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

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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

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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

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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.

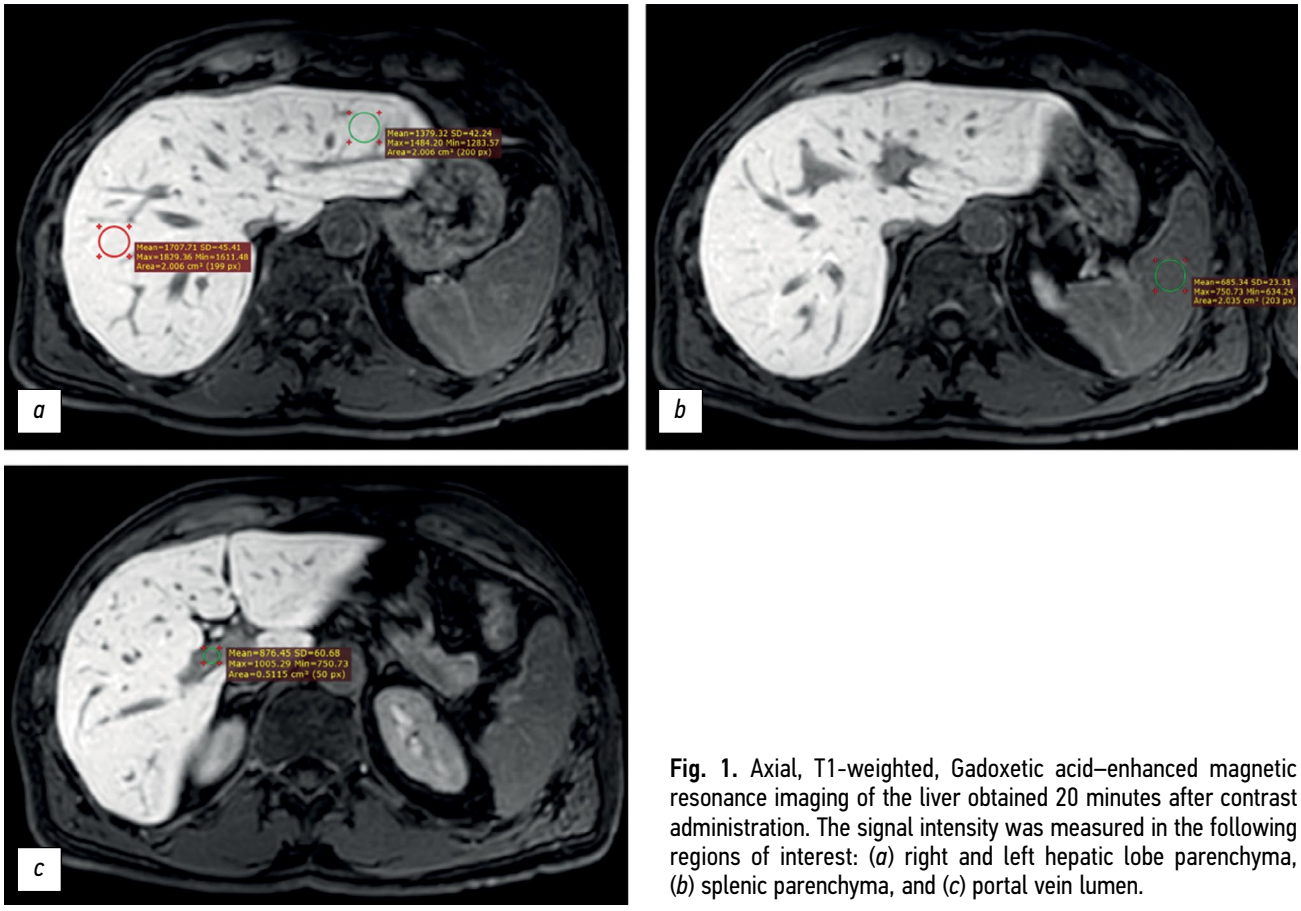

Fig. 1. Axial, T1-weighted, Gadoxetic acid–enhanced magnetic resonance imaging of the liver obtained 20 minutes after contrast administration. The signal intensity was measured in the following regions of interest: (*a*) right and left hepatic lobe parenchyma, (*b*) splenic parenchyma, and (*c*) portal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

