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Liver Function Assessment Based on Hepatobiliary Contrast Agent–Enhanced Magnetic Resonance Imaging

Sofiia F. Ageeva[1], Valentin E. Sinitsyn[1], Elena A. Mershina[1], Natalia A. Rucheva[2], Ekaterina I. Petrova[3]

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ABSTRACT

BACKGROUND: Liver function assessment is very important in clinical practice. The use of magnetic resonance imaging for the anatomical and functional evaluation of the liver is possible in actual clinical practice.

AIM: To examine the possibility of using hepatobiliary contrast-enhanced magnetic resonance imaging for the evaluation of liver function.

MATERIALS AND METHODS: Datasets of patients who underwent gadoxetic acid-enhanced magnetic resonance imaging were retrospectively reviewed. Patients were divided into two groups: group 1 included patients with impaired liver function, and group 2 included those with normal liver function. Based on magnetic resonance imaging in the hepatobiliary phase, the liver parenchyma signal intensity and its ratio to spleen signal intensity and portal vein signal intensity were estimated. Differences among these parameters were compared between groups. The correlation between liver parenchyma signal intensity and laboratory blood tests reflecting liver function (total bilirubin, albumen, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma glutamyl transpeptidase, and prothrombin time) were analyzed.

RESULTS: Datasets of 53 patients (25 men and 28 women, aged 24–84 years) were analyzed. Group 1 included 19 patients, whereas group 2 included 34. The median liver parenchyma signal intensity was 919.05 [669.65; 1258.35] in group 1 and 1525.13 [1460.5; 1631.4] in group 2 ($P = 0.0000001$). The median ratio of liver parenchyma signal intensity to spleen signal intensity was 1.2 [1.04;1.7] in group 1 and 1.7 [1.46; 1.96] in group 2 ($P = 0.00076$). The median ratio of liver parenchyma signal intensity to portal vein signal intensity was 1.44 [1.29; 1.83] in group 1 and 1.6 [1.43; 1.83] in group 2 ($P = 0.1$). The estimated correlation values between liver parenchyma signal intensity and blood tests parameters were as follows: total bilirubin (r=–0.61; $P = 0.000001$), albumen (r=0.13; $P = 0.61$), aspartate aminotransferase (r=–0.57; $P = 0.000009$), alanine aminotransferase (r=–0.44; $P = 0.001$), alkaline phosphatase (r=–0.45; $P = 0.0007$), gamma glutamyl transpeptidase (r=–0.5; $P = 0.0003$), prothrombin time (r=–0.34; $P = 0.04$).

CONCLUSION: The study reflects the ability to assess liver function using indices (liver parenchyma signal intensity and its ratio to spleen signal intensity) derived from gadoxetic acid-enhanced magnetic resonance imaging. However, this study did not confirm the assumed effectiveness of using the liver parenchyma signal intensity to portal vein signal intensity ratio as an index of liver function. A significant inverse correlation was identified between liver parenchyma signal intensity and blood test parameters in reflecting liver function, except for albumin. The results indicate the possibility of using magnetic resonance imaging to assess liver function.

Keywords: magnetic resonance imaging; liver; cirrhosis; contrast study; hepatotropic contrast agent; gadoxetic acid.

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Возможности применения магнитно-резонансной томографии с использованием гепатотропных контрастных веществ для функциональной оценки печени

С.Ф. Агеева[1], В.Е. Синицын[1], Е.А. Мершина[1], Н.А. Ручьева[2], Е.И. Петрова[3]

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АННОТАЦИЯ

Обоснование. Оценка функции печени при различных заболеваниях остаётся важной клинической задачей. Применение магнитно-резонансной томографии с гепатотропным контрастным веществом для оценки функции печени представляет существенный научный и практический интерес.

Цель — изучить возможность функциональной оценки печени на основании показателей, полученных по данным магнитно-резонансной томографии с контрастированием гепатотропным веществом.

Материалы и методы. Были проанализированы данные пациентов, которым выполнялась магнитно-резонансная томография с внутривенным контрастированием гадоксетовой кислотой. Пациенты были разделены на две группы: с нарушенной (первая группа) и с нормальной (вторая группа) функцией печени. По данным магнитно-резонансных исследований оценивались следующие параметры: интенсивность сигнала печени, её отношение к интенсивности сигнала селезёнки и к интенсивности сигнала в просвете воротной вены. Были оценены показатели лабораторных анализов крови, отражающие функции печени: общий билирубин, альбумин, аланинаминотрансфераза, аспартатаминотрансфераза, γ-глутамилтранспептидаза, щелочная фосфатаза, протромбиновое время. Был проведён анализ статистической значимости различий между группами по параметрам магнитно-резонансной томографии, оценивалось наличие корреляционной связи между значениями интенсивности сигнала печени и данными лабораторных анализов крови.

Результаты. Были проанализированы данные 53 пациентов (25 мужчин и 28 женщин в возрасте от 24 до 84 лет). В первую группу вошло 19 человек, во вторую — 34 человека. Были установлены статистически значимые различия показателей интенсивности сигнала печени и её отношения к интенсивности сигнала селезёнки между исследуемыми группами. В первой группе значение интенсивности сигнала печени составило 919,05 [669,65; 1258,35], во второй — 1525,13 [1460,5; 1631,4] (p=0,0000001). Отношение интенсивности сигнала печени к интенсивности сигнала селезёнки в первой группе составило 1,2 [1,04; 1,7], во второй — 1,7 [1,46; 1,96] (p=0,00076). Отношение интенсивности сигнала печени к интенсивности сигнала в просвете воротной вены составило 1,44 [1,29; 1,83] в первой группе, 1,6 [1,43; 1,83] — во второй (p=0,1). Была оценена корреляция между интенсивностью сигнала печени и общим билирубином (r=–0,61; p=0,000001), альбумином (r=0,13; p=0,61), аспартатаминотрансферазой (r=–0,57; p=0,000009), аланинаминотрансферазой (r=–0,44; p=0,001), щелочной фосфатазой (r=–0,45; p=0,0007), γ-глутамилтранспептидазой (r=–0,5; p=0,0003), протромбиновым временем (r=–0,34; p=0,04). По шкале Чеддока заметная сила корреляционной связи была выявлена между показателем интенсивности сигнала печени и значениями общего билирубина, аспартатаминотрансферазы. Умеренная сила — между показателем интенсивности сигнала печени и значениями аланинаминотрансферазы, щелочной фосфатазы, γ-глутамилтранспептидазы, протромбинового времени.

Заключение. Продемонстрирована эффективность применения параметров магнитно-резонансной томографии (интенсивность сигнала печени и её отношение к интенсивности сигнала селезёнки) в функциональной оценке печени. В исследовании не подтвердилось предположение об эффективности применения такого параметра, как отношение значения интенсивности сигнала печени к интенсивности сигнала в просвете воротной вены. Были установлены статистически значимые обратные связи между значениями интенсивности сигнала печени и показателями лабораторных анализов крови, отражающих функции печени, за исключением альбумина. Результаты свидетельствуют о возможности использования магнитно-резонансной томографии для функциональной оценки печени.

Ключевые слова: магнитно-резонансная томография; печень; цирроз; контрастное исследование; гепатотропный контрастный агент; гадоксетовая кислота.

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使用亲肝造影剂进行磁共振成像以评估肝脏功能的可能性

Sofiia F. Ageeva[1], Valentin E. Sinitsyn[1], Elena A. Mershina[1], Natalia A. Rucheva[2], Ekaterina I. Petrova[3]

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摘要

论证。评估各种疾病的肝功能仍然是一项重要的临床任务。使用亲肝造影剂的磁共振成像来评估肝功能具有相当大的科学和实用意义。

目的是研究根据亲肝造影剂 磁共振成像获得的指数对肝脏进行功能评估的可能性。

材料和方法。对接受静脉注射钆塞酸造影剂磁共振成像的患者数据进行了分析。患者分为两组：肝功能受损组（第一组）和肝功能正常组（第二组）。根据磁共振成像数据评估了以下参数：肝脏信号强度、肝脏信号强度与脾脏信号强度的比值以及肝脏信号强度与门静脉管腔信号强度的比值。对反映肝功能的实验室血液检查指标进行了评估：总胆红素、白蛋白、丙氨酸氨基转移酶、天门冬氨酸氨基转移酶、γ-谷氨酰转肽酶、碱性磷酸酶、凝血酶原时间。我们分析了组间磁共振参数差异的统计学意义，评估了肝脏信号强度值与实验室血液检查数据之间是否存在相关性。

结果。对 53 名患者（25 名男性和 28 名女性，年龄在 24 至 84 岁之间）的数据进行了分析。第一组包括 19 人，第二组包括 34 人。研究组之间的肝脏信号强度和肝脏信号强度与脾脏信号强度的比值差异具有统计学意义。第一组的肝信号强度值为 919.05 [669.65; 1258.35]，第二组为 1525.13 [1460.5; 1631.4]（P=0.0000001）。第一组肝脏信号强度与脾脏信号强度的比值为 1.2 [1.04; 1.7]，第二组为 1.7 [1.46; 1.96]（P=0.00076）。第一组肝脏信号强度与门静脉管腔信号强度的比值为 1.44 [1.29; 1.83]，第二组为 1.6 [1.43; 1.83]（P=0.1）。对肝脏信号强度与总胆红素（r=−0.61; P=0.000001）、白蛋白（r=0.13; P=0.61）、天冬氨酸氨基转移酶（r=−0.57; P=0.000009）、丙氨酸氨基转移酶（r=−0.44; P=0.001）、碱性磷酸酶（r=−0.45; P=0.0007）、γ-谷氨酰转肽酶（r=−0.5; P=0.0003）、凝血酶原时间（r=−0.34; P=0.04）的相关性也进行了评估。在 Chaddock 标上，肝脏信号强度指数与总胆红素、天门冬氨酸氨基转移酶值之间存在明显的相关性。肝脏信号强度指数与丙氨酸氨基转移酶、碱性磷酸酶、γ-谷氨酰转肽酶、凝血酶原时间之间的相关性中等。

结论。磁共振成像参数（肝脏信号强度及其与脾脏信号强度的比值）在肝脏功能评估中的有效性得到了证实。研究并未证实肝脏信号强度与门静脉管腔信号强度的比值等参数的有效性假设。除白蛋白外，肝脏信号强度值与反映肝功能的实验室血液化验指标之间建立了统计学意义上的反相关关系。结果表明，磁共振成像可用于肝脏功能评估。

关键词：磁共振成像；肝脏；肝硬化；造影剂检查；亲肝造影剂；钆塞酸。

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BACKGROUND

The liver is a vital organ that performs several functions such as detoxification, metabolism (e.g., protein synthesis and fat and carbohydrate metabolism), and exocrine functions. Liver dysfunction can occur in several different conditions (e.g., infections, autoimmune diseases, and drug-induced injuries), and it may be asymptomatic in the early stages. Liver function should be assessed to determine the management strategy of patients with liver disease, especially when planning for surgery to avoid complications associated with post-resection liver failure. Existing laboratory tests and imaging modalities for the analysis of liver function have some advantages and disadvantages [1, 2].

Magnetic resonance imaging (MRI) with extracellular contrast enhancement is extensively used to evaluate the anatomy and characteristics of liver lesions. The development of hepatotropic contrast agents has expanded the diagnostic capabilities of the method with the introduction of a new hepato-specific phase (HSP).

Hepatobiliary-specific contrast agents include gadobenic acid (Gd-BOPTA, MultiHance; Bracco Diagnostics Inc.) and gadoxetic acid (Gd-EOB-DTPA, Eovist or Primovist; Bayer Healthcare) [3, 4]. These agents differ significantly. Approximately 5% of the administered dose of Gd-BOPTA is taken up by hepatocytes, and the HSP uptake is evaluated 1–3 h after contrast administration. When gadoxetic acid (GA) is used as a contrast agent, significantly more substance (up to 50%) enters the liver cells, and the HSP uptake is evaluated 15–25 min after contrast administration. Due to its characteristics, GA is more commonly used than Gd-BOPTA in clinical practice to evaluate HSP uptake [3].

Preliminary evidence suggests that MRI enhanced with hepatobiliary-specific contrast agents may aid in assessing liver function. The feasibility of using MRI to assess the liver anatomy and function is a relevant scientific and practical issue.

STUDY AIM

To evaluate the feasibility of the functional assessment of the liver using parameters of liver obtained from MRI enhanced with a hepatobiliary-specific contrast agent.

MATERIALS AND METHODS

Study Design

This is a retrospective, multicenter, selective study.

Eligibility Criteria

The data of patients aged ⩾18 years who had undergone abdominal MRI enhanced with intravenous GA (Primovist; Bayer Healthcare) were evaluated. Laboratory blood test (complete blood count, blood biochemistry, and coagulation profile) results were also evaluated.

For subsequent statistical analysis, the patients were divided into two groups. Group 1 included patients with cirrhosis of various origins and clinical and laboratory evidence of liver dysfunction. Group 2 included patients with an intact liver parenchyma, benign liver tumors, or arteriovenous shunts without any clinical or laboratory evidence of liver dysfunction.

Study Setting

Data were collected from the following three institutions over from 2020 to 2023: Shumakov National Medical Research Center of Transplantology and Artificial Organs of the Russian Federation's Ministry of Health, the Medical Research and Education Center of Lomonosov Moscow State University, and the Industrial Clinic and Diagnostic Center of PJSC Gazprom.

Magnetic Resonance Imaging Protocol

GA-enhanced MRIs were obtained using one of three models. The Shumakov National Medical Research Center of Transplantology and Artificial Organs used the 1.5 T Signa Voyager (GE Healthcare, USA), the Medical Research and Education Center of Lomonosov Moscow State University used the 3 T Magnetom Vida (Siemens Healthineers, Germany), and the Industrial Clinical and Diagnostic Center of PJSC Gazprom used the 1.5 T Ingenia (Philips, the Netherlands).

The contrast enhancement agent (Primovist; Bayer Healthcare, Germany) was administered intravenously at a rate of 0.025 mmol/kg of body weight. Table 1 shows the MRI protocol.

A series of T1-weighted images (WIs) of 3–6 mm slice thickness obtained before and 15–20 min after contrast administration were analyzed.

The signal intensity (in arbitrary units, au) was measured in the following regions of interest (ROIs, Fig. 1):

- Liver parenchyma (left and right lobes), outside the margins of the tumors, vessels, bile ducts and artifacts (if any) (ROI, at least 2 cm^2 in diameter),
- Spleen parenchyma (ROI, at least 2 cm^2 in diameter), and
- Lumen of the portal vein (ROI, at least 0.5 cm^2 in diameter).

Using the GA-enhanced MRI, the following parameters were calculated:

- Liver Signal Intensity (LSI), which is the mean signal intensity (SI) of the left and right lobes of the liver:

$$LSI = \frac{SI_{left\ lobe} + SI_{right\ lobe}}{2},$$

- LSI to Spleen Signal Intensity (SSI) ratio: LSI/SSI, and
- LSI to Portal Vein Signal Intensity (PVSI) ratio: LSI/PVSI.

Additionally, the following laboratory blood test data obtained closest to the date of the GA-enhanced MRI were analyzed: levels of total bilirubin, albumin, alanine

Table 1. Protocol of gadoxetic acid–enhanced magnetic resonance imaging of the liver.

Program	MRI sequence	TR, msec	TE, msec	FA, degrees	Slice thickness, mm	Number of slices
Topography	HASTE	2000	90	110	5	3
T2-WIs, transverse plane	TSE	3000	90	140	5	20–30
T2-WIs with fat suppression, transverse and frontal planes	TSE	3000	90	140	5	20–30
T2-WIs, transverse and frontal planes	VIBE	9	4	10	3	25
T2-WIs with phase shift, transverse plane	VIBE	9	2 and 5	10	3	25
DWIs (b-value, 0, 500, and 1,000), transverse plane	DWI	6000	90	–	3	20
T1-WIs for dynamic contrast enhancement (six phases), transverse plane	VIBE	9	4	10	3	30
MR cholangiography, frontal plane	HASTE	2500	110	130	3	35
T1-WIs in delayed phase, transverse plane	VIBE	9	4	10	3	30

Note. WI, weighted image; MRI, magnetic resonance imaging; DWI, diffusion-weighted image; TR, repetition time; TE, echo time; FA, fractional anisotropy.

aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), and prothrombin time (PT).

Statistical Analysis

STATISTICA (version 12.0; TIBCO Software, USA) was used for statistical processing of all the data. The statistical significance of the differences in LSI, LSI/SSI, LSI/PVSI between Groups 1 and 2 was evaluated using the Mann–Whitney U test. The Spearman's rank correlation coefficient was used to determine the association between LSI and laboratory test results such as the levels of total bilirubin, albumin, AST, ALT, ALP, GGT, and PT.

RESULTS

Study Subjects

In this study, the data of 53 patients (25 men and 28 women) who underwent abdominal MRI with intravenous GA contrast enhancement were analyzed.

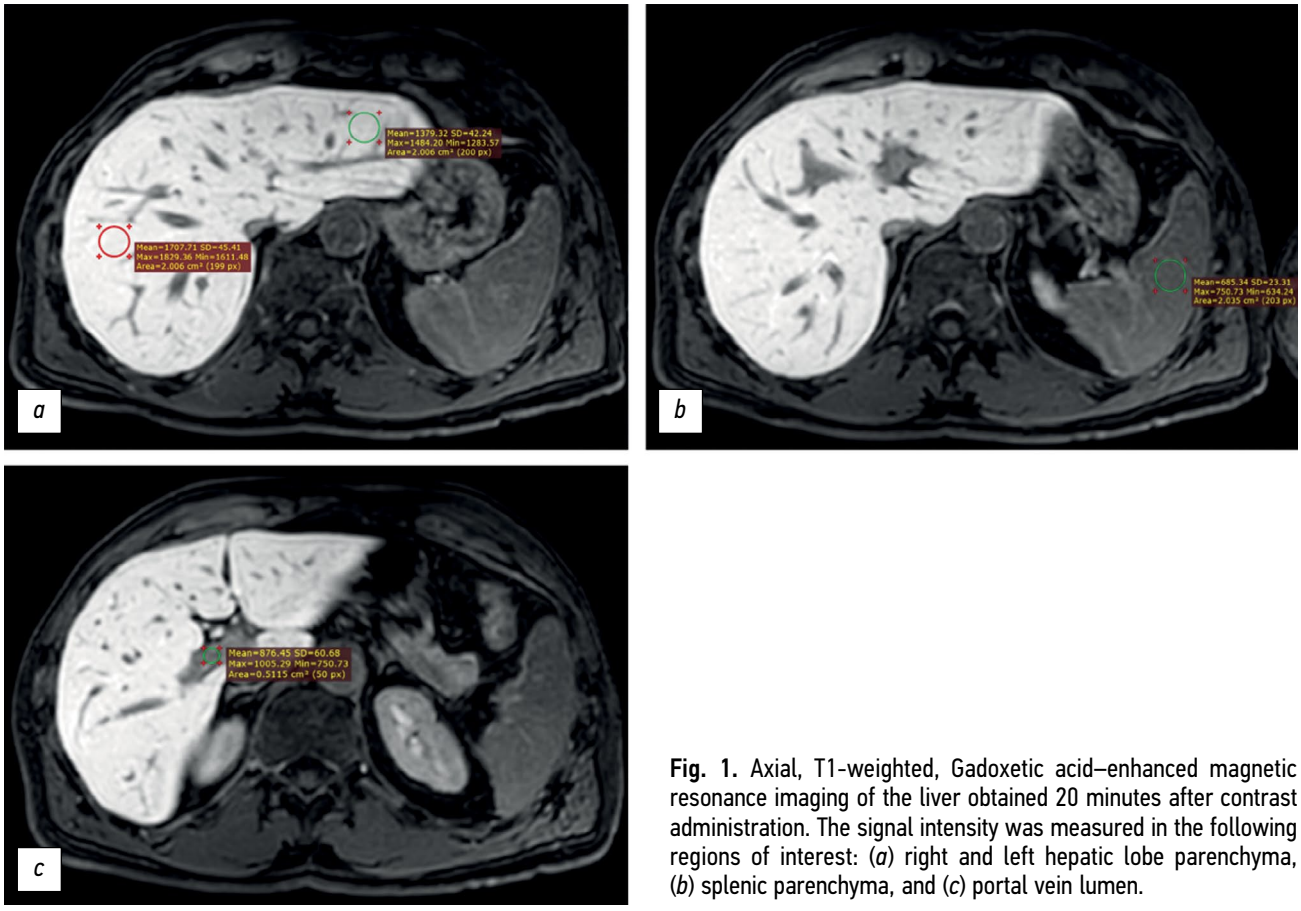

Fig. 1. Axial, T1-weighted, Gadoxetic acid–enhanced magnetic resonance imaging of the liver obtained 20 minutes after contrast administration. The signal intensity was measured in the following regions of interest: (*a*) right and left hepatic lobe parenchyma, (*b*) splenic parenchyma, and (*c*) portal vein lumen.

Group 1 included 19 patients, aged 34–71 years (mean age: 51.2 ± 9.8 years), who had liver cirrhosis of various origins (Table 2).

Group 2 included 34 patients, aged 24–84 years (mean age: 57.6 ± 15.8 years), in whom the liver function was preserved (Table 3).

Primary Findings

Table 4 shows the statistical analysis of the differences in LSI, LSI/SSI, LSI/PVSI between the two groups. The LSI was statistically significantly higher in patients in Group 2 than in patients in Group 1 ($P < 0.001$). The LSI/SSI was also statistically significantly different between the groups; the median LSI/SSI value was significantly higher in Group 2 than in Group 1 ($P < 0.001$). There was no statistically significant difference in the LSI/PVSI between the groups ($P > 0.05$) (Fig. 2).

The correlation analysis showed a statistically significant negative correlation between LSI and the following blood test results: total bilirubin level (r = –0.61; $P = 0.000001$), AST level (r = –0.57; $P = 0.000009$), ALT level (r = –0.44; $P = 0.001$), ALP level (r = –0.45; $P = 0.0007$), GGT level (r = –0.5; $P = 0.0003$), and PT (r = –0.34; $P = 0.04$) (Fig. 3). According to the Chaddock scale, there were significant correlations between the LSI and the total bilirubin and AST levels. Furthermore, there was a moderate correlation between the LSI and the levels of ALT, ALP, GGT, and PT.

Because data regarding serum albumin levels in the patients in Group 2 was insufficient, the laboratory blood test results of patients in Group 1 were used in the correlation analysis. There was no statistically significant correlation between serum albumin levels and LSI (r = 0.13; $P = 0.61$) (Fig. 4).

DISCUSSION

Statistical analyses in our study revealed a significant difference in the LSI between the study groups. The high LSI in Group 2 may be attributable to the active uptake of GA by the functional hepatocytes [5, 6]. In Group 1, the cellular uptake of the contrast agent may be attributed to the impaired liver function and decreased number of

Table 2. Characteristics of the patients in Group 1 on the basis of the etiology of liver abnormalities

Etiology of liver abnormalities	Number of patients	Malignancy
Hepatitis C	8	Four patients had histologically confirmed HCC. Two patients were diagnosed with HCC on the basis of GA-enhanced MRI; the diagnosis was not confirmed histologically
Hepatitis B	2	One patient had histologically confirmed cholangiocellular carcinoma
Alimentary origin	2	–
Unspecified origin	1	–
Toxic origin	1	–
Nonalcoholic fatty liver disease	1	–
Primary sclerosing cholangitis	2	–
Budd–Chiari syndrome	1	–
Wilson's disease	1	–

Note. GA, gadoxetic acid; HCC, hepatocellular carcinoma; MRI, magnetic resonance imaging.

Table 3. Characteristics of the patients in Group 2 on the basis of the etiology of liver abnormalities

Etiology of liver abnormalities	Number of patients
Intact liver parenchyma	7
Benign hepatic tumors (liver adenomas, focal nodular hyperplasia, hemangiomas, and liver cysts)	25
Arteriovenous shunts	2

Table 4. Statistical differences between Groups 1 and 2

	LSI	LSI/SSI	LSI/PVSI
Group 1	919.05 [669.65; 1258.35]	1.2 [1.04; 1.7]	1.44 [1.29; 1.83]
Group 2	1525.13 [1460.5; 1631.4]	1.7 [1.46; 1.96]	1.6 [1.43; 1.83]
P-value	0.0000001	0.00076	0.1

Note. LSI, liver signal intensity; LSI/SSI, liver signal intensity to spleen signal intensity ratio; LSI/PVSI, liver signal intensity to portal vein signal intensity ratio.

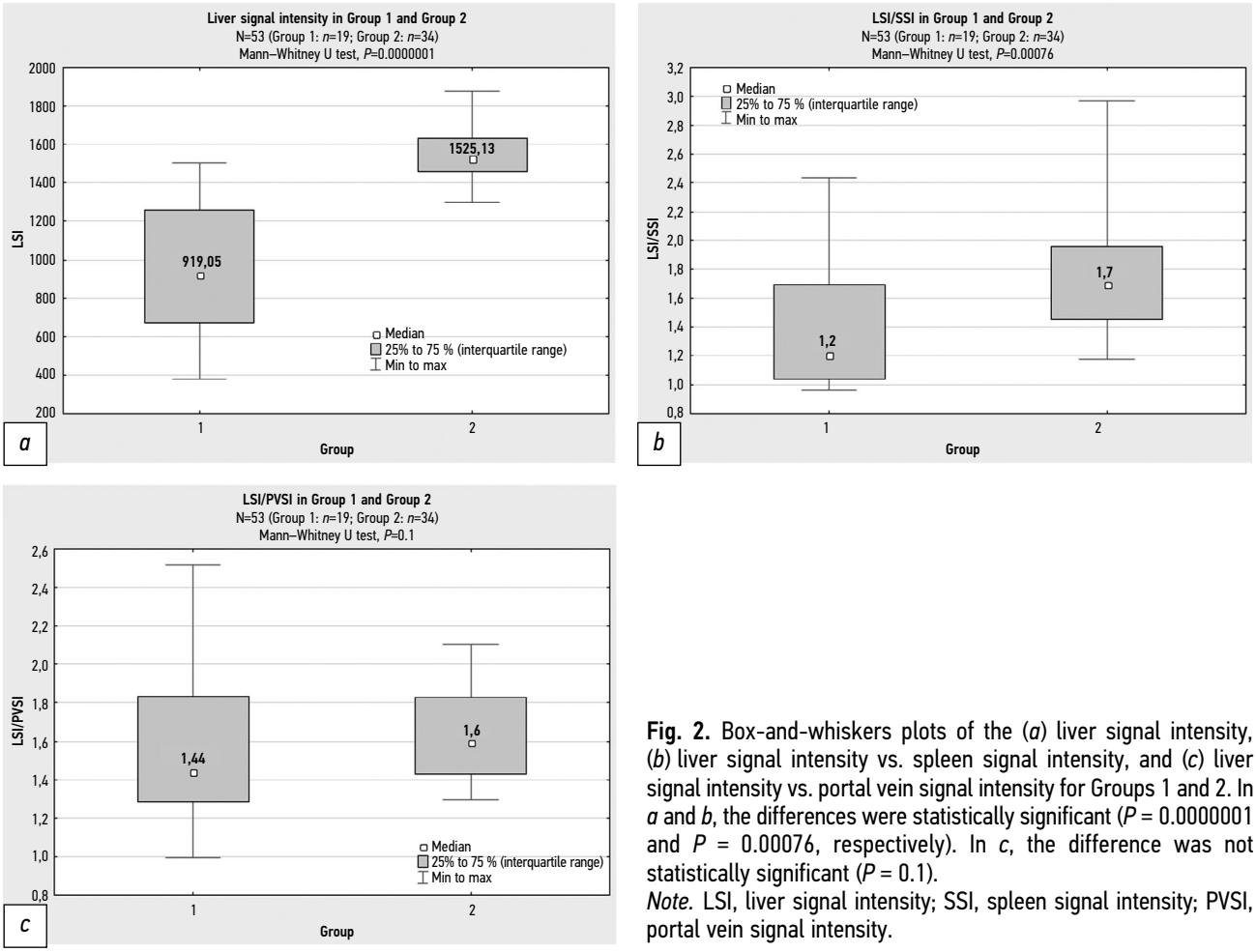

Fig. 2. Box-and-whiskers plots of the (*a*) liver signal intensity, (*b*) liver signal intensity vs. spleen signal intensity, and (*c*) liver signal intensity vs. portal vein signal intensity for Groups 1 and 2. In *a* and *b*, the differences were statistically significant ($P = 0.0000001$ and $P = 0.00076$, respectively). In *c*, the difference was not statistically significant ($P = 0.1$).
Note. LSI, liver signal intensity; SSI, spleen signal intensity; PVSI, portal vein signal intensity.

hepatocytes, resulting in a decreased signal intensity in the liver parenchymal on MRI [7, 8].

In the spleen, GA serves as an extracellular enhancing agent because the spleen cells do not contain proteins that can transport GA into the cells [9]. It has been proposed that the functional status of the liver is reflected by the LSI/SSI ratio. In our study, there was a statistically significant difference in the LSI/SSI between the study groups, indicating that it may be an effective parameter to assess liver function.

Our finding that LSI and LSI/SSI may reflect liver function is consistent with that of previous studies. Yang et al. evaluated the laboratory test results and GA-enhanced MRI data of 120 patients with normal and impaired liver function. The following HSP parameters were evaluated: LSI, PVSI, SSI, LSI/PVSI, LSI, SSI, and PVSI/SSI. They found significant differences in the LSI, LSI/PVSI, and LSI/SSI between their study groups. Thus, they concluded that these parameters may be used to assess the liver function [9].

Bastati et al. evaluated the data of 128 patients and concluded that GA-enhanced MRI may be used to assess the liver engraftment potential in patients who have undergone orthotopic organ transplantation. The authors used a functional liver imaging score (FLIS) with the sum of three criteria (LSI, biliary excretion of GA, LSI/PVSI), each of which was scored from 0 to 2 points. Furthermore, the relative liver enhancement (RLE) was assessed using the following formula [10]:

$$RLE = \frac{LSI_{HSP} - LSI}{LSI} \times 100.$$

Mnatsakanyan et al. compared the effectiveness of using MRI to assess the liver function in surgical candidates with that of the combined use of hepatobiliary scintigraphy (with ^{99m}Tc mebrofenin) and single-photon emission computed tomography (CT). The MRI parameters used were future liver remnant function (FunctFLR) and the hepatocellular uptake index (HUI) in the HSP. A FLIS system was also used for the evaluation.

FunctFLR was calculated using the following formula:

$$FunctFLR = FLR \times \frac{RLE}{m},$$

where FLR is the future liver remnant assessed by CT- or MRI-volumetry, m is the weight of the patient, and RLE is the relative liver enhancement.

The RLE was calculated using the following formula:

$$RLE = \frac{SI_{hb} - SI_{pre}}{SI_{pre}},$$

where SI_{hb} is the mean signal intensity of three ROIs in the HSP and SI_{pre} is the mean signal intensity of three ROIs in the native phase.

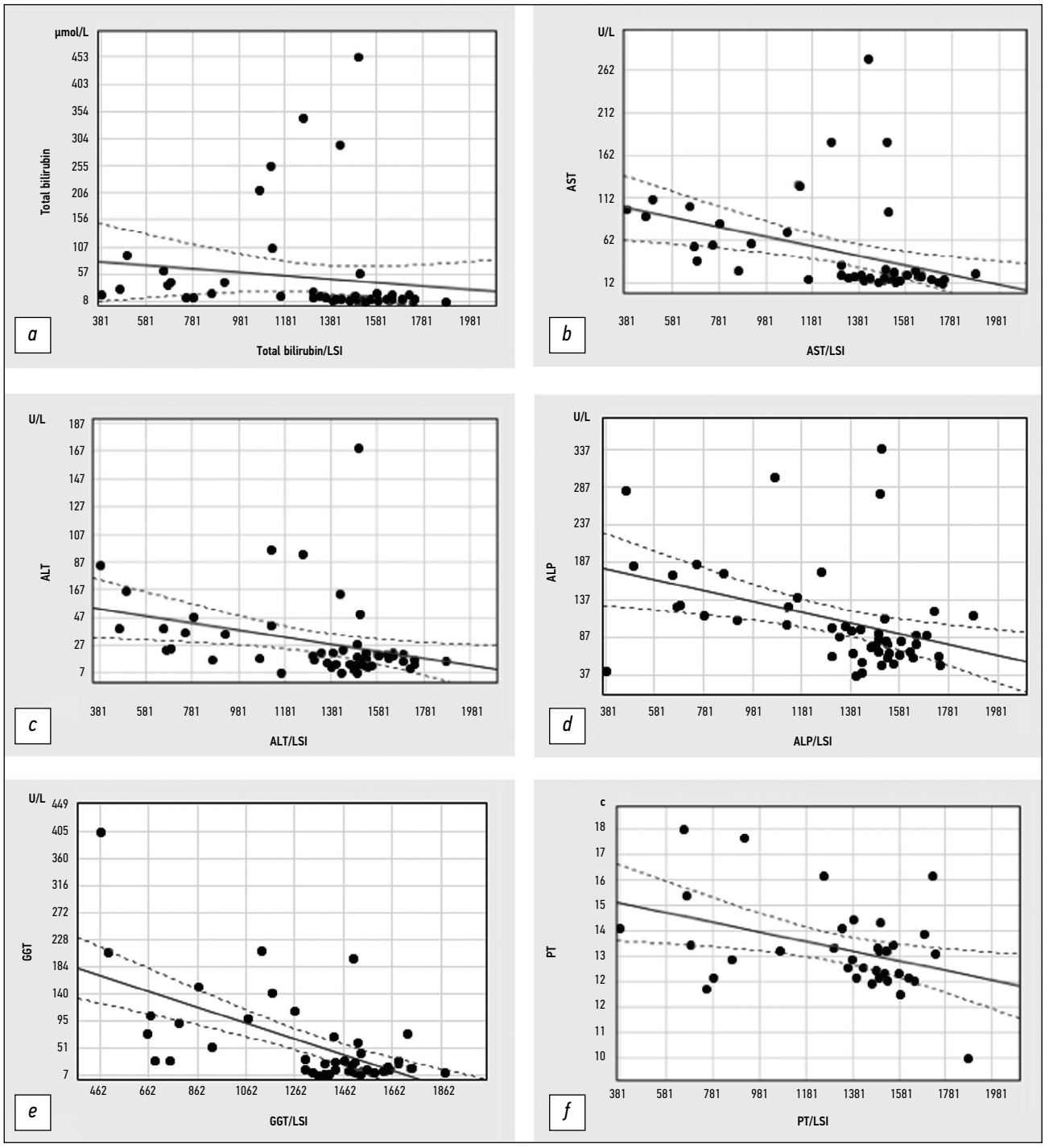

Fig. 3. Scatter plots showing the correlation between liver signal intensity and the following parameters: (*a*) total bilirubin level (r = –0.61; P = 0.000001), (*b*) aspartate aminotransferase level (r = –0.57; P = 0.000009), (*c*) alanine aminotransferase level (r = –0.44; P = 0.001), (*d*) alkaline phosphatase level (r = –0.45; P = 0.0007); (*e*), gamma-glutamyl transferase level (r = –0.5; P = 0.0003), and (*f*) prothrombin time (r = –0.34; P = 0.04). *Note.* LSI, liver signal intensity; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phospatase; GGT, gamma-glutamyl transferase; PT, prothrombine time.

The HUI was calculated using the following formula:

$$HUI = VL \times \left(\frac{L20}{S20} - 1 \right),$$

where VL is the volume of the liver, L20 is the mean LSI on contrast-enhanced T1-WIs with fat suppression, and S20 is the mean SSI on contrast-enhanced T1-WIs with fat suppression.

Mnatsakanyan et al. concluded that GA-enhanced MRI can be used as an alternative modality for the functional assessment of the liver when planning extensive resections [11].

Some studies have demonstrated the efficacy of the LSI/PVSI in assessing liver function [9, 12]. Zhang et al. evaluated GA-enhanced MRIs of 92 patients with normal liver function or hepatitis B-related cirrhosis. They

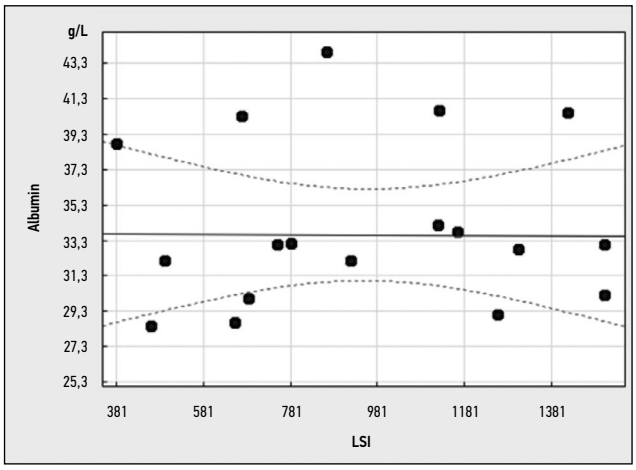

Fig. 4. Scatter plot showing the correlation between liver signal intensity and serum albumin level (r = 0.13; P = 0.61).
Note. LSI, liver signal intensity.

evaluated the following parameters: LSI/PVSI in the HSP and laboratory blood test results (total bilirubin level, albumin level, and platelet count). They found that the LSI/PVSI in the HSP was associated with the severity of functional impairment in patients with hepatitis B-related liver cirrhosis, which was consistent with their laboratory data. Thus, the authors concluded that LSI/PVSI in the HSP may be used as a biomarker of liver function [12].

However, in our study, there was no statistically significant difference in the LSI/PVSI between the study groups. This may be attributable to the significant hyperbilirubinemia reported in some patients in Group 1, particularly those with primary sclerosing cholangitis. Lee et al. demonstrated that in patients with significant hyperbilirubinemia, bilirubin competes with GA for uptake by the hepatocytes, resulting in delayed uptake and slowed GA clearance from the blood [13]. In our study, the etiology of liver cirrhosis in Group 1 was heterogeneous, and the median total bilirubin level was 43.25 [22.4–211.17] μmol/L. In some patients in Group 1, the significant hyperbilirubinemia may have affected the LSI/PVSI. However, given the small sample size, there was no statistically significant difference in the LSI/PVSI between the groups.

The correlation analysis also supports the hypothesis that MRI can be used to assess liver function, which is largely consistent with the results of the study by Yang et al. [9]. They found a statistically significant negative correlation between the LSI and the total bilirubin (r = –0.52; P < 0.001), albumin (r = 0.48; P < 0.001), AST (r = –0.5; P < 0.001), and ALT (r = –0.49; P < 0.001) levels as well as the PT (r = –0.52; P < 0.001) [9]. Contrary to the finding in the study by Yang et al., we did not observe a correlation between the LSI and the serum albumin level. This may be attributed to the small sample size. Furthermore, because serum albumin level is rarely included in the routine laboratory blood tests of patients in Group 2, the correlation analysis was performed using the data of patients in Group 1.

In our study, there was a significant correlation between the LSI and total bilirubin level (r = –0.61; P < 0.001). This specific marker has been used in some scales to assess the functional status of the liver. For example, liver dysfunction can be assessed using the Chronic Liver Failure Consortium scoring system and Sequential Organ Failure Assessment scale, which include the total bilirubin level as a criterion [14, 15]. The Asian Pacific Association for the Study of the Liver recommends that acute-on-chronic liver failure be defined on the basis of two laboratory blood parameters such as total bilirubin and international normalized ratio or prothrombin activity [15]. Therefore, the correlation obtained in our study demonstrated the potential of GA-enhanced MRI in the assessment of liver function.

Study Limitations

Insufficient data may explain the lack of correlation between the LSI and serum albumin level in our study. Thus, further studies with larger sample sizes are required. Furthermore, the heterogeneous etiology of cirrhosis in the patients in Group 1 may have resulted in the lack of a statistically significant difference in the LSI/PVSI between the study groups. Thus, further studies with larger sample sizes are required.

CONCLUSION

The correlation analysis in our study revealed statistically significant differences in MRI parameters such as LSI and LSI/SSI between the patients with normal liver function and those with impaired liver function. The study's findings validate the feasibility using GA-enhanced MRI for the assessment of liver function. The lack of a statistically significant difference in LSI/PVSI between the study groups may be attributed to the significant hyperbilirubinemia in some patients in Group 1.

The correlation analysis in our study also demonstrated a statistically significant negative correlation between the LSI and the total bilirubin, AST, ALT, GGT, ALP, and PT levels. These findings also support the use of GA-enhanced MRI to assess liver function. The lack of a statistically significant correlation between the serum albumin level and LSI in Group 1 may be attributable to the insufficient amount of data evaluated.

In conclusion, GA-enhanced MRI can be used for the functional assessment of the liver in addition to its main indications (diagnosis and characterization of lesions). Thus, it is a promising assessment modality that is based on the physiology of GA uptake by the hepatocytes.

ADDITIONAL INFORMATION

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Possibilities and Limitations of Magnetic Resonance Imaging in the Diagnostics of Endocervical Adenocarcinomas

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ABSTRACT

BACKGROUND: In recent decades, the incidence of cervical adenocarcinomas has increased from 5% to 20%. Endocervical adenocarcinomas are characterized by a more aggressive course and early metastasis. Owing to the difficulties in the cytological diagnosis of cervical adenocarcinoma, early radiation diagnostics and staging subsequently play a key role. Very few studies have examined the use of magnetic resonance imaging in diagnosing cervical adenocarcinomas.

AIM: To determine the diagnostic informativeness of magnetic resonance imaging in the staging of cervical adenocarcinomas according to the T-criterion and assessing the depth of tumor invasion into the stroma of the cervix and clarify the semiotic signs of adenocarcinoma and features of tumor growth in the uterus.

MATERIALS AND METHODS: In total, 123 patients diagnosed with cervical cancer (C53), who underwent diagnosis and treatment between 2020 and 2023, were examined. The examination results of 22 (18%) patients with cervical adenocarcinoma were analyzed. The average patient age was 56 years. A multiparametric magnetic resonance examination of the pelvic organs was performed on 22 patients using tomographs with a magnetic field strength of 1.5 T. Moreover, 14 (64%) patients underwent surgery including extirpation of the uterus and appendages with pelvic lymphadenectomy. The information value of magnetic resonance imaging was evaluated in 11 patients, whose first stage was surgical treatment.

RESULTS: In this study, cervical adenocarcinoma was detected in 18% among all cases of cervical cancer. The information value of magnetic resonance imaging in assessing the local prevalence of endocervical adenocarcinoma according to the T-criterion was as follows (main value with the corresponding 95% confidence interval): sensitivity, 77.78% (39.99%–97.19%); specificity, 50.00% (1.26%–98.74%); positive predictive value, 87.50% (62.64%–96.69%); negative predictive value, 33.33% (7.30%–76.04%); and accuracy, 72.73% (39.03%–93.98%). The information value of magnetic resonance imaging in assessing the depth of tumor invasion into the cervical stroma was as follows: odds ratio, 3.500 (0.145%–84.694%); sensitivity, 85.7% (0.757%–0.993%); specificity, 33.3% (0.018%–0.0648%); positive predictive value, 75% (0.673%–0.883%); negative predictive value, 50% (0.027%–0.972%).

CONCLUSIONS: The results of this study showed that magnetic resonance imaging is a good tool with high diagnostic informativeness in detecting endocervical cervical adenocarcinoma. The four macrostructures of tumor growth in endocervical adenocarcinoma identified during magnetic resonance imaging data analysis indicate locally aggressive tumor growth and a high frequency of endometrial dropouts. This finding will allow radiologists to structure a descriptive picture, including the verified cervical adenocarcinoma, to enhance methods of developing a treatment plan for the patient.

Keywords: endocervical adenocarcinoma; cervical cancer; magnetic resonance imaging; diagnostics in gynecology.

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Возможности и ограничения магнитно-резонансной томографии для диагностики эндоцервикальных аденокарцином шейки матки

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АННОТАЦИЯ

Обоснование. В последние десятилетия отмечается рост аденокарцином шейки матки с 5% до 20%. Установлено, что эндоцервикальные аденокарциномы характеризуются более агрессивным течением и ранним метастазированием. В связи с трудностями цитологической диагностики аденокарциномы шейки матки лучевая диагностика играет ключевую роль на этапе установления диагноза и стадирования впоследствии. На настоящий момент исследований, посвящённых использованию магнитно-резонансной томографии в диагностике аденокарцином шейки матки, очень мало.

Цель — определить диагностическую информативность магнитно-резонансной томографии в стадировании аденокарцином шейки матки по Т-критерию, а также в оценке глубины инвазии опухоли в строму шейки матки, уточнить семиотические признаки аденокарциномы и особенности роста опухоли в матке.

Материалы и методы. В период с 2020 по 2023 год обследовано 123 пациентки с диагнозом рак шейки матки (С53). Детально проанализированы результаты обследования 22 (18%) пациенток с аденокарциномой шейки матки (средний возраст 56 лет), которым проводилась магнитно-резонансная томография органов малого таза на томографе с напряжённостью магнитного поля 1,5 Тл. Анализ информативности магнитно-резонансной томографии оценивался у 11/22 (50%) пациенток, у которых первым этапом было проведено хирургическое лечение в объёме экстирпации матки с придатками. Для анализа диагностической информативности проводилось сравнение данных магнитно-резонансной томографии и патоморфологического исследования операционного материала. Статистическая обработка результатов исследования проводилась с использованием программного приложения Microsoft Excel, JavaStat.

Результаты. В нашем исследовании аденокарцинома шейки матки определялась в 18% наблюдений среди всех случаев рака шейки матки. Информативность магнитно-резонансной томографии в оценке местной распространённости эндоцервикальных аденокарцином (по Т-критерию) составила (здесь и далее в скобках после основного значения указан 95% доверительный интервал): чувствительность — 77,78% (39,99–97,19%); специфичность — 50,00% (1,26–98,74%); предсказательная ценность положительного результата — 87,50% (62,64–96,69%); предсказательная ценность отрицательного результата — 33,33% (7,30–76,04%); точность — 72,73% (39,03–93,98%). Информативность магнитно-резонансной томографии в оценке глубины инвазии опухоли в строму шейки матки составила: отношение шансов — 3,500 (0,145–84,694); чувствительность — 85,7% (0,757–0,993), специфичность — 33,3% (0,018–0,0648), предсказательная ценность положительного результата — 75% (0,673–0,883), предсказательная ценность отрицательного результата — 50% (0,027–0,972).

Заключение. Настоящее исследование показало, что магнитно-резонансная томография является хорошим инструментом с высокими показателями диагностической информативности метода в выявлении эндоцервикальной аденокарциномы шейки матки. Выделенные в ходе анализа данных магнитно-резонансной томографии 4 типа макроструктуры опухолевого роста аденокарциномы шейки матки указывают на местноагрессивный рост опухоли, высокую частоту отсевов в эндометрий, а также позволят структурировать описательную картину врачу-рентгенологу в том числе при верифицированной аденокарциноме шейки матки, что в дальнейшем позволит лучшим образом выработать план лечения пациентки.

Ключевые слова: эндоцервикальная аденокарцинома; рак шейки матки; магнитно-резонансная томография; диагностика в гинекологии.

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磁共振成像诊断宫颈内膜腺癌的可能性和局限性

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摘要

论证。近几十年来，宫颈腺癌的发病率从 5% 上升到 20%。已证实宫颈内膜腺癌的特点是病程较长，转移较早。由于宫颈腺癌细胞学诊断的困难，放射诊断在诊断和分期阶段发挥着关键作用。迄今为止，关于磁共振成像在宫颈腺癌诊断中的应用的研究还很少。

目的是确定磁共振成像在根据 T 标准对宫颈腺癌进行分期时的诊断信息量，以及在评估肿瘤侵入宫颈基质的深度时的诊断信息量，明确腺癌的符号标志和肿瘤在子宫内生长的特殊性。

材料和方法。2020 年至 2023 年间，123 名确诊为宫颈癌（C53）的患者接受了检查。我们详细分析了 22 名（18%）宫颈腺癌患者（平均年龄 56 岁）使用 1.5 特斯拉磁场强度断层扫描仪接受盆腔器官磁共振成像的结果。对 11/22 例（50%）患者的磁共振成像信息分析进行了评估，这些患者接受了第一阶段手术治疗，切除了子宫和附件。为了分析诊断的信息量，对磁共振成像数据和手术材料的病理形态学检查数据进行了比较。研究结果的统计处理使用 Microsoft Excel 和 JavaStat 软件应用程序进行。

结果。磁共振成像在评估宫颈内膜腺癌局部患病率方面的信息量（根据 T 标准）为（以下主要值后的括号中给出了 95% 的置信区间）：灵敏度为 77.78%（39.99%–97.19%）；特异性为 50.00%（1.26%–98.74%）；阳性结果预测值为 87.50%（62.64%–96.69%）；阴性结果预测值为 33.33%（7.30%–76.04%）；准确度为 72.73%（39.03%–93.98%）。磁共振成像在评估肿瘤侵入宫颈基质深度方面的信息量为：机会比率为 3.500（0.145–84.694）；灵敏度为 85.7%（0.757–0.993），特异性为 33.3%（0.018–0.0648），阳性结果预测值为 75%（0.673–0.883），阴性结果预测值为 50%（0.027–0.972）。

结论。本研究表明了，磁共振成像是检测宫颈内膜腺癌的良好工具，具有很高的诊断信息量。在磁共振成像数据分析过程中发现的宫颈腺癌肿瘤生长宏观结构的 4 种类型表明，肿瘤生长具有局部侵袭性，向子宫内膜脱落的频率较高。这样就能为放射科医生提供描述性的图片结构，在宫颈腺癌得到证实的情况下也是如此，从而为患者制定更好的治疗方案。

关键词：宫颈内膜腺癌；宫颈癌；磁共振成像；妇科诊断。

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BACKGROUND

Despite widespread adoption of preventive measures, cytology screening, and active treatment for precancerous conditions, the incidence of cervical cancer (CC) remains high. According to the World Health Organization, CC is the fourth most common cancer in women worldwide in terms of prevalence and mortality [1]. In developed countries, the incidence rate tends to decrease [1, 2]. In Russia, CC is consistently the fifth common cause of cancer morbidity and the tenth common cause of cancer mortality. Additionally, most *de novo* cases occur in women of reproductive age (40–49 years). Over the past decade, the CC population has increased by 10% [3].

In 2011, a meta-analysis showed that the increased number of CC cases was associated with human papillomavirus (HPV) types 16, 18, and 31 and other types. In cervical squamous cell carcinoma, which is associated with HPV in up to 90% of cases, type 16 was the most common (59.3%) [4]. Cervical adenocarcinoma (CA) is the second most common histologic variant of CC, with 75% of cases associated with HPV; either type 18 or 16 predominate, depending on the country. HPV type 18 was detected in 36.8% of all HPV-positive adenocarcinomas [5, 6]. The incidence of other histologic types of cancer does not exceed 1% [7, 8]. CA is characterized by significant histologic heterogeneity. The association of CA with HPV served as the basis for a new pathogenetic classification published in 2018 (IECC, International Endocervical Adenocarcinoma Criteria and Classification). HPV-positive adenocarcinomas are classified as usual, villoglandular, mucinous, intestinal, and signet ring cell adenocarcinomas and HPV-associated adenocarcinoma not otherwise specified. HPV-negative CAs, which account for 15%–20%, include gastric, clear cell, mesonephric, serous, and endometrioid subtypes and adenocarcinoma not otherwise specified [9, 10].

The classification of HPV-positive and HPV-negative endocervical adenocarcinomas is based on clinical features, differences in tumor biology, prognosis, and response to treatment. The most common HPV-associated endocervical adenocarcinoma is the most typical subtype, accounting for ~75% of all endocervical adenocarcinomas [10]. Mucinous endocervical adenocarcinomas account for ~10% of all HPV-associated endocervical adenocarcinomas [9, 11]. Additionally, endometrioid endocervical adenocarcinoma is rare. With strict diagnostic criteria, it accounts for <1% of all CAs and is associated with endometriosis [9, 11].

CC screening and prevention reduces morbidity and mortality from invasive cervical squamous cell carcinoma. However, in recent decades, CA incidence has increased from 5% to 20% [4, 10, 12]. In addition to diagnostic issues, CA is characterized by a more aggressive course, early metastasis, and lower sensitivity to radiation and drug therapy and represents a serious problem in gynecologic oncology practice [13–15]. The specific location and course of CA with obvious diagnostic problems lead to late detection of the tumor and a high frequency of recurrence and mortality [4, 12]. Therefore, improving diagnostics and developing early detection algorithms are crucial for successful treatment.

According to the 2019 International Federation of Gynecology and Obstetrics (FIGO) classification, stages IA2, IB1, and IIA1 are considered local CC forms; stages IB2 and IIA2–IVA are considered locally advanced; and tumors with distant metastases are classified as advanced stage IVB tumors [16]. Clinical staging of CC (including CA), particularly according to the revised 2018 FIGO classification, is based on a comprehensive evaluation, which includes history-taking and physical examination, morphologic review, and imaging data, such as magnetic resonance imaging (MRI), ultrasound (US), computed tomography (CT), and positron emission tomography (PET). Accuracy of clinical staging at initial diagnosis is critical to the success of subsequent treatment and prognosis [7, 16]. Staging of local CC is based on tumor size; however, the size of the primary cervical lesion does not define the stage of locally advanced tumor when the vagina, parametrium, ureters, and adjacent organs are involved. Although in CC staging, the size of the primary tumor is considered, the recent FIGO report indicated that cervical stromal invasion of >50% and involvement of the outer parts of the stromal ring are associated with poor prognosis and increased recurrence rate [16].

CA does not develop from the squamocolumnar junction (as in cervical squamous cell carcinoma), but from the deep part of the cervical canal, within the crypts; this defines the type of tumor growth, which is predominantly endophytic, resulting in the absence of early clinical manifestations and late detection of the tumor. Tumor progression in the deep endocervix, closer to the internal orifice of the cervix, leads to tumor spread in the adjacent isthmus and endometrium, infiltrating the cervical stroma and myometrium, mimicking endometrial cancer (EC). When tumor imaging (using US, MRI, and CT) is performed at the stage of simultaneous uterine body and cervical involvement, determination of the primary lesion and staging become extremely difficult. According to the FIGO classification, in CC, tumor spread to the body of the uterus does not affect the stage, whereas in EC with cervical involvement, the tumor progresses from stage T1 to T2, which significantly affects the treatment choice and prognosis. In these cases, histology and immunohistochemistry are the definitive diagnostic tests. Immunohistochemical markers for differential diagnosis include p16, estrogen and progesterone receptors, and p53 [17]. Positive staining for p16 is more characteristic for usual-type HPV-associated endocervical adenocarcinoma, and a positive test for estrogen and/or progesterone receptors is more common in endometrioid adenocarcinoma of the endometrium, although it may also be seen in CA [17]. In 2022, a Korean research group led

by Song JY trained artificial intelligence to differentiate between different subtypes of cervical and uterine body cancer. The study demonstrated high diagnostic efficacy of the proposed algorithm (AUC of 0.977 for CC, 0.944 for EC, and 0.939 for differentiation of cervical and uterine body adenocarcinoma) [18].

A 2020 meta-analysis evaluated the diagnostic efficacy of various imaging modalities (i.e., MRI, US, CT, and PET) in assessing local tumor spread and lymph node metastases in patients with newly diagnosed CC and showed that MRI had the highest sensitivity and specificity for local spread of CC. All the above modalities have a high specificity for detecting metastases in lymph nodes [19]. In some studies, including Russian studies (Rubtsova NA et al.), the overall accuracy of MRI in staging invasive CC was 77%–90% [20, 21]. MRI provides high resolution of soft tissues and more accurately determines the depth of invasion and preoperative tumor size, especially with T2-weighted images (WI). However, the diagnostic value of MRI in assessing parametrial invasion remains controversial, with a borderline sensitivity rate (~73%–76%), associated with a high percentage of false-positive results [22, 23]. Studies that evaluated the characteristics of MRI in endocervical adenocarcinoma are few.

STUDY AIM

To determine the diagnostic efficacy of MRI in T-staging CC and in assessing the depth of cervical stromal invasion of endocervical adenocarcinoma and identify semiotic signs of adenocarcinoma and characteristics of uterine tumor growth.

MATERIALS AND METHODS

Study Materials. Study Design

This single-center, retrospective, selective study included 123 patients with histologically confirmed CC (ICD code: C53) to evaluate the incidence trend of CA. They were examined and treated at the Scientific Center for Radiography and Radiology of the Ministry of Health of the Russian Federation from 2020 to 2023.

Patients with CA were comprehensively evaluated; the results of 22 (18%) patients with this histologic cancer type were reviewed. The mean age of patients with CA was 56 years (range: 35–74 years). Data analysis excluded patients with squamous cell carcinoma.

Fig. 1 shows the study design. Table 1 presents the distribution of patients by histologic tumor type and grade of differentiation. The distribution by FIGO stages is presented in Table 2.

Study Methods

Overall, 123 women were examined by an obstetrician-gynecologist. The study included assessment of symptoms and medical history, bimanual rectovaginal examination, vaginal and cervical speculum examination, cytology of cervical and endocervical smears, and cervical histology.

In 22 patients (18%), multiparametric pelvic MRI was performed using 1.5 T scanners. It was conducted using a flexible body coil and with the patient in supine position. The multiparametric MRI protocol included T1-WI and T2-WI; STIR; diffusion-weighted images with b-factors of 0, 800, and 1000 sec/mm^2; and dynamic contrast enhancement with gadolinium

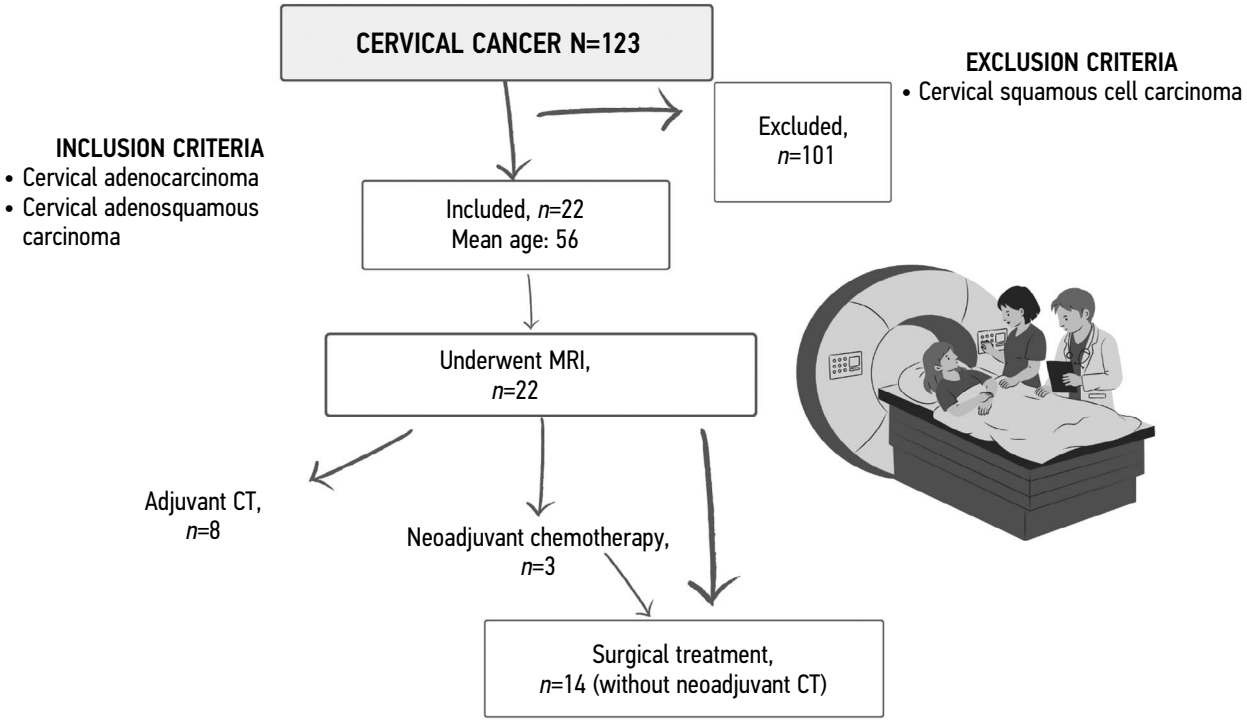

Fig. 1. Study design. MRI, magnetic resonance imaging; CT, computed tomography.

Table 1. Distribution of patients depending on the histological type of tumor and degree of differentiation

Histologic type		No. of patients (*n*=22)
Endocervical adenocarcinoma	Low-grade	7
	Intermediate-grade	4
	High-grade	2
Serous adenocarcinoma		3
Endometrioid adenocarcinoma		5
Adenosquamous carcinoma		1

Table 2. Distribution of patients by disease according to the International Federation of Gynecology and Obstetrics classification

Stage	Number of patients (*n*=22)
Cancer in situ	2
IB	4
IB1	3
IB2	1
IIA	1
IIB	2
IIIB	1
IIIC	1
IIIC1	3
IV	2
IVB	2

salts, which met the European Society of Urogenital Radiology (ESUR) requirements for MRI [24]. According to ESUR guidelines, a b-factor of 1000 sec/mm^2 is sufficient for the diagnosis of uterine disorders in routine practice.

T2-WI MRI data were used to evaluate the size and depth of cervical stromal invasion (Fig. 2); the presence of parametrial invasion; involvement of the internal orifice and isthmus of the uterus, endometrial lining, uterine appendages, and lymph nodes; and the presence of a "feeding pedicle" in the tumor. The tumor pedicle was used to designate the junction between the tumor and uterine wall, considered as the tumor origin, with tumor feeding vessels visualized in the arterial and venous phases of dynamic contrast enhancement.

Extirpation of the uterus and appendages with pelvic lymphadenectomy was performed in 14 patients (64%). Three patients (21%) underwent surgery after neoadjuvant polychemotherapy. Pathologists assessed the size and depth of cervical stromal invasion in 11 patients with CA who started anticancer treatment at the surgical stage. In the excised specimens, the presence of cervical stromal invasion, vaginal transition, parametrial invasion, uterine body involvement (depth of myometrial invasion), uterine appendages, and lymph nodes were also evaluated. In 11 patients, preoperative MRI data, obtained not more than 1 month prior to the start of the treatment, were compared

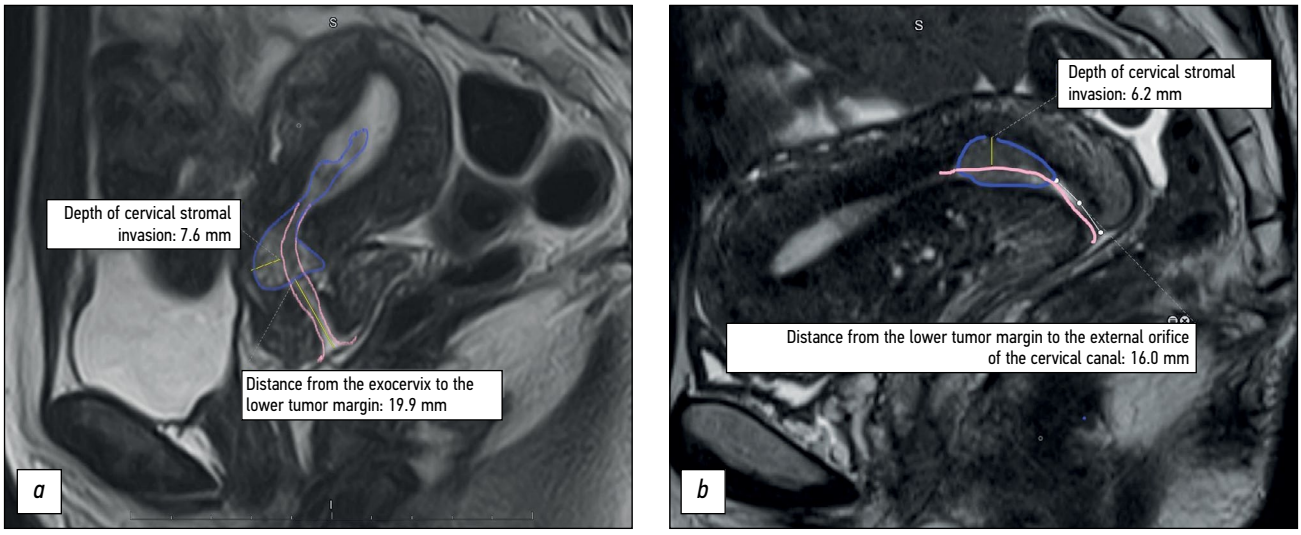

Fig. 2. An example of measuring the depth of cervical adenocarcinoma invasion into the stroma and the distance from the tumor to the exocervix: (*a*) the tumor is located in the upper third of the cervix, has a depth of invasion of 8 mm and is located at a distance of 20 mm from the exocervix; (*b*) the tumor is located in the upper third and middle third of the cervix, has a depth of invasion of 6 mm and is located at a distance of 16 mm from the exocervix. The tumor is outlined with a purple line, the endocervical canal is marked with pink lines. Conclusion of the pathomorphological study: endocervical adenocarcinoma of the cervix grade 2; depth of invasion into the cervical stroma 5 mm (less than 1/2 the thickness of the cervical wall); lymphovascular invasion was detected; the tumor grows into the internal os; endometrium in the secretion phase.

with postoperative pathology data. Eight patients (36%) received a combination of chemotherapy and radiotherapy.

Microsoft Excel (Microsoft, USA) and JavaStat were used for statistical processing of the results.

Ethical Review

According to the Independent Ethics Committee at the Russian Scientific Center for Radiography and Radiology of the Ministry of Health of the Russian Federation (minutes of meeting no. 9, dated September 29, 2023), the study "Possibilities and Limitations of Magnetic Resonance Imaging in the Diagnostics of Endocervical Adenocarcinomas" did not require the opinion of the Independent Ethics Committee.

RESULTS

CA was detected in 18% (22/123) of CC patients examined between 2020 and 2023.

In 5 patients (23%), CC was discovered incidentally during a routine gynecologic examination. The disease manifested with spotting in 13 patients (59%), serous discharge in 2 patients (9%), dragging pain in lower abdomen in 6 patients (27%), and painful urination in 1 patient (5%).

Preexisting cervical conditions (ectropion, erosion, and chronic cervicitis) were noted in 8 patients (36%) and cervical dysplasia (grade 1–3) in 3 patients (14%). In 11 patients (50%), no cervical abnormalities were detected prior to the diagnosis of CA. Table 3 shows the gynecological examination data.

In 2 women (9%), the MRI scan did not show a tumor. Table 4 shows the MRI data of 22 patients. The mean tumor volume in T2-WI was 25 cm^3 (range: 1–71 cm^3). The following results were obtained when evaluating the diagnostic efficacy of MRI in assessing the local extent of CA (T-staging) in 11 patients after surgery as the first treatment step:

- Sensitivity: 77.78% (95% confidence interval [CI]: 39.99%, 97.19%)
- Specificity: 50.00% (95% CI: 1.26%, 98.74%)
- Positive predictive value: 87.50% (95% CI: 62.64%, 96.69%)
- Negative predictive value: 33.33% (95% CI: 7.30%, 76.04%)
- Accuracy: 72.73% (95% CI: 39.03%, 93.98%)

In 8 patients (40%), the CC was located at a distance from the external orifice (mean: 11 mm; range: 4–18 mm). In this location, the tumors cannot be visualized during gynecologic examination because the external orifice is intact. Infiltration of the vaginal cervix was reported in 9 patients (45%). The mean apparent diffusion coefficient (ADC) of the tumor was 0.833×10^{-3} mm/sec (range: from 0.440×10^{-3} to 0.1282×10^{-3} mm/sec).

We identified two types of tumor growth in the cervical stroma: the most common were the endophytic type (75%, $n = 15$), characterized by diffuse enlargement and barrel-shaped cervical transformation (Fig. 3), and exophytic type, which occurred in 25% of cases in the present study ($n = 5$). Exophytic tumors were most commonly located in the vaginal cervix, with tumor masses prolapsing into the vagina or cervical canal lumen (Fig. 3). The exophytic tumor was represented by different histologic subtypes of CA:

- Poorly and moderately differentiated typical endocervical adenocarcinoma, 2 cases
- Poorly differentiated serous adenocarcinoma, 1 case
- Adenosquamous carcinoma, 1 case
- Endometrioid endocervical adenocarcinoma, 1 case

Table 3. Results of gynecological examination

Gynecological examination data	Yes *n* (%)	No *n* (%)
Cervical lesion	10 (45)	12 (55)
Parametrial lesion (clinically as thickened fornixes)	11 (50)	11 (50)
Vaginal involvement	11 (50)	11 (50)

Table 4. Magnetic resonance imaging data

Parameter	Yes *n* (%)	No *n* (%)
Cervical stroma invasion	17 (77)	5 (23)
Parametrial invasion	9 (41)	13 (59)
Involvement of the internal cervix	12 (55)	10 (45)
Involvement of the isthmus	9 (41)	13 (59)
Involvement of the endometrium	6 (27)	16 (73)
Involvement of the adnexa	4 (18)	18 (82)
Involvement of lymph nodes	9 (41)	13 (59)
Presence of a central feeding vessel	9 (41)	13 (59)

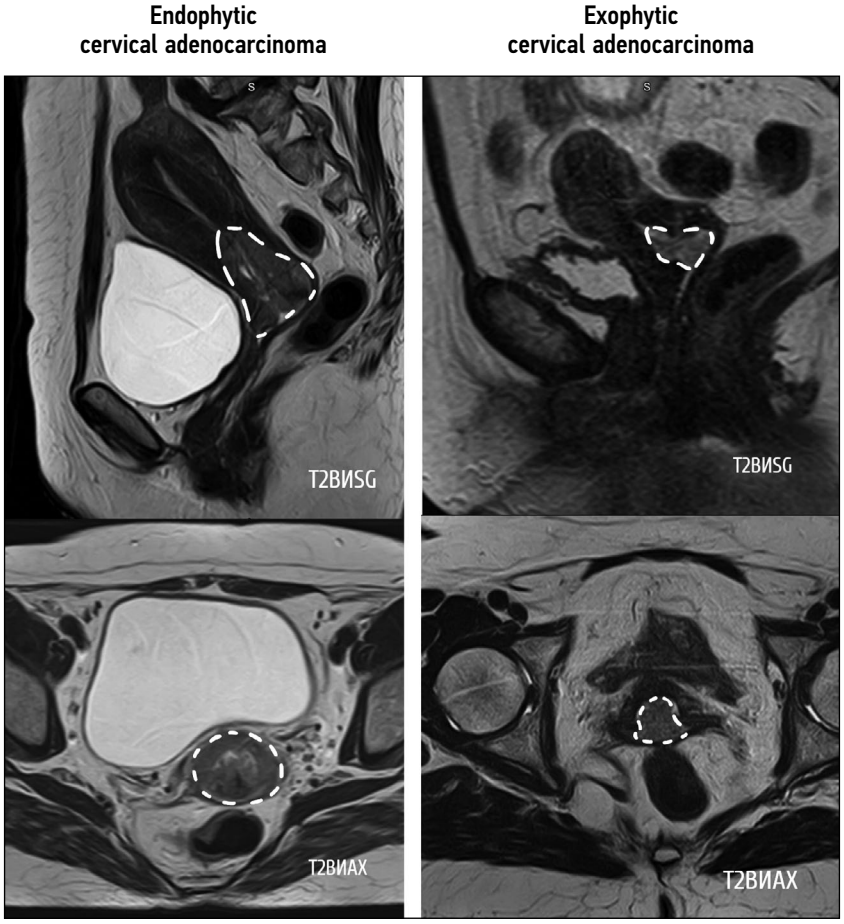

Fig. 3. Cervical adenocarcinoma growth pattern. The upper row of images is T2-weighted images in sagittal plane, the lower one — in axial plane.

Furthermore, endophytic tumors were characterized by different histologic types and differentiation patterns. No correlation was found for the type of tumor growth and its histologic subtype.

Differential diagnosis of the location of the primary tumor (whether the observed uterine abnormalities were endometrial carcinoma with cervical involvement or cervical carcinoma with endometrial involvement) was critical in the diagnostic search of gynecologists and radiologists for detecting uterine adenocarcinoma. All diagnostic controversies with predominant involvement in the uterine cavity were further reviewed by pathologists, and in all patients, endocervical adenocarcinoma (tumor of the cervix) was confirmed. Therefore, four types of tumor macrostructure were retrospectively classified based on the predominant location of the tumor according to MRI and pathology data (Fig. 4):

1) Predominance of tumor in the cervix (*n* = 13; 65%)
2) Predominance of tumor in the uterine body (*n* = 2; 10%)
3) Equal involvement of endocervix and endometrium (*n* = 2; 10%)
4) Isolated cervical lesion with CA lesion seeding into the uterine cavity (in the endometrium), confirmed by pathology and immunohistochemistry data (*n* = 3; 15%)

Notably, type 2, 3, and 4 tumors were described as uterine body cancer on MRI, and only pathology examination confirmed primary CA.

According to pathology data, the mean depth of cervical stromal invasion of adenocarcinoma was 8.2 mm (range: 2–15 mm). Surgical material examination data are presented in Table 5.

A comparative analysis of the invasion depth according to MRI and postoperative pathology was performed in 11 patients who did not receive neoadjuvant chemotherapy (Table 6). MRI data on cervical stromal invasion depth revealed a false-positive result (overdiagnosis) in 2 patients (18%) and a false-negative result (underdiagnosis) in 1 patient (9%). In 8 patients (73%), MRI and pathology data were consistent. The thickness of the MRI slice (T2-WI) was 4 mm; thus, a difference between MRI and pathology data ≤4 mm was considered a method error.

Therefore, the diagnostic value of MRI in assessing the depth of cervical stromal invasion of CA was as follows:

- Odds ratio: 3.500 (95% CI: 0.145, 84.694)
- Sensitivity: 85.7% (95% CI: 0.757, 0.993)
- Specificity: 33.3% (95% CI: 0.018, 0.0648)
- Positive predictive value: 75% (95% CI: 0.673, 0.883)
- Negative predictive value: 50% (95% CI: 0.027, 0.972)

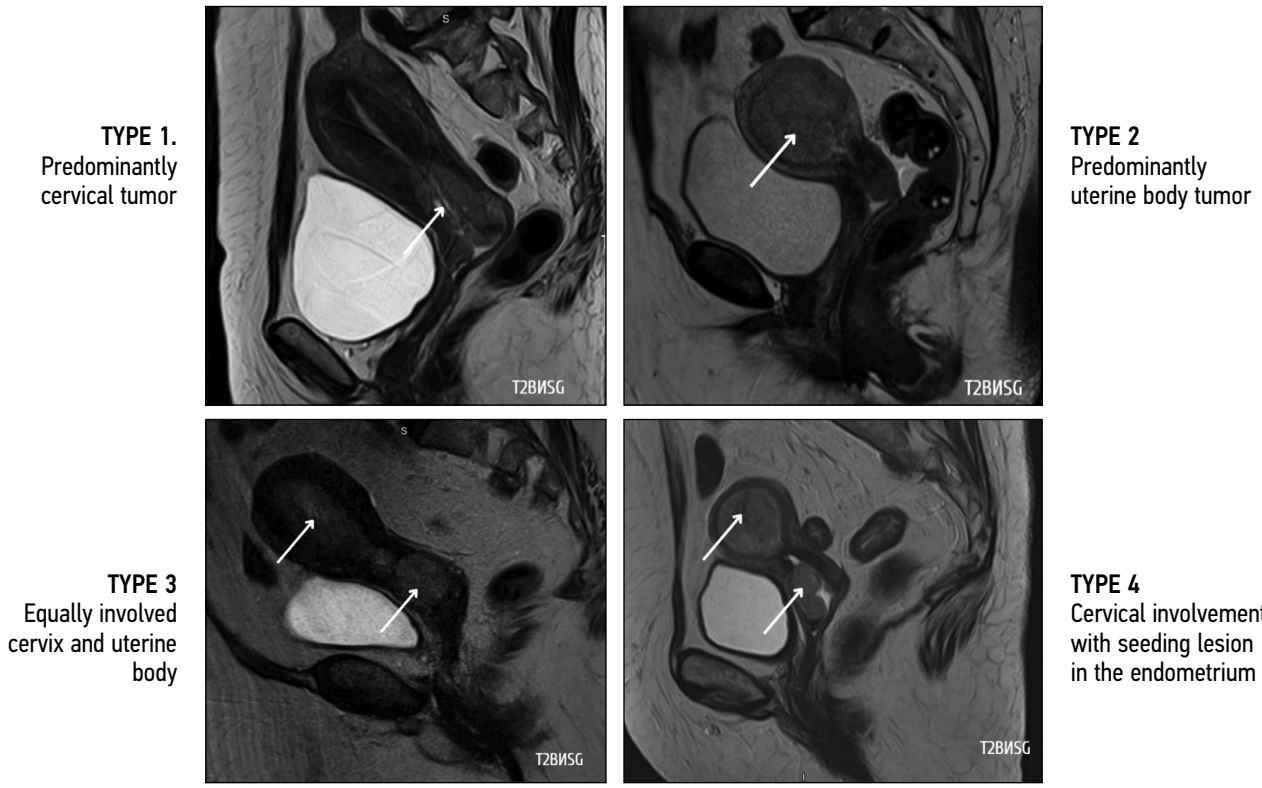

Fig. 4. Type of tumor macrostructure, T2-weighted images in sagittal plane, cervical adenocarcinoma.

The locally invasive growth pattern with tumor pedicle formation was observed, and feeding vessels were visualized (41%) in the endometrial CA seeding lesions (Fig. 5).

DISCUSSION

In our study, 18% (22/123) of patients diagnosed with CC had adenocarcinoma and mixed adenosquamous lesions of the cervix. This confirms the relative increase in CA morbidity reported in global (Chan ZF et al. and Islami F et al.) and Russian (Grigoruk OG et al.) studies [4, 10, 12]. We believe that the relative increase in CA morbidity is related to the lack of signs of the disease (in our study, 48% of patients had no visual cervical lesions on gynecologic examination and had an intact external orifice on MRI) and the lack of effective screening strategies. A population study by Castanon A et al. showed that current cytology screening is ineffective in the diagnosis of cervical pre-cancer (adenocarcinoma *in situ* or

Table 5. Surgical material data of 14 patients

Parameter	Yes *n* (%)	No *n* (%)
Cervical stroma invasion	13 (93)	1 (7)
Parametrial invasion	0 (0)	14 (100)
Involvement of the endometrium	4 (29)	10 (71)
Involvement of the adnexa	2 (14)	12 (86)
Involvement of lymph nodes	2 (14)	12 (86)

Table 6. Diagnostic value of magnetic resonance imaging in the diagnosis of cervical adenocarcinoma

Parameter	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Cervical stroma invasion evaluation	85.7% (CI, 0.757–0.993)	33.3% (CI, 0.018–0.0648)	75% (CI, 0.673–0.883)	50% (CI, 0.027–0.972)
T-staging	77.78% (CI, 39.99%–97.19%)	50.00% (CI, 1.26%–98.74%)	87.50% (CI, 62.64%–96.69%)	33.33% (CI, 7.30%–76.04%)

Note. CI, 95% confidence interval.

