Multiparametric ultrasound Diagnosis of Endometrial Cancer in the Preoperative Preparation of Menopausal Patients

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ABSTRACT:

Endometrial cancer is one of the most common tumors of the female reproductive organs. Tumor size, depth of myometrial invasion , and cervical stromal involvement cannot be determined by clinical examination. In this regard, the article discusses the diagnostic value of multiparametric ultrasound diagnostics, which, along with magnetic resonance imaging, currently represents the "gold standard" in confirming endometrial cancer in premenopausal and menopausal women at the stage of preoperative preparation. Based on the study, it was found that the most informative is transvaginal access using energy and color mapping modes, which makes it possible to judge the presence or absence of invasion of the endometrial malignancy into the myometrium in stages I B and I C. The use of spectral Doppler ultrasound provides information about the intensity of the neoangiogenesis process.

Key words: endometrial cancer, ultrasound diagnosis, myometrial invasion, endometrial doppler, neoangiogenesis

Introduction.

Malignant formation of the endometrium is one of the most common tumors of the female reproductive organs. According to statistics, every year 200,000 women develop endometrial cancer, the mortality rate is 50,000 women per year [1]. The incidence of uterine cancer in developed countries is 12.9/100,000 (mortality 1.6/100,000), while in undeveloped countries it is 5.7/100,000 (mortality 0.7/100,000) [2].

The incidence of endometrial carcinoma increases with age (5–10 years before menopause) with a peak incidence between 65 and 70 years [3].

The majority of patients diagnosed with EC are postmenopausal women; the average age at diagnosis is 68 years. However, up to 15% of cases may occur in premenopausal women [4].

Endometrial carcinoma usually presents with abnormal uterine bleeding in postmenopausal women, and the diagnosis is confirmed by evaluation of an endometrial curettage biopsy or hysterectomy specimen [5].

Traditionally, endometrial cancer is classified into two pathogenetic variants based on clinical and hormonal features with different pathophysiological and histological characteristics.

The prognosis depends on the patient's age, histological type of malignancy, tumor size, metastasis to regional and retroperitoneal lymph nodes , depth of invasion into the myometrium, and involvement of the cervix [6].

Tumor size, depth of myometrial invasion, and cervical stromal involvement cannot be determined by clinical examination. Thus, multiparametric ultrasound and magnetic resonance imaging (MRI) are increasingly used to improve preoperative assessment, i.e. to identify women requiring more extensive surgical intervention, including pelvic and para-aortic lymph node dissection. According to the literature, the systematic use of echography contributes to earlier diagnosis of endometrial cancer, increasing the incidence of stage I cancer by 50% and reducing the incidence of stage III - IV cancer by 1.5 times [7,8].

The purpose of the study is to determine the sequence of a multiparametric study of endometrial cancer depending on the tumor size, degree of invasion, clinical picture, followed by histological verification at the stage of preoperative preparation.

Materials and methods.

An examination of women undergoing treatment in the gynecological department of the regional oncology clinic was carried out. The age of the patients ranged from 48 to 77 years. We included in the study group 68 women with complaints of postmenopausal bleeding and a history of dysfunctional vaginal bleeding during hormone replacement therapy (HRT). The number of patients at the age of menopause is 57 (83.8%), at the age of premenopause - 11 (16.1%). The average postmenopausal period was 11 years. Menopause was defined as amenorrhea lasting at least 12 months in women over 45 years of age. All women were examined according to a general scheme: collection of anamnestic data, gynecological examination, assessment of risk factors, comprehensive ultrasound examination of the pelvic organs, internal organs and retroperitoneal lymph nodes. The most common comorbidities in patients were: hypertension (58.8%), obesity (70.5%), diabetes mellitus (29.4%), thromboembolic diseases (22%) and calculous cholecystitis (14%). Malignant diseases of other locations: ovarian tumors were registered in 8 (11.7%) patients, breast tumors in 4 (5.8%) women. Malignant diseases in close relatives were present in 3 (4.4%) patients (Table 1).