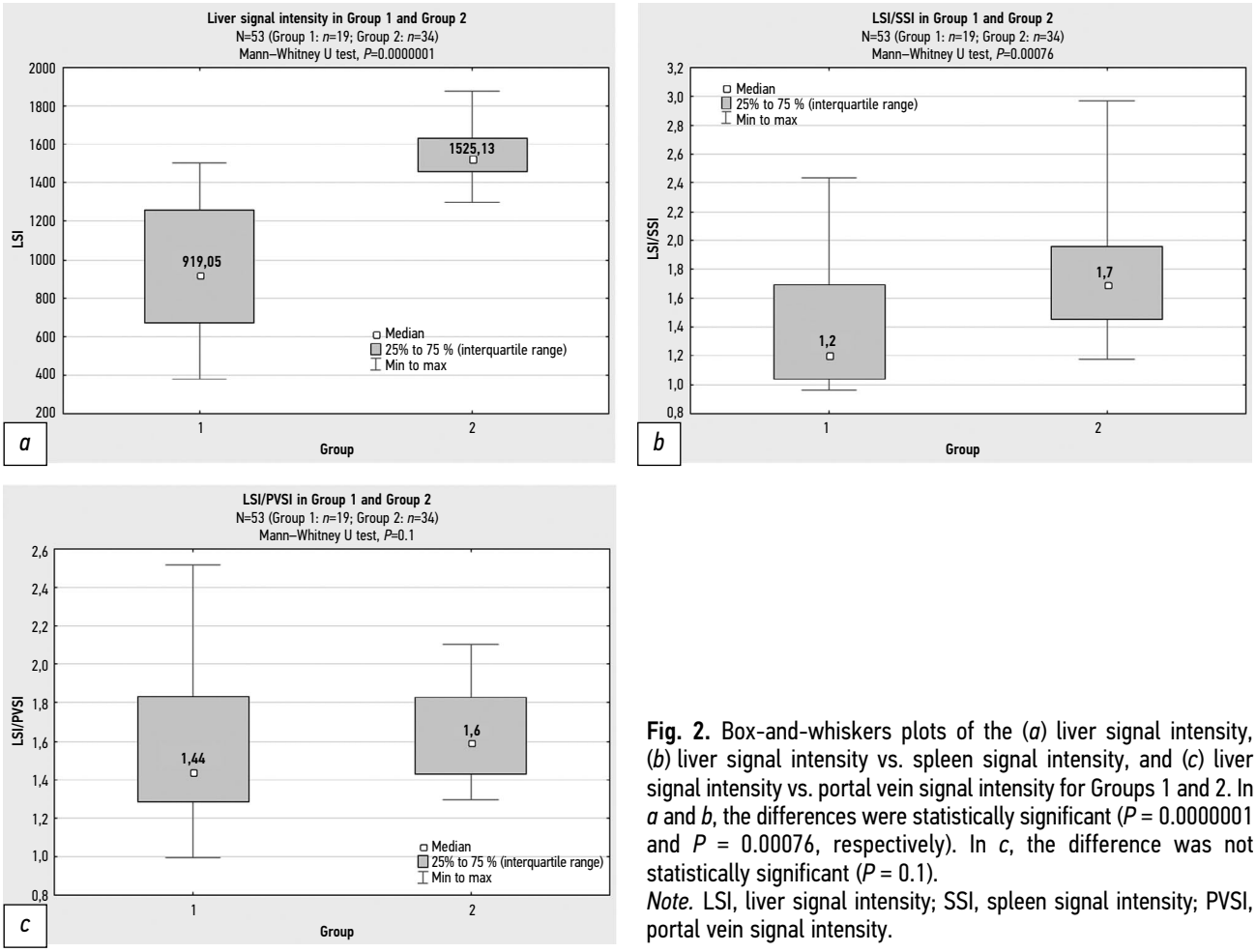

Fig. 2. Box-and-whiskers plots of the (*a*) liver signal intensity, (*b*) liver signal intensity vs. spleen signal intensity, and (*c*) liver signal intensity vs. portal vein signal intensity for Groups 1 and 2. In *a* and *b*, the differences were statistically significant ($P = 0.0000001$ and $P = 0.00076$, 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.