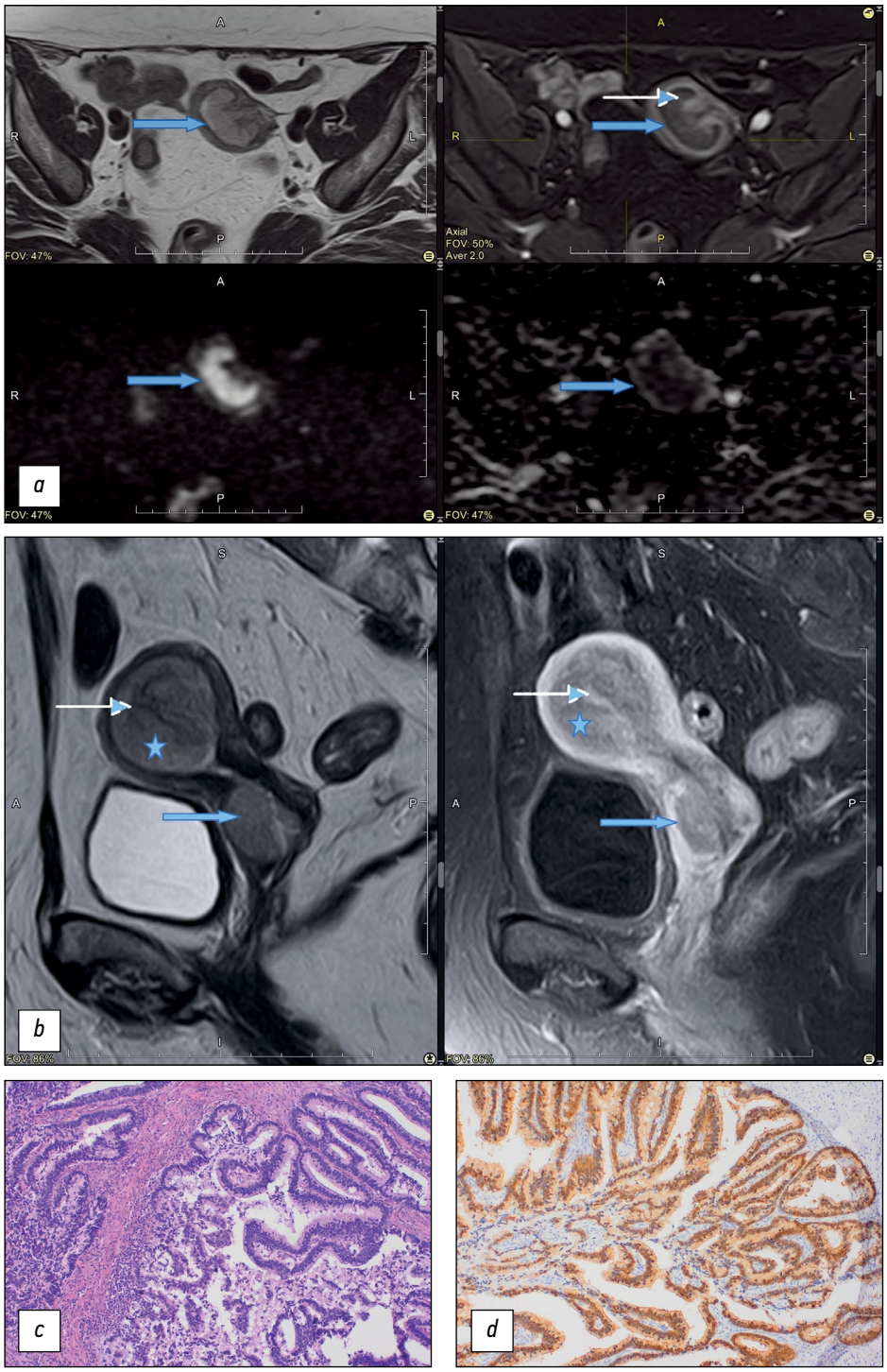

Fig. 5. Magnetic resonance imaging of the pelvis (cervical adenocarcinoma), metastasis in endometrium:
(*a*) from left to right and from top to bottom: T2-weighted image, T1FS-weighted image with contrast enhancement in the arterial phase, diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) map. The tumor (metastasis in endometrium) is marked with an arrow. The region of the "leg" of the tumor and feeding vessels are marked with a dotted arrow; (*b*) sagittal plane, T2-weighted image (left) and T1FS+C (right): primary tumor (arrow), metastasis in the body of the uterus (star), vessels in the focus of tumor (dotted arrow). In the arterial phase of DCE, the accumulation of paramagnetic by the basal layer of the endometrium and the vessels in the "feeding leg" of the tumor is determined; (*c*) histological examination of the surgical material, stained with hematoxylin and eosin, ×10; *d,* immunohistochemical study, expression of p16.
Conclusion of the pathomorphological study: Moderately differentiated endocervical adenocarcinoma. The tumor grows into the stroma of the cervix to a depth of 1.3 cm (2/3 of the thickness of the wall of the cervix in the transition zone). The tumor grows into the myometrium (to a depth of 0.6 cm, 1/3 of the thickness of the uterine body wall) and endometrium. The vaginal part of the cervix is covered with a multilayer flat epithelium.

low-grade cervical glandular intraepithelial neoplasia), but it is effective in the detection of the earlier stage CA (stage IA). This is attributed to the predominantly endocervical location of CA, within the cervical crypts, which complicates the sampling of material containing atypical cells [25]. Islami F et al. found the increased incidence of CA *in situ* and invasive CA, mainly in young women aged 35–54 years, owing to improved CC screening [12]. Similar data were obtained in studies by Chan ZF et al. and Suh DH et al. [4, 26].

Regarding precancerous conditions, gastric-type endocervical carcinoma is preceded by endocervical glandular hyperplasia, including atypical adenocarcinoma *in situ* [27, 28]. In the present study, 50% of the patients had preexisting cervical diseases (e.g., chronic cervicitis); atypical adenocarcinoma *in situ* was found in one patient with history of multiple cervical conization caused by severe dysplasia (CIN III). Ten patients had endometriosis.

In this study, despite the high diagnostic value of MRI in detecting and assessing the extent of CC, the tumor was not visualized with multiparametric scanning tomography in 2 patients (9%) with histologically confirmed CA. This may be due to the small volume of the tumor and its lateral-spreading growth along the cervical canal and the technical limitations of this imaging modality.

Good results were obtained when comparing MRI and pathology examination data:

- The overall accuracy of MRI in assessing the depth of cervical stromal invasion was 70%, with a sensitivity of 87.5%.
- In assessing tumor extent (T-staging), the accuracy was 72.3% and the sensitivity was 77.8%.

In our study, in the case of underdiagnosis (n = 1), differences were associated with tumor necrosis leading to magnetic resonance signal heterogeneity in T2-WI and not accounted for in size measurement. In cases of overdiagnosis (n = 2), difference was due to severe uterine deformity in mixed adenomyosis and submucosal leiomyomas.

Despite the several advantages of MRI, foreign literature showed frequent discrepancies between clinical staging and surgical findings, with a tendency to underestimate stage; the higher the stage, the greater the discrepancy. For CA, these differences were even more significant [29, 30].

In addition to objective errors in assessing the extent of the various histologic forms of CC, overdiagnosis results from the concomitant inflammatory infiltration following invasive cervical manipulation or necrosis of large tumors. Underdiagnosis may result from the accumulation of retention cysts in the vaginal cervix, including the area around the external orifice, which complicates assessment of the structure of the epithelial lining and underlying cervical stroma [31].

For CA seeding in the endometrium, a locally invasive growth of endometrial seeding lesions and some CA lesions located in the isthmus and in the middle third (m/3) of the endocervical canal were noted, along with the formation of a pedicle and visualized feeding vessels (41%). This finding is described for the first time and has not been analyzed in previous studies. We believe that the neoangiogenesis in the tumor, which is fed by arcuate and large intramural vessels of the myometrium on MRI, indicates aggressive tumor growth, a high probability of lymphovascular invasion (LVI+), an increased probability of lymph node metastasis, and a poor prognosis. However, owing to the small number of reports and the lack of comparison with pathology data (because of the retrospective nature of the data analysis), the characteristics identified are rather observational and require further scientific research.

The ability of CA to seed the endometrium has been reported in several studies and is explained by a "seed and soil" theory, i.e., the detachment of some cancer cells from the primary tumor site, their migration into the uterine cavity, and their implantation in the endometrium [32]. Cell implantation with subsequent formation of feeding vessels and the predominantly uterine location of the growing seeding lesion can be explained by the better blood supply to the myometrium compared to the cervix with dominating fibrous tissue in the stroma.

The use of diffusion-WI and analysis of ADC maps increases the efficiency of this modality compared to standard MRI [33, 34]. Kuang F. et al. showed that ADC is a reliable marker for differentiating CC from normal cervix, with high diagnostic accuracy (ADC for CC was significantly lower than for normal cervix: $0.81 \pm 0.13 \times 10^{-3}$ mm^2/sec vs. $1.41 \pm 0.10 \times 10^{-3}$ mm^2/sec). Moreover, ADC can be used to determine the grade of differentiation and histologic type of CC. However, there is some overlap between the values. The higher the ACD, the more differentiated the tumor is [34, 35]. In the present study, the mean ADC in the region of interest was 0.833×10^{-3} mm^2/sec (range: from 440×10^{-3} mm^2/sec; to $1{,}282 \times 10^{-3}$ mm^2/sec), which is generally consistent with literature data.

There are data on the difference in ADC between cervical squamous cell carcinoma and CA; ADC is significantly lower in squamous cell carcinoma [36].

Lin Y-C. et al. demonstrated that in cases of inconsistent morphology, the tumor ADC can be used to differentiate its histologic type: the mean ADC was significantly lower in EC (0.766×10^{-3} mm^2/sec) than in CC (0.969×10^{-3} mm^2/sec). In EC, the tumor was reported to have predominantly longitudinal growth in the cervix, whereas in CC, the growth pattern was predominantly oval [37, 38]. Tarachkova EV et al. evaluated semiotic differences between CA and cervical squamous cell carcinoma. In 90 patients with histologically confirmed CC, adenocarcinoma was found to have a more intense and less heterogeneous signal on T2-WI, with fat suppression compared to squamous cell carcinoma [39].

Determining the location of the primary tumor was crucial in the differential diagnosis of uterine adenocarcinoma based on MRI data. Endocervical adenocarcinoma with endometrial involvement and endometrial adenocarcinoma with cervical involvement cannot be distinguished based on signal

characteristics in most cases. As this study has shown, one should not rely solely on the location of a larger tumor volume.

In the current study, only 65% (13 of 20) of histologically confirmed endocervical CAs were localized exclusively in the cervix. In 35% of cases (7 of 20), the tumor mimicked EC, with tumor lesions found in the uterine cavity and along the cervical canal. In cases with endocervical adenocarcinoma seeding lesions in the endometrium (3/20, 15%), the size of the tumor implantation in the endometrium exceeded the size of the primary cervical tumor in 2 patients (Fig. 5d). In 2009, a similar pattern in CA growth was reported by Yemelyanova A et al. from the Johns Hopkins University. Scientists evaluated 10 cases of CA with concomitant involvement of the uterine body and cervix and concluded that endometrioid adenocarcinoma with minimal cervical involvement often turned out to be cervical adenocarcinoma [40].

Pathology and immunohistochemistry are objective methods for differential diagnosis of complicated cases of adenocarcinoma of the cervix and uterine body. However, it should be noted that even pathology and immunohistochemistry do not reveal a definitive diagnosis in 100% of cases, as some endometrioid adenocarcinomas are difficult to distinguish from endocervical CA; partial staining of the latter for p16 and estrogen and progesterone receptors is possible [17]. Endometrioid CA should be diagnosed with caution. Generally, endometrioid adenocarcinoma of the cervix and uterine body may have a similar immunohistochemical profile [41]. In the case of simultaneous lesions of the uterine body and cervix, it is crucial to exclude advanced endometrial and ovarian adenocarcinoma and correlate clinical and diagnostic data, as the primary location of the tumor will be critical in the choice of treatment strategy and chemotherapy regimens. According to the IECC, the term "endometrioid carcinoma" refers to tumors with low-grade endometrioid glands and confirmatory endometrioid features (squamous metaplasia or endometriosis) [41].

Therefore, differential diagnosis of complicated cases of adenocarcinoma of the uterine cervix and body should be based on a comprehensive examination of a patient, including history-taking and physical examination, confirmatory morphology, immunohistochemistry, and MRI.

CONCLUSION

Owing to infiltrative tumor growth, frequent location in the upper cervical canal and mucosa of the isthmus, endocervical CA is diagnosed at late stages. This is related to the difficulty in obtaining sufficient cytology material for PAP smear and failure to visualize cervical abnormalities during gynecologic examination, which prevents prompt tumor detection. Late diagnosis of endocervical CA results in the detection of a locally advanced process with frequent direct or metastatic lesions of the endometrium, mimicking primary EC.

This study showed that MRI is an instrumental tool with a high value in the diagnosis of uterine tumors. Four MRI-based macrostructural types of CA growth indicate locally aggressive tumor growth and a high frequency of seeding into the endometrium and allow a radiologist to structure the descriptive image, even in the presence of CA, and subsequently develop a better treatment plan for a patient.

The limitations of MRI in the detection of small cervical tumors are related to the predominantly infiltrative and lateral-spreading tumor growth without increasing the uterine size and changing the endocervical signal characteristics. However, if MRI shows heterogeneous expansion and hyperplasia of the cervical canal, a tumor may be suspected, and the patient should be urgently referred to a gynecologic oncologist. In the absence of clear guidelines for the management of patients with CA *in situ*, MRI is the preferred method for follow-up. If the primary lesion of uterine adenocarcinoma cannot be determined, a combination of physical (gynecologic) examination, imaging (MRI), and morphologic diagnostic methods should be used.

ADDITIONAL INFORMATION

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Magnetic Resonance Imaging in the Evaluation of Pectus Excavatum

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ABSTRACT

BACKGROUND: Magnetic resonance imaging is more often used to confirm the presence of pectus excavatum and assess compression changes in the heart at this level.

AIM: To evaluate pectus excavatum preoperatively according to magnetic resonance imaging findings.

MATERIALS AND METHODS: A retrospective evaluation of chest magnetic resonance imaging data of 38 patients (male, *n* = 30; female, *n* = 8) was performed. The average age was 19.9 years (±9 years).Cardiac magnetic resonance imaging was performed on a 1.5-T General Electric Optima MR450w GEM scanner with 2D-FIESTA-C pulse sequences, as well as functional assessment of the left and right ventricles. Parameters for surgical treatment of pectus excavatum were as follows: the Haller index, correction index, and sternum rotation angle. Statistical analysis of the relationship between the Haller index, correction index, and sternum rotation angle and ejection fraction of the right ventricle was conducted. A p-value <0.05 was considered significant.

RESULTS: Moderate and severe pectus excavatum were found in 92% of the cases. No significant Pearson correlation was obtained between the Haller index and right ventricular ejection fraction (inspiratory and expiratory ejection fraction, *P* = 0.777 and 0.798, respectively). The mean right ventricular ejection fraction was 46%. A correlation was noted between the Haller index and the correction index (*P* < 0.05). The rotation angle of the sternum, which required modification of surgical intervention, was detected in 44.7% of patients.

CONCLUSION: Magnetic resonance imaging is an informative diagnostic method for pectus excavatum pectus excavatum without radiation exposure and enables detailed preoperative assessment. A correlation was noted between the Haller index and the correction index (*P* < 0.05). Magnetic resonance imaging revealed a decrease in the ejection fraction of the right ventricle.

Keywords: pectus excavatum; magnetic resonance imaging; right ventricle ejection fraction; Haller index; correction index; sternal torsion angle.

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Магнитно-резонансная томография при воронкообразной деформации грудной клетки

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АННОТАЦИЯ

Обоснование. Магнитно-резонансная томография чаще применяется для подтверждения факта наличия воронкообразной деформации грудной клетки, а также для оценки компрессионных изменений сердца на этом уровне.

Цель — прицельная предоперационная оценка воронкообразной деформации грудной клетки по данным магнитно-резонансной томографии.

Материалы и методы. Проведена ретроспективная оценка магнитно-резонансной томографии органов грудной клетки у 38 пациентов (30 мужского пола, 8 женского пола). Средний возраст — 19,9 года (±9 лет).

Магнитно-резонансная томография сердца выполнялась на аппарате General Electric Optima MR450w GEM 1,5 Тл с использованием импульсных последовательностей 2D-FIESTA-C с электрокардиографической синхронизацией с функциональной оценкой состояния левого и правого желудочков. Были получены параметры, необходимые для дальнейшего оперативного лечения пациентов по поводу воронкообразной деформации грудины — индекс Галлера, индекс коррекции, угол ротации грудины.

Проведена статистическая обработка полученных данных, поиск взаимосвязи между индексом Галлера, индексом коррекции, углом ротации грудины и фракцией выброса правого желудочка. Значение p <0,05 считали границей статистической значимости.

Результаты. В 92% случаев у пациентов выявлена умеренная и тяжёлая воронкообразная деформация грудной клетки. При поиске взаимосвязи между значениями индекса Галлера и фракцией выброса правого желудочка не было получено статистически значимой корреляции Пирсона (p=0,777 для значений фракции выброса на вдохе и p=0,798 для значений фракции выброса на выдохе). Среднее значение фракции выброса правого желудочка составило 46%.

При статистическом анализе по мере увеличения индекса Галлера (увеличение степени деформации органов грудной клетки) было отмечено увеличение индекса коррекции (p <0,05). Значения угла ротации грудины, потребовавшие модификации оперативного вмешательства (более 15°), были выявлены у 44,7% пациентов.

Заключение. Магнитно-резонансная томография — высокоинформативный метод диагностики при воронкообразной деформации грудной клетки: без лучевой нагрузки и с возможностью подробной предоперационной оценки патологических изменений.

Получены данные о наличии корреляции между значениями индекса Галлера и индекса коррекции (p <0,05). Кроме того, по данным магнитно-резонансной томографии выявлено уменьшение фракции выброса правого желудочка.

Ключевые слова: воронкообразная деформация грудной клетки; магнитно-резонансная томография; фракция выброса правого желудочка; индекс Галлера; индекс коррекции; угол ротации грудины.

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漏斗胸畸形的磁共振成像

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摘要

论证。磁共振成像更常用于确认是否存在漏斗胸畸形，并评估该水平的心脏压迫变化。

目的是通过磁共振成像对漏斗胸畸形进行术前评估。

材料和方法。我们对 38 名患者（30 名男性，8 名女性）的胸部器官磁共振成像进行了回顾性评估。平均年龄为 19.9 岁（±9 岁）。

心脏磁共振成像是在 General Electric Optima MR450w GEM 1.5 特斯拉设备上进行的，使用的是 2D-FIESTA-C 脉冲序列，同时进行了伴有左心室和右心室功能评估的心电图同步。获得了对漏斗胸畸形患者进行进一步手术治疗所需的参数：Haller 指数、矫正指数、胸骨旋转角度。

对获得的数据进行统计处理，寻找 Haller 指数、矫正指数、胸骨旋转角度和右心室射血分数之间的相关性。P<0.05的值被认为是统计学意义的边界。

结果。在 92% 的患者中发现了中度和重度漏斗胸畸形。在寻找 Haller指数值与右心室射血分数之间的相关性时，未发现有统计学意义的 Pearson 相关性（吸气射血分数值的相关性为 P=0.777，呼气射血分数值的相关性为 P=0.798）。右心室射血分数的平均值为 46%。在统计分析中，随着 Haller 指数（胸腔器官畸形程度的增加）的增加，矫正指数也在增加（P<0.05）。44.7% 的患者的胸骨旋转角度值需要修改手术干预（超过15°）。

结论。磁共振成像是一种对漏斗胸畸形有高度参考价值的诊断方法：无需放射线照射，还能对病理变化进行详细的术前评估。

数据显示了，Haller 指数与矫正指数值之间存在相关性（P<0.05）。此外，磁共振成像数据显示了，右心室射血分数有所下降。

关键词：漏斗胸畸形；磁共振成像；右心室射血分数；Haller 指数；矫正指数；胸骨旋转角度。

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BACKGROUND

Pectus excavatum (PE) is a prevalent developmental chest wall deformity affecting 1:300–1:1,000 newborns, with clinical manifestations most commonly observed at 10–12 years of age and during puberty [1, 2].

The sternum and anterior ribs "sink" into the thorax in PE, resulting in a depression of varying depth and shape. The chest wall deformity is believed to be the result of aberrant rib cartilage development, which causes progressive displacement of the sternum due to their excessive growth. The attachment of ribs 6 and 7 to the sternum is where the most substantial alterations are observed. Pectus carinatum, a protrusion chest deformity also known as "keel chest," is diagnosed when the sternum is displaced forward. "PE," or "funnel chest" deformity, is diagnosed when the sternum is displaced inward [2].

In addition to cosmetic defects, PE is linked to displacement of mediastinal organs and structures and compression of lung tissue, which can impact heart and lung function and reduce physical activity [3–6].

Due to its accessibility and speed, computed tomography (CT) is widely employed to evaluate the degree of deformity and the position of the mediastinal organs in relation to the deformed chest wall [3].

Magnetic resonance imaging (MRI) is also used to verify the presence of a deformity and evaluate possible compression of the heart [3]. MRI does not involve radiation exposure and offers comparable diagnostic information regarding the sternum and ribs to CT. Nevertheless, there are only a limited number of sources that provide comprehensive information regarding the informative value of MRI in evaluating the parameters required for surgical planning [4].

Given the significance of establishing the appropriate indications for the surgical treatment of PE, the severity of this malformation is assessed using several parameters, including the Haller index, the correction index, and the sternal rotation angle.

The Haller index is determined using axial scanning. This index is calculated by dividing the transverse diameter of the chest wall (the maximum distance between the inner surfaces of the ribs) by the anteroposterior diameter of the chest (the distance between the posterior aspect of the sternum and the anterior aspect of the vertebra) [7]. In PE, the anteroposterior diameter decreases because of the depression of the sternocostal complex, which causes the Haller index to increase [8]. The Haller index is classified as follows:

- Normal: <2.0
- Mild PE: 2.0–3.2
- Moderate PE: 3.2–3.5
- Severe PE: >3.5

Surgical treatment of PE is indicated when the Haller index exceeds 3.25.

The correction index is defined as the ratio of the expected increase in thoracic deformity of the corrected sternum (as reflected by the formula calculating the difference between the maximum size and the available minimum size) to the maximum anterior and posterior internal chest size, expressed as a percentage. The correction index has been used to guide the treatment of PE patients only recently [9].

The sternal rotation angle is a critical parameter in PE patients, as understanding the severity and direction of the angle is required for appropriate subsequent surgical planning [10].

STUDY AIM

To construct a targeted evaluation of PE parameters using MRI.

MATERIALS AND METHODS

Study Design

This single-center retrospective study evaluated heart and chest findings in 38 patients.

Eligibility Criteria

Inclusion criteria:

- Examination for PE
- Available heart and chest MRI scans
- Signed informed consent form

Exclusion criteria:

- Electronic pacemaker, metal elements inside body
- Claustrophobia
- Inadequate patient behavior

Description of Medical Intervention

Heart MRI was performed as part of the preoperative evaluation employing a General Electric Optima MR450w GEM 1.5 T scanner (GE Healthcare, USA) with 2D-FIESTA-C pulse sequences. A functional evaluation of the left and right ventricular myocardium was incorporated into the electrocardiographic synchronization protocol. The functional examination used standard sequences to acquire cine images of the heart (balanced gradient echo) in standard cardiac axes (long 2- and 4-chamber, short 2-chamber axes). The right ventricular ejection fraction was determined in a semiautomatic mode (with manual adjustment of the values obtained) during inspiration and expiration.

Haller index, correction index, and sternal rotation angle were also evaluated as parameters necessary for the further surgical management of patients with PE during the cardiac function assessment.

Ethical Review

The heart MRI was conducted as part of the preoperative evaluation in response to the request of clinicians. Therefore,

no ethical review was performed during the retrospective evaluation of the studies conducted.

Statistical Analysis

The sample size required for the study was not precalculated. The mean values and standard deviations of the measured parameters were calculated for the statistical analysis of the data obtained. The Shapiro–Wilk test was used to determine the normality of distribution of the quantitative parameters. Pearson correlation coefficient and Spearman's rank correlation coefficient were used to evaluate the correlation between the quantitative characteristics. The P-value, along with the 95% confidence interval limits and correlation coefficients, were reported. A two-sided significance level was estimated. A *P*-value of <0.05 was considered to be statistically significant. The GraphPad Prism 9 (GraphPad Software, USA) was employed for the analysis.

RESULTS

Study Subjects

This retrospective study analyzed the heart and chest MRI data of 38 patients (30 males, 8 females). The mean age was 19.9 years (±9 years).

Haller Index

Patients were divided into three subgroups based on the Haller index (Fig. 1, Table 1). Mild PE patients did not require further surgery. The surgery was performed for patients with moderate to severe chest wall deformities.

When assessing the correlation between the Haller index and the right ventricular ejection fraction, no statistically significant Pearson correlation was observed (*P* = 0.777 for inspiratory ejection fraction and *P* = 0.798 for expiratory ejection fraction) (Fig. 2, Table 2). The mean right ventricular ejection fraction was 46%.

There was no statistically significant association between the Haller index and the sternal rotation angle (*P* = 0.9489).

Correction Index

The mean correction index in this study was 31.5 (±11) (Fig. 3). The correction index increased in tandem with the Haller index (the degree of chest wall deformity), as indicated by the statistical analysis *P* < 0.05 (Fig. 4). For instance, the mean correction index was 13, 24, and 35 in patients with mild, moderate, and severe PE, respectively.

No statistically significant association was detected between the sternal rotation angle and the correction index (*P* = 0.35) as well as between the correction index and the right ventricular ejection fraction (*P* = 0.1).

Sternal Rotation Angle

The sternal rotation angle is a crucial factor in planning the treatment strategy (Fig. 5).

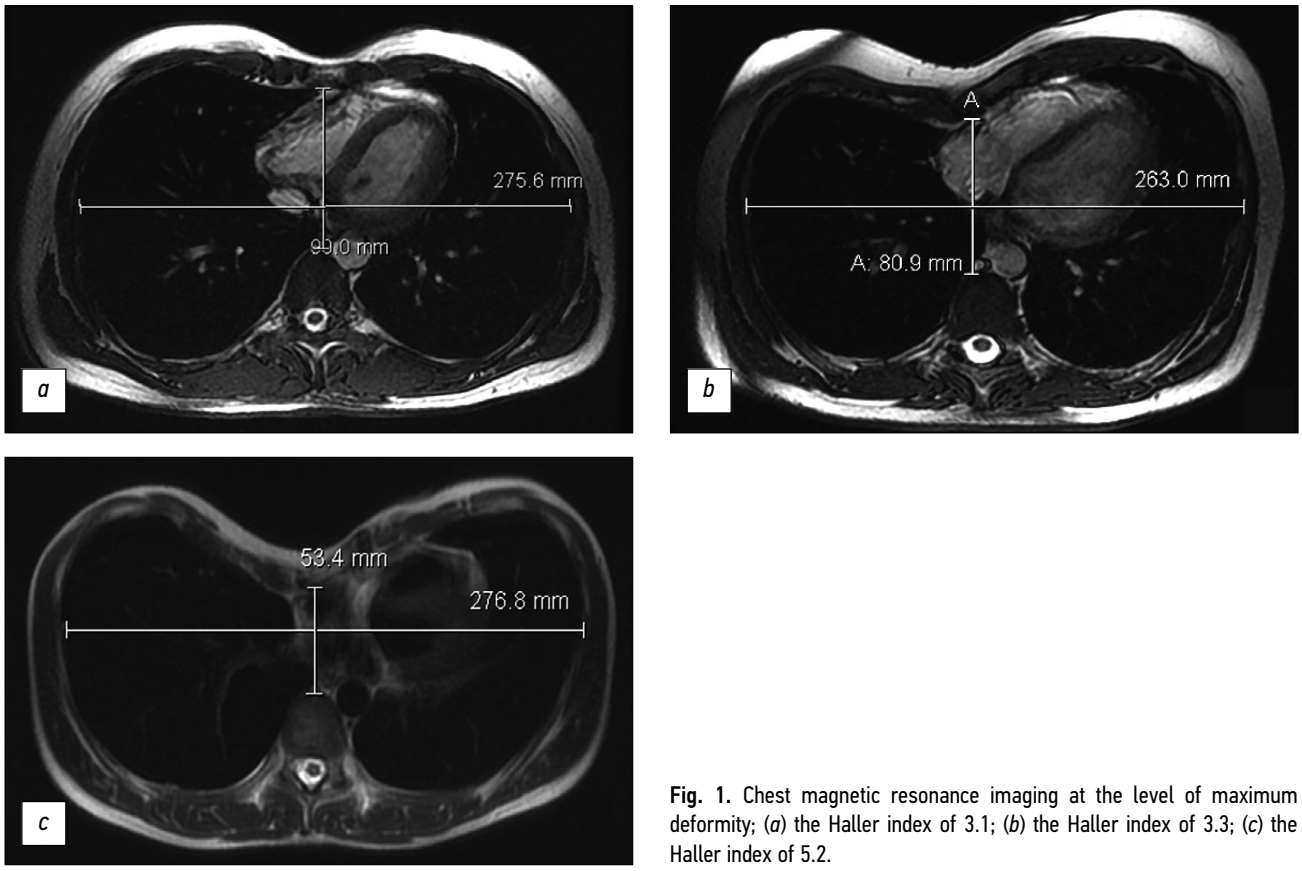

Fig. 1. Chest magnetic resonance imaging at the level of maximum deformity; (*a*) the Haller index of 3.1; (*b*) the Haller index of 3.3; (*c*) the Haller index of 5.2.

Table 1. Patient distribution based on the Haller index

	Pectus excavatum		
	Mild	**Moderate**	**Severe**
Number of patients	3	6	29
The mean Haller index	2.8	3.3	5.1
The standard deviation for the Haller index	0.4	0.1	1.8

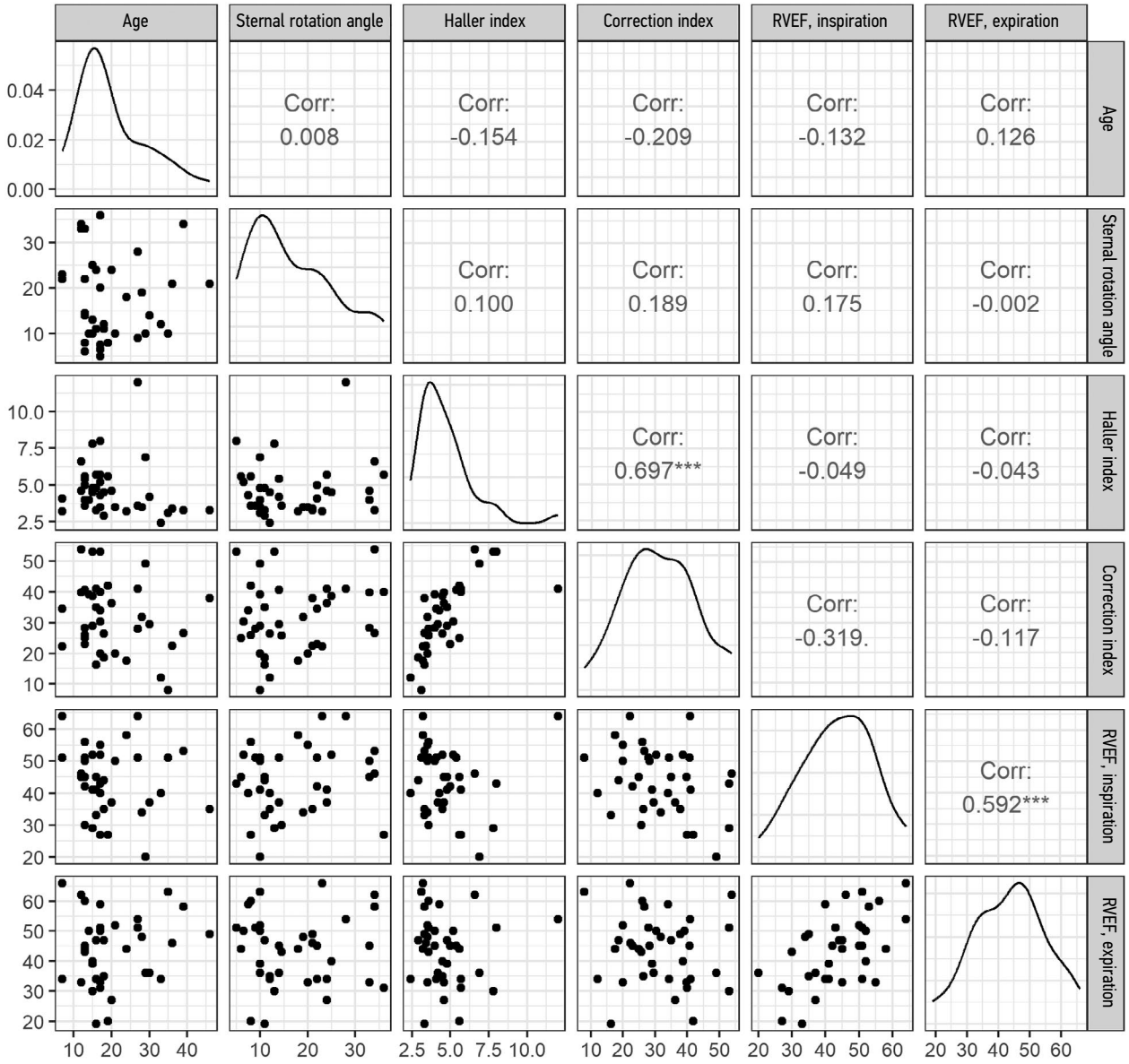

Fig. 2. Correlation data for the study parameters. RVEF, right ventricular ejection fraction.

Table 2. Correlation between variables (the Haller index, sternal rotation angle) and the right ventricle ejection fraction on inspiration and expiration

Variable	**Correction index**	**Right ventricular ejection fraction**	
		Inspiration	**Expiration**
Sternal rotation angle	R=0.19 *P* = 0.255	R=0.18 *P* = 0.306	R=0 *P* = 0.99
Haller index	R=0.7 *P* < 0.001	R=–0.05 *P* = 0.777	R=–0.04 *P* = 0.798

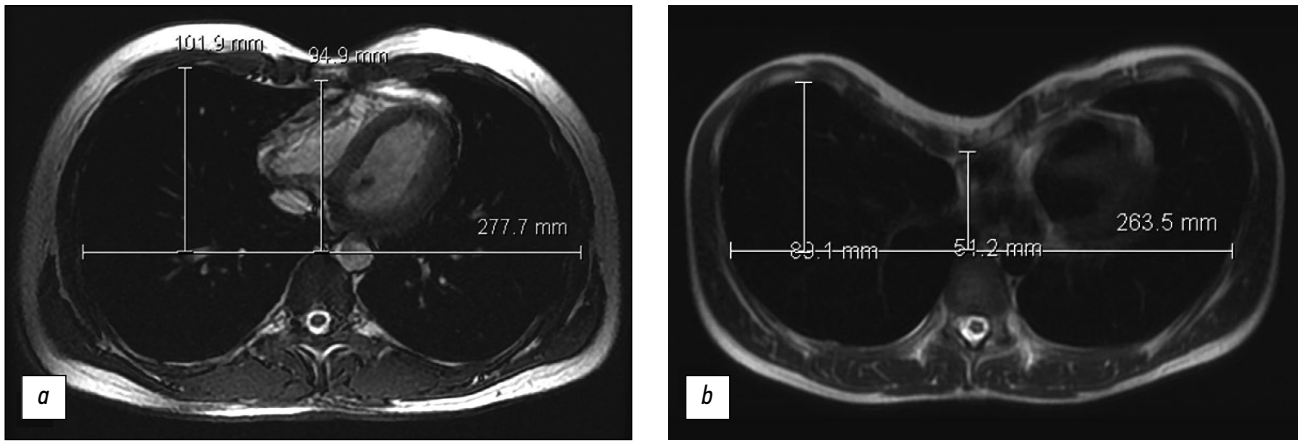

Fig. 3. Chest magnetic resonance imaging at the level of maximum deformity; (*a*) the correction index of 7%; (*b*) the correction index of 32%.

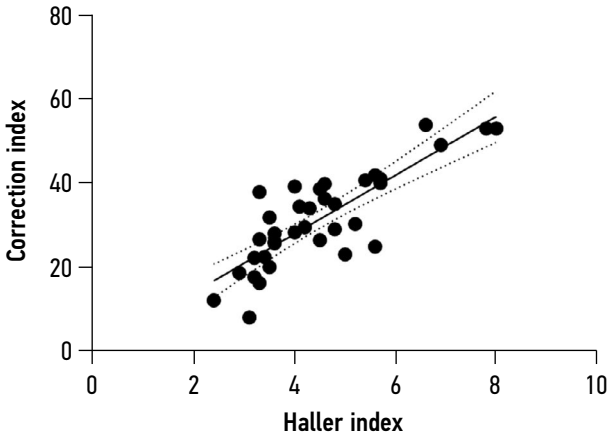

Fig. 4. Correlation data for the Haller index and the correction index ($P < 0.05$).

An angle of ⩾150° was considered significant for surgery and was reported in 44.7% of the total number of patients (Table 3). This position of the sternum required a unique oblique positioning of the sternal plate. The plate was positioned "toward" the acute sternal angle in preparation for subsequent rotation. Consequently, the sternal plate was transferred from the upper intercostal space on the right to the lower intercostal space on the left by traversing the apex of the deformity with sternal rotation when the acute angle expanded to the right (Fig. 6*a*). This occurred in 86% of all sternal rotation cases. In the case of the acute angle expanded to the left (14% of all cases), the sternal plate was accessed from the lower intercostal space on the right, through the apex of the deformity to the higher intercostal space on the left (Fig. 6*b*).

DISCUSSION

Conventionally, CT has been widely employed for diagnosing PE and evaluating diverse parameters due to its accessibility [11]. Radiation exposure is a clear limitation of chest CT; consequently, scanning protocols have been altered in recent years to mitigate this concern [12].

MRI is less frequently used to diagnose PE and is more time-consuming. However, it has the advantage of not exposing the patient to radiation and enables evaluation of compressive changes in the heart.

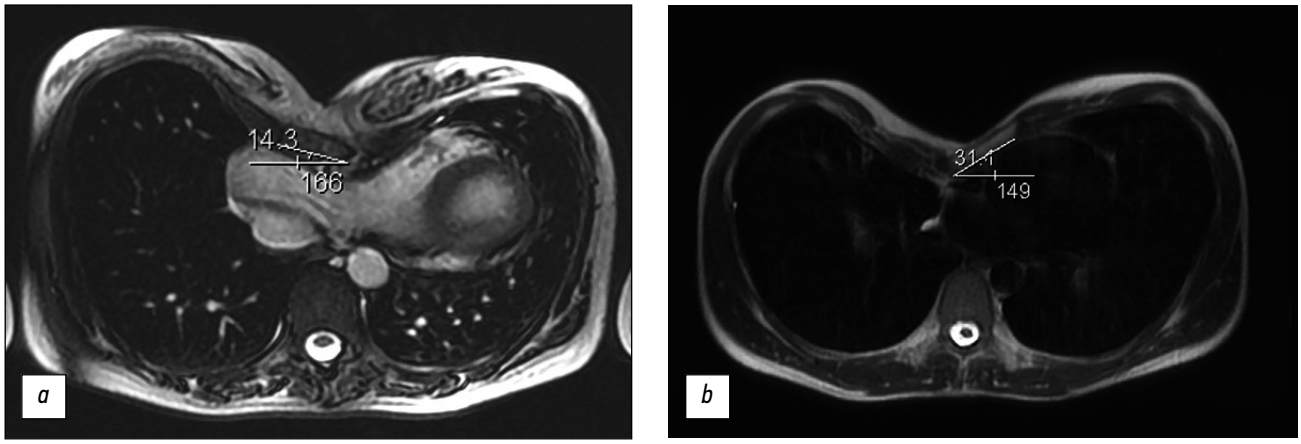

Fig. 5. Chest magnetic resonance imaging at the level of maximum deformity; (*a*) the sternal angle rotation of 14.3°; (*b*) the sternal angle rotation of 31.1°.

Table 3. Patient distribution based on the sternal rotation angle

Sternal rotation angle <15°	
Number of patients	21
The mean angle	10°
Sternal rotation angle >15°	
Number of patients	17
The mean angle	26°

Several different indices are described in the literature to evaluate PE. The Haller index is one of the most used indices to identify patients requiring surgical treatment of the deformity. The threshold value for surgery is 3.25. However, some studies have recently demonstrated potential problems associated with the exclusive use of the Haller index for surgical planning. For example, the Haller index does not correlate with age, other parameters of surgical treatment, or potential postoperative complications [13]. Furthermore, a separate study of the Haller index revealed that 48% of the Haller index numerical values for PE patients and controls overlapped [9].

Such data indicates the need to standardize data and devise additional preoperative and postoperative indices [9, 13, 14]. The correction index is one of these parameters; surgery is indicated when it is >28%, provided it correlates with the Haller index [15]. The correction index can also be utilized to compare postoperative outcomes.

In our study, the Haller index, the correction index, and the sternal rotation angle are consistent with the clinical status of the patients and the previous studies on the preoperative evaluation of chest wall deformities using CT and MRI [16, 17].

The mean right ventricular ejection fraction in patients with PE was decreased to 46% in our study. Such findings align with research data reporting the diminished right ventricular ejection fraction in patients with chest wall deformities [18–20]. However, statistical analysis did not reveal a correlation between the numerical values of the Haller index and ejection fraction. This may be attributed to the uneven distribution of patients based on the severity of their deformity and requires further study.

Study Limitations

Our study is limited by its retrospective nature, a relatively small patient sample size, an imbalanced distribution of patients by progression of changes, and the absence of a comparison with chest CT as the gold standard.

CONCLUSION

Our study revealed that MRI is a highly informative diagnostic tool for PE that does not expose patients to radiation and provides a comprehensive preoperative assessment of abnormalities.

The Haller index and the correction index were found to be correlated ($P < 0.05$).

Our study demonstrated the decreased right ventricular ejection fractions in PE patients. Nevertheless, no correlation was detected between this parameter and the Haller index, and this may be attributed to the study limitations.

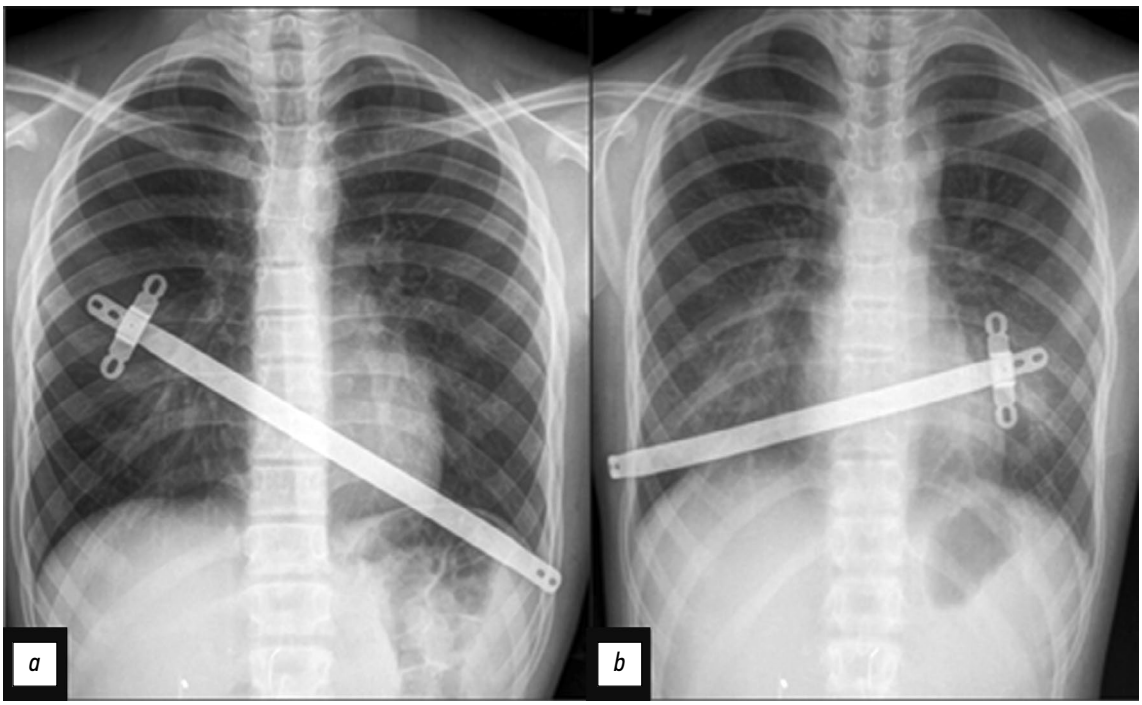

Fig. 6. Frontal chest X-ray following pectus excavatum treatment. Plates positioned if the angle opens: (*a*) right; (*b*) left.

ADDITIONAL INFORMATION

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Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. M.V. Vishnyakova — study concept and design, text editing; G.S. Muzafarova — writing text, collecting and processing materials; A.S. Abramenko — collection and processing of materials; V.A. Kuzmichev, V.V Gatsutsyn — research concept, text editing.

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Identification of Indicators Used to Assess Needs for Telemedicine Consultations in Various Profiles of Medical Care

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ABSTRACT

BACKGROUND: A unified system for assessing the results and real contributions of telemedicine consultations to improving medical care quality in the healthcare system of the Russian Federation has not yet been developed.

AIM: To develop a system of indicators for differentiated assessment of the needs for telemedicine consultations in the provision of medical care.

MATERIALS AND METHODS: In the first stage, reports on the results of on-site activities of national medical research centers in regions of the Russian Federation and their annual public reports (2020–2022) were analyzed to identify indicators that determine the need for telemedicine consultations. The identified indicators were clarified and validated in an open interview with the representatives of the national medical research centers. In the second stage, the value of each indicator was determined based on the expert survey: 18 experts assessed each indicator on a scale of 1–5. Then, the weight coefficient of each indicator was calculated for their subsequent use in planning the coverage of telemedicine consultations.

RESULTS: Three groups of indicators that determined the need for telemedicine consultations for different medical care profiles were as follows: (1) indicators that affect the planned volumes of telemedicine consultations, (2) indicators that characterize the efficiency and effectiveness of telemedicine consultations, and (3) indicators that characterize the validity of requests for telemedicine consultations. Group 1 included indicators of lethality, disability, hospital mortality, frequency of emergency/urgent consultations, and frequency of consultations of patients requiring intensive care. Group 2 included indicators for assessing the effectiveness and efficiency of telemedicine consultations, both subjective (result satisfaction) and objective (number of positive and negative treatment and hospitalization outcomes for cases that received where telemedicine consultations). Group 3 included indicators that characterize the validity of requests for telemedicine consultations: thoroughness of a patient's examination before a telemedicine consultation and accuracy of the diagnosis. The weight coefficients of group 1 indicators ranged from 0.05 to 1.61 and varied for different profiles.

CONCLUSION: A system of indicators was proposed for the differentiated assessment of the needs for telemedicine consultations when providing medical care.

Keywords: need for telemedicine consultations; effectiveness; national medical research centers; profile of medical care; indicator; weight coefficient.

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Разработка системы показателей, определяющих потребность в проведении телемедицинских консультаций при оказании медицинской помощи различных профилей

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АННОТАЦИЯ

Обоснование. На данный момент не существует разработанной единой системы оценки результатов и реального вклада телемедицинских консультаций в повышение качества оказания медицинской помощи в системе здравоохранения Российской Федерации.

Цель — разработка системы показателей для дифференцированной оценки потребности в проведении телемедицинских консультаций при оказании медицинской помощи различных профилей.

Материалы и методы. Исследование проходило в два этапа. На первом этапе были проанализированы отчёты по результатам выездных мероприятий национальных медицинских исследовательских центров в субъекты Российской Федерации и годовые публичные отчёты об их деятельности за 2020–2022 гг. на предмет выявления показателей, определяющих потребность в телемедицинских консультациях. Выявленные показатели уточняли и валидировали в открытом интервью с представителями национальных медицинских исследовательских центров. По результатам первого этапа был сформирован перечень показателей для определения потребности в телемедицинских консультациях по различным профилям медицинской помощи. На втором этапе 18 экспертов проходили опрос, в котором оценивалась значимость каждого показателя в баллах от 1 до 5 и рассчитывались весовые коэффициенты каждого показателя для их последующего использования при планировании объёмов телемедицинских консультаций.

Результаты. Выделено три группы показателей, определяющих потребность в телемедицинских консультациях для различных профилей медицинской помощи: 1) показатели, влияющие на плановые объёмы телемедицинских консультаций; 2) показатели, характеризующие результативность и эффективность проведения телемедицинских консультаций; 3) показатели, характеризующие обоснованность запросов на телемедицинские консультации. К первой группе относятся показатели, отражающие состояние здоровья пациентов и некоторые особенности оказания медицинской помощи этого профиля (смертность, инвалидность, больничная летальность, частота экстренных/неотложных консультаций и консультаций реанимационных пациентов). Вторая группа включает показатели субъективной и объективной оценки результативности и эффективности проведения телемедицинских консультаций, где субъективная оценка включает удовлетворённость результатами ТМК, а объективная — число положительных и отрицательных исходов заболевания и исходов госпитализаций, по которым были проведены телемедицинские консультации. К третьей группе отнесены показатели, характеризующие обоснованность запросов на телемедицинские консультации: полнота обследования пациента перед консультацией, корректность установленного диагноза, экспертная оценка возможности принятия самостоятельного решения на уровне региона или медицинской организации. Весовые коэффициенты значимости показателей первой группы варьировали от 0,05 до 1,61 и отличались для разных профилей.

Заключение. Предложена система показателей для дифференцированной оценки потребности в проведении телемедицинских консультаций при оказании медицинской помощи различных профилей.

Ключевые слова: потребность в телемедицинских консультациях; эффективность; национальные медицинские исследовательские центры; профиль медицинской помощи; показатель; весовой коэффициент значимости.

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制定一套指标体系，确定在提供各种医疗服务时对远程医疗会诊的需求

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摘要

论证。目前，还没有一个完善的统一体系来评估远程医疗会诊在提高俄罗斯联邦医疗系统医疗质量方面的成果和实际贡献。

目的是制定一套指标体系，用于区别评估在提供各种医疗服务时对远程医疗会诊的需求。

材料和方法。研究分两个阶段进行。在第一阶段，分析了俄罗斯联邦各主体国家医学研究中心的实地活动成果报告。此外，还分析了关于其 2020–2022 年活动的年度公开报告，以发现确定远程医疗会诊需求的指标。在与国家医学研究中心代表的公开访谈中，对确定的指标进行了澄清和验证。根据第一阶段的结果，形成了一份指标清单，以确定在各种医疗保健情况下对远程医疗会诊的需求。在第二阶段，对 18 名专家进行了访谈，以 1 至 5 分评估每项指标的重要性。在同一阶段，还计算了每项指标的加权系数，以便随后在规划远程医疗会诊量时使用。

结果。确定了三组指标，这些指标决定不同医疗保健情况下的远程医疗会诊需求：1）影响远程医疗会诊计划量的指标；2）表明远程医疗会诊效率和效果的指标；3）表明远程医疗会诊申请有效性的指标。第一组包括反映病人健康状况的指标和医疗护理的一些特征（死亡率、残疾、住院致死率、急诊/非急诊会诊频率和重症监护病人的会诊）。第二组包括对远程医疗会诊效果和效率的主观和客观评估指标。主观评估包括对远程医疗会诊结果的满意度，客观评估包括进行远程医疗会诊的疾病正负结果和住院结果的数量。第三组包括描述远程医疗会诊申请有效性的指标。这些指标包括会诊前病人检查的完整性、确定诊断的正确性、专家对在地区或医疗组织层面做出独立决定的可能性的评估。第一组指标的显著性加权系数从 0.05 到 1.61 不等，不同情况下的加权系数也不同。

结论。提出了一套指标体系，用于区别评估在提供各种医疗服务时对远程医疗会诊的需求。

关键词：远程医疗会诊需求；效率；国家医学研究中心；医疗护理概况；指标；显著性加权系数。

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BACKGROUND

Telemedicine is a highly effective and innovative healthcare service in different treatment areas [1]. Its widespread use reduces the time patients spend in healthcare organizations, increases the availability of healthcare—especially in underpopulated countries—by increasing the coverage of diagnostic tests and outpatient follow-up, and increases patient satisfaction with the overall quality of healthcare [2].

Telemedicine has been shown to increase the accessibility and clinical effectiveness of care and improve patient satisfaction across treatment areas [3, 4]. Additionally, evidence suggests that it helped contain the spread of COVID-19 during the pandemic [5]. Telemedicine has also proven effective in remotely monitoring the health status of patients with various diseases [6–9].

In the Russian Federation, a significant proportion of telemedicine consultations (TMCs) are performed by National Medical Research Centers (NMRCs). One of the primary objectives of the Federal Project "Development of the NMRC Network and Implementation of Innovative Medical Technologies" is the implementation of TMCs for regional, republican, territorial, and district healthcare organizations across the constituent entities of the Russian Federation. Positive experiences with TMCs have been described in some treatment areas:

- General Practice [10],
- Psychiatry and Psychiatry/Narcology [11–13],
- Ophthalmology [14],
- Oncology [15],
- Surgery (Transplantology) [16],
- Anesthesiology and Intensive Care in Pregnancy [17],
- Obstetrics/Gynecology and Neonatology [18].

Positive experiences of using TMCs are confirmed by "anchor" healthcare organizations of the constituent entities of the Russian Federation [19]. However, there is still no unified system for assessing the results and real contribution of TMCs toward improving the quality of care in the Russian healthcare system. Additionally, no factors have been identified to enhance the efficient use of financial resources allocated to the implementation of TMCs.

STUDY AIM

The aim of this study was to develop a system of parameters to differentiate the need for TMC in different treatment areas.

MATERIALS AND METHODS

The study included two phases:

1. Creating a list of parameters that determine the need for TMC in the delivery of healthcare services in various treatment areas,

2. Conducting a quantitative assessment of the significance of each parameter using a weighting coefficient.

The list of parameters was based on studying the established practice of TMC and its evaluation, including the following:

- Analysis of analytical reports on NMRC field events in the constituent entities of the Russian Federation and annual public reports on the activities of NMRCs for 2020–2022 in order to identify parameters influencing the need for TMC,
- Open interviews with representatives of the NMRCs to clarify and validate the identified parameters.

The expert survey was used to assess the quantitative significance of each parameter. Based on the results of the expert survey, weighting coefficients were calculated to assess the significance of parameters that determine the need for TMC in different treatment areas.

A structured form was developed to analyze the NMRC reports, including the following:

- Parameters used by the NMRC to determine the need for TMC,
- Specific and general suggestions for improving the effectiveness and efficiency of TMC,
- Parameters that determine the technical feasibility of TMC implementation in the constituent entities of the Russian Federation,
- Results of the assessment of the implementation of the recommendations made by the NMRC professionals during the TMC (if any).

Similar parameters determining the need for TMC were grouped for subsequent validation through open interviews with NMRC experts.

To clarify and validate the key parameters determining the need for TMC, face-to-face open interviews were conducted with 14 experts from five NMRCs. The experts were asked to determine the relevance of the parameters selected in the field report analysis phase, determine the scope of TMC for each treatment area, and formulate additional conditions that should be considered in determining the need for TMC for different treatment areas.

Based on the results of the first phase, a list of potential parameters was created to determine the need for TMC in different treatment areas.

In the second phase, experts assessed the significance of the listed parameters using a standardized form. To participate in the interview, experts had to meet the following criteria:

- At least 1 year of experience participating in the Federal Project "Development of the NMRC Network and Implementation of Innovative Medical Technologies,"
- At least 5 years of experience in management and methodology development at the level of constituent entities of the Russian Federation,
- Experience in planning and implementing TMC, calculating the cost of implementing TMC, and/or

analyzing the effectiveness of implementing TMC at various levels,

- A self-assessed expertise level of ⩾0.5 points[1] [20].

In total, 18 experts participated in the survey: heads of structural departments responsible either for management and methodology development in the constituent entities of the Russian Federation or for TMCs, as well as specialists of NMRCs and the Federal State Budgetary Institution "The Center of Expertise and Quality Control of Medical Care" of the Ministry of Health of the Russian Federation. The mean coefficient of expertise was 0.58.

Each expert was asked to rate the significance of considering each parameter on a scale of 1 to 5, with 1 being the least significant and 5 being the most significant. It was suggested that the significance of the parameters influencing the planned scope of TMC be evaluated separately for each treatment area. To assess the significance of parameters of effectiveness and efficacy of the TMC implementation and the validity of corresponding requests, it was decided not to use reference to specific treatment areas since, in an open interview, the majority of experts agreed that the significance of these parameters does not vary depending on the treatment area.

For each parameter, an average score (based on all expert responses) was calculated in points. Subsequently, the concordance of expert opinions was assessed using Kendall's W [21], which is a statistic ranging from 0 to 1 that characterizes the concordance of expert opinions (ranks) for a set of criteria. The degree of expert opinion concordance was considered unsatisfactory at $W < 0.3$, intermediate at $0.3 < W < 0.7$, and high at $W > 0.7$. To ensure the significance of the differences in the identified parameter correlation, the coefficient of concordance was evaluated using the Friedman test. Statistical analysis was conducted using Statistica 10 (StatSoft, Tulsa, OK, USA).

The final weighting coefficients for all parameter profiles were calculated by multiplying the mean assessment value by Kendall's coefficient of concordance. Weighting coefficients for parameters influencing the planned scope of TMC were calculated for each profile separately. This was done for parameters of TMC effectiveness and efficacy and the validity of corresponding requests without reference to specific treatment areas.

RESULTS

A review of the NMRC reports and open interviews with NMRC experts identified three groups of parameters that determine the necessity of TMC for a range of treatment areas:

1. Parameters influencing the planned scope of TMC,
2. Parameters characterizing the effectiveness and efficacy of TMC implementation,
3. Parameters characterizing the validity of requests for TMC.

Parameters Influencing the Planned Scope of Telemedicine Consultations

The planned scope of TMC is defined by specific parameters that reflect the health status of patients who are receiving healthcare services in the specific treatment area, as well as certain characteristics of such services. The parameters are divided into five subgroups:

1. Mortality rates from diseases covered by the treatment area,
2. Disability rates,
3. In-hospital mortality rates,
4. Rates of emergency/urgent consultations (among all TMCs),
5. Rates of intensive care consultations (among all TMCs).

Table 1 shows the most used parameters in the various subgroups.

Parameters Characterizing the Effectiveness and Efficacy of Telemedicine Consultations

The effectiveness and efficacy of the TMC are evaluated using subjective and objective parameters.

Subjective parameters include the satisfaction level of healthcare professionals in the constituent entities of the Russian Federation with the TMC outcomes, which can be assessed through surveys using a structured feedback form. At some NMRCs, experts are already using forms that ask questions, such as:

- Are you satisfied with the outcomes of the consultation?
- Does the outcome of the consultation meet the goals?
- Are you satisfied with the conclusion based on TMC results?
- Were the recommendations made during the consultation followed?
- Was the diagnosis clarified/changed as a result of the consultation?
- Was the treatment plan changed as a result of the consultation?
- Did you have any difficulties creating a TMC request?
- Please rate whether the expectation of the request matches the priority of the consultation (scheduled, urgent, emergency).
- Please rate your level of satisfaction with the work of the TMC NMRC Group.
- Based on the TMC results, the patient was referred to a federal healthcare organization for treatment/further examination ("yes" or "no").

[1] Each expert was asked to evaluate their level of expertise in three domains: k1 for the level of theoretical knowledge of a subject matter, k2 for the level of practical knowledge (experience) of a subject matter, and k3 for the level of ability to predict future development of a subject matter. Each of the three domains was rated by an expert using the following scale: 1 point for the high level, 0.5 points for the intermediate level, 0 points for the low level. The coefficient of expertise (k) was calculated by averaging k1, k2, and k3.

Table 1. Parameters influencing the planned scope of telemedicine consultations (most frequently used by National Medical Research Centers)

Subgroup	Parameters
Mortality rates from diseases covered by the treatment area	Mortality rates per 100,000 for individual diseases or groups of diseases by treatment area Overall mortality rate 100,000 for all diseases by treatment area
Disability rates	Disability rates per 10,000 for individual diseases or groups of diseases by treatment area Overall mortality rate 10,000 for all diseases by treatment area
In-hospital mortality rates	In-hospital mortality in different surgeries by treatment area
Rates of emergency/urgent consultations (among all TMCs)	Percentage of patients with various acute disease complications by treatment area
Rates of intensive care consultations (among all TMCs)	Rates of major emergency and urgent conditions (ICD-10) Prescription rate for a range of healthcare services (dialysis, ECMO, etc.)

Note. ECMO, extracorporeal membrane oxygenation; ICD-10, International Classification of Diseases, 10th revision; TMC, telemedicine consultations

Each question is suggested to be answered in points, usually ranging from 1 to 5, with the overall score being the final result.

To objectively assess the effectiveness and efficacy of TMCs conducted by a constituent entity of the Russian Federation, experts most often consider it necessary to evaluate outcomes of diseases and hospitalizations for which the TMC was performed. Based on open interviews with TMC department heads, two parameters were recommended for an objective assessment:

1. The percentage (or absolute number) of positive TMC outcomes: recovery/improvement/remission + discharged/referred to another healthcare organization, federal healthcare organization, or NMRC,

2. The percentage (or absolute number) of negative TMC outcomes: deterioration/progression/complications/death + discharged/referred to another healthcare facility, federal healthcare facility, or NMRC.

Parameters Characterizing the Validity of Requests for Telemedicine Consultations

According to NMRC field reports and interviews with NMRC specialists, the validity of TMC referral by healthcare organizations of constituent entities of the Russian Federation is influenced by the following:

- Scope of examination prior to the consultation,
- The accuracy of the diagnosis,
- Expert assessment of the possibility for independent decision-making at the level of region or healthcare organization.

A complete examination of the patient before the consultation indicates that all necessary tests, including laboratory tests and imaging modalities, are conducted in accordance with clinical guidelines.

Accuracy of the established diagnosis means that the patient's diagnosis is fully consistent with the clinical picture of the disease and that the wording and coding of the diagnosis are consistent with the current International Classification of Diseases and other generally accepted classifications.

Experts evaluate the possibility of making independent decisions at the regional or healthcare organization level, considering the availability of human and material resources for accurate diagnosis, the ability to perform appropriate examinations and tests, prescribe the necessary treatment, and the need for timely referral of a patient to another healthcare organization, without conducting TMC with the NMRC.

To determine the need for TMC, most experts have suggested evaluating the share of justified TMC requests from the total number of requests from a constituent entity of the Russian Federation.

Assessment of Parameter Significance and Calculation of the Weighting Coefficients

Table 2 shows the weighting coefficients based on expert assessment for Group 1 (separately for different treatment areas).

In Group 1, the significance of each parameter varied by treatment area. For example, in Obstetrics/Gynecology, the percentage of intensive care patients was the most significant (coefficient of 0.92), and the disability rate was the least significant (0.66). In Cardiology, the in-hospital mortality rate was the most significant parameter (0.66), with the disability rate being the least significant parameter (0.49). In Oncology, the mortality rate was the most significant parameter (0.57), whereas the disability rates and the percentage of emergency/urgent TMCs were the least significant parameters (0.45). In Medical Rehabilitation, the percentage of intensive care patients and the disability rates were the most significant parameters (0.14 and 0.13, respectively), and the mortality rate was the least significant parameter (0.10). However, all parameters had lower coefficients compared to other treatment areas (except for Coloproctology and Geriatrics).

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Table 2. Weighting coefficients for the significance of parameters influencing the planned scope of telemedicine consultations

Treatment area	Coefficient of concordance	*P*-value	Weighting coefficient of parameter significance				
			Mortality rate	Disability rate	In-hospital mortality rate	Percentage of emergency TMCs	Percentage of intensive care patients
Obstetrics/Gynecology	0.2171	0.0036	0.74	0.66	0.87	0.77	0.92
Anesthesiology and Intensive Care (Pregnancy)	0.3188	0.0001	1.28	0.81	1.36	1.20	1.36
Anesthesiology and Intensive Care (Adults)	0.3723	0.0000	1.45	0.95	1.61	1.41	1.59
Anesthesiology and Intensive Care (Children)	0.3486	0.0001	1.39	0.91	1.53	1.32	1.49
Hematology	0.1151	0.0817	0.43	0.32	0.44	0.36	0.43
Geriatrics	0.0240	0.7863	0.06	0.05	0.06	0.05	0.06
Oncology and Hematology (Children)	0.1761	0.0130	0.76	0.58	0.69	0.63	0.67
Traumatology and Orthopedics (Children)	0.1734	0.0141	0.54	0.60	0.67	0.61	0.69
Infectious Diseases	0.3406	0.0001	1.02	0.78	1.31	1.06	1.23
Cardiology	0.1541	0.0255	0.59	0.49	0.66	0.52	0.62
Coloproctology	0.0201	0.8355	0.06	0.05	0.06	0.06	0.07
Medical Rehabilitation	0.0547	0.4146	0.10	0.13	0.11	0.11	0.14
Neurology	0.0425	0.5477	0.15	0.13	0.16	0.14	0.16
Neurosurgery	0.2201	0.0032	0.93	0.71	0.97	0.89	0.95
Neonatology	0.1307	0.0516	0.52	0.45	0.57	0.51	0.56
Oncology	0.1342	0.0466	0.57	0.45	0.49	0.45	0.48
Otorhinolaryngology	0.0973	0.1355	0.22	0.22	0.28	0.27	0.30
Ophthalmology	0.0859	0.1859	0.20	0.24	0.24	0.20	0.26
Pediatrics	0.1611	0.0206	0.59	0.47	0.66	0.55	0.64
Psychiatry and Psychiatry/Narcology	0.0760	0.2424	0.18	0.19	0.19	0.21	0.22
Pulmonology	0.0509	0.4536	0.16	0.37	0.47	0.40	0.47
Health Resort Treatment	0.0316	0.6852	0.05	0.05	0.06	0.05	0.05
Cardiovascular Surgery	0.2363	0.0019	0.95	0.75	1.05	0.93	1.02
Dentistry	0.0973	0.1811	0.22	0.22	0.28	0.27	0.30
General Practice	0.0582	0.3806	0.16	0.15	0.19	0.15	0.19
Traumatology and Orthopedics	0.1118	0.0898	0.35	0.37	0.44	0.37	0.42
Urology	0.0928	0.1539	0.26	0.23	0.29	0.27	0.31
Phthisiology	0.1376	0.0421	0.47	0.36	0.45	0.34	0.44
Surgery	0.1844	0.0100	0.64	0.53	0.72	0.63	0.73
Surgery (Organ and/or Tissue Transplantation)	0.0836	0.1979	0.32	0.26	0.33	0.29	0.33
Maxillofacial Surgery	0.0578	0.3850	0.15	0.15	0.18	0.16	0.19
Endocrinology	0.0458	0.5099	0.15	0.13	0.17	0.14	0.17

Note. TMC, telemedicine consultations

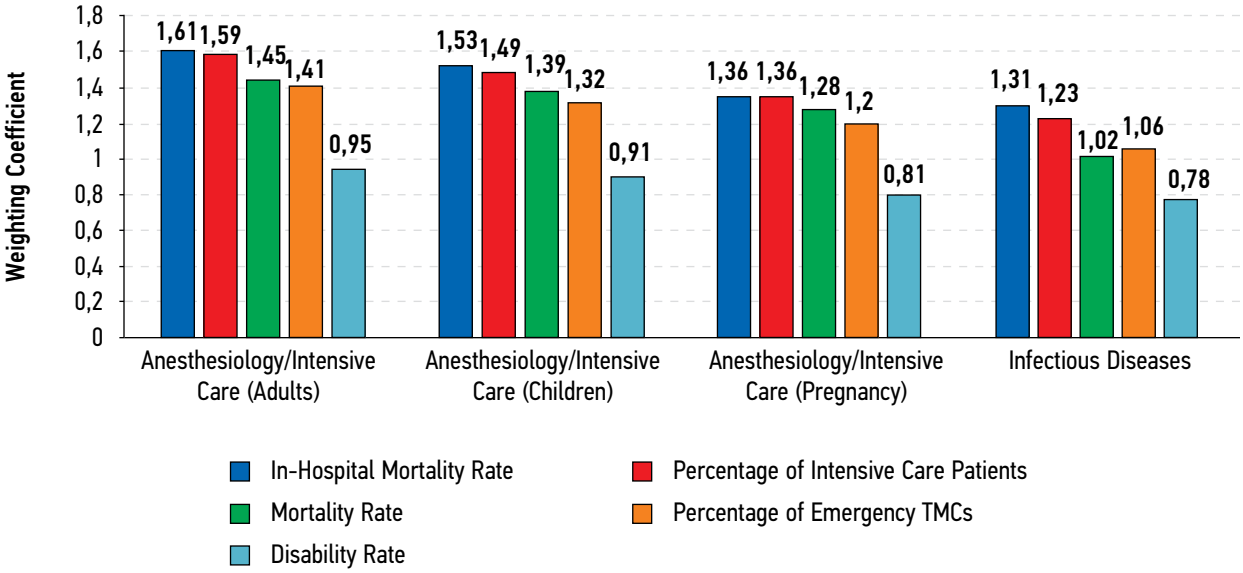

Fig. 1. Four treatment areas with the highest weighting coefficients of the parameters influencing the planned scope of telemedicine consultations. TMC, telemedicine consultations.

The highest weighting coefficients for all five subgroups were found in four treatment areas such as Anesthesiology/Intensive Care (Adults), Anesthesiology/Intensive Care (Children), Anesthesiology/Intensive Care (Pregnancy), and Infectious Diseases (Fig. 1). In these treatment areas, the in-hospital mortality rate and the percentage of intensive care consultations were the most significant parameters. Less significant parameters for Intensive Care included the mortality rate and the percentage of emergency TMCs, and vice versa for Infectious Diseases. The disability parameters were the least significant.

Table 3 shows the weighting coefficients of the parameter significance for Groups 2 and 3 (not related to the treatment areas). The percentage of justified TMC requests from the total number of requests from a constituent entity of the Russian Federation was the most significant parameter (0.0743). Subjective quality of TMC (0.0679), the number of positive TMC outcomes (0.0658), and the absolute number of negative TMC outcomes (0.0638) followed.

DISCUSSION

Based on the analysis of established expert TMC practices, our study generated a list of parameters to assess the need for TMC in different treatment areas. The significance of each parameter was evaluated using a weighting coefficient.

Most of Russian studies included a qualitative assessment of the effectiveness of TMC. For example, in several treatment areas, the active use of TMC in constituent entities of the Russian Federation has the following:

- Reduced length of hospital stays by optimizing drug therapy (Psychiatry and Psychiatry/Narcology [11–13]),
- Improved the effectiveness of minimally invasive surgery through adaptation of surgical techniques (Ophthalmology [14]),
- Supported criteria for initiation of anticancer drug therapy (Oncology [15]),
- Reduced postoperative morbidity and in-hospital mortality rates in some healthcare organizations (Anesthesiology/Intensive Care (Pregnancy) [17], Obstetrics/Gynecology and Neonatology [18]).

Table 3. Weighting coefficients of parameters characterizing the effectiveness and efficacy of telemedicine consultations

Parameter	Coefficient of concordance	*P*-value	Weighting coefficient
Significance of the subjective quality of telemedicine consultations based on a feedback form obtained from a constituent entity of the Russian Federation	0.01852	0.71653	0.0679
Significance of percentage (or absolute number) of positive TMC outcomes			0.0658
Significance of percentage (or absolute number) of negative TMC outcomes			0.0638
Significance of percentage of justified TMC requests from the total number of requests from a constituent entity of the Russian Federation			0.0743

Note. TMC, telemedicine consultations

Our parameters for determining the need for TMC are partially consistent with those from other studies. For example, a systematic review by Khanal S et al. [22] evaluated 46 papers on 36 TMC programs in different countries and identified some predictors for the most appropriate and effective telemedicine use. For example, such criteria included treatment of urgent conditions (if real-time TMC is possible); this parameter was also highlighted in our study. However, Khanal S et al. did not quantify the significance of the identified factors.

In an open interview, we clarified the parameters that influence the need for TMC. A similar approach was used in a Norwegian study, which also conducted open interviews with key stakeholders at the national, regional, and local levels to identify the main factors determining the use of telemedicine by health authorities and healthcare organizations [23]. However, according to the study, organizational factors were critical, including the integration of telemedicine into daily healthcare services, a single body for telemedicine management, and training of healthcare professionals in the proper use of telemedicine.

Both studies emphasized the need for a quantitative assessment of the parameters and factors that determine the use of telemedicine and its necessity. The aim of our study was not only to identify the most significant parameters and factors that determine the need for TMC in different treatment areas but also to develop a methodology for quantitative assessment of parameter significance using weighting coefficients.

A quantitative assessment of the parameter significance and differentiated approach to treatment areas are the main differences between our study and other similar studies, which, in most cases, only conducted a qualitative assessment of the factors influencing the use of TMC. Similar studies that quantitatively assessed the significance of parameters and factors were not found.

However, our study had some limitations. It may be difficult or inaccurate to obtain primary data to calculate some parameters. The weighting coefficients reflecting the significance of the factors were determined by a small panel of experts, and a larger study may be needed to refine them in the future.

CONCLUSION

A system of parameters (with their significance considered) has been developed that can be used for a differentiated assessment of the need for TMC in different treatment areas.

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Conventional Structural Magnetic Resonance Imaging in Differentiating Chronic Disorders of Consciousness

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ABSTRACT

BACKGROUND: Differential diagnosis of chronic disorders of consciousness remains one of the most difficult problems even for experienced clinicians.

AIM: To evaluate the inter-expert consistency and capacity of the researcher-developed structural scale based on magnetic resonance imaging to differentiate chronic disorders of consciousness, named, DOC-MRIDS, on a larger sample of patients.

MATERIALS AND METHODS: Sixty patients with a clinically stable status diagnosed with consciousness disorders (vegetative state, $n = 32$; minimally conscious state, $n = 28$) were enrolled. The revised coma recovery scale (CRS-R) was included in the clinical assessment. All patients underwent structural magnetic resonance imaging with 3.0-T Siemens scanners including T2 and T1 sequences. Structural changes were assessed using the DOC-MRIDS scale and included the following features: diffuse cortical atrophy, ventricular enlargement, gyri dilatation, leukoaraiosis, brainstem and/or thalamic degeneration, corpus callosum degeneration, and focal corpus callosum lesions. A total score was calculated. Magnetic resonance imaging data were analyzed by three neuroradiologists, and inter-observer agreement (Krippendorf's alpha) was assessed.

RESULTS: A high inter-examiner agreement of the DOC-MRIDS scale score was found, with $\alpha = 0.806$ (95% confidence interval 0.757–0.849). The vegetative state group had a higher DOC-MRIDS score than the minimally conscious state group ($P < 0.005$). A negative correlation was obtained between CRS-R and DOC-MRIDS scale scores ($\rho = -0.457$, $P < 0.0001$), individual clinical scale domains, and magnetic resonance imaging features.

CONCLUSION: When assessing structural changes in patients with chronic consciousness disorders, the use of the DOC-MRIDS scale helps differentiate the type of such disorders with sufficient specificity, sensitivity, and inter-rater agreement. This scale can be used in clinical practice as an additional differential diagnostic tool.

Keywords: magnetic resonance imaging; structural assessment; chronic disorders of consciousness; unresponsive wakefulness syndrome; minimally conscious state; differential diagnosis.

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Дифференциальная диагностика хронических нарушений сознания по данным структурной магнитно-резонансной томографии

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АННОТАЦИЯ

Обоснование. Дифференциальная диагностика хронических нарушений сознания остаётся сложной задачей даже для опытных клиницистов. В связи с этим для оценки таких пациентов актуальной является разработка инструментальных подходов, предоставляющих дополнительную информацию о диагнозе.

Цель — оценка межэкспертной согласованности и возможностей практического применения ранее предложенной шкалы оценки изменений на основе структурной магнитно-резонансной томографии для дифференциальной диагностики хронических нарушений сознания (DOC-MRIDS) на более крупной выборке пациентов.

Материалы и методы. Исследованы 60 соматически стабильных пациентов с клинически диагностированными хроническими нарушениями сознания: 32 — в вегетативном состоянии, и 28 — в состоянии минимального сознания. Клиническая оценка проводилась с использованием пересмотренной шкалы восстановления после комы (CRS-R). Всем пациентам была проведена структурная магнитно-резонансная томография с использованием томографов 3.0 T Siemens, включающая T2- и T1-последовательности. При оценке структурных изменений по шкале DOC-MRIDS учитывались наличие и выраженность следующих признаков: диффузная атрофия коры, увеличение желудочков, расширение борозд, лейкоареоз, дегенерация ствола мозга и/или таламуса, дегенерация мозолистого тела, очаговое поражение мозолистого тела; производился подсчёт суммарного балла. Данные магнитно-резонансной томографии анализировались тремя нейрорадиологами с оценкой межэкспертной согласованности (коэффициент альфа Криппендорфа).

Результаты. Выявлена высокая межэкспертная согласованность оценки по шкале DOC-MRIDS: α=0,806 (95% доверительный интервал 0,757–0,849). Пациенты в вегетативном состоянии имели более высокий балл по шкале магнитно-резонансной томографии DOC-MRIDS по сравнению с пациентами в состоянии минимального сознания (p <0,005). Получена отрицательная корреляция между оценкой по шкалам CRS-R и DOC-MRIDS (ρ=–0,457, p <0,0001) между отдельными доменами клинической шкалы и признаками по магнитно-резонансной томографии.

Заключение. Оценка структурных изменений у пациентов с хроническими нарушениями сознания с помощью шкалы DOC-MRIDS помогает установить вероятный клинический тип нарушения сознания с достаточной специфичностью, чувствительностью и межэкспертной согласованностью и может использоваться в клинической практике как дополнительный к клиническим данным дифференциально-диагностический метод.

Ключевые слова: магнитно-резонансная томография; структурная оценка, хронические нарушения сознания; вегетативное состояние; состояние минимального сознания; дифференциальная диагностика.

