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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 строуму 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 (C53). 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 строуму 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 позволяют 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/mm²; and dynamic contrast enhancement with gadolinium

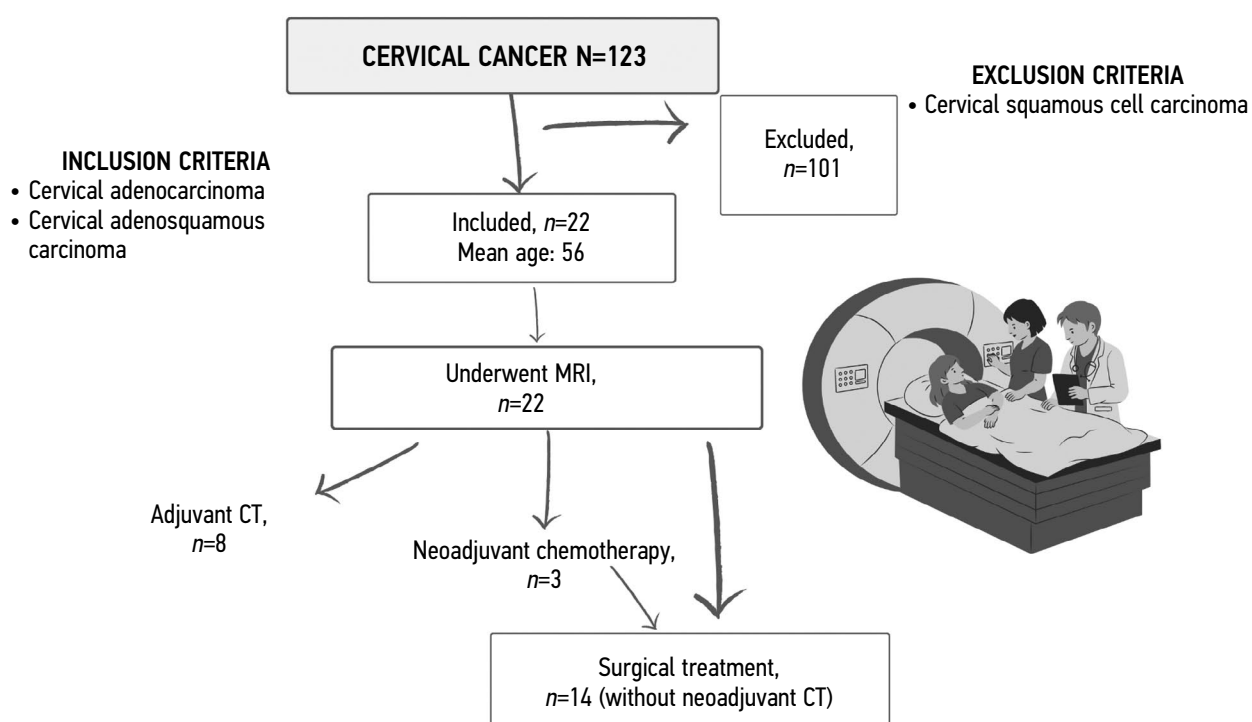


Fig. 1. Study design. MRI, magnetic resonance imaging; CT, computed tomography.

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/mm² 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