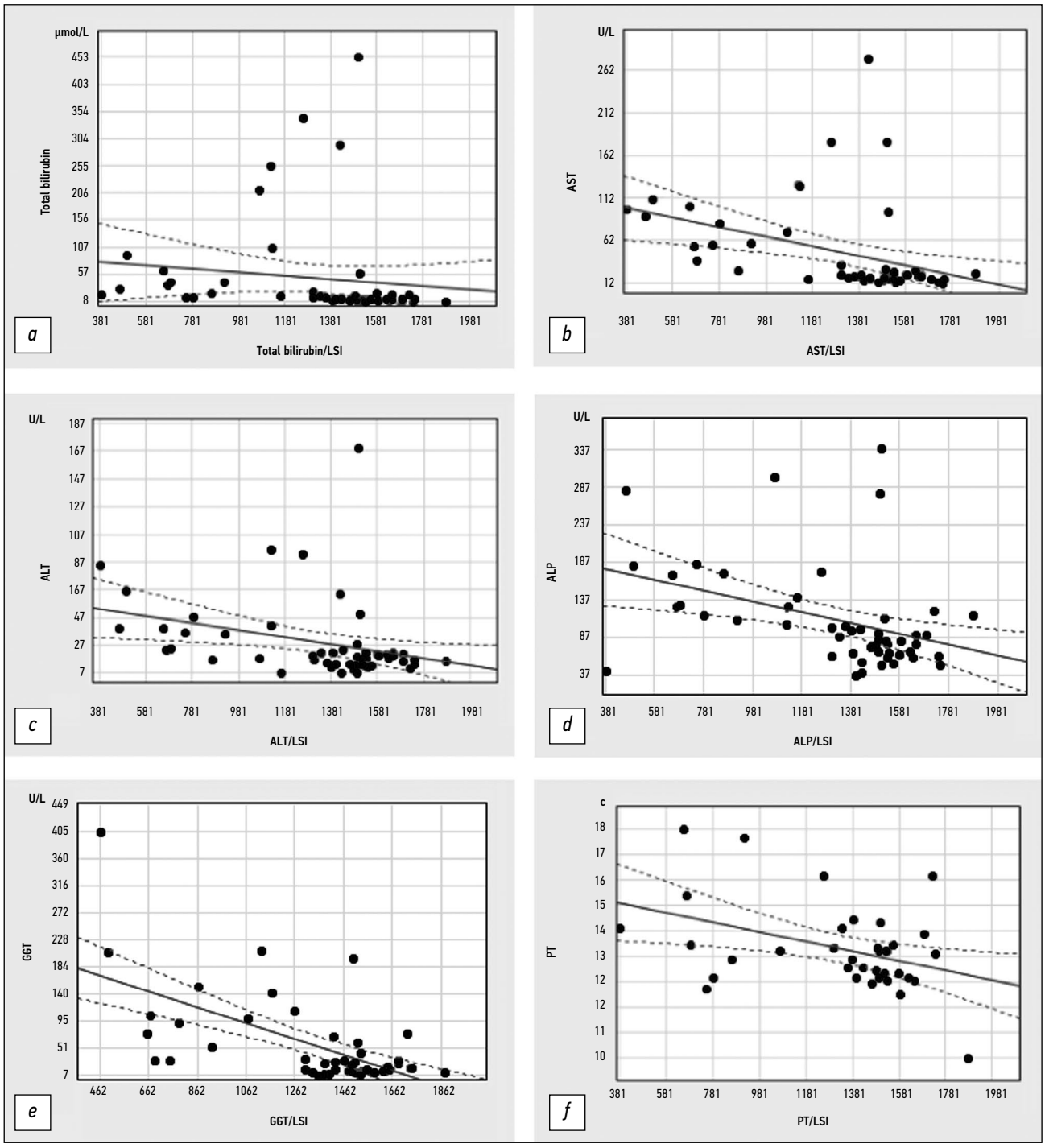

Fig. 3. Scatter plots showing the correlation between liver signal intensity and the following parameters: (*a*) total bilirubin level (r = –0.61; P = 0.000001), (*b*) aspartate aminotransferase level (r = –0.57; P = 0.000009), (*c*) alanine aminotransferase level (r = –0.44; P = 0.001), (*d*) alkaline 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

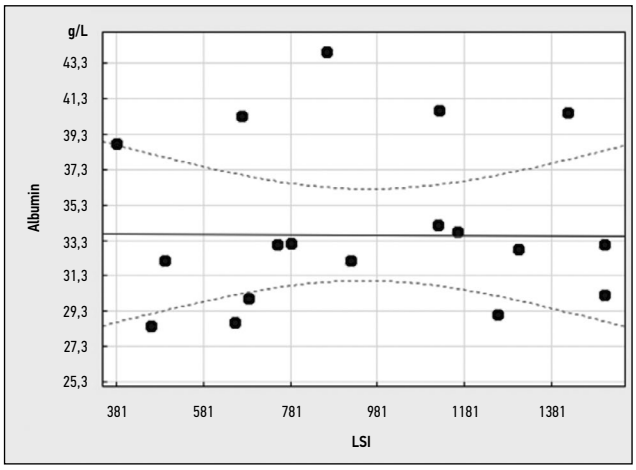

Fig. 4. Scatter plot showing the correlation between liver signal intensity and serum albumin level (r = 0.13; P = 0.61).
Note. LSI, liver signal intensity.