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根据结构性磁共振成像数据对慢性意识障碍进行鉴别诊断

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摘要

论证。即使对于经验丰富的临床医生来说，慢性意识障碍的鉴别诊断仍然是一项艰巨的任务。在这方面，开发评估这些患者的工具性方法具有重要意义，它能为诊断提供更多信息。

目的是评估之前提出的基于结构性磁共振成像的慢性意识障碍鉴别诊断变化评估量表（DOC-MRIDS）在更多患者样本中的专家间一致性和实际应用的可行性。

材料和方法。研究对象为 60 名经临床诊断为慢性意识障碍的躯体稳定患者：32 名处于植物人状态，28 名处于微意识状态。临床评估采用昏迷恢复量表修订版（CRS-R）进行。所有患者均使用 3.0 T Siemens 断层扫描仪进行了 T2 和 T1 序列结构性磁共振成像。在根据 DOC-MRIDS 量表评估结构变化时，考虑了以下特征的存在和严重程度：弥漫性皮质萎缩、脑室扩大、脑沟扩张、白质疏松、脑干和/或丘脑变性、胼胝体变性和胼胝体局灶性病变；并计算了总分。磁共振成像数据由三位神经放射学专家进行分析，并评估专家间的一致性（Krippendorff 的 α系数）。

结果。DOC-MRIDS量表评分的专家间一致性很高：α=0.806（95%置信区间为0.757-0.849）。与处于微意识状态的患者相比，植物人患者的 DOC-MRIDS 磁共振成像量表得分更高（P<0.005）。CRS-R和DOC-MRIDS评分之间呈负相关（P=-0.457，P<0.0001），临床量表的各个领域与磁共振成像特征之间呈负相关。

结论。使用 DOC-MRIDS 量表对慢性意识障碍患者的结构变化进行评估，有助于确定意识障碍的可能临床类型，具有足够的特异性、灵敏度和专家间的一致性，可在临床实践中作为临床数据的补充鉴别诊断方法。

关键词：磁共振成像；慢性意识障碍；植物人状态；微意识状态；鉴别诊断。

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BACKGROUND

Chronic disorders of consciousness (CDoC), defined as the chronic failure to regain conscious behavior after a coma despite restored wakefulness, are typically caused by extensive damage to several brain structures [1]. In CDoC, the vegetative functions of the hypothalamus and brain stem (specifically circulatory control and spontaneous breathing) are either fully or partially preserved, allowing patients to survive for extended periods [2]. The two main types of CDoC are vegetative state (VS, or unresponsive wakefulness syndrome) and minimally conscious state (MCS) [2,3]. VS is a clinical condition characterized by a complete absence of awareness of oneself and the environment. In contrast, patients in an MCS demonstrate unstable but distinct and reproducible behavioral signs of self-awareness or responses to their surroundings [3,4].

In the differential diagnosis of VS and MCS, identifying signs of consciousness is crucial, which largely determines the subsequent rehabilitation strategy [3]. Diagnostic criteria for distinguishing between VS and MCS include clinical signs of conscious responses to external stimuli and the possibility of purposeful communication. A detailed, standardized clinical examination remains the gold standard for detecting signs of consciousness [5]. The Coma Recovery Scale-Revised (CRS-R) is widely used to assess CDoC patients. This scale provides optimal results for the differential diagnosis of VS and MCS [6]. However, its use is frequently challenging due to the complex interpretation of observed responses, variations in the patient's activity level, severe motor deficiency, aphasia, mechanical obstacles (such as a tracheostomy tube), pain syndrome, and various other factors. As a result, the diagnosis error rate can reach 40% [7].

Numerous studies have been performed to improve the differential diagnosis of CDoC and predict the outcomes using neuroimaging techniques, such as brain positron emission tomography with 18F-fludeoxyglucose. This method has been shown to complement clinical evaluations and help predict the long-term recovery of CDoC patients [8]. Monti et al. demonstrate brain activation in a small proportion of patients using functional magnetic resonance imaging (fMRI) when performing specific mental imagery tasks, which also implies the presence of consciousness [9]. Another study found a correlation between the restoration of frontal-thalamic interactions according to resting-state fMRI and the recovery of cognitive function [10]. Moreover, another study [11] that evaluated the functional connectivity of resting-state networks (default mode network, frontoparietal network, salience network, auditory network, sensorimotor network, and visual network) found differences between VS and MCS patients in more than 80% of cases.

However, functional imaging techniques are not widely used because they require complex data processing, and the findings can be conflicting. Structural imaging is a far more accessible tool for determining the severity of brain injury in CDoC. In a large patient sample (n = 143), this method has demonstrated that CDoC is characterized by severe atrophy of basal nuclei and the thalamus [12]. Moreover, several attempts were made to identify brain injury patterns that could help distinguish between VS and MCS patients. For example, studies have shown that patients in a VS had more severe atrophy of the left putamen and globus pallidus, decreased volume of the thalamus, and more pronounced changes in the ventromedial prefrontal cortex, posterior cingulate cortex, and precuneus compared to MCS patients. Furthermore, MCS subtypes were examined based on the intricacy of the observed behavioral response: MCS– and MCS+. In MCS+ patients, the left cerebral cortex was more intact, including the middle temporal gyrus, superior temporal gyrus, and inferior frontal gyrus (the Broca area) [13]. The prognostic value of structural MRI findings in posttraumatic VS patients has been confirmed: damage to the corpus callosum and dorsolateral brain stem were predictors of failure to recover. Additionally, a study using a morphometric approach demonstrated differences between VS and MCS patients in terms of gray matter volume in the paracentral, parahippocampal, inferior parietal, and medial orbitofrontal cortex, as well as thalami and caudate nuclei [14].

However, complex analysis of imaging findings may not be available in routine practice. Considering the wide use of structural MRI, its necessity in the majority of CDoC patients, and the confirmed association between MRI changes and the clinical presentation in CDoC patients, the Research Center of Neurology developed the Disorders of Consciousness MRI-Based Distinguishing Scale (DOC-MRIDS) [15]. This scale evaluates the most common and clinically significant MRI changes reported in CDoC patients, providing further evidence for the differential diagnosis of VS and MCS. The scale was tested in 30 patients and demonstrated high sensitivity and specificity (82% and 92%, respectively); however, its wider clinical use requires further reliability assessment.

STUDY AIM

This study aimed to evaluate the potential of DOC-MRIDS for the differential diagnosis of CDoC in a larger sample of patients and to determine the inter-rater consistency of assessment findings.

MATERIALS AND METHODS

Study Design

This was an experimental, single-center, cross-sectional study.

Eligibility Criteria

The inclusion criteria include the following:

- confirmed CDoC;
- age above 18 years;

- time from the onset of disorder of consciousness of at least 28 days;
- stable somatic condition;
- informed consent of the patient's legal representative.

Patients with contraindications to MRI were excluded.

Investigational Site

The study was performed in the intensive care unit of the Research Center of Neurology (Moscow).

Study Duration

Study subjects were enrolled between 2015 and 2021.

Therapeutic Intervention

All patients underwent structural MRI using MAGNETOM Verio 3T и MAGNETOM Prisma 3T scanners (Siemens Healthineers, Germany). The imaging protocol included T2-weighted images using a spin echo sequence (repetition time: 4,000 msec; echo time: 118 msec; slice thickness: 5.0 mm; slice spacing: 1.5 mm; duration: 2 min 02 sec) and T1-weighted images using a 3D gradient echo sequence (repetition time: 1,900 ms; echo time: 2.5 msec; slice thickness: 1.0 mm; slice spacing: 1.0 mm; slice number: 176; duration: 4 min 18 sec) to assess the brain matter.

To assess structural changes according to DOC-MRIDS, the most commonly reported indicators were selected, including diffuse cortical atrophy, ventricular enlargement, sulcus widening, leukoaraiosis, degeneration of the brain stem and/or thalamus, corpus callosum degeneration, and focal lesion of the corpus callosum (Fig. 1).

In diffuse cortical atrophy, brain stem and/or thalamus degeneration, and corpus callosum damage, the changes were classified as the presence (1) or absence (0) of pathology. Confirmed extensive cortical thinning and symmetrical bilateral decrease in thalamic and/or brain stem size were considered. Unilateral damage due to stroke or injury was considered to be the absence of the sign. The

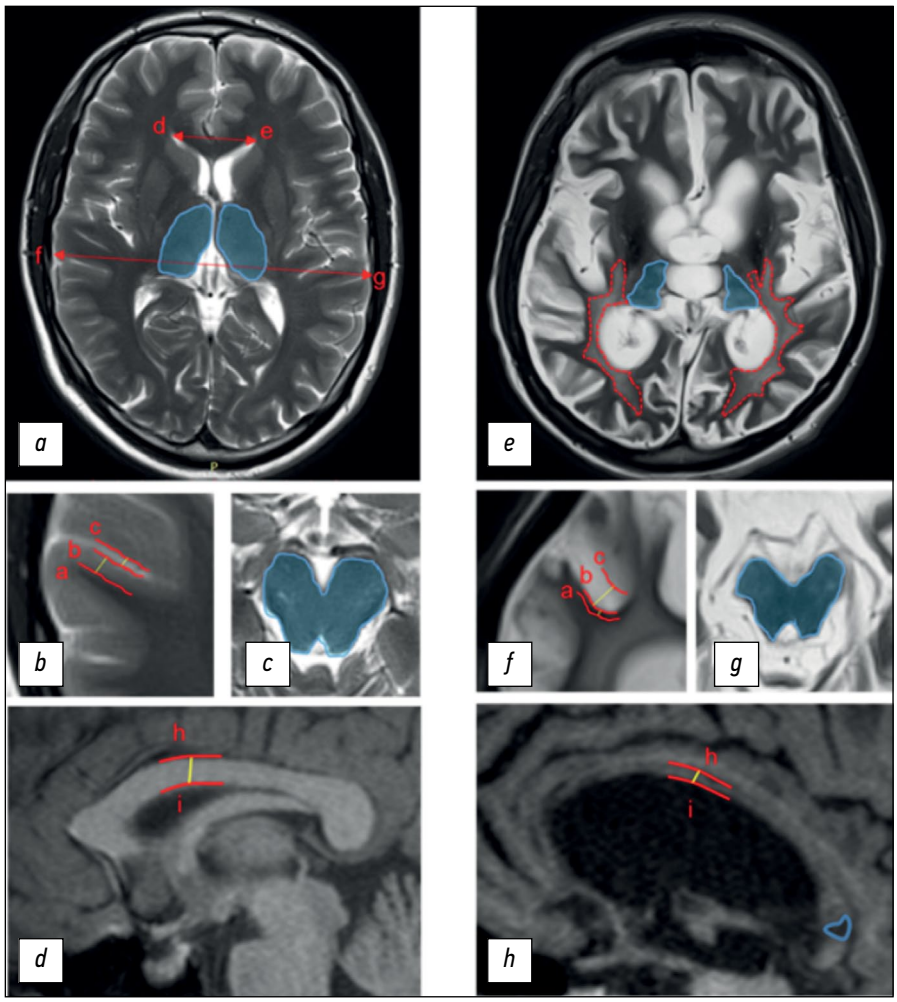

Fig. 1. Disorders of Consciousness MRI-Based Distinguishing Scale (DOC-MRIDS) score: (*a–d*) in a healthy volunteer; (*e–h*) in a CDoC patient. Specified distances: (*a–b*) cortex thickness; (*b–c*) sulcus width; (*h–i*) thickness of the central part of the corpus callosum; distances (*d–e*; *f–g*) were used to calculate the Evans index. Blue areas: (*a*) unchanged thalami; (*c*) brain stem; (*e*) thalamic degeneration; (*g*) brain stem degeneration. Lines: (*e*) red dotted lines represent the extent of leukoaraiosis; (*h*) the solid blue line corresponds to hypointense lesions in the corpus callosum.

remaining parameters were assessed as follows: 0 = no changes; 1 = moderate changes; 2 = severe changes:

- moderate and severe ventricular enlargement corresponded to the Evans index of 0.31 to 0.74 (1) and >0.74 (2), respectively;
- subarachnoid space enlargement of 0.2–0.4 cm was classified as moderate sulcus widening (1) and of >0.4 cm as severe sulcus widening (2);
- periventricular caps and diffuse periventricular changes in the signal intensity in the white matter were classified as moderate leukoaraiosis (1); large, confluent T2 hyperintense areas extending to deep white matter and the subcortex were classified as severe leukoaraiosis (2);
- corpus callosum degeneration was assessed by the thickness of its central part: 0.4–0.2 cm for moderate degeneration (1) and <0.2 cm for severe degeneration (2).

Following a visual assessment of the aforementioned changes, the total score was calculated on a scale of 0 (unchanged brain) to 11 (extensive brain injury) (Table 1).

All these MRI parameters were independently assessed based on T2- and T1-weighted images by three neuroradiologists (work experience over 15 years) who were blinded to the clinical diagnosis.

Three neurologists (with at least three years of experience in the treatment of CDoC patients) conducted the clinical assessment. They made the diagnosis of VS or MCS using a validated version of the CRS-R in Russian [4]. The assessment was performed at least five times, and the best result was used.

Subgroup Analysis

The study included 60 patients (28 women and 32 men) aged 18 to 67 years (median age: 32 [24; 49] years) with a clinical diagnosis of CDoC (VS: n = 31; MCS: n = 29). All patients were in a stable somatic condition.

Ethics Review

All legal representatives of patients provided informed consent. All procedures involving humans in this study adhered to the ethical standards of the Institutional and/or National Research Committee and the 1964 Declaration of Helsinki, as amended, or comparable ethical standards. The informed consent protocol was approved by the Ethics Committee of the Research Center of Neurology on November 19, 2014 (project ID: 11/14).

Statistical Analysis

When calculating the sample size according to a well-established algorithm, it was shown that a sample size of 60 patients is sufficiently representative. The data distribution in the sample (n = 60) was non-normal; thus, nonparametric statistical methods were used for the analysis, such as the Kruskal–Wallis test and the Mann–Whitney U test, to compare patients across three or more parameters, the Benjamini–Hochberg multiplicity adjustment was applied. The nonparametric Spearman's correlation coefficient was used to assess the association between parameters. The chi-squared test with continuity correction was used to analyze categorical variables. Receiver operating characteristic (ROC) analysis was used to assess the informative value of the scale by calculating the area under the curve (AUC), as well as sensitivity and specificity parameters.

The inter-rater consistency was assessed using Krippendorff's alpha. The significance level for all hypothesis tests corresponded to $P < 0.05$.

The descriptive statistics results are presented as median (Me) and interquartile range (Q25–Q75). The statistical analysis was performed using SPSS Statistics 22 (IBM, Chicago, IL, USA) and Rstudio (Posit PBC, Boston, MA, USA).

RESULTS

Study Subjects

The duration of CDoC was 2 to 72 months after emerging from coma. CDoC was due to a traumatic brain injury (TBI; n = 19) and non-traumatic causes (anoxic brain injury, acute ischemic or hemorrhagic cerebrovascular accident, demyelinating disease, intoxication, etc.; n = 41).

Table 1. Magnetic resonance imaging parameters for assessment according to Disorders of Consciousness Magnetic Resonance Imaging-Based Distinguishing Scale

Parameters	DOC-MRIDS			
	Absence	Presence	Moderate changes	Severe changes
Diffuse cortical atrophy	0	1	–	–
Brain stem/thalamus degeneration	0	1	–	–
Focal lesion of the corpus callosum	0	1	–	–
Ventricular enlargement	0	–	1	2
Sulcus widening	0	–	1	2
Leukoaraiosis	0	–	1	2
Corpus callosum degeneration	0	–	1	2

DOC-MRIDS, Disorders of Consciousness MRI-Based Distinguishing Scale

Table 2. Demographic and clinical data

	Vegetative state	Minimally conscious state	All patients
Number	31	29	60
Age, years	34 [24; 51]	32 [25; 45]	32 [24; 49]
Sex, male/female	15/16	17/12	28/32
Traumatic brain injury/non-traumatic causes	4/27*	15/14*	19/41
Duration of the disease, months	14 (2–72)	12 (2–56)	13 (2–72)
DOC-MRIDS	4**	6**	5,5
CRS-R	6*	12,0*	9

CRS-R, Coma Recovery Scale-Revised; DOC-MRIDS, Disorders of Consciousness MRI-Based Distinguishing Scale; *$P < 0.05$; **$P < 0.005$ (Mann–Whitney U test).

Table 2 summarizes demographic and clinical data for VS and MCS patients. The median total CRS-R score in VS and MCS patients was 6 and 12 points, respectively.

Primary Findings

There were no significant differences between VS and MCS patients in terms of age (Mann–Whitney U test, $P = 0.982$), disease duration ($P = 0.807$), and sex (chi-squared test with continuity correction, $P = 0.453$). Non-TBI in VS patients was significantly more common than TBI (chi-squared test, $P = 0.003$), while MCS patients had a similar incidence of non-traumatic and TBI (chi-squared test, $P = 0.268$). In general, the clinical presentation in patients with non-TBI was more severe than in patients with TBI. The median total CRS-R score was 6.0 (5.0–10.0) and 11.0 (8.0–16.0), respectively (Mann–Whitney U test with the Benjamini–Hochberg multiplicity adjustment, $P = 0.001$).

Three experts demonstrated strong inter-rater consistency when assessing images according to DOC-MRIDS, as measured by Krippendorff's alpha: $\alpha = 0.806$ (95% confidence interval: 0.757–0.849). The Kruskal–Wallis test was used to select findings from one of the three experts. There were no significant differences between the experts ($P = 0.363$); hence, the findings of the second experts were used for further analysis.

When assessing the association between the duration of CDoC and the DOC-MRIDS score, there was a weak positive correlation (Spearman's correlation coefficient 0.338; $P = 0.008$). Spearman's correlation analysis showed a significant negative correlation between the CRS-R and DOC-MRIDS scores ($\rho = -0.457$, $P < 0.0001$) (Fig. 2). Moreover, significant negative correlations were observed between the total CRS-R score and the following parameters: diffuse cortical atrophy ($\rho = -0.457$); lesions in the corpus callosum ($\rho = 0.349$); ventricular enlargement ($\rho = -0.342$); sulcus widening ($\rho = 0.442$); and leukoaraiosis ($\rho = 0.502$); $P < 0.001$ in all cases. There was also a significant correlation between individual CRS-R domains and nearly all structural scale parameters (Table 3).

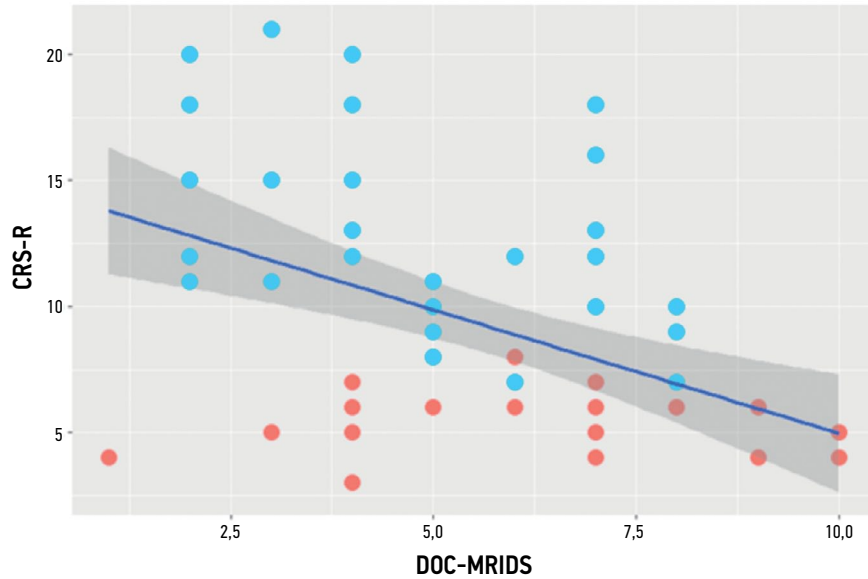

Fig. 2. Negative correlation between the Coma Recovery Scale-Revised (CRS-R) and Disorders of Consciousness MRI-Based Distinguishing Scale (DOC-MRIDS) scores ($\rho = -0.457$, $P < 0.0001$). Red dots: vegetative state group; blue dots: minimally conscious state group.

Table 3. Correlation coefficients between individual the Coma Recovery Scale-Revised domains and Disorders of Consciousness Magnetic Resonance Imaging-Based Distinguishing Scale parameters

Statistical parameter	Auditory function	Visual function	Motor function	Oromotor function	Communication	Wakefulness
Diffuse cortical atrophy						
Correlation coefficient (ρ)	–0.472**	–0.382**	–0.492**	–0.152	–0.315*	–0.159
P-value	0.000	0.005	0.000	0.278	0.022	0.255
Brain stem and/or thalamus degeneration						
Correlation coefficient (ρ)	–0.288*	–0.212	–0.209	–0.091	–0.140	–0.137
P-value	0.035	0.124	0.130	0.513	0.314	0.323
Lesions in the corpus callosum						
Correlation coefficient (ρ)	0.289*	0.360**	0.355**	0.229	0.164	0.142
P-value	0.032	0.007	0.008	0.093	0.232	0.301
Ventricular enlargement						
Correlation coefficient (ρ)	–0.276*	–0.318*	–0.379**	–0.149	–0.309*	–0.256
P-value	0.041	0.018	0.004	0.276	0.022	0.059
Sulcus widening						
Correlation coefficient (ρ)	–0.502**	–0.425**	–0.516**	–0.169	–0.341*	–0.201
P-value	0.000	0.001	0.000	0.218	0.011	0.141
Leukoaraiosis						
Correlation coefficient (ρ)	–0.405**	–0.451**	–0.480**	–0.338*	–0.396**	–0.250
P-value	0.002	0.001	0.000	0.012	0.003	0.066
Corpus callosum atrophy						
Correlation coefficient (ρ)	–0.165	–0.135	–0.049	–0.174	–0.001	–0.141
P-value	0.229	0.324	0.722	0.204	0.996	0.305

*$P < 0.05$; **$P < 0.005$ (Spearman's correlation analysis).

Additionally, statistical between-group differences were observed according to DOC-MRIDS. For example, VS patients had a lower DOC-MRIDS score compared to MCS patients (Mann–Whitney *U* test, $P < 0.005$). According to ROC analysis in this sample, the threshold DOC-MRIDS score for distinguishing between VS and MCS patients was 5.5, with an optimal sensitivity of 68% and a specificity of 64% (AUC = 0.71; $P = 0.005$; Fig. 3).

There were significant differences between causative factors. Signs, such as cortical atrophy (chi-squared test, $P < 0.0001$), sulcus widening ($P = 0.001$), and leukoaraiosis, were significantly more common in patients with non-TBI ($P = 0.004$), whereas patients with traumatic CDoC had a higher incidence of lesions in the corpus callosum ($P = 0.002$).

DISCUSSION

Summary of Primary Findings

The MRI scale for quantitative assessment of structural brain changes characteristic of CDoC was proposed as an additional tool for the differential diagnosis of clinical variants of CDoC. A pilot study demonstrated that the scale can be used in routine practice with sufficiently high sensitivity and specificity [15]. This study was the next step in the scale's development and attempted to assess its reliability when used by different radiologists and in a larger sample of patients.

Discussion of Primary Findings

The findings obtained in a twofold larger patient population balanced by the CDoC type show that DOC-MRIDS has a lower sensitivity and specificity than the pilot study: 82% and 92% vs. 68% and 64%, respectively. This could be related to a considerable variation in the duration of CDoC (2–72 months). However, these values are high enough to use the scale in clinical practice. A high inter-rater consistency indicates that reliable results can be obtained when different radiologists perform the assessment.

Notably, the assessment included data from clinically stable patients with no somatic conditions that could compromise the results of neurological consciousness assessment (such as infectious diseases, elevated intracranial pressure, etc.). Moreover, clinical data on the state of consciousness were obtained by repeated evaluation

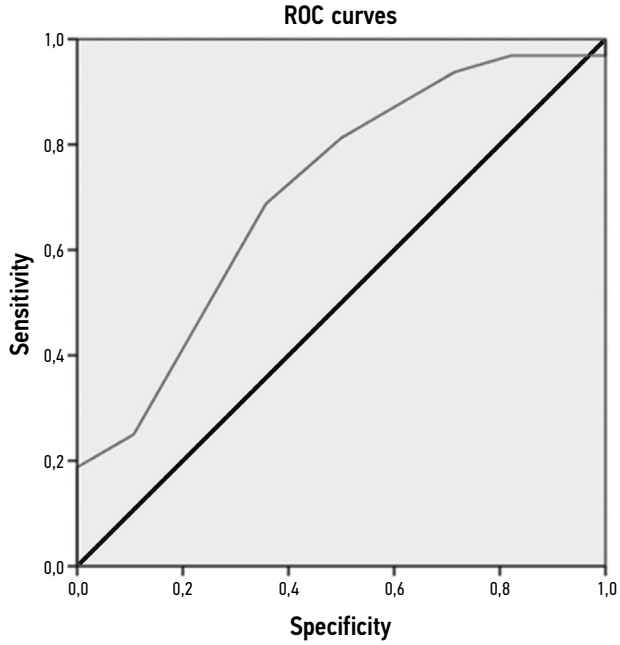

Fig. 3. ROC curve for distinguishing between vegetative state and minimally conscious state patients (AUC = 0.71; *P* = 0.005).
ROC, receiver operating characteristic

using the most reliable scale, CRS-R; the assessment was performed by neurologists with sufficient experience in the treatment of CDoC patients [16,17]. This approach ensures the most accurate diagnosis of CDoC type. Furthermore, inconsistencies between X-ray findings according to DOC-MRIDS and the clinical presentation in CDoC patients may indicate the need for repeated neurological assessment in some cases.

Notably, most VS patients had non-traumatic disorders of consciousness. This reflects the challenges in enrolling CDoC patients: the prognosis after TBI is somewhat better, and this group of patients develops MCS more frequently. As a result, it would take longer to enroll VS patients with non-TBI and form a population balanced by the causative factor. This characteristic of the study group could affect the interpretation of assessment according to DOC-MRIDS because patients with non-TBI had more severe changes in such parameters as cortical atrophy, sulcus widening, and leukoaraiosis. Thus, further assessment of the effect of the causative factor on the DOC-MRIDS score in VS patients requires a study in a larger sample of patients, balanced by the number of traumatic and non-traumatic brain injuries.

A weak positive correlation between the duration of CDoC and the DOC-MRIDS score may reflect morphological changes over time. There have been no detailed long-term studies on this subject.

DOC-MRIDS has an undeniable advantage in terms of availability because the assessment requires structural MRI findings (T2-weighted spin echo sequence and T1-weighted gradient echo sequence with the specified imaging parameters), which can be obtained using any high-field scanner with a magnetic field intensity above 1.0 T.

Patient motion artifacts are a common problem in MRI examinations, making the assessment, according to DOC-MRIDS, challenging, especially for MCS patients. Mitigating the artifacts may require sedation, which is associated with potential risks for patients and makes the study more challenging to conduct. However, when using structural MRI, special image reconstruction algorithms can minimize the effect of artifacts. Furthermore, structural MRI findings, including the DOC-MRIDS score, are substantially less susceptible to the impact of motion artifacts compared to functional MRI, emphasizing the availability of this method in routine practice.

Our study is one of the first to incorporate morphological signs of brain injury in CDoC patients into a single scale. Our findings are consistent with some previous studies in patients with early posttraumatic brain injuries causing disorders of consciousness. For example, it was shown that traumatic injuries of the corpus callosum and dorsolateral brain stem are predictors of failure to recover and may result in unfavorable outcomes [14]. In our study, severe corpus callosum atrophy and brain stem and thalamus degeneration were most commonly observed in VS patients.

Individual domains and the total CRS-R score significantly correlated with the total DOC-MRIDS score and changes in its individual parameters, indicating the significance of the morphological integrity of anatomical structures included in the consciousness assessment scale [18]. Some brain areas may contribute to consciousness formation and maintenance, but their structural integrity alone is insufficient for clear consciousness formation. Moreover, the maintenance of consciousness requires the integrity of thalamocortical interactions and interactions within and between various

brain networks [19]. This may explain the observed strongest correlations between individual CRS-R domains and diffuse changes in the white matter and focal lesions of the corpus callosum, which form the structural basis for intracerebral interactions. However, automatic group analysis of data on brain connectivity in CDoC patients collected using structural and functional MRI is difficult due to high variability and severe changes in the brain matter. Despite advances in CDoC studies, recent findings [19–21] highlight the need for more extensive, simultaneous examination of structural and functional characteristics of the brain in CDoC patients, as well as the development of computational data processing methods, including using artificial intelligence [20].

CONCLUSION

A comprehensive analysis of structural changes in CDoC patients, along with their attempted quantitative assessment using the DOC-MRIDS scale, helps to determine the likely clinical variant of CDoC with sufficient specificity, sensitivity, and inter-rater consistency. This method can be used in clinical practice in addition to the findings of a structured neurological examination.

ADDITIONAL INFORMATION

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Remote Monitoring of Patients with Chronic Heart Failure: A Prospective Randomized Study

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ABSTRACT

BACKGROUND: Chronic heart failure is one of the key problems of the Russian domestic healthcare system. E-health can be used to improve medical care quality and reduce the of hospitalizations and mortality.

AIM: To examine the effect of telemedicine monitoring on mortality, frequency of hospitalizations, and clinical and functional states of patients with chronic heart failure.

MATERIALS AND METHODS: A prospective, controlled, randomized study was conducted in the Central City Hospital No. 20 in Ekaterinburg (Russia), covering the period from December 2020 to December 2022. Patients with a confirmed diagnosis of chronic heart failure were randomized using the envelope method into three groups: group 1, a telephone control group ($n = 58$); group 2, a remote control group using a Russian medical platform Medsenger ($n = 52$); and group 3, the standard control group ($n = 103$). All patients were examined, including NT-proBNP measurement and echocardiography on the first day of the study and at 3, 6, and 12 months. The occurrence of primary and secondary outcomes was evaluated at these reference points. Stata14 and jamovi software were used for statistical processing.

RESULTS: The study involved 213 participants, and all three groups were comparable in terms of basic demographic and clinical characteristics. The advantage of remote control (groups 1 and 2) over face-to-face observation in reducing cardiovascular mortality was observed after 3 (odds ratio 2.73, 95% confidence interval 1.1–7.39; $P = 0.042$) and 12 (odds ratio 2.1, 95% confidence interval 1.1–3.7; $P = 0.027$) months and that in reducing the occurrence of the combined primary endpoint (odds ratio 2.1, 95% confidence interval 1.1–5.6; $P = 0.015$) after 12 months. The use of the Medsenger platform also demonstrated an advantage over face-to-face observation in the development of the combined secondary endpoint (odds ratio 1.39, 95% confidence interval 0.19–0.81; $P = 0.011$) after 3 months and over telephone control by a nurse after 12 months in reducing cardiovascular mortality (odds ratio 0.177, 95% confidence interval 0.06–0.487; $P = 0.021$) and development of the combined secondary endpoint (odds ratio 0.427, 95% confidence interval 0.189–0.964; $P = 0.041$). When using the Medsenger platform, the ejection fraction increased from 47% initially to 55% after 12 months ($P = 0.004$). The NT-proBNP level decreased from 817 to 582 pg/mL ($P < 0.001$) after 3 months and then to 233 pg/mL after 12 months ($P < 0.001$).

CONCLUSION: Remote monitoring protocols can be a good alternative to the traditional face-to-face monitoring of patients with chronic heart failure, which may improve clinical and functional health indicators.

Keywords: chronic heart failure; remote control; telemedicine monitoring.

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Телемедицинский мониторинг пациентов с хронической сердечной недостаточностью: проспективное рандомизированное исследование

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АННОТАЦИЯ

Обоснование. Хроническая сердечная недостаточность — одна из ключевых проблем отечественной системы здравоохранения. Для повышения качества оказания медицинской помощи и снижения частоты госпитализаций и смертности могут использоваться возможности электронного здравоохранения.

Цель — изучить влияние телемедицинского мониторинга на смертность, количество повторных госпитализаций и клинико-функциональный статус пациентов с хронической сердечной недостаточностью.

Материалы и методы. Проспективное, контролируемое, рандомизированное исследование проходило на базе Центральной городской больницы № 20 (г. Екатеринбург) с декабря 2020 года по декабрь 2022 года. Пациенты с подтверждённым диагнозом хронической сердечной недостаточности были рандомизированы методом конвертов на 3 группы: 1-я группа — группа телефонного диспансерного наблюдения (n=58), 2-я группа — группа диспансерного наблюдения на российской медицинской платформе Medsenger (n=52), 3-я группа — группа стандартного очного наблюдения у кардиолога поликлиники (n=103). Всем пациентам проводился осмотр, исследование концентрации NT-proBNP и эхокардиография при включении в исследование и во временных промежутках 3, 6 и 12 месяцев. В референсных точках оценивалось наступление первичной и вторичной конечных точек. Статистическая обработка была выполнена с использованием программ Stata 14 и jamovi.

Результаты. В исследовании приняли участие 213 человек, все 3 группы были сопоставимы между собой по основным демографическим и клиническим характеристикам. Было выявлено преимущество дистанционного (группы 1 и 2) перед очным (группа 3) наблюдением по снижению сердечно-сосудистой смертности через 3 месяца (отношение шансов 2,73, 95% доверительный интервал 1,1–7,39: p=0,042) и через 12 месяцев (отношение шансов 2,1, 95% доверительный интервал 1,1–3,7; p=0,027), а также показателю комбинированной первичной конечной точки через 12 месяцев (отношение шансов 2,1, 95% доверительный интервал 1,1–5,6; p=0,015).

Использование платформы Medsenger обладает преимуществом перед очным наблюдением в развитии событий комбинированной вторичной точки через 3 месяца (отношение шансов 1,39, 95% доверительный интервал 0,19–0,81; p=0,011); перед проведением структурированного телефонного опроса медицинской сестрой через 12 месяцев наблюдения по показателю сердечно-сосудистой смертности (отношение шансов 0,177, 95% доверительный интервал 0,06–0,487; p=0,021) и по развитию событий комбинированной вторичной конечной точки (отношение шансов 0,427, 95% доверительный интервал 0,189–0,964; p=0,041).

При использовании платформы Medsenger фракция выброса левого желудочка выросла с 47% исходно до 55% через 12 месяцев (p=0,004). Концентрация NT-proBNP снизилась с 817 пг/мл до 582 пг/мл (p <0,001) через 3 месяца, и до 233 пг/мл — через 12 месяцев (p <0,001).

Заключение. Разработка протоколов дистанционного наблюдения может стать хорошей альтернативой традиционному очному наблюдению пациентов с хронической сердечной недостаточностью, приводя к улучшению клинических и функциональных показателей здоровья.

Ключевые слова: хроническая сердечная недостаточность; дистанционное диспансерное наблюдение; телемедицинский мониторинг.

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对慢性心力衰竭患者进行远程医疗监控：一项前瞻性随机研究

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摘要

论证。慢性心力衰竭是国家医疗系统的主要问题之一。电子医疗可用于提高医疗质量，降低住院率和死亡率。

目的是研究远程医疗监控对慢性心力衰竭患者的死亡率、再次住院次数以及临床和功能状态的影响。

材料和方法。这项前瞻性、对照、随机研究于 2020 年 12 月至 2022 年 12 月在 Central City Hospital №20（叶卡捷琳堡）进行。确诊为慢性心力衰竭的患者通过信封法随机分为三组：第一组——电话防治所随访组（n=58），第二组——俄罗斯医疗平台 Medsenger 上的防治所随访组（n=52），第三组——综合医院心脏病专家面对面标准随访组（n=103）。所有患者在加入研究时以及 3、6 和 12 个月时都接受了 NT-proBNP 浓度和超声心动图检查。主要和次要终点的发生情况在参考点进行评估。统计处理使用 Stata 14 和 jamovi 程序进行。

结果。共有 213 人参加了这项研究。就基本人口统计和临床特征而言，所有三组均具有可比性。远程随访（第 1 组和第 2 组）比面对面随访（第 3 组）更能降低 3 个月和 12 个月的心血管死亡率（为 3 个月：机会比率 2.73，95% 置信区间 1.1-7.39；P=0.042），（为 12 个月：机会比率 2.1，95% 置信区间 1.1-3.7；P=0.027）。在 12 个月的综合主要终点也观察到了获益（机会比率 2.1，95% 置信区间 1.1-5.6；P=0.015）。

与面对面随访相比，使用 Medsenger 平台在 3 个月后发生合并次要终点事件方面（机会比率 1.39，95% 置信区间 0.19-0.81；P=0.011），在随访 12 个月时，由护士进行结构化电话访谈前，心血管死亡率方面（机会比率 0.177，95% 置信区间 0.06-0.487；P=0.021）和合并次要终点事件的发生率方面（机会比率 0.427，95% 置信区间 0.189-0.964；P=0.041）更具优势。

使用 Medsenger 平台后，左心室射血分数从基线的 47% 增加到 12 个月后的 55%（P=0.004）。3 个月后，NT-proBNP 浓度从 817 pg/ml 降至 582 pg/ml（P<0.001），12 个月后降至 233 pg/ml（P<0.001）。

结论。制定远程监控协议可能是替代传统的面对面随访慢性心衰患者的一个好办法，从而改善临床和功能性健康结果。

关键词：慢性心力衰竭；远程防治所监控；远程医疗监控。

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BACKGROUND

Chronic heart failure (CHF) is one of the major problems of the Russian healthcare system. High mortality and readmission rates, regional demographic imbalances, poor treatment adherence, staffing shortages, and other outpatient challenges require improved management of this patient population [1, 2]. All these issues require a comprehensive approach, and eHealth can be used to address the journey of patients with CHF.

In the age of modern technology, numerous healthcare tasks are solved by systems that automate much of the work of healthcare professionals (HCPs), increasing the accessibility and quality of care at a lower cost. Patients can learn about their disease online, monitor their vital signs, communicate with their doctor, and receive medical care remotely [3, 4].

Studies of the clinical effectiveness of telemedicine monitoring have evaluated the effect of technology on all-cause and cardiovascular mortality, rate of readmission for decompensated CHF, and quality of follow-up (FU) [5]. Comparative studies of routine FU with telephone monitoring or noninvasive telemonitoring have provided valuable information on the advantages and disadvantages of these methods [6, 7]. However, the current results are highly inconsistent. The number of patients enrolled, study design, and length of FU vary widely; thus, conclusions are often quite opposite. In addition, not enough studies of high-quality design have evaluated the effect of telemedicine monitoring in the CHF population in Russia. Therefore, this study is relevant.

STUDY AIM

This study aimed to evaluate the effect of telemedicine monitoring on mortality, readmission rates, and clinical and functional status of patients with CHF.

MATERIALS AND METHODS

Study Design

This study employed an interventional, single-center, prospective, controlled, randomized, selective, unblinded design.

Eligibility Criteria

Inclusion criteria:

- Signed informed consent for outpatient CHF FU in Yekaterinburg Central City Hospital No. 20.
- Confirmed stage II–III (Strazhesko–Vasilenko classification) CHF and New York Heart Association (NYHA) functional classes (FC) I–IV.

Exclusion criteria:

- Age <18 years
- Pregnancy and lactation
- Unexplained shortness of breath
- Noncardiac edema syndrome
- Patient refusal of FU
- End-stage CHF: stage III (Strazhesko–Vasilenko classification) CHF and NYHA FC IV.

Investigational Site

Patients were enrolled in the Outpatient Heart Failure Center of Yekaterinburg Central City Hospital No. 20.

Study Duration

Patients were recruited from December 2020 to December 2021, with a post-randomization FU of 12 months.

A Medsenger electronic platform (OOO TelePat, Russia) for remote monitoring of patients with CHF was implemented after a trial period from December 1, 2020, to December 14, 2020. During this period, the system was tested on eight patients. Vital parameters such as blood pressure (BP), heart rate (HR), and body weight were evaluated in the test mode. Other elements of the system were also tested, including patient wellness data transmission, audio messaging, and video-calling options. This preparation helped in identifying some of the platform's shortcomings in terms of CHF monitoring and developing a more convenient version of the program for all stakeholders. After the test period and following the implementation of major changes, the enrollment of patients with CHF was initiated.

Description of Medical Intervention

CHF was diagnosed according to the clinical guidelines for CHF of the Russian Society of Cardiology, which were approved by the Research and Practice Council of the Ministry of Health of the Russian Federation in 2020. The screening to confirm CHF included a medical history, general physical examination, and assessment of the FC of CHF using the 6-min walk test. All patients underwent a series of standard clinical laboratory tests (complete blood count, blood biochemistry with plasma glucose, potassium, sodium, creatinine, and calculation of the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] glomerular filtration rate), and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) measurement.

Study investigations included:

- 12-lead electrocardiography
- Echocardiography (EchoCG)
- Neck Doppler ultrasound scan
- Abdominal and pleural ultrasonography (as indicated)
- Chest X-ray imaging

After a baseline visit to a cardiologist and confirmation of a diagnosis of CHF, patients were randomized to three FU groups by the envelope method:

Group 1: Telemedicine monitoring included a structured telephone interview conducted by a nurse using a specific questionnaire (Table 2). This was done once or twice a month, depending on the baseline severity of CHF.

Group 2: Monitoring using Medsenger telemedicine monitoring software. The methodology of telemedicine monitoring is described below.

Group 3: Control group; standard face-to-face FU with a cardiologist at a local outpatient facility in accordance with current guidelines for CHF management.

A comparative analysis was also conducted at months 3, 6, and 12. Groups 1 and 2 used remote monitoring as the main FU method (Table 1).

In Group 1, a telephone survey and remote software monitoring were conducted by a nurse using a predesigned algorithm, with further strategies based on patient responses. Validated algorithms developed at the National Medical Research Center of Cardiology named after Academician E.I. Chazov of the Ministry of Health of the Russian Federation were used to determine the urgency of medical care [8].

In Group 2, patients received a daily notification about the need to enter their parameters (BP, HR, and body weight) into the system for clinical disease monitoring. Well-being and adherence questionnaires were sent every 3 days. In addition, all patients were instructed in advance (at the randomization visit) to perform daily self-monitoring of BP, HR, and body weight.

The remote monitoring in Groups 1 and 2 included the major and minor criteria for CHF decompensation (Table 2) based on national guidelines for CHF diagnosis and treatment.

Major CHF decompensation criteria:

- Increased shortness of breath and fatigue
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Decreased exercise tolerance
- Ankle swelling

Minor CHF decompensation criteria:

- Night cough
- Weight gain >2 kg per week
- Depressive disorder
- Heart palpitations

All data obtained were processed automatically. If BP, HR, and body weight were out of range, or if the major/minor criteria for CHF decompensation were met, the program automatically sent a notification to the administrator (nurse and/or physician), who then decided on the need for a face-to-face or telemedicine consultation to change monitoring and treatment strategies. If the emergency criteria were met, an ambulance would be called. In accordance with the algorithm, the patient should receive a response to this notification within 24 h. Patients were not monitored on nonworking days, weekends, and holidays. They were instructed in advance about the need to seek medical care independently (at the local emergency room or by calling an ambulance) if their condition deteriorated. This response algorithm was used in both remote FU groups (Groups 1 and 2).

Primary Findings

The study evaluated primary and secondary endpoints.

Primary endpoints:

- Cardiovascular death
- Readmission caused by CHF decompensation
- Number of ambulance or emergency room visits caused by CHF decompensation.

Secondary endpoints:

- Death from noncardiovascular causes
- Hospital admission or emergency care visit for other cardiovascular causes (acute coronary syndrome, cerebrovascular accident, COVID-19, hypertension, etc.)

Table 1. Study visit procedures.

Visit Procedures	Screening and randomization (day 0)	Visit 1 (day 90 ± 30)	Visit 2 (day 180 ± 30)	Visit 3 (day 365 ± 30)
Informed consent	+	–	–	–
Evaluation of inclusion/exclusion criteria	+	–	–	–
Evaluation of exclusion criteria	+	+	+	+
Collection of medical history and previous drug therapy	+	–	–	–
Collection of demographic and anthropometric data	+	+	+	+
Physical examination	+	+	+	+
Handout of a self-monitoring diary with control of its fill-out	+	+	+	+
Treatment recommendations	+	+	+	+
Laboratory tests and instrumental examinations	+	+	+	+
Adherence questionnaire	+	+	+	+
Reporting endpoints	–	+	+	+
Assessment of satisfaction with follow-up monitoring	–	+	+	+

Table 2. Structure of remote follow-up monitoring for patients with chronic heart failure

Question	Yes	No
Domain 1 (Patient subjective assessment)		
Major criteria for decompensated chronic heart failure		
Did you experience any shortness of breath during usual physical activity in the last week?		
Did you experience any shortness of breath while lying down during the week? Did you need to raise your pillow higher and/or add more pillows while sleeping?		
Did you experience any nighttime shortness of breath in the last week?		
Did you find it harder to be physically active than before in the last week?		
Did you feel weak, tired, or needed to rest for a long time in the last week?		
Did you notice swollen shins, swollen ankles, or newly appearing sock/shoe marks in the last week?		
Did you notice your waist getting bigger in the last week?		
Minor criteria for decompensated chronic heart failure		
Did you have night cough in the last week?		
Did your gain 2 kg in the last week?		
Did your lose 2 kg in the last week?		
Did you feel depressed or apathetic in the last week?		
Did you have heart palpitations in the last week?		
Domain 2 (Treatment assessment)		
Have you ever missed a medication dose?		
Do you find that you sometimes do not pay enough attention to your medication timing?		
Do you miss doses even when you feel well?		
Do you miss a dose if you feel ill after taking your medicine?		

- Deterioration of the patient's clinical and laboratory status as assessed by CHF progression: based on CHF FC, NT-proBNP levels, and left ventricular ejection fraction (LVEF).

Additional Findings

In addition, the effect of the FU option on the clinical status of a patient with CHF (NYHA FC), LVEF, and NT-proBNP levels was evaluated.

Outcome Reporting Methods

Outcomes were analyzed using medical records.

Ethical Review

The Study Protocol No. 4 dated November 25, 2020, was approved by the Local Ethics Committee of Yekaterinburg Central City Hospital No. 20. All patients provided written informed consent to participate in the study.

Statistical Analysis

Sample Size Calculation

The sample size was calculated using the method by Otdelnova KA. At a significance level of 0.05, 100 participants are sufficient for moderate precision studies [9].

Statistical Analysis

All remote and standard (face-to-face) monitoring patients were included in the data analysis. For an additional analysis, a separate remote FU group was created by pooling patients from Groups 1 and 2. Stata 14 (StataCorp, USA) and jamovi (The jamovi Project, Australia) were used in the statistical processing. Absolute values were expressed as numbers, and relative values were expressed as percentages (%). The data distribution type was determined using the Shapiro–Wilk test. Quantitative data were expressed as mean and standard deviation (M ± SD) for normal distribution and as median and interquartile range for nonnormal distribution: Me (25; 75).

Unpaired Student's *t*-test and univariate analysis of variance (Mann–Whitney *U* and Wilcoxon tests for nonnormal distributions) were used to compare quantitative parameters in independent groups. Tukey's post hoc analysis was performed. In the dependent groups, quantitative characteristics with a normal distribution were compared using Student's *t*-test. To compare the three groups, repeated-measures analysis of variance was used. Pearson's chi-squared test was used to compare qualitative parameters. Ordinal regression was used to compare ordinal parameters. The significance level was set at $P < 0.05$.

RESULTS

Study Subjects

The study enrolled a total of 213 participants. Three groups were matched for key clinical and demographic parameters, including BP, CHF duration, LVEF, estimated glomerular filtration rate (eGFR by CKD-EPI formula), hemoglobin, and NT-proBNP (Table 3). The compared groups also did not differ in the distribution of cardiovascular and noncardiac morbidity (Table 4).

Primary Findings

When comparing face-to-face CHF monitoring with two remote monitoring options (pooled Groups 1 and 2), a benefit of remote monitoring in reducing cardiovascular mortality was observed at 3 months with an odds ratio (OR) of 2.73 (95% confidence interval [CI], 1.1–7.39, $P = 0.042$). No benefit was seen in terms of the effect on the composite secondary endpoint (all-cause mortality, hospital admission, or emergency visits for other cardiovascular causes, deterioration of the patient's clinical and laboratory status) at 3 months: OR 0.5; 95% CI 0.27–0.92; $P = 0.03$ (Fig. 1).

When comparing groups 1 and 2 of remote FU in terms of the effect on month 3 endpoints, the Medsenger platform demonstrated an advantage over face-to-face monitoring in the composite secondary endpoint: OR 0.39; 95% CI, 0.19–0.81; $P = 0.011$.

After 6 months of FU, no significant differences were found between distance and face-to-face FU (Fig. 2). However, the number of readmissions due to acute CHF decompensation was significantly higher in the face-to-face FU group than

Table 3. Clinical and demographic characteristics of the study groups

Parameter	Group 1 (*n*=58)	Group 2 (*n*=52)	Group 3 (*n*=103)	*P*
Male	36 (62.1%)	22 (42.3%)	42 (40.1%)	0.143
Female	22 (37.9%)	30 (57.7%)	61 (59.8%)	0.265
Age, years	67 (58; 72.8)	69.5 (61.8; 79)	69 (62; 74)	0.159
BMI, kg/m^2	32.38±5.92	28.71±5.46	32.09±6.43	0.236
SBP, mmHg	129±22.9	132±16.3	133±17.5	0.305
DBP, mmHg	73 (70; 90)	80 (71; 90)	80 (70; 90)	0.206
Heart rate, bpm	80.1±12.3	79.1±14.8	79.1±15.0	0.79
CHF duration, years	2 (1; 5.25)	2 (0.33; 5)	2 (0.23; 5)	0.167
LVEF, %	47 (37.8; 55)	42 (39; 47)	47 (39; 55)	0.285
Glucose, mmol/L	6 (5; 6)	6.5 (6; 7)	5 (5; 7)	0.258
GFR, mL/(min × 1.73 m^2)	69 (60; 87)	74.5 (54; 89)	65 (55.5; 87.5)	0.942
Hemoglobin, g/L	133 (122; 146)	133 (119; 142)	128 (118; 141)	0.529
NT-proBNP, pg/mL	817 (331; 1480)	617 (262; 2131)	1082 (445; 2124)	0.117

Note. BMI, body mass index; DBP, diastolic blood pressure; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure. Quality parameters are expressed as: absolute number (percentage).

Table 4. Distribution of cardiovascular and noncardiac comorbidities in the study groups

Parameter	Group 1 (*n*=58)	Group 2 (*n*=52)	Group 3 (*n*=103)	*P*
Atrial fibrillation/atrial flutter	32 (55,2%)	29 (55,8%)	62 (60,2%)	0,467
Hypertension	50 (86,2%)	51 (98,1%)	101 (98,1%)	0,067
CHD	32 (55,2%)	40 (76,9%)	83 (80,6%)	0,087
Coronary revascularization	10 (17,2%)	7 (13,5%)	27 (26,2%)	0,799
Type 2 diabetes mellitus	7 (12,1%)	22 (42,3%)	40 (38,8%)	0,301
COPD	7 (12,1%)	13 (25,0%)	24 (23,3%)	0,216
ACE/TIA	5 (8,6%)	8 (15,4%)	11 (10,7%)	0,813

Note. CHD, coronary heart disease; COPD, chronic obstructive pulmonary ACE, acute cerebrovascular event; TIA, transient ischemic attack.

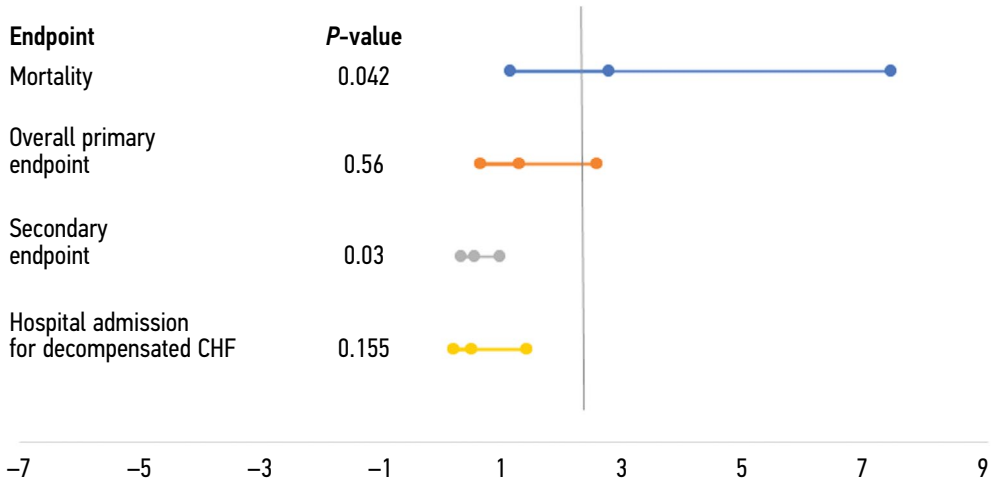

Fig. 1. Effect of outpatient follow-up option (remote/face-to-face) on month 3 endpoints. CHF, chronic heart failure.

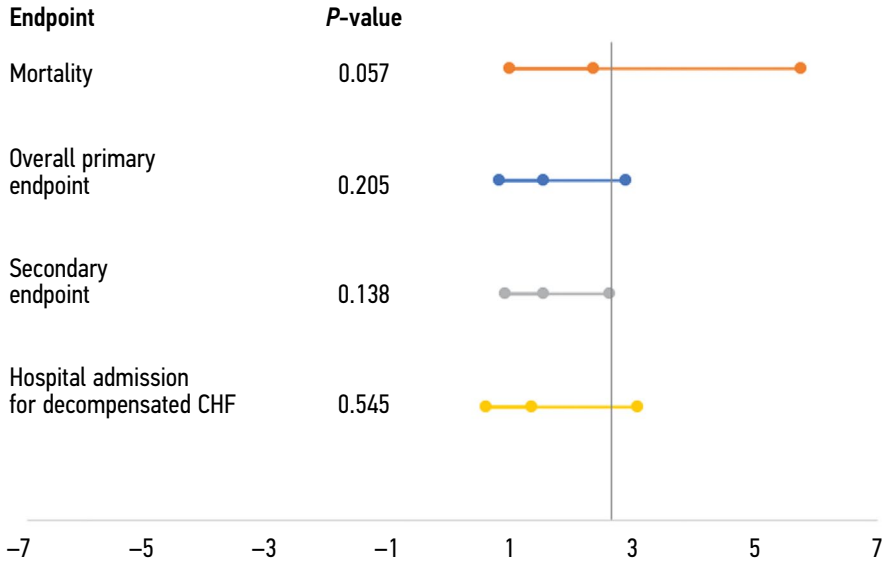

Fig. 2. Effect of outpatient follow-up option (remote/face-to-face) on month 6 endpoints. CHF, chronic heart failure.

in the Medsenger group: OR 0.171; 95% CI: 0.04 to 0.83; *P* = 0.029.

After 12 months of FU, the remote monitoring options demonstrated superiority over face-to-face FU for patients with CHF in terms of reducing cardiovascular mortality (OR 2.1; 95% CI, 1.1–3.7; *P* = 0.027) and the combined primary endpoint (OR 2.1, 95% CI 1.1–5.6; *P* = 0.015) (Fig. 3).

However, when comparing the remote monitoring options, the Medsenger platform was found superior to a structured telephone survey conducted by a nurse at 12 months of FU for cardiovascular mortality (OR 0.177, 95% CI 0.06–0.487; *P* = 0.021) and a composite secondary endpoint (OR 0.427, 95% CI 0.189–0.964; *P* = 0.041).

Additional Findings

In the remote FU group (Groups 1 and 2), LVEF increased significantly by 6%–7%, from 43% (38–54) at the randomization visit to 49% (41–56) at the month 3 visit (*P* < 0.001) and up to 50% at the month 6 visit (*P* = 0.045). However, no further increase in LVEF (at month 6 and 12 visits) was reported in the remote FU group.

No significant increase in LVEF was found in the face-to-face FU group (Group 3). During the period from the randomization visit to month 3 FU visit, LVEF increased by 4%, from 47% (39–55) to 51% (42–60), and then decreased to 48% (38.8–55.3) at month 6 visit (*P* = 0.475).

In the remote FU group using the Medsenger platform, LVEF increased significantly from 47% (37.8–55) at baseline to 55% (41.3–60) at the end of FU (*P* = 0.004) (Fig. 4).

In the remote FU group (pooled groups 1 and 2), NT-proBNP levels decreased both in the short term (at month 3, from 717 [296.5–1805.5] pg/mL to 464.4 [181.5–861] pg/mL, *P* < 0.001) and during the entire FU period (from 717 [296.5–1805.5] pg/mL to 294.5 [133.5–817] pg/mL, *P* < 0.001). In the face-to-face group, a positive trend was reported for this marker; however, only at months 3 and 6 (*P* < 0.001) (Fig. 5).

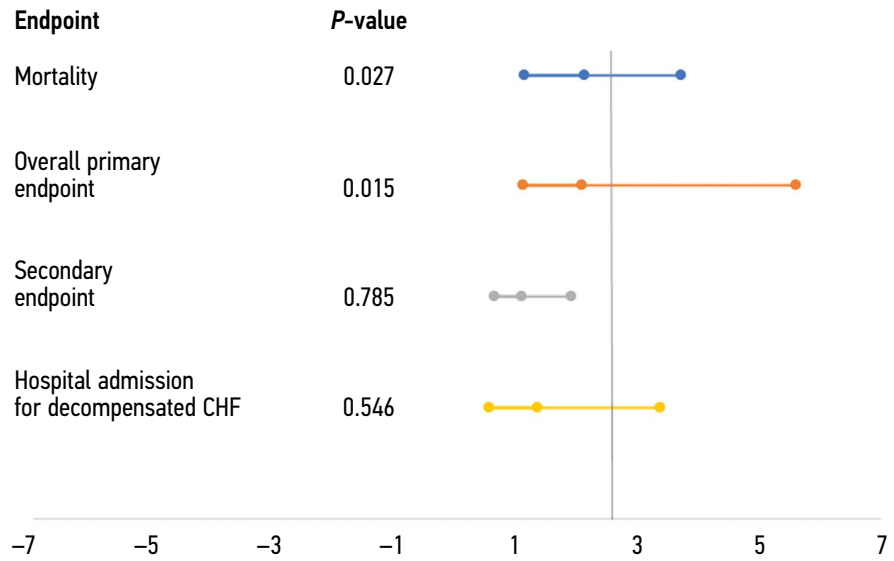

Fig. 3. Effect of outpatient follow-up option (remote/face-to-face) on month 6 endpoints. CHF, chronic heart failure.

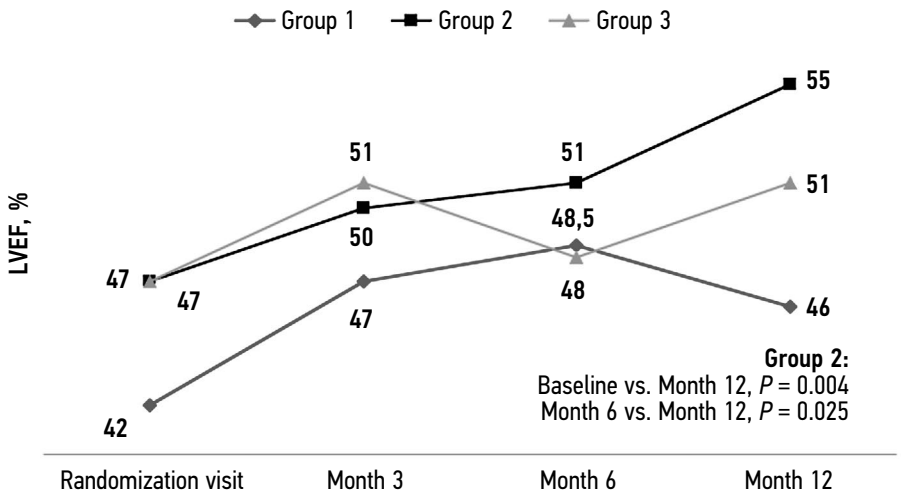

Fig. 4. Changes in the left ventricular ejection fraction in the study groups. Group 1, telephone follow-up (*n* = 58); Group 2, Medsenger follow-up (*n* = 52); Group 3, standard follow-up (*n* = 103).

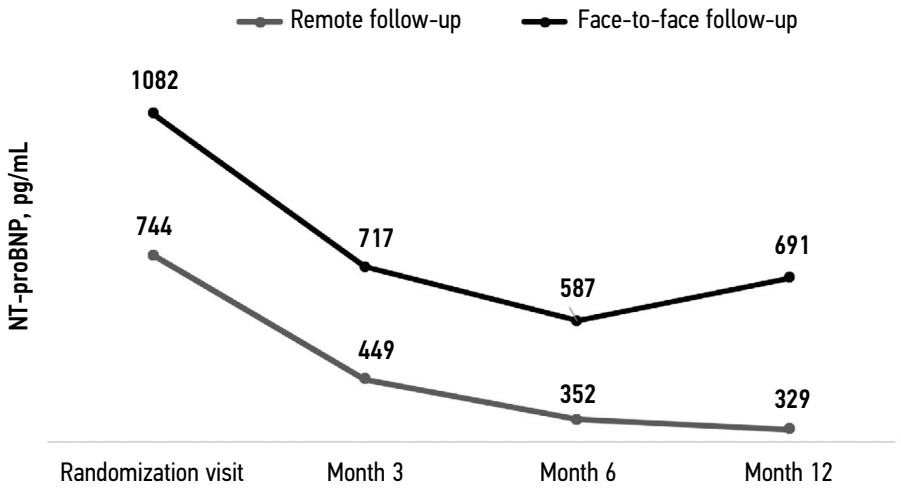

Fig. 5. Changes in NT-proBNP levels by follow-up options; remote follow-up: pooled group (groups 1 and 2, *n* = 110); face-to-face follow-up: standard follow-up group (*n* = 103).

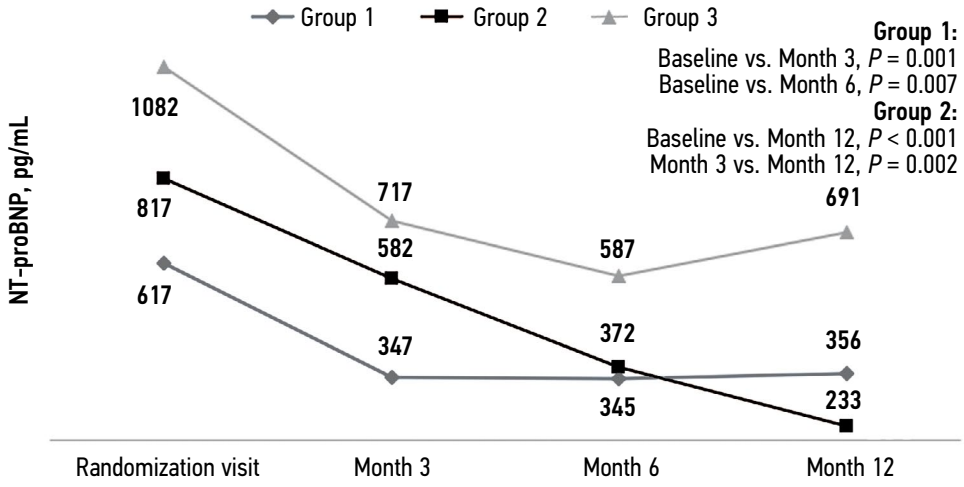

Fig. 6. Changes in NT-proBNP levels in the study groups; Group 1, telephone follow-up (*n* = 58); Group 2, Medsenger follow-up (*n* = 52); Group 3, standard follow-up (*n* = 103).

When evaluating the effect of the different FU options on changes in NT-proBNP levels in the study groups, the greatest decrease in this parameter at months 3 and 6 was found in the structured telephone survey group: from 617 (262–2,131) pg/mL to 345 (321–923) pg/mL at month 6 ($P = 0.007$). No difference was reported over 12 months. The Medsenger medical platform was superior at months 3 and 6: at 3 months, the NT-proBNP levels decreased from 817 (331–1,480) pg/mL to 582 (208–896) pg/mL ($P < 0.001$), and at 1 year, it decreased by 3.5 times to 233 (128–638) pg/mL ($P < 0.001$) (Fig. 6).

From a technical perspective, assessing the effect of FC on outcomes and determining the effectiveness of the monitoring options are challenging owing to the ordinal nature of the variable, missing data (patient deaths), and presence of related groups (groups were assessed at different time points). Therefore, a method was chosen to assess the effect of the FC on the outcomes in each FU group by using ordinal regression.

In Group 1, no significant influence of FC on the outcomes was found by telephone interviews. Group 2 using the Medsenger platform showed that at 3 months, the FC level had a significant effect on the secondary endpoint ($P = 0.016$) and the admission rate due to CHF decompensation ($P = 0.006$). Similar results were reported at 12 months ($P < 0.001$), and no difference was seen at 6 months. In Group 3, standard FU showed that the FC affected the primary endpoint only after 12 months ($P = 0.021$), without affecting other outcomes. No significant effects were found when comparing the remote and face-to-face FU groups.

Adverse Events

No adverse events were reported for the study technology.

DISCUSSION

Summary of Primary Findings

The study demonstrated the superiority of remote FU over routine monitoring in patients with CHF in reducing cardiovascular mortality at 3 and 12 months of FU. In the remote FU group, LVEF increased by a significant 6% during the first 3 months, and NT-proBNP levels decreased at all reference points. The Medsenger platform was superior to a telephone survey at 12 months of FU for cardiovascular mortality and a composite secondary endpoint. It was also associated with an increase in LVEF (from 47% at baseline to 55% at the end of FU) and a decrease in NT-proBNP levels (from 817 pg/mL to 233 pg/mL).

Discussion of Primary Findings

To date, many clinical studies have evaluated various telemedicine technologies, including telemedicine monitoring for chronic noncommunicable diseases [10]. However, even today, no clear understanding of its clinical effectiveness has been reached in terms of its effect on cardiovascular mortality and readmissions. As a result, the implementation of telemedicine technologies in the routine practice for the long-term care of patients with chronic noncommunicable diseases is limited.

In the multicenter European iCOR study, remote monitoring of the health status of patients with CHF using videoconferencing and telemetry of biological parameters was associated with a significant reduction in the rates of acute LV failure from 56% to 22% and a decrease in the treatment cost from €8,163 to €4,993 over 6 months [11].

The first Cochrane review of the effectiveness of CHF telephone support and telemonitoring was published in 2007 and updated in 2010. The latest version of the review included 30 randomized clinical studies with 9,806 patients. The primary outcome of this meta-analysis was that patients followed up using telemonitoring systems had lower all-cause mortality (relative risk [RR] 0.66, 95% CI 0.54–0.81; $P < 0.001$) and heart failure (HF) admissions (RR 0.79, 95% CI 0.67–0.94, $P = 0.008$), whereas telephone patient support affected only on HF admissions (RR 0.77, 95% CI 0.68–0.87; $P < 0.0001$) [12].

Some studies have shown that remote monitoring is effective in reducing all-cause mortality, CHF admission, and mortality in this patient population [13, 14].

OSICAT was a multicenter, randomized study (n = 937) that enrolled patients with decompensated HF within ⩽1 year before the study started. Remote monitoring was associated with a 21% decrease in the relative risk of first emergency admission (OR 0.79, 95% CI 0.62–0.99; P = 0.044), a 29% decrease in the relative risk in patients with NYHA FC III or IV HF (OR 0.71, 95% CI 0.53–0.95; P = 0.02), and a 38% relative risk decrease in socially isolated patients (OR 0.62, 95% CI 0.39–0.98; P = 0.043) [15].

In subsequent years, the publication of several large randomized clinical studies with negative [16–18] and neutral [19, 20] results led to increasing uncertainty about the benefits of telephone support and telemonitoring.

A systematic review and meta-analysis of studies enrolling patients with recently decompensated HF revealed that remote FU was not superior to standard FU in terms of all-cause admission (OR 0.95, 95% CI 0.84–1.08, P = 0.43) and all-cause mortality (OR 0.83, 95% CI 0.63–1.09, P = 0.17) rates [21].

A systematic review of 34 randomized clinical studies (2000–2021) found that remote monitoring had no significant effect on reducing hospital admissions or mortality. American studies in patients with CHF and a high risk of readmission showed positive trends in reducing mortality/admission rates; however, no significant differences were reported [22].

Notably, these studies had several limitations, such as recruitment of patients with severe HF with LVEF <35%, differences in treatment adherence between groups, low study power, short duration of patient FU, and lack of uniform standards for telemedicine monitoring. All these factors prevent a comprehensive assessment of the effectiveness of FU options.

This study showed a clear association between the effect of the remote monitoring option and the primary endpoint, remote monitoring resulted in 2.73-fold decrease in mortality rate, and these differences persisted throughout the study. When comparing the remote FU options in the short term, no differences were found; however, at 12 months, Medsenger monitoring was superior to structured telephone support with a 17% decrease in cardiovascular mortality (P = 0.029). Such results may be related to the ability of a physician to adjust therapy remotely through telemedicine consultation, which may prevent further HF decompensation and death. In addition, educating patients on what to do if their condition worsens also helps prevent adverse outcomes [23].

The decreased number of deaths and admissions in the remote monitoring group is explained by the improvement in the clinical and functional profiles of patients. Our data show that this monitoring option is associated with an increase in LVEF and a decrease in NT-proBNP levels, indicating CHF stabilization and improvement in the quality of life. Patients in the remote monitoring groups received regular support from HCPs, and this had a positive effect on adherence.

Literature data on the effect of the FU option on laboratory tests and investigations are limited, probably due to the high cost of these types of diagnostics. Single studies evaluated the effect of the FU option on FC in patients with CHF. For example, Pyrikova NV et al. [25] demonstrated a positive effect of remote FU on the functional status of patients with CHF. At 6 months, the number of patients with FC III decreased by 1.7 times (P = 0.03), and in the control group with routine monitoring, it increased by 1.9 times (P = 0.002). FC IV was 6.5 times more frequent in the control group than in the telemedicine groups, indirectly indicating the effectiveness of the latter. The present study reported the superiority of Group 2 monitoring: when using the Medsenger platform, the FC level showed a significant effect on the secondary endpoint and admission rate due to decompensated CHF at 3 months (P = 0.006). This may also indicate that the improved clinical status of patients in this group positively affected the outcome. In the standard monitoring group, FC affected the primary endpoint only at 12 months, whereas no association was found in the telephone survey group.

Thus, remote FU positively affects LVEF, NT-proBNP levels, and FC. The normalization of these clinical and functional parameters is likely to decrease the cardiovascular mortality rate and the incidence of composite secondary endpoint events and explains the positive results in remote FU.

Study Limitations

The sample size was calculated using the moderate precision test and a significance level of 0.05. To increase the power of the study and the representativeness of the results with a similar design, more participants would be required.

CONCLUSION

One of the most important and challenging issues in modern healthcare is finding a way to best monitor patients with CHF to improve outcomes and reduce mortality and admission rates. Remote monitoring protocol based on our data can become a good alternative to traditional face-to-face monitoring. The results showed the superiority of remote monitoring to standard monitoring, with decreased cardiovascular mortality rates at 3 and 12 months (OR 2.73, 95% CI 1.1–7.39, P = 0.042, and OR 2.1, 95% CI 1.1–3.7, P = 0.027, respectively).

Improving the clinical and functional status of patients will also improve patient outcomes, their quality of life and level of self-care, contribute to adherence and trust in the healthcare system, and drive the development of related IT technologies. The widespread adoption of such solutions is currently limited by barriers such as low patient digital literacy, a lack of clear attitudes toward remote monitoring in the healthcare community, and need for additional

technological equipment in medical facilities. However, the demographic characteristics of our population, growing number of patients with CHF, and need for high-quality, personalized care will ultimately drive the universal adoption of remote monitoring technologies.

ADDITIONAL INFORMATION

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Mitral Valve Calcinosis as an Important Finding During Heart Examination

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ABSTRACT

BACKGROUND: Mitral valve calcinosis is a chronic degenerative process in the fibrous structures of the mitral valve. Advanced stages increase the risk of endocarditis and cardiac rhythm disturbances and contribute to cardiovascular mortality. The cause of mitral valve calcinosis is still controversial; however, the contribution of atherosclerosis to its development is currently undisputed. The prevalence of mitral valve calcinosis varies in different age groups and on average is higher in people with cardiovascular disease.

AIM: To assess the prevalence of mitral valve calcinosis in patients undergoing computed tomography angiography and identify the relationship between aortic and mitral valve calcinosis and coronary calcium index and signs of remodeling.

MATERIALS AND METHODS: A retrospective study of 336 patients who underwent computed tomography coronary angiography with intravenous contrast enhancement at the Lomonosov Moscow State University Clinic between November 13, 2020, and May 14, 2022, was conducted.

RESULTS: The prevalence of aortic (16.4%) and mitral (11%) valve calcinosis was high in people undergoing cardiovascular examination, and a relationship was noted between valve calcinosis and coronary calcium index.

CONCLUSION: The detection of mitral valve calcinosis in patients during routine examination is important in predicting further treatment and outcomes because valve calcinosis is an indirect indicator of coronary heart disease risk. Although valve calcinosis is usually an incidental examination finding, it may indicate a high cardiovascular risk and should prompt further evaluation, if clinically necessary.

Keywords: mitral valve; calcinosis; computed tomography; magnetic resonance imaging; echocardiography.

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Кальциноз митрального клапана как важная находка при сердечно-сосудистой визуализации

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АННОТАЦИЯ

Обоснование. Кальциноз митрального клапана — это хронический дегенеративный процесс в фиброзных структурах митрального клапана, на продвинутых стадиях повышающий риск развития эндокардита и нарушений ритма сердца, а также вносящий вклад в структуру сердечно-сосудистой смертности. Этиология кальциноза митрального клапана пока является дискутабельным вопросом, однако вклад атеросклероза в его развитие в настоящее время не вызывает сомнений. Распространённость кальциноза митрального клапана варьирует в разных возрастных группах и в среднем выше у людей с заболеваниями сердечно-сосудистой системы.

Цель — оценка распространённости кальциноза митрального клапана у пациентов, проходящих компьютерную томографическую ангиографию; выявление взаимосвязи между кальцинозом аортального и митрального клапанов и индексом коронарного кальция, а также признаками ремоделирования.

Материалы и методы. Проведено ретроспективное исследование 336 пациентов, проходивших компьютерную томографическую коронароангиографию с внутривенным контрастированием на базе Медицинского научно-образовательного центра Московского государственного университета имени М.В. Ломоносова в период с 13.11.2020 по 14.05.2022.

Результаты. Исследование показало высокую распространённость кальциноза аортального (16,4%) и митрального (11%) клапанов в популяции людей, проходящих обследование сердечно-сосудистой системы, а также наличие взаимосвязи между кальцинозом клапанов и индексом коронарного кальция.

Заключение. Выявление кальциноза митрального клапана у пациентов при рутинном обследовании играет важную роль для прогнозирования дальнейшего лечения и исхода, поскольку кальциноз клапанов является косвенным показателем риска ишемической болезни сердца. Будучи, как правило, случайной находкой при обследовании, кальциноз клапанов может свидетельствовать о наличии у пациента повышенного сердечно-сосудистого риска и должен быть поводом для дополнительного обследования при клинической необходимости.

Ключевые слова: митральный клапан; кальциноз; компьютерная томография; магнитно-резонансная томография; эхокардиография.

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二尖瓣钙化作为心血管成像的一个重要发现

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摘要

论证。二尖瓣钙化好机会是二尖瓣纤维结构的一种慢性退行性过程。二尖瓣钙化在晚期会增加心内膜炎和心律失常的风险，并导致心血管死亡。二尖瓣钙化的病因仍存在争议。不过，动脉粥样硬化对二尖瓣钙化的发展所起的作用目前是毋庸置疑的。二尖瓣钙化在不同年龄段的发病率各不相同，平均而言，心血管疾病患者的发病率较高。

目的是评估接受计算机断层扫描血管造影术的患者中二尖瓣钙化的发病率；确定主动脉瓣和二尖瓣钙化与冠状动脉钙化指数和重塑迹象之间的关系。

材料和方法。该回顾性研究实对 2020 年 11 月 13 日至 2022 年 5 月 14 日期间在 Medical Scientific and Educational Center, Lomonosov Moscow State University 接受静脉注射造影剂的计算机断层扫描冠状动脉造影术的 336 名患者进行的。

结果。研究显示了，在接受心血管筛查的人群中，主动脉瓣（16.4%）和二尖瓣（11%）钙化的发病率很高，而且瓣膜钙化与冠状动脉钙化指数之间存在关系。

结论。在常规检查中发现患者的二尖瓣钙化对于预测进一步的治疗和结果非常重要，因为瓣膜钙化是冠心病风险的间接指标。虽然瓣膜钙化通常是检查中的偶然发现，但它可能预示着患者的心血管风险增加，临床上有必要时应考虑对其进行进一步评估。

关键词：二尖瓣；钙化；计算机断层扫描；磁共振成像；超声心动图。

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BACKGROUND

Mitral valve calcinosis (MVC) is a chronic degenerative condition of the fibrous ring of the mitral valve (MV). It is characterized by calcium deposition, primarily in the posterior leaflet. Caseous calcinosis is a distinct type of MV damage, with a biochemical transformation of calcium and the formation of caseous masses (thus the name). MVC (ordinary or caseous) is frequently mistakenly regarded as a neoplasm based on imaging findings; thus, the appropriate use of different methods is critical for the differential diagnosis.

The overall incidence of MVC is approximately at 13% [1]; however, it can range from 4.6% to 15.8%, depending on the population [2]. The incidence of MVC is 35% in patients with symptoms of cardiovascular diseases [3] and 36% in patients with advanced renal insufficiency [1]. MVC is typically asymptomatic and is discovered by accident during examinations, contributing to this substantial variability. The Framingham Heart Study revealed that MVC is extremely rarely detected in patients aged <40 years [4]. This has a major effect on cardiovascular morbidity and mortality and outcomes of cardiovascular surgery. Unlike rheumatic diseases, calcinosis usually does not significantly impair MV function; however, severe MVC can cause mitral regurgitation.

STUDY AIM

This study aimed to assess the incidence and characteristics of MVC and aortic valve calcinosis (AVC) in patients who were tested for coronary artery atherosclerosis using computed tomography (CT) coronary angiography. Moreover, the study assessed the potential relationship between these processes and the effect of calcinosis on MV function and cardiac chamber morphology.

METHODS

Study Design

This retrospective, observational, single-center cohort study enrolled patients who underwent CT coronary angiography in the X-ray diagnosis department of the Medical Research and Educational Center of the Lomonosov Moscow State University.