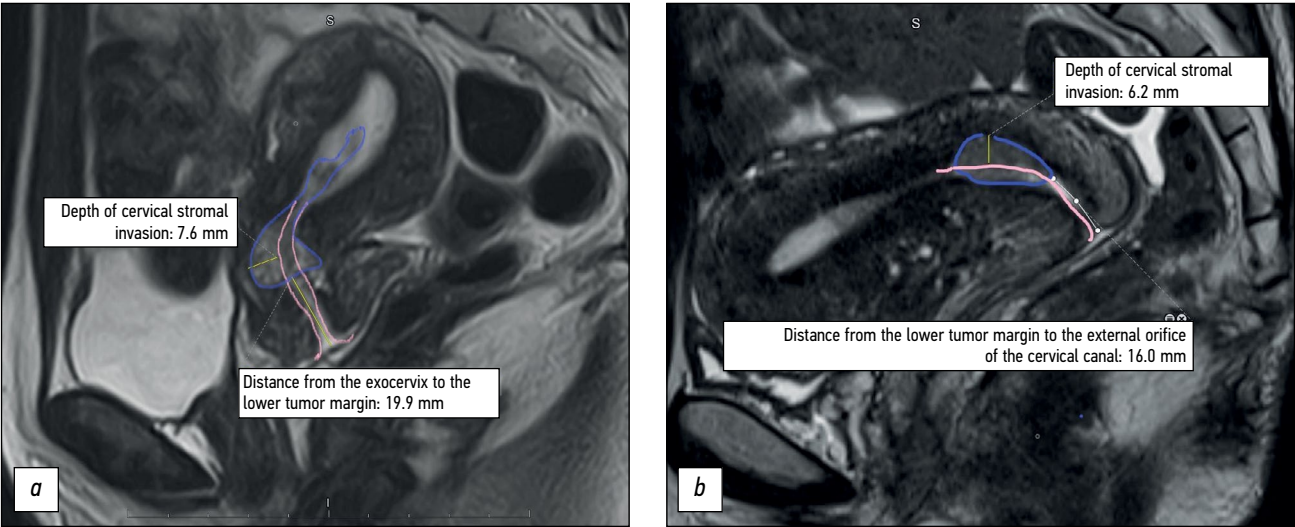


Fig. 2. An example of measuring the depth of cervical adenocarcinoma invasion into the stroma and the distance from the tumor to the exocervix: (a) the tumor is located in the upper third of the cervix, has a depth of invasion of 8 mm and is located at a distance of 20 mm from the exocervix; (b) the 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 cm³ (range: 1–71 cm³). 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 <i>n</i> (%)	No <i>n</i> (%)
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 <i>n</i> (%)	No <i>n</i> (%)
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)

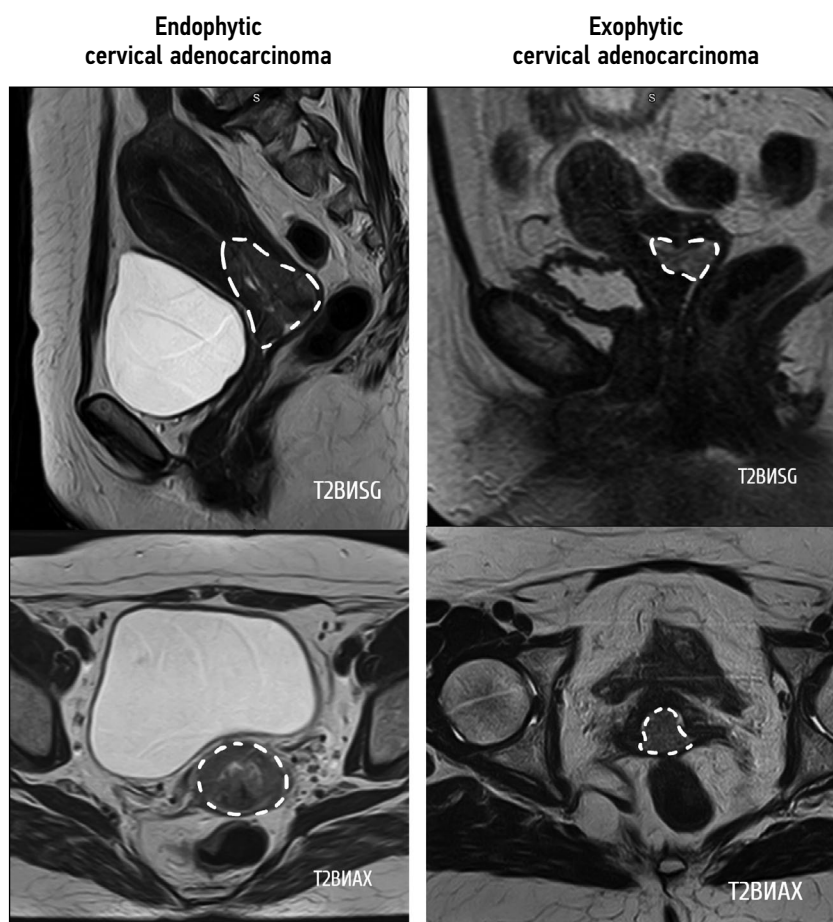


Fig. 3. Cervical adenocarcinoma growth pattern. The upper row of images is T2-weighted images in sagittal plane, the lower one — in axial plane.