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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REFERENCES

1. Peng Y, Qi X, Guo X. Child–Pugh Versus MELD Score for the Assessment of Prognosis in Liver Cirrhosis. *Medicine.* 2016;95(8):e2877. doi: 10.1097/MD.0000000000002877

2. Likar YuN, Akhaladze DG, Rumyantsev AG. Hepatobiliary scintigraphy in the preoperative assessment of the future remnant liver function (literature review and own examples). *The Russian Journal of Pediatric Hematology and Oncology.* 2020;7(1):62–69. EDN: VWDZUW doi: 10.21682/2311-1267-2020-7-1-62-69

3. Chernyak V, Fowler KJ, Heiken JP, Sirlin CB. Use of gadoxetate disodium in patients with chronic liver disease and its implications for liver imaging reporting and data system (LI-RADS). *Journal of Magnetic Resonance Imaging.* 2019;49(5):1236–1252. doi: 10.1002/jmri.26540

4. Welle CL, Guglielmo FF, Venkatesh SK. MRI of the liver: choosing the right contrast agent. *Abdominal Radiology.* 2020;45(2):384–392. doi: 10.1007/s00261-019-02162-5

5. Furlan A, Borhani AA, Heller MT, Yu RK, Tublin ME. Non-focal liver signal abnormalities on hepatobiliary phase of gadoxetate disodium-enhanced MR imaging: a review and differential diagnosis. *Abdominal Radiology.* 2016;41(7):1399–1410. doi: 10.1007/s00261-016-0685-z

6. Cho SH, Kang UR, Kim JD, Han YS, Choi DL. The value of gadoxetate disodium-enhanced MR imaging for predicting posthepatectomy liver failure after major hepatic resection: A preliminary study. *Eur J Radiol.* 2011;80(2):e195–e200. doi: 10.1016/j.ejrad.2011.08.008

7. Collettini F, Elkilany A, Seta MD, et al. MR imaging of hepatocellular carcinoma: prospective intraindividual head-to-head comparison of the contrast agents gadoxetic acid and gadoteric acid. *Sci Rep.* 2022;12(1):18583. doi: 10.1038/s41598-022-23397-1

8. Galle PR, Forner A, Llovet JM, et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol.* 2018;69(1):182–236. doi: 10.1016/j.jhep.2018.03.019

9. Yang M, Zhang Y, Zhao W, et al. Evaluation of liver function using liver parenchyma, spleen and portal vein signal intensities during the hepatobiliary phase in Gd-EOB-DTPA-enhanced MRI. *BMC Med Imaging.* 2020;20(1):119. doi: 10.1186/s12880-020-00519-7

10. Bastati N, Wibmer A, Tamandl D, et al. Assessment of Orthotopic Liver Transplant Graft Survival on Gadoxetic Acid-Enhanced Magnetic Resonance Imaging Using Qualitative and Quantitative Parameters. *Invest Radiol.* 2016;51(11):728–734. doi: 10.1097/RLI.0000000000000286

11. Mnatsakanyan MK, Rubtsova NA, Kabanov DO, et al. The role of magnetic resonance imaging with gadoxetic acid in the assessment of the functional reserve of the liver. *Russian Electronic Journal of Radiology.* 2022;12(1):43–55. EDN: GXFGZS doi: 10.21569/2222-7415-2022-12-1-43-55

12. Zhang W, Wang X, Miao Y, Hu C, Zhao W. Liver function correlates with liver-to-portal vein contrast ratio during the hepatobiliary phase with Gd-EOB-DTPA-enhanced MR at 3 Tesla. *Abdominal Radiology.* 2018;43(9):2262–2269. doi: 10.1007/s00261-018-1462-y

13. Lee NK, Kim S, Kim GH, et al. Significance of the "Delayed hyperintense portal vein sign" in the hepatobiliary phase MRI obtained with Gd-EOB-DTPA. *Journal of Magnetic Resonance Imaging.* 2012;36(3):678–685. doi: 10.1002/jmri.23700

14. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med.* 1996;22(7):707–710. doi: 10.1007/BF01709751

15. Zaccherini G, Weiss E, Moreau R. Acute-on-chronic liver failure: Definitions, pathophysiology and principles of treatment. *JHEP Reports.* 2021;3(1):100176. doi: 10.1016/j.jhepr.2020.100176

СПИСОК ЛИТЕРАТУРЫ

1. Peng Y., Qi X., Guo X. Child–Pugh Versus MELD Score for the Assessment of Prognosis in Liver Cirrhosis // Medicine. 2016. Vol. 95, N 8. P. e2877. doi: 10.1097/MD.0000000000002877