Eligibility Criteria

Inclusion criteria: patients referred for contrast-enhanced CT coronary angiography to rule out coronary artery atherosclerosis.

Noninclusion criteria:

- Condition after coronary artery stenting or bypass grafting (calcium score assessment was not feasible)
- Condition after valve replacement
- Congenital heart disorders and heart neoplasms
- History of severe allergic reaction to an iodine-containing contrast enhancement agent
- Severe condition preventing a diagnostically valuable examination

Exclusion criteria: refusal to participate in the study.

Study Duration

The study was performed between November 13, 2020, and May 14, 2022.

Therapeutic Intervention

CT coronary angiography with electrocardiogram (ECG) gating was performed, which included two successive scans: a native scan to determine the cardiac calcium score (CCS) and an arterial enhancement scan (using an iodine-containing contrast enhancement agent at a dose of 300 mg iodine per 1 mL, or 1 mL per 1 kg body weight). Retrospective ECG gating was employed in all cases, which enabled additional visualization of cardiac chambers during various phases of the cardiac cycle. Coronary artery reconstruction in the multiplanar reformation (MPR) mode was used for the analysis of images.

Primary Outcome

Detection of MVC and AVC and calcified plaques in coronary artery walls.

Secondary Outcomes

Detection of cardiac remodeling signs (left atrial enlargement).

Subgroup Analysis

The patients were divided into subgroups depending on the presence of valvular calcinosis:

- MVC group
- AVC group
- MVC and AVC group
- Group without valvular calcinosis

Moreover, the patients were divided into subgroups depending on the CCS:

- 0 (no coronary artery lesion)
- 1–10 (minimal lesion)
- 11–100 (insignificant lesion)
- 101–400 (moderate lesion)
- >400 (severe lesion)

Ethics Review

The study was approved by the Ethics Committee of the Medical Research and Educational Center of the Lomonosov Moscow State University on September 24, 2020.

Statistical Analysis

Statistical analysis was performed using Microsoft Office Excel 2010 (Microsoft Corporation, USA). Data were analyzed using the Kruskal–Wallis, Mann–Whitney *U*, and chi-squared tests. The significance level was $P < 0.05$.

Table 1. Incidence of valvular calcification in the study groups

	MVC	AVC	MVC, AVC	No calcification
Number of patients	37	55	13	251
Mean age, years	66.1±8.9	66.7±7.9	67.0±9.7	60.1±11.6
Men/women	16/21	32/23	5/8	149/102
CCS, units	582.3±875.3	435.3±591.4	314.2±215.2	176.5±402.9

Note. AVC, aortic valve calcification; MVC, mitral valve calcification; CCS, cardiac calcium score.

RESULTS

Study Subjects

The study included 336 patients, of which 195 were men (58%). The mean age was 61.1 ± 11.8 years.

Primary Findings

The incidence rates of MVC and AVC in the study groups were 11% (n = 37) and 16.4% (n = 55), respectively. Calcification of both valves was observed in 3.9% of cases (n = 13). Caseous MVC was reported in 7 (2.1%) patients.

Table 1 provides information on the study groups and the detected incidence of valvular calcinosis.

When dividing patients into groups depending on the presence of valvular calcinosis, significant differences in the CCS were revealed. The analysis was performed using the Kruskal–Wallis test ($P < 0.001$). The MVC group had the highest CCS, whereas the group without calcinosis had the lowest value.

When analyzing arbitrary-sized contingency tables using the chi-squared test, a positive correlation was found between the CCS and the incidence of MVC and AVC ($P < 0.01$) (Fig. 1). However, the association was less significant for AVC compared with that for MVC.

The severity of valvular calcinosis was assessed by calculating the CCS and the estimated calcium volume. When comparing the coronary artery CCS and severity of valvular calcinosis using the Mann–Whitney U test, no significant association was found. This pattern was observed in both the MVC and AVC groups.

Additional Findings

A potential association between left atrial enlargement (an indirect factor of mitral valve disease) and MVC was assessed. The analysis using the chi-squared test revealed a significant association between the MVC factor and left atrial enlargement as an outcome ($P = 0.002$).

Adverse Events

No adverse events or side effects of the contrast agent were reported during the study.

DISCUSSION

Summary Of Primary Findings

This retrospective study demonstrated a high incidence of MVC and AVC in patients undergoing a cardiovascular examination using CT coronary angiography and an association between valvular calcinosis and the CCS, with a more significant correlation for MVC. However, the severity of calcinosis was not associated with the coronary artery CCS.

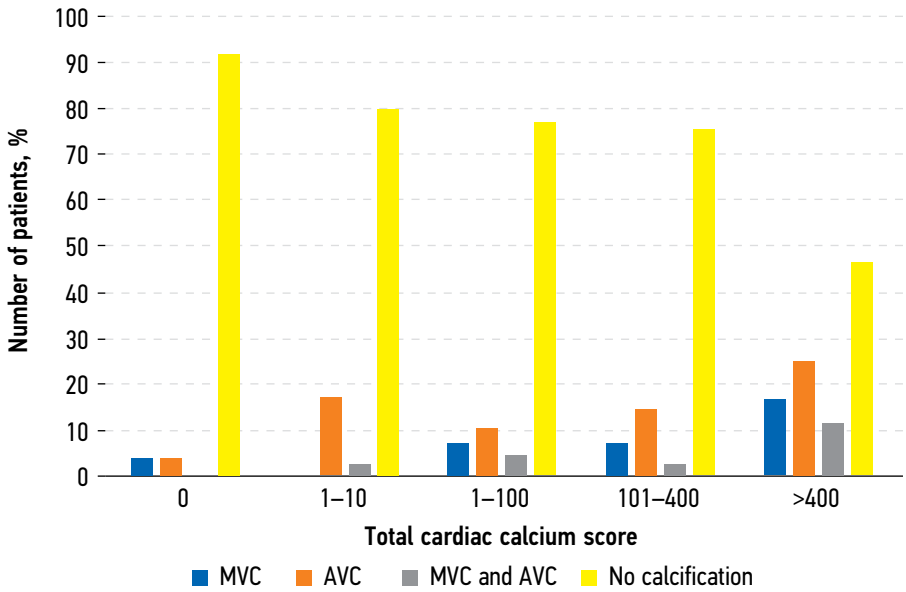

Fig. 1. Number of patients with valvular calcification in groups with different cardiac calcium score: AVC, aortic valve calcification; MVC, mitral valve calcification.

Moreover, a relationship was found between MVC and left atrial enlargement.

Discussion of Primary Findings

According to the literature, a correlation was found among MVC, AVC, and coronary artery atherosclerosis [5]. Moreover, a correlation was noted between coronary artery atherosclerosis and systemic atherosclerosis. Our findings are of relevance given that AVC exhibited a less significant correlation with the CCS than MVC. This emphasizes that the likelihood of valvular calcinosis is determined not only by systemic atherosclerosis and associated risk factors but also by other conditions. Timely diagnosis of MVC is clinically significant because MVC can be considered a predictor of atherosclerosis and MV disease in the future.

The pathophysiology of MVC is not fully understood. Nestico et al. defined MVC as a chronic, age-related degenerative condition that affects the fibrous support structure of the MV [6]. During the first decade of life, the mitral annulus is made up of parallel thin collagen fibers and some elastic fibers. The thickness and density of collagen fibers increase with age, as does the number of elastic fibers. Lipid spots form between collagen fibers, accompanied by calcinosis areas. Over time, collagen fiber misalignment increases, and lipid and calcium deposits grow. Areas with decreased shear stress and increased blood flow turbulence are susceptible to atherosclerosis [7]. Calcification and lipid deposition in the mitral annulus are commonly reported during autopsy in patients without macroscopic signs of MVC [8].

Studies have demonstrated significant similarities between atherosclerotic cardiovascular disease and chronic degenerative changes in the mitral and aortic valves [9]; all these events are typically caused by endothelial damage or dysfunction [10]. Moreover, as calcinosis forms, the mitral valve changes typical of atherosclerosis, such as inflammation [11], lipid buildup [12], and matrix metalloproteinase activation [13]. The renin–angiotensin–aldosterone system also plays a role in the development of valvular calcinosis [14]. Over time, focal calcium and lipoprotein deposits at microdamage areas transform into dense, rigid structures that form MVC. Moreover, numerous studies have demonstrated a significant correlation between the severity of systemic atherosclerosis and associated risk factors with MVC [15–17]. Thus, several researchers propose that MVC and atherosclerotic cardiovascular disease are two variants of the same condition.

However, an essential feature of MVC pathogenesis is that MVC more frequently affects women, whereas classic atherosclerosis is more common in men [18]. Women also have larger deposits in the mitral annulus. The formation of extrauterine calcium deposits in older women was assumed to be associated with severe bone loss due to osteoporosis in postmenopause [19]. Moreover, bisphosphonate therapy is associated with a lower incidence of cardiovascular calcinosis in women aged >65 years [20].

In addition to atherosclerosis, conditions associated with a long-term MV overload, such as hypertension, aortic stenosis, and hypertrophic cardiomyopathy, are also significant contributors to MVC development. In these conditions, the peak systolic pressure and MV closing pressure increase, resulting in an increased load on the mitral annulus and causing its degeneration [21].

Chronic renal failure is another significant risk factor for MVC. Reduced glomerular filtration rate, end-stage renal disease, and hemodialysis are linked to the incidence of MVC [22]. This association can be attributable to various reasons, including a high incidence of cardiovascular risk factors and atherosclerosis in these patients, more severe comorbidities, and impaired calcium–phosphorus metabolism [23, 24]. Jesri et al. demonstrated that nearly 60% of patients with MVC have a reduced glomerular filtration rate of ⩽60 mL/min × 1.73 m^2 [25]. Notably, no such association was found between chronic kidney disease and MVC [26]. Moreover, patients with specific congenital disorders, such as Marfan syndrome, which is characterized by systemic connective tissue and cardiovascular system damage, are more susceptible to MVC [27].

The Framingham Heart Study revealed a correlation between MVC and the incidence of adverse cardiovascular events and cardiovascular mortality [28]; the risk of the latter depends on the severity of MVC [17]. The main reason is that MVC is considered a marker of systemic atherosclerosis and coronary artery atherosclerosis [29]. Inflammatory, immune, and metabolic processes can also participate in this relationship. MVC in patients aged <65 years with chest pain is an important, independent predictor of significant stenosis of at least one coronary artery. The absence of MVC in women aged <65 years is an independent predictor of the absence of coronary heart disease [3]. Thus, MVC in patients aged <65 years must be considered by practitioners as a significant marker of coronary heart disease. It is relevant in patients without clinical signs of this disease, and these patients require risk factor and lifestyle modifications to reduce the risk of adverse coronary events.

The literature data on the relationship between MVC and stroke are less consistent. Some studies (e.g., Kizer et al. [30]) confirm this correlation, whereas others (Rodriguez et al. [31]) found that it significantly decreased after making adjustments for classic risk factors for stroke. MVC is associated with coronary artery atherosclerosis and ventricular fibrillation, which can explain the reported correlation between MVC and stroke [32, 33].

Evidence shows that calcinosis can affect the MV function because the mobility of the posterior leaflet decreases when the base is densely infiltrated. This, in turn, increases the risk of elongation and rupture of the chordae tendineae, resulting in secondary mitral regurgitation [34]. The incidence of endocarditis in MVC is unknown. Although it is rare, it is a potentially fatal condition characterized by vegetation on the MV leaflets or mitral annulus [35].

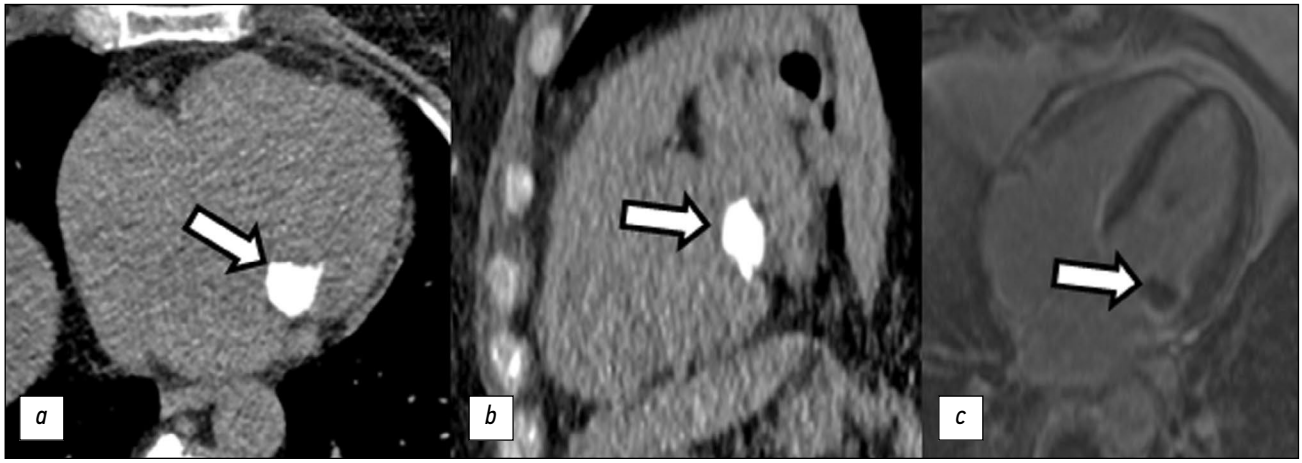

Fig. 2. Female patient, aged 65 years. Mitral valve calcification according to various methods: (*a*, *b*) computed tomography (axial and sagittal planes, without contrast enhancement); (*c*) magnetic resonance imaging (four-chamber long-axis view, delayed contrast enhancement).

The association between MVC and cardiac rhythm disorders is well-known. The most common disorders are atrioventricular block, bundle branch block, and intraventricular conduction block [36]. According to the literature, the incidence of cardiac rhythm disorders was significantly higher in patients with MVC than in the control group (70% vs. 34%) [37]. This could be because calcinosis directly extends to the atrioventricular node and the bundle of His. A significant correlation between MVC and atrial fibrillation was also associated with left atrial enlargement [38].

Given that MVC is mostly asymptomatic and can have potentially life-threatening consequences, its timely diagnosis is critical. In some cases, distinguishing between MVC, thrombosis, and neoplasms is difficult. Moreover, some authors report that calcinosis may appear similar to a myocardial abscess [39].

Echocardiography (EchoCG) is used for the primary diagnosis of MVC, which is visualized as a static hyperechoic structure with sharp edges, usually in the subvalvular space, beneath the MV posterior leaflet. Moreover, MVC is sometimes visualized as a heterogeneous structure with hypoechoic areas. Large calcinosiss may form an acoustic shadow, preventing clear visualization. Observation of typical MVC characteristics does not require further examination; however, the sensitivity of EchoCG is often insufficient to distinguish between calcium and other dense structures (such as collagen). Advanced abscesses can resemble MVC caused by consolidation and calcinosis areas. Magnetic resonance imaging (MRI) and CT can be used for follow-up examinations in cases in which visualization using EchoCG is difficult when there is a nonspecific increase in inflammatory markers (which does not allow ruling out an abscess or neoplasm), and in some other doubtful situations.

MVC typically has a decreased signal on standard cine MRI sequences, which sometimes makes it difficult to distinguish between calcium, adjacent cardiac muscles, and neoplasms in this location. T2-weighted images make it easier to differentiate MVC from other surrounding structures. Contrast enhancement does not result in significant perfusion during the early phase or delayed enhancement during the late phase (Fig. 2*c*). A thin rim of contrast is sometimes observed along the margin during the late phase. MVC can be distinguished from benign or malignant neoplasms based on the absence of vascularization and necrosis in the central part. MVC is displayed as a hypointense central part on T1- and T2-weighted images, whereas myxoma and lipoma are characterized by a hypointense signal due to mucin or fat in the stroma [40]. MR signs of abscesses depend on the stage; however, they are typically visualized as structures with a hypointense signal in the center and a hypointense signal in the periphery. However, the sensitivity and specificity of MRI are not always sufficient for an accurate differential diagnosis among MVC, thrombosis, and tumors. In these cases, CT is employed for follow-up examination.

On CT, MVC is visualized as a hyperdense structure without signs of contrast uptake, with an avascular, "soft" center. A fibrous capsule with heterogeneous, dense calcium areas is sometimes observed in the periphery [41] (Fig. 2*a*, *b*). CT allows determining the location and extent of MVC and its effect on valve function. Calculating the CCS enables a quantitative assessment of MVC.

Thus, a multimodal approach is recommended to make an accurate diagnosis of MVC. EchoCG is the first-line method, and ambiguous results necessitate additional examination using both MRI and CT. Notably, the use of various imaging methods not only allows for a correct diagnosis but also provides valuable information about the other conditions (coronary artery atherosclerosis, valve stenosis, reduced ventricular contractility, reduced ventricular contractility, hypokinesia or dyskinesia areas, etc.) of the patient, which may affect the treatment strategy.

Study Limitations

The study limitations include the analysis of calcified coronary artery plaques solely disregarding soft plaques. The

correlation between the severity of coronary artery stenosis and soft plaques will be assessed in the next phase of the study. In addition, clinical data, as well as EchoCG findings, were not analyzed.

CONCLUSION

MVC is commonly observed and is typically asymptomatic. The etiology of this condition is not fully understood; however, it shows a clear association with systemic atherosclerosis. MVC is associated with atherosclerosis and MV disease; thus, early disease diagnosis is clinically significant for the prevention of potentially dangerous conditions.

This study revealed a high incidence of valvular calcinosis in the population (the incidence rates of MVC, AVC, and calcinosis of both valves were 11%, 16.4%, and 3.9%, respectively). Moreover, a correlation was found between valvular calcinosis and coronary artery atherosclerosis, with a more significant association for the MV. Moreover, a relationship was found between MVC and left atrial enlargement.

Distinguishing between MVC, heart neoplasms, thrombosis, and some other conditions is difficult. EchoCG is used for the primary diagnosis of MVC; however, this condition can be mistaken for a neoplasm or thrombosis. Thus, when the findings are insufficient, follow-up examinations using cardiac MRI and CT are recommended. The use of a comprehensive approach and ensuring appropriate follow-up in patients with MVC and concomitant conditions, including calcinosis of other heart valves, are encouraged.

ADDITIONAL INFORMATION

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Competing interests. The authors declare that they have no competing interests.

Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

D.A. Filatova — forming the research group, conducting data statistical analysis, writing the text of the article; E.A. Mershina — developing the research concept, editing the text of the article; M.L. Plotnikova — editing the text of the article; M.V. Lisitskaya — development of the research concept, editing the text of the article; V.E. Sinitsyn — development of the research concept, approval of the final version of the text.

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Role of Teleradiology in the Interpretation of Ultrasound Images Acquired in the Emergency Setting

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ABSTRACT

BACKGROUND: Teleradiology has become an important tool in emergency medicine, particularly in the interpretation of emergency ultrasonography. In emergency situations, where time is essential, rapid diagnosis and treatment can mean the difference between life and death. Teleradiology is an innovative alternative to augment the staffing and fill the gaps of onsite radiology personnel in emergency departments or during off-hours.

AIM: To assess the effectiveness/impact of teleradiology in emergency ultrasound interpretation.

MATERIALS AND METHODS: A retrospective study was performed in a cohort of 33,616 patients from 86 hospitals across the USA between January and December 2022. The study involved radiological interpretations of 37,253 ultrasound images acquired in the emergency setting by American Board Certified Radiologists empaneled by a teleradiology service provider, headquartered in Bangalore, India.

RESULTS: The proposed telehealth model provided timely and quality reporting of 37,253 scans of patients with a mean turnaround time of 35.71 min (95% confidence interval 35.50–35.91).

CONCLUSION: This study demonstrates that a structured telesonography program with defined protocols for image capture, transmission, and clinical communication can allow for successful immediate reporting of ultrasound data in the emergency care setting.

Keywords: teleradiology; emergency; ultrasound; turnaround time; healthcare.

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Роль телерадиологии в интерпретации изображений, полученных при проведении ультразвукового исследования в условиях неотложной медицинской помощи

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АННОТАЦИЯ

Обоснование. Телерадиология — важный инструмент в условиях неотложной медицинской помощи, особенно при интерпретации изображений, полученных в ходе проведения ультразвуковых исследований. В чрезвычайных ситуациях, когда время имеет решающее значение, своевременная диагностика и лечение могут стать решающим фактором в спасении жизни пациентов. Телерадиология — инновационная альтернатива, позволяющая расширить кадровый состав и устранить нехватку радиологов, работающих в отделениях неотложной помощи в штатном режиме или в сверхурочное время.

Цель — оценить эффективность и влияние телерадиологии на интерпретацию изображений, полученных в ходе проведения ультразвуковых исследований, в условиях неотложной медицинской помощи.

Материалы и методы. Проведено ретроспективное исследование, в котором приняли участие 33 616 пациентов из 86 больниц США, обращавшихся за медицинской помощью в период с января по декабрь 2022 года. Сертифицированные специалисты Американского радиологического общества — официального провайдера телерадиологических услуг со штаб-квартирой в Бангалоре (Индия) — выполнили радиологическую оценку 37 253 изображений, полученных при проведении ультразвукового исследования в условиях неотложной медицинской помощи.

Результаты. Предложенная модель телемедицинской помощи обеспечила своевременную и качественную интерпретацию 37 253 снимков ультразвукового исследования пациентов со средним временем выполнения 35,71 мин (95% доверительный интервал 35,50–35,91).

Заключение. Данное исследование демонстрирует, что структурированная программа дистанционного ультразвукового исследования с установленными протоколами получения изображений, их передачи и последующей коммуникации между участниками процесса позволяет оперативно обмениваться данными в условиях неотложной медицинской помощи.

Ключевые слова: телерадиология; неотложная медицинская помощь; ультразвуковое исследование; время получения результатов; здравоохранение.

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远程放射学在急诊超声图像解读中的作用

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摘要

论证。远程放射学是急诊医疗环境中的一项重要工具，尤其是在解读超声波图像时。在时间紧迫的紧急情况下，及时诊断和治疗是挽救病人生命的关键因素。远程放射学是一种创新的替代方法，可以扩大人员编制，解决急诊科放射科医生正常工作或加班不足的问题。

目的是评估远程放射学对急症护理环境中超声波图像解读的效果和影响。

材料和方法。这项回顾性研究涉及 2022 年 1 月至 12 月期间在美国 86 家医院就诊的 33 616 名患者。美国放射学会（总部位于印度班加罗尔的远程放射学服务官方提供商）的认证专家对急诊超声检查中获得的 37 253 张图像进行了放射学评估。

结果。拟议的远程医疗护理模式为 37 253 名患者提供了及时、高质量的超声图像解读，平均周转时间为 35.71 分钟（95% 置信区间为 35.50–35.91）。

结论。这项研究表明，结构化远程超声计划具有既定的图像采集、传输和参与者之间后续沟通的协议，能够在急症护理环境中实现快速的数据共享。

关键词：远程放射学；紧急医疗护理；超声检查；得出结果的时间；卫生保健。

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BACKGROUND

Teleradiology epitomizes healthcare innovation and efficient healthcare delivery and represents a success story within the wider field of telemedicine [1]. This rapidly expanding field involves the transmission of radiological images from one location to another for interpretation by a radiologist [2]. It is an indispensable tool in emergency medicine, significantly improving patient care. Prompt interpretation and reporting of radiologic examinations by a teleradiologist in the evaluation of specific emergent complaints render it a significant part of the emergency medicine diagnostic paradigm [3].

Emergency cases within emergency departments (EDs) have notably increased over the past couple years, which was strongly associated with population growth and further heightened during the COVID pandemic [4]. EDs are also vulnerable to crowding during catastrophic disasters, such as earthquakes, tsunamis, cyclones, and urban flooding [5]. According to the National Hospital Ambulatory Medical Care Survey: 2020, the total number of visits to EDs of the hospitals in the US was 131.3 million [6], which is a matter of concern. In India, the NITI Aayog (2021) reported that 16% of all patients presenting to a health facility have emergency and injury cases, accounting for 19%–36% of admissions in district hospitals annually [5]. In addition, a report released by the Department of Emergency Medicine, AIIMS, on Emergency and Injury Care at Secondary and Tertiary level centers in India revealed that the number of beds available at EDs to cater to emergency cases, represents only 3%–5% of the total beds available in the country [7]. With a yearly rise in the number of people who visit EDs, nearly half of all EDs operate at or exceeding their capacity. This trend is very concerning and must be addressed [8]. Moreover, there is a shortage of physicians, particularly radiologists, i.e., approximately 22,000 radiologists for a large population of over 1.2 billion, resulting in a skewed ratio of 1:100,000 [9]. Considering the severity of trauma, stroke, and other critical illness of patients presenting to the EDs, diagnostic and treatment delays can lead to serious consequences for patients. Thus, timely and accurate interpretation of patients' imaging is pivotal. However, the availability of in-house trained radiologists is limited in EDs, particularly after working hours or on holidays. The challenge is to work toward efficiency and quality despite the rising workload and the shortage of medical personnel [10]. Under such circumstances, teleradiology is an obvious alternative to augment, assist, and fill in the gaps of the onsite radiology personnel in meeting the rising demand for imaging in trauma and acute illnesses in an emergency setting with a limited radiology workforce [8].

Emergency ultrasonography (USG) is a diagnostic imaging technique that utilizes high-frequency sound waves to create images of internal organs and structures [12]. It is a fast and noninvasive method of evaluating various clinical conditions, including trauma, abdominal and pelvic pain, appendicitis, cholecystitis, acute kidney dysfunction, abscess, complications of pregnancy, complications of organ transplantation [13]. Doppler USG is a real-time imaging technology that plays a pivotal role in emergency radiology for quick evaluation of vascular conditions and blood flow. It allows the identification of potentially fatal conditions such as deep vein thrombosis, arterial blockage, and insufficient organ perfusion. Diagnosing vascular damage in trauma cases facilitates timely performance of surgical intervention [14].

The major benefit of teleradiology in emergency sonography is not only the ability to provide timely diagnosis and treatment but also to offer adequate after-hour and specialist coverage including support for onsite ultrasound technologists/sonographers. Teleradiology in emergency USG can also lead to cost reductions for hospitals and patients [15]. Several studies have documented the benefits of teleradiology for patients [1, 11, 16, 17], and the present study aimed to evaluate the benefits of teleradiology in emergency ultrasound interpretation.

The advent of digital imaging technologies, picture archiving and communication systems (PACS), radiology information systems (RIS), high-speed Internet connections, and artificial intelligence have further improved the value proposition of teleradiology in providing timely radiological services under emergency settings, even to remote and underserved areas [11, 18, 19]. Moreover, stringent service-level agreements between the hospital and the teleradiology service guarantee a very short reporting turnaround time (TAT), which is advantageous to the patient and the attending emergency physician. The standard for clinical service in emergency care has thus been enhanced thanks to teleradiology [1, 20].

AIM STUDY

This retrospective study aimed to evaluate the role of teleradiology in USG performed on a cohort of patients in the emergency setting.

MATERIALS AND METHODS

Study Design

A retrospective study enrolled a cohort of 33,616 patients from 86 hospitals across the USA between January and December 2022. The study involved analysis of radiological ultrasonogram interpretations performed in the emergency setting by American Board Certified Radiologists empanelled by a teleradiology service provider, headquartered in Bangalore, India. DICOM static images and cine-series of the ultrasound images of the patients were uploaded onto the telereporting workflow platform "RADspa," a cloud-based RIS/PACS system over a high-speed Internet connection. In addition to uploading the images, the technologists at

the hospitals also provided observations in a worksheet submitted along with the images. The worksheet was typically a combination of an annotated graphic image with measurements and free text comments. The images (static images and cine-series) and worksheets were reviewed by the radiologists, and the reports were transmitted back to the hospitals over the same workflow platform, as well as conveyed verbally/telephonically in cases with critical findings. Other information, such as prior images and reports, patient clinical and surgical history records, are also uploaded to the RIS so that they are available to the radiologists along with the images.

A distribution of studies for different procedures performed in the emergency setting was analyzed. The mean reporting TAT from the time when the DICOM images of emergency ultrasound studies were received in the worklist up until the reports were uploaded in RADspa or verbally communicated to the referring physician was calculated.

Eligibility Criteria

The study included patients who had registered in the EDs of the hospitals and undergone USG.

Study Duration

The study enrolled a cohort of 33,616 patients from 86 hospitals across the USA between January and December 2022.

Ethical Review

This retrospective study was approved by the institutional review board.

RESULTS

Study Subjects

A total of 37,253 ultrasound scans of 33,616 patients from 86 hospitals across the US were evaluated.

Primary Findings

The hospitals were categorized based on the bed count and number of images received (Table 1).

Among all hospitals under study, 28 had in-house technologists to perform ultrasound scans for the patients, out of which 4 had on-call technologists on weekends. In addition, 51 hospitals had on-call technologists, whereas in one hospital, radiology residents reported ultrasound cases. In six hospitals, technologists do not perform ultrasound scans after 11 pm.

In a teleradiology practice, technologists communicate in three ways and provide brief descriptions of the cases to the teleradiologists. Technologists create worksheets with case observations and upload these in the RADspa either as pdf or jpeg file, may convert them into DICOM, or may write down their comments or notes directly into the textbox provided in RADspa. In this study, out of 37,253 ultrasound scans, the technologists had provided notes for 27,138 (72.84%) cases, and for the remaining cases, worksheets were attached.

Demographic information, such as the sex and age of the patients, was also loaded into the cloud-based server. Out of 33,616 patients in this study, 70.56% were women and 29.44% were men. The mean age of the patients was 40.95 (95% confidence interval, 40.73–41.17) years. The group aged 21–40 years accounted for the maximum number of patients (Fig. 1).

To help in making diagnosis and treatment decisions, ultrasound scans of different body parts were performed (Table 2). Among the ultrasound procedures performed, lower and upper extremity USG comprised 26.28% (n = 9,792); abdomen, 18.62% (n = 6,937); obstetrics, 17.41% (n = 6,488), and pelvis, 15.62% (n = 5,820). Out of 33616 patients, 9496 had followed up with computed tomography.

Teleradiology services were provided to the patients under different clinical situations. Patient clinical texts were categorized based on the presenting symptoms, and a systems-based approach was employed (Fig. 2). The majority of the presenting symptoms were categorized as reproductive (35%), gastrointestinal (31%), cardiovascular (9%), and musculoskeletal (6%). Other categories, shown in Fig. 2, make up smaller proportions of the presenting symptoms of the overall study cohort.

Cine-series of 4,025 patients were also uploaded into the cloud server for interpretation by teleradiologists. Out of 4,025 cine-series, 1,731 (43%), 1,048 (26.03%), and 655 (16.27%) were performed for issues related to the reproductive, gastrointestinal, and cardiovascular systems, respectively (Fig. 3).

Table 1. Distribution of hospitals according to bed count and imaging

Hospital bed count	Number of hospitals	Number of cases
Small hospitals (<100 beds)	22	1,621
Medium-size hospitals (100–499 beds)	54	29,692
Large hospitals (≥500 beds)	7	981
Imaging centers	3	4,959
Total	86	37,253

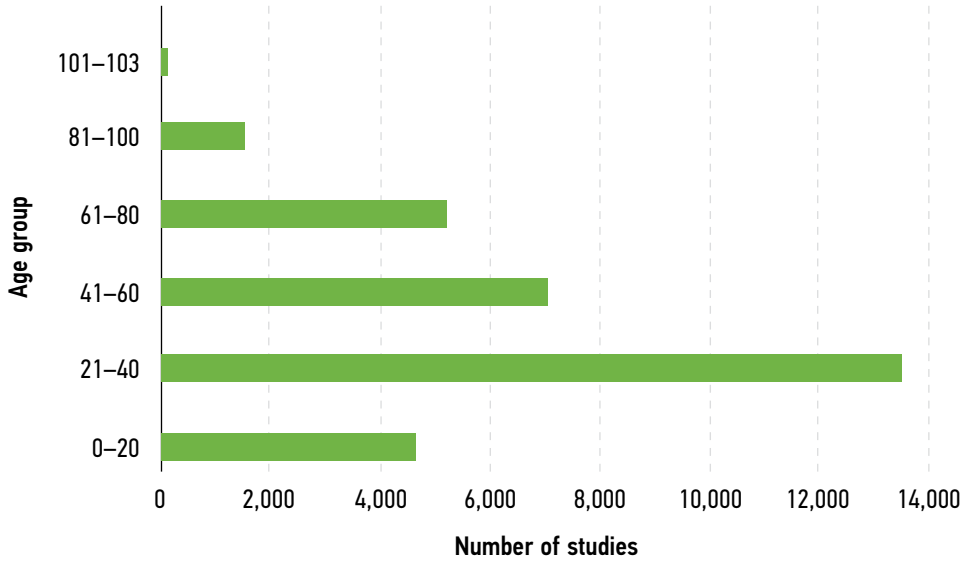

Fig. 1. Age group categorization of the patients.

In this study, 1,262 patients had undergone Doppler, of which 569 patients who had clinical history of scrotal or testicular pain, swelling, torsion and hydrocele underwent scrotal Doppler. Further, 497 patients having cysts, suspected ovarian torsion, pelvic pain, cramps, vaginal bleeding during pregnancy, post-menopausal bleeding, and lower abdominal pain had undergone pelvic Doppler. In addition, 152 patients with numbness, vertigo, slurred speech, syncope, CVA,

Table 2. Distribution of studies for different procedures

Procedures	Number of cases
Venous Doppler (lower/upper extremity)	9,792
Abdomen	6,937
Obstetrics biophysical profile	6,488
Pelvis (non-pregnant female)/transvaginal /endovaginal	5,820
Gallbladder/right upper quadrant/appendix/liver/right lower quadrant	3,965
Scrotal/testicular/scrotum Doppler	1,977
Renal/retroperitoneal	1,393
Breast	184
Carotid Doppler	152
Neck	115
Soft Tissue	79
Intussusception	69
Carotid Duplex	60
Groin	35
Chest	29
Urinary bladder	24
Extracranial arteries, both	19
Fistula graft	18
Head	18
Thyroid	18
Kidney transplantation	12
Other procedures	49

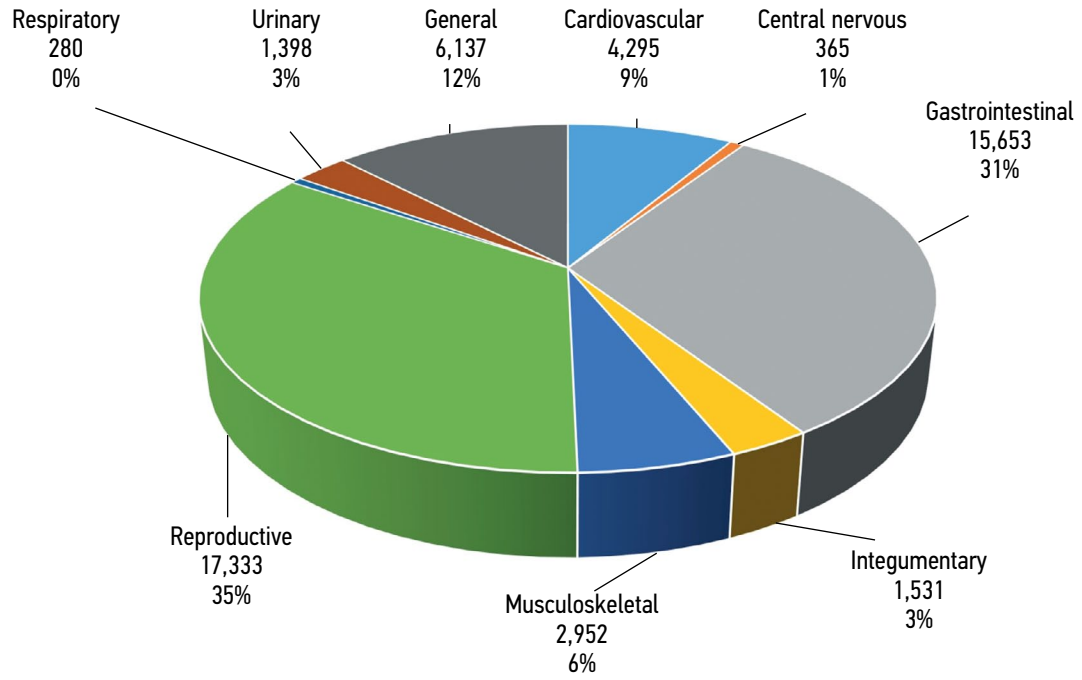

Fig. 2. Distribution of cases based on clinical presentation and symptoms using a systems-based approach.

transient ischemic stroke and stenosis underwent carotid Doppler. Twenty-eight patients with abnormal gallbladder, liver or spleen, hepatic encephalopathy, liver failure, cirrhosis, hepatic vein thrombosis, and liver transplantation underwent liver Doppler, and 16 cases with renal failure underwent renal Doppler (Fig. 4).

The mean reporting TAT for all emergency ultrasound studies was 35.71 min (95% CI, 35.50–35.91).

Additional Findings

All ultrasound scans were peer-reviewed under a quality assurance program to assess diagnostic accuracy and clinical performance. Out of 37,253 ultrasound scans, 99.9% of the studies showed accurate and concurrent interpretations, and 39 (0.1%) studies showed discrepancies. Among these 39 cases, 24 had nonclinically significant discrepancies, whereas 15 were clinically significant ones.

DISCUSSION

Emergency care is the provision of immediate interventions required to prevent death and disability, wherein delays over hours may worsen prognoses or reduce the efficacy of care [21]. With the development of emergency radiology as a distinct radiology specialty, a unique set of expertise is essential to diagnose patients

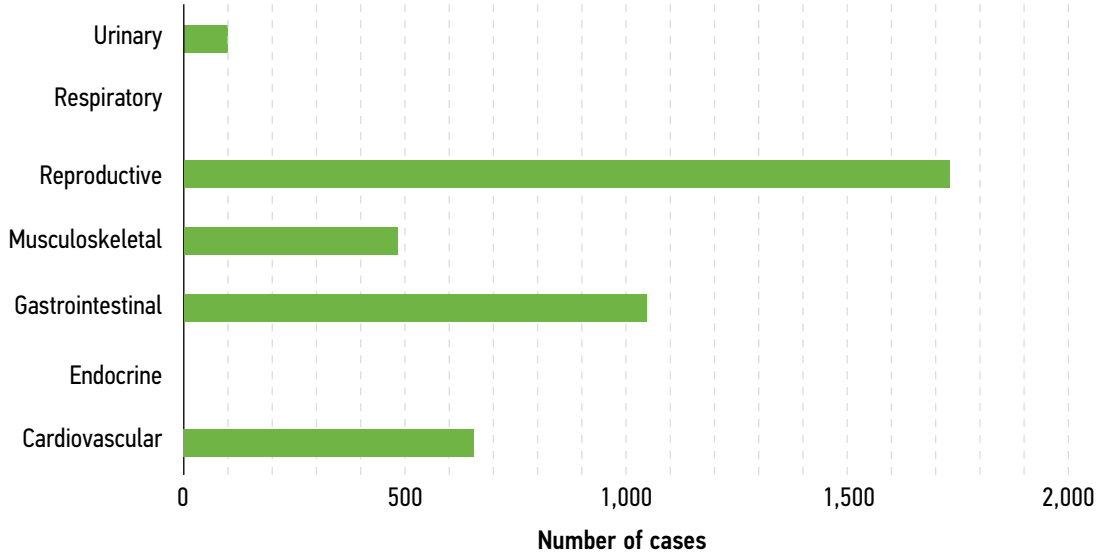

Fig. 3. Distribution of cases with cine-series using a systems-based approach.

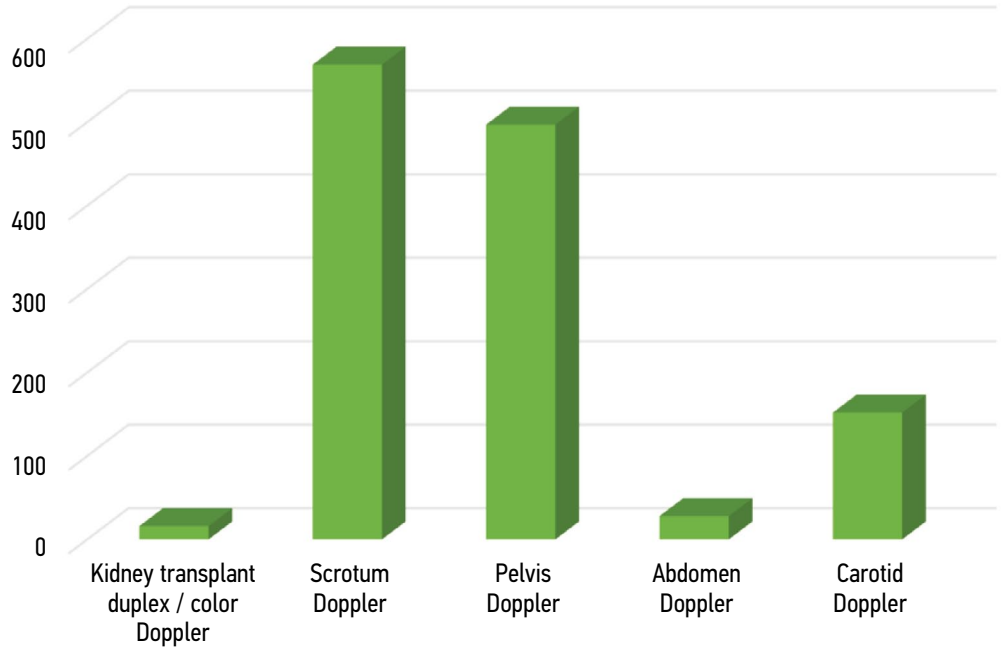

Fig. 4. Distribution of cases for Doppler ultrasound.

with critical illnesses or trauma promptly and accurately [11]. Teleradiology is an innovative solution that enables quick interpretation of imaging and accurate diagnosis of patients with critical injuries or illnesses requiring immediate resuscitation, intensive care, or emergent surgery, allowing emergency physicians to make informed decisions about patient care and treatment plans. Further, the proposed emergency teleradiology model, where night-to-day teleradiology services are leveraged, i.e., emergency scans performed at night in the USA can be reported from India during the day by appropriately certified radiologists, and vice versa, could be a front-line driver in healthcare. At present, emergency radiology subspecialty training or dedicated emergency radiology positions are not available. Several emergency radiology and medicine societies, namely, the Society of Emergency Radiology, European Society of Emergency Radiology, American Society of Emergency Radiology, Society for Emergency Medicine India, and Indian Society for Trauma and Acute Care have been founded to promote the exchange of best practices in the area and enable integration of clinical care and imaging [22].

This retrospective study involves the evaluation and interpretation of imaging of emergency cases transmitted from 86 hospitals across the USA. According to the information obtained from the Annual Survey of Hospitals, the total staffed beds in all US hospitals is 919,649 [23]. The hospitals are broadly categorized based on the bed count as small (<100 beds), medium (100–499 beds), and large (≥500 beds) hospitals. In this study, the hospitals were categorized based on the bed count and number of imaging studies received (Table 1). The majority of the studies (79.7%) were transmitted by 54 medium hospitals, and 13% were transmitted by three imaging centers. This study demonstrates that hospitals of any size may benefit from telesonography.

Telesonography may be effectively practiced in either model (in-house or on-call technologist). Out of 86 hospitals, 28 had in-house technologists who helped in establishing better communication of results compared with hospitals having on-call technologists.

Of all ultrasound scans, 17,333 (35%) were from patients presenting reproductive-related issues, followed by 15,653 (31%) with gastrointestinal/biliary issues, 4,295 (9%) with vascular problems, and 2,952 (6%) with musculoskeletal-related issues that required immediate medical attention. Other smaller categories included 1,531 studies of skin-related cases, 1,398 of urinary system-related problems, 365 of neurologic issues, and 280 of respiratory-related problems (Fig. 2). Thus, teleradiology in USG covers the entire gamut of organ systems and clinical presentations to address emergent clinical needs.

The mean TAT is the interval from when the DICOM images of emergency ultrasound studies were received in the worklist to the time the reports were uploaded in RADspa or verbally communicated to the referring physician/results were sent to hospitals. The mean reporting TAT for all emergency ultrasound studies was 35.71 min (95% CI, 35.50–35.91). Szabo et al. reported a mean TAT of 58.27 min for USG within the ED of a hospital system with in-house radiologists. In the present study, the mean TAT using teleradiology is quite reasonable and satisfactory compared with the mean TAT for USG by other published studies with onsite radiologists, thus displaying the effect of teleradiology on patient care in the emergency setting [24].

In addition, this study demonstrates that static images of standard views accompanied by the sonographer's worksheets are adequate for the interpretation of ultrasound studies via telesonography in most cases. Additional cine sequences can be used in complex cases to provide additional details.

With reference to the communication of findings, in critical cases requiring immediate patient management, referring physicians were informed either by direct telephonic communication with the radiologist or the call center team of the teleradiology service provider [25]. In this study, a total of 752 calls were made to communicate with the hospitals. Out of these calls, 49 direct calls were made between the radiologist and the referring physician, and 70 calls were made by the support staff to relate positive findings and 47 calls to communicate negative findings. In addition, 619 calls were performed for the verbal communication of important findings to physician assistants at hospitals who ensured further actions.

A peer review plays an indispensable role in a radiology interpretation QA program. A QA program is the most common method for assessing diagnostic accuracy and clinical performance. In this study, a very high accuracy (99.9%) was observed during the peer review. Only 39 (0.1%) studies showed discrepancies. Among these 39 cases, 24 were nonclinically significant discrepancies, whereas 15 were clinically significant ones. In a study by Iyer et al. (2013), 85.9% of the cases had concurrent interpretations. Some discrepancies analyzed during peer review were under-reading, faulty reasoning, failure to provide appropriate differential diagnosis, overcall, typographical error, failure to consult before imaging studies, and failure to suggest further imaging or follow-up.

CONCLUSION

Teleradiology has become an important tool in emergency medicine where time is essential, and rapid diagnosis and treatment can mean the difference between life and death. Many EDs do not have a radiologist on site to interpret ultrasound images, which can lead to diagnostic and treatment delays. Under such circumstances, the deployment of teleradiology services can be a game changer owing to its ability to provide quick and accurate diagnoses, further leading to the expedient and safer disposition of patients. This study demonstrates that a structured telesonography program with defined protocols for image capture, transmission, and clinical communication can allow for the successful immediate reporting of ultrasound examinations in the emergency care setting. The findings of the proposed telehealth model seek to provide a platform for constructing a similar telesonography model in developing countries.

ADDITIONAL INFORMATION

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Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

A. Kalyanpur — conceptualization, formal analysis and investigation, writing and editing, supervision; N. Mathur — formal analysis and investigation, writing, original draft preparation.

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A New Artificial Intelligence Program for the Automatic Evaluation of Scoliosis on Frontal Spinal Radiographs: Accuracy, Advantages and Limitations

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ABSTRACT

BACKGROUND: Scoliosis is one of the most common spinal deformations that are usually diagnosed on frontal radiographs using Cobb's method. Automatic measurement methods based on artificial intelligence can overcome many drawbacks of the usual method and can significantly save radiologist's time.

AIM: To analyze the accuracy, advantages, and disadvantages of a newly developed artificial intelligence program for the automatic diagnosis of scoliosis and measurement of Cobb's angle on frontal radiographs.

MATERIALS AND METHODS: In total, 114 digital radiographs were used to test the agreement of Cobb's angle measurements between the new automatic method and the radiologist using the Bland–Altman method on Microsoft Excel. A limited clinical accuracy test was also conducted using 120 radiographs. The accuracy of the system in defining the scoliosis grade was evaluated by sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve.

RESULTS: The agreement of Cobb's angle measurement between the system and the radiologist's calculation was found mostly in grade 1 and 2 scoliosis. Only 2.8% of the results showed a clinically significant angle variability of >5°. The diagnostic accuracy metrics of the limited clinical trial in City Mariinsky Hospital (Saint Petersburg, Russia) also proved the reliability of the system, with a sensitivity of 0.97, specificity of 0.88, accuracy (general validity) of 0.93, and area under the receiver operating characteristic curve of 0.93.

CONCLUSION: Overall, the artificial intelligence program can automatically and accurately define the scoliosis grade and measure the angles of spinal curvatures on frontal radiographs.

Keywords: scoliosis; artificial intelligence; spine.

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Новая интеллектуальная система для автоматической диагностики сколиоза по фронтальным рентгенограммам позвоночника: точность, преимущества и ограничения

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АННОТАЦИЯ

Обоснование. Сколиоз — одна из самых распространённых деформаций позвоночника, которую обычно диагностируют с помощью фронтальных спондилограмм по методу Кобба. Автоматические методы измерения, основанные на искусственном интеллекте, компенсируют многие недостатки стандартных методов и могут значительно сэкономить время врача-рентгенолога.

Цель — проанализировать точность, преимущества и недостатки новой программы искусственного интеллекта при автоматическом определении степени сколиоза и измерении угла Кобба на фронтальных рентгенограммах.

Материалы и методы. Всего исследовано 114 рентгенограмм на предмет соответствия измерений угла Кобба, выполняемых автоматически программой искусственного интеллекта и рентгенологом с использованием метода Бленда–Альтмана в программе Microsoft Excel. Кроме того, были проведены клинические испытание точности системы с использованием ограниченных данных (120 рентгенограмм). Точность системы в определении степени выраженности сколиоза оценивали по показателям чувствительности, специфичности, точности и площади под ROC-кривой.

Результаты. Больше согласованности в измерениях угла Кобба, вычисляемых программой искусственного интеллекта и рентгенологом, найдено в группах сколиоза I и II степени. Только в 2,8% случаев наблюдалась клинически значимая разница в измерении углов Кобба (вариабельность >5°). Показатели диагностической точности, полученные в ходе ограниченного клинического исследования в городской Мариинской больнице (Санкт-Петербург), также подтвердили надёжность системы: чувствительность составила 0,97, специфичность — 0,88, точность (общая валидность) — 0,93, а площадь под ROC-кривой — 0,93.

Заключение. В целом, программа искусственного интеллекта может автоматически точно определять степень выраженности сколиоза, а также измерять углы искривления позвоночника на фронтальных спондилограммах.

Ключевые слова: сколиоз; искусственный интеллект; позвоночник.

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用脊柱正面 X 光片自动诊断脊柱侧弯的新型智能系统：准确度、优势和局限性

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摘要

论证。脊柱侧弯是最常见的脊柱畸形之一，通常使用 Cobb 方法正面 X 光片进行诊断。基于人工智能的自动测量方法弥补了标准方法的许多不足，可以大大节省放射科医生的时间。

目的是分析一种新的人工智能程序在通过自动测量正面 X 光片上的 Cobb 角来评估脊柱侧弯程度方面的准确度和优缺点。

材料和方法。共检查了 114 张 X 光片，以确定人工智能软件自动测量的 Cobb 角与放射科医生使用 Microsoft Excel 中的 Bland-Altman 方法测量的 Cobb 角是否一致。此外，还使用有限的数据（120 张 X 光片）进行了临床准确度测试。通过灵敏度、特异性、准确度和 ROC 曲线下面积评估了该系统在确定脊柱侧弯严重程度方面的准确度。

结果。I度和II度脊柱侧弯组中，人工智能程序和放射科医生计算出的 Cobb 角测量值更加一致。只有 2.8% 的病例在 Cobb 角测量值上存在显著的临床差异（差异大于 5°）。在 Mariinsky City Hospital（圣彼得堡）进行的有限临床试验中获得的诊断准确度值也证实了该系统的可靠性：灵敏度为 0.97，特异性为 0.88，准确度（总体有效性）为 0.93，ROC 曲线下的面积为 0.93。

结论。一般来说，人工智能程序可以自动准确地确定脊柱侧弯的严重程度，并利用正面 X 光片测量脊柱弯曲的角度。

关键词：脊柱侧弯；人工智能；脊柱。

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INTRODUCTION

Scoliosis is a common spinal pathology that can affect any age group. It is usually defined as a lateral spinal curvature in the coronal plane with an angle of ⩾10° and torsion of the vertebral bodies and their posterior elements. Scoliosis is mainly diagnosed based on frontal radiographs. Cobb's method is considered the gold standard method to measure the scoliosis angle [1-8]. In recent years, many researchers have actively explored the use of artificial intelligence (AI) for evaluating scoliosis on different imaging modalities to objectify scoliosis evaluation and decrease intra- and interobserver measurement variability of Cobb's method [9–14].

In this study, a new program based on machine learning was developed. In the first stage of system development, an artificial neural network was trained so that it can identify vertebral bodies automatically. Accordingly, 1,000 images were selected from the database (XrScl) [15]. Vertebral bodies in each image were marked by identifying their boreder susing four reference points, and all thoracic and lumbar vertebrae found on each image were numbered. After the training, the network could independently define the vertebral bodies and their numbers. In the second stage, Cobb's angle was measured automatically, and scoliosis grade was determined automatically by the algorithm. Three methods can be used to measure Cobb's angle using the automatic system: (1) the classical Cobb's method, where the scoliosis angle is measured between the upper and lower endplates of the upper and lower end vertebrae (EV), respectively; (2) the method which is used in practice by radiologists (at Mariinsky City Hospital), where the scoliosis angle is constructed between the maximally inclined upper or lower endplates of the EV, and (3) the method of middle lines, in which the scoliosis angle is constructed between the lines drawn along the midpart of the vertebral bodies of the EV. The accuracy of the new automatic system was tested in measuring Cobb's angle and in defining the scoliosis grade**.**

STUDY AIM

To analyze the accuracy, advantages, and disadvantages of a newly developed AI program for automatic diagnosis of scoliosis and measurement of Cobb's angle on frontal spinal radiographs.

MATERIALS AND METHOD

Study Design

This is a diagnostic accuracy study.

Study Description and Statistical Analysis

To assess the reliability of the program in measuring Cobb's angle, 114 digital spinal radiographs and chest X-ray (CXR) images, were selected from the database XrScl *(test set 1)* [15]. This database includes >2,500 radiographs; thus, we could use different sets of images for the training and evaluation of the system. The agreement of Cobb's angles measured by the new automatic program and the radiologist was tested using the Blant–Altman method on Microsoft Excel. The mean difference between the two methods ("bias") and 95% limits of agreement (2 standard deviations [SD]) was calculated. Only the angles that were obtained by both the radiologist and the AI system were compared.

To test the possibility of using the new system in medical practice, a limited clinical test was conducted in Mariinsky City Hospital. For this study, 120 radiographs were collected from the archive of Mariinsky City Hospital and G.A. Albrecht Federal State Budgetary Research Center *(test set 2).* The reliability of the system in defining the scoliosis grade was tested by calculating sensitivity as TP/(TP + FN), specificity as TN/(TN + FP), accuracy as (TP + TN)/(TP + TN + FP + FN), and area under the receiver operating characteristic curve (ROC AUC), where TP, TN, FP, and FN indicated true positive, true negative, false positive, and false negative, respectively.

The radiographs in data sets 1 and 2 were evaluated by two radiologists, one with more than 25 years of experience and the other of more than 9 year-experience.

RESULTS

Study Subjects

In *test set 1*, the radiographs were distributed into four severity groups (according to Russian Federation Law No. 565 [16]) as follows: grade I (5°–10°, 16%); grade II (11°–25°, 15%); grade III (26°–50°, 16%), and grade IV (>50°, 16%). A normal group (grade 0) was added to this classification (<5°, 37%). Moreover, 179 angles which ranged from 5.1° to 91.3°were found by both the radiologist and the system.

For the limited clinical test of the system, *test set 2* was divided into normal or pathologic (with scoliosis) in equal groups (60 radiographs for each). The images with scoliosis were evenly distributed into four grades from 1 to 4 (15 studies for each grade).

Primary Findings

The agreement of Cobb's angle measurements between the system and the radiologist was found mostly in grade 1 and 2 scoliosis, with an average measurement difference of –0.10 and 0.46 and SDs of 1.29 and 1.73, respectively. Angles measured by the two methods differed by <4.5° in 95% of cases in all scoliosis grades, except for the group with grade 3 scoliosis, where the 95% of the variability (limits of agreement) ranged from –6.60° to 7.85°. The largest SD (3.69°) was found also in this group. The results of statistical data analysis for each scoliosis grade are presented in Fig. 1 and 2 (Bland–Altman plots) and Table 1. Only 2.8% of the results were clinically unsatisfying with an angle variability of >5°.

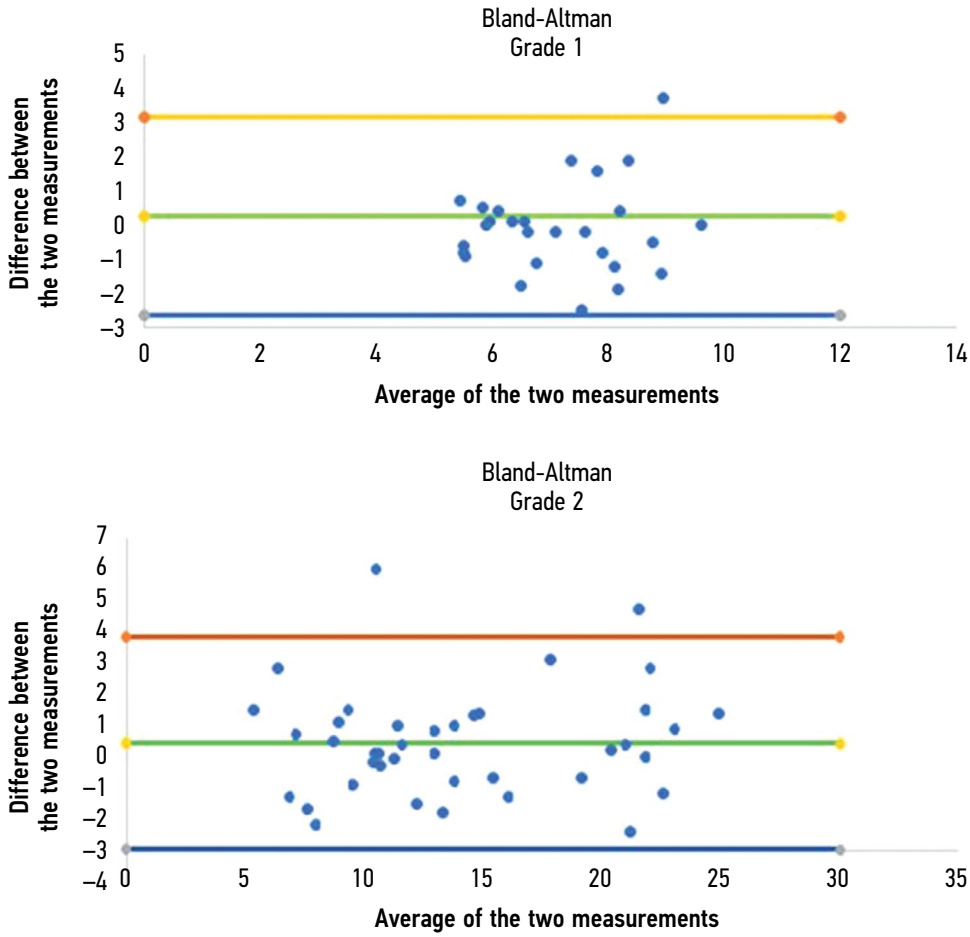

Fig. 1. Results of the Bland–Altman method. Agreement between measurements of the two methods in radiographs with grade 1 and 2 scoliosis.

The diagnostic accuracy metrics of the limited clinical test in Mariinsky City Hospital using *(test set 2)* also proved the reliability of the system in defining the scoliosis grade, with a sensitivity of 0.97, specificity of 0.88, accuracy (general validity) of 0.93, and ROC AUC of 0.93 (Fig. 3). For each study, the average analysis time of the image by the newly proposed system was 5 s. These results confirm the effectiveness of the system in determining the scoliosis grade.

DISCUSSION

Summary of Primary Findings

The bulk of this work was performed in a hospital where adolescents are screened for scoliosis, as part of multiple examinations for medical commissions, to determine whether adolescents match the criteria for army enlistment. Thus, radiographs *in test set 1* and *test set 2* were divided according to the severity classification included in Federal Law No. 565, where any small curves with angles <10° are considered grade 1 scoliosis [16]. The new automatic system for evaluating scoliosis on digital radiographs can help radiologists to define the scoliosis grade and measure the curve's angle, particularly in situations such as screening for scoliosis and at times of heavy workload in outpatient clinics. In these situations, radiologists can use the program as an objective tool, increasing the accuracy of scoliosis evaluation on frontal radiographs because the interobserver variability can

Table 1. Statistical parameters for evaluating the agreement between the two methods

Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Mean difference	–0.10	0.46	0.62	0.00
Standard deviation	1.29	1.73	3.69	2.32
Upper limit of agreement	2.43	3.84	7.85	4.56
Lower limit of agreement	–2.63	–2.93	–6.60	–4.55

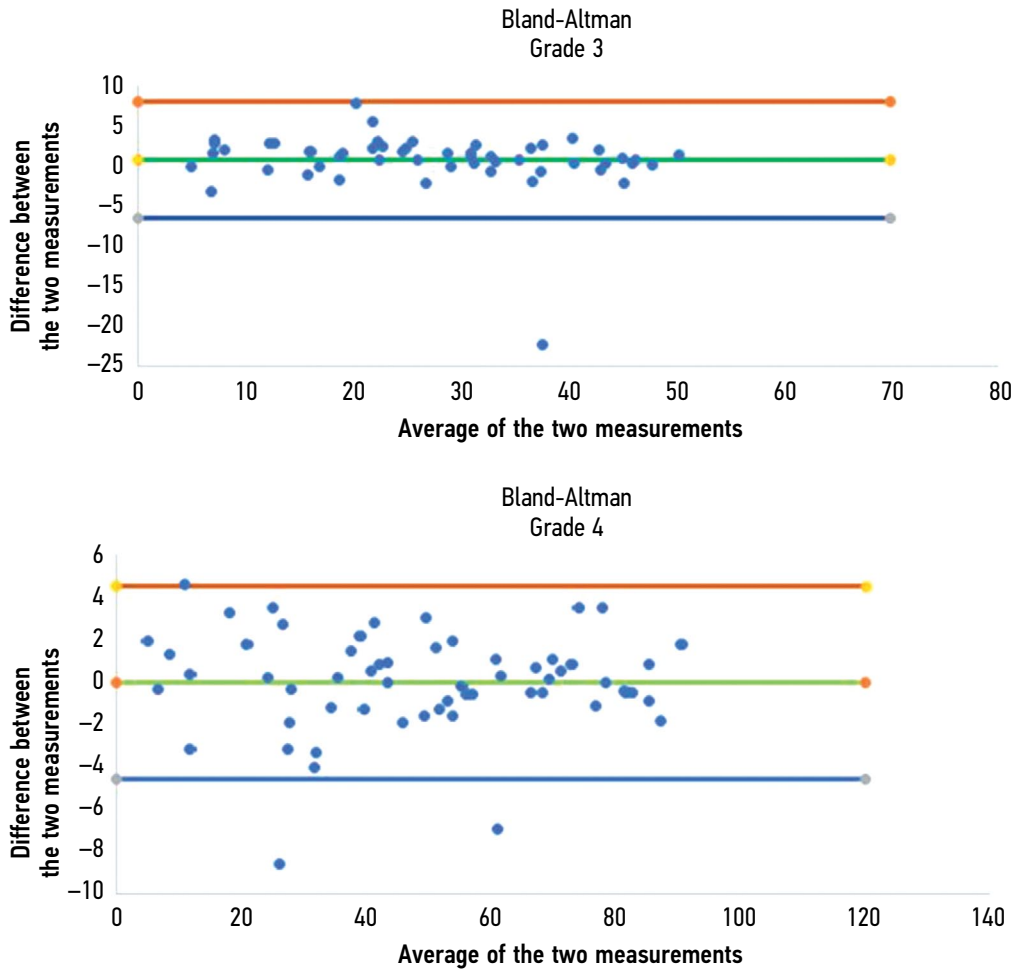

Fig. 2. Results of the Bland–Altman method. Agreement between measurements of the two methods in radiographs with grade 4 scoliosis.

be avoided if radiologists use the same instrument. Moreover, it can significantly save the radiologist's time. In addition, Cobb's angles measured by the system were acceptable, with no significant clinical variability in most of the evaluated curves. Fig. 4 shows an example of how the system works.

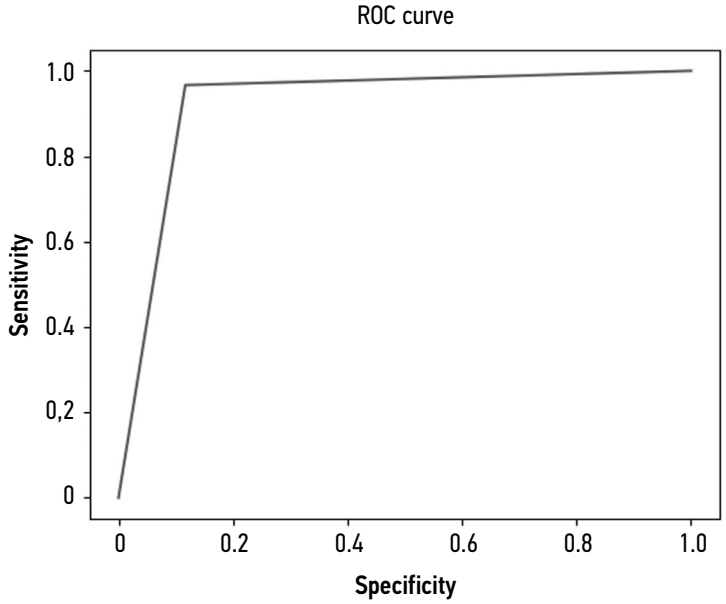

Fig. 3. ROC curve confirms the accuracy of the new AI program in defining the scoliosis grade.

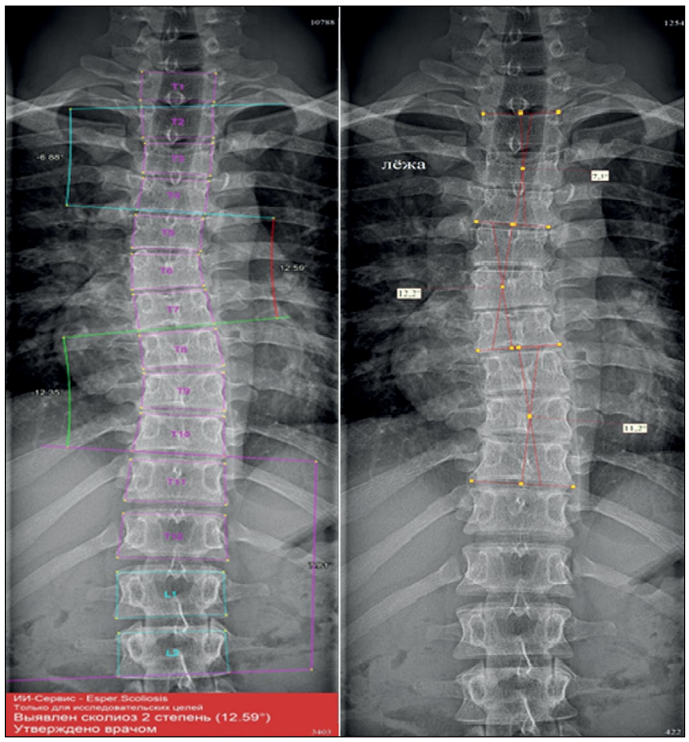

Fig. 4. X-ray image showing grade 2 scoliosis. Analysis by the system (left) and by the radiologist (right). The radiologist did not measure the thoracolumbar curve as the lower EV is not shown in the image.

Discussion of Primary Findings

The proposed program provides multiple options for the radiologist to measure Cobb's angle in three different methods. These options can help radiologists, particularly if he/she does not use the standard Cobb's angle measurement method (such as that used in Mariinsky City Hospital when screening for scoliosis). The step of choosing the most tilted endplate is time consuming and can cause interobserver measurement variability. Therefore, the ability to objectively and automatically define the most tilted endplates, which form the largest angle in one curve, would be beneficial for the radiologist.

In addition, when using the program, the radiologist can change vertebral markings made by the system automatically. This is very essential to overcome any errors in vertebral markings that can cause a false final result. Further analysis of the results showed that the inaccurate marking of vertebral bodies and their borders predominantly led to less accurate results of angle measurement and scoliosis grade definition. This was mainly seen when evaluating scoliosis in poor-quality images and CXR images. The borders of the midthoracic vertebrae in CXR images usually are not seen posterior to the mediastinum. Multiple normal CXR images (grade 0, defined by the radiologist) were recognized by the system as grade 1 scoliosis because of detecting an FP curve (proximal or midthoracic curve) (Fig. 5). Other common error was also seen in marking the borders of L5 vertebral body

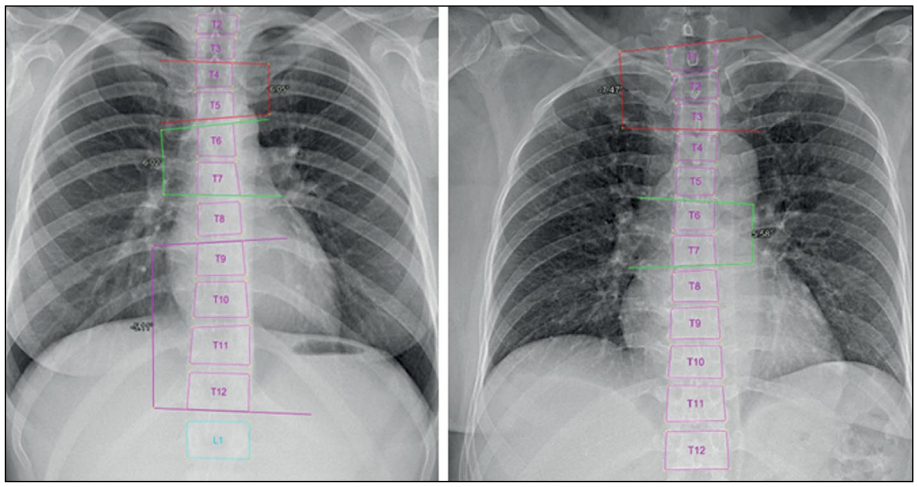

Fig. 5. Errors in vertebral markings on radiographs with grade 0 (normal). In CXR images, poor definition of the vertebral borders may lead to false measurements.

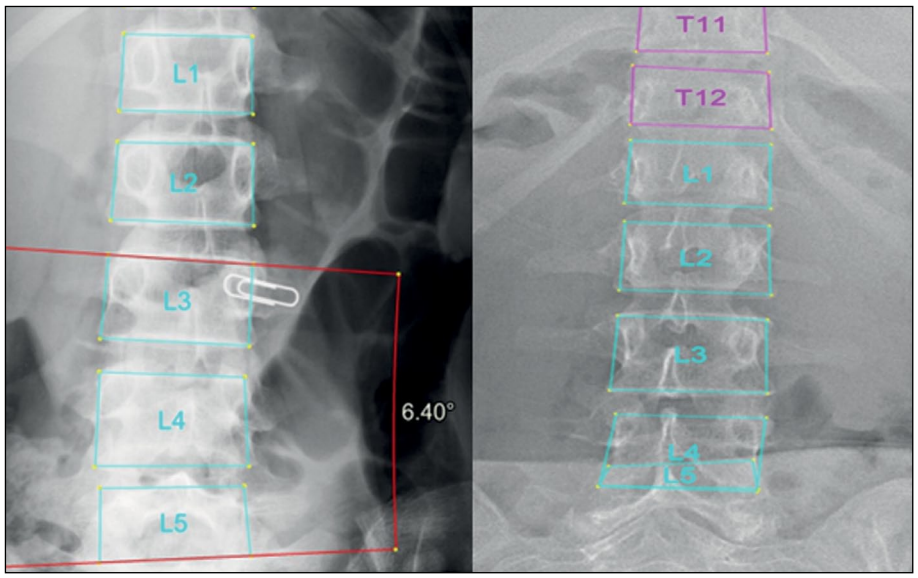

Fig. 6. Errors in vertebral markings on radiographs with grade 0 (normal). Errors in defining the L5 vertebral body may lead to false positive curve detection (left).

(Fig. 6). The adjacent bony structures (adjacent sacrum and iliac bones) limit the definition of L5 borders, particularly its lower endplate.

Regarding errors in evaluating images with group 0 scoliosis, most of the measurements by the AI system resulted in angles with >5° but very close to it. However, such minimal variability in measurements between the system and the radiologist led to a change in the grade from 0 to 1 (Fig. 7). The majority of such angles (70%) were found in the range of 5°–6°, as shown in the pie chart (Fig. 8).

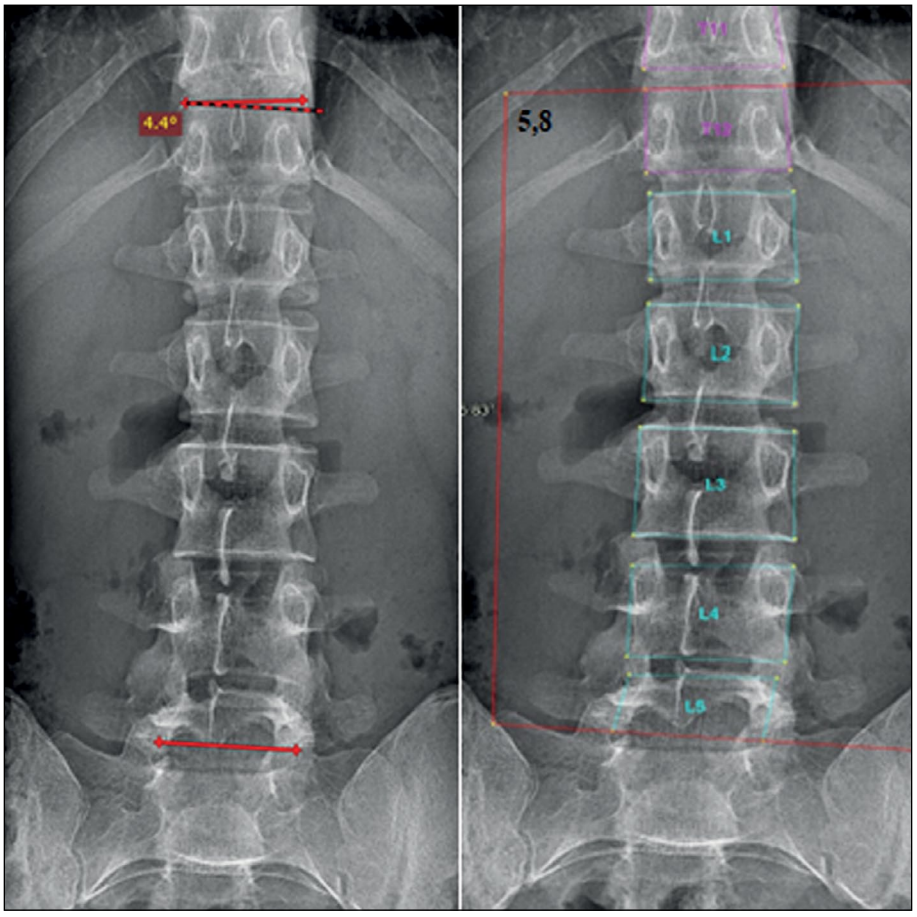

Fig. 7. Errors of the system in evaluating images with grade 0 scoliosis. Cobb's angles measured by the radiologist (left) and the AI system (right). Measurement variability is not significant (1.4°); however, the scoliosis grade is 0 by the doctor and 1 by the system.

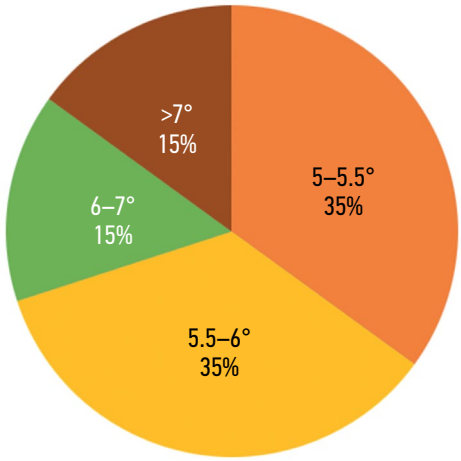

Fig. 8. Distribution of angles measured by the AI system on normal X-ray images; 70% of the 5°–6° range.

In addition, in most cases, the system accurately evaluated radiographs with severe scoliosis (grades III and IV), although errors in vertebral detection and numbering or errors in measuring Cobb's angle sometimes were noted. Grade IV scoliosis is characterized by maximum vertebral rotation, with displacement of the pedicle beyond the midline and deformation of the vertebral body. Thus, the usual shape of the vertebra changes, and the edges of its body become less defined (Fig. 9).

In some cases, the accuracy of the system in diagnosing grade III or IV scoliosis was not affected by significant measurement variability of Cobb's angle between the system and the radiologist. Usually, these errors had been mainly found when assessing a nonprimary (secondary) curvature (Fig. 10).

As another limitation, the proposed AI program can only be used to evaluate frontal radiographs. This system cannot evaluate scoliosis on sagittal radiographs and other modalities such as CT.

Most of the abovementioned errors of the system can be fixed by the radiologists when they are using the system because they are provided with an access to change vertebral markings to get more accurate results. The time needed to obtain the results even if the radiologist must make changes in the automatic vertebral markings done by the system was still shorter than getting the results through the usual Cobb's method. In addition, in the future, we believe that vertebral marking will be more accurate when providing the network with a much larger dataset.

CONCLUSION

The automatic system can be used as a reliable objective tool to define the scoliosis grade and measure Cobb's angle on frontal spinal radiographs, significantly saving the radiologist's time. Major factors that can affect the results of the program are the quality of the radiographs and accuracy of the vertebral markings. Those factors can

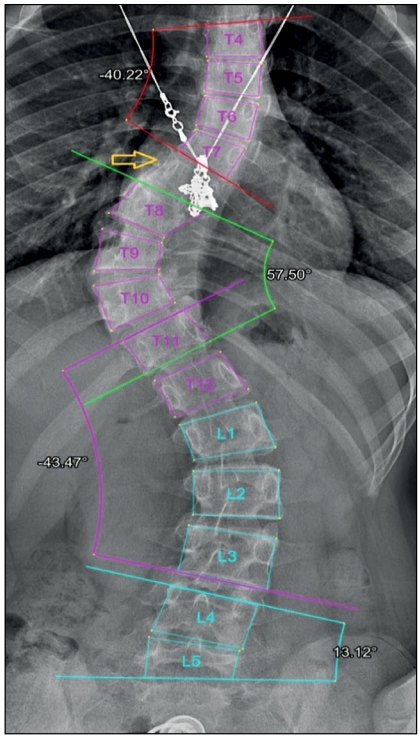

Fig. 9. Specifications of vertebral marking in radiographs with grade 3 and 4 scoliosis. Errors in detection and numbering of vertebrae caused by the unusual shape of the vertebrae (yellow arrow).