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)

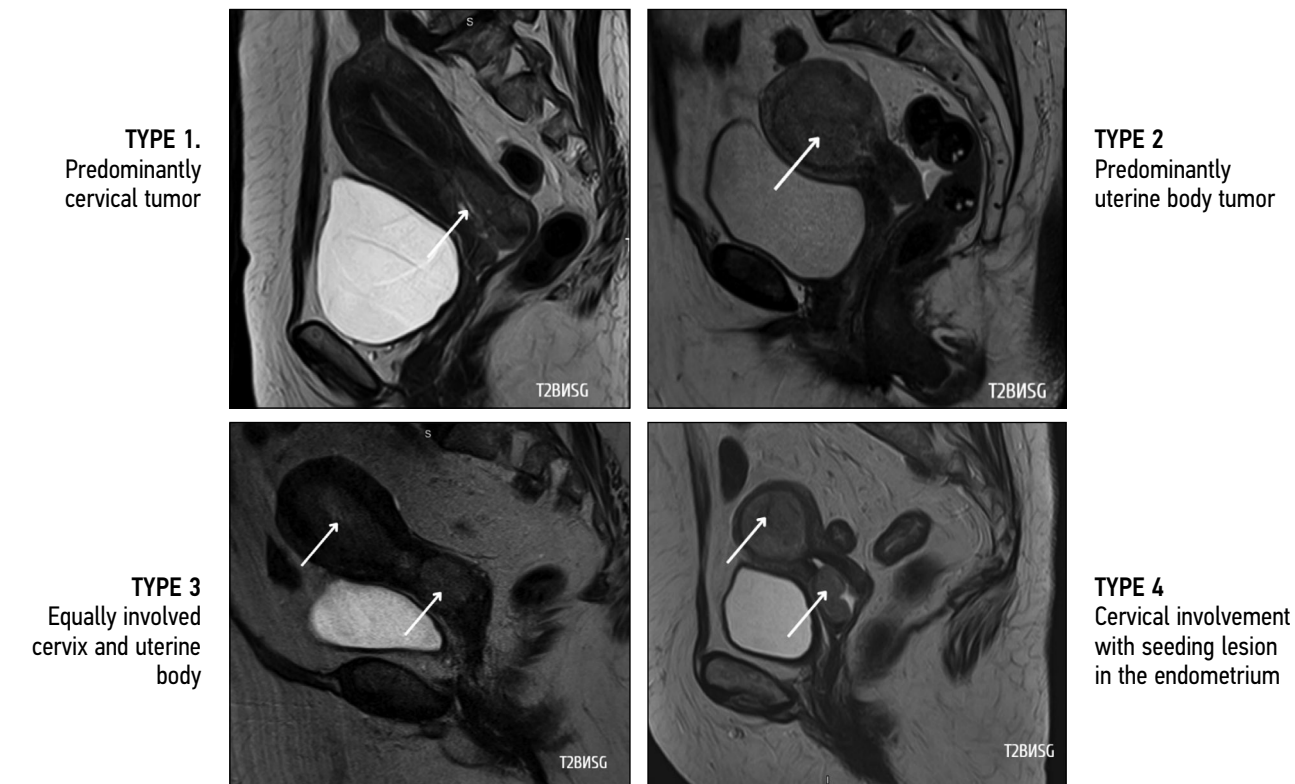


Fig. 4. Type of tumor macrostructure, T2-weighted images in sagittal plane, cervical adenocarcinoma.

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 <i>n</i> (%)	No <i>n</i> (%)
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.