Table 1. Comorbidities in patients with endometrial cancer

Characteristic	Menopause		Total number of patients (n=68)
	Yes (n= 5 7)	No (n=11)	
Arterial hypertension			
Eat	38 (66.6%)	2 (18.2%)	40 (58.8%)
No	19 (33.4%)	9 (81.8%)	28 (41.2%)
Obesity			
Eat	41(71.9%)	7 (63.6%)	48 (70.5%)
No	16 (28.1%)	4 (36.4%)	20 (29.5%)
Diabetes			
Eat	17 (29.8%)	3 (27.3%)	20 (29.4%)
No	40 (70.2%)	8 (72.7%)	48 (70.6%)
Thromboembolic diseases			
Eat	13 (22.8%)	2 (18.2%)	15 (22.0%)
No	44 (77.2%)	9 (81.8%)	53 (78.0%)
Ovarian tumors			
Eat	12 (21%)	4 (36.4%)	16 (23.5%)
No	45 (79%)	7 (63.6%)	52 (76.5%)

All patients underwent ultrasound examination after histological confirmation of the diagnosis. Echography was performed using the MINDRAY device RESONA I 9 using a transvaginal sensor with a frequency of 5-7 MHz . Due to the fact that a large number of women diagnosed with uterine cancer are obese, transabdominal examination of the pelvic organs is not very informative . In this group of patients, it is most advisable to widely use transvaginal echography . In our study, we used mode B, color and energy mapping modes, compression elastography and shear wave elastography . The uterus was scanned in the sagittal plane from the fundus to the internal os and in the transverse plane from the cervix to the fundus. We noted the presence of adenomyosis in 37 (54.4%) and fibroids in 16 (23.5%) women. We measured the anterior -posterior diameter of the uterus and the thickness of the endometrium in the sagittal plane (Fig. 1), and the width of the uterus in the transverse plane. Endometrial tumor size was measured in three orthogonal planes: anteroposterior (tumor thickness), craniocaudal (tumor length), and laterolateral diameter (tumor width).

Results and discussion

In the study group of patients, we did not notice a significant increase in the size of the uterus. In 59 (86.7%) women, the uterus was of normal size or with signs of involution. In most cases, the uterus had smooth, clear contours. In 12 (17.6%) cases, the contour of the uterus was tuberous, which was explained by the subserous location of myomatous nodular formations. The uterine cavity was dilated with the presence of anechoic contents in 8 cases. But this echographic sign is not pathognomic for endometrial cancer (Fig. 2).

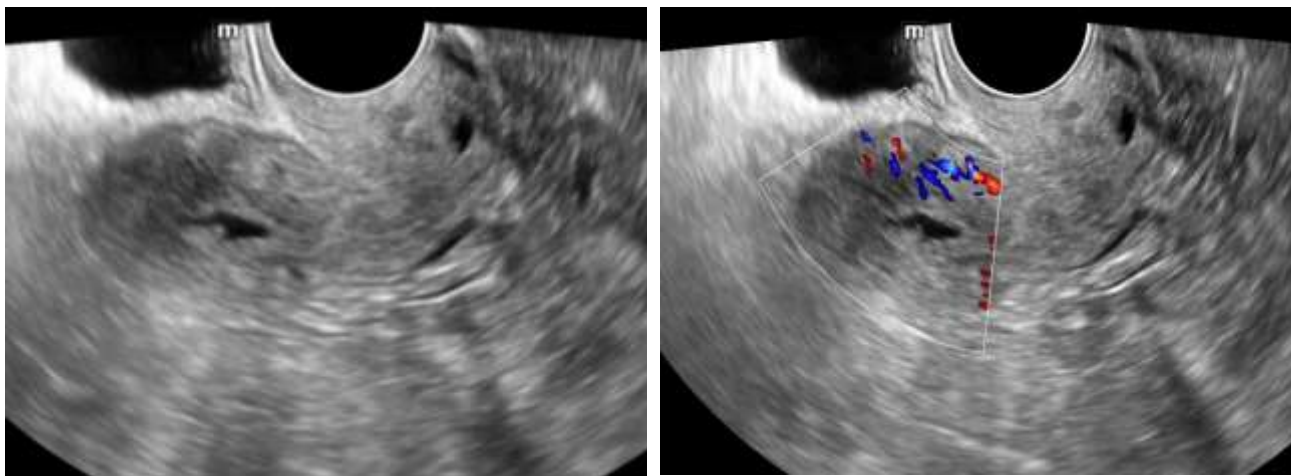**Fig. 1.** Transvaginal examination. Mode B. Histologists: Endometrial cancer

Fig. 2. Patient 70 years old. Transvaginal examination. B-mode. Against the background of the expansion of the cavity, an uneven internal contour of the endometrium is visualized. Histology: endometrial cancer.