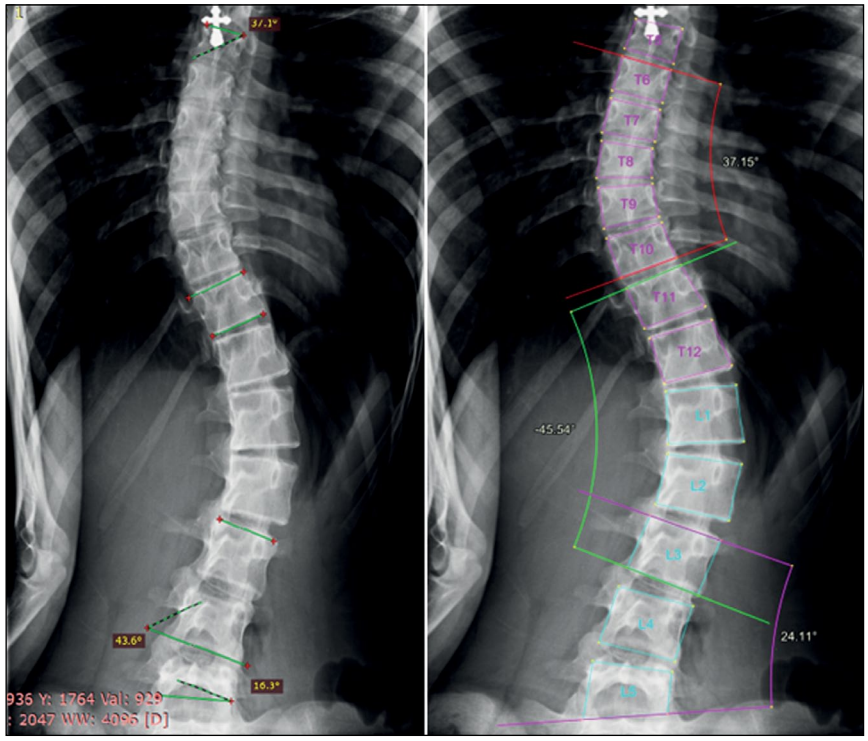

Fig. 10. Grade 3 scoliosis diagnosed by the radiologist (left) and the AI system (right). Significant variability in measuring the lumbar curve (7.8°) did not affect the overall scoliosis grade.

be overcome in practice when using the program, as the radiologist can correct the vertebral markings and obtain the best results.

ADDITIONAL INFORMATION

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Priority Radiomic Parameters for Computed Tomography of Head and Neck Malignancies: A Systematic Review

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ABSTRACT

BACKGROUND: Radiomics is the newest and most promising direction in modern radiographic diagnostics. The number of head and neck cancer studies employing radiomics is increasing annually. A systematic review of recent publications (2021–2023) on computed tomography (CT) of head and neck malignancies was performed.

AIM: To present systematized data on parameters for radiomic analysis for head and neck malignancies identified by CT data.

MATERIALS AND METHODS: The literature search was carried out in PubMed. The basic characteristics of the selected articles were extracted, and their quality was assessed using RQS 2.0 and the modified QUADAS-CAD questionnaire. The reproducibility level of radiomic parameters selected for predictive models in different studies was assessed. Eleven articles were selected for the review. In most cases, a high risk of systematic error associated with data imbalance in terms of demographic parameters and level of pathologies was noted.

RESULTS: The range of RQS 2.0 scores for the included articles varied from 19.44% to 50.00% of the maximum possible score. The decreasing research quality was mainly caused by the lack of external result validation (73% of the analyzed articles) and data accessibility and transparency (82%). Inter-study reproducibility of radiomic parameters was low owing to the wide variety of techniques used for image acquisition, image post-processing, extraction, and statistical processing of radiomic parameters.

CONCLUSION: A set of stable radiomic parameters must be successfully introduced into clinical practice. The standardization of radiomics method and creation of an open radiomics database are necessary for this purpose.

Keywords: radiomics; head and neck cancer; radiomic parameters.

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Приоритетные параметры радиомического анализа для компьютерной томографии при злокачественных новообразованиях головы и шеи: систематический обзор

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АННОТАЦИЯ

Обоснование. Радиомика — новейшее и многообещающее направление современной лучевой диагностики. Число исследований злокачественных новообразований головы и шеи с помощью этого метода увеличивается с каждым годом. Мы провели систематический обзор новейших публикаций (2021–2023) по злокачественным новообразованиям головы и шеи, выполненным на основе компьютерной томографии.

Цель — систематизация данных по используемым параметрам радиомического анализа при раке головы и шеи, выявленным по данным компьютерной томографии.

Материалы и методы. Поиск статей осуществлялся в базе PubMed. Произведены извлечение базовых характеристик отобранных статей и оценка их качества по RQS 2.0 и модифицированному опроснику QUADAS-CAD. Оценили уровень воспроизводимости радиомических параметров, отобранных для прогностических моделей, в разных исследованиях. Для обзора отобрано 11 статей. В большинстве случаев отмечался высокий риск систематической ошибки, связанный с несбалансированностью выборки по демографическим параметрам и уровню патологий.

Результаты. При оценке качества радиомики диапазон баллов для исследованных статей изменяется от 19,44% до 50,00% максимально возможной суммы. Основные проблемы, влекущие за собой снижение качества исследований, обусловлены отсутствием внешней валидации результатов (73% проанализированных статей), а также недоступностью или непрозрачностью исследовательских данных (82%). Воспроизводимость радиомических параметров между исследованиями низкая из-за большого разнообразия используемых методик получения и постобработки изображений, а также извлечения и статистической обработки радиомических параметров.

Заключение. Обсуждается необходимость выделения базового блока устойчивых радиомических параметров для внедрения метода в клиническую практику, что возможно сделать только при стандартизации методов радиомики и создания открытой базы радиомических данных.

Ключевые слова: радиомика; злокачественные образования головы и шеи; радиомические параметры.

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头颈部恶性肿瘤计算机断层扫描的优先放射组学分析参数：系统综述

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摘要

论证。放射组学是现代放射治疗诊断中最新、最有前途的领域。使用这种方法对头颈部恶性肿瘤进行检查的数量每年都在增加。我们对基于计算机断层扫描的头颈部恶性肿瘤最新出版物（2021–2023 年）进行了系统综述。

目的是系统整理通过计算机断层扫描检测到的头颈部癌症的放射组学分析参数数据。

材料和方法。这些文章在 PubMed 数据库中进行了检索。我们提取了所选文章的基线特征，并使用 RQS 2.0 和修改后的 QUADAS-CAD 问卷对其质量进行了评估。我们评估了不同研究中预后模型所选放射组学参数的可重复性水平。我们选择了 11 篇文章进行审查。在大多数情况下，由于人口统计参数和病理学水平的取样不平衡，系统误差的风险很高。

结果。在评估放射组学的质量时，所分析文章的得分范围从最高可能得分的 19.44% 到 50.00% 不等。导致研究质量下降的主要问题是研究结果缺乏外部验证（占所分析文章的 73%），以及研究数据无法获取或缺乏透明度（占 82%）。由于所使用的图像采集和后处理技术种类繁多，以及对放射组学参数的提取和统计处理，不同研究之间放射组学参数的可重复性很低。

结论。讨论将该方法引入临床实践的基本稳定放射组学参数分配的必要性，这只有在放射组学方法标准化和建立开放的放射组学数据库的情况下才能实现。

关键词：放射组学；头颈部恶性肿瘤；放射组学参数。

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BACKGROUND

Radiomics is the latest modern medicine innovation. This technique aims to improve the diagnostic quality using radiomic features, i.e., medical image parameters invisible to the human eye [1]. Radiomics analysis is a rapidly developing area in radiology [2]. This approach is expected to be widely used as an additional tool for assessing the prognosis and determining the treatment strategy.

Several thousand radiomic parameters [3] are currently classified into three major groups:

- Curve parameters describing image properties
- Texture parameters (gray-scale matrices) representative of pixel ratios
- Shape parameters

Several subgroups were observed within each group of radiomics features.

Dozens to thousands of parameters were used in studies, depending on whether radiomic features are extracted manually or via machine learning algorithms [3, 4]. Furthermore, approaches to assigning specific parameters to major groups vary. In some cases, all groups of features can be included in varying proportions, whereas only texture parameters are included in others, excluding shape parameters. Currently, the number and composition of radiomic features during manual extraction (handcrafted features) are primarily determined using the selected analysis software and per the researcher's perception.

The set of radiomic features should be standardized for the potential use of radiomics as an additional diagnostic tool in clinical practice [5, 6]. Features selected for a wide practical use should ensure inter-study reproducibility. However, these studies differ in various ways, including the structures examined, the type of prognosis, the method of obtaining and processing images, and the statistical analysis methods of radiomic features.

STUDY AIM

To organize data on the used radiomic parameters in head and neck cancer detected based on computed tomography (CT) findings. Head and neck cancer, including throat, larynx, nasal cavity, paranasal sinus, and oral cavity malignancies [7], was selected as one of the most common cancers [8] requiring multimodal diagnostics, beginning with CT [9–11].

STUDY OBJECTIVES

The study objectives are as follows:

1. To review the most recent publications (2021–2023) on radiomics in head and neck cancer using CT findings, including an assessment of distribution by study objectives, methods used, and article quality based on modern radiomics standards.

2. To assess the intra- and inter-study reproducibility (robustness) of radiomic features.

3. To compare the most recent publications with previous studies.

MATERIALS AND METHODS

Search Strategy

The search was performed in PubMed. The search terms were in English only. The search period—November 15, 2020, to June 1, 2023—was selected so that the reference lists of our and other studies would not overlap for the most part [12–14].

The search terms included the following:

"head and neck neoplasms" [MeSH Terms] AND ("artificial intelligence" [MeSH Terms] OR ("artificial" [All Fields] AND "intelligence" [All Fields]) OR "artificial intelligence" [All Fields] OR ("deep learning" [MeSH Terms] OR ("deep" [All Fields] AND "learning" [All Fields]) OR "deep learning" [All Fields]) OR ("machine learning" [MeSH Terms] OR ("machine" [All Fields] AND "learning" [All Fields]) OR "machine learning" [All Fields]) OR ("neural networks, computer" [MeSH Terms] OR ("neural" [All Fields] AND "networks" [All Fields] AND "computer" [All Fields]) OR "computer neural networks" [All Fields] OR ("neural" [All Fields] AND "network" [All Fields]) OR "neural network" [All Fields]) OR ("radiomic*" [All Fields]) OR "radiomic features*" [All Fields]) OR ("radiomics features*" [All Fields]) AND ("node*" [All Fields] OR "lymph node*" [All Fields] OR ("nodal" [All Fields] OR "nodally" [All Fields] OR "nodals" [All Fields]) OR "metastas*" [All Fields])

Inclusion criteria: Original research articles

Exclusion criteria: Reviews, meta-analyses, and case reports on radiomics in head and neck cancer

The study design adheres to the Preferred Reporting Items for Systematic reviews and Meta-Analyses [15].

Two experts independently reviewed the article titles and abstracts found using the search terms. This review identified several articles for full-text analysis. The third expert made the final decision in case of disagreement over including an article in the analysis. Further review of reference lists of included articles to identify eligible publications (snowballing) was not performed.

Data Extraction and Article Quality Assessment

The following information was extracted from the selected full-text articles:

- Original author and corresponding author
- Article title, year of publication, and DOI
- Journal and impact factor
- Country where the study was performed
- Study objectives
- Study design (prospective/retrospective, single-center/multicenter)
- Inclusion/exclusion criteria
- Number, sex, and age of patients
- Tumor site and type

- Total number of extracted radiomic features
- Assignment of radiomic features to classes (assessed or not assessed); if assessed, the following classes were analyzed:
  - Shape parameters (2D and 3D)
  - Type 1 parameters
  - Type 2 parameters: texture parameters with several subgroups (Gray Level Co-occurrence Matrix [GLCM], Gray Level Run Length Matrix [GLRLM], Gray Level Size Zone Matrix [GLSZM], Neighboring Gray Tone Difference Matrix [NGTDM], and Gray Level Dependence Matrix [GLDM])
- Radiomic feature analysis method:
  - Machine learning (used or not used)
  - For handcrafted radiomics, statistical methods were used for the selection of radiomic features
- Number of radiomic features selected by the authors as prognostically valuable and their significance.

Two approaches were used to assess the quality of selected articles: the Radiomics Quality Score 2.0 (RQS 2.0) [16], specific to radiomics studies, and Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [17, 18], commonly used in medical studies and has been modified for computer aided detection (QUADAS-CAD).

Analysis of Radiomic Features

Radiomic features identified with prognostic value were extracted from each selected article. Features extracted from both original and post-processed images were analyzed. Various statistical methods, including machine learning, regression analysis, analysis of variance, resampling, and assessment by intraclass correlation coefficient, were used to select features to be considered. If several hypotheses were evaluated in a study, radiomic features were extracted separately for each hypothesis. Two studies provided statistics for the robustness of all extracted radiomic parameters (the intraclass correlation coefficient [19] and the *P*-level for the analysis of variance [20]), without reducing the number of parameters. In such cases, the most robust radiomic parameters were independently selected for our analysis, based on the available data.

Moreover, the inter- and intra-study overlap of significant radiomic feature sets was assessed for different endpoints.

RESULTS

Literature Search and Selection of Articles

The initial search identified 804 publications. After reviewing the titles and abstracts, 762 publications were excluded as irrelevant (other types of cancer were investigated, radiomics analysis was not used, etc.). Forty-two publications were included for analysis after reviewing the titles and abstracts (Fig. 1). Of these, 11 studies were included in the final analysis, whereas 31 were excluded (11 studies used magnetic resonance imaging, 2 used ultrasound examination, 7 focused on thyroid cancer,

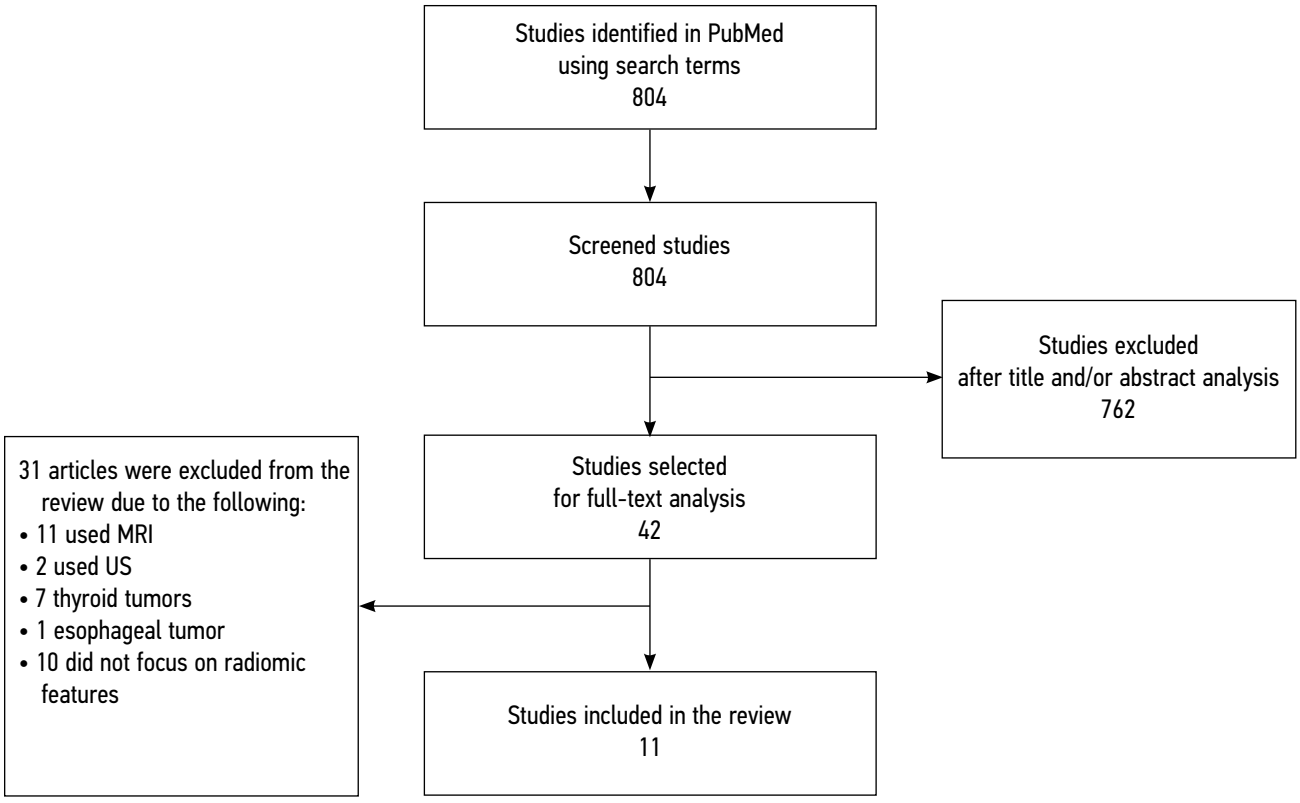

Fig. 1. Flow chart of systematic literature search flow chart
Abbreviations: MRI, magnetic resonance imaging; US, ultrasound.

1 focused on esophageal cancer, and 10 did not specify the radiomic parameters used).

Basic Characteristics of Articles

The basic characteristics of articles selected for the review are summarized in Appendix 1. Of these 11 studies, five were performed in China [19, 21–24], three in Europe (of them one in Italy) [25], and one each in Portugal/Austria/Germany [26], the Netherlands [27], the USA [28], Canada [20], and Thailand [29]. Articles with the highest ratings were published in *Cancers* (impact factor 6.575) [20] and *European Radiology* (impact factor 6.020) [21]. All studies were retrospective. Eight were single-center [20–23, 25, 27–29] and three were multicenter [19, 24, 26] studies.

Radiomic features were used to predict overall survival [25, 26, 29], progression-free survival [25, 29], distant disease-free survival [28], risk of locoregional recurrence [25, 26, 28], and risk of distant metastases [26]; to preoperatively predict lymph node involvement [21, 23, 24]; and to classify enlarged cervical lymph nodes [22]. One study examined the relationship between the robustness of radiomics parameters and the quality of radiomics models [18]. Another investigated the differences in radiomic features depending on the tumor site [20]. One used additional data to validate a previously created model [27].

Quality of Included Articles According to RQS 2.0

The quality assessment of articles using the specialized radiomics analysis scoring system RQS 2.0 is summarized in Appendix 2. The scores for the reviewed articles range from 7 (19.44%) [20] to 18 (50.00%) [22], with a maximum score of 36 (100%) points; the mean and standard deviation are 10 and 4, respectively.

In 7 (64%) of 11 cases, the imaging protocol was well-documented [21–26, 28]. Five studies (45%) considered the effects of segmentation (resegmentation by two researchers, segmentation algorithms, random noise) on the extraction of radiomic features [22, 23, 25, 29, 30]. Teng et al. [20] assessed the reliability of radiomic features in multicenter studies and the effects of various features on the overall reliability of models. None of the reviewed studies evaluated the robustness of radiomic features against temporal variations, such as organ movement or increased/decreased organ size. Ten (91%) studies examined model retraining and reduced number of radiomic features to select the most significant ones [19, 21–29]. Eight (73%) studies reported that models were developed using pooled sets of radiomic and clinical features and compared mixed, radiomic, and clinical models [22, 24–30]. All studies (100%) provided significance and discrimination quality metrics (area under the curve [AUC] and *P*-level, including those obtained during data resampling) [31]. The obtained radiomic models were rarely validated. Specifically, validation was performed in as few as three studies (27%) [20, 23, 26], with only one (9%) using data from another study site [26]. Data transparency was also limited, with only two studies providing open access to images [25] and extracted radiomic features [18].

Quality of Included Articles Based on QUADAS-CAD

The risk of bias according to QUADAS-CAD is summarized in Tables 3 and 4 [17]. The overall risk of bias was high in 6 of 11 reviewed articles (54.5%) [19, 20, 25, 26, 28, 29]. Five (45.5%) of 11 articles had a low risk of bias [21–24, 27]. Seven (64%) studies reported a high risk of bias due to data imbalance [19, 20, 23, 25, 26, 28, 29], and four (36%) reported low [21, 22, 24, 27]. In most cases, this risk was caused by a sample imbalance in terms of demographics and pathology. Machine learning was used in six studies [19, 20, 22, 24, 26, 28]; thus, some questions in D2 block are only applicable to them. The risk of bias due to the selected method for the use and interpretation of index tests was high in four studies (36%) [19, 20, 26, 29], moderate in one (9.5%) [28], and low in six (54.5%) [21–25, 27]. The risk of bias from the reference standard assessment was low in most cases (64%) [19, 21–24, 27, 29]. In some cases, the expertise level of physicians assessing the reference values was unclear; therefore, the risk of bias was considered high (27%) [28] or moderate (9%) [20, 25, 26]. The risk of bias due to data heterogeneity was high in three studies (27%) [20, 25, 28] and low in eight (73%) [19, 21–24, 26, 27, 29]. In some cases, ambiguous assessment results were due to a detailed level when describing data analysis methods.

Methods Used in the Studies

The number of extracted radiomic features ranges from 36 [20] to 5,486 [19]. Five articles included detailed information on the distribution of extracted radiomic features [22, 23, 25, 26, 28].

Six studies used machine learning for radiomics analysis [19, 20, 22, 24, 26, 28]. The remaining five studies used regression analysis [25, 29], analysis of variance (ANOVA) [23], intraclass correlation coefficient (ICC) [29], data resampling [28], and one-way tests for pairwise comparison of features (Student's *t*-test, Mann–Whitney *U* test, chi-squared test, Fisher's exact test) to assess the significance of radiomic features [21, 23, 27].

The number of selected features in studies ranges from 2 [25, 27] to 19 [26]. Two articles did not select the most significant features; instead, they reported the corresponding statistics for each extracted feature (ICC) [19] and the percentage of repeated features in replicates [28].

Feature Reproducibility Analysis

In 11 studies, 191 radiomic features considered valid for prognostic models were selected (see Appendix 1), including 47 first-order features. Of these, the same feature is used in two different studies with five (11%) cases; in the remaining cases, features do not overlap between studies. Shape parameters include 25 radiomic features. Of these, the same feature is used in two different studies with five (20%) cases. Moreover, the same feature is used in three different studies in two (8%) cases. In the remaining cases, features do not overlap between studies. Second-order features include

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Table 1. Quality Assessment of Diagnostic Accuracy Studies for Computer Aided Detection

Domain	Questions	Franzese C., 2023	Gonçalves M., 2022	Zhao X., 2023	Teng X., 2022	Zhang W., 2022	Yang G., 2022	Intarak S., 2022	Morgan H., 2021	Li J., 2021	Liu X., 2021	Zhai T., 2021
D1	Were the data (training and test sets) balanced in terms of the target pathology severity (including its absence)?	No	No	Yes	Unclear	Yes	Yes	No	No	Yes	No	Yes
	Were the data (training and test sets) balanced in terms of demographic factors?	No	No	Yes	Unclear	Yes	No	No	Unclear	Yes	No	Yes
	Was the study free of needless exclusions?	Yes	No	Yes	Unclear	Yes	Yes	Unclear	Unclear	Yes	Unclear	Yes
D2	If a neural network was used, were the training and test data sets distinct or similar?	X	Yes	X	Unclear	Yes	X	X	Yes	Yes	Unclear	X
	If a neural network was used, was the size of each data set appropriate?	X	No	X	Yes	Yes	X	X	Yes	Yes	Yes	X
	If a pathology threshold was used, was it predefined?	Yes	X	Yes	X	Yes	Yes	No	Unclear	Yes	Unclear	Yes
	If a decision threshold was used (for AI), was it predefined?	X	X	X	X	X	X	X	Unclear	X	X	X
D3	Can the reference standard accurately classify the target condition?	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes
	Were the results for reference standards generated or validated with the required expertise level?	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes
D4	Were the results obtained in a transparent manner?	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
	Was the same reference standard used for all patient data?	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	No	Unclear	No	Yes

Table 4. Risk-of-bias assessment according to Quality Assessment of Diagnostic Accuracy Studies for Computer Aided Detection

Original author, year	D1	D2	D3	D4	Total score	Weight (%)
Franzese C., 2023	High	Low	Somewhat doubtful	High	High	2
Gonçalves M., 2022	High	High	Somewhat doubtful	Low	High	4
Zhao X., 2023	Low	Low	Low	Low	Low	10
Teng X., 2022	High	High	Low	Low	High	32
Zhang W., 2022	Low	Low	Low	Low	Low	6
Yang G., 2022	High	Low	Low	Low	Low	4
Intarak S., 2022	High	High	Low	Low	High	4
Morgan H., 2021	High	Somewhat doubtful	High	High	High	1
Li J., 2021	Low	Low	Low	Low	Low	15
Liu X., 2021	High	High	Somewhat doubtful	High	High	14
Zhai T., 2021	Low	Low	Low	Low	Low	6

119 radiomic features. Of these, the same feature is used in two different studies in one case (0.8%).

In two studies, radiomic features were completely reproducible between different models [23, 29]. In two more studies, radiomic features were not reproducible between different models [25, 28].

DISCUSSION

This review analyzed studies on radiomics analysis in head and neck malignancies based on CT findings performed between 2021 and 2023, focusing on a list of frequently used, reliable radiomic parameters. The reviewed publications used a wide range of approaches, from image acquisition and post-processing methods to software used for radiomic parameter extraction and statistical processing. Furthermore, creating a predictive radiomics model always requires reducing the number of radiomic parameters. Parameters are selected using different methods, from univariate statistical tests to machine learning; this is entirely up to the authors. The selected statistical methods for reducing the number of features also have a significant impact on the selection results of parameters. The most recent meta-analyses highlighted that the difficulty of summarizing and implementing individual successful practices remains a significant barrier in current radiomics [30].

Study Quality

When comparing previous systematic reviews of radiomic studies in head and neck malignancies [13, 32] and our new study, several methodological challenges persisting for a decade were encountered.

One of the major challenges in radiomic studies is the lack of validation of obtained radiomic models using external data. Only one of the reviewed studies validated data from another study site [33].

Another major challenge is the lack of data transparency and insufficient detailed description of analysis methods, preventing the reproduction of results of such studies. However, reproducibility of results is widely considered one of the fundamental criteria of scientific approach and the basis for practical implementation of a method [34].

Our conclusions are consistent with the findings of other systematic reviews. For example, all four identified reviews of studies evaluating head and neck cancer [12, 13, 32, 35] lacked result validation using external data. Moreover, Giannitto et al. [13] reported a lack of transparency of methodologies used in studies due to an inadequate description of the study conduct and a lack of assessment of the possible implementation of results in clinical practice. Guha et al. [12] revealed substantial heterogeneity of methodologies, making it difficult to generalize study findings.

The Image Biomarker Standardization Initiative (IBSI) is currently in progress [36]. Considering the detailed level in addressing the issues and numbers of community members involved, this initiative could be a significant step toward resolving the lack of transparency in radiomic analysis. The reproducibility and reliability of results can also be improved by appropriately designed clinical studies of intelligent technology-based algorithms [37].

Creating an open platform for radiomic studies will enable reporting negative results, which are not published in

peer-reviewed journals due to the so-called publication bias [38]. Minimizing the risk of bias is critically important when assessing the efficacy of radiomic analysis. Furthermore, Kocak et al.'s [39] meta-study made it possible to highlight issues caused by a largely retrospective design (95%, 142/149) and a lack of a reference test in a significant number of studies (44%, 66/149) [39].

The assessed method is based on radiomic parameters describing the relationships among voxels, 2D and 3D characteristics of malignancies, and other properties. Several thousands of these parameters are currently known; however, the consensus regarding the diagnostic value of each parameter and its various combinations is not yet established. The number of selected features in reviewed studies dramatically varies, ranging from a few to several thousands. Less than half of studies provide detailed descriptions of the groups of features representing various characteristics of malignancies. Three studies did not specify the radiomic parameters used in the models. Only one reviewed article examined the robustness of radiomic parameters in multicenter studies.

To promote the widespread use of prognostic radiomics models in clinical practice, priority parameters must be identified based on their robustness and reproducibility assessment. Radiomic parameters most used in prognostic models were selected. Our findings demonstrated that the reproducibility of radiomic parameters is extremely low due to the wide range of methodologies used. This is consistent with earlier studies suggesting that radiomic parameters might be random and non-reproducible [40]. Recommending a specific set of radiomic parameters for clinical use is difficult. Therefore, radiomic methods must be standardized, and recommended standards must be implemented. Consequently, a basic set of radiomic parameters can be created for the use of radiomic analysis in diagnostic imaging [41]. Standardization of radiomic analysis can also be achieved through efforts in the field of study protocol standardization and post-processing control standardization [42].

Limitations of Our Approach

Our study has several limitations inherent for systematic reviews. With the aim to provide the most comprehensive review of currently available studies of head and neck malignancies, this review includes studies of both primary and secondary tumors and histologically heterogeneous head and neck cancers.

The search was limited to PubMed and English publications, which may have reduced the number of identified studies.

Data imbalance was observed in all studies. Only pathological cases were included, while non-pathological cases were excluded. Moreover, data imbalance was also observed in demographics.

These limitations prevented comprehensive meta-analysis, allowing only qualitative synthesis with descriptive statistics. However, our study highlighted the major challenges of modern radiomics and the direction of future research in this area.

CONCLUSION

Radiomics is a rapidly evolving modern medicine area. Studies increasingly used radiomics analysis. Our findings revealed that major challenges in this area preventing the wide clinical use of this promising method include low transparency of studies and the absence of open-access databases and standardized approaches to radiomics studies. The fundamental objective of radiomics development is to adopt accepted standards for image acquisition and processing, as well as modeling strategies. Assessment tools for the risk of bias should be used during studies, such as QUADAS-2 or its versions modified for specific tasks, and recommendations should be considered for reducing these risks. Free access to radiomics data should be enabled, similarly to genetic studies. A set of robust radiomic parameters should be developed to use this method in clinical practice. The IBSI platform is an effective solution for the standardization of radiomics data and its open-access publication.

ADDITIONAL INFORMATION

Additional materials.

Supplement 1. Basic characteristics of articles.
DOI: https://doi.org/10.17816/DD623240-4214843

Suplement 2. Radiomics quality assessment according to RQS-2.0.
DOI: https://doi.org/10.17816/DD623240-4214842

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Authors' contribution. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept, conduct of the study and preparation of the article, read and approved the final version before publication. The contribution is distributed as follows: Yu.A. Vasilev, A.V. Vladzymyrskyy, O.V. Omelyanskaya — study concept, approval of the final version of the manuscript; R.V. Reshetnikov, I.A. Blokhin, O.G. Nanova — literature review, data analysis, writing the text of the article.

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Optimization of Magnetic Resonance Imaging of the Hand

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ABSTRACT

BACKGROUND: Magnetic resonance imaging is one of the leading imaging modalities of the musculoskeletal system. However, when imaging the hand, major problems in magnetic resonance imaging include the lack of specialized coils and reliable fixation devices for the hand, uncomfortable patient posture, motion artifacts, and small anatomical structures in the wrist. These factors inevitably lead to incorrect interpretation.

AIM: To improve the quality of magnetic resonance imaging of the hand by developing an approach to coil selection, scanning protocol, and hand positioning and fixation.

MATERIALS AND METHODS: A positioning device was developed to prevent hand movements. Two types of coils were evaluated. Magnetic resonance images were evaluated comparatively, as well as by a musculoskeletal radiologist.

RESULTS: A head coil is more appropriate when scanning the entire hand, for example, in rheumatic diseases. A knee coil is more appropriate when studying smaller anatomical structures (including the wrist) owing to a smaller field of view and higher resolution. Based on the obtained data, guidelines for the selection of scanning parameters, sequences, and coils for magnetic resonance imaging of the hand were formulated. To prevent motion artifacts, a special fixation device of the patient's hand was introduced.

CONCLUSION: Certain factors directly affect the qualitative magnetic resonance imaging study of the hand, such as safety protocols, scanning parameters, and hand fixation. The guidelines presented in this study and the use of the developed specialized fixation device may improve the quality of magnetic resonance imaging of the hand.

Keywords: magnetic resonance imaging; hand; wrist; optimization.

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Магнитно-резонансная томография кисти: оптимизация сканирования

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АННОТАЦИЯ

Обоснование. Магнитно-резонансная томография — один из ведущих методов лучевой диагностики патологических изменений опорно-двигательного аппарата, в том числе лучезапястного сустава и кисти. Основными проблемами, с которыми встречаются рентгенолаборанты и врачи-рентгенологи при выполнении магнитно-резонансной томографии кисти, являются отсутствие специализированной катушки и надёжного фиксирующего устройства для кисти, а также неудобная поза пациента, что в итоге приводит к чрезмерной двигательной активности пациента во время исследования и снижению качества получаемых изображений. В дополнение к этому, лучезапястный сустав и кисть состоят из множества небольших анатомических структур, детальная визуализация которых требует удлинения времени сканирования, что в свою очередь является дополнительным фактором риска получения некачественных изображений из-за двигательной активности пациента, повышая вероятность некорректной интерпретации исследования врачом-рентгенологом.

Цель — улучшить качество изображений, полученных в ходе магнитно-резонансной томографии кисти, путём разработки стандартизованного подхода к выполнению исследования: выбор катушки, укладка пациента, осуществление фиксации кисти, а также выбор протокола сканирования и параметров импульсных последовательностей.

Материалы и методы. Разработана лонгета для предупреждения движений кисти и выполнены исследования с применением двух видов радиочастотных катушек. Проведена сравнительная оценка изображений по техническим параметрам, а также оценка врачом-рентгенологом, специализирующимся на скелетно-мышечной визуализации, на предмет качества изображений в зависимости от цели исследования.

Результаты. Применение катушки для исследования головы (головной катушки) более целесообразно при необходимости сканирования всей кисти (например, при ревматологических заболеваниях), применение коленной катушки — при необходимости более детальной оценки анатомических структур (в том числе запястья), ввиду меньшего поля обзора и более высокого разрешения. На основании полученных данных были сформулированы рекомендации по проведению магнитно-резонансной томографии кисти: выбор радиочастотной катушки, протокола сканирования, параметров импульсных последовательностей. Кроме того, нами предложена лонгета для фиксации кисти пациента с целью нивелирования избыточных движений и предотвращения возникновения артефактов.

Заключение. Для качественного выполнения магнитно-резонансной томографии кисти требуется учитывать ряд факторов: правила безопасности при проведении магнитно-резонансной томографии, настройка параметров сканирования, грамотная фиксация кисти в катушке. Соблюдение рекомендаций, которые предлагаются в данной работе, а также применение разработанной лонгеты позволяют улучшить качество полученных изображений при магнитно-резонансной томографии кисти.

Ключевые слова: магнитно-резонансная томография; кисть; лучезапястный сустав; оптимизация.

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手部磁共振成像：扫描优化

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摘要

论证。磁共振成像是对包括腕关节和手部在内的肌肉骨骼系统病变进行放射诊断的主要方法之一。放射技师和放射科医生在进行手部磁共振成像时遇到的主要问题是缺乏专用线圈和可靠的手部固定装置，以及病人的姿势不舒适。这最终会导致患者在检查过程中过度移动，并降低所获图像的质量。此外，腕关节和手部由许多细小的解剖结构组成，对这些结构的详细观察需要更长的扫描时间。反过来，由于患者的运动活动，这也是造成图像质量差的一个额外风险因素。这就增加了放射科医生对检查做出错误解释的可能性。

目的是通过制定标准化的检查方法，提高手部磁共振成像的图像质量：线圈选择、患者定位、手部固定以及扫描方案和脉冲序列参数的选择。

材料和方法。开发了一种防止手部运动的绷带，并使用两种射频线圈进行了检查。一名专门从事肌肉骨骼成像的放射科医生对图像的技术参数进行了比较评估，并根据研究目的对图像质量进行了评估。

结果。当需要扫描整个手部（如风湿病）时，头部线圈更为合适。膝部线圈的视野较小，分辨率较高，可用于对解剖结构（包括腕部）进行更详细的评估。根据获得的数据，我们制定了手部磁共振成像的建议：选择射频线圈、扫描方案和脉冲序列参数。此外，我们还提出了固定患者手部的绷带，以平缓过度运动和防止伪影。

结论。要保证手部磁共振成像的质量，需要考虑以下几个因素：磁共振成像过程中的安全规则、扫描参数的调整以及手部在线圈中的正确固定。遵守本文提出的建议以及使用开发的绷带可以提高手部磁共振成像的质量。

关键词：磁共振成像；手部；腕关节；优化。

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BACKGROUND

Magnetic resonance imaging (MRI) is a crucial imaging modality for diagnosing abnormalities in human musculoskeletal structures. It is widely used owing to the absence of radiation exposure and high contrast enhancement of soft tissues. MRI has a high diagnostic accuracy in evaluating lesions of cartilage, ligaments, mass lesions, and bone marrow [1]. However, to evaluate the small structures of the hand and obtain high-quality MRI scans, several conditions should be met: the radiologist should follow general MRI precautions [2], use correct sequences, and use special radiofrequency (RF) coils and accessories to fix the hand position. The disadvantages of MRI include its limited availability [3] and high cost [4].

For radiologists, one of the challenging aspects in interpreting hand MRI is that the hand is composed of small structures; thus, imaging and interpretation of pathological changes in the hand tissues is directly dependent on the skill and expertise of the radiologist and on the quality of the image [5]. For example, radiologists with expertise in diagnosing musculoskeletal disorders were shown to provide more detailed interpretations than those with less experience [1]. For patients, the key factors for obtaining high-quality images are proper positioning and fixation of the patient's hand and minimizing motor activity throughout the examination. Motion is a common source of MRI artifacts. Artifacts appear as blurred margins of structures and thus reduce the informational value of the examination [6]. Two types of motion can cause artifacts: internal, caused by physiological processes (e.g., blood flow in the vessels), and external, which are directly related to the patient's active or passive movements during the examination. Flow artifacts are less significant owing to the small vessel caliber. They can be mitigated by using special saturation pulses applied distal and proximal to the area being scanned and by changing the direction of the phase encoding gradient. The patient's movements can be minimized by choosing a comfortable position for the hand and fixing it securely [6].

STUDY AIM

This study aimed to improve the quality of hand MRI by standardizing coil selection, patient positioning, hand fixation, scan protocol, and sequence parameters.

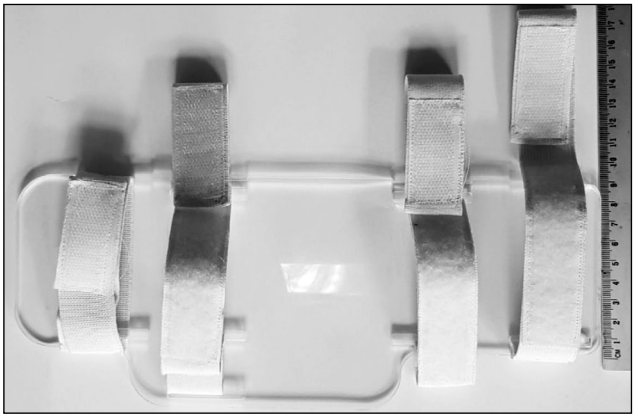

Fig. 1. A device (splint) for positioning the patient's hand.

MATERIALS AND METHODS

Currently, various problems in performing hand MRI have been identified. Healthcare facilities of the Moscow City Health Department are no exception to these issues, including lack of a special coil, uncomfortable patient position, motion artifacts, and small anatomical structures that require increased scanning time for detailed imaging. The lack of reliable hand fixing device in the coil is another crucial problem. Therefore, an immobilizing splint was developed and evaluated in studies using different RF coils (head and knee) to compare quality and provide recommendations for MRI scanning based on the data obtained, depending on the purpose of the examination.

The present study included a healthy volunteer using Excelart Vantage 1.5T (Toshiba, Japan), a commonly used MR scanner model in healthcare facilities of the Moscow City Health Department at the time of the study.

A splint made of polymethyl methacrylate (organic glass) with four textile fasteners on elastic straps was developed to immobilize the hand (Fig. 1). The splint had the dimensions 30 × 12 cm and thickness of 0.5 cm. A pad for the distal forearm (Fig. 2*b*) and disposable covers (gloves, sleeves) were also provided.

The splint was placed to keep the hand close to the body, and the wrist was comfortably positioned on a special pad. Then, the splint was secured with four textile fasteners on elastic straps (Fig. 2). The patient was put in the prone position, with the arm extended forward (the superman position) and the splint fixed to the hand (Fig. 3).

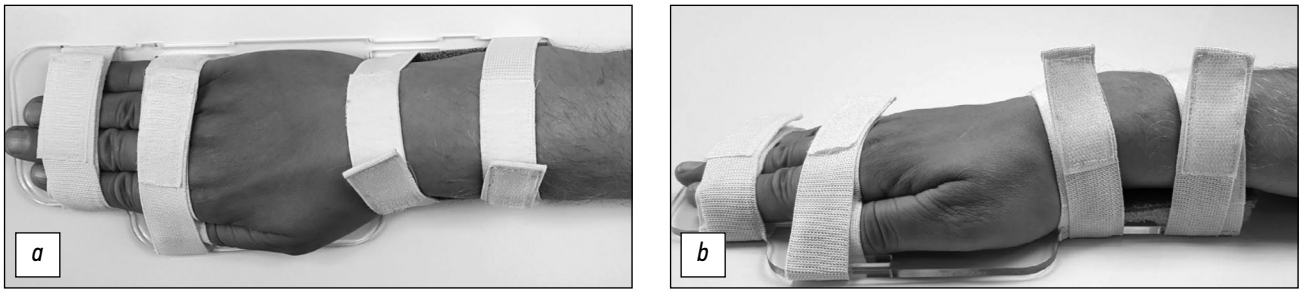

Fig. 2. Fixing a splint to immobilize the patient's hand; (*a*) top view; (*b*) side view.

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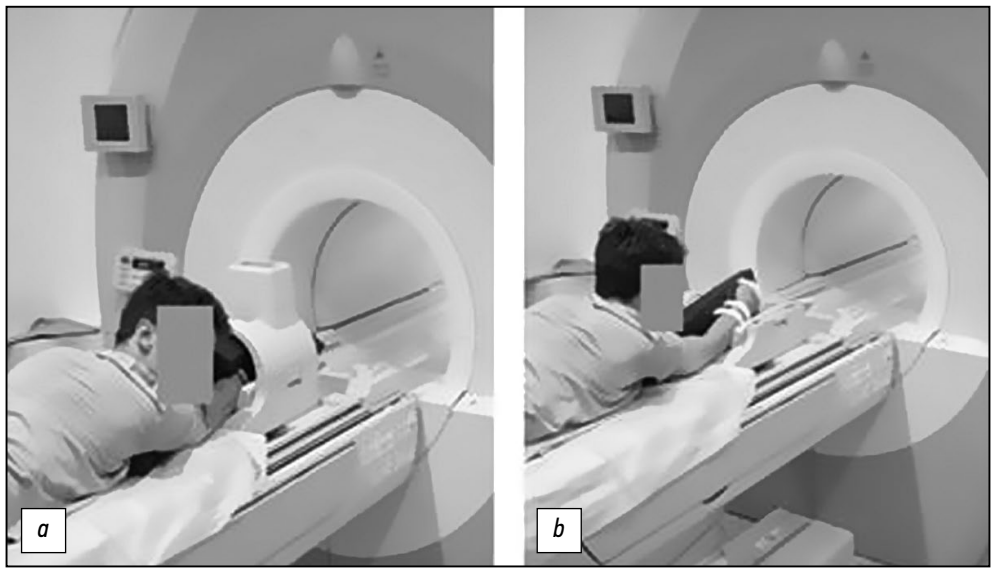

Fig. 3. Patient in the prone position with the arm extended forward (the superman position) and the hand placed on a splint for immobilization; (*a*) positioning of the device in the assembled radiofrequency coil; (*b*) positioning of the device in the volume radiofrequency coil with the upper part open.

Signal-to-noise ratio (SNR) is a crucial parameter of MRI quality; the higher the SNR, the better the anatomical structures are visualized. Therefore, the first step was to evaluate the images by SNR, depending on the scanning region. Two methods were used to calculate the SNR for the head and knee coils.

The first method calculated the ratio of the thenar muscle signal and the standard deviation (SD) of the background (formula (1)):

$$SNR = \frac{\text{Thenar Signal}}{\text{Background SD}} \quad (1)$$

The second method uses the ratio of the thenar signal to the background signal (formula (2)):

$$SNR = \frac{\text{Thenar Signal}}{\text{Background Signal}} \quad (2)$$

The signal was determined for the thenar as the muscle signal was not suppressed by the short tau inversion recovery (STIR) and fat suppression (FS) modes; hence, the obtained data for different scan modes were averaged. The SNR was calculated for three main pulse sequences: T1-weighted (WI) images, STIR, and proton-density weighted images with fat suppression (PD-WI FS). Furthermore, the presence of vascular artifacts, the possibility of vertical and horizontal placement, the need for scan program adjustments, and patient comfort were evaluated. The images were interpreted by a radiologist with 10 years of experience.

RESULTS

Table 1 shows the SNR comparison data for the head and knee coils. When using the knee coil, the SNR was higher for both calculation methods. This is more clearly seen when presented as the mean SNR, which was 1.39 times higher when using formula (1) and 5.3 times higher when using formula (2).

Table 2 presents data comparing head and knee coils. Fig. 4 and 5 display images obtained with the head and knee RF coils. When using the head coil (Fig. 4), the SNR was lower; however, the signal intensity was more evenly distributed, allowing evaluation of the entire hand. However,

Table 1. Signal-to-noise ratio comparison for head and knee coils

	SNR with formula (1)			SNR with formula (2)		
	T1-WI	STIR	PD FS	T1-WI	STIR	PD FS
Head coil	6.62	11.51	30.81	1.67	1.65	4.08
Knee coil	10.13	15.54	39.97	11.29	7.16	20.39
SNR	1.53	1.35	1.30	6.76	4.34	5.00
Mean		1.39			5.3	

Note: WI, weighted images; PD FS, proton density with fat suppression; SNR, signal-to-noise ratio; STIR, short tau inversion recovery. SNR is calculated using the following formula: knee coil SNR / head coil SNR.

Table 2. Comparison of hand magnetic resonance imaging parameters for the head and knee coils

Parameter	Head coil	Knee coil
Type	Multichannel	Quadrature
Signal-to-noise ratio (SNR)	Higher position for the knee coil relative to the head coil	
Scan region	Evenly distributed Convenient scanning of the entire hand (rheumatology)	Locally high (up to 150 mm) Convenient scanning, two regions (radiocarpal region and wrist/metacarpal bones and finger phalanges [traumatology])
Vascular artifacts	Mild	Significant, to be suppressed in some programs
Vertical and horizontal positions are possible	Yes	Yes
Scanning programs	Setup required	Setup required
Patient comfort	Comfortable	Relatively comfortable

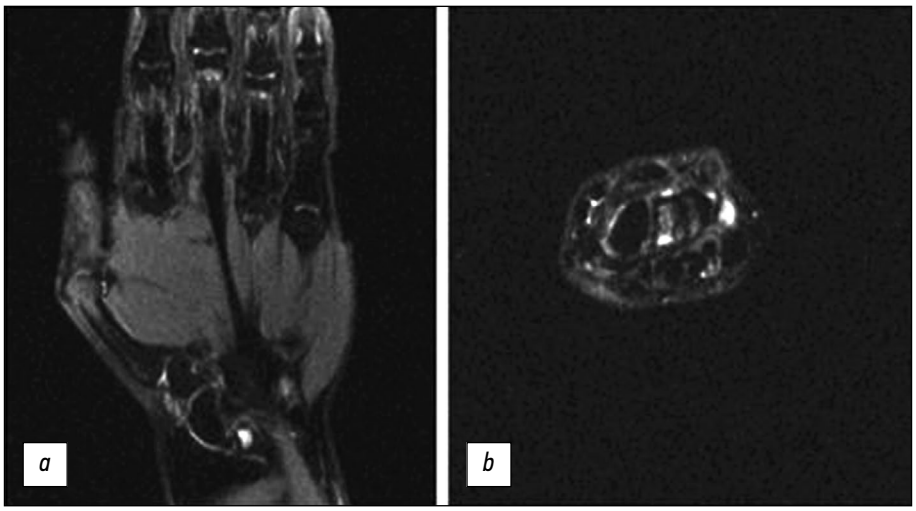

Fig. 4. Magnetic resonance imaging of the hand using a head radiofrequency coil, with a splint to immobilize the hand. PD-weighted images with fat suppression; (*a*) coronal plane; (*b*) axial plane.

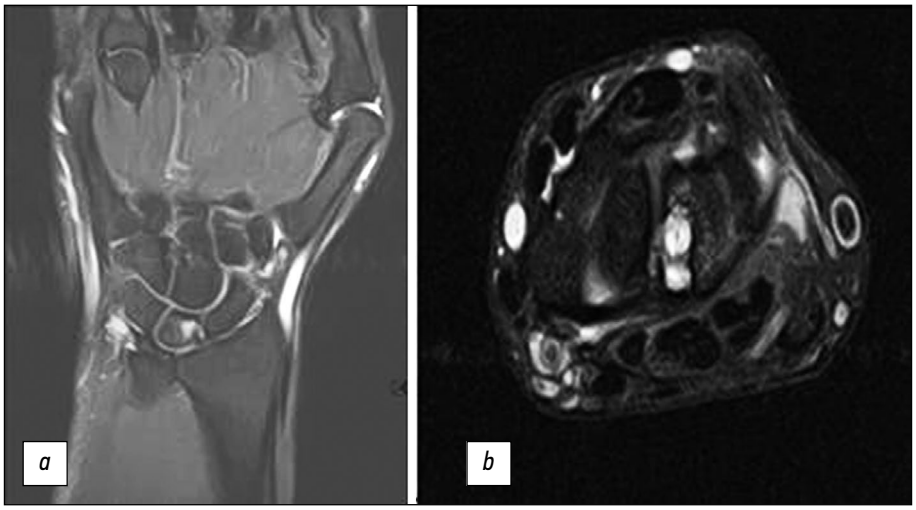

Fig. 5. Magnetic resonance imaging of the hand using a knee radiofrequency coil, with a splint to immobilize the hand. PD-weighted images with fat suppression; (*a*) coronal plane; (*b*) axial plane.

when the knee coil was used (Fig. 5), the SNR was higher locally, allowing assessment of smaller wrist structures. This was because the knee RF coil was quadrature, not multichannel, and the working field of view was smaller. A survey showed that the head coil was more comfortable for the patient.

Therefore, a head coil is preferred when the entire hand needs to be scanned, such as in rheumatic diseases, whereas a knee coil is more appropriate when small wrist structures need to be examined, for example, in hyaline cartilage lesions, stress and pathologic fractures, triangular fibrocartilage complex (TFCC) lesions, and tunnel syndrome.

Recommendations for clinicians and X-ray technicians have been developed based on these data:

1. Ensure that there are no metal objects that could cause artifacts and patient injury.
2. Select an RF coil appropriate for the clinical task: a volume knee RF coil is recommended for thorough evaluation of local anatomical structures (e.g., wrist, TFCC, etc.); a head RF coil is recommended to scan the entire hand.
3. Fix the patient's hand firmly to the splint, placing the wrist on a special pad for comfortable hand positioning and securing with four textile fasteners on elastic straps (Fig. 2*a, b*).
4. Place the patient in the prone position, with one arm extended forward (the superman position) (Fig. 3). It is not always possible to place the patient's arm along the central axis of the scanner bore with the hand exactly isocentered; hence, the hand is often rotated and/or moved to the edge of the bore. Additionally, the choice of coil matters. Some manufacturers attach a coil rigidly to the patient table, whereas others allow enough space for movement to position the hand precisely in the isocenter.
5. Use the following scan protocol [7–10]:
   a) For the entire hand scan, e.g., in rheumatic diseases (Table 3):
   - Pre-scan to set up and position the slices
   - PD-WI FS in the sagittal plane
   - PD-WI FS in the coronal plane
   - PD-WI FS in the axial plane
   - STIR in the coronal plane
   - T1-WI in the coronal plane

   Position the locator sequences, i.e., low-resolution images, in three planes obtained in less than 25 seconds:
   - Axial plane: the resulting slices should cover the entire hand for three slices above the carpometacarpal joint and three slices below the distal radioulnar joint.
   - Coronal plane: the resulting slices should cover the entire hand from the dorsal surface to the palmar surface.
   - Sagittal plane: the resulting slices should cover the entire hand from the medial surface to the lateral surface of the wrist joint area.

   b) For a hand scan, e.g., in case of an injury (Table 4):
   - Pre-scan to set up and position the slices
   - T1-WI in the coronal plane
   - T2-WI in the coronal plane
   - PD FS in the axial plane

Table 3. Recommended parameters for hand scan (Toshiba scanner, head radiofrequency coil)

Sequence	TR	TE	Slice thickness (mm)	FOV (cm)	ETL	Matrix
PD-WI FS, sag	2050	36	3	15×20	7	320x224
PD-WI FS, cor	2700	36	3	15×15	7	320x224
PD-WI FS, ax	2700	36	3	15×15	7	320x224
STIR, cor	3632	36	3	15×15	7	320×224
T1-WI, cor	646	15	3	15×15	1	320x224

Note: ax/cor/sag, axial, coronal, and sagittal planes; WI, weighted images; ETL, echo train length; FOV, field of view; PD FS, proton density with fat suppression; STIR, short tau inversion recovery; TE, echo time; TR, repetition time. The gap between slices is 10% of the slice thickness. STRI time: 130 msec.

Table 4. Recommended parameters for hand scan (Toshiba scanner, knee radiofrequency coil)

	TR	TE	Slice thickness (mm)	FOV (cm)	ETL	Matrix
T1-WI, cor	273	10	3	20×16	1	368×240
T2-WI, cor	3,660	45	3	12×12	7	320×256
PD FS, ax	3,630	36	3	12×12	7	256×224
PD FS, cor	2,116	45	3	18×16	7	256×256
STIR, sag	2,464	12	3	15×15	7	320×224

Note: ax/cor/sag, axial, coronal, and sagittal planes; WI, weighted images; ETL, echo train length; FOV, field of view; PD FS, proton density with fat suppression; STIR, short tau inversion recovery; TE, echo time; TR, repetition time. The gap between slices is 10% of the slice thickness. STRI time: 130 msec.

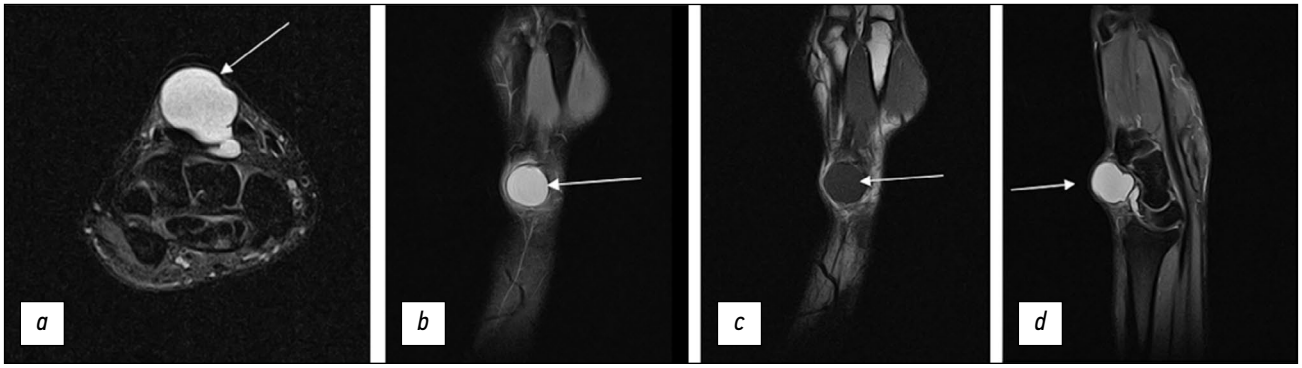

Fig. 6. Large encapsulated ganglion cyst of the dorsal hand with neck-like connection to the wrist cavity; (*a*) PD-weighted images with fat suppression in the axial plane; (*b*) PD-weighted images with fat suppression in the coronal plane; (*c*) T1-weighted images in the coronal plane; (*d*) PD-weighted images with fat suppression in the sagittal plane.

- PD FS in the coronal plane
- STIR in the sagittal plane
- 3D WET in the coronal plane (optional)

Position the locator sequences, i.e., low-resolution images, in three planes obtained in less than 25 seconds:

- Axial plane: the resulting slices should cover the entire area of the hand from the distal phalanges to the level of the distal radioulnar joint.
- Coronal plane: the resulting slices should cover the entire hand from the dorsal surface to the palmar surface.
- Sagittal plane: the resulting slices should cover the entire hand from digit 1 to digit 5.

For survey scans, such as for the diagnosis of rheumatic processes, STIR is recommended as this sequence allows a comprehensive volumetric assessment of inflammatory lesions, whereas PD-WI FS is more selective and provides higher spatial resolution, which is critical in evaluating smaller structures.

The limitations of the proposed fixation method include the potential inability to use the described splint in patients with contractures or large-space-occupying masses resulting in gross deformation of the contours (Fig. 6). However, in this case, the remaining recommendations should be followed regardless.

DISCUSSION

The hand is the distal part of the upper extremity, which includes the bones of the wrist, metacarpal bones, and phalanges, as well as ligaments, vessels, and nerves. The wrist consists of two rows of bones: the proximal row, consisting of the scaphoid (os scaphoideum), lunate (os lunatum), triquetrum (os triquetrum), and pisiform (os pisiforme) bones, and the distal row, consisting of the trapezium (os trapezium), trapezoid (os trapezoideum), capitate (os capitatum), and hamate (os hamatum) bones [11] (Fig. 7).

MRI is a leading imaging method for evaluating hand structures; however, radiography is more commonly used for initial evaluation [12]. MRI may be used to investigate the TFCC, which is the structure that provides shock absorption, because in the neutral position, the TFCC

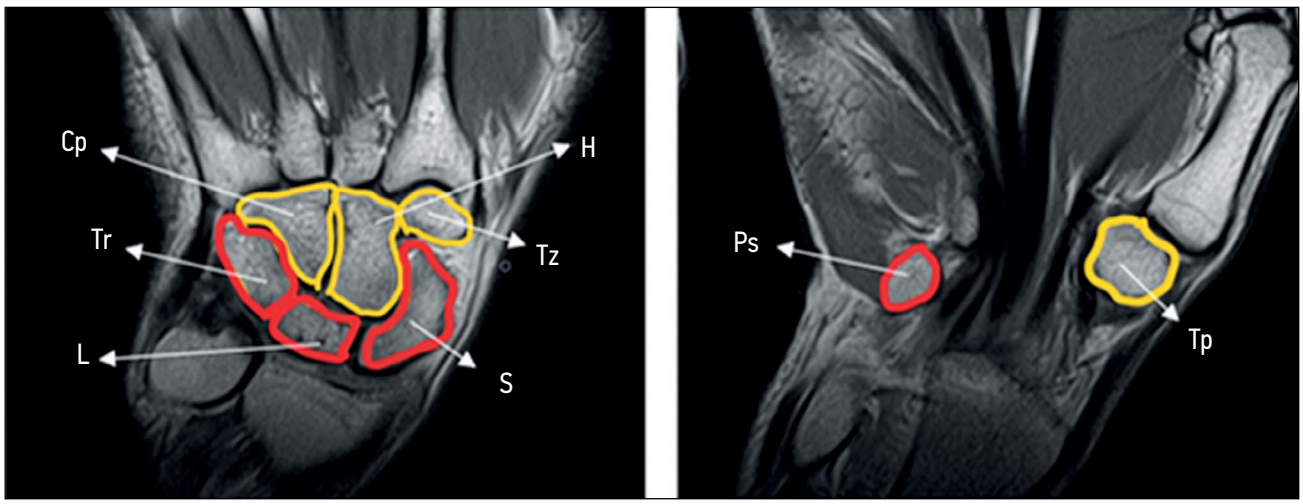

Fig. 7. Left hand, wrist bones, and magnetic resonance imaging (T1-weighted images, coronal plane). The proximal bone row is marked in red; the distal bone row is marked in yellow. S, scaphoid bone; L, lunate bone; Tr, triquetral bone; Ps, pisiform bone; Tp, trapezium bone; Tz, trapezoid bone; H, hamatum, Cp, capitate bone.

absorbs approximately 18%–20% of the axial wrist load [4]. Notably, MRI has been shown to be a useful diagnostic tool in chronic wrist pain to detect central TFCC tears and lesions at the articulation site with the radial bone, although ulnar articulation tears are often not visualized [13]. A study by El-Deek et al. compared the sensitivity, specificity, and accuracy of MRI and ultrasound (US) in the evaluation of hand pathology. US was shown to be as effective as MRI in evaluating tendon disorders and slightly more effective than MRI in diagnosing carpal tunnel syndrome and presence of foreign bodies. However, MRI is superior to US in evaluating TFCC and in assessing edema and characterizing masses [14]. A study showed that 7T MRI scanners can visualize hand structures better than 3T MRI scanners [15].

In 2018, the American College of Radiology (ACR) published guidelines for imaging modalities for chronic wrist pain (Table 5). However, recommendations regarding the technical aspects and methodology of hand MRI were few; further, a special birdcage RF coil is required for better visualization, and 3T MRI scanners should be preferred over 1.5T or lower ones [12].

Radiofrequency Coils Used for Hand Magnetic Resonance Imaging

In 2002, a published article presented a birdcage RF coil optimized for the hands. This coil improved SNR by 50%–90% [16]. This was reflected in the ACR guidelines at the time [12].

Currently, there are several RF coils for hand imaging. For example, Siemens (Germany) offers the Hand/Wrist 16 RF coil with 16 channels. The core features of this RF coil are as follows:

- Special internal design for quick and easy hand positioning
- Stabilizing pads to keep the hand in a comfortable position
- A holder to shift the center
- Easy installation in the MRI scanner [17]

Further, ScanMed (USA) offers a Hand and Wrist MRI Coil that is compatible with MRI scanners from various manufacturers, including Siemens, General Electric (USA), and Philips (the Netherlands). The manufacturer claims that this wrist, hand, and phalange imaging coil showed a significant improvement in image quality over a scan area of up to 8 cm compared to other commonly used coils (e.g., knee RF coils, quadrature extremity RF coils, wrist 4-channel RF coils, etc.). This RF coil enables the patient's arm to be positioned at the side (in the supine position) or above the head in the superman position (in the prone position). Moreover, it has two design options with two removable bases that allow scanning in craniocaudal and caudocranial directions [18].

Available Equivalents of the Proposed Splint

Peterfy et al. [19] described an equivalent of the proposed splint presented by Spire Sciences, Inc., wherein the hand is placed on a special M-shaped acrylic frame so that the thumb and the remaining four fingers are brought together and are in the same plane. Then, the hand and wrist are secured to the frame with a self-adhesive elastic bandage [19].

Patient Positioning Options

There are several ways to position a patient. In the superman position, the patient is placed in the prone position with the arm extended above the head so that the wrist is as close as possible to the isocenter of the magnetic field, which provides the highest SNR and the most uniform signal.

This is an uncomfortable position for many patients; hence, the patient can be placed in the supine position with the arms at the sides of the body. In this position, the hand is away from the magnet isocenter, resulting in a reduced signal and consequently poor and uneven fat signal suppression [20].

Other foreign studies described the prayer position, wherein the patient lies on his/her side with the elbow bent so that the wrist is next to the face and thus closer to the isocenter of

Table 5. Summary of the American College of Radiology recommendations for the use of radiologic modalities in chronic wrist pain

Purpose/indication	Modality
Primary diagnosis	Radiography
Radiographic results are inconclusive and the symptoms persist	Hand MRI without intravenous contrast enhancement
Diagnosis of arthritis to treat or predict course	Hand MRI with/without intravenous contrast enhancement
Kienböck's disease suspected	Radiography; for negative radiograms, hand MRI without intravenous contrast enhancement
Palpable hand mass or suspected hygroma	Hand MRI/US without intravenous contrast enhancement
Suspected occult or stress fractures of the hand	Hand MRI/CT without intravenous contrast enhancement
History of scaphoid fractures and chronic wrist pain to assess fracture complications	Hand MRI/CT without intravenous contrast enhancement
Diagnosis of tunnel syndromes	Clinical evaluation combined with electrophysiology (stimulating electroneuromyography). Further imaging is usually not needed; in some cases, a wrist US or MRI without contrast enhancement may be indicated

Note: MRI, magnetic resonance imaging; CT, computed tomography; US, ultrasound.

the magnet [20]. In the Standards of MRI, Bazhin et al. [10] revealed two similar positioning options: the prone position with the head toward the magnet bore and arms extended and raised (the superman position) and the supine position with the examined arm placed in a neutral position along the body.

Scan Protocols

In the Standards of MRI, Bazhin et al. [10] determined the following hand scan protocol:

1. T1-WI in the coronal plane
2. T2-WI in the coronal plane
3. STIR in the coronal plane
4. T1-WI in the sagittal plane
5. STIR in the sagittal plane
6. STIR in the axial plane
7. GRE in the axial plane

Nonetheless, the European Society of Skeletal Radiology Sports Subcommittee [7] recommends the following protocol, primarily for hand digits:

1. PD-WI FS in the axial plane
2. T1-WI in the axial plane
3. PD-WI FS in the coronal plane
4. PD-WI FS in the sagittal plane
5. STIR in the coronal plane

Moreover, the European Society of Skeletal Radiology Arthritis Subcommittee [8] recommends the following protocol for rheumatic diseases:

1. STIR/T2-WI FS in the coronal plane
2. T1-WI in the coronal plane
3. PD-WI FS/STIR/T2-WI FS in the axial plane
4. T1-WI in the axial plane
5. PD-WI FS in the sagittal plane
6. Contrast-enhanced T1-WI in the axial plane (optional)

Images with Artifacts

A review of hand MRI showed that MRI scans may often be of low diagnostic value, with low resolution and low contrast enhancement (low SNR), and present motion or metal artifacts in the scan field (Fig. 8–10).

The technique to be used for hand MRI to ensure maximum patient comfort and high image quality remains controversial.

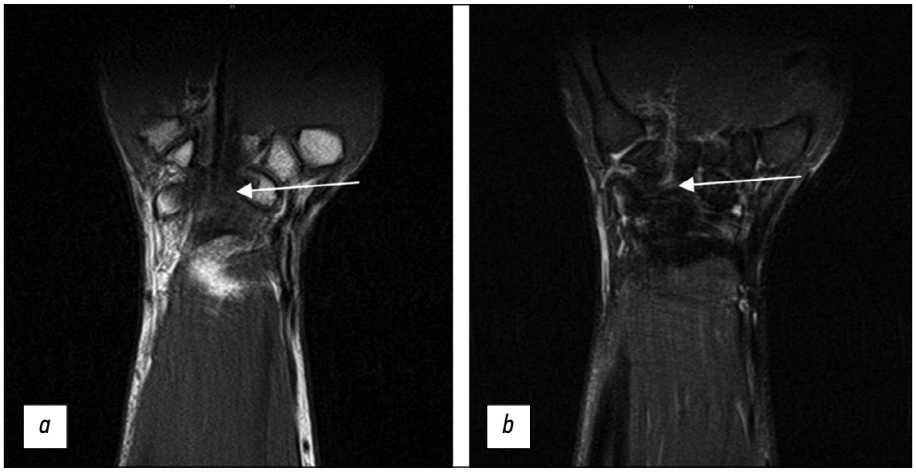

Fig. 8. Reduced imaging quality because of movement artifacts without using a splint (arrows); (*a*) T1-weighted images in the coronal plane; (*b*) STIR protocol in the coronal plane.

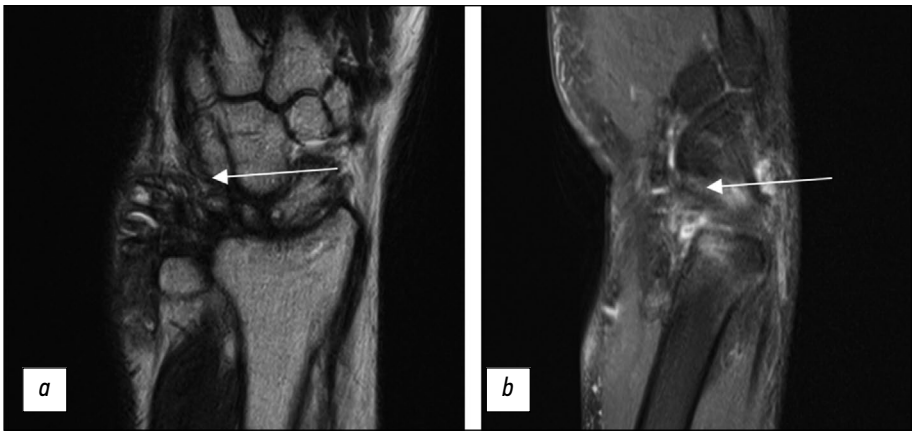

Fig. 9. Reduced imaging quality in a patient with triangular fibrocartilage complex disorder because of motion artifacts (arrows) and atypical positioning (without a splint); (*a*) T2-weighted images in the coronal plane; (*b*) PD-weighted images with fat suppression in the sagittal plane.

Fig. 10. Reduced imaging quality because of technical artifacts from the ring: T1-weighted images in the coronal plane.

CONCLUSION

The hand is a complex anatomic structure. MRI is a commonly used imaging modality for evaluating the musculoskeletal system owing to the absence of radiation exposure, high contrast enhancement of soft tissues, and ability to detect radiographic abnormalities in the bone tissue. Several factors should be considered to obtain high-quality MRI scans, including general MRI precautions, scan settings, and proper hand fixation in the coil. Implementation of the proposed splint will standardize examinations and reduce motion artifacts with convenient fixation and use. Therefore, following the recommendations can improve the quality of MRI scans, reduce overall scan time, and reduce interpretation errors for hand MRI scans.

ADDITIONAL INFORMATION

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Multiparametric Magnetic Resonance Imaging and Magnetic Resonance Imaging Fusion-Guided Biopsy for the Diagnosis of Prostate Cancer: Current Status

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ABSTRACT

This review explains the role of multiparametric magnetic resonance imaging, particularly in prostate biopsy, in the detection of prostate cancer. The use of multiparametric magnetic resonance imaging in the diagnosis of prostate cancer has also allowed its use in magnetic resonance imaging-guided biopsies, which according to many studies present high sensitivity and specificity in early diagnosis and staging, in patients with persistently high prostate-specific antigen levels despite previous negative prostate biopsies, and in the follow-up of patients under active surveillance.

To perform a targeted prostate biopsy, three types of magnetic resonance imaging guidance are available: cognitive fusion, direct magnetic resonance imaging-guided biopsy performed within a tomograph (in-bore biopsies), and software coregistration of stored magnetic resonance images with real-time ultrasound using a fusion device, with multiparametric magnetic resonance imaging findings digitally overlaid on real-time transrectal ultrasound images for targeted biopsy.

Each method has its advantages and disadvantages. Magnetic resonance imaging-targeted biopsy improves the quality of histological results compared with other approaches, with approximately 90% correct detection of significant index lesions. Correct staging allows the selection of the best therapeutic options, adequate evaluation of the prognosis, and reduction of the incidence of new biopsies and complications. The current objective is to make magnetic resonance imaging-guided biopsy increasingly available and standardize the technique to minimize inter-operator variability depending on the available system.

Keywords: multiparametric magnetic resonance imaging; prostate cancer; fusion biopsy; targeted biopsy.

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Возможности мультипараметрической магнитно-резонансной томографии при проведении фьюжн-биопсии под её контролем в диагностике рака предстательной железы: текущий статус

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АННОТАЦИЯ

В данном обзоре освещается роль мультипараметрической магнитно-резонансной томографии в выявлении рака предстательной железы, в частности — при биопсии простаты. Использование мультипараметрической магнитно-резонансной томографии в диагностике рака простаты позволяет также применять её для биопсии. Мультипараметрическая магнитно-резонансная томография, по данным многих исследований, обладает высокой чувствительностью и специфичностью в ранней диагностике и стадировании у пациентов с сохраняющимся высоким уровнем простатспецифического антигена, несмотря на предыдущие отрицательные биопсии простаты, а также при ведении пациентов, находящихся под активным наблюдением.

Для проведения прицельной биопсии простаты существует три типа наведения: когнитивная фьюжн-биопсия; прямая биопсия, направляемая магнитно-резонансной томографией и выполняемая внутри томографа (in-bore); программная корегистрация снимков предоперационной магнитно-резонансной томографии с интраоперационным ультразвуковым исследованием с помощью фьюжн-устройства. При этом при проведении прицельной биопсии результаты мультипараметрической магнитно-резонансной томографии накладываются в цифровом виде на изображения трансректального ультразвукового исследования в реальном времени.

Каждый метод имеет свои преимущества и недостатки. Прицельная биопсия с помощью магнитно-резонансной томографии улучшает качество гистологических результатов по сравнению с другими подходами, выявляя значимые индексные поражения с точностью до 90%. Правильное стадирование позволяет выбрать оптимальные варианты лечения, адекватно оценить прогноз, снизить частоту новых биопсий и осложнений. В настоящее время главная задача состоит в том, чтобы сделать биопсию в сочетании с магнитно-резонансной томографией более доступной и стандартизировать технику проведения процедуры, что позволит минимизировать межоператорскую вариабельность в зависимости от используемой системы.

Ключевые слова: мультипараметрическая магнитно-резонансная томография; рак предстательной железы; фьюжн-биопсия; прицельная биопсия.

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融合引导活检在前列腺癌诊断中的多参数磁共振成像功能：现状

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摘要

本综述强调了多参数磁共振成像在前列腺癌检测中的作用，特别是在前列腺活检中的作用。多参数磁共振成像技术在前列腺癌诊断中的应用也可用于活检。许多研究报告称，多参数磁共振成像在前列腺活检阴性但前列腺特异性抗原水平持续偏高的患者的早期诊断和分期方面具有很高的灵敏度和特异性，在主动监测患者的管理方面也是如此。

前列腺靶向活检有三种引导方式：认知融合引导活检；由磁共振成像引导并在计算机断层扫描仪内（in-bore）进行的直接活检；以及使用融合设备对术前磁共振成像图像和术中超声检查进行的软件联合注册。在这种靶向活检中，多参数磁共振成像结果以数字方式叠加在实时经直肠超声图像上。

每种方法都有其优缺点。与其他方法相比，利用磁共振成像进行靶向活检可提高组织学结果的质量，检测重要指标病变的准确率高达 90%。正确的分期可以选择最佳治疗方案，充分评估预后，减少新的活检和并发症的发生。目前的主要任务是使活检与磁共振成像相结合的应用更加广泛，并使手术技术标准化，以最大限度地减少因所使用的系统不同而造成的操作者之间的差异。

关键词：多参数磁共振成像；前列腺癌；融合引导活检；靶向活检。

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INTRODUCTION

In Western countries, prostate cancer (PCa) is the most frequent noncutaneous tumor in men [1]. According to the European Association of Urology (EAU) recommendations, prostate biopsy is the gold standard for PCa diagnosis.

The first diagnostic biopsy method is the random technique (rather than sextant), with 12 samples taken only in the peripheral zone [2]. This technique has limitations such as undersampling (insufficient number of samples in relation to the prostate volume), oversampling (excessive core number, with identification of the nonsignificant microfoci), overstaging, with a diagnosis of nonsignificant tumors (low sensitivity), understaging, with failure to diagnose clinically significant cancers (low specificity), and operator experience-related errors [3].

The new therapeutic trend of active surveillance (AS; for low-risk tumors and minimally invasive targeted procedures necessitates more precision in prostate examination, necessitating advancements in the biopsy approach.

Prostate biopsy is currently recommended for men aged 50–69 years with high serum prostate-specific antigen (PSA) levels (>3 ng/mL) or abnormal digital rectal examination findings (nodules, induration, and asymmetry). After the first set of negative biopsy results, when suspicion of PCa remains high, the number of samples (i.e., saturation biopsy) and sampling of the transitional zone should be increased [4].

Since its initial application in 1983, MRI has been widely used for PCa diagnosis because of its increased availability and multiparametric imaging, which combines anatomical and functional data [5, 6].

In 2012, the European Society of Urogenital Radiology published guidelines based on expert consensus to standardize the evaluation and reporting of prostate MRI: the Prostate Imaging Reporting and Data System (Pirads) [7]. Since then, the Pirads score has been externally evaluated and found to be reliable for more accurate PCa detection [8].

In 2019, the Pirads Steering Committee published updated reporting guidelines describing the assessment categories and technical parameters described in version 2 of the Pirads [9].

With these premises, the role of multiparametric MRI (mpMRI) has become central not only in the diagnosis of PCa but also in biopsy as a tool for correct staging and assessment of tumor extension (Gleason score [GS]).

The current goal is to make MR-guided biopsy increasingly available, thereby minimizing interoperator variability depending on the available system.

METHODS OF MAGNETIC RESONANCE IMAGING GUIDED PROSTATE BIOPSY

To perform a targeted prostate biopsy, three types of MRI guidance are available:

- Cognitive fusion, in which the operator visually directs the transrectal ultrasound (TRUS)-guided biopsy to the prostate area of abnormalities on mpMRI.
- Direct MRI-guided biopsy, performed within an MRI tube (in-bore biopsies): This technique is quite precise for identifying areas of interest within the prostate; however, it is time-consuming, expensive, and impractical because the entire process is performed within the MRI gantry [10].
- Software coregistration of stored MRI with real-time US using a fusion device, with mpMRI findings digitally overlaid on real-time TRUS images for targeted biopsy (TB). This procedure can be performed using elastic fusion systems (*e.g.*, Koelis Urostation and Eigen Artemis) or rigid fusion systems (*e.g.*, Philips Uronav, Eindhoven, The Netherlands; Medcom BiopSee, Darmstadt, Germany).

Each method has its advantages and disadvantages.

Despite substantial variation in the sensitivity of detecting clinically indolent disease across studies, most studies have shown that the sensitivity of MR–US fusion (cognitive or device) ranges between 80% and 95% [11].

The main clinical indications for MR–US fusion biopsy are persistently high PSA levels despite previous negative prostate biopsies and follow-up of patients on AS [12].

Cognitive Fusion

Cognitive fusion is performed easily and rapidly and does not require any additional equipment other than an MRI and a standard TRUS facility. The US operator does not need any additional training beyond the standard TRUS-guided biopsy. Cognitive fusion is based on the sonographer's ability to localize the region of interest by imaging its location within the prostate after viewing the worrisome lesion on MRI [12].

MRI and TRUS images are superimposed by a cognitive overlay during biopsy, which can be performed with a printed document or by presenting MR images on the screen of a workstation in the TRUS room adjacent to the TRUS platform [13].