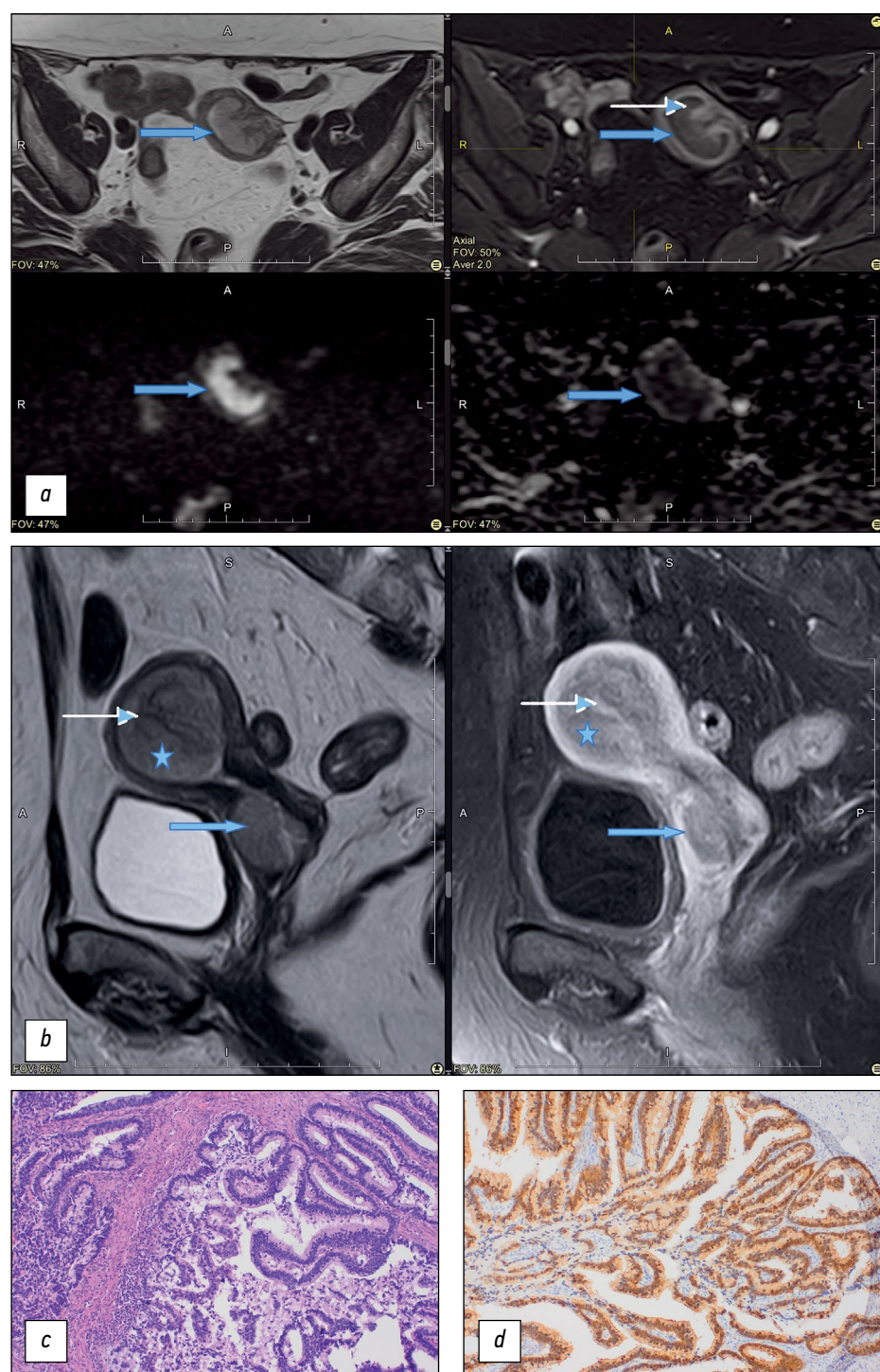


Fig. 5. Magnetic resonance imaging of the pelvis (cervical adenocarcinoma), metastasis in endometrium:

(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, $\times 10$; 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: $0.81 \pm 0.13 \times 10^{-3} \text{ mm}^2/\text{sec}$ vs. $1.41 \pm 0.10 \times 10^{-3} \text{ mm}^2/\text{sec}$). 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 $0.833 \times 10^{-3} \text{ mm}^2/\text{sec}$ (range: from $440 \times 10^{-3} \text{ mm}^2/\text{sec}$; to $1,282 \times 10^{-3} \text{ mm}^2/\text{sec}$), 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 ($0.766 \times 10^{-3} \text{ mm}^2/\text{sec}$) than in CC ($0.969 \times 10^{-3} \text{ mm}^2/\text{sec}$). 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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