2. Ликарь Ю.Н., Ахаладзе Д.Г., Румянцев А.Г. Гепатобилиарная сцинтиграфия в предоперационной оценке функции планируемого остатка печени (обзор литературы и собственные примеры) // Российский журнал детской гематологии и онкологии. 2020. Т. 7, № 1. С. 62–69. EDN: VWDZUW doi: 10.21682/2311-1267-2020-7-1-62-69

3. Chernyak V., Fowler K.J., Heiken J.P., Sirlin C.B. Use of gadoxetate disodium in patients with chronic liver disease and its implications for liver imaging reporting and data system (LI-RADS) // Journal of Magnetic Resonance Imaging. 2019. Vol. 49, N 5. P. 1236–1252. doi: 10.1002/jmri.26540

4. Welle C.L., Guglielmo F.F., Venkatesh S.K. MRI of the liver: choosing the right contrast agent // Abdominal Radiology. 2020. Vol. 45, N 2. P. 384–392. doi: 10.1007/s00261-019-02162-5

5. Furlan A., Borhani A.A., Heller M.T., Yu R.K., Tublin M.E. Non-focal liver signal abnormalities on hepatobiliary phase of gadoxetate disodium-enhanced MR imaging: a review and differential diagnosis // Abdominal Radiology. 2016. Vol. 41, N 7. P. 1399–1410. doi: 10.1007/s00261-016-0685-z

6. Cho S.H., Kang U.R., Kim J.D., Han Y.S., Choi D.L. The value of gadoxetate disodium-enhanced MR imaging for predicting

posthepatectomy liver failure after major hepatic resection: A preliminary study // Eur J Radiol. 2011. Vol. 80, N 2. P. e195–e200. doi: 10.1016/j.ejrad.2011.08.008

7. Collettini F., Elkilany A., Seta M.D., et al. MR imaging of hepatocellular carcinoma: prospective intraindividual head-to-head comparison of the contrast agents gadoxetic acid and gadoteric acid // Sci Rep. 2022. Vol. 12, N 1. P. 18583. doi: 10.1038/s41598-022-23397-1

8. Galle P.R., Forner A., Llovet J.M., et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma // J Hepatol. 2018. Vol. 69, N 1. P. 182–236. doi: 10.1016/j.jhep.2018.03.019

9. Yang M., Zhang Y., Zhao W., et al. Evaluation of liver function using liver parenchyma, spleen and portal vein signal intensities during the hepatobiliary phase in Gd-EOB-DTPA-enhanced MRI // BMC Med Imaging. 2020. Vol. 20, N 1. P. 119. doi: 10.1186/s12880-020-00519-7

10. Bastati N., Wibmer A., Tamandl D., et al. Assessment of Orthotopic Liver Transplant Graft Survival on Gadoxetic Acid–Enhanced Magnetic Resonance Imaging Using Qualitative and Quantitative Parameters // Invest Radiol. 2016. Vol. 51, N 11. P. 728–734. doi: 10.1097/RLI.0000000000000286

11. Мнацаканян М.К., Рубцова Н.А., Кабанов Д.О., и др. Роль магнитно-резонансной томографии с гадоксетовой кислотой в оценке функционального резерва печени // Российский электронный журнал лучевой диагностики. 2022. Т. 12, № 1. С. 43–55. EDN: GXFGZS doi: 10.21569/2222-7415-2022-12-1-43-55

12. Zhang W., Wang X., Miao Y., Hu C., Zhao W. Liver function correlates with liver-to-portal vein contrast ratio during the hepatobiliary phase with Gd-EOB-DTPA-enhanced MR at 3 Tesla // Abdominal Radiology. 2018. Vol. 43, N 9. P. 2262–2269. doi: 10.1007/s00261-018-1462-y

13. Lee N.K., Kim S., Kim G.H., et al. Significance of the "Delayed hyperintense portal vein sign" in the hepatobiliary phase MRI obtained with Gd-EOB-DTPA // Journal of Magnetic Resonance Imaging. 2012. Vol. 36, N 3. P. 678–685. doi: 10.1002/jmri.23700

14. Vincent J.L., Moreno R., Takala J., et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure // Intensive Care Med. 1996. Vol. 22, N 7. P. 707–710. doi: 10.1007/BF01709751

15. Zaccherini G., Weiss E., Moreau R. Acute-on-chronic liver failure: Definitions, pathophysiology and principles of treatment // JHEP Reports. 2021. Vol. 3, N 1. P. 100176. doi: 10.1016/j.jhepr.2020.100176

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