Endometrial thickness within 7-10 mm was observed in 34 (50.0%); 11-16 mm – in 14 (20.5%); 17-23 mm – in 10 (14.7%); 24-30 mm – in 3 (4.4%) women. Endometrial thickness was more than 40 mm in 7 (10.3%) patients. The endometrium in most patients had increased echogenicity (Fig. 3). A diffusely heterogeneous echostructure with alternating areas of increased and decreased echogenicity was detected in 53 (77.9%) patients. Noteworthy is the change in the nature of the echo picture of the endometrium depending on its size. According to our observations, when the thickness of the endometrium is up to 15-18 mm, the echostructure is visualized as hyperechoic , while when the thickness increases to 25-30 mm, it becomes more heterogeneous due to the visualization of cavity inclusions of regular and irregular shape. This gives the endometrium a heteroechoic appearance.
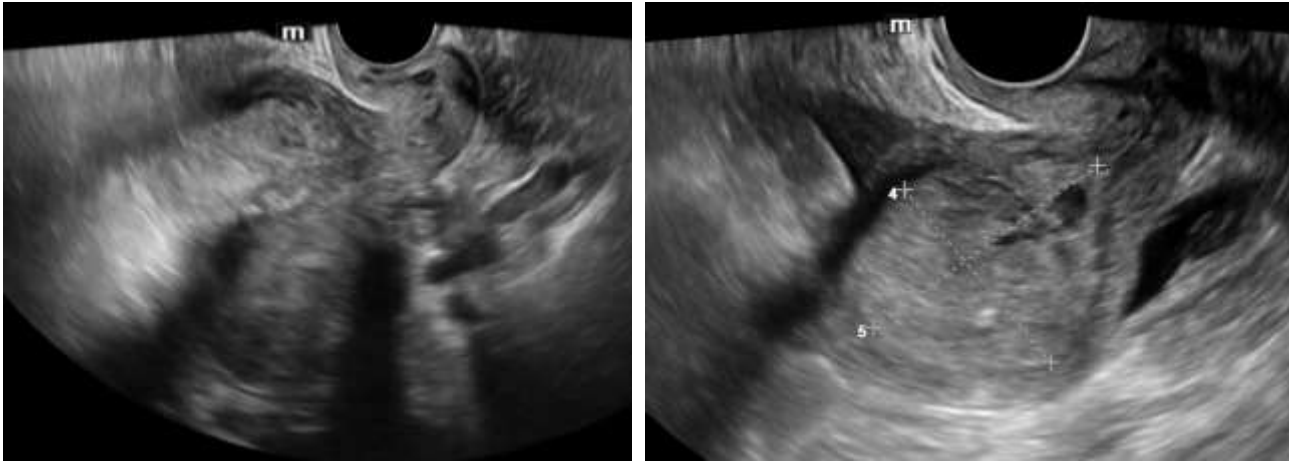
Fig. 3. Transvaginal examination. Mode B. Endometrial cancer

When the thickness of the endometrium was more than 30 mm, the endometrium had a "spotty" appearance due to the presence of zones of reduced and increased echogenicity

Thus, we observed that ultrasound signs of endometrial cancer, such as echostructure and echogenicity , vary depending on the size of the tumor and the stage of the disease. The larger the tumor size and the greater the degree of invasion into the myometrium , the more heterogeneous the structure.

In 10 (14.7%) cases, a false negative result was obtained due to the presence of microinvasive cancer. In this group of patients, tumor structures in the projection of the uterine cavity were not visualized. During transabdominal examination, we noted diffuse uniform or uneven thickening of the M-echo along the entire length of the uterine cavity. However, it was not possible to speak more precisely about the location, shape of the tumor and the degree of invasion.

This may be due to the anatomical features of the uterus, the growth pattern of endometrial cancer and the limited capabilities of the transabdominal method. In our opinion, a more promising method for determining the degree of tumor invasion into the myometrium is a comprehensive transvaginal ultrasound examination in the modes of colorectal dosing and elastography . This method is simple, accessible, highly informative, allowing for ultrasound differential diagnosis of various types of uterine cancer pathology.