The physician aims at the target lesion with knowledge of lesion localization on MRI. The advantages of cognitive fusion are speed and simplicity; that is, it does not require additional equipment beyond what is ordinarily necessary for a TRUS-guided biopsy [14].

However, one of the downsides of cognitive fusion biopsy approaches is the possibility of sampling error when attempting to conceptualize the region of interest, which is particularly problematic for smaller tumors. Another disadvantage is the inability to track the position of each previous biopsy.

Despite this, the tumor detection rate of cognitive fusion is comparable to that of device-mediated fusion, and in most investigations, both cognitive and device-mediated fusions appear to be superior to random systematic sampling alone [15,16].

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The disadvantage of cognitive fusion is the possibility of human error in extrapolating from MRI to TRUS in the absence of a real overlay.

Several studies have assessed the value of cognitively performed TB. Lawrentschuk et al. found that cognitive TB performed better than random cores, particularly in anterior lesions [17]. In a retrospective analysis, Haffner et al. compared TB results with those of 12 random biopsies in 555 patients [18]. A TB approach alone would have required just 3.8 cores per patient, thereby avoiding unnecessary biopsies in 38% of patients with normal MRI findings and avoiding the detection of minor cancer discovered by random biopsies in 13% of cases [18].

In this study, 13 significant cancers were missed with TB alone, whereas 12 significant cancers were missed with the standard approach [18].

In another study, Puech et al. discovered that MRI before biopsy increased the cancer detection rate (CDR) from 59% by 12-core saturation biopsy (SB) to 65% by cognitive TB [15].

In terms of significant cancer (cancer core length > 3 mm on any core and GS > 3 + 3), the CDRs were 67% for TB and 52% for conventional biopsies [15].

Labanaris et al. demonstrated that TB allowed for a 90% match between biopsy and surgical GS and indicated that MRI should be performed before biopsy to decrease SB underestimation of GS [19].

Thus, current research suggests that MRI-guided biopsy has higher accuracy and CDRs than standard TRUS-guided biopsy.

Haffner et al. reported that cognitive fusion is no better than systematic biopsies in men with questionable MRIs, highlighting the major risk associated with cognitive fusion: interobserver variability [18]. Although the present literature on cognitive fusion shows potential in the hands of professional cognitive fusionists, most urologists are now shifting toward commercially accessible device-mediated platforms because of the lack of tracking and digital overlay.

Direct Magnetic Resonance Imaging Guided Biopsy is Performed 'In-Bore'

A radiologist performs direct MRI-guided biopsy "in-bore," that is, within the MRI tube, by fusing a previous MR image indicating a lesion with a contemporaneous MR image to confirm biopsy needle localization. The transrectal route is employed. After each biopsy sample, the patient is scanned to ensure localization. Typically, only a few targeted cores are taken, and systematic sampling is not conducted.

The in-bore biopsy method provides the benefits of precision needle placement, fewer sampled cores, and a low risk of missed targets if they are visible by MRI [20]. Its disadvantages include greater expense and time consumption and the inability to regularly sample the residual gland [20]. This is relevant because MRI misses approximately 10% of severe lesions compared with final RP pathology [21,22].

Quentin et al. showed that in-bore TB has an excellent significant CDR of 92.2% [23]. Hoeks et al. reported that 265 patients with dubious lesions on mpMRI who had previously negative TRUS biopsies had transrectal in-bore TB, resulting in a CDR of 41%, with 87% of the identified tumors being clinically significant [24].

The Barentsz group at Radboud University in Nijmegen, The Netherlands, presented a vast experience with in-bore biopsy [25]. The benefits of this procedure include a reduced number of cores taken, precise localization of the biopsy, and less detection of insignificant tumors. The downsides of this procedure include the time and cost, including the in-bore time, and two MRI sessions are required to obtain the biopsy specimens.

Furthermore, because only suspicious lesions are sampled, tissues with a "normal" MRI appearance are not collected, which is problematic because any false-negative characteristics of prostate MRI are unknown [25].

Fusion of Magnetic Resonance Imaging and Transrectal Ultrasound

In this method, the operator images the prostate using US, as has been used for decades. While viewing the prostate, the MR images of that prostate, in which imaging was performed beforehand and images were stored in the device, are fused with real-time US images using a digital overlay, allowing the target(s) previously delineated by a radiologist to be brought into the US machine's aiming mechanism. Fusion produces a three-dimensional (3D) reconstruction of the prostate, and the aiming and tracking of biopsy sites occur on the reconstructed model (Fig. 1 and 2) [25]. Several commercial platforms are now available, each with a different method of coregistration and a different hardware platform for lining up the biopsy with the coregistered picture [3]. Compared with VE, MRI–TRUS fusion-guided biopsy may have higher reproducibility because of less operator dependence and delivery of real-time feedback on actual biopsied areas [3]. The disadvantages include higher software/device costs, dependence on software for accuracy, and the associated learning curve and operator training [26] (Fig. 3 and 4).

This method has the disadvantage of being an indirect method, requiring the use of an additional device, and requiring specialized operator training. The benefit is that it may be performed in minutes in an outpatient clinic environment under local anesthesia, using techniques that have been used for years. The results obtained using the fusion device are highly encouraging [25].

Device-mediated fusion allows for the targeting of biopsies into previously defined MRI regions of interest using a 3D rendering apparatus that superimposes saved MR images on real-time US images, a technique known as coregistration. Although several commercial MR–US fusion platforms are available, all use some types of image coregistration and needle/probe tracking (mechanical or electromagnetic). These technologies enable the acquisition, storage, and reconstruction of real-time US images and the creation of 3D maps of lesion locations and prior biopsy sites for future reference [27]. Because any movement of the patient or the prostate affects image coregistration, these fusion devices

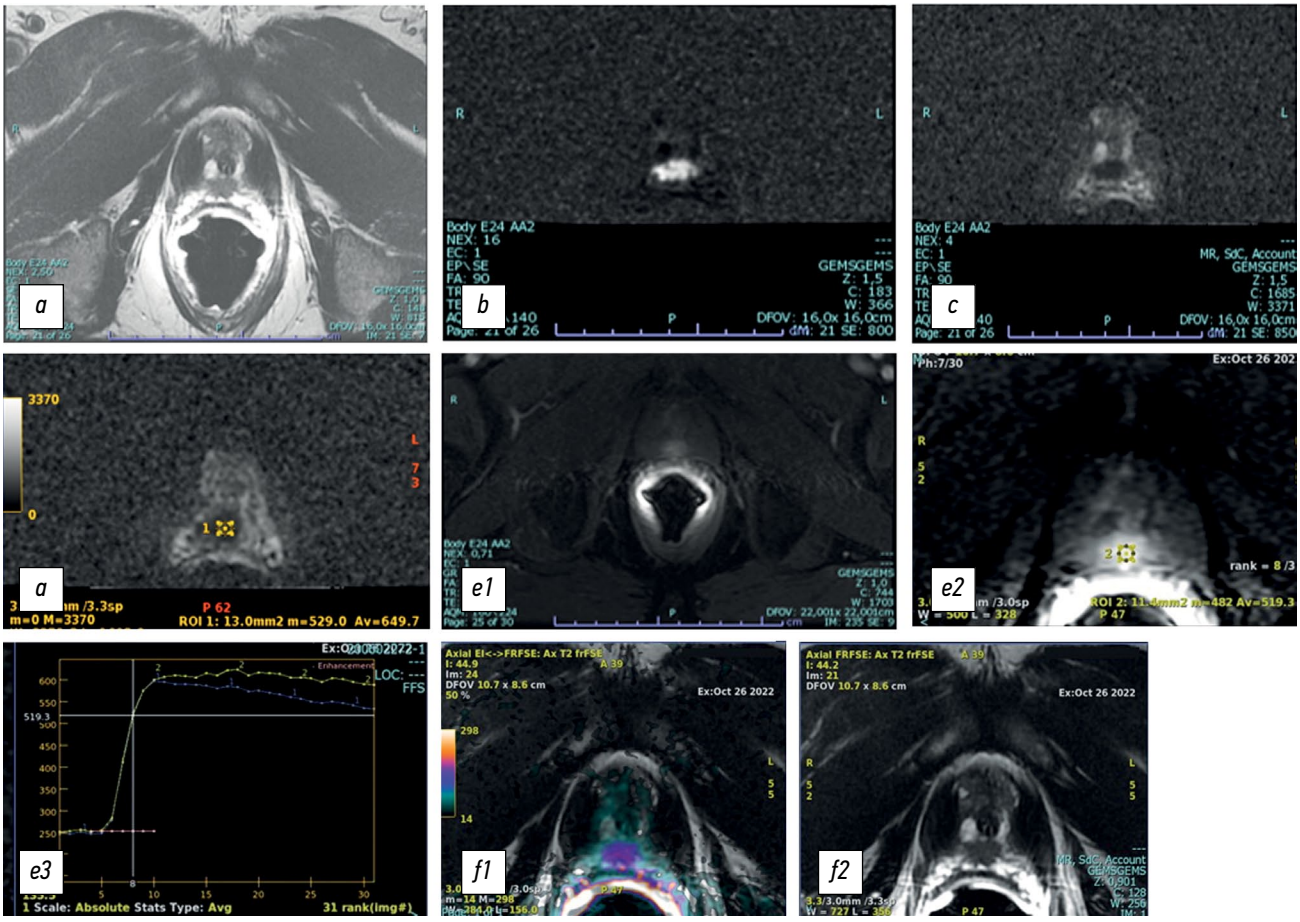

Fig. 1. T2-weighted (*a*) magnetic resonance image (axial plane) showing a hypointense nodular lesion in the peripheral zone at the apical posterior site. Axial diffusion-weighted MR image (*b*) with an apparent diffusion coefficient (ADC) (*c*) of put value × 10^{-3} m^2/sec in the corresponding area. Reduced water diffusion in prostate cancer (PCa) is related to increased cellularity of malignant lesions, with a reduction in the extracellular space and restriction of movement of a larger portion of water molecules into the intracellular space. Therefore, DWI with the corresponding ADC map provides an important quantitative biophysical parameter that can be used to diagnose PCa (*d*). The tumor is characterized by intense early hyperenhancement of the normal adjacent tissue (*e*). Colorimetric map generated by the DCE evaluation of PCa in the peripheral area at the apical site. The suspicious area is coded in red (*f*).

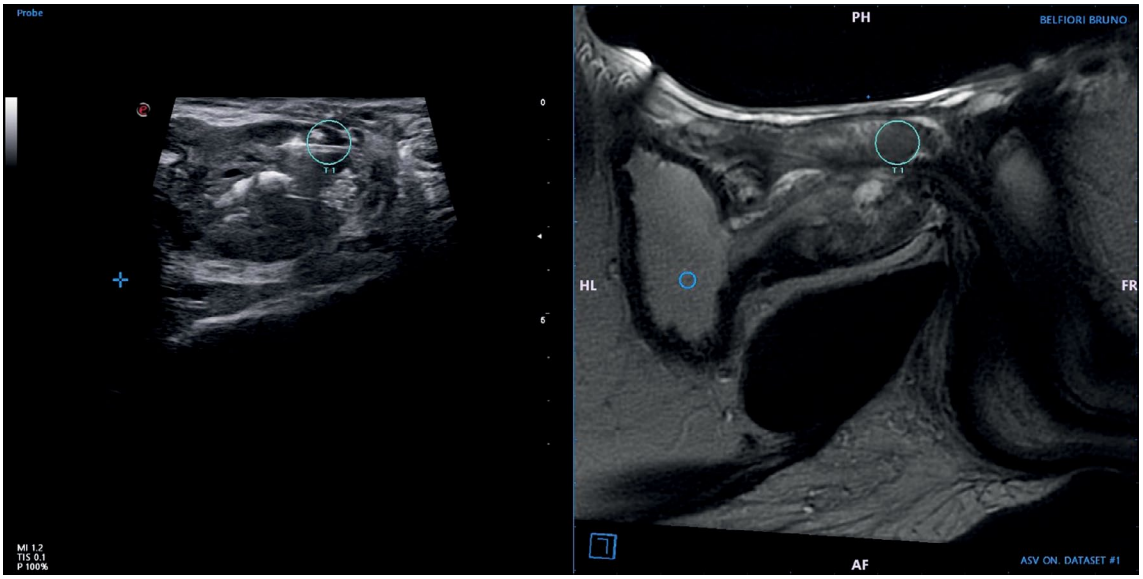

Fig. 2. MRI–TRUS fusion-guided prostate biopsy. The prostate and lesions identified on MR images (in this case, on T2W imaging) are segmented. During the procedure, a 2D TRUS scan of the prostate was performed. Images were recorded semiautomatically. Co-viewing images can be tiled or overlaid. By merging the two images, the urologist can locate the lesion during a biopsy using real-time ultrasound guidance.

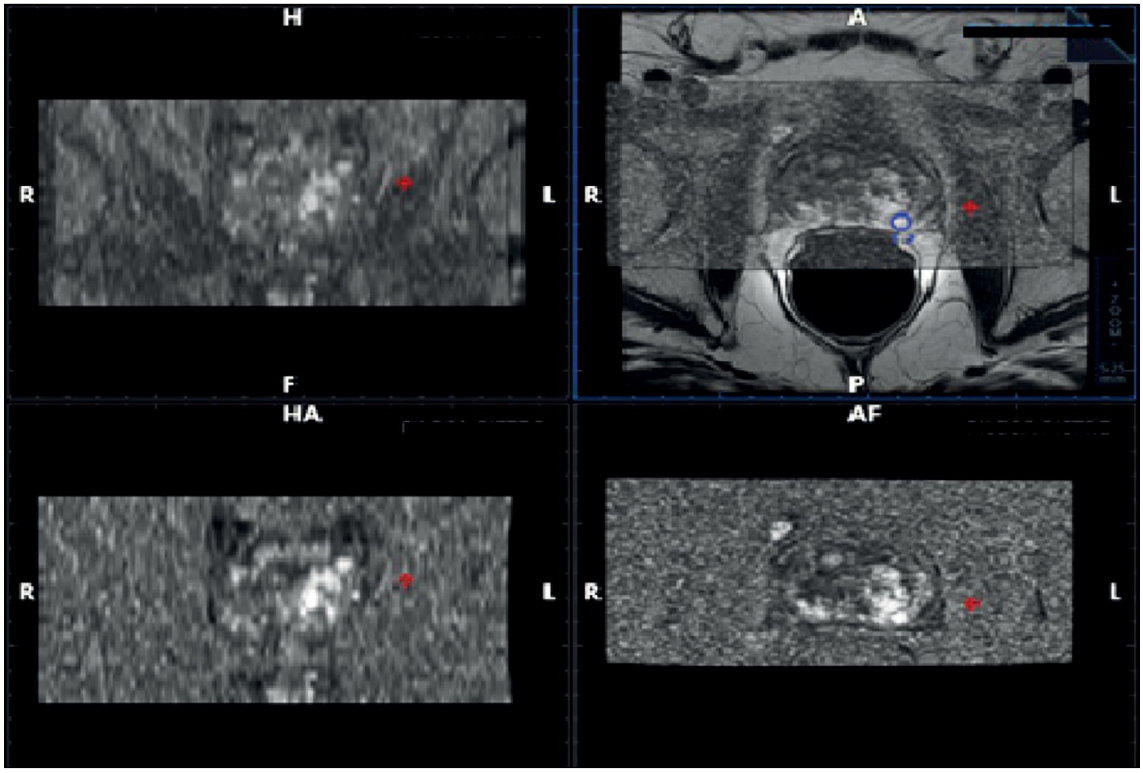

Fig. 3. Magnetic resonance (MR) imaging of prostate cancer: axial diffusion-weighted MR image (up on the left) with an apparent diffusion coefficient map (down on the left), T2-weighted MRI image (up on the right), and T1-weighted image after contrast media (down on the right).

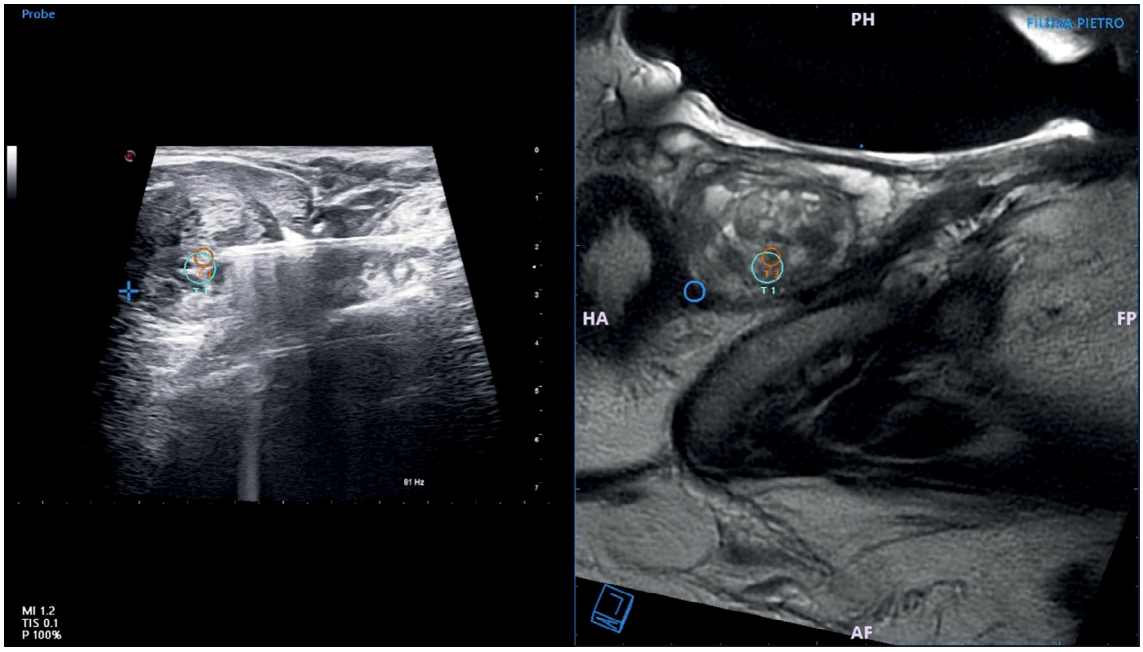

Fig. 4. Magnetic resonance imaging is fused with real-time TRUS using a digital overlay, allowing the target(s) previously delineated by a radiologist to be brought into the ultrasound machine's aiming mechanism. Fusion enables the reconstruction of the prostate, and the aiming and tracking of biopsy sites occur on the reconstructed model.

also employ dynamic repeat registration methods using motion-compensation algorithms to guarantee accurate and reproducible index lesion targeting [12].

Recent studies have compared the detection of PCa and severe disease using traditional SB or TPMB as a reference test [22, 28, 29].

In a cohort of >1000 patients, Siddiqui et al. used the Uronav system and conventional 12-core TRUS-guided biopsy as a reference test and reported that TB diagnosed 30% more high-risk cancers than standard biopsy (P = 0.001) and 17% fewer low-risk cancers (P = 0.002) using primary GS 4 as the significance level [22]. Rastinehad et al. defined GS 3 + 4 as

clinically significant PCa (sPCa) and reported that 14.3%–20.9% of sPCa cases were discovered by TB alone but ignored by the traditional TRUS technique [30]. Furthermore, 23.5% of cases were upgraded from insignificant to sPCa through MRI–TRUS fusion-guided biopsy [30]. In contrast, 4/105 sPCa cases were missed by MRI–TRUS fusion-guided biopsy [30].

Baco et al. demonstrated that 98% of index tumors defined as the highest GS or biggest volume in the case of multifocality with equal GS, were diagnosed by MRI and that 98% of the correct location was diagnosed by MRI–TRUS fusion-guided TB using the Koelis Urostation® [31].

Regarding public health, Cerantola et al. published a cost-effectiveness analysis comparing TRUS biopsy with MRI target biopsy (MRTB) in 2016. They assessed the cumulative effects after 5, 10, 15, and 20 years and determined that including MRI and MRTB in PCa diagnosis and care is a cost-effective measure after 5, 10, 15, and 20 years [32].

COMPARATIVE STUDIES OF DIFFERENT TARGETED BIOPSY APPROACHES

Only a few studies have examined the CDRs of various targeting strategies, and the results are contradictory [26].

Delongchamps et al. reported that cognitive fusion biopsy was not significantly better than SB in a study comparing VE with two MRI–TRUS fusion devices; however, both software coregistration devices tested (Esaote/MyLabTMTwice and Koelis/Urostation) significantly increased the CDRs compared with SB in a cohort of 391 patients using conditional logistic regression analysis [33].

In a prospective trial of 125 men with worrisome lesions, Wysock et al. compared MRI–TRUS fusion-guided biopsies using the Eigen/Artemis system with VE targeting [34]. They found that MRI–TRUS fusion-guided biopsies had a slightly improved CDR compared with VE for all cancers (32% *vs.* 26.7%, $P = 0.1374$) and for GS $\geqslant 3 + 4$ (20.3% *vs.* 15.1%, $P = 0.0523$).

Puech et al. found no difference in the CDR of PCa for rigid software coregistration using MedCom Navigator versus cognitive fusion TB (53% vs. 47%). Furthermore, no variations in cancer positivity were observed in the categories of posterior (46 of 79, 58%), anterior (33 of 79, 42%), or smallest (25 of 79, 32%) MRI targets [15]. In 2013, Bjurlin et al. conducted a literature review, and their findings indicated that the use of MRI to target prostate biopsies can reduce sampling errors associated with conventional biopsy by providing better disease localization and sampling. They discovered that increased cancer sampling allows more accurate risk classification, which may influence therapeutic decision making. However, the best clinical application of MRB has not yet been determined [3].

EARLY DETECTION OF PROSTATE CANCER

The US Preventive Services Task Force (USPSTF) updated its recommendations in 2018, largely based on the publication of longer follow-up data from large screening trials and emerging evidence that the use of AS in low-risk PCa reduces the harms associated with screening overtreatment. The USPSTF now recommends that men aged 55–69 years undergo PSA testing following a discussion with their clinicians about the relative benefits and harms, although it still advises against PSA screening in younger men (aged 40–55 years) or those aged >70 years [35].

In the absence of widespread organized PSA testing, opportunistic testing has become a routine practice in many EU member countries. However, a recent study revealed reveals that while this strategy has minimal influence on PCa-specific mortality, it is associated with overdiagnosis than organized risk-adapted PSA testing [36]. This lack of effect is largely attributed to testing individuals who will not benefit (e.g., those with a 10-year life expectancy) without sufficient informed decision making [37], as well as repeated testing in men who are not at risk of developing severe PCa [38].

Overdiagnosis can be reduced by employing a risk-adapted detection strategy based on PSA values in conjunction with risk calculators and mpMRI, which can distinguish between significant and insignificant PCa and modify treatment accordingly. As a result, many cases of early PCa diagnosis can be handled with AS, thereby avoiding overtreatment [39]. Those with a lower-risk profile may benefit from local treatment, which has fewer adverse effects and produces better results than if the condition was diagnosed and treated later, thereby enhancing or maintaining the patient's quality of life [40].

The EAU has created an algorithm to explain a risk-adapted strategy for PCa detection. This algorithm is intended for use in well-informed men aged >50 years with a life expectancy longer than 10–15 years. This algorithm clearly demonstrates how to achieve early detection of serious PCa while avoiding overdiagnosis and overtreatment. Following a clinical risk assessment and appropriate counseling, the PSA test represents the first step in identifying a large proportion of men with a low PSA value who do not require any further immediate investigations for 2–4 years (for those with a PSA value of 1–3 ng/mL) or 5 years (for those with a PSA value of 1 ng/mL and aged 60 years) [39].

A risk stratification nomogram (which considers factors such as age, family history, digital rectal examination, and prostate volume [PSA density] in a risk calculator) will identify a subgroup of men (approximately 35% of all men with an initial PSA test of >3 ng/mL [41]) as those with a low risk who require clinical follow-up only, avoiding the need for further testing, including MRI and biopsy. Men with a PSA value of >3 ng/mL who were classified as intermediate or high risk would then undergo mpMRI, leading to the identification of a further subgroup (approximately 54% of all men undergoing MRI [41]) with a Prostate Imaging Reporting and Data System (PIRADS) score of 1–2 considered at a low risk of having sPCa and requiring clinical follow-up only.

Further risk categorization of men with a PIRADS score of 3 using PSA density and other clinical characteristics would reveal an additional category requiring only clinical follow-up (a PIRADS score of 1, 2 or "low-risk" 3 accounts for approximately 57% of men tested by PIRADS [41]). As a result, the remaining subset of the original population could be regarded as intermediate or high risk and should undergo targeted and/or systematic biopsy. Within this subgroup, those with a positive diagnosis and a favorable grading group (approximately 25% of all confirmed diagnoses [41]) may be eligible for AS rather than active treatment.

However, as part of a collaborative decision-making process, all final treatment decisions should consider the patient's values and preferences [40]. This algorithm demonstrates how PSA testing can be used more intelligently by incorporating risk calculators, such as those developed by the European Randomised Study of Screening for PC (ERSPC) and the Prostate Cancer Prevention Trial [42], as well as mpMRI and the Pirads score [43, 44], to reduce the number of men undergoing biopsy. The proposed time intervals for repeat PSA testing depending on age and initial PSA test result reflect the risk of a future clinically significant cancer diagnosis [45] and thus help reduce false-positive biopsies.

The risk calculator to be used must also be carefully selected. Although the ERSPC risk calculator has been well verified and may thus be regarded as superior, a recalibration step may be required to account for regional variations in prevalence and the link between PSA and PCa risk [46].

CANCER RISK ASSESSMENT USING TARGET BIOPSY

The change from systematic biopsy to image TB raises significant concerns regarding the clinical care of PCa. More men should choose AS if new biopsy techniques provide them with greater confidence.

However, the use of targeted biopsies will be exploited to justify additional overtreatment. Currently, risk classification systems based on biopsy results greatly affect therapy decisions [47]. These systems evolved from traditional systematic biopsies. When tumors are sampled more thoroughly with TB, the proportion of positive cores and maximum CCL are higher than with traditional biopsy [48,18].

As a result, compared with systematic biopsy, TB increased risk attribution. In a computer simulation study that included 107 reconstructed 3D models of whole-mount prostatectomy specimens, Robertson et al. [49] revealed this critical issue. They discovered that a 12-core TRUS biopsy properly categorized only 24% of clinically significant cancer-containing prostates as high risk, compared with 74% of cases using a transperineal TB with four cores. Furthermore, the targeted biopsies had a higher proportion of positive cores and higher maximum CCLs. They concluded that when risk models derived from conventional TRUS biopsy are used for image-directed biopsy, there is a systematic rise in risk attribution.

At UCLA, one hundred and ninety-four AS men were treated with MR-US fusion TB, which included systematic and targeted sampling. Using only systematic biopsy and the Epstein histological criteria (Gleason score 6, 2 cores cancer, and 50% of any core), 28% of men were categorized as poor candidates for surveillance on confirmatory biopsy.

Incorporating TB increased the number of reclassified patients to 41%. In some circumstances, this is caused by the discovery of additional dangerous malignancies, whereas in others (i.e., numerous malignant cores from a single MRI target), it is the result of using a classification system that does not consider TB.

Given the inflation in risk attribution, TB may be used to justify aggressive treatment of more men, exacerbating the overtreatment problem. To avoid this unwanted effect, new risk stratification criteria based on image-targeted biopsy must be developed and verified. Consider a man who underwent a conventional biopsy with a low-volume GS of 3 + 3 and a TB with a low-volume GS of 3 + 4. TB combined with device-based tracking of malignant detects could be used to safely follow tumors that are now thought to require treatment [47].

INCORPORATION OF MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY WITH RISK MODELING FOR PROSTATE CANCER

When compared with RP specimens, mpMRI detects 85%–95% of index lesions and sPCa [50]. The use of TB of dubious mpMRI lesions in a fusion biopsy context increases the identification of sPCa by 30% [22].

Multivariate risk-based techniques have been established to identify men with sPCa while avoiding needless biopsies [51,52]. A risk calculator based on data from the ERSPC was created to quantify the sPCa risk. Roobol et al. revealed that in men with a PCa risk of 12.5%, 33% of routine biopsies might be avoided [52].

Although TB of mpMRI-suspicious lesions alone is a potential technique for reducing the overdetection of minor illnesses, MRI-invisible sPCa can be missed [22, 53, 54].

Unlike Alberts et al., Radtke et al. and van Leeuwen et al. developed risk calculators and added prebiopsy mpMRI to clinical parameters to determine an individual sPCa risk using a validated biopsy approach combining fusion-guided TB and transperineal systematic SBs as reference on the one hand and transperineal mapping and TB plus 12-core TRUS on the other [55, 56].

In the area under the curve (AUC) of the receiver operating characteristics curve analysis, Van Leeuwen et al. demonstrated that a model combining age, PSA, DRE, prostate volume, previous biopsy result, and mpMRI Pirads Likert score outperformed the model of clinical parameters

alone with discrimination of 0.90 [56]. In addition to the model for biopsy-naive men, Radtke et al. internally validated a risk model for men with a previous negative biopsy that combined PSA, prostate volume, DRE, age, and mpMRI Pirads Likert scoring [55]. When compared with a validated clinical parameter risk calculator and Pirads, the model beat both instruments [55]. When risk models that include mpMRI and clinical parameters are compared with risk models that only use clinical parameters or PIRADS, the accuracy of the decision to perform a biopsy in a patient with sPCa suspicion can be increased. In conclusion, risk models that include mpMRI are superior to risk models that exclude mpMRI not only for men before initial biopsy but also for patients who have had previous negative biopsy results [55, 56].

While detection of sPCa can be improved, an unsuspicious mpMRI or a low PIRADS score cannot be used to justify not proceeding with a biopsy in the case of PCa suspicion. MRI fusion biopsy was claimed to help diagnose indolent PCa. However, finding low-risk PCa can improve patient safety by avoiding unnecessary treatment and improving disease monitoring accuracy and reliability when selecting individuals for AS.

Avoiding Multuparametric Magnetic Resonance Imaging Fusion Biopsy Failure

Although mpMRI offers helpful details regarding the diagnostic route for sPCa, mpMRI fusion biopsy can fail. To date, four potential mechanisms for mpMRI fusion biopsy failure have been identified: mpMRI-invisible cancer, improper sampling, mpMRI reader oversight, and intralesion GS heterogeneity [57]. Muthigi et al. demonstrated that in 71% of cases when SB discovered sPCa but TB did not, the malignant finding was within the sextant of the target lesion, correlating with the findings of Cash et al., who identified inaccurate sampling as one of the primary causes of fusion biopsy failure [58].

Similarly, Bryk et al. identified a combination of TB and ipsilateral SB as the best strategy to detect sPCa and avoid detection of low-risk PCa in patients with unilateral mpMRI lesions using TB, and both sided SB as a reference [59]. The findings of these two studies imply that increasing the number of samples taken from the target area can help minimize erroneous sampling and intralesion GS heterogeneity. However, Porpiglia et al. discovered that two targeted cores inserted in the center of the lesion are sufficient to precisely portray the index lesion [60].

More research on this topic is required. The mpMRI fusion biopsy failure caused by mpMRI-invisible cancer, which has a consistent negative predictive value (NPV) for mpMRI of 63%–98%, can only be solved with further SB [61, 62]. However, most groups that combined TB with 12-core SB found no substantial benefit in detecting sPCa by combining both approaches over TB alone [22, 63].

In contrast, Filson et al. discovered that the combination biopsy approach detected much more sPCa than TB or SB alone [64].

These controversial results lead to the conclusion that the superiority of sPCa detection in a combined biopsy approach compared to a TB-only approach increases with the amount of SB, but with the risk of finding significantly lower-risk diseases.

The question of whether to omit SB might never be entirely solved, and decisions should be made individually according to biopsy indications and patient needs.

The technique used to perform the biopsy is another point regarding the quality and possible reasons for failure of mpMRI fusion biopsy.

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY IN MEN REQUIRING A REPEAT BIOPSY

Men with a previous negative biopsy and an ongoing suspicion of PCa should be continuously monitored. Prior sampling reduces overall disease incidence relative to a biopsy-naive group; however, individuals with continuous suspicion for PCa suffer from inadequate NPV of 12-core TRUS-guided biopsy. MpMRI has been proven in many studies to be effective in monitoring this patient group and should thus be suggested in a repeat biopsy setting [65, 1].

Most recent studies have examined these patients as a subset of a larger cohort; however, some studies have paid special attention to this patient group: Simmons et al. evaluated the diagnostic accuracy of mpMRI in men requiring repeat prostate biopsy (PICTURE study), although only 31% of men had a previous negative biopsy [66]. When used as a positive test result, an mpMRI score of 3 has a sensitivity of 97%, specificity of 22%, NPV of 91%, and positive predictive value of 47% [66].

The authors conclude that a repeat biopsy can be avoided in 14% of men at the cost of missing 9% of sPCa [66]. Hansen et al. reported a significantly improved AUC when Pirads and PSA density were combined (0.82 vs. 0.85), implying that repeat biopsy should be avoided only in cases of worrying mpMRI and low PSA density [67]. Again, data are unclear on when it is safe to exclude SB. Arsov et al. compared in-bore TB to fusion-guided TB plus 12-core TRUS-SB in a prospective randomized experiment. They discovered that adding SB had no further benefit in detecting sPCa [10].

In contrast, recent papers comparing TB alone methods with 24- or 12-core SB reveal that TB alone misses a significant amount of sPCa [67].

MULTIPARAMETRIC MAGNETIC RESONANCE IMAGING FUSION-GUIDED BIOPSY IN MEN UNDER AS

Men with PCa who are eligible for AS are another important patient category because proper risk assessment of potentially less serious conditions is essential. To achieve this purpose, mpMRI in conjunction

with fusion biopsy can aid in initial candidate screening and disease progression monitoring. Radtke et al. analyzed in a sample of 149 men whose initial mpMRI and fusion biopsy before AS resulted in significantly reduced rates of later AS qualifying (20% vs. 48%) during a 2-year follow-up compared with those selected for AS based on 12-core TRUS-guided biopsy [68].

These findings are supported by Henderson et al., who revealed in a prospective study that the apparent diffusion coefficient (ADC) is a good marker for choosing patients for AS because a low ADC value is associated with a shorter time to unfavorable histology [69]. Several recent studies have examined mpMRI and fusion biopsy for disease progression detection. Most of them reveal that mpMRI accurately predicts the likelihood of clinical progression and that patients with stable mpMRI findings have a low probability of developing the disease [70–72].

The inclusion of clinical criteria in the decision-making process appears to be advantageous when selecting patients for AS. Alberts et al. discovered in a cohort of 210 men without upgrade at baseline, confirmatory, or surveillance biopsy in instances of unsuspicious mpMRI and PSA density <0.15 ng/mL, implying that follow-up biopsy should be avoided in these individuals [10]. However, whether following up with fusion biopsy confined to mpMRI-visible targets is sufficient is still being debated. Meng et al. and Frey et al. showed that on combined SB and TB follow-up mpMRI fusion biopsy, TB detected significantly more upgrades than SB, supporting the rationale for removing SB [70, 53].

Conversely, Tran et al., Ma et al., and Recabal et al. found that a significant fraction of higher-grade malignancies could only be diagnosed by SB, suggesting the necessity for additional SB [71, 72]. These contradictory results can be explained in part by differences in study parameters such as median TB and SB cores; however, they also highlight the need for additional research on long-term results, serial mpMRI for replacing repeat biopsies, and sufficiency of follow-up biopsies limited to mpMRI targets.

CONCLUSIONS

MRTB improves the quality of histological results compared with other approaches, with a correct detection of approximately 90% of significant index lesions.

The systematic 12-core TRUS-guided biopsy is still a widely used technique despite its limited sensitivity for the clinical detection of sPCa.

MRI-guided biopsies provide a higher detection rate for clinically detected sPCa and increase the percentage of positive cores.

Although currently used in patients who remain at high clinical suspicion of PCa despite a negative TRUS-guided systematic biopsy, with the increasing use of upfront diagnostic MRI, these biopsies are expected to replace standard systematic biopsies.

Correct staging allows the selection of the best treatment options, including focal treatments, and adequate evaluation of the prognosis. It also reduces the incidence of re-biopsy, costs, and complications.

It is crucial to standardize the bioptic technique and improve the fusion technique to reduce understaging caused by errors in estimating the tumor volume. The role of mpMRI in the presurgical phase of RP is emerging because mpMRI can help in planning the initial surgical strategy, referring to clinical decision making.

ADDITIONAL INFORMATION

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SWOT-Analysis: Remote Monitoring of Blood Pressure

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ABSTRACT

Global political and socioeconomic changes have caused a huge strain on the healthcare system. To transition into a new level of medical care, modern technological solutions are needed. Accelerated development of innovations in medicine and the formation of a personalized approach will improve the quality and accessibility of medical services. One of the directions of healthcare development is the use of digital technologies and remote monitoring in assessing the health indicators of citizens. Currently, the federal project of remote monitoring of patients with arterial hypertension, named, "Personal Medical Assistants," is being implemented in the Russian Federation. Similar to any new technology, remote monitoring has advantages and disadvantages. In this article, a strategic analysis (SWOT-analysis) was performed, considering medical, economic, social, and political aspects that may affect the results of the federal project. For effective implementation of remote monitoring technology in clinical practice, the strengths and weaknesses in the healthcare system and the state as a whole must be emphasized. SWOT-analysis can be used in formulating strategies for the widespread use of new digital technologies in clinical practice.

Keywords: SWOT-analysis; remote monitoring; blood pressure; federal projects; personal medical assistants; healthcare.

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SWOT-анализ: дистанционный мониторинг артериального давления

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АННОТАЦИЯ

В связи с глобальными политическими и социально-экономическими изменениями система здравоохранения испытывает огромную нагрузку. Переход на новый уровень оказания медицинской помощи требует внедрения современных технологических решений. Ускоренное развитие инноваций в медицине и формирование персонализированного подхода позволит повысить качество и доступность медицинских услуг.

Одним из направлений развития здравоохранения является использование цифровых технологий и применение дистанционного мониторирования для оценки показателей здоровья граждан. В настоящее время на территории Российской Федерации реализуется Федеральный проект дистанционного наблюдения за пациентами с артериальной гипертензией «Персональные медицинские помощники». Как и любая новая технология, дистанционное мониторирование имеет свои преимущества и недостатки. В данной статье проведён стратегический анализ (SWOT-анализ), а также рассмотрены медицинские, экономические, социальные и политические аспекты, которые могут оказать влияние конечный результат федерального проекта. Для эффективного внедрения в практику технологии дистанционного мониторирования требуется акцентуация сильных и проработка слабых сторон как в системе здравоохранения, так и в государстве в целом. Проведённый SWOT-анализ может быть использован для построения дальнейшей стратегии широкого использования в клинической практике новых цифровых технологий.

Ключевые слова: SWOT-анализ; дистанционное мониторирование; артериальное давление; федеральные проекты; персональные медицинские помощники; здравоохранение.

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SWOT 分析：远程血压监控

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摘要

由于全球政治和社会经济的变化，医疗保健系统面临着巨大的压力。向新的医疗水平过渡需要引入现代技术解决方案。医学创新的加速发展和个性化方法的形成将提高医疗服务的质量和可及性。

保健发展的一个领域是使用数字技术和应用远程监控来评估公民的健康指标。目前，俄罗斯联邦正在实施对动脉高血压患者进行远程监控的联邦项目《个人医疗助理》。与任何新技术一样，远程监控也有其优缺点。本文进行了战略分析（SWOT 分析），并考虑了可能影响联邦项目最终结果的医疗、经济、社会和政治方面。要有效实施远程监控技术，就必须强调医疗保健系统和整个国家的优势并克服其不足。所进行的 SWOT 分析可用于制定进一步的战略，以便在临床实践中广泛使用新的数字技术。

关键词： SWOT 分析；远程监控；血压；联邦项目；个人医疗助理；医疗保健。

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INTRODUCTION

Healthcare systems are currently under great strain due to sociodemographic (e.g., decreasing working-age population, population aging, and increasing population with chronic noncommunicable disease risk factors) and economic (e.g., economic volatility and understaffing of healthcare facilities) factors [1–4].

Scientific and technological advancements in medicine and healthcare systems allows finding solutions to some existing problems. Digital transformation in healthcare requires innovative approaches for providing medical care [5]. Remote monitoring based on automatic reporting of the patient's health status is a key technology for personalized medicine [6]. The wide clinical use of innovative remote monitoring technologies is crucial in healthcare as it can determine the risk factors of chronic noncommunicable diseases [7–11].

Strengths, weaknesses, opportunities, and threats (SWOT) analysis is a universal tool for strategic analysis. It is applied in all sectors of the economy (commercial, nonprofit, and governmental organizations) to assess brands, products, and projects. A benefit of SWOT analysis is the ability to examine external and internal factors, determine the relationship between strengths and weaknesses, and evaluate external threats and opportunities [12].

Hypertension is a common health condition and significant modifiable cardiovascular risk factor [4]. According to research, in Russia, the prevalence of hypertension is constantly high, reaching 40%–45%. The current population aging in Russia can further increase the number of hypertension patients [3]. Epidemiological studies of hypertension performed in Russia between 2010 and 2020 revealed several unresolved challenges in providing medical care, including unwillingness of patients to take medicines, failure to reach the target blood pressure (BP) on antihypertensive therapy, and low motivation and BP control in rural areas [2].

Successful BP control is an effective preventive strategy in cardiovascular diseases[1]. A meta-analysis of 61 randomized clinical studies showed that a decrease in BP even by 2 mmHg resulted in a decreased mortality due to stroke and coronary heart disease; moreover, effective and timely hypertension therapy could be life-saving for approximately 30% of patients [13].

Suboptimal BP control by patients is a global concern [14]. In most countries, poor compliance and irregular or nonexistent physician visits for hypertension management are believed to be the main reasons for unsatisfactory control of the disease [15]. Low compliance with antihypertensive therapy prevents from reaching target BP levels and raises hospitalization rate and duration, thus increasing healthcare system expenses [8].

Currently, Russia is undertaking large-scale initiatives to implement remote BP monitoring. Therefore, a SWOT analysis of this strategic task is critical.

S: STRENGTHS

Remote monitoring of patients with cardiovascular diseases using wearable devices is regarded feasible, because these devices are efficient, readily available, small-sized, and user-friendly for prolonged use. Moreover, they enable remote monitoring of patients in a comfortable environment (at home) and provide prompt alerts on events that require emergency care or hospitalization [7]. Some wearable devices do not require hospital visits for maintenance. Their operation can be controlled remotely, which is critical for patients living far from large cities with a well-organized cardiovascular care service, including in rural areas [9]. Telemedicine solutions provide several benefits, including easy planning of monitoring and treatment [16] and easier communication between patients and physicians [17].

Patients who use remote technologies can better observe and understand the association between their daily behaviors, such as diet, sleeping habits, and adherence to medication, and health. Telemedicine technologies allow patients to monitor and record their health parameters. This raises awareness and encourages patients to take better care of their health [18, 19]. Patients benefit from telemedicine because it allows for long-term monitoring, long-term disease control by physicians, greater patient health literacy, and convenient communication without the need for hospital visits [20, 21].

Furthermore, remote monitoring increases access to healthcare in remote areas [22]. A healthcare professional (physician or physician assistant) can assess the patient's daily activities and behaviors, allowing for timely treatment plan adjustments [23]. Moreover, a study showed that BP levels measured at home are closer to actual levels, because stress caused by hospital visits and the white coat effect are avoided [24].

Healthcare facilities using remote technologies have various advantages, such as more patients enrolled in care, improved satisfaction with treatment, and more capacity in the facility owing to effective remote consultations. A direct short-term economic effect remains to be demonstrated; nevertheless, the long-term cost-effectiveness of these solutions is clear [19, 24, 25].

Several foreign studies have shown the cost-effectiveness of telemetric reporting of BP self-monitoring [26–29]. Russian studies have assessed the potential socioeconomic effect of

[1] WHO. Global report on hypertension. The race against a silent killer. Geneva, 2013. URL: http://apps.who.int/iris/bitstream/handle/10665/79059/WHO_DCO_WHD_2013.2_rus.pdf Last accessed: February 13, 2023

remote technologies in patients with elevated BP. According to mathematical estimates, in a region with a population of 1 million, with 30% involved in remote monitoring, over 600 patients could be spared over 5 years, and with 90% involved in remote monitoring, about 2,000 lives could be saved [30].

Additionally, economic benefits to patients have been confirmed. BP self-monitoring is more effective than standard therapy in both men and women (assuming the effect of lowered BP was maintained for at least 2 years in men and 5 years in women) [20]. Notably, long-term monitoring was not associated with reduced quality of life [31]. Furthermore, other studies demonstrated a varying economic effect of short-term use of remote technologies; however, this effect becomes apparent starting from 2 years of use [19, 20].

Thus, the advantages of remote monitoring in patients with hypertension include the possibility of BP control and improved access to healthcare in remote areas, providing long-term economic benefits both for patients and healthcare facilities.

W: WEAKNESSES

Despite the advantages of remote monitoring, several weaknesses have been discovered when using digital technologies for BP monitoring in clinical practice, which should be considered when upscaling ongoing and future projects.

Low technology literacy of patients is a limiting factor for remote monitoring. Many patients are unfamiliar with new possibilities and hence unable to integrate them in their everyday life [32]. This is especially true for older patients and requires training to extend the group of patients who comprehend and actively use remote monitoring systems [31].

Personal characteristics and emotional profile of patients considerably affect the efficacy of implementing innovative technologies [33]. A study conducted at the University of Pennsylvania investigated patient interaction phenotypes with a remote BP monitoring system. Three main patterns of engagement style were observed:

- The enthusiast, who tended to submit unprompted messages with high word counts (10.9%)
- The student, who inconsistently engaged with the remote monitoring system (22.6%)
- The minimalist, who engaged only when prompted (66.5%)

A significant association between the communication pattern and reaching the target BP was observed only in the group of patients demonstrating the minimalist communication style ($P < 0.001$) [34].

A study conducted in Belgium examined the effect of anxiety and depression on adherence to remote monitoring in women with pregnancy-induced hypertension using PHQ-9 and ECR-R questionnaires. The moderate adherence group showed significantly higher anxiety and depression levels, whereas no such association was observed in patients with good adherence and over-adherence [35].

Many patients are concerned about personal data safety; hence, some patients refuse to employ biometric data monitoring devices. Some of these patients, who finally consent to use monitoring devices, show high anxiety and depression levels [36].

According to some studies, the absence of interpersonal interaction could hinder the widespread use of remote monitoring [37]. A previous study found that patients valued such communication components as the ability to visit a hospital, meet a physician personally, and ask questions [38]. Moreover, the patient's passive role in remote monitoring is a risk factor, as evidenced by the absence of adequate and timely responses from physicians to suboptimal BP control [39].

The duration of remote monitoring has a significant effect on compliance. Short-term programs showed good adherence to monitoring in approximately 80% of 1,662 patients; 87% of patients found this monitoring option useful and convenient [40]. In long-term follow-up, the number of active patients decreased: an observational clinical trial using the Hello Heart software found that nearly half of patients ceased keeping the electronic diary between 3 months and 1 year [41]. Russian studies revealed similar tendencies: manual reporting of measurements is associated with low adherence to remote monitoring [42, 43]. More than 50% of patients in these studies discontinued monitoring, with most of these cases observed during the first 1.5–3 months of monitoring.

Research showed that patients require extensive support from healthcare professionals to use telemedicine technologies independently and regularly [16]. Moreover, some patients struggle to understand and follow the rules of remote monitoring [44] and resort to self-medication, which poses significant health risks [24].

In addition to the patient-related limitations of remote monitoring, weaknesses associated with the processes and staff management in healthcare systems were noted.

Russian studies revealed that outpatient physicians are hesitant about the widespread use of remote monitoring because of a lack of practical experience. For example, Kalinina et al. conducted a survey of 93 physicians from 6 outpatient clinics in Bryansk [45]. The survey found that respondents struggled the most with questions on the organizational structure of remote monitoring. More than 34.4% of physicians were unable to convey their opinions on the feasibility of establishing a separate system for follow-up remote monitoring, despite this topic being widely discussed presently. Thus, practitioners today cannot comprehend the functions of such an organizational structure. Further, the survey highlighted the ideas of physicians on potential barriers to the implementation of remote monitoring in follow-up care. The majority of respondents (80.6%) indicated insufficient time for monitoring as a barrier; economic

reasons (cost of equipment) were mentioned by 44.1%, technical issues by 45.2%, and challenges in patient training and uncertain reliability of data collection and reporting tools by 39.8%.

Additionally, several foreign countries have observed low digital literacy and reluctance among healthcare professionals. Shaw et al. highlighted the factors reducing technology acceptance by nurses, including additional workload, the need for integration into existing work processes, additional contacts with patients, and understaffing [25]. Moreover, physicians expect the use of telemedicine to increase the workload in the long term [19, 24, 46]. Practitioners are concerned that the cost of remote monitoring will exceed the insurance amount [46], leveling off the economic benefit [21]. Moreover, implementing this technology may make the professional roles in healthcare less clear [18].

In addition to staff-related limitations, economic factors significantly impede future development of information technology in follow-up care.

For example, when incorporating remote technologies into clinical practice, the high cost of devices and the need to train healthcare professionals in their use may become a barrier. Furthermore, the limitations of regulatory documents and the lack of general guidelines for the use of remote monitoring should be considered [10]. Another weakness is low engagement of insurance companies in the field of telemedicine for BP monitoring [39].

The development of remote monitoring technology demands attention to another poorly addressed issue, namely, the time and effort required for the physician to regularly assess the measurements obtained by patients at home and provide remote consultations during monitoring. Moreover, physician labor costs increase, because patients need to be trained on how to use applications. This issue requires adjustments in working time management and modifications in the compulsory/voluntary healthcare insurance system or the introduction of new sources of funding by a healthcare facility [22].

The third group of weaknesses of remote monitoring in hypertension includes methodology-related issues. The most significant unresolved difficulty is the diagnosis of white coat and masked hypertension based on office or home BP measurement. The PAMELA study found similar BP levels when measured at home and during ambulatory blood pressure monitoring [47]. Another study found variations in the diagnosis of white coat hypertension based on home BP measurement and ambulatory monitoring in 13% of participants [48]. Regarding masked hypertension, only 57% and 45% of patients with hypertension confirmed by elevated systolic and diastolic BP, respectively, had similar BP levels during home monitoring. However, the systolic and diastolic BP levels varied in 23% and 30% of patients, respectively [49]. Therefore, home BP monitoring confirms the diagnosis in the case of elevated office BP, whereas ambulatory monitoring is most effective in the diagnosis of masked or white coat hypertension [49]. The disparity in findings does not imply that one method is inferior to the other. Despite appearing similar, the methods address different aspects of the BP profile [50, 51]. According to Barochiner et al., the diagnosis of masked hypertension based on home monitoring can be rarely established owing to low reproducibility of office measurements (Cohen's kappa coefficient $\kappa = 0.19$; 95% confidence interval: 0.0002, 0.38; $P = 0.02$) [52].

Currently, no clear guidelines for addressing variations between office and home BP measurements have been established; thus, overtreatment and undertreatment are possible. This is not a limitation of telemedicine, but rather a methodological feature of hypertension detection. Home BP monitoring and reporting should be standardized to prevent bias in the assessment of findings and data misrepresentation [53].

When making therapeutic decisions, reliability of home BP measurements is critical. Technical errors or blood pressure monitor malfunction may result in inaccurate BP measurements. Hence, BP monitors should be validated and tested for accuracy. Furthermore, the data should be compared to measurements taken by a qualified healthcare professional. In addition to the technical serviceability of the BP monitor, a properly sized cuff is required. According to NHANES, 51% of adults in the USA, including 65% of patients aged 18–34 years and 84% of patients with obesity, required large or very large cuffs [54–56].

Thus, remote monitoring technology for hypertension is not free of weaknesses. Low digital literacy, distrust of innovative technologies, and the desire to maintain current patient–physician interaction style hinder the widespread use of this technique. Moreover, healthcare professionals show a certain degree of reluctance: a potential increase in time and labor input due to additional work results in a hesitation over the widespread use of remote monitoring. The methodological and technical challenges of remote monitoring in patients with hypertension result in a less than enthusiastic attitude toward this technology in the medical community.

O: OPPORTUNITIES

Despite its weaknesses, remote BP monitoring in patients with cardiovascular diseases has shown favorable outcomes, including a significant reduction in hospitalization rate and duration, a decrease in mortality, and improved BP control compared to standard therapy and follow-up. In the TEN-HMS study (UK, Germany, and the Netherlands), the 1-year mortality in the control, remote monitoring, and structured telephone support groups was 45%, 29%, and 27%, respectively [10]. A meta-analysis of 46 randomized clinical studies assessed the efficacy of remote BP monitoring compared to standard hypertension management. Remote monitoring was associated with a decrease in office systolic and diastolic BP by 3.99 mmHg ($P < 0.001$) [11]. The Home BP

study (UK) demonstrated improved systolic BP control when using a remote monitoring system. The mean difference in systolic BP was 3.4 mmHg (95% confidence interval: 6.1, 0.8; $P < 0.05$) [57].

Bubnova et al. conducted a study in 342 hypertension patients and found that remote monitoring provided significant benefits regarding the number of emergency calls, hospitalization rate, and time on sick leave. After 12 months, 92.2% of patients in the treatment group and 43.3% of patients in the control group achieved the target BP level [58].

Remote monitoring enables the collection of large amounts of patient data. Big data and intelligent computer systems have an increasing effect on conventional approaches in medicine [59, 60]. Data collection and integration and feedback to a physician will be automated. Big data collection from various devices, trend prediction via machine learning, and long-term analysis of vital and geographical characteristics will help improve our understanding of cardiovascular disease development on a population level [61].

Improvements to remote monitoring systems may make them more adaptive and flexible. For example, if a patient struggles to follow the remote monitoring protocol, a behavioral module will activate, adapting to the patient's needs to help overcome the challenges. Drug prescription algorithms can also be automated: large datasets allow for case-by-case analysis and real-time decision-making [62].

Remote monitoring has been widely used in healthcare systems of the USA and Europe, confirming its long-term economic and clinical efficacy. Telemedicine allows for more effective health management and efficient utilization of limited medical resources:

- Less time spent on follow-up visits and selecting effective antihypertensive therapy
- Improved BP control in hypertension and the resulting decrease in complication rates
- Shorter hospital stay for complications of hypertension
- Implementation of the technology in remote areas and consistently understaffed healthcare facilities
- Improved availability and quality of medical care for patients with disabilities [40]

T: THREATS

In the implementation of remote monitoring, several threats were identified that limit its wide clinical use.

The development of remote monitoring requires wide implementation of advanced solutions and modern technologies in healthcare systems. However, the current geopolitical environment has its own rules. Previously, most information technology (IT) products and their components were imported, which was significantly more convenient than developing domestic solutions with a long pay-off period. Thus, Russia became severely disadvantaged by sanctions due to weak domestic IT infrastructure. Major western IT companies, such as Microsoft, Oracle, Cisco, IBM, Adobe, SAP, Intel, and AMD[2], have limited their activities or stopped operating in Russia. According to Dmitry Pshichenko, lecturer of the IT Management School of the Russian Presidential Academy of National Economy and Public Administration, the main risks are currently associated with data security and server maintenance, because the majority of western software is cloud-based, and purchasing components for maintenance is difficult. This affects the development of digital technology in medicine[3].

In addition to software issues, the Russian IT industry faces a shortage of expertise. According to Vice Prime Minister Dmitry Chernyshenko, the deficit of IT specialists currently stands at 1 million people[4], with projections of 2 million by 2027. This impedes the rapid development of the IT industry, particularly in healthcare.

Furthermore, economic issues and resource shortages may cause delays in digitization. According to the HSE University, the healthcare industry spent 39.5 billion rubles on the development, distribution, and use of digital technologies and related products and services in 2019, which accounted for 1.6% of the total industry gross added value. When compared to total expenses, the share of expenses for digitization does not exceed 0.6%–0.7% [63].

In 2021, healthcare digitization expenses accounted for 2.6% of the total economic activity. When considering the expenses of Russian companies for digitization, the share of healthcare has increased insignificantly over the last 2 years: 1.6% in 2019 and 2.2% in 2020.

Cybersecurity concerns add to the doubts in the use of remote monitoring systems. Telemedicine involves the collection of large amounts of data, which should be stored in a specific manner to prevent them from being leaked into open sources. Fraudsters may gain access to patient data and use it for criminal purposes[5].

According to Kaspersky Lab, 54% of healthcare facilities use outdated software, because of the high cost of updates and issues with old and new system compatibility. A lack of updates makes a system more vulnerable to cyberattacks; attackers can break into the corporate system and use the databases for their own gain. According to statistics, owing

[2] Gone for good: IT companies that have exited Russia. URL: https://hightech.fm/2022/05/26/it-companies-went-away. Last accessed: March 1, 2023

[3] Major risks in IT stem from a shortage of expertise. URL: https://rg.ru/2023/02/17/vitaiut-v-oblakah.html. Last accessed: March 1, 2023

[4] This year, the number of certified IT companies in Russia has grown sevenfold. URL: https://www.ixbt.com/news/2022/10/24/v-jetom-godu-akkreditovannyh-itkompanij-v-rossii-stalo-v-sem-raz-bolshe.html. Last accessed: March 1, 2023

[5] The risks, threats, and lack of systemic approach in digitization. URL: https://www.infowatch.ru/resources/blog/tochka-zreniya-kasperskoy/o-riskakh-ugrozakh-i-otsutstvii-sistemnosti-v-tsifrovizatsii. Last accessed: March 1, 2023

to increased vulnerability of Russian medical systems, 32%, 32%, and 30% have experienced data leaks, DDoS attacks, and ransomware attacks, respectively[6]. A study by Buldakova et al. identified potential threats to information security: data leaks can occur at almost any point, from sensors and cloud-based medical information systems to healthcare professionals and patients [64]. Furthermore, the rapid development of mobile technologies and m-Health has resulted in numerous mobile applications and ready-made wireless devices. The majority of them have not been certified [65, 66] and thus cannot be used as medical devices, because of noncompliance with cybersecurity rules (such applications are only suitable for use by patients) [67].

Certain issues with remote monitoring are related to remote patient identification. Accurate and reliable identification of the patient being monitored is challenging. Hence, remote monitoring cannot be used in expert settings or in problematic situations, and the patient is solely accountable for the appropriate use of devices [68].

CONCLUSION

The widespread use of remote monitoring technologies in Russia requires large-scale threat analysis, which is not limited to healthcare. In our country, medicine advances at the same rate as IT. Digitization in medicine cannot be considered a standalone industry; it is linked to external and internal factors and political, economic, and social considerations. Certainly, healthcare-specific aspects (personal data and patient confidentiality) should be considered. However, the foundation for the development of IT solutions in Russia is consistent.

SWOT analysis involves developing a further strategy. To accomplish this, the Weihrich model is used to predict the interaction of factors from different squares:

- Strengths—opportunities
- Strengths—threats
- Weaknesses—opportunities
- Weaknesses—threats

A comprehensive approach enables seamless integration of remote monitoring technologies into healthcare systems, making the benefits of digital medicine available to all.

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Conventional and Innovative Imaging Modalities in Bladder Cancer: Techniques and Applications

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ABSTRACT

This narrative review describes the current status of imaging in the evaluation of bladder cancer, considering conventional technologies such as ultrasonography, computed tomography urography, and magnetic resonance imaging, as well as novel technologies such as contrast-enhanced ultrasonography and dual-energy computed tomography.

The article is organized by first presenting an introduction on both the anatomy of the bladder (to understand its normal appearance on imaging) and the main features of bladder cancer with reference to epidemiology, clinical picture, classification, and treatment. Subsequently, the role of imaging is discussed, with an explanation of the technique and applications in bladder cancer assessment for each modality.

Imaging plays a critical role in the detection and staging of bladder cancer. In particular, the role of magnetic resonance imaging is expanding because it enables differentiating muscle-invasive bladder cancer from non-muscle-invasive bladder cancer using the Vesical Imaging-Reporting and Data System (VI-RADS), along with conventional technologies, such as computed tomography urography and ultrasonography. Contrast-enhanced ultrasound and dual-energy computed tomography are new imaging modalities that offer special advantages and provide the right approach to patients with oncological conditions. This review ends with the presentation of integrated imaging modalities such as positron emission tomography combined with computed tomography or magnetic resonance imaging, which are promising methods for bladder cancer staging.

Keywords: urinary bladder neoplasms; ultrasonography; multiparametric magnetic resonance imaging; diagnostic imaging.

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Традиционные и инновационные методы визуализации при раке мочевого пузыря: технология выполнения и применение

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АННОТАЦИЯ

В статье описаны современные методы визуализации при оценке рака мочевого пузыря с учётом традиционных технологий (ультразвуковое исследование, компьютерно-томографическая урография и магнитно-резонансная томография), а также новых технологий, таких как ультразвуковое исследование с контрастным усилением и двухэнергетическая компьютерная томография.

В начале статьи представлены общие данные об анатомии мочевого пузыря для понимания его нормального внешнего вида при визуализации, а также основные особенности рака мочевого пузыря с учётом эпидемиологии, клинической картины, классификации и лечения. Затем обсуждается роль каждого метода визуализации с объяснением техники выполнения процедуры и применения в оценке рака мочевого пузыря.

Визуализация играет важнейшую роль в выявлении и стадировании рака мочевого пузыря. В частности, в последнее время возрастает роль магнитно-резонансной томографии, которая, дополняя результаты компьютерно-томографической урографии и ультразвукового исследования, позволяет дифференцировать мышечно-инвазивный рак мочевого пузыря от немышечно-инвазивного с помощью системы отчётности и данных о визуализации (VI-RADS). Ультразвуковое исследование с контрастным усилением и двухэнергетическая компьютерная томография — новые методы визуализации, которые обладают особыми преимуществами и обеспечивают правильный подход к пациенту с онкологическими заболеваниями. В конце обзора представлены комбинированные методы визуализации, включающие позитронно-эмиссионную томографию, совмещённую с компьютерной или магнитно-резонансной томографией, которые также перспективны при стадировании рака мочевого пузыря.

Ключевые слова: новообразования мочевого пузыря; ультразвуковое исследование; мультипараметрическая магнитно-резонансная томография; диагностическая визуализация.

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膀胱癌的传统和创新成像技术：技术与应用

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摘要

这篇叙述性综述旨在描述成像技术在膀胱癌评估中的现状，其中考虑到了超声检查（US）、计算机断层扫描尿路造影（CTU）和磁共振成像（MRI）等传统技术，以及对比增强超声检查（CEUS）和双能量计算机断层扫描（DECT）等新型技术。文章首先介绍了膀胱的解剖结构，以了解正常的影像学表现，并结合流行病学、临床、分类和治疗介绍了膀胱癌的主要特征。随后，文章讨论了成像技术的作用，并解释了每种成像方式在膀胱癌评估中的技术和应用。影像学在膀胱癌的检测和分期中起着至关重要的作用。尤其是磁共振成像的作用正在不断扩大，因为它能利用膀胱成像报告和数据系统（VI-RADS）以及 CTU 和 US 等传统技术区分肌层浸润性膀胱癌和非肌层浸润性膀胱癌。为确保对肿瘤患者采取正确的治疗方法，CEUS 和 DECT 代表了具有特殊优势的新兴模式。本综述最后介绍了正电子发射断层扫描（PET）/CT 和 PET/MRI 等综合成像模式，它们是膀胱癌分期的理想方法。

关键词： 膀胱肿瘤；超声检查；多参数磁共振成像；诊断成像。

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INTRODUCTION

BLADDER ANATOMY

The urinary bladder is a subperitoneal, hollow muscular sac that serves as the reservoir of urine and allows its expulsion. This highly deformable organ is located in the pelvic cavity, behind the symphysis pubis, and below the parietal peritoneum. The size and shape of the urinary bladder change depending on how much urine it holds, with a total storage volume of up to 500 mL, and the pressure exerted by other organs. In particular, when filled, the bladder acquires a round or oval form [1].

The bladder's anatomical structure is complex. Macroscopically, it is divided into four parts: the apex or dome, which is directed anterosuperiorly; the body; the fundus; and the neck, which is positioned inferiorly. The bladder's floor has three openings, creating the trigone. The base of the trigone is formed by two openings from the ureters, which come from a short, oblique, intramuscular course. The third is the urethral opening, located at the bladder neck, precisely at the inferior angle of the trigone, where urine is expelled from the bladder [2, 3].

Microscopically, the bladder has a layered composition, similar to that of the ureters. The inner lining is made up of a transitional epithelium, known as the urothelium, which consists of transitional cells. In a relaxed state, the urothelium is 5–7 layers thick; however, it can stretch to accommodate increased urine volume. The lamina propria or submucosa, which is a subepithelial connective tissue containing muscle fibers with variable disposition, lies beneath the urothelium. Then, the muscularis propria is composed of the detrusor muscle, featuring the inner longitudinal, middle circular, and outer longitudinal layers. This smooth muscle is responsible for contracting and releasing urine from the bladder. Bladder walls are covered by serosa, a thin connective tissue layer that continues with the peritoneal layer of the abdominal wall and contains blood vessels. In areas without serosa, the bladder is enveloped by the adventitia, a layer of loose connective tissue [4, 5].

BLADDER CANCER

Bladder cancer (BCa) is a prevalent and aggressive malignancy worldwide, secondary to prostate cancer considering urogenital tumors [6]. The International Agency for Research on Cancer has documented that the following risk factors are associated with BC: tobacco smoking; certain occupational exposures, such as working in industries like aluminum production, rubber production, painting, firefighting, and exposure to various dyes (e.g., magenta and auramine) or dye intermediates (e.g., 4-aminobiphenyl); environmental factors such as X-ray radiation, gamma radiation, and arsenic; specific medications such as cyclophosphamide; opium consumption; and Schistosoma infection. Other risk factors, such as dietary elements, microbiome imbalances, gene–environment interactions, exposure to diesel exhaust emissions, and pelvic radiotherapy, have shown correlations with BCa development [7].

The most common presentation symptom of BCa is an asymptomatic macro or microhematuria, known as "painless hematuria," which occurs in approximately 85% of patients. To identify the origin of the bleeding, hematuria must be carefully characterized as initial, terminal, and total [8]. Other frequent presenting symptoms of BCa are linked to bladder irritability, such as urinary frequency, urgency, and dysuria. Flank pain appears when ureteral obstruction occurs. Less common symptoms are lower extremity edema and palpable pelvic masses. In advanced cases, patients present with weight loss and abdominal or bone pain because of distant metastases [9, 10].

Urothelial carcinoma (UC) is the most common BCa subtype, followed by squamous cell carcinoma, sarcoma, lymphoma, and adenocarcinoma. Two-thirds of all BCa cases are non-muscle-invasive BC (NMIBC), whereas one-third are muscle-invasive BC (MIBC) and are related to a higher risk for metastasis and a significantly worse prognosis [7]. BCa morphology can vary depending on tumor growth and progression. For example, horizontal growth is typical of carcinoma in situ (CIS), whereas exophytic polypoid masses or sessile infiltrative lesions are typical of invasive forms [8, 6].

BCa is staged using the standard TNM system; as with other hollow organs, the T parameter is based on the depth of invasion of the layers. In particular, pTa refers to papillary carcinoma, an NMIBC type that presents as an exophytic mass lesion, whereas pTis refers to the flat CIS, included in NMIBC. At T1 stage, the tumor invades the lamina propria and is typically treated with transurethral resection of the bladder tumor (TURBT) and adjuvant intravesical therapy. At T2, the tumor invades the detrusor muscle, becoming an MIBC. T3 occurs when a tumor infiltrates the perivesical fat, and when it affects the surrounding organs, T4 commences. Tumors at T2 and above require more aggressive management, such as radical cystectomy [11]. The N parameter considers the lymph node involvement. N1 and N2 require the presence in the true pelvis of one or multiple nodes, respectively. In N3, the metastasis reaches the common iliac node. M1 indicates the presence of metastasis, with subclassifications of M1a when there is no regional lymph node involvement and M1b when other distant metastases are present [5,12].

IMAGING MODALITIES

Imaging modalities, including ultrasonography (US), computed tomography urography (CTU), and magnetic resonance imaging (MRI), play an important role in diagnosing and staging BCa. They are crucial for BCa detection and differentiating a T1 from a T2, considering that the treatment changes significantly between the two stages [13].

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Considering the sensitivity of BCa detection, this parameter increases from US to CTU, reaching a very high rate with MRI. Nevertheless, the latter is gaining wider applications because it is essential in differentiating an NMIBC from an MIBC.

International guidelines recommend US, not excluding physical examination, as the first step in the diagnostic workup of a suspicious tumor, as in the case of painless hematuria, and requires cystoscopy and subsequent biopsy for the final diagnosis [8].

Radionuclide diagnostics such as positron emission tomography (PET)/CT and PET/MRI have been discussed because hybrid imaging methods appear to be promising imaging tools in BCa staging, particularly for the detection of lymph node and distant metastases, as they are more accurate than conventional CT.

This narrative review also includes imaging modalities such as dual-energy CT (DECT) and contrast-enhanced US (CEUS) that are not mentioned in the habitual diagnostic workup but have utility in particular applications.

ULTRASONOGRAPHY

Technique

The patient should drink 300–500 mL of water before the examination to enable adequate distension of the bladder, which should be filled moderately. If underdistended, the evaluation of the bladder wall is limited because a wall thickening or a focal mass can be overestimated, whereas overdistention leads to patient discomfort and low cooperation.

Transabdominal US is mostly performed, which is analyzed in this review. Transvaginal US is performed in women to improve spatial resolution if needed, whereas in men, transrectal US can be performed if the transabdominal approach is limited. The examination is performed with the patient in the supine position, with lateral decubitus when required.

A convex probe (4.5–6 MHz) is more appropriate, and an abdomen/renal preset is suggested. For correct evaluation of the organ, the probe should be placed just above the symphysis pubis and angled caudally, and scanning should be performed in two orthogonal planes and in the oblique direction. In this way, the bladder is always centered within the field of view during the examination.

The bladder wall appears as layered with the hypoechoic muscle between two hyperechoic layers corresponding to the serosa and mucosa. The lateral and posterior walls are well visualized in US, and the anterior wall is affected by the reverberation phenomena, which can be adjusted with the time–gain compensation. To selectively explore the anterior wall and the vesical cupola, the examination can be performed using a higher-frequency linear transducer (>7.5 MHz). To evaluate the ureteral jet, which is a normal and periodic efflux of urine from the ureter into the bladder, color Doppler is necessary for the trigone of the posterior wall to exclude a complete ureteral obstruction.

US allows for the evaluation of the vesical capacity and residual urine volume. The urine volume is estimated by taking the three dimensions in the two orthogonal planes and applying an automated formula that includes a correction factor (k) that considers the complex shape of the bladder [11, 14].

Applications

Transabdominal US is influenced by various factors, such as the amount of vesical filling, the patient's constitution, tumor size and distribution, or previous treatments (radiotherapeutic, chemotherapeutic, or surgical) [13]. US is reported to be 63% sensitive; in particular, the sensitivity rate decreases when male patients suffer from prostate hypertrophy, which indicates irregularity of the bladder base wall. On the contrary, the sensitivity rate increases when compared with cystoscopy in the case of a tumor within the diverticula because evaluation of the narrow neck by cystoscopy is limited [14].

Generally, BCa can be easily detected when is localized on the lateral and posterior walls, considering that most UC cases are localized in the posterior walls, and larger, which is the most important factor that influences the diagnostic sensitivity of US. Tumors can only be detected if their maximum diameter is >5 mm. A larger tumor is often associated with other signs such as wall rigidity and asymmetrical bladder distension. The site of origin of the tumor is a less important factor that influences sensitivity, although some regions (dome, anterior wall, and base) are more difficult to evaluate because of technical reasons [11].

Bladder masses are commonly echogenic, and shaped irregularly such as cauliflower-like, and are found either mounted on the bladder wall or in areas of the bladder wall with irregularly increased thickness. However, BCa features in US can differ depending on morphology and appear as papillary, infiltrating, or invasive, as well as with mixed features of papillary and infiltrating. Papillary forms appear as small echogenic masses originating from the bladder wall and projecting into the lumen, which are easily detected when larger than 2–3 mm. Conversely, if the tumor is a superficial carcinoma, it can be recognized only based on a soft wall thickening, which presents a normal echo structure and is not a sign of invasion. Infiltrating tumors have typical small papillary components and hypoechogenicity compared with the echogenicity of the vesical wall and the perivesical adipose tissue [11, 13, 14].

If a focal mass is detected in the US image, the presence of additional lesions must be further explored, considering that one-third of tumors are multifocal, and an additional evaluation with Doppler that helps in identifying the internal vascularity with a rich blood flow signal or a stellate morphology and differentiating a potential tumor from a blood clot. The latter can be excluded by asking the patient to change position from supine to lateral to assess for lesion mobility typical of a clot or performing bladder irrigation, followed by another US scan [11] (Fig.1).

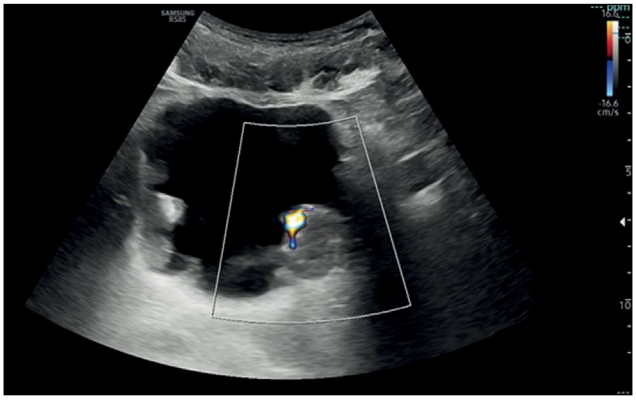

Fig. 1. Transverse ultrasound image of the bladder showing diffuse irregular wall thickening with multiple masses and endoluminal development. Color Doppler on the largest echogenic lesion, localized on the left posterior bladder wall, showed vascularity within the mass.

CONTRAST-ENHANCED ULTRASONOGRAPHY

Technique

CEUS, a novel technology, can objectively reflect tissue perfusion, using ultrasound contrast agent (UCA). In conventional US, the bladder should be adequately distended before the examination. Initially, a complete baseline US evaluation should be performed before CEUS. The most commonly used UCA is sulfur hexafluoride (SonoVue), which is a blood pool tracer that never leaves the blood vessel and can be used for real-time dynamic imaging of microcirculation perfusion. It is injected intravenously (IV) in an amount of 2.4 mL, using a 21-G peripheral cannula, followed by approximately 5 mL of saline. The UCA remains in the circulation for a period sufficient to reach the organ and guarantee adequate interpretation of both arterial and venous phases. The study is conducted in basal B-mode conditions with a low mechanical index to reduce the incidence of microbubble rupture.

A normally distended bladder has a thin wall of approximately 2 mm, with little signal to the CD, and is nearly imperceptible in the initial phase of administration of the contrast medium, with a progressive signal enhancement up to approximately 2 min [15].

Applications

CEUS utilizes the biological principle that tumors exhibit distinct neovascularization patterns, leading to variations in contrast agent wash-in and washout times compared with non-neoplastic conditions. A key advantage of CEUS is its real-time capability. Unlike CT or MRI, which requires determining the optimal acquisition time for better differentiation of tumors from the surrounding bladder wall, CEUS does not necessitate such precise timing because the enhancement pattern can vary among patients due to factors such as cardiovascular health or the extent of microvascularization in BCa. With CEUS, a dynamic real-time assessment of enhancement can be performed continuously, eliminating the need to pinpoint a specific moment.

Moreover, prolonged BCa enhancement allows for a comprehensive exploration of bladder walls with just one dose of contrast agent, making it useful in detecting multiple cancer foci in multicentric cancers. With arterial neovascularization, a common feature of BCa, the signal enhancement in papillary and sessile lesions or small focal thickening areas is immediately noticeable, similar to that in the arterial phase of uro-CT. The signal increase is typically uniform, except in larger, high-grade, invasive cases where it may be non-uniform, particularly in necrotic regions within the tumor [16].

After the rapid arterial phase, most tumors reach a plateau with slow washout, although the venous phase can vary based on size and cellular differentiation. CEUS is valuable for differential diagnosis, helping distinguish neoplastic growths from other bladder wall alterations that may mimic tumors, such as intravesical clots, adherent lithiasis, benign prostatic hypertrophy-related thickening, or inflammation-induced wall thickening. Focal or nodular enhancement indicates neoplasia in these situations.

BCa detection with CEUS relies on identifying areas of focal hyperenhanced wall thickening or enhancing masses protruding into the bladder lumen. The use of a contrast agent in US improves BCa detection, particularly in cases where traditional US studies may be inconclusive because of factors such as inadequate bladder distension, history of bladder surgeries, obesity, or the presence of an intravesical catheter.

The depth of wall invasion, histological grade, and extension beyond the bladder are the main factors for determining the prognosis and treatment approach for BCa. Although MRI and CT are the preferred modalities for local staging, CEUS can aid in evaluating wall invasion by assessing the enhancement pattern of the bladder wall. It can help differentiate a noninvasive UC from an infiltrating carcinoma based on the presence or absence of a hypoechoic layer and the enhancement pattern after arterial enhancement [15].

Malignant bladder tumors exhibit distinct enhancement patterns compared with benign lesions, making CEUS a valuable tool for distinguishing between them and improving diagnostic accuracy. CEUS enables real-time observation of the blood flow in bladder tumors, aiding in the differentiation of benign from malignant tumors. However, compared with CT and MRI, its usefulness in bladder staging for infiltrating carcinomas is limited because it cannot assess perivesical fat infiltration and retroperitoneal lymph nodes (Fig. 2) [16].