An important sign of invasion of the tumor process into the myometrium is the definition of the contours of the endometrium and the presence of a hypoechoic rim that defines the boundary between the tumor and the myometrium . On histological examination, this area appeared to be infiltrative changes around the glandular elements of well-differentiated cancer. The endometrium has a heterogeneous structure. There is thinning of the myometrium and infiltrative changes in the form of a hypoechoic rim.

The next stage of our research was to conduct qualitative and quantitative Doppler sonography. The color mapping mode allowed us to assess the presence of blood flow, location (peripheral or central) and the number of color loci. Spectral Doppler measurements were carried out to measure three main parameters of blood flow: the velocity of arterial (Vmax) and venous flow (VVmax) and the nature of the resistance index (RI) in the uterine arteries and in the tumor area (Fig. 4).
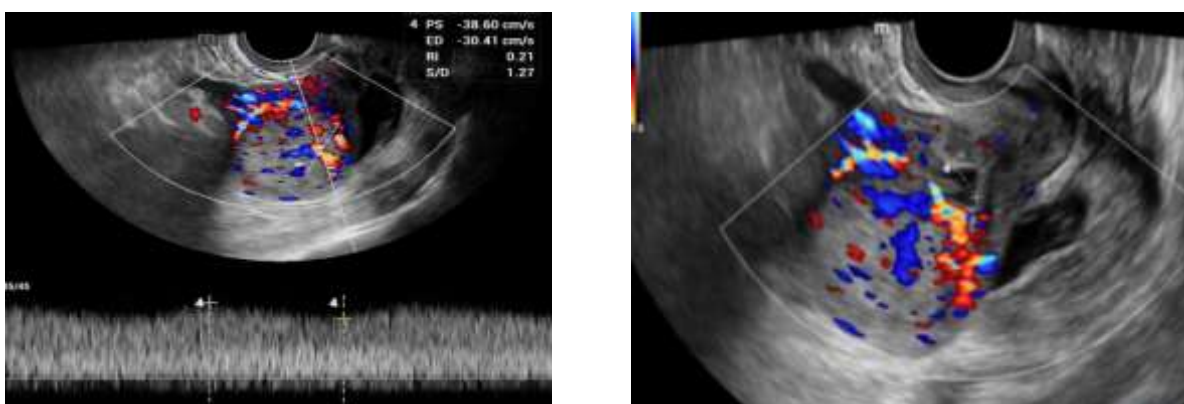

Fig. 4. Transvaginal examination. High-velocity, low-resistance intratumoral blood flow.

In power Doppler mode , it is possible to visualize blood flow in the smallest vessels down to the microcirculatory system. Measurements were carried out repeatedly at the largest possible number of available color loci.

Color and energy mapping data were compared with the results of histological examination of the endometrium obtained during diagnostic curettage or after hysterectomy.

In assessing the intensity of intratumoral hemodynamics, we chose the blood flow scale. In four freeze frames we recorded the number of color signals from the vessels of the neoplasm (Fig. 5):

1. Blood flow was taken as "Zero" in the absence of color loci in the formation;

2. The "scanty" intratumoral blood flow was represented by single color signals from the vessels - no more than 5 (in one plane);

3. "Moderately expressed" corresponded to 5-10 color signals;

4. "Increased blood flow" , with more than 10 color signals from the vessels.
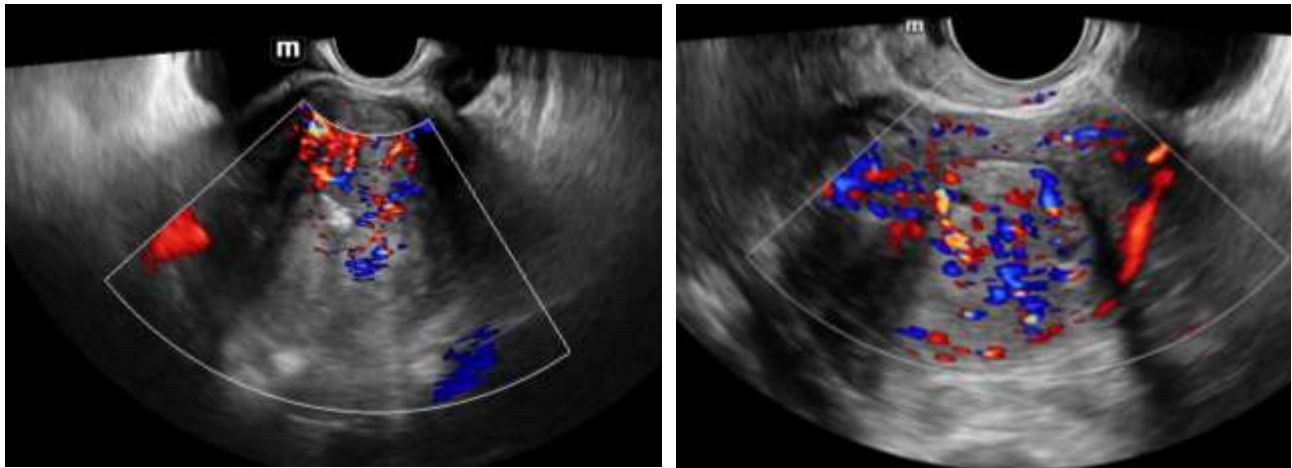