COMPUTED TOMOGRAPHY UROGRAPHY

Technique

CTU, a CT examination of the urinary tract, is performed with an unenhanced scan and after IV contrast material

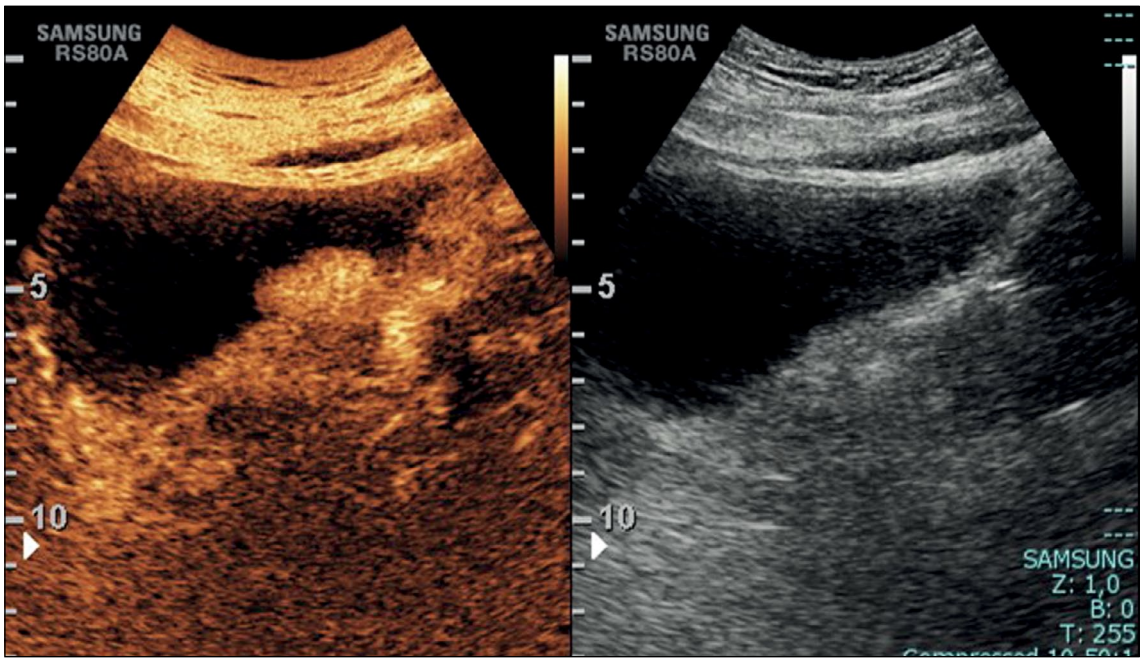

Fig. 2. Sagittal contrast-enhanced ultrasound images showing an enhancing mass of the left bladder wall, not well definable in the B-mode as noticed on the left side of the image.

administration with a multiphasic acquisition to obtain a set of images that show a fully opacified and distended intrarenal collecting system, ureters, and bladder [17].

More precisely, the protocol includes an unenhanced scan of the abdomen and pelvis. After IV administration of contrast agent, the phases obtained are as follows: a corticomedullary phase 30–40 sec after the injection, resulting in an arterial phase; a nephrographic phase 100 sec after the injection; and an excretory phase 8–12 min after the injection. The scan should be in a craniocaudal direction, and the extension on the Z-axes should start from the diaphragmatic dome to reach the pubic symphysis, particularly in the unenhanced and nephrographic scan, whereas the corticomedullary and excretory phases can start from the upper pole of the kidney.

However, the main limitation of a multiphasic protocol is the high radiation exposure, ranging from 25 to 35 mSv. For this reason, particularly in young patients, a split-bolus technique is suggested. This includes a two-phase protocol with an unenhanced scan, followed by two IV injections of contrast agent of approximately 80 and 40 mL. After the first administration, the corticomedullary scan is obtained after 20 sec. After an 8-min delay, the second bolus is administered, followed by a scan at 100 sec to obtain the nephrographic–excretory phase. The scan should be in a craniocaudal direction, and the extension on the Z-axes should start from the diaphragmatic dome to reach the pubic symphysis, particularly in the unenhanced and nephrographic–excretory scan, whereas the corticomedullary phase can start from the upper pole of the kidney [18].

Both protocols may be completed with an IV administration of 10 mg of furosemide 2–3 min before the corticomedullary scan to obtain adequate distension of the upper urinary tracts and the bladder. Therefore, an underdistended bladder can appear thickened, particularly along its anterior wall, and the lumen can show an incomplete mixing of nonopacified urine and contrast material, resulting in a urine contrast level because the specific gravity of the contrast medium is higher than that of urine [17].

Applications

Abdominal CTU is the most commonly used technique, thanks to its many advantages, such as wide availability, fast scanning, and creation of multiplanar reformatted and three-dimensional (3d) reconstructed images. In patients suspected or diagnosed with BCa, the examination is performed for BCa detection and staging, in the latter case to assess the locoregional and distant extension of the disease.

Each phase of the protocol required in a CTU has advantages. The unenhanced CT scan is used to measure the basal attenuation of the mass to compare it after contrast enhancement and identify the presence of stones, calcifications, hemorrhages, and clots. The corticomedullary phase is used to evaluate suspected vascular abnormalities or arterial enhancements. The nephrographic phase is used to detect and characterize renal masses. The excretory phase is used to assess the urothelium because the bladder is filled with dense contrast material and an endoluminal soft tissue lesion will appear as a filling defect [19].

BCa can appear as a focal region of bladder wall thickening or as a mass protruding into the bladder lumen or extending into adjacent tissues in advanced cases. If the bladder distension is not adequate, the asymmetry of the thickening must be examined. Generally, masses have

soft tissue attenuation and may be encrusted with small calcifications.

CTU has the highest accuracy, with a pooled sensitivity of 92% and a pooled specificity of 95% in detection and staging. Concerning T stages, it is limited in differentiating NMIBC from MIBC but can distinguish T3 and T4 tumors. Regarding N stages, it enables the assessment of lymph node morphology and size. As regards the size, a suspect is made when the pelvic, abdominal, and retroperitoneal lymph nodes have a short axis, greater than 8 and 10 mm. Regarding the morphological criterion, the presence of confluent lymph nodes or those with a necrotic center is considered a clear sign of lymph node metastasis. In the study of lymph nodes, CTU is limited by potential overstaging, detected in approximately 30% of cases with reactive lymphadenopathies, with a short axis >10 mm, and potential substaging when lymph nodes are malignant but have dimensions within the limits. Concerning M stages, BCa most frequently metastasizes to the pelvic and retroperitoneal lymph nodes. The bone is the most common site for distant BCa metastases; most appear sclerotic but can also be lytic or mixed lytic sclerotic. In solid organs, the liver and lung are the most frequent sites of metastasis, and other organs are far less frequently involved [11].

After the diagnostic workup, for detection requiring further examination, an endoscopy with biopsy may be indicated to confirm the diagnosis and determine the number, extent, and localization of the urothelial tumors [18].

DUAL-ENERGY COMPUTED TOMOGRAPHY

Technique

DECT is a novel imaging technology that operates two X-ray tubes with different kilovoltages (one lower and one higher) to images reconstructed in post-processing.

Considering the purpose of the examination such as the detection of a suspicious BCa or its staging, the most useful types of images are the virtual monochromatic (VMC), virtual non-contrast (VNC), iodine map, and atomic map.

VMC generates images similar to those of conventional single-energy CT considering quality; however, it provides more reliable attenuation values. The lower-energy kilovoltage setting can increase contrast among near structures, thanks to the high beam attenuation of iodine. Consequently, a parietal lesion is easier to recognize. The higher-energy kilovoltage setting can decrease noise and artifacts. The comparison between the two different kilovoltages settings, from VMC-acquired images, also produces a spectral attenuation curve, which is a function of energies. The latter is attributed to its properties, which are useful to improve lesion characterization.

VNC generates images "without contrast" by suppressing the iodine material uptake from scans acquired post-contrast. Therefore, VNC images are also known as iodine-removed images. Accordingly, the radiation dose could be reduced because the patient has not undergone the first unenhanced scan.

The iodine map is a material-specific image in opposition to the iodine-removed image, as iodine is selected and not suppressed to show all areas with iodine uptake. This image results in a color map that can quantify the iodine uptake expressing it in mg/mL. Moreover, it allows for distinguishing a vascularized lesion from a nonvascularized lesion considering the amount of iodine filling the aorta.

The effective atomic number map is a quantitative method for assessing material differentiation and evaluating attenuation variations as a function of energy [3].

Applications

DECT, a new imaging method, may help overcome the main limitations of CT such as ionizing radiation overexposure typical of patients with oncological conditions who underwent repeated acquisitions and tight follow-up.

Moreover, DECT allows for better lesion characterization, thanks to post-processing reconstruction.

VNC images provide a true unenhanced image that helps exclude the presence of stones, calcifications, and fresh bleeding that appears hyperdense in the typical basal scan and in measuring the attenuation value of reference for the subsequent post-contrast graphic scans.

The spectral curve, in the case of bladder wall thickening, shows a curve tending to increase from lower values of kilovoltage setting.

VMC images at low-energy kilovoltage settings generate better contrast of the tumor despite the nearby regions and increase the sensitivity in tumor detection. Moreover, by normalizing the iodine quantification to that of the aorta, in the nephrographic phase, this image type had increased specificity when a threshold of ⩾3.0 mg/mL is reached and allows the differentiation of a vascular from a nonvascular lesion. The formula is as follows: |I| normalized=|I| lesion/|I| aorta [20, 21].

DECT advantages also concern BCa staging because iodine maps enable easier evaluation of the tumor infiltration of wall layers, including the muscular layer in differentiating an NMIBC from an MIBC and evaluating lymph node involvement and presence of metastases.

For treatment planning, the application of this technology may be crucial because it can better assess the relationship between the tumor and a vascular structure, with increased contrast obtained with the VMC at a lower kilovoltage setting, offering an important parameter (Fig. 3 and 4) [22].

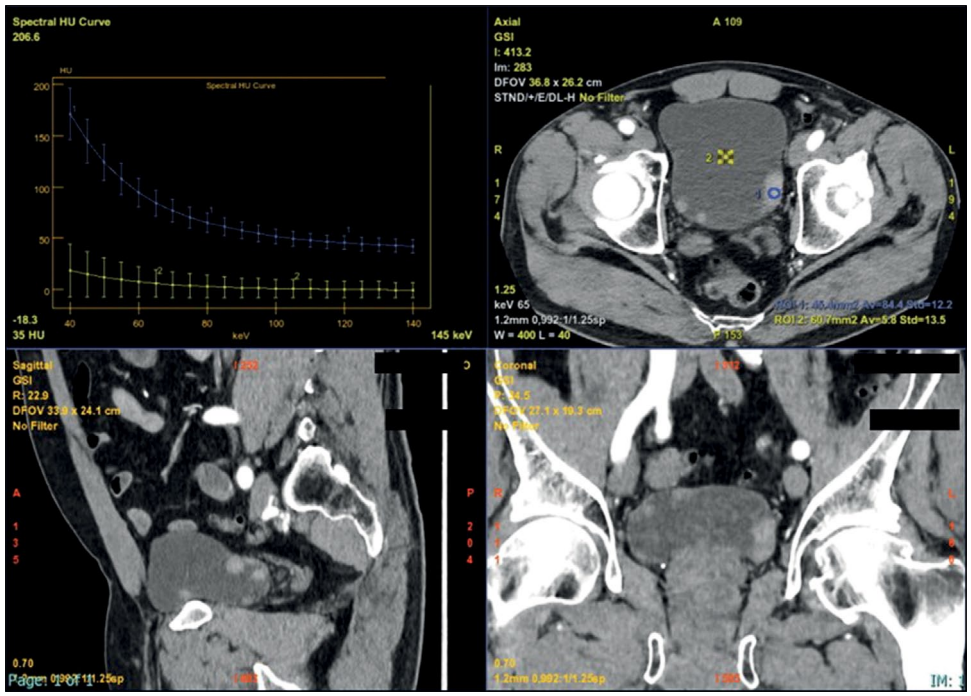

Fig. 3. Multiplanar iodine map images showing different attenuations of multifocal masses, the main localized on the left posterior wall, with different Av values compared with the Av endoluminal value. The spectral curve (upper left side) allowed the characterization of materials because each material has a different attenuation curve.

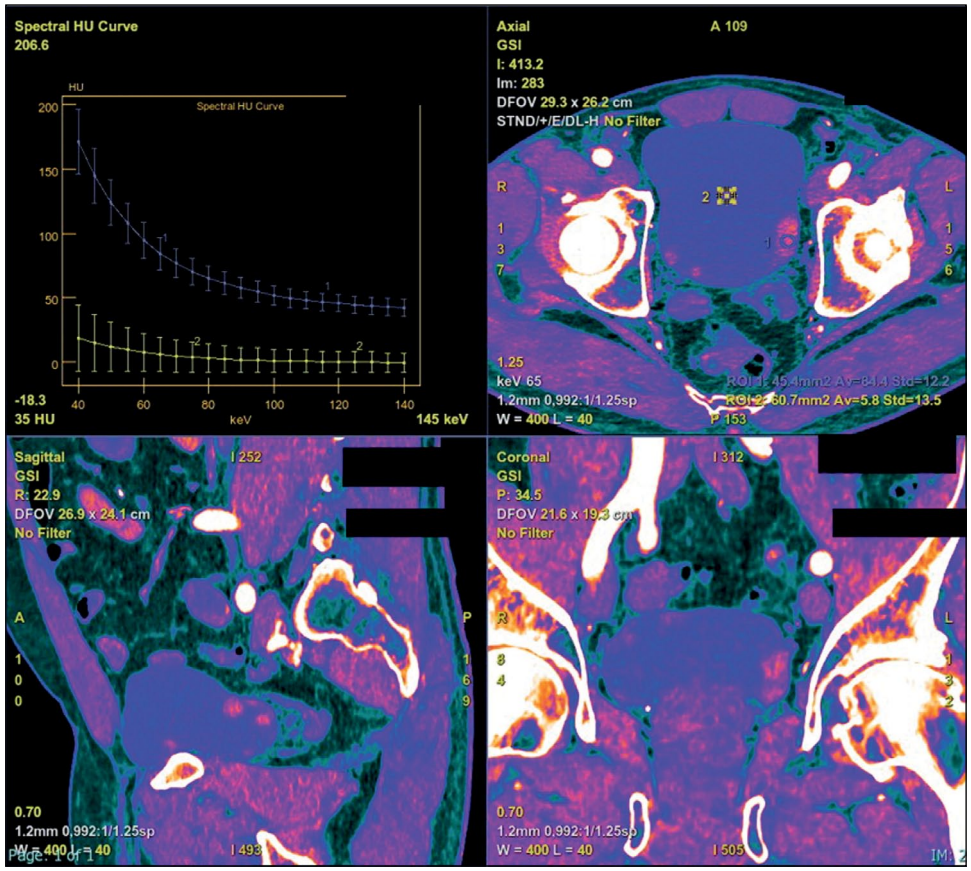

Fig. 4. Multiplanar iodine map with coloring overlap showing different attenuations of multifocal masses, the main localized on the left posterior wall, with different Av values compared with the endoluminal Av value. The spectral curve (upper left side) allowed the characterization of materials because each material has a different attenuation curve.

MAGNETIC RESONANCE IMAGING

Technique

For adequate examination, the preparation of the patient with moderate bladder distention is crucial. The patient should urinate and start drinking 500 mL of water about 2.5 h before MRI.

A targeted scan with the localizer can guide the technician in starting the test when the bladder is properly distended.

Bladder distension, as mentioned before, is essential in BCa evaluation. The bladder wall may appear thickened, and underdistension may lead to a misdiagnosis. Conversely, overdistension may cause discomfort in patients, who would move during artifact detection, or interrupt the examination if the patient could not hold more urine.

Generally, using a 1.5-T MRI scanner, the examination is performed with the patient in a supine position, and sequences necessary for a proper bladder evaluation are as follows: T1-weighted (T1W) fast spin echo on the axial plane; T2W sequences with high resolution and narrow field of view on axial, sagittal, or coronal plane and with fat suppression; diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC); and finally, DCE-MRI with T1W 3D gradient echo and the Dixon three-point method.

In female patients, images must include not only the urinary bladder but also the uterus, ovaries, and vagina, whereas in male patients, the images must include the prostate [5].

Applications

In BCa evaluation, MRI is mainly applied in local tumor staging because it allows distinguishing the presence and absence of muscular infiltration, resulting in the differentiation between NMIBC and MIBC, and stages ranging from T1 to >T2.

The bladder wall has multilayers, with the urothelium and lamina propria appearing as a hyperintense line only after contrast agent administration, in the early phase of DCE-MRI sequences. The muscular layer appears as a low-intensity line on T2W, medium-intensity line in DWI and ADC sequences, and with a late and gradual enhancement in DCE-MRI [5].

The development of the vesical imaging-reporting and data system (VI-RADS) score helps standardize the approach to MRI acquisition, interpretation, and reporting in patients diagnosed with BCa through TURBT. The score ranges from 1 to 5 and expresses the increasing risk of invasion of the detrusor muscle [6]. For accurate examination, the sequences include T2W, DWI/ADC, and DCE with each sequence generating a score of 1–5. T1W is not useful for differentiating MIBC from NMIBC because the detrusor muscle shows intermediate-signal intensity as well as a cancerous process [23].

Initially, the structural information in the T2W must be analyzed, evaluating the integrity of the muscular layer in T2W that should appear as homogeneously hypointense in contrast with a hyperintense signal of the bladder content. Then, the signal on DWI/ADC and DCE sequences must be evaluated. In tumors, the signal would appear hyperintense on DWI and hypointense on the ADC map, and there is an early enhancement of the inner layer. After obtaining information from each sequence, the combination of the different scores is compared to obtain the final VI-RADS score.

VI-RADS 1 is assigned when there is an interruption of the intensity signal line corresponding to the muscular layer in T2W. The maximum size reached from the lesion (sessile or vegetating) is 1 cm. VI-RADS 1 suggests an NMIBC.

VI-RADS 2 is assigned when there is an interruption of the intensity signal line but with a diameter >1 cm. The lesion could be associated with edema, appearing with a thickening line, and related to an increasing probability of invasion. VI-RADS 3 expresses a doubt: there is no clear disruption of the low-signal intensity of the muscular layer in T2W. VI-RADS 4 is assigned when there is a certain invasion of the muscular layer. VI-RADS 5 is assigned when the muscular layer invasion is associated with the involvement of the nearly adipose tissue.

In case of a discrepancy in results, the DWI/ADC map and DCE will prevail to downgrade and upgrade lesions [5].

MRI also plays a role in post-therapeutic approach in BCa, concerning patient evaluation after neoadjuvant chemotherapy and immunotherapy, which is the last revolution in the treatment MIBC. The purpose is to assess the lesion after treatment under T2W, DWI/ADC, and DCE sequences and establish the response to the therapy, which can be partial, complete, or absent. In this context, the VI-RADS scoring system has shown promising results [24].

In conclusion, MRI is rapidly becoming a leading imaging modality in BCa diagnostic workup, assessment of response to therapies, and longitudinal surveillance and plays an important role in treatment planning for BCa surgical and radiation therapy. Nevertheless, transurethral resection biopsy is required for tumor grading and cannot be replaced by MRI (Fig. 5 and 6).

RADIONUCLIDE HYBRID IMAGING: POSITRON EMISSION TOMOGRAPHY/ COMPUTED TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY/ MAGNETIC RESONANCE IMAGING

PET/CT combines PET and CT into a single imaging modality. 2-Fluorine-18-fluoro-2-deoxy-d-glucose (FDG) is the most common radiotracer in oncology; therefore, FDG PET/CT is widely used in the clinical management in many cancer types [25, 26].

As an analog of glucose, 18F-FDG is taken up within tumor cells via GLUT and other transporters where it is phosphorylated by hexokinase but not further metabolized, leading to intracellular accumulation. PET/CT offers a high-sensitivity scan for metabolic activity with precise anatomical localization [27].

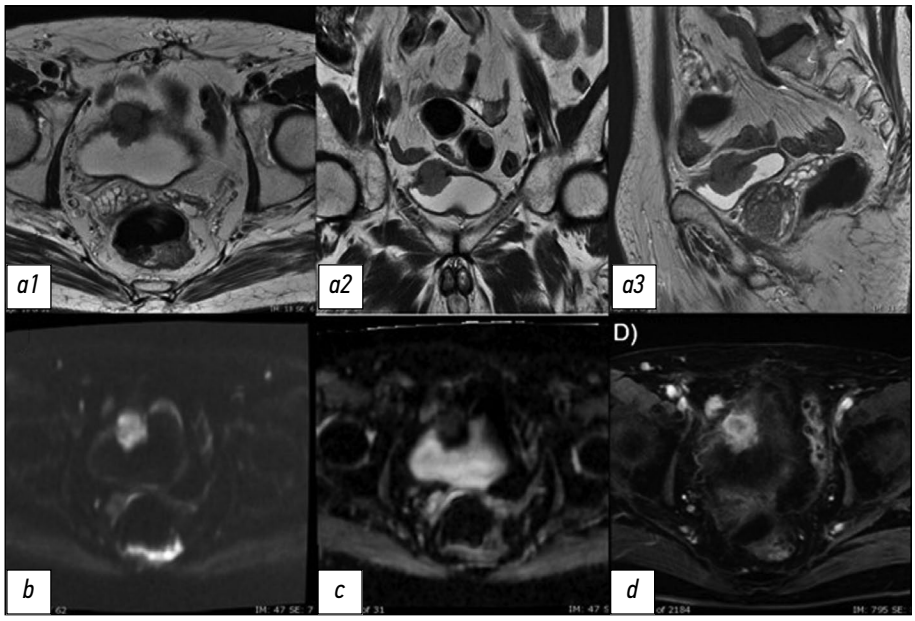

Fig. 5. (*a*) Multiplanar T2W sequences showing a mass on the left posterior wall, >1 cm in size, with an intermediate signal of the muscular layer (VI-RADS 4). (*b*) DWI sequence and ADC maps showing a lesion with significantly limited diffusion, extending through the muscular layer. The low ADC value of approximately 0.9×10^{-3} mm^2/sec denote malignancy (VI-RADS 4). (*c*, *d*) DCE sequence showing early and heterogeneous enhancement of the lesion, extending through the muscular layer (VI-RADS 4). The VI-RADS overall score was four. Image source: Eusebi Laura, Masino Federica, Gifuni Rossella, Fierro Davide, Michele Bertolotto, Cova Maria Assunta, Giuseppe Guglielmi. Role of Multiparametric-MRI in Bladder Cancer. Current Radiology Reports 11, 69–80 (2023). https://doi.org/10.1007/s40134-023-00412-5. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license 4.0 (http://creativecommons.org/licenses/by/4.0/).

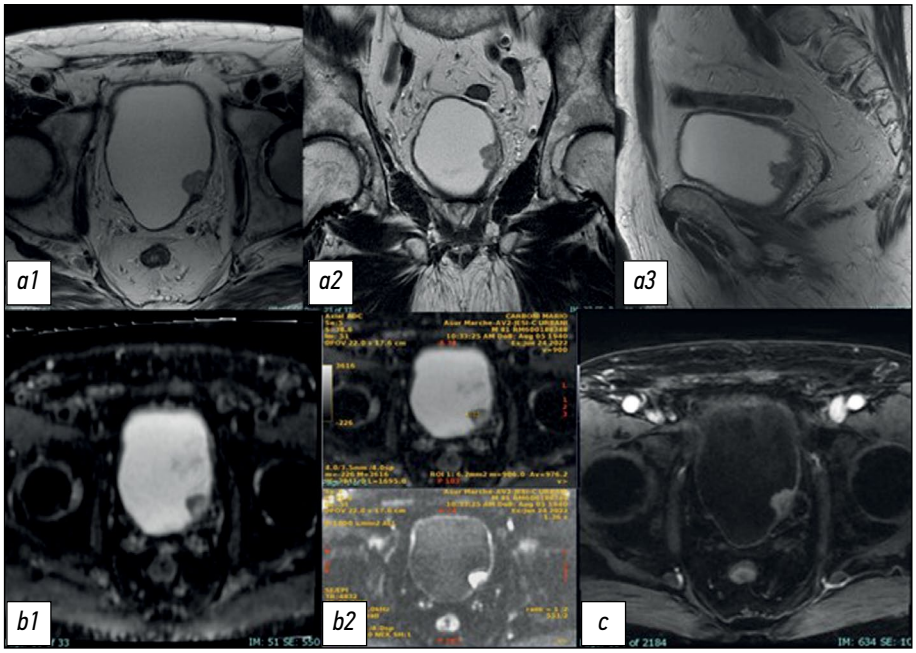

Fig. 6. (*a*) Multiplanar T2W sequences showing a mass, >1 cm, on the right lateral wall of the bladder dome, with an intermediate signal extending through the muscular layer and invading the perivesical adipose tissue (VI-RADS 5). (*b*) DWI sequence and c ADC map showing a significantly limited diffusion lesion extending through the muscular layer and invading the perivesical adipose tissue (VI-RADS 5). (*c*) DCE showing an early and heterogeneous improvement of the lesion extending through the muscular layer and the perivesical adipose tissue (VI-RADS 5). The VI-RADS overall score was five. Image source: Eusebi Laura, Masino Federica, Gifuni Rossella, Fierro Davide, Michele Bertolotto, Cova Maria Assunta, Giuseppe Guglielmi. Role of Multiparametric-MRI in Bladder Cancer. Current Radiology Reports 11, 69–80 (2023). https://doi.org/10.1007/s40134-023-00412-5. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license 4.0 (http://creativecommons.org/licenses/by/4.0/).

In BCa, in recent years, this hybrid imaging technique is increasingly used for recurrence detection after radical cystectomy [25, 26].

Considering that urothelial tumors have a high FDG uptake, urinary excretion of FDG may mask tumors in all the urinary tract extension, particularly in the bladder. Because of this important limitation in this technique, several methods have been investigated and tested to reduce urine FDG activities, particularly profuse water uptake, diuretic administration, and catheterization are helpful. However, catheterization that involves flushing and retrograde bladder filling can increase the risk of iatrogenic urinary tract infection and consequently increase hospitalization times. Conversely, this limitation consists in the application of early dynamic images that could be useful for BCa detection before the excretion and collection of FDG in the bladder [25].

Currently, FDG PET/CT is not recommended as the initial diagnostic or as a primary staging tool because it is assumed to be unable to evaluate microscopic perivesical fat invasion and adjacent-organ involvement. Nevertheless, it may be used to assess treatment response, detect any residual or recurrent diseases, and differentiate scar tissue from active tumors [26].

PET/MRI is a hybrid imaging modality that combines the functional information provided by PET and the detailed anatomical images obtained through MRI. The PET component, typically using FDG as a tracer, highlights areas with increased metabolic activity, which is often indicative of cancerous tissue. Conversely, the MRI component provides a great contrast of soft tissue. Considering these premises, PET/MRI could overcome the intrinsic limitation of PET/CT in assessing local disease extent because quality MR images can help in assessing the spread of malignant tissue in the perivesical fat and the involvement of the muscular layer [28]. Nevertheless, the sensitivity of PET/MRI is still very low in diagnosing early-stage BCa because of the renal excretion of the FDG PET tracer; thus, small lesions in the bladder wall can be missed [29].

CONCLUSIONS

Imaging is crucial in BCa evaluation, particularly in detection and staging. Conventional technologies such as US, particularly CTU, are nowadays flanked by MRI, which is acquiring importance because it allows the differentiation of NMIBC from MIBC through VI-RADS. Combined imaging techniques such as PET/CT and PET/MRI are promising tools in BCa staging. Emerging modalities such as CEUS and DECT are not included in the typical diagnostic and staging process but have applications in particular conditions and can provide useful information for both the clinicians and radiologists to guarantee the proper approach to patients with oncological conditions, with a future eye on increasingly personalized medicine.

ADDITIONAL INFORMATION

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Multiple Biliary Microhamartomas Diagnosed in an Unsuspecting Elderly Patient

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ABSTRACT

Multiple biliary hamartomas are a benign incidental finding in the liver. They are not easily detected if one has never seen them, and if appropriate imaging tests are unavailable, and also can be challenging to differentiate from other liver lesions based on imaging alone. Thus, this study aimed to expand the radiologist's digital image library, enabling a quick and precise differential diagnosis. This paper also highlights the importance of thorough radiological assessment and need for a multidisciplinary approach, involving radiologists, hepatologists, and pathologists, to ensure a precise diagnosis.

The patient presented at the hospital for a computed tomography scan and an abdominal magnetic resonance imaging recommended by his general practitioner to assess the biliary tree (magnetic resonance cholangiopancreatography), owing to persistent abdominal pain. The patient had never undergone an abdominal magnetic resonance imaging previously; hence, the discovery of hepatic lesions was incidental and unexpected.

Magnetic resonance imaging revealed multiple benign lesions in both the hepatic lobes comparable to the Von Meyenburg complex. These lesions are multiple hamartomas and behave differently in all magnetic resonance imaging sequences.

Images acquired with different magnetic resonance imaging sequences were carefully examined. Multiple lesions were found scattered throughout the liver; however, the lesions were benign and consistent with the diagnosis of multiple biliary hamartomas.

Medical practitioners should examine the presence of multiple biliary hamartomas and consider them in the differential diagnosis when patients present with hepatic abnormalities. This can prevent unnecessary interventions and guide appropriate patient management.

Keywords: liver; hamartomas; Von Meyenburg complex; magnetic resonance imaging; diagnostic imaging; magnetic resonance cholangiography; bile duct neoplasms.

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Множественные билиарные микрогамартомы, случайно диагностированные у пожилого пациента

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АННОТАЦИЯ

Множественные билиарные гамартомы, также называемые комплексами фон Мейенбурга — это доброкачественные новообразования печени, которые могут быть выявлены случайно. Их нелегко обнаружить, если ранее не доводилось с ними встречаться, а также если соответствующие методы визуализации на момент обследования недоступны. К тому же их сложно отличить от других поражений печени на основании визуализационных данных. Таким образом, описание данного клинического случая направлено на пополнение библиотеки цифровых изображений, что позволит радиологу быстро и точно провести дифференциальную диагностику. Кроме того, подчёркивается важность тщательной рентгенологической оценки этого заболевания и необходимость мультидисциплинарного подхода с участием радиологов, гепатологов и патологов для постановки точного диагноза.

Пациент поступил в больницу для проведения компьютерной томографии и магнитно-резонансной томографии брюшной полости по рекомендации терапевта для оценки состояния билиарного дерева (магнитно-резонансная холангиопанкреатография) в связи с постоянными болями в животе. Пациенту никогда ранее не проводили инструментальное обследование брюшной полости, поэтому новообразования печени оказались случайной и неожиданной находкой.

Магнитно-резонансная томография выявила множественные доброкачественные образования в обеих печёночных долях, сопоставимые с комплексами фон Мейенбурга. Эти поражения представляют собой множественные гамартомы и ведут себя по-разному во всех последовательностях сканирования.

В ходе исследования были тщательно изучены изображения, полученные с помощью различных последовательностей магнитно-резонансной томографии. В печени обнаружены множественные очаги поражения с признаками доброкачественности, которые соответствовали диагнозу «множественные билиарные гамартомы».

Практикующие специалисты должны уметь распознать это заболевание и учитывать его при дифференциальной диагностике у пациентов с патологиями печени. Это позволит предотвратить ненужные вмешательства и выбрать правильную тактику ведения пациентов.

Ключевые слова: печень; гамартомы; комплекс фон Мейенбурга; магнитно-резонансная томография; диагностическая визуализация; магнитно-резонансная холангиография; новообразования желчных протоков.

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一名老年患者偶然诊断出的多发性胆管微小错构瘤

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摘要

多发性胆管错构瘤又称 von Meyenburg 复合体，是一种可能偶然发现的良性肝肿瘤。如果以前没有遇到过，而且在检查时没有适当的成像技术，就不容易被发现。根据影像学检查结果，它们也很难与其他肝脏病变区分开来。因此，本病例的描述旨在为数字图像库增添新的内容，使放射科医生能够做出快速准确的鉴别诊断。此外，该病例还强调了对该疾病进行全面放射学评估的重要性，以及放射科医生、肝病科医生和病理科医生多学科合作以做出准确诊断的必要性。

患者因持续腹痛，在全科医生的建议下入院进行腹腔计算机断层扫描和磁共振成像，以评估胆道树的状况（磁共振胰胆管造影）。患者以前从未接受过腹腔器械检查，因此肝脏肿瘤是一个偶然的意外发现。

磁共振成像显示了，两个肝叶都有多发性良性病变，与 von Meyenburg 复合体相似。这些病变代表多发性错构瘤，在所有扫描序列中表现不同。

研究仔细检查了不同磁共振成像序列获得的图像。在肝脏中发现了多个具有良性迹象的病灶，符合“多发性胆管错构瘤”的诊断。

医生应该能够识别这种疾病，并在肝脏病变患者的鉴别诊断中加以考虑。这将有助于避免不必要的干预，并能选择正确的治疗策略。

关键词：肝脏；错构瘤；von Meyenburg 复合体；磁共振成像；诊断成像；磁共振胰胆管造影；胆管肿瘤。

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INTRODUCTION

Multiple biliary hamartomas are relatively rare and often an incidental finding during imaging studies. Identifying and accurately diagnosing these lesions are crucial because they can mimic other hepatic lesions, such as cysts or tumors, leading to potentially unnecessary invasive procedures or treatments [1-4].

DESCRIPTION OF THE CASE

Medical History

An 82-year-old male presented to the hospital with a primary complaint of abdominal pain persisting for more than 6 weeks. The patient has no personal/family history significant for liver disease. A thorough medical evaluation, including physical examination and blood tests, was conducted. However, these initial assessments did not yield conclusive results nor provide a clear diagnosis.

Diagnostic Assessment

The patient underwent contrast-enhanced CT (computed tomography) and subsequently MRI [5–6].

Multiple millimetric disorganized hypodense lesions, both subcapsular and intraparenchymal, were detected incidentally in both hepatic lobes on CT.

After the administration of contrast medium, enhancement of lesions was not observed (Fig. 1).

Subsequent MRI examination identified the same lesions with different characteristics in various sequences. In T2-weighted MRI images, the areas appear homogeneously and intensely hyperintense (Fig. 2).

In T1-weighted images, all the lesions were homogeneously hypointense.

In diffusion-weighted imaging (DWI), the lesions persist as hyperintense at a low B-value (50 sec/mm^2) but disappear at a high B-value (800) (Fig. 3).

In T2-weighted MRI–cholangiography sequences, the liver presents a "starry sky" appearance due to the presence of multiple small hyperintense lesions; however, the communication with the bile duct are usually not recognized [7] (Fig. 4).

The dynamic study after contrast administration did not show enhancement in the arterial and venous phases (Fig. 5).

Differential Diagnosis

Radiographic findings may be nonspecific and may not differentiate biliary hamartomas from other lesions.

The differential diagnosis is made with polycystic liver disease, multiple simple hepatic cysts, metastases, micro-abscesses, and Caroli's disease [8]. A more heterogeneous appearance of lesions and communication with the bile duct is observed in the latter.

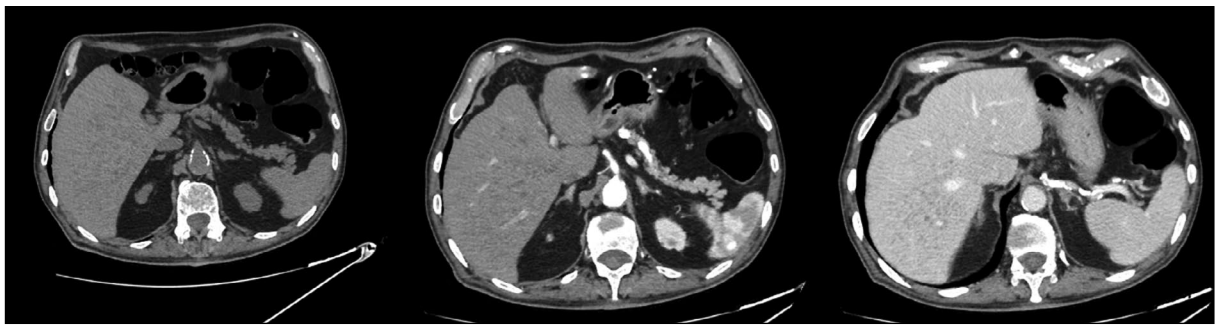

Fig. 1. Axial CT image: hypodense lesions without significant contrast enhancement in the arterial and venous phases.

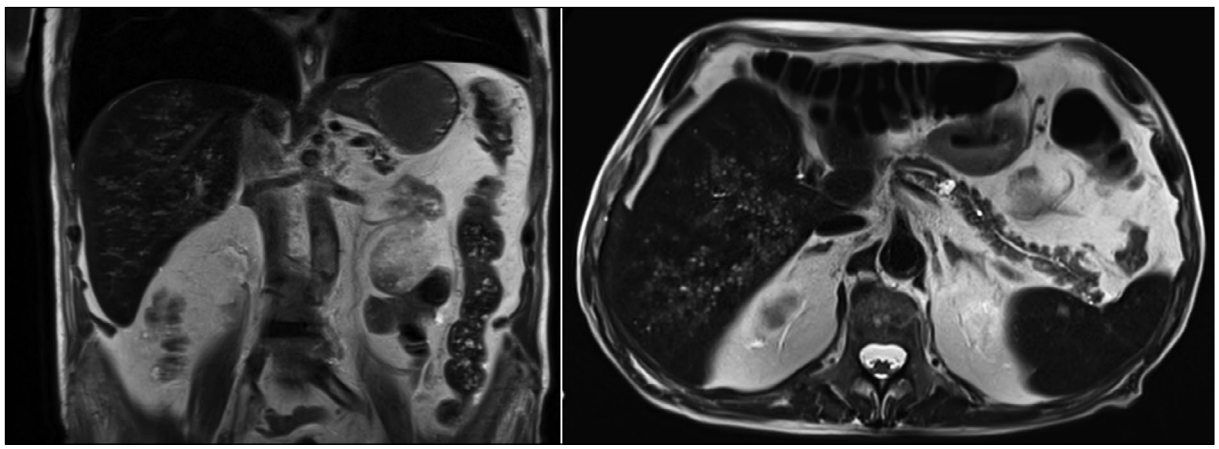

Fig. 2. Coronal and axial MRI images with HASTE T2 sequence: multiple small hyperintense lesions throughout the hepatic area.

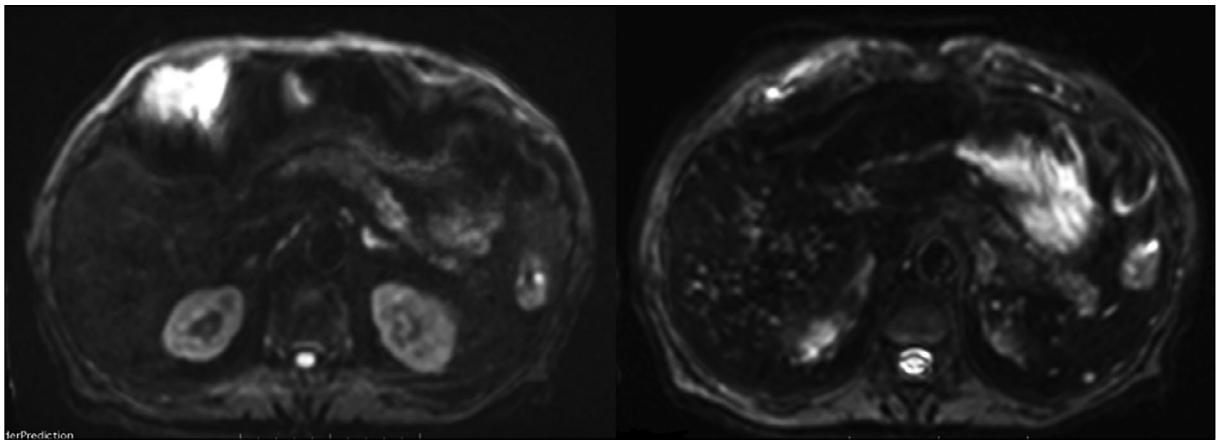

Fig. 3. Axial MRI image with DWI sequence: hyperintense lesions at low B-value (50 sec/mm^2) on the right, disappearing at high B-values on the left (800).

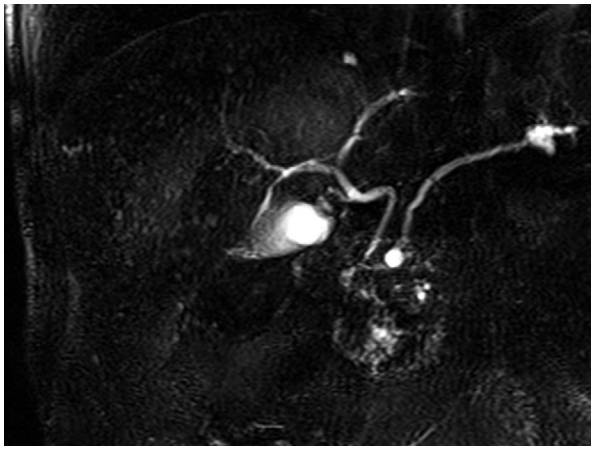

Fig. 4. MRI image with T2 MRI–cholangiography sequence: multiple small hyperintense lesions; the liver with a "starry sky" appearance.

Interventions

In the present case, the lesions were not directly related to symptoms or complications therefore, no surgical or pharmacological treatment was required.

If Von Meyenburg complexes are causing symptoms or complications, treatment may include surgical removal of the affected liver tissue or drainage of large cysts [9–11].

It is critical for individuals diagnosed with these complexes to consult a hepatologist or liver specialist to determine the appropriate management approach based on their specific case.

Follow-up and Outcomes

The management of the patient's condition was based on observation and scheduled monitoring, allowing for the timely assessment of any potential alterations. However, no significant changes led to alterations in the diagnostic choices made.

DISCUSSION

Multiple biliary hamartomas, also called Von Meyenburg complexes, are rare benign liver lesions characterized by small disorganized cystic structures affecting both hepatic lobes with some predilection for subcapsular regions [12–13]. They are multiple small round, or irregular lesions and are usually 5–30 mm in size on imaging.

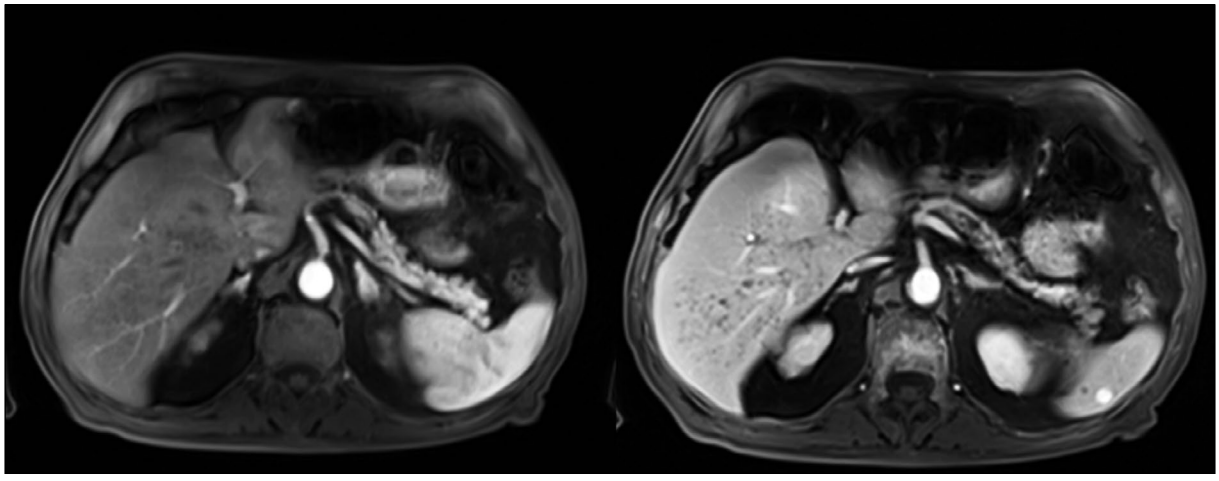

Fig. 5. Axial MRI image with T1 sequence showing hypointense lesions without significant contrast enhancement in the arterial and venous phases.

These structures are composed of abnormal bile ducts and are typically discovered incidentally during medical imaging studies, such as ultrasound, CT, and MRI, which are often performed for other reasons. Although hamartomas can communicate with the biliary tree, but usually not. They are believed to arise from embryonic bile duct remnants that have failed to involute.

Von Meyenburg complexes are considered noncancerous and are usually asymptomatic. They are generally not associated with liver dysfunction or clinical symptoms. Laboratory data are generally nonspecific and within normal limits. Most individuals with these lesions do not require treatment. In some cases, Von Meyenburg complexes can be associated with various liver conditions, including polycystic liver disease, Caroli's disease, and congenital hepatic fibrosis [14].

When these conditions are present, they can lead to more significant liver-related problems and may require medical management.

CONCLUSION

Von Meyenburg complexes a rare medical condition that is often detected incidentally. This study highlights the importance of accurate diagnosis and challenges in distinguishing these lesions from other hepatic lesions. Management based on observation and periodic monitoring is a feasible approach when the lesions are asymptomatic. However, clinical awareness on multiple biliary hamartomas is crucial to avoid misdiagnosis and unnecessary invasive interventions. Future studies may further our understanding of this condition and its clinical implications.

ADDITIONAL INFORMATION

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Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information and all of accompanying images within the manuscript in Digital Diagnostics Journal.

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Prospective Evaluation of the Extensibility of the Ascending Aorta Wall and its Vascular Prosthesis in a Patient with an Aneurysm with Technically Flawless Surgical Correction and Postoperative Decrease in Functional Parameters: Description of the Case

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ABSTRACT

In this clinical case, a patient who had an instrumentally detected aneurysm with the lumen expanding up to 60 mm underwent a surgically flawless prosthetic replacement of the ascending aorta. This treatment led to decreased exercise tolerance, decreased contractile function of the left ventricular myocardium at rest, and enlarged pulmonary artery. The leading factor was a decrease in the volume of systolic expansion of the aorta down to 5 mL (at the initial 13 mL), despite a noticeable increase in the extensibility and a decrease in mechanical stiffness compared with initial indexes of the affected aortic wall. In the literature review, considering mechanical extensibility and elasticity, problems in creating aortic prostheses equivalent to those for healthy biological tissues were discussed.

Keywords: aneurysm of the ascending aorta; prosthetics of the ascending aorta; extensibility; Young's modulus; systolic stretching of the aorta; coronary blood supply to the myocardium; case report.

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Проспективная оценка показателей растяжимости стенки восходящей аорты и её сосудистого протеза у пациентки с аневризмой при технически безупречной хирургической коррекции и послеоперационном снижении функциональных показателей: клинический случай

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АННОТАЦИЯ

Представлен и обсуждён клинический случай, когда у пациентки после выполнения хирургически безупречного протезирования восходящей аорты отмечалось выраженное снижение толерантности к физической нагрузке, снижение сократительной функции миокарда левого желудочка в покое и расширение лёгочной артерии вследствие усиления лёгочной артериальной гипертензии. Протезирование было выполнено в связи с инструментально выявленной при расширенном магнитно-резонансном томографическом исследовании аневризмой восходящей аорты с увеличением просвета в поперечном сечении аорты до 60 мм. Показано, что единственным и ведущим фактором к развитию негативных последствий протезирования явилось снижение объёма систолического расширения аорты до 5 мл, при исходных 13 мл, несмотря на заметное увеличение показателей растяжимости и снижения механической жёсткости по сравнению с показателями поражённой стенки аорты. Представлен обзор литературы и обсуждены в этой связи настоятельная необходимость и проблемы создания протезов аорты, эквивалентных по показателям механической растяжимости и упругости таковым для здоровых биологических тканей.

Ключевые слова: аневризма восходящей аорты; протезирование восходящей аорты; растяжимость; модуль Юнга; коронарное кровоснабжение миокарда; клинический случай.

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对一名动脉瘤患者升主动脉壁及其血管假体的伸展性参数进行前瞻性评估，手术矫正技术完美，但术后功能下降

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摘要

本文介绍并讨论了一例临床病例，患者在对升主动脉进行无暇假体修复手术后，运动耐力明显下降，左心室静息时心肌收缩功能减弱，肺动脉高压加重导致肺动脉扩张。通过增强磁共振成像器械检测到升主动脉瘤，主动脉横截面的管腔扩大到 60 毫米，在这种情况下进行了假体植入术。结果表明了，尽管与病变主动脉壁的指数相比，主动脉的伸展性指数明显增加，机械硬度指数下降，但假体造成不良后果的唯一和主要因素是主动脉收缩期的扩张量从最初的 13 毫升减少到 5 毫升。本文对文献进行了综述，并就此讨论了制作在机械延伸性和弹性方面与健康生物组织相当的主动脉假体的迫切性和问题。

关键词：升主动脉瘤；升主动脉假体；伸展性；Young 模块；冠状动脉心肌血流；临床病例。

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INTRODUCTION

Surgical treatment of ascending aortic aneurysms with a >5 cm lumen expansion [1] has been the technique of choice in preventing the risk of aneurysm rupture, with a mortality rate of up to 100% in acute cases [2–4].

Several cardiac surgery techniques, involving complete or partial arch replacement, have been developed [5].

The outcomes of such replacement are assessed based on the significant decrease in the risk of mortality in such patients [2]. The quantitative assessment of physiological and biomechanical parameters of the ascending aorta, quality of life, and the presence and severity of angina and other coronary ischemia markers is often regarded as less significant [3]. This may be justified, as saving the patient's life is always the top concern.

However, a sustained decrease in the mortality rate with the surgical treatment of ascending aortic aneurysm requires further clarification of pathophysiological criteria determining the functional status of patients, possibility of recovery and vocational rehabilitation, state of the cardiac muscle, and factors affecting coronary blood supply.

The ascending aorta is a crucial anatomical and functional component of the vascular system. It provides blood supply to the cardiac muscle, which invariably occurs during diastole, within the systolic expansion volume of the ascending aorta [6]. Physiologists and sports medicine specialists [6], as well as prosthetic valve and vessel manufacturers [7], have long been interested in the elastic properties of the ascending aorta in the context of adequate blood supply to the cardiac muscle, when the aorta, which stretches during systole, collapses during diastole. However, single-center and multicenter studies of the clinical use of biophysical and biomechanical assessments of aortic elasticity are limited [4]. It has been previously demonstrated that decreased elasticity and distensibility and increased stiffness of the ascending aorta are significant pathological factors contributing to the risk of acute myocardial infarction [8, 9]. Studies of ascending aortic elasticity in cardiac surgery patients with aneurysms are equally clinically significant. Insufficient graft elasticity can be a limiting and pathological factor.

Thus, this study presents a clinical case of a female patient who failed to reach the target pO_2 level post-surgery, as well as other parameters required for a good performance status (e.g., exercise tolerance), despite uncomplicated ascending aortic replacement. These metrics did not improve, but rather worsened, and the patient has been dependent on an oxygen concentrator for breathing several months after surgery.

DESCRIPTION OF THE CASE

We present a clinical case of prospective follow-up of changes in biomechanical parameters of aortic aneurysm during surgical treatment of a 65-year-old female (patient B-k). The patient has a history of hypertension for 10 years (with full pharmacological blood pressure control). Additionally, she has type 2 diabetes mellitus, with glucose and glycated hemoglobin levels controlled to the limit of normal with oral antidiabetic drugs. She was otherwise healthy for the last 15 years.

The patient initially presented to a neurologist with increasingly frequent episodes of dizziness and weakness with fatigue, and transient, short-term episodes of loss of speech. Critical stenosis of the internal carotid artery or its branches was suspected, and the patient was referred for ultrasound examination and carotid magnetic resonance (MR) angiography. These examinations did not confirm the carotid artery pathology. Narrowing of the internal carotid arteries or their branches by more than 15%–20% was not observed. However, carotid MR angiography showed a pathological radial expansion of the ascending aorta lumen of up to 57–60 mm. This was confirmed by MR aortography (Fig. 2*a*), and the patient was referred to the Research Institute of Cardiology of the Tomsk National Medical Research Center for consultation and cardiac surgery.

Further, the patient had preoperative coronary angiography and aortography, which confirmed the nature and extent of the aortic lesion and ruled out coronary stenosis. The proximal right coronary artery showed the most severe stenosis, of up to 35% of the lumen. Stenoses in the left coronary artery did not exceed 25% in any of its branches.

Prior to aortic replacement, the exercise tolerance threshold according to a cycle ergometer exercise test with electrocardiography (ECG) monitoring was 25 W. The test was stopped because of shortness of breath and muscular weakness. The test did not reveal ECG signs of coronary insufficiency.

As previously mentioned, the patient had magnetic resonance imaging (MRI) of the heart and aortic wall with ECG gating [8], including the thoracic aorta up to the diaphragm. In particular, heart MRI along its short and long axes was performed, which included the following:

- T1 weighted images (WI): time of repetition (TR), 500 msec; time of echo (TE), 12 msec
- T2WI: TR, 4,000 msec; TE, 25 msec
- Steady-state free precession (SSFP) images

Slice thickness: 5–8 mm; matrix: 256 × 392 or 256 × 256. Axial T1WI chest MRI with respiration and ECG gating, with increased TR of 1,850–1,900 ms and TE of 32 ms, was performed as a component of cardiac and chest MRI with ECG gating (Fig. 1). This mode provides visualization of large thoracic vessels, including their walls. Owing to the borderline glomerular filtration rate (<30 mL/min × 1.73 m^2), additional paramagnetic contrast enhancement was not used.

Following cardiac MRI, the patient underwent MRI of the ascending aorta with ECG gating, at the level of crossover with the pulmonary artery bifurcation level, in axial plane,

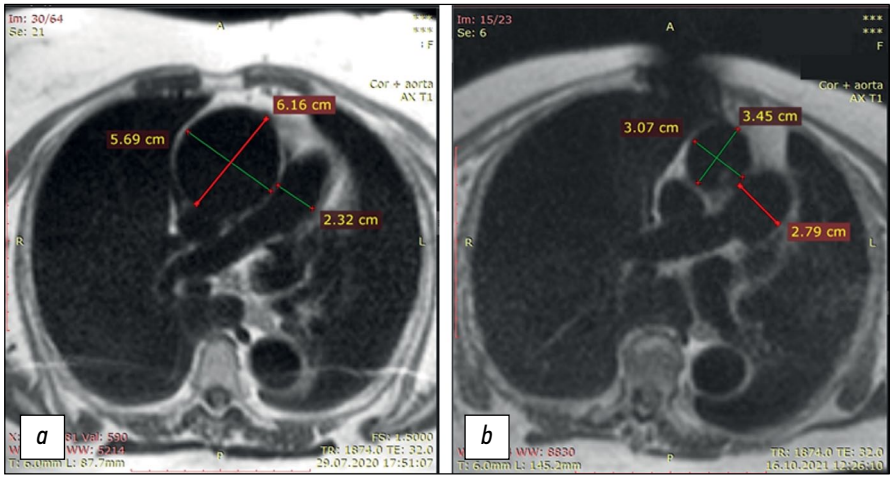

Fig.1. Transverse slices of T1-weighted images of the chest organs, including the thoracic aorta, at the pulmonary artery bifurcation level in patient B-k: (*a*) before prosthetic replacement of the thoracic aorta expanded due to aneurysm; critical ascending aortic aneurysm with a >6 cm lumen expansion; (*b*) after prosthetic replacement of the thoracic aorta expanded due to aneurysm; normal lumen of the ascending aorta. The descending aorta was normal before and after surgery. The pulmonary artery expanded to 27 mm after surgery, compared to 23 mm at admission. Postoperative tomography revealed an artifact in the chest area due to a wire fixator.

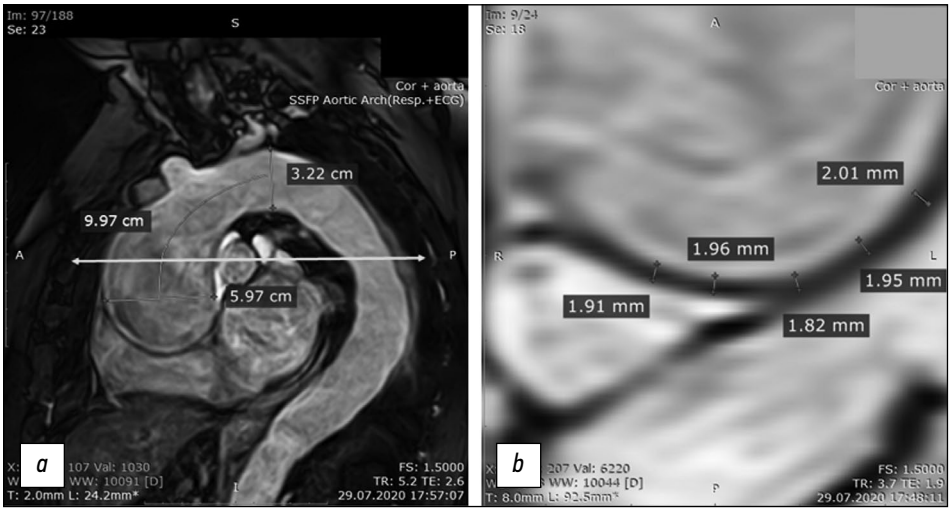

Fig. 2. Magnetic resonance imaging with ECG gating in patient B-k: (*a*) magnetic resonance angiography of the thoracic aorta. The lumen at the supravalvular and aortic arch levels and the distances between them, which are used to calculate the ascending aorta volume during systole and diastole and the systolic expansion volume, are shown. The turquoise horizontal line with arrows at the ends represents the tomographic slice level; (*b*) transverse tomographic slice of the ascending aorta in the wall area, with thickness measurements for the subsequent calculations of Young's modulus parameters. The measurements are marked by thin green lines, with respective values.

in the cine mode (24 cine frames per cardiac cycle), with the assessment of changes in the aortic wall thickness during a cardiac cycle (Fig. 2*b*) and diameter and cross-sectional area of the lumen at the study level (marked with an arrow in Fig. 2*a*). The cardiac MRI findings were processed using a standard method; the left ventricular end-diastolic volume, left ventricular end-systolic volume, and left ventricular ejection fraction were calculated. Moreover, biomechanical parameters of aortic distensibility were obtained based on non-contrast-enhanced cine mode MRI findings.

These measurements and a linear biophysical model [10, 11] were used to calculate the distensibility (radial expansion) of the aorta [12]:

$$Distensibility_{adj} = S_{syst} - S_{diast} / S_{diast} \quad (1)$$

Moreover, the distensibility adjusted for pulse pressure was calculated:

$$Distensibility_{adj} = \frac{S_{syst} - S_{diast} / S_{diast}}{BP_{pulse}} \quad (2),$$

where S_{syst} and S_{diast} are the cross-sectional areas of the aorta during systole and diastole, respectively, and BP_{pulse} is the pulse pressure (Fig. 3).

The transverse Young's modulus for the ascending aorta wall was calculated based on the findings of MR

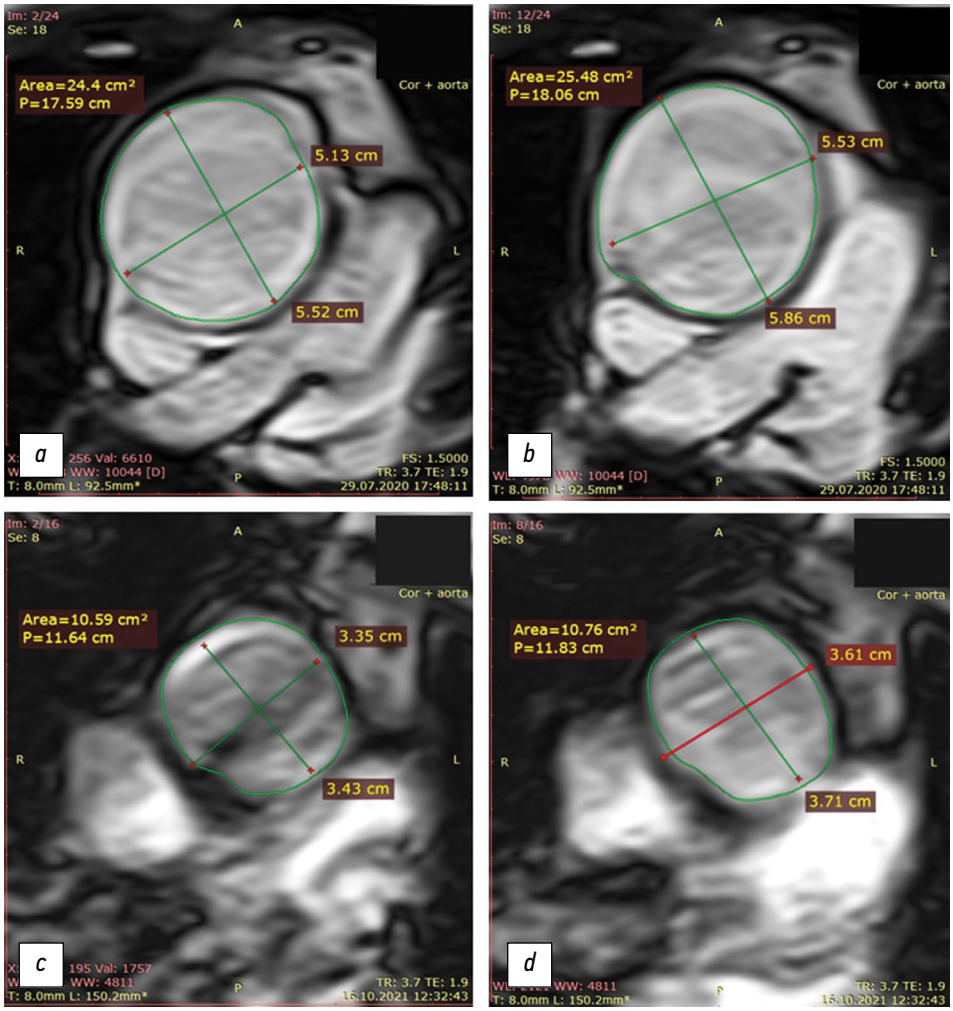

Fig. 3. Cross-sectional dimensions and areas of the ascending aorta during systole and diastole: top row: baseline (at admission; before replacement of the aorta that expanded due to aneurysm); bottom row: after replacement with a synthetic graft; (*a*, *c*) diastole; (*b*, *d*) systole. Of note is a considerable lumen narrowing after surgery, with a relatively small distensibility of the ascending aorta.

aortography with ECG gating, according to the method well-studied in biomechanical experiments [10, 11]:

$$E = \frac{d_{diast}^{\ 2} \times (1 - 0{,}25) \times BP_{pulse}}{2 \times h \times \Delta d_{pulse}} \times 133{,}3 \quad (3),$$

where E = Young's modulus (Pa),

d_{diast} = transverse aortic diameter during diastole,

Δd_{pulse} = increase in the aortic diameter during systole,

0.25 = squared Poisson's ratio for the aortic wall, which is known to be 0.5 [11],

h = aortic wall thickness during diastole (Fig. 2*b*),

BP_{pulse} = pulse pressure, and

133.3 = conversion factor (mmHg to Pa).

The ascending aortic volume was calculated, from the supravalvular level to the middle of the aortic arch (between the brachiocephalic trunk and opening of the left common carotid artery), during systole and diastole. The ascending aorta was visualized as a deformed, incompressibly curved, truncated cone with the length l (length of the aortic valve–middle of the aortic arch area; Fig. 1*a*), with the base radius determined by transverse slices in the cine mode: lower base radius, R, and upper base radius, r. In this case, the volume of the deformed truncated cone (the ascending aorta) can be with high accuracy estimated as follows [13]:

$$V = \frac{1}{3}\pi l\,(R^2 + Rr + r^2) \quad (4)$$

The systolic expansion volume of the aorta ΔV_{syst} was determined by the difference between systolic and diastolic volumes of the ascending aorta. This parameter determines the blood volume available for the coronary blood supply to the cardiac muscle during diastole, when the primary blood supply to the cardiac muscle occurs [6, 14].

The patient underwent replacement of the ascending aorta and partial arch replacement with assisted circulation, using a 35 mm synthetic graft GORE-TEX (W.L. Gore & Associates, USA). Aortic valve replacement was not performed, as no significant aortic valve insufficiency was noted, and the area of the effective hemodynamic lumen during systole was >2.0 cm^2. The brachiocephalic trunk ostium was implanted in the respective branch of the graft; postoperatively, no blood supply disturbances in the right common carotid artery and subclavian artery territories were observed.

No postoperative surgical complications, including inflammation, and signs of vital organ blood supply disturbances were noted. Sinus tachycardia at rest was reported (82–92 bpm), which worsened significantly on mild exertion. The preoperative glomerular filtration rate was 57–65 mL/min × 1.73 m^2, which was maintained after surgery. The patient required long-term oxygen support, because only with then her condition was subjectively close to normal. Imaging and clinical biochemistry studies revealed no signs of postoperative myocardial infarction. Without oxygen support using a membrane oxygen concentrator, the pO_2 level was 81%–83%; when a concentrator was used, this parameter increased to 93%–95% or higher (occasionally, at rest). Perfusion single-photon computed tomography with ^{99m}Tc-labeled beads revealed no signs of thrombosis or pulmonary embolism.

Following the surgery, the exercise tolerance decreased significantly compared to baseline and remained minimal during the inpatient postoperative period and after discharge. The patient resides on the second floor and can only get there by elevator; an outpatient MRI required the use of an oxygen concentrator.

A follow-up examination (cardiac MRI and MR elastography of the aortic wall) was performed 4 months after surgery; the findings compared to baseline are presented in Tables 1 and 2.

Aortic elasticity parameters improved dramatically following surgery; however, they still exceeded the normal value [8]. However, the systolic expansion volume of the ascending aorta (ΔV_{syst}) decreased significantly due to a decrease in the aortic diameter by 2 cm.

The postoperative Young's modulus for the aortic wall (specifically, for the ascending aortic graft) decreased, whereas the elasticity increased. However, generally, the systolic expansion volume of the aorta decreased to approximately 5 mL (Table 2), which is insufficient for adequate coronary blood supply [8]. The physical dimensions of the graft corresponded to those specified in the documents. Thus, even in the absence of significant coronary stenoses and with an ideal surgical technique of ascending aortic replacement, insufficient distensibility of the aortic wall became a critical factor, limiting exercise tolerance after surgery and contributing to left ventricular failure, although without acute myocardial infarction.

DISCUSSION

When assessing aortic stiffness, methods initially tested in animal studies are used [15, 16, 17], such as external transmission of a high-frequency mechanical wave to the aorta, using a special MRI-compatible vibration generator, followed by an MRI recording of wave transmission along the aortic wall [15, 18, 19]. This method, adapted from solid-organ elasticity studies, is commonly used [18, 19, 20].

The high-frequency method of mechanical aortic elasticity assessment allows for the calculation of this parameter throughout the anatomical study area (along the length of the aorta) [19]. However, the aortic volume at a specific level, particularly at the level of the ascending aorta, is not considered [2]. The volume of various parts of the aorta in the case of pathologies has recently become a subject of interest [15].

In this context, the distensibility of the aortic lumen during a cardiac cycle following changes in aortic pressure is a more physiological parameter [12]. Regarding the ascending aorta, it allows for direct assessment of the blood volume available for pumping into the coronary bed during diastole [12]. In the present case, this parameter allowed determining the

Table 1. Cardiac magnetic resonance imaging findings in patient B-k before and after aortic replacement

	Left ventricular myocardium mass, g	LVEDV, mL	LVEF, %	LVESV, g	Left atrial volume, mL	Pulmonary artery diameter, mm
Baseline (at admission)	165	79.4	83	165	55.7	23
After ascending aortic replacement	161	**94.2**	**73**	161	**69.4**	**28**

Note: LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume. Parameters indicating the progression of heart failure (increased LVEDV, decreased LVEF, increased left atrial volume, and pulmonary artery expansion by 4 mm) are in bold text.

Table 2. Magnetic resonance elastometry of the ascending aortic wall in patient B-k before and after aortic replacement

	Young's modulus for the ascending aortic wall, Pa	Ascending aortic distensibility		ΔV_{syst}, mL
		Absolute	Adjusted = absolute/pulse pressure	
Baseline (at admission)	$0{,}58\times10^6$	0.0043	$0.0043/25 = 1.72\times10^{-4}$	13.28
After ascending aortic replacement	$0{,}260\times10^6$	0.0161	$0.0161/20 = 8.05\times10^{-4}$	4.95

exact cause of the patient's postoperative condition, which was initially attributed to undetected flaws of the surgical technique; however, the existence of these flaws was later disproved.

This demonstrates that the aorta is crucial for adequate coronary blood supply to the cardiac muscle [6, 12]. In the case of ascending aortic replacement, the graft elasticity plays a critical role [7]. It is even more relevant considering that aortic wall inflammation [24] and stiffness [25] are associated with the incidence and severity of cerebrovascular accidents. Single-center [12] and multicenter studies [8, 26] confirmed that increased aortic wall stiffness is a predictor of increased incidence of coronary disorders in patients with myocardial infarction. In patients with cardiovascular diseases that do not require cardiac surgery, drug therapy can significantly improve aortic distensibility and elasticity [27].

As previously stated, further development of ascending aortic grafts is focused on the use of synthetic and multicomponent materials with preserved elasticity, which ensure adequate diastolic blood supply to the cardiac muscle and exercise tolerance [7]. Manufacturers are aware of this issue [28, 29], which is shown in the present case: the mechanical aortic wall stiffness after surgery decreased more than twofold compared to the aorta with aneurysm before surgery, whereas the distensibility increased more than threefold (Table 2). However, considering the graft diameter, which is decreased compared to the baseline aneurysm, modern synthetic materials cannot maintain the systolic expansion volume of the ascending aorta (ΔV_{syst}).

In this regard, biological aortic grafts [29, 30] produced using special technologies from major vessels of cattle, with preserved structure of collagen and elastin fibers, provide an advantage regarding mechanical distensibility and elasticity. Currently, these are the only grafts capable of maintaining the wall distensibility of a complex hemodynamic structure such as the aorta [30]. MR elastometry can be used for aortic elasticity monitoring after replacement, with the desired frequency and duration of follow-up [8]. It can be used to assess the aortic wall and mechanical distensibility parameters in patients with ascending aortic replacement and in experimental settings.

CONCLUSION

MR elastometry provides therapeutically valuable information when used for the quantitative assessment of the biomechanical state of the ascending aorta. This should be considered when conducting studies in patients with aortic diseases, both atherosclerotic and due to other causes, and during prosthetic graft replacement of the ascending aorta irreversibly changed due to aneurysm.

MR elastometry with ECG gating for assessing the distensibility and calculating the Young's modulus for the damaged aortic wall currently has no alternatives, because X-ray computed tomography-based elastometry, which is methodologically equivalent, is inherently associated with radiation exposure.

MR elastometry is expected to gain more clinical use, as calculating the systolic expansion volume of the aorta is clinically relevant in other aortic biomechanics and coronary circulation disorders of various origins.

ADDITIONAL INFORMATION

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Idiopathic Enterocolic Intussusception: Imaging Findings in an Abdominal Emergency

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ABSTRACT

Adult intussusceptions are a rare cause of abdominal obstruction and are usually associated with a neoplastic disease; idiopathic forms are extremely rare. We report a case of enterocolic intussusception in a young woman who experienced symptoms of abdominal obstruction. Imaging findings were reported. On histological examination, no underlying diseases were found. The patient presented at the hospital for computed tomography because of persistent abdominal pain. Computed tomography revealed an enterocolic invagination involving the ileocecal valve and cecum and widespread edematous thickening of the colonic parietal walls.

Idiopathic enterocolic intussusception is an uncommon abdominal urgency in adults. Symptoms can be vague and persistent, delaying an accurate diagnosis. Imaging is crucial in these circumstances to make a diagnosis. Some computed tomography findings, such as a target-like bulk, may be suggestive.

Keywords: intussusception; laparoscopy; colectomy; computed tomography; abdomen.

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Идиопатическая инвагинация кишечника: результаты визуализации неотложной абдоминальной патологии

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АННОТАЦИЯ

Инвагинация кишечника у взрослых — редкая причина кишечной непроходимости и обычно связана с неопластическими заболеваниями. Идиопатические формы встречаются крайне редко. В статье описывается случай инвагинации кишечника у молодой женщины, которая испытывала симптомы кишечной непроходимости. Представлены результаты визуализации.

Первичных заболеваний при гистологическом исследовании выявлено не было. Пациентка поступила в больницу для проведения компьютерной томографии из-за постоянных болей в животе. Компьютерная томография выявила инвагинацию кишечника с вовлечением илеоцекального клапана и купола слепой кишки, а также отёчность и утолщение стенок париетальной брюшины. Идиопатическая инвагинация кишечника — редкое неотложное состояние органов брюшной полости у взрослых. Симптомы могут быть персистирующими, стёртыми и неясными, что затрудняет постановку точного диагноза. В таких случаях решающее значение имеет диагностическая визуализация. Некоторые результаты компьютерной томографии, такие как мишеневидное содержимое кишечника, могут указывать на данное заболевание.

Ключевые слова: инвагинация, лапароскопия; колэктомия; компьютерная томография; брюшная полость.

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特发性肠套叠：急诊腹部病理成像结果

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摘要

成人肠套叠是一种罕见的肠梗阻病因，通常与肿瘤疾病有关。特发性肠套叠极为罕见。本文描述了一例年轻女性肠套叠病例，她曾出现过肠梗阻症状。本文还介绍了影像学检查结果。组织学检查未发现原发性疾病。患者因持续腹痛入院进行计算机断层扫描。计算机断层扫描显示了，肠套叠累及回盲瓣和盲肠穹隆，壁层腹膜壁肿胀增厚。特发性肠套叠是一种罕见的成人急腹症。症状可能是持续性的、磨灭的和模糊的，因此很难做出明确诊断。在这种情况下，影像学诊断至关重要。某些计算机断层扫描结果（如靶形肠内容物）可能预示着这种疾病。

关键词：肠套叠；腹腔镜检查；结肠切除术；计算机断层扫描；腹部。

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INTRODUCTION

Adult intussusception is an uncommon abdominal emergency [1]. Intussusception consists of the invagination of a bowel segment (intussusceptum) and its mesentery into the lumen of a distal portion (intussuscipiens) because of the abnormal mobility of the peristalsis [1, 2]. It can involve any part of the intestine; however, it usually occurs at the coupling between a mobile loop and a fixed retroperitoneal segment [1, 3]. Among adults, intussusceptions are frequently associated with an organic lesion common in children, whereas they are less frequently encountered in adults; symptoms tend to be nonspecific, making the diagnosis more challenging [4, 5].

DESCRIPTION OF THE CASE

Medical History

A 37-year-old woman was admitted to the emergency room complaining of 4-day abdominal pain that had increased in the last few hours. She reported no fever but noticed changes in her bowel habits, alternating diarrhea, and constipation.

Diagnostic Assessment and Differential Diagnosis

To exclude any possible causes of intestinal obstruction, computed tomography (CT) was performed before and after the administration of intravenous iodinated contrast medium. CT revealed an enterocolic invagination involving the ileocecal valve and the cecum with diffuse edematous thickening of the colonic parietal walls. Edematous strains in the adjacent peritoneal fat, satellite lymphadenopathy levels, and a small amount of fluid collection in the right iliac fossa were also present (Fig. 1).

Multiplanar reconstruction (MPR) revealed the "target" appearance of the intestinal walls (Fig. 2).

Interventions

Owing to the rapid progression of the clinical signs, surgical treatment was suggested, and a laparoscopic right colectomy was performed. Oral intake was initiated with fluids on the second postoperative day and solid food on the third postoperative day.

Follow-up and Outcomes

The patient was discharged on the sixth postoperative day. No complications were observed. Histology revealed

Fig. 1. Abdominal computed tomography, portal phase. Sagittal multiplanar reconstruction: (*a*) enterocolic invagination with the involvement of the mesenteric fat and vascular structures. Thick edematous walls, stranding of the surrounding fatty tissue (*b*), and satellite nodes (11 mm in *c*).

Fig. 2. Oblique sagittal multiplanar reconstruction, orthogonal to the intussusception, shows the "target sign" due to the alternating of edematous walls and mesenteric fat.

inflammatory changes in the intestinal walls with reactive satellite nodes; no other diseases were associated with intussusception.

DISCUSSION

Adult intussusception is an uncommon cause of intestinal blockage. In contrast to pediatric patients in whom intussusception is primary and benign, adult intussusception, particularly of the colon, has a high probability of neoplasia; therefore, operative management is often necessary.

In some patients, conservative treatment by reduction is also recommended provided that the bowel appears viable. In the remaining cases, reduction should not be attempted if signs of inflammation or ischemia of the bowel wall are present.

In this case, we performed a laparoscopic right colectomy.

Oral intake was initiated with fluid on the second postoperative day and solid food on the third postoperative day. The patient was discharged on the sixth postoperative day. No complications were observed. According to the location, intussusception can be classified as enterocolic, when limited to the small bowel; colonocolonic, if it involves the colon; and enterocolonic, which can be ileocecal and ileocolic [1, 2]. The obstruction of venous blood flow can lead to edema and ischemia of the involved intestinal loop, and necrosis may eventually develop [6].

Intussusceptions are more common in children; they are mostly idiopathic and classically present with a triad of cramping abdominal pain, currant jelly-like faces, and a palpable sausage-like abdominal mass [6, 7].

Conversely, adult intussusceptions are very rare, accounting for approximately 5% of all cases [5, 8]; they may manifest with long-standing nonspecific abdominal symptoms (such as nausea, vomiting, bowel habit changes, abdominal distension, and gastrointestinal bleeding), which make the diagnosis more challenging [4, 6]. In children, intussusceptions are mostly idiopathic [6].

In adults, intussusceptions are generally associated with both benign and malignant diseases in most cases; however, idiopathic forms are less common and generally involve the small bowel, contrary to our case. Imaging is fundamental for diagnosis, particularly in the most problematic cases [9]. Abdominal CT is considered the modality of choice because it can evaluate the intussusception site, its extension, and the bowel segment involved [10]. In addition, it can demonstrate the presence of a leading point and is important to exclude possible complications, such as bowel wall ischemia and perforation. The invagination the intussusceptum into the intussuscipiens appears on CT as a "target" because of the alternating of intestinal walls and mesentery fat when observed on a plane perpendicular to the main axis of the involved segment [1].

In contrast to pediatric intussusception, which is primary and benign, adult intussusception (particularly of the colon) is associated with neoplastic disorders [6]. Therefore, a surgical approach is often necessary.

In some patients, conservative treatment by reduction is also recommended after the bowel appears viable. In the remaining cases, reduction should not be attempted if signs of inflammation or ischemia of the bowel walls are present.

CONCLUSION

Idiopathic enterocolic intussusception is a rare abdominal urgency in adults. Symptoms can be nonspecific and long-standing, which may delay the correct diagnosis. In these cases, imaging plays a central role in the diagnosis. Some CT findings, such as a mass with a target appearance, can be suggestive. Laparoscopic surgery is comparable to open surgery in the setting of right colectomy. The obvious advantages of laparoscopic surgery are the lower surgical site infection rates, shorter nasogastric tube duration, less postoperative pain, and better esthetic results. The safety and efficacy of laparoscopic right colectomy in an emergency with bowel occlusion is possible in the hands of expert surgeons.

ADDITIONAL INFORMATION

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Unilateral Pulmonary Vein Atresia: Difficulties of Radiological Diagnosis

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ABSTRACT

Pulmonary vein atresia is a rare congenital abnormality that could manifest in isolation or in association with other congenital abnormalities in the cardiovascular system such as pulmonary vein hypoplasia. Pulmonary vein atresia leads to changes in cardiovascular functioning. This abnormality is often diagnosed in children with recurrent pneumonia and hemoptysis. In adulthood, pulmonary vein atresia is much less common, with clinical symptoms such as dyspnea during physical exercises and hemoptysis. However, some patients are asymptomatic. Owing to the nonspecific imaging findings, lung parenchymal changes are often misdiagnosed as another lung disease, including inflammatory genesis disease. In this article, a case of a young man with asymptomatic unilateral pulmonary vein atresia combined with pulmonary artery hypoplasia and interstitial lung changes in a lung with hypoplasia was presented. These pathologies were first identified in a 21-year-old patient by contrast-enhanced computed tomography.

Keywords: pulmonary vein; atresia; pulmonary artery; hypoplasia; inferior vena cava; case report; computed tomography.

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Односторонняя атрезия лёгочных вен: сложности лучевой диагностики

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АННОТАЦИЯ

Атрезия лёгочных вен — редкий порок развития, который может возникать как изолированно, так и в сочетании с другими врождёнными пороками развития сердечно-сосудистой системы, например, с таким как гипоплазия лёгочной артерии. Атрезия лёгочных вен приводит к изменениям в работе сердечно-сосудистой системы. Данный порок развития чаще диагностируется в младенческом и раннем детском возрастем ввиду рецидивирующих эпизодов пневмонии и кровохарканья. Во взрослом возрасте атрезия лёгочных вен встречается намного реже, клинически характеризуется такими проявлениями, как одышка при физической нагрузке и кровохарканье. Однако в редких случаях клинические симптомы отсутствуют, при этом изменения в паренхиме лёгких носят неспецифический характер, ввиду чего могут быть ошибочно расценены как проявления различных лёгочных заболеваний в том числе воспалительного генеза. В представленной статье описано клиническое наблюдение сочетания односторонней атрезии лёгочных вен с гипоплазией лёгочной артерии и интерстициальными изменениями в гипоплазированном лёгком у молодого мужчины без жалоб со стороны органов дыхания. Патологии впервые выявлены в 21 год по данным компьютерной томографии с контрастным усилением.

Ключевые слова: атрезия; лёгочные вены; гипоплазия; лёгочные артерии; нижняя полая вена; клинический случай; компьютерная томография.

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单侧肺静脉闭锁：放射诊断中的难题

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摘要

肺静脉闭锁是一种罕见的畸形，既可单独发生，也可与其他先天性心血管系统畸形（如肺动脉发育不全）同时发生。肺静脉闭锁会导致心血管系统发生变化。这种畸形通常在婴儿期和幼儿期因反复发作肺炎和咯血而被诊断出来。在成年人中，肺静脉闭锁的发病率要低得多。在临床上，这种疾病主要表现为呼吸困难和咯血。然而，在极少数病例中没有临床症状。在这种情况下，肺实质的变化是非特异性的，可能会被误认为是各种肺部疾病的表现，包括炎症性成因。本文描述的是一名无呼吸道症状的单侧肺静脉闭锁合并肺动脉发育不全和发育不全肺间质改变的年轻男子临床观察结果。造影剂增强计算机断层扫描首次发现异常是在 21 岁。

关键词：闭锁；肺静脉；发育不全；肺动脉；下腔静脉；临床病例；计算机断层扫描。

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INTRODUCTION

Pulmonary vein atresia is a congenital malformation that commonly manifests in infants and young children with recurrent hemoptysis and pneumonia [1]. It is extremely rare in adults, with less than 40 cases of asymptomatic unilateral pulmonary vein atresia newly diagnosed in adults reported in foreign studies [2]. No such cases have been described in Russian studies. This study presents a case of a 21-year-old male with right pulmonary vein atresia associated with hypoplasia of the right pulmonary artery and interstitial lesions in the right lung first identified with computed tomography (CT).

DESCRIPTION OF THE CASE

Patient V, 21 years old, was referred to the City Clinical Oncology Hospital No. 1 of the Moscow City Health Department for a routine examination because of a history of left kidney cancer (pT3N0M0) and status post left nephrectomy for nephroblastoma in 2003.

Medical History

In 2020, a tumor was found in the solitary right kidney. However, immunohistochemistry performed at another healthcare facility showed no evidence of cancer. The patient was followed up by an endocrinologist for Denys–Drash syndrome (karyotype 46, XY; gonadectomy for gonadal dysgenesis), hypergonadotropic hypogonadism, gynecomastia, and short stature. The patient reported a history of heart surgery in childhood. No additional data on examinations and diagnostic and therapeutic interventions performed before 2020 were available.

Physical Examination, Laboratory Tests, and Investigations

In 2020, a routine chest X-ray showed decreased right lung volume and a shaded, ill-defined lesion in the lower part of the right lung (Fig. 1). During examination, the patient presented no complaints.

Chest CT without contrast was performed to further diagnose the abnormalities. The scan showed interstitial lesions in the right lung, presenting as thickened intra- and interlobular septa, mainly in the middle and lower parts of the right lung, and thickened bronchial walls. Moreover, in the mediastinum, an irregular soft tissue conglomerate was detected in the right tracheobronchial and subcarinal lymph nodes, with a homogeneous structure and density of +40 HU. The findings indicated intrathoracic lymphadenopathy and interstitial disease of the right lung with evidence of bullous emphysema (Fig. 2).

Owing to the lung CT findings, the patient was referred to a pulmonologist for further consultation, and a pulmonary function test was conducted. Decreased respiratory function of the lungs and restrictive and obstructive defects (forced expiratory volume in 1 second was 53%) were detected. In the absence of clinical manifestations, watchful waiting and consultation with an oncologist regarding the right kidney mass and mediastinal lymphadenopathy were recommended.

In 2023, after consultation with an oncologist, the patient was referred for laboratory tests (results within reference limits). As part of watchful waiting, chest, abdominal, and pelvic CT was performed with intravenous contrast. The scan showed persisting decreased volume of the right lung with significant interstitial abnormalities, ground-glass opacity, and cysts in the affected lung. No changes from the previous scan dated 2020 were noted.

Arterial and venous phase scanning along the margins of the right main bronchus revealed multiple dilated, tortuous arterial and venous vessels (bronchial and intercostal) in the intrathoracic lymph nodes; without contrast enhancement, they were previously interpreted as manifestations of intrathoracic lymphadenopathy (Fig. 3). The decreased diameter of the right pulmonary artery to 7 mm (vs. 14 mm on the contralateral side) and absence of contrast enhancement in the right pulmonary veins were clearly visualized in the three-dimensional reconstruction of the heart (Fig. 4).

DISCUSSION

Pulmonary vein atresia is a rare congenital malformation, with an incidence of 1.7 cases per 100,000 children aged >2 years [3]. It is believed to occur during intrauterine

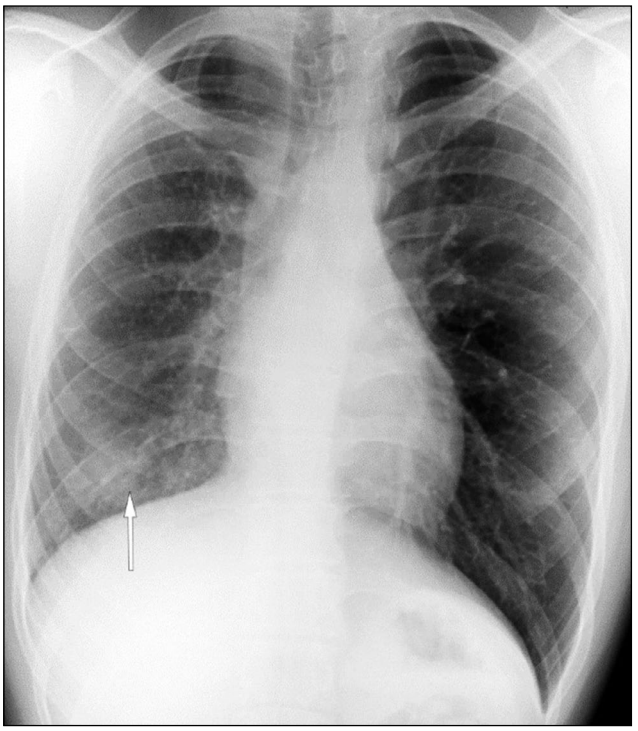

Fig. 1. Lung X-ray. Decreased volume of the right lung; a shaded ill-defined lesion in the lower part of the right lung field (white arrow).

development when the common pulmonary vein fails to incorporate into the left atrium [4–6]. In most cases, this abnormality is diagnosed in infants and young children with recurrent pneumonia and/or hemoptysis [1, 7, 11]. This malformation can occur on either side, without left or right predominance, and is often associated with a cardiovascular disease, as in our patient with a history of heart surgery in childhood. Additionally, in our case, indirect signs of tricuspid regurgitation were detected, such as blood reflux into the hepatic portion of the inferior vena cava and hepatic veins.

In adults, the main complaints include shortness of breath on exertion and hemoptysis, often associated with pulmonary hypertension [5]. However, in rare cases, the disease may be asymptomatic [3, 8].

In 50% of cases, pulmonary vein atresia is isolated; in the remaining cases, it is associated with other malformations, such as pulmonary artery hypoplasia, resulting in hypoperfusion and decreased size of the affected lung [9, 12]. Pulmonary vascular malformations cause vascular collaterals to form, characterized by dilated intercostal and bronchial arteries and veins. They fuse with newly formed vessels, resulting in thickened interlobular septa, perifissural lesions, and ground-glass opacity as a manifestation of lymphostasis and venous congestion [2, 9]. When blood flow in individual capillaries, small arteries, and veins stops and the vascular network is dilated and blood overflows into these vessels due to impaired normal outflow, the affected lung parenchyma is

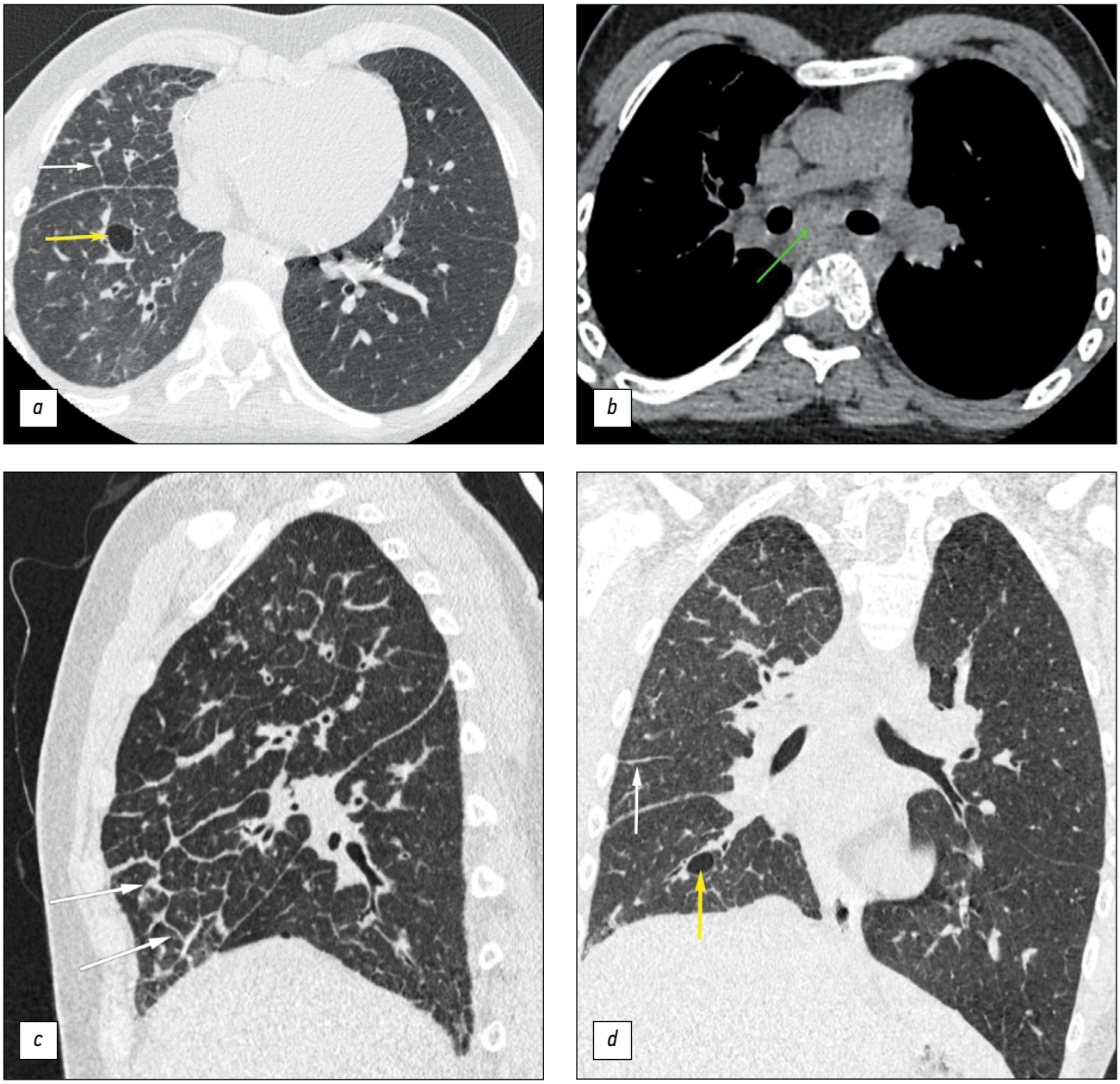

Fig. 2. Computed tomography of the lungs; (*a*, *b*) axial plane; (*c*) sagittal plane; (*d*) coronal plane. The volume of the right lung is decreased. White arrows: thickened interlobular interstitium. Yellow arrows: lung cyst. Green arrow: homogeneous soft tissue conglomerate with a density of +40 HU in the mediastinum. Computed tomography in 2023 showed no changes over time.

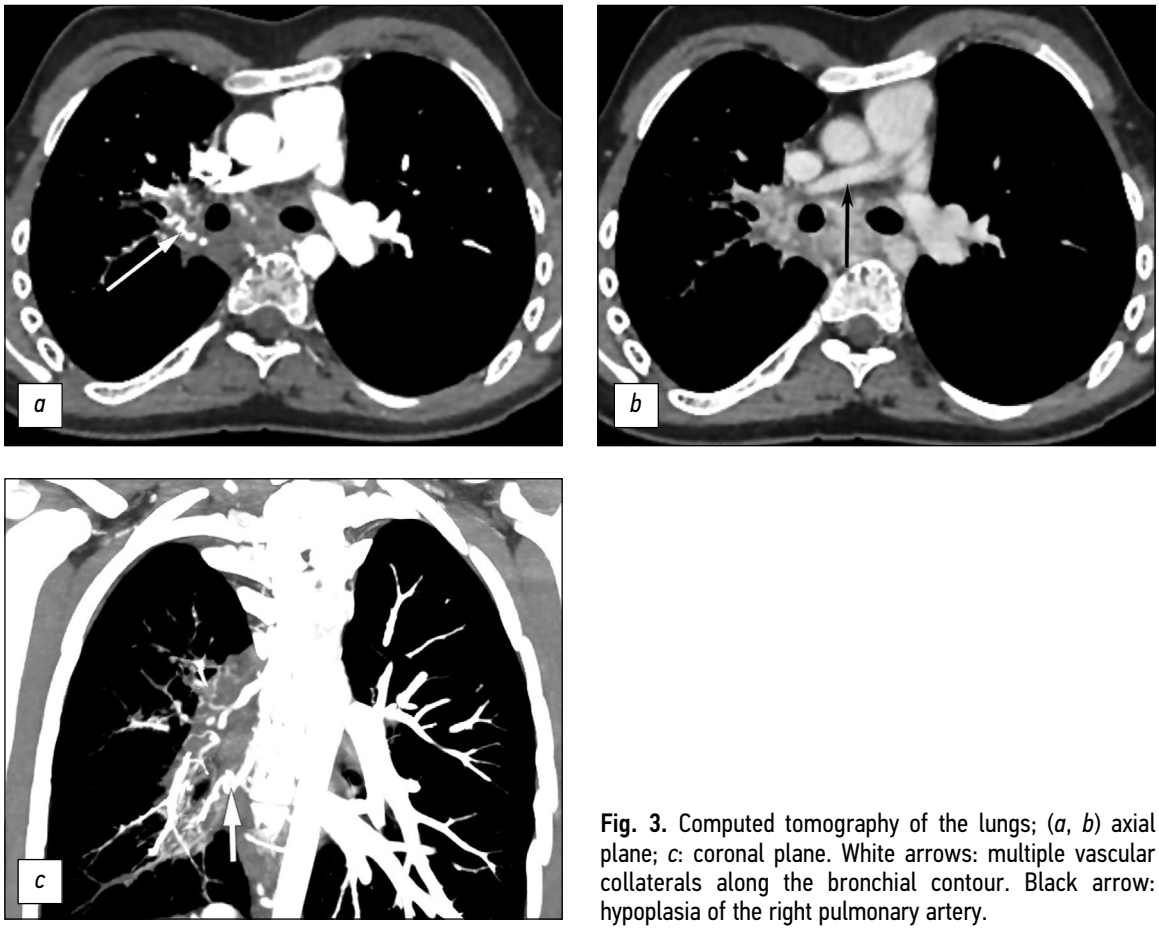

Fig. 3. Computed tomography of the lungs; (*a*, *b*) axial plane; *c*: coronal plane. White arrows: multiple vascular collaterals along the bronchial contour. Black arrow: hypoplasia of the right pulmonary artery.

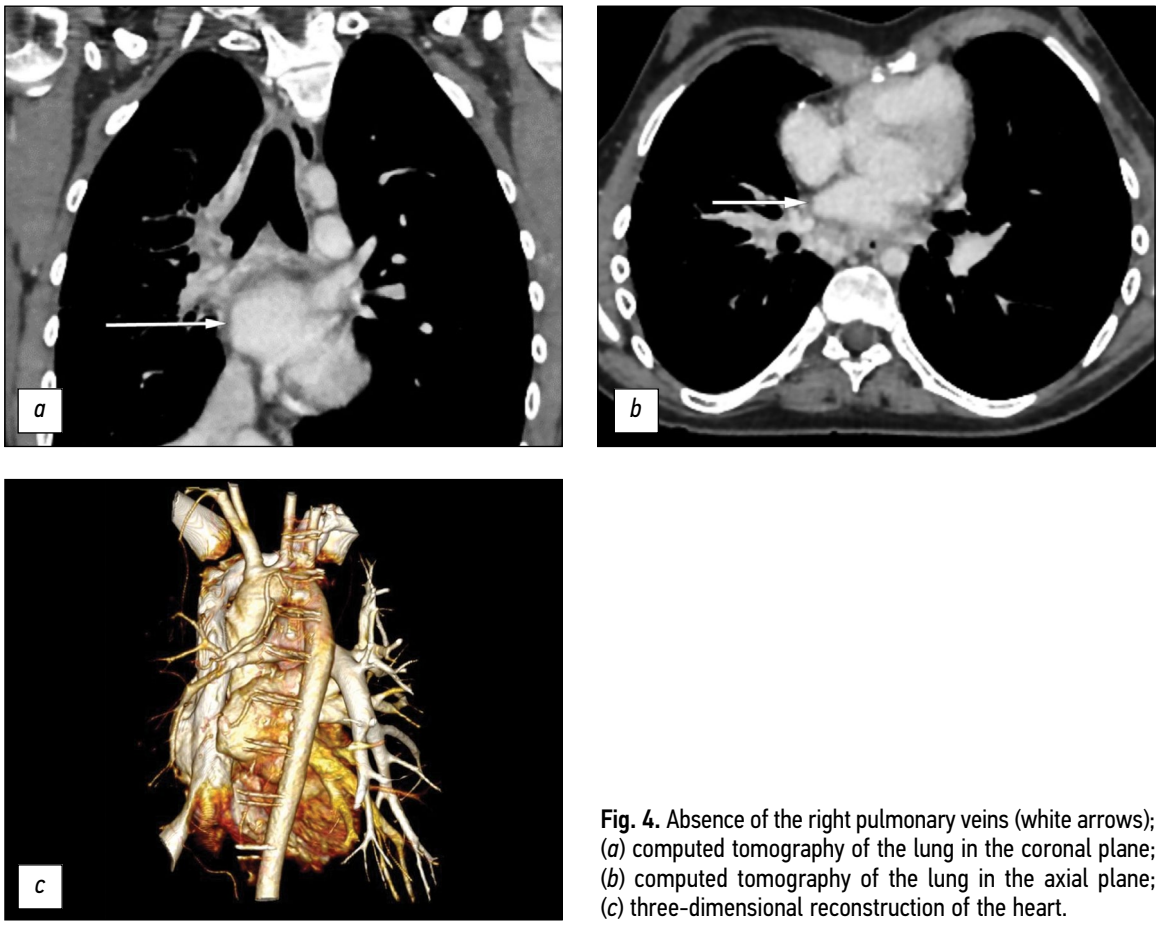

Fig. 4. Absence of the right pulmonary veins (white arrows); (*a*) computed tomography of the lung in the coronal plane; (*b*) computed tomography of the lung in the axial plane; (*c*) three-dimensional reconstruction of the heart.

inadequately supplied with blood. Consequently, the lung tissue is compacted, and the alveolar capillary membrane and interalveolar septa thicken due to increased connective tissue proliferation. This leads to impaired pulmonary gas exchange and hypoxemia [10].

In the present case, cysts were found in the affected lung. This was not an incidental finding, but a consequence of the destruction or underdevelopment of capillary networks at the alveolar level due to insufficient blood supply [2, 7].

Among the primary noninvasive diagnostic methods for congenital cardiovascular abnormalities, echocardiography is crucial for determining anatomical variability, size of the main pulmonary vessels, and blood supply parameters. In the present case, this examination was scheduled; however, the patient did not show up.

A standard chest X-ray may show the decreased volume of the affected lung and increased pulmonary vascularity due to the reticular component. Follow-up noninvasive diagnostics may include CT angiography and heart magnetic resonance imaging (MRI) [9]. In our case, heart MRI was not performed because CT visualized both venous and arterial abnormalities, allowing the diagnosis of venous insufficiency without using other modalities. Moreover, contrast-enhanced CT showed the absence of pulmonary veins, pulmonary artery hypoplasia, decreased size of the right lung, and interlobular septa thickening due to venous congestion.

Unilateral pulmonary venous atresia is a rare congenital malformation often confused with secondary malignancy, pneumonia, and pulmonary tuberculosis [3, 9]. In case of clinical symptoms, pneumonectomy or lung transplantation is recommended [9].

CONCLUSION

Unilateral pulmonary vein atresia is a rare congenital malformation that is often associated with other cardiovascular abnormalities. A rare case of combined asymptomatic congenital malformations of the pulmonary vessels in a young man is presented. In some cases, mediastinal and pulmonary lesions found in such patients may be misinterpreted as a manifestation of pneumonia, pulmonary tuberculosis, or cancer. However, a combination of radiologic signs on contrast-enhanced chest CT may be beneficial in the early diagnosis of this malformation.

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Consent for publication. Written consent was obtained from the patient for publication of relevant medical information and all of accompanying images within the manuscript Digital Diagnostics Journal.

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An Unknown Situs Viscerum Inversus Totalis, Accidentally Discovered After Computed Tomography

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ABSTRACT

Benign *situs inversus totalis* of the viscerum is often diagnosed accidentally, rarely in adults, and more frequently in children and neonates, affecting both sexes. In this report, a young female patient accidentally discovered a situs inversus totalis after computed tomography for acute abdominal pain. In this uncommon anatomical abnormality, the major visceral organs are reversed in the opposite direction. This report highlights the importance of being aware of and considering situs inversus in clinical practice, particularly when interpreting imaging findings and planning medical procedures. This is critical for differential diagnosis and comorbidities that may affect those patients.

The cause of *situs inversus totalis* is still unknown; however, this condition is frequently asymptomatic, particularly in infants, and is sometimes associated with other syndromes. The patient arrived at the emergency department with left flank pain, nausea, and fever. In the first ultrasonography, a strange anatomy was suspected; thus, a contrasted computed tomography was performed. The patient had never had a computed tomography scan before. The identification of situs inversus totalis was unexpected and coincidental; the computed tomography images were carefully examined. In patients with chest or abdominal pain, clinicians may consider situs inversus totalis based on computed tomography, particularly if without clinical and imaging history. This knowledge can help in the differential diagnosis, avoiding unneeded interventions. Moreover, comorbidities that affect several systems, particularly cardiovascular and pulmonary systems, affect quite a few patients with situs inversus totalis, who require careful examination and lifelong monitoring.

Keywords: computed tomography; diagnostic imaging; situs inversus totalis; viscerum inversus; anatomic variation; dextrocardia; left-sided gallbladder; left-right asymmetry; mirror-image transposition.

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Полная транспозиция внутренних органов неясной этиологии, случайно выявленная при компьютерной томографии

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АННОТАЦИЯ

Доброкачественная транспозиция внутренних органов (*situs inversus totalis*) часто диагностируется случайно, редко у взрослых и чаще у детей и новорождённых, как правило, у представителей обоих полов. В данной статье описан случай молодой пациентки, у которой случайно обнаружили *situs inversus totalis* при компьютерной томографии по поводу острой боли в животе. При этой редкой аномалии основные внутренние органы имеют зеркальное расположение. Данный случай подчёркивает важность информированности врачей и учёта *situs inversus* в клинической практике, особенно при интерпретации результатов визуализации и планировании медицинских процедур. Знания о подобных аномалиях очень важны для дифференциальной диагностики и выявления сопутствующих заболеваний у таких пациентов.

Этиология *situs inversus totalis* до сих пор не ясна, однако это состояние часто протекает бессимптомно, особенно у младенцев, и иногда ассоциируется с другими синдромами. Наша пациентка поступила в отделение неотложной помощи с болью в левом боку, тошнотой и лихорадкой. При первом ультразвуковом исследовании было выявлено нетипичное расположение внутренних органов. По этой причине была назначена компьютерная томография с контрастированием, после чего снимки были тщательно изучены. Ранее пациентка никогда не проходила компьютерную томографию, поэтому *situs inversus totalis* оказалась неожиданной и случайной находкой. При болях в груди или животе врачи могут предположить наличие *situs inversus totalis* по результатам компьютерной томографии, особенно если нет других клинических и визуализационных данных в анамнезе. Эти знания могут помочь в дифференциальной диагностике, позволяя избежать ненужных вмешательств. Более того, сопутствующие заболевания, затрагивающие несколько систем органов, в частности сердечно-сосудистую и лёгочную, встречаются у многих пациентов с situs inversus totalis, что требует тщательного обследования и наблюдения за ними в течение всей жизни.

Ключевые слова: компьютерная томография; диагностическая визуализация; *situs inversus totalis*; *viscerum inversus*; анатомический вариант; декстрокардия; левосторонний желчный пузырь; лево-правая асимметрия; зеркальная транспозиция.

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计算机断层扫描中偶然发现的病因不明的内脏器官完全移位

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摘要

良性内脏器官移位（situs inversus totalis）通常是偶然诊断出来的，很少发生在成人身上，更常见于儿童和新生儿，通常男女均可患病。本文描述了一名年轻患者的病例，她因急性腹痛而在接受计算机断层扫描时意外被诊断出患有 situs inversus totalis。在这种罕见的异常中，主要内脏器官呈镜像。本病例强调了医生在临床实践中认识和考虑 situs inversus 的重要性，尤其是在解释成像结果和规划医疗程序时。了解这类异常对于鉴别诊断和发现这些患者的合并症非常重要。

Situs inversus totalis 的病因尚不清楚，但这种疾病通常没有症状，尤其是在婴儿身上，有时还伴有其他综合征。我们的患者因左侧腹痛、恶心和发热被送入急诊科。第一次超声检查发现内脏器官的位置不典型。因此，医生要求患者接受造影剂计算机断层扫描，并对图像进行了仔细检查。患者以前从未做过计算机断层扫描，因此 situs inversus totalis 是一个意外的偶然发现。在胸痛或腹痛的情况下，按照计算机断层扫描结果，医生可能会假设有 situs inversus totalis，尤其是在没有其他临床或影像学病史的情况下。这些知识有助于鉴别诊断，避免不必要的干预。此外，涉及多个器官系统（尤其是心血管和肺部）的合并症在许多 situs inversus totalis 患者中很常见，需要进行仔细评估和终身随访。

关键词： 计算机断层扫描；诊断成像；situs inversus totalis；viscerum inversus；解剖变异；右旋心；左侧胆囊；左右不对称；镜像移位。

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INTRODUCTION

Situs viscerum inversus (SI) is a congenital anatomical disorder characterized by a mirror-image reversal of the major visceral organs (complete or incomplete), and the organs are arranged as opposed to the typical arrangement [1–6].

The term "situs" refers to the visceral pattern and individual asymmetric internal organs, which include the gastrointestinal tract, liver, spleen, and lung [7]. SI is classified into solitus (normal), inversus (mirror-image of normal), and situs ambiguous. Thus, situs solitus means normal anatomy, situs inversus describes total reversal, and situs ambiguous denotes any other anomalies of left–right development.

SI could be divided into totalis (SIT) or incomplete; this second condition is also known as "partial," in which only some visceral organs are transposed, whereas others remain normal. The extent of organ reversal varies; usually, the patient has a normal left-side heart and abdominal organ transposition [8–10]. The origin of these conditions is still unknown; however, they are frequently asymptomatic, particularly in infants. This clinical condition could create several thoracic problems, particularly in the heart level, and abdominal complications [11]. SIT could also complicate the diagnostic assessment and future treatment.

DESCRIPTION OF THE CASE

Medical History

A 56-year-old female patient presented to the emergency department with recurrent and colic left flank pain, particularly on the left side of the abdomen. She experienced intermittent pain migrating upward, to the back, under the shoulder blade and left shoulder [7–12].

She also reported nausea and vomiting, and the first hypothesis of the physician was biliary colic. Thus, some blood test was required, and ultrasonography (US) was initially performed. Due to precarious social conditions, the patient had never had any imaging tests until that moment. The US results were suspicious of something strange in the abdominal anatomy; thus, a contrasted CT was performed (Fig. 1).

The patient had not experienced any other significant cardiac or respiratory symptoms or previous CT. The first CT image of the thorax showed dextrocardia and a new diagnostic hypothesis was created. Further imaging studies of the thorax and abdomen confirmed the diagnosis of an unknown SIT (Fig. 2 and 3).

Diagnostic Assessment

The contrasted CT confirmed the SIT: an asymptomatic situs viscerum inversus totalis (Fig. 4).

In addition, the images from the high abdomen show a left-sided gallbladder with some micro-calculi, which could explain the clinical condition of recurrent flank pain on the left [1–7]. For the most part, this unsuspected discovery appeared completely innocuous for the patient's health [9].

Differential Diagnosis

was a crucial point in this case. The first problem was to know the causes of the acute flank pain on the left [11–13]. The patient has opposing anatomy; thus, the causes of this pain differ from the normal: biliary colic on the left, which is normally localized on the right [9]. This clinical condition was also confirmed by laboratory tests, which revealed a small increase in C-reactive protein level, white blood cell count, and transaminase levels.

Interventions

This case is not directly related to significant symptoms or acute problems due to SIT; instead, the interventions were focused on critical symptoms and the management and prevention of complications [12–16]. Biliary colic treatment aims to reduce pain with painkillers and antispasmodics to relieve symptoms (Fig. 5).

The future treatment regimen and follow-up for SIT are frequently interdisciplinary, comprising pulmonologists, cardiologists, and gastroenterologists. The management plan is adapted to the needs of each patient.

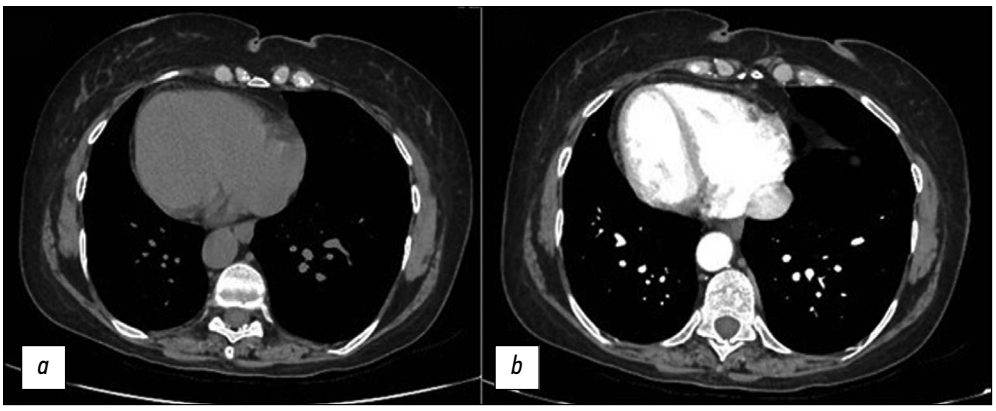

Fig. 1. Axial-computer CT images of the chest without (*a*) and with contrast medium (*b*) that show dextrocardia. In this case of *situs inversus*, the left lung has three lobes, the right lung has two lobes, and the heart apex is on the right.

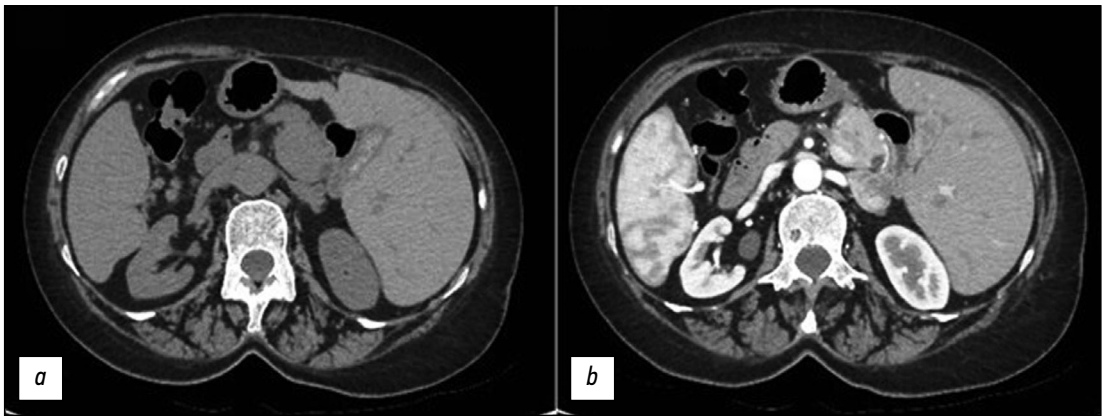

Fig. 2. Axial CT images of the abdomen without (*a*) and with contrast medium (*b*) show SIT and some calcific calculi in the gallbladder. The stomach and spleen are on the left, and the bigger lobe of the liver is on the right.

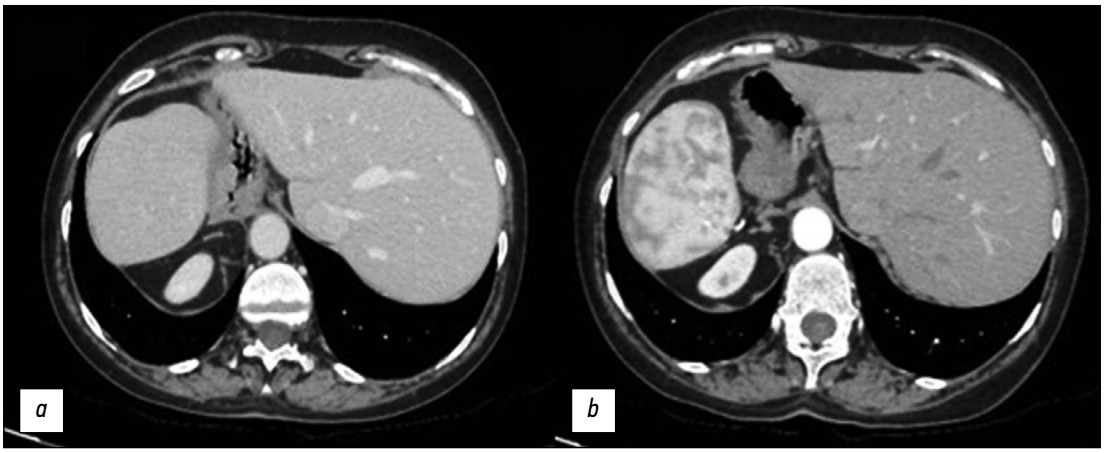

Fig. 3. Axial CT image without (*a*) and with contrast medium (*b*) that shows the stomach on the right side.

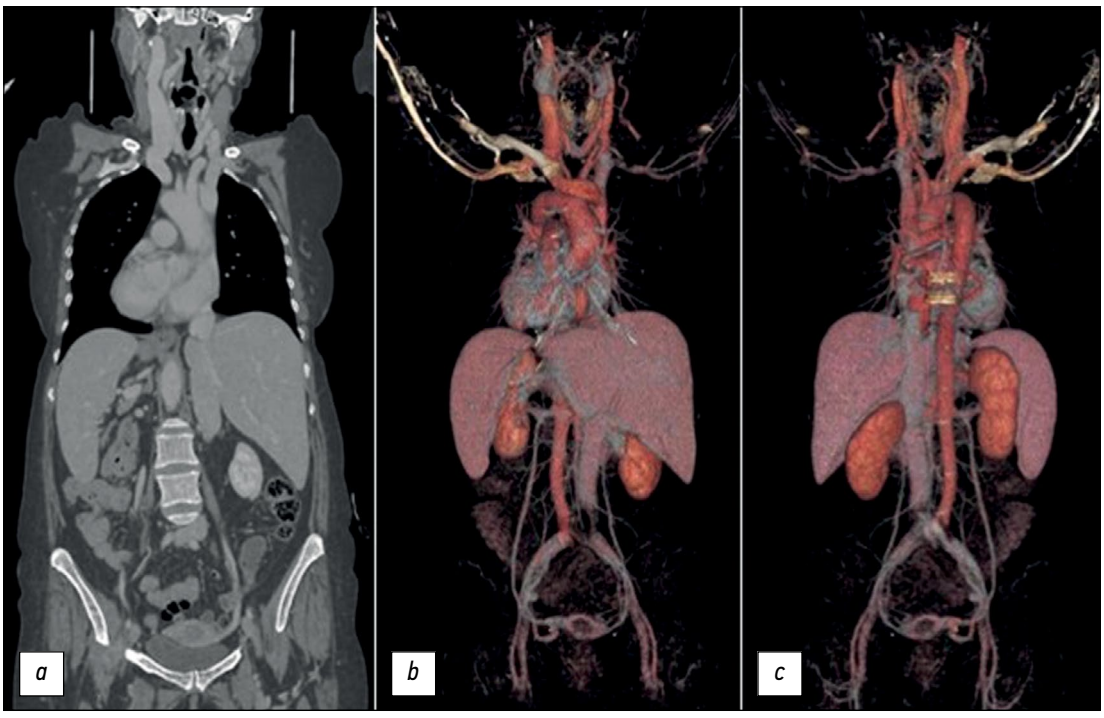

Fig. 4. The SIT is in a coronal plane of the CT (*a*) and two volume rendering (VR) VR images: (*b*) from the front and (c) behind.

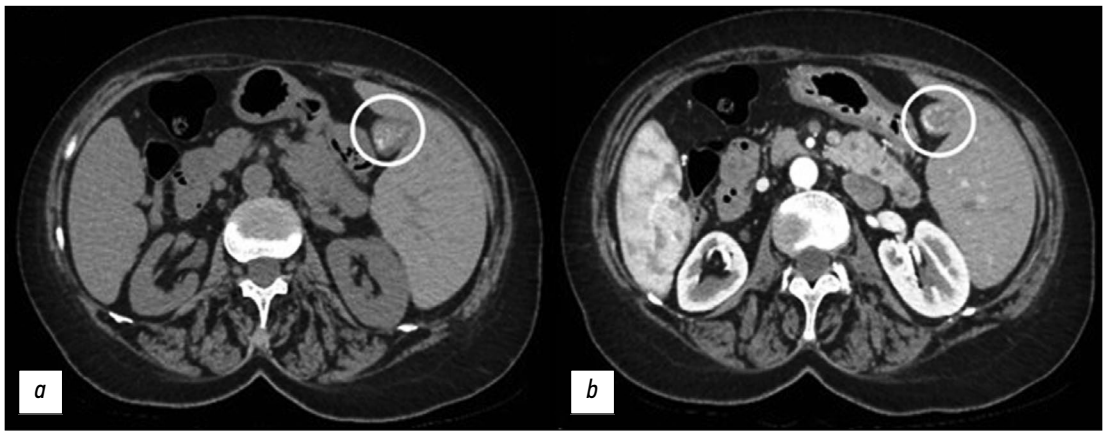

Fig. 5. The gallbladder appears with multiple calcific calculi. These CT images without (*a*) and with (*b*) contrast medium justify the left-sided abdominal pain.

Follow-up and Outcomes

To optimize care and maintain the best possible quality of life, regular follow-up and communication between physicians and patients are essential in the present and future conditions [15–17].

DISCUSSION

SI refers to a reversal positioning of the heart and major internal organs [1-4]. It is an uncommon congenital anomaly that manifests as a mirror-image transposition of both the abdominal and thoracic organs [5]. Dextrocardia (true mirror-image) is commonly related to SI, and the aorta is up-directed on the opposite side (Fig. 6).

This condition could affect the chest, particularly the heart and large blood vessels because each cardiac chamber is asymmetrical; situs also applies to the heart. In addition, the anatomy of the arteries and the abdomen is mirrored (Fig. 7).

Currently, SIT still has no clear and recognized causes. Given the frequent relationship between aberrant situs and other unusual congenital abnormalities, a study proposed an acquired etiology originating from an in-utero insult that disrupts the normal process of differentiation and orientation [8].

This anatomical condition could complicate the diagnostic process and diagnostic/treatment procedures, particularly invasive ones. Because of their rarity, practicing doctors, such as gastroenterologists, radiologists, and surgeons, typically have little experience with these patients [14–17].

CONCLUSION

Many people with SI are unaware of this condition until they experience some symptoms that require treatment or

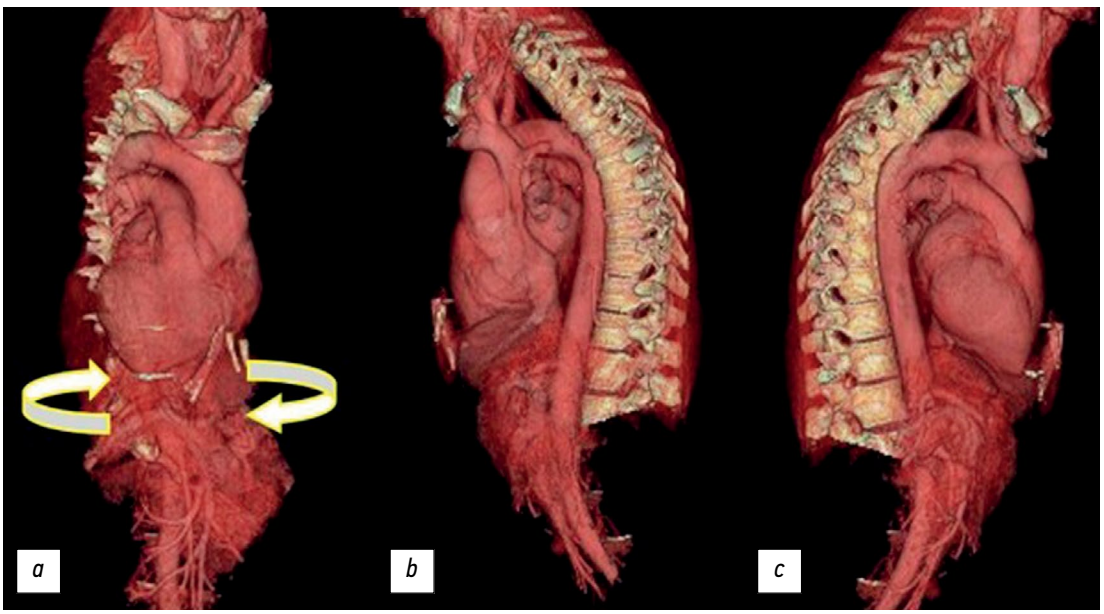

Fig. 6. A series of VR images of the mediastinum that show the heart and aorta directed on the right from different perspectives (*a* in front) (*b* behind, on the left) (*c* behind, on the right) on rotation.

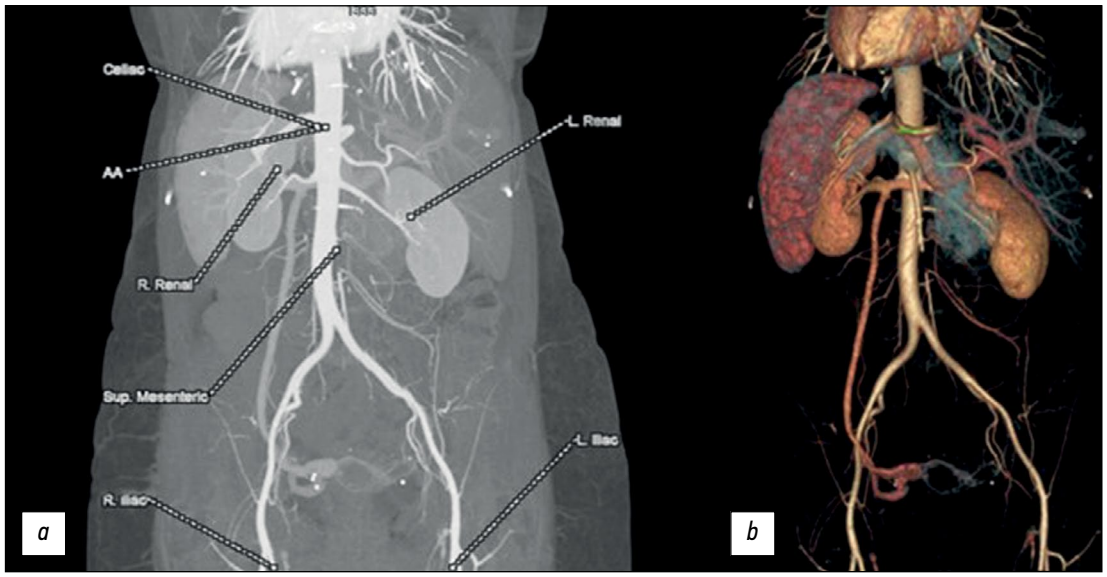

Fig. 7. The artery's anatomy of the abdomen in the case of SIT: on the left, there is the liver, and the spleen is on the opposite side. The first is an angio-map (*a*) while the second is a VR image (*b*).

until they undergo clinical examinations, for example, chest auscultation or US of the abdomen. However, follow-up is required because mirrored architecture can make future disorders more difficult to detect. Thus, regular evaluations and communication between doctors and patients with SIT are critical for optimizing care and preserving the highest possible quality of life, against the resolution of future pathologies and syndromes.

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F. Masino, R. Tupputi — data collection; F. Masino, G. Guglielmi — analysis and interpretation of results; M. Montatore, M. Balbino — draft manuscript preparation, editing the manuscript.

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Difficulties in the Radiological Diagnosis of Mature Adrenal Teratoma Mimicking Neuroblastoma in a Child

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ABSTRACT

The most common adrenal tumor in young children is neuroblastoma, which can be difficult to differentiate from other conditions such as nephroblastoma, adrenal hemorrhage, angiomyolipoma, myelolipoma, and adenoma. This article describes a case of teratoma, one of the rarest adrenal tumors in children. Initially, despite its large size, it demonstrated all the radiological and histological signs of neuroblastoma. Teratomas are germ cell tumors usually found in the gonads. Adrenal teratomas are extremely rare, accounting for approximately 0.13% of all adrenal tumors. Typically, adrenal teratomas are asymptomatic, as the retroperitoneal space is large enough to accommodate the growth of the tumor without causing symptoms. For the first time in domestic literature, we present a clinical case of adrenal teratoma in a 3-month-old child. The article also presents a detailed description of the diagnostic process and challenges that radiologists and clinicians face when encountering a common tumor in a very rare location for children. This report aimed to help physicians increase awareness of this rare condition and include adrenal teratomas in the potential differential diagnosis of adrenal neoplasms.

Keywords: adrenal teratoma; case report; pediatrics; radiology.

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Трудности лучевой диагностики зрелой тератомы надпочечника, имитирующей нейробластому, у ребёнка

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АННОТАЦИЯ

Наиболее частое образование надпочечников у детей раннего возраста — это нейробластома, в дифференциальный ряд которой включены такие образования, как нефробластома, кровоизлияние в надпочечник, ангиомиолипома, миелолипома и аденома. В данной статье описан случай одной из самых редких опухолей надпочечников у детей — тератомы, которая на начальных этапах диагностики, несмотря на крупный размер, демонстрировала все рентгенологические и гистологические признаки нейробластомы.

Тератомы — это герминогенно-клеточные опухоли, обычно обнаруживаемые в области гонад. Тератомы надпочечников встречаются крайне редко и составляют около 0,13% всех образований надпочечников. Как правило, тератомы надпочечников протекают бессимптомно за счёт того, что забрюшинное пространство достаточно обширно для свободного роста образования.

Впервые в отечественной литературе нами представлен клинический случай тератомы надпочечника у ребёнка в возрасте 3 месяцев. В статье также подробно описан ход диагностических исследований и те сложности, с которыми рентгенологи и клиницисты столкнулись, встретив распространённую в детском возрасте опухоль в очень редкой для неё локализации.

Данная статья может помочь врачам повысить осведомлённость о таком редком заболевании и включить тератому надпочечников в потенциальный дифференциальный ряд новообразований надпочечников.

Ключевые слова: тератома надпочечника; клинический случай; педиатрия; лучевая диагностика.

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一名患有模仿神经母细胞瘤的肾上腺成熟性畸胎瘤的儿童的放射诊断难题

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摘要

神经母细胞瘤是幼儿最常见的肾上腺肿块，其鉴别系列包括肾母细胞瘤、肾上腺出血、血管肌脂肪瘤、骨髓脂肪瘤和腺瘤。本文描述了一例最罕见的儿童肾上腺肿瘤，即畸胎瘤，尽管其体积较大，但在诊断初期却显示出神经母细胞瘤的所有放射学和组织学特征。

畸胎瘤是生殖细胞肿瘤，通常出现在性腺区域。肾上腺畸胎瘤极为罕见，约占所有肾上腺肿块的0.13%。肾上腺畸胎瘤通常没有症状，这是因为腹膜后间隙足够大，肿块可以自由生长。

我们首次在俄罗斯文献中介绍了一个 3 个月大儿童肾上腺畸胎瘤的临床病例。文章还详细描述了诊断检查的过程，以及放射科医生和临床医生在罕见部位遇到常见儿童肿瘤时所遇到的困难。

文章旨在帮助医生提高对这种罕见疾病的认识，并将肾上腺畸胎瘤纳入肾上腺肿瘤的潜在鉴别系列。

关键词：肾上腺畸胎瘤；临床病例；儿科；放射诊断。

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INTRODUCTION

Primary adrenal tumors are a critical area of clinical oncology that presents diagnostic and therapeutic challenges.

Based on the fourth edition of Classification of Tumors of Endocrine Organs by the World Health Organization published in 2017, all adrenal tumors can be classified into two large groups [1]:

1) Tumors of the adrenal cortex;
2) Tumors of the adrenal medulla and extra-adrenal paraganglia.

The first group comprises tumors that originate from the adrenal cortex or predominantly affect it, including adenocarcinoma, adenoma, sex cord stromal tumors, adenomatoid tumors, mesenchymal and stromal tumors (myelolipoma and schwannoma), and hematolymphoid tumors.

The second group encompasses pheochromocytoma, paraganglioma, and neuroblastic adrenal tumors (neuroblastoma, ganglioneuroblastoma, and ganglioneuroma).

Currently, neuroblastoma is the most prevalent adrenal tumor in children and incorporates such differential diagnosis categories as nephroblastoma, adrenal hemorrhage, angiomyolipoma, myelolipoma, and adenoma [2–4].

This article details a case report of primary mature teratoma of the left adrenal gland in a child. The tumor was initially diagnosed as neuroblastoma. The article also provides differential diagnosis categories for this condition.

As per the literature review, approximately 20 comparable cases in children have been reported worldwide [3, 5, 6]. However, we were unable to locate relevant case reports in Russian literature.

DESCRIPTION OF THE CASE

Medical History

The patient has been unwell since August 2020 (age of 2 months), when a routine abdominal ultrasound (US) revealed a left kidney space-occupying mass (197 cm^3). The patient's previous medical history was unremarkable.

According to the medical history:

On **September 21, 2020**, the patient was admitted to the Urology Department. The tumor markers assessed as of September 22, 2020 were:

- Neuron-specific enolase (NSE) elevated to 24.7 ng/mL (normal range: 0–16.3 ng/mL);
- Alpha-fetoprotein (AFP) elevated to 971 ng/mL (normal range: 323 ± 278 ng/mL).

September 23, 2020: A contrast-enhanced abdominal multislice computed tomography (MSCT) revealed a retroperitoneal space-occupying mass on the left, measuring 81 × 71 × 87 mm (volume: 260 cm^3), with a heterogeneous structure incorporating areas of calcification and inclusion cysts; the contrast uptake was weak. The neoplasm extended to the renal sinus area, without discernible signs of extension into the renal parenchyma. The adrenal gland extended across the lateral contour. The renal vessels on the left side followed the tumor contour; the superior mesenteric artery was displaced to the right, while the celiac artery was displaced upward (Fig. 1).

September 29, 2020: No tumor cells were detected in myelogram findings.

The surgery, which involved laparotomy and retroperitoneal tumor biopsy, was conducted in early October. The histological examination revealed the tumor to be a high-grade neuroblastoma. The diagnosis was further corroborated by the examination of histologic specimens at the Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology, and Immunology. A cytogenetic test was not performed because of insufficient sample size.

Following the examination, a clinical diagnosis of left-sided retroperitoneal neuroblastoma extending to the abdominal cavity was established. Therapy was initiated in accordance with the NB-2004 protocol.

October 16, 2020: The patient was referred for follow-up magnetic resonance imaging (MRI) at their place of residence. The MRI revealed disease progression, with a tumor size increase to 104 × 77 × 118 mm (volume: 491 cm^3). The tumor exhibited a cystic and solid structure, with areas of hemorrhage and signs of active contrast uptake. The adrenal gland was spread along the lateral contour of the tumor. The tumor contour was followed by the renal vessels on the left; the superior mesenteric artery was displaced to the right, and the celiac artery was displaced upward. The study did not incorporate contrast sequences or weighted sequences with fat suppression (Fig. 2).

Hospitalization

Because of the disease progression, the patient was admitted to the Clinical Oncology Department of the Dmitry Rogachev National Medical Research Center for further examination and determining the suitable treatment strategy.

Upon admission, the test for NSE was repeated, revealing elevated levels of 19.64 ng/mL (normal range: 0–16.3 ng/mL). A blood test for cortisol was conducted to exclude a hormone-producing tumor, yielding a value of 17.3 μg/dL (normal range: 3.7–19.4 μg/dL).

October 30, 2020: A metaiodobenzylguanidine scintigraphy demonstrated no reliable signs of radiopharmaceutical uptake (Fig. 3).

November 1, 2020: A contrast-enhanced MRI was conducted as a follow-up to ascertain the type of the tumor. A series of abdominal scans revealed persistent signs of a cystic and solid retroperitoneal mass lesion on the left, which was irregularly shaped had relatively clear and smooth contours with areas of intratumor hemorrhage (restricted diffusion areas in diffusion-weighted images) and fat deposits (signal dropout in the spectral pre-saturation with inversion recovery (SPIR) mode). The total dimensions of the lesion were up to

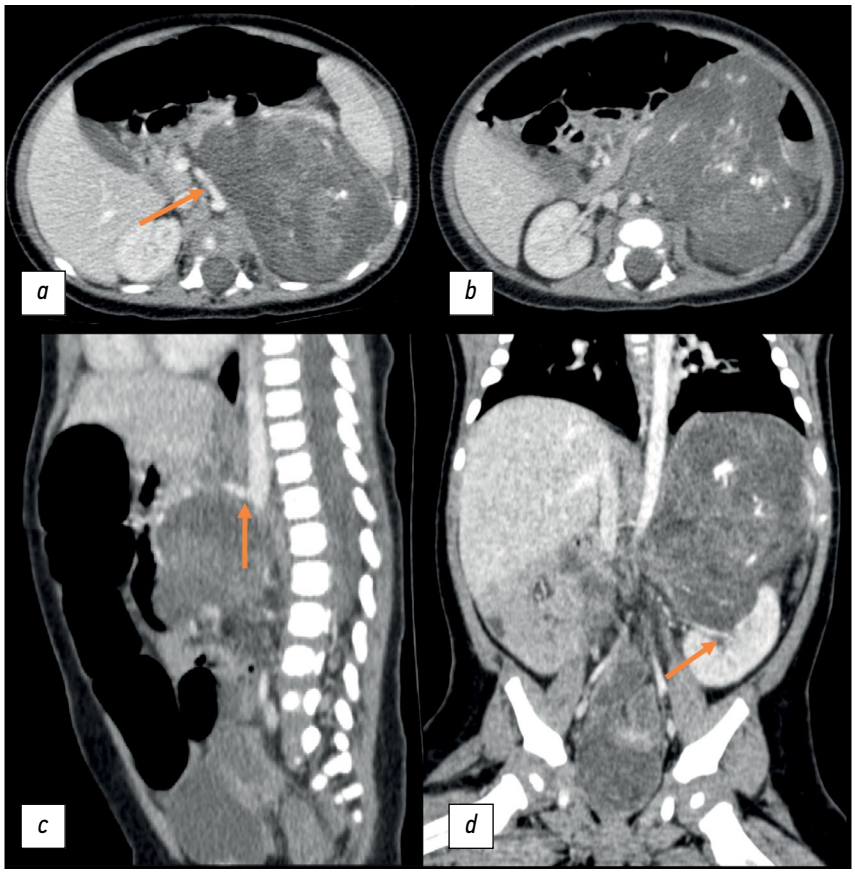

Fig. 1. Initial abdominal computed tomography using intravenous contrast dated September 23, 2020, a pattern of a space-occupying retroperitoneal mass on the left: (*a*) axial plane; the arrow indicates the displacement of the superior mesenteric artery to the right; (*b*) axial plane; (*c*) sagittal plane; the arrow indicates the upward displacement of the celiac artery; (*d*) coronal plane; the arrow indicates the tumor extension into the renal sinus.

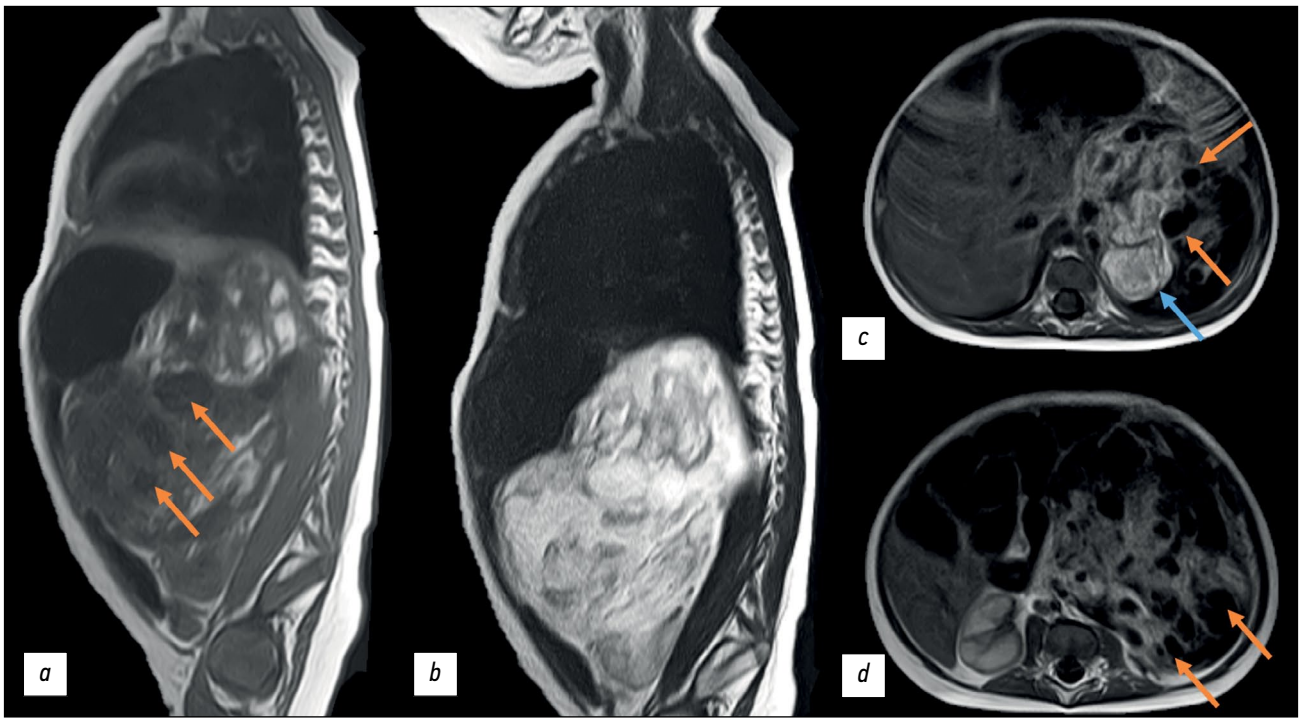

Fig. 2. Abdominal magnetic resonance imaging dated November 16, 2020: (*a*) T1-weighted image, sagittal plane; (*b*) T2-weighted image, sagittal plane; (*c*, *d*) T1-weighted images, axial plane; a space-occupying mass of the left adrenal gland, with an increase in the size over time. Orange arrows indicate an attenuated signal from the cystic tumor component; the blue arrow indicates an enhanced signal from the solid tumor component.

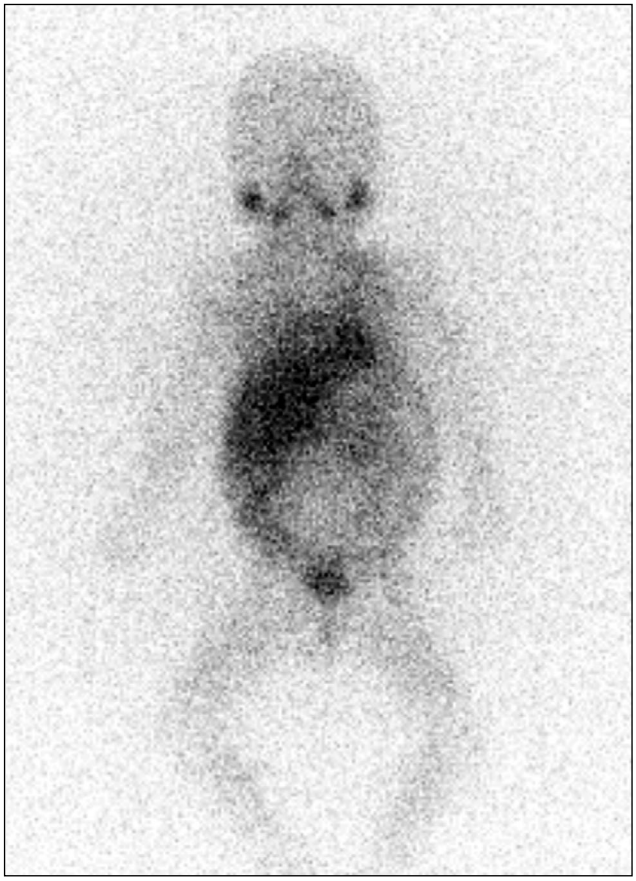

Fig. 3. Metaiodobenzylguanidine scintigraphy dated October 30, 2020. There was no indication of radiopharmaceutical uptake.

89 × 112 × 141 mm (volume: 731 cm^3). The tumor volume increased by 49% in comparison to the previous investigation. A focal MRI contrast absorption in solid components was observed because of intravenous contrast enhancement. The tumor caused caudal displacement of the left kidney to the small pelvic area. The left adrenal gland was not visualized. The spleen was displaced forward, and the tumor margin was clearly visible. The celiac artery followed the medial contour, while the spleen vessels followed the anterior tumor contour. The pancreas extended across the anterior tumor contour and was in close proximity to the tumor. The caudal misplacement of the left hemidiaphragm was a result of the tumor's upper margin being contiguous to it, which in turn reduced the volume of the left lung (Fig. 4).

The MRI revealed fat deposits (signal dropout in the SPIR mode) that are atypical for neuroblastoma. Hence, for the first time, a germ cell tumor, i.e., retroperitoneal teratoma (possibly, left adrenal gland teratoma) or a mesenchymal tumor, was suspected.

The following day, abdominal computed tomography was conducted, which verified calcification and fat deposits in the mass with the cystic and solid components, with a weak contrast uptake (Fig. 5).

Considering an increase in the tumor size during the initial chemotherapy course, tumor characteristics with signs of fat deposits and tumor infiltration of the renal sinus area, as well as the absence of cytogenetic test findings, surgery was recommended. This procedure included repeated laparotomy

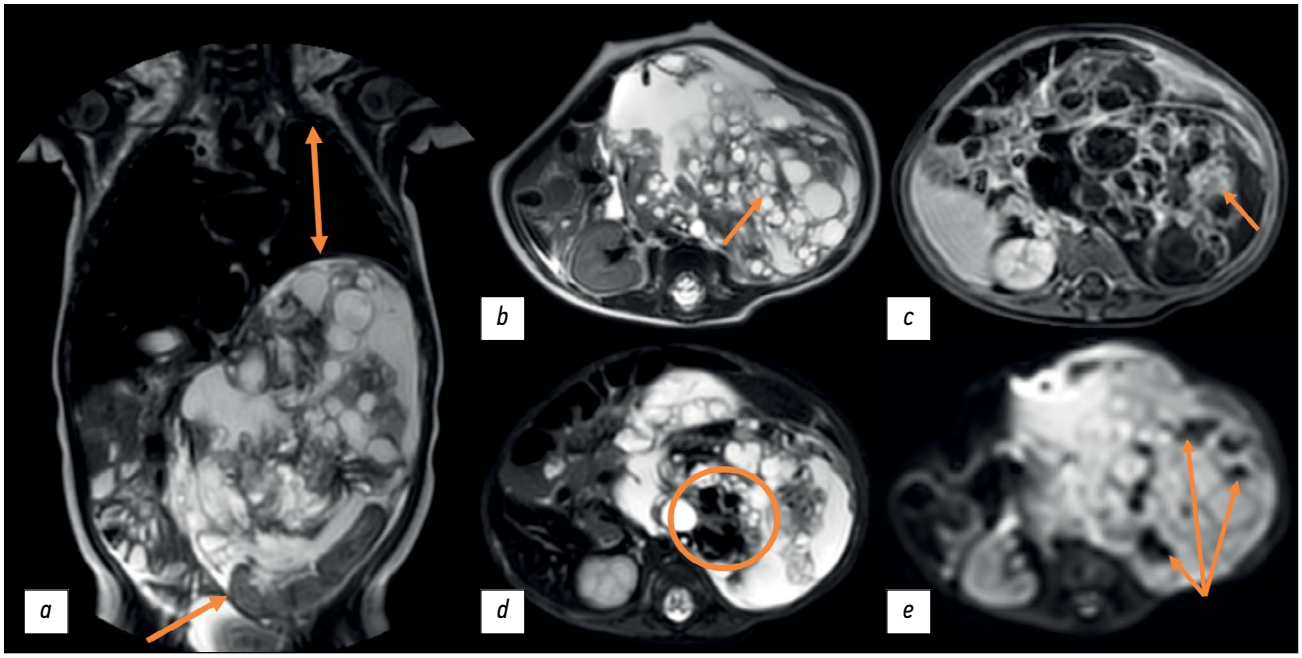

Fig. 4. Contrast-enhanced abdominal magnetic resonance imaging dated November 11, 2020, coronal (*a*) and axial (*b–e*) planes: (*a*) T2-weighted image; diminished volume of the left lung caused by the tumor pressing on the left hemidiaphragm (double orange arrow), displacement of the left kidney to the pelvic area (orange arrow); (*b*) T2-weighted image; multiple cysts in the tumor (orange arrow); (*c*) T1-weighted image +C; focal contrast uptake in solid components (orange arrow); (*d*) T2 SPIR; signal dropout because of fat deposits in the tumor (orange circle); (*e*) diffusion-weighted image; restricted diffusion areas due to intratumor hemorrhages (orange arrows).

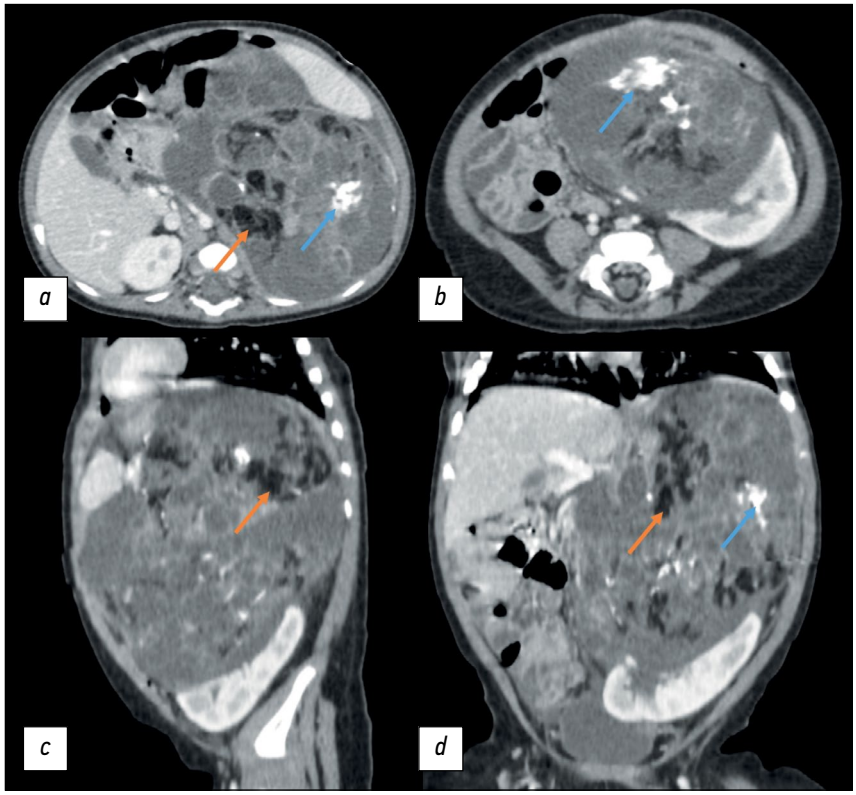

Fig. 5. Contrast-enhanced abdominal computed tomography dated November 1, 2020: (*a*, *b*) axial plane; (*c*) sagittal plane; (*d*) coronal plane. Orange arrows indicate the hypodense areas (fat deposits) of the tumor, with a density of –80 HU; blue arrows indicate calcification.

and retroperitoneal tumor resection to conduct routine histopathological examination and cytogenetic testing.

November 4, 2020: Laparotomy, retroperitoneal tumor resection, and left ureter stenting were performed as part of surgical treatment.

November 9, 2020: The laboratory findings revealed that the AFP levels returned to normal (51 ng/mL).

Histopathological findings: the morphological pattern was consistent with mature teratoma of the left adrenal gland. The tumor originated from the adrenal medulla.

Thus, the final diagnosis of ature teratoma of the left adrenal gland was established.

The patient was discharged in stable condition at the age of 5 months to be dynamically observed by a pediatric oncologist at their place of residence. There were no indications to continue any particular therapy.

DISCUSSION

Teratomas are germ cell tumors that develop from totipotent cells [5]. They comprise well-differentiated or not fully differentiated elements of at least two germ cell layers (endoderm, ectoderm, and/or mesoderm).

It is hypothesized that the initial involvement of the retroperitoneal space is a consequence of the disruption of normal embryological migration of primary germ cells at various points between their development in the yolk sack and their “final destination” in the labioscrotal swellings [7]. There are four histological variants of teratomas: mature, immature, with malignant transformation, and monodermal [7]. Mature teratomas are well-differentiated relative to germ cell layers. Immature teratomas are not completely differentiated and are comparable to fetal or embryonic tissue [8]. Teratomas may contain hair, skin, teeth, nerves, adipose tissue, cartilages, etc. [3]. Adrenal teratomas are exceedingly uncommon, and teratomas that originate outside the gonads are exceedingly unusual. The Peking Union Medical College in China conducted the most extensive study of adrenal disorders, treating 3,901 patients between March 2009 and February 2014. Of these, five patients (four adults and one child) were diagnosed with primary adrenal teratoma, accounting for 0.13% [9].

Adrenal teratoma patients typically do not exhibit any clinical symptoms of the disease since the retroperitoneal space is sufficiently vast to accommodate unrestricted tumor growth. Certain patients complain of lower back pain, a palpable mass in the abdomen, and upper abdominal pain [3].

In children, abdominal ultrasound is typically the preferred imaging method, The detection rate of masses in the early phases has been enhanced by the combination of prophylactic abdominal and retroperitoneal ultrasound one month after birth and antenatal ultrasound examination of the fetus [10]. Ultrasound enables the identification of cystic, solid, and other complex tumor components [11].

MSCT and MRI are essential for evaluating the size of tumors in the retroperitoneal space and their association

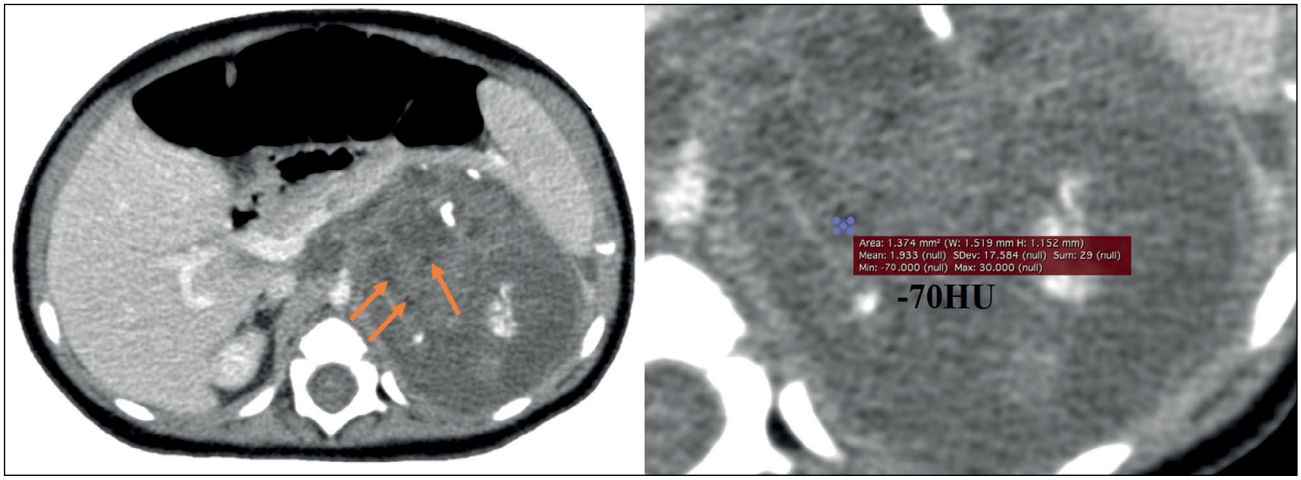

Fig. 6. Initial contrast-enhanced abdominal computed tomography dated September 23, 2020, axial plane. Arrows indicate small hypodense areas of the tumor, with a density of –70 HU.

with large vessels. This enhances preoperative planning and increases the possibility of total tumor resection with a lower risk of iatrogenic injury [12]. Fat deposits, cysts, and calcification are considered significant predictors of a benign teratoma on MSCT [13]. MRI exhibits a high natural contrast of soft tissues; moreover, it is overly sensitive to small fat deposits when sequences with fat suppression are employed. Retroperitoneal teratomas can express AFP; thus, its serum levels are a reliable parameter for the diagnosis and evaluation of tumor recurrence [14].

This case report underscores the need to thoroughly examine the tumor node structure and assess the density of different tumor components. The retrospective examination of the diagnostic errors revealed that teratoma could have been suspected as early as the initial abdominal MSCT, as the presence of small hypodense inclusions (–70 HU) consistent with the lipid component of the tumor and uncharacteristic of neuroblastoma should have been considered (Fig. 6).

Moreover, the diagnosis of adrenal teratoma was inferred from the clear and smooth contours of the tumor, which displaced vessels without surrounding them; in contrast, neuroblastoma exhibits indistinct, irregular contours and affects vessels by infiltrating them. The presence of a cystic and solid component and calcification is typical for both tumors. The absence of radiopharmaceutical uptake during scintigraphy, low NSE levels, and high AFP levels are also suggestive of teratoma. The histopathological examination's errors may be attributed to a biopsy performed at a less informative site and a limited sample size.

Notably, adrenal tumors, except for neuroblastomas, are exceedingly uncommon in children. Teratomas should be differentiated from other tumors that contain a fat component and calcification.

Fat-containing adrenal tumors include myelolipoma, lipoma, and myelosarcoma; microscopic fat inclusions can be found in adenoma, pheochromocytoma, and adrenocortical carcinoma.

Myelolipoma is typically detected at the age of 50–70 years, more commonly in the right adrenal gland [15]. Large adipose deposits are depicted on MSCT, with cloudy or mottled tissue areas that have a higher density of 20–30 HU (myeloid elements). In rare cases, small, calcified inclusion may be observed.

Adrenal lipoma is an extremely rare condition that primarily impacts the right adrenal gland, with a median diagnosis age of 54 years. Unlike teratoma, it is a hypodense mass that exclusively contains a fat component [16].

Despite the rarity of liposarcoma in children, it should not be disregarded during the differential diagnosis. It is characterized by indistinct, irregular contours and invasion into the surrounding tissues and vessels. Metastases are frequently observed [17].

The most prevalent adrenal neoplasms with calcified components are metastatic lesions (in our case, this was a primary tumor, and no other neoplasms were identified) and tuberculosis involvement (in the present case, the patient was not exposed to infectious diseases, and there were no signs of tuberculosis) [3].

CONCLUSION

Primary adrenal teratoma is extremely rare; however, it exhibits distinct radiographic signs that, in certain cases, may be remarkably comparable to those of other common pediatric tumors at this site. In our case, the radiologist could have suspected this disease as early as at the initial phases of the diagnostic search. Misdiagnosis was the consequence of a lack of awareness regarding an uncommon tumor site, inaccurate interpretation of histopathological examination findings, and a lack of attention to detail during the assessment of the tumor node structure. To enhance the quality of diagnostic radiology, it is imperative to discuss rare clinical cases and analyze the mistakes.

ADDITIONAL INFORMATION

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