Fig. 5. Doppler assessment of endometrial cancer. Severe atypical vascularization

Color Dopplerography revealed a scattered type of blood supply to the uterus along the vascular bundle, as well as neovascularization of the endometrium with a "mosaic" form of mapping and a low level of peripheral resistance of newly formed vessels. For the uterine arteries, a frequency filter of 100 and 50 Hz was used, for the arcuate and intratumoral vessels, with a Doppler beam control volume size of 4 and 2 mm, respectively.

In our group of patients, intratumoral blood flow was not recorded in 21 (30.8%) patients with endometrial thickness less than 8 mm. The reason for this could be the removal of a small tumor as a result of preliminary diagnostic curettage of the uterine cavity and the occurrence of a malignant process against the background of endometrial atrophy in well-differentiated adenocarcinoma I a stage.

The remaining 47 women had low-resistance high-velocity blood flow, both inside the tumor and along its periphery. The study of blood circulation characteristics depending on the degree of histological differentiation of uterine cancer revealed a number of patterns. Thus, the study showed that as the degree of differentiation decreases, there is a change in blood circulation indicators along with an increase in intratumoral blood flow, and indicators of vascular resistance decrease (Table 2).

Table 2. Hemodynamic parameters in endometrial cancer

Hemodynamic parameters	Well-differentiated adenocarcinoma (n = 3 8)	Moderately differentiated adenocarcinoma (n = 14)	Poorly differentiated adenocarcinoma (n= 1 6)
Vmax (cm/s)	15.8 ± 0.5	22.5 ± 0.6	38.9 ± 0.8
VV max (cm/s)	10.6 ± 0.2	12.9 ± 0.8	14.1 ± 0.5
R.I.	0.44 ± 0.01	0.37 ± 0.02	0.31 ± 0.04

Conclusions.

Analysis of the histopathological report showed that in 28 (41.2%) patients there was no invasion into the myometrium ; Invasion of the uterine wall was verified to be less than half its thickness in 19 (27.9%) and more than half the thickness of the uterine wall in 15 (22.1%) women. Cervical invasion was detected in 6 (8.8%) patients. Metastatic lesions (spread to the appendages, regional and retroperitoneal lymph nodes) were confirmed in 35.3% of patients. Liver metastases were diagnosed in 3 (4.4%). These results were confirmed by magnetic resonance imaging.

We noted several sonographic features that may indicate malignant endometrial morphology and tumor invasion into the myometrium:

1) Heterogeneity of the endometrial structure;

2) Higher echogenicity of the endometrium compared to the myometrium ;

3) A zone of reduced echogenicity around the tumor, which determines the formation of the endometrium;

4) An uneven, "eaten" contour, penetrating into the myometrium to varying depths;

5) High speed low resistance intratumoral blood flow, as well as increased blood flow in the uterine arteries and its branches.

Malignant transformation of the endometrium is characterized by the presence of neovascularization of the tumor: intense central and peripheral tumor blood flow, chaotic arrangement of vessels with a low level of peripheral vascular resistance. Ultrasound examination using color Doppler mapping, power Doppler , pulsed Doppler does not allow assessing the tumor histotype before surgery. But the level of vascularization of the process revealed using color Doppler sonography makes it possible to predict the rate of growth of the detected neoplasm.

Thus, a comprehensive ultrasound examination using color and power Doppler, pulsed Doppler is a highly informative method of non-invasive diagnostics.

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