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FEATURES OF DOPPLER INDICATORS OF UTERINE BLOOD FLOW IN PATIENTS WITH ADENOMYOSIS

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The purpose of study was to establish the incidence, clinical and anamnestic features of patients with adenomyosis. A comprehensive clinical, laboratory and instrumental prospective examination was carried out on 224 patients aged 30 to 50 years (average age – 42.0±1.8 years) with adenomyosis. These patients constituted the main study group. Patients of the main group were divided into 2 subgroups depending on the form of adenomyosis (Group I – diffuse form – 106 women, Group II – nodular form – 118 women). The control group consisted of 84 relatively healthy women of reproductive age, with a regular ovulatory menstrual cycle and no history of gynecological diseases. The largest number of adenomyosis are registered in patients aged 36–40 years – 92 women, 41.1±3.3 %. The most common pathologies in patients with various forms of the adenomyosis were the diseases of the cervix (114 women, 50.89±3.3 %), uterine fibroids (113 women, 50.45±3.4 %) and inflammatory diseases of the pelvic organs (113 women, 50.45±3.4 %). Resistance index values in the follicular phase and luteal phase have statistically significant differences between groups of patients with adenomyosis ($p<0.05$).

Key words: adenomyosis, diagnosis, resistance index, blood flow, uterus, differential diagnosis

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ОСОБЛИВОСТІ ДОППЛЕРІВСЬКИХ ПОКАЗНИКІВ МАТОЧНОГО КРОВОТОКУ У ХВОРИХ НА АДЕНОМІОЗ

Метою дослідження було встановити захворюваність, клініко-анамнестичні особливості хворих на аденоміоз. Проведено комплексне клініко-лабораторне та інструментальне проспективне обстеження 224 пацієнток віком від 30 до 50 років (середній вік – 42,0±1,8 роки) з аденоміозом. Ці пацієнтки становили основну групу дослідження. Хворі основної групи були поділені на 2 підгрупи залежно від форми аденоміозу (I група – дифузна форма, 106 жінок, II група – вузлова форма, 118 жінок). Групу контролю склали 84 практично здорові жінки репродуктивного віку з регулярним овуляторним менструальним циклом і без гінекологічних захворювань в анамнезі. Найбільше випадків аденоміозу зареєстровано у хворих віком 36–40 років – 92 жінки, 41,1±3,3 %. Найбільш поширеною патологією у хворих з різними формами аденоміозу були захворювання шийки матки (114 жінок, 50,89±3,3 %), міома матки (113 жінок, 50,45±3,4 %) та запальні захворювання органів малого тазу (113 жінок, 50,45±3,4 %). Значення індексу резистентності у фолікулярну та лютеїнову фази мають статистично значущі відмінності між групами хворих на аденоміоз ($p<0,05$).

Ключові слова: аденоміоз, діагностика, індекс резистентності, кровообіг, матка, диференціальний діагноз.

Adenomyosis is a common gynecological disease manifested by infiltration of the myometrium by glands and endometrial stroma. Depending on the scale of the lesion, adenomyosis is divided into diffuse and focal forms. The most common form is diffuse adenomyosis. Focal adenomyosis, especially on cystic uterine glands, is much less common [2, 9].

The incidence of adenomyosis usually occurs in the population of women aged 30 to 50 years, given that endometriosis and adenomyosis are diseases that predominantly affect women of reproductive age. The manifestations of adenomyosis are interrelated with the menstrual cycle, a period when endometriotic tissue located outside the endometrium bleeds, causing swelling and inflammation [10]. Indeed, despite the standard approach which considers that after menopause there is a tendency for endometrioid tissue to atrophy and reabsorb, there are studies showing that endometrial deposits are still potentially active in older patients and can be reactivated in the presence of certain hormones [2, 8].

In recent years, epidemiological studies have been conducted to determine the prevalence of endometriosis and adenomyosis. The incidence of adenomyosis varies from 7.4 to 53 % of women of reproductive age [3, 4]. In addition to its high prevalence, the relevance of studying the problem of adenomyosis is due to the severity and versatility of the clinical picture of the disease [14].

There are many treatment modalities for this disease and choosing the appropriate treatment metod is necessary after comprehensive consideration of the patient's age, course of the disease, reproductive requirements and clinical symptoms. Therefore, accurate diagnosis of the disease is of great importance for doctors to select scientific treatment methods [1, 15].

Despite certain successes in the study of certain aspects of the pathogenesis, diagnosis and treatment of adenomyosis of various localizations, this problem has not lost its relevance [5, 12]. The data on the effect of adenomyosis on reproductive function and perinatal outcomes data are ambiguous [6, 7, 13]. The main instrumental method for diagnosing adenomyosis is ultrasound examination with determination of resistance indices.

The purpose of study was to establish the incidence, clinical and anamnestic features of patients with adenomyosis.

Material and methods. During the study, a comprehensive clinical, laboratory and instrumental prospective examination was carried out on 224 patients aged 30 to 50 years (average age – 42.0±1.8 years) with adenomyosis. These patients constituted the main study group. Patients of the main group were divided into 2 subgroups depending on the form of adenomyosis (Group I – diffuse form – 106 women, Group II – nodular form – 118 women). The control group consisted of 84 relatively healthy women of reproductive age, with a regular ovulatory menstrual cycle and no history of gynecological diseases. Cohort studies are prospective. Inclusion criteria for the study: patient diagnosed with adenomyosis; patient age from 30 to 50 years; obtaining written consent from the patient to participate in examinations.

Exclusion criteria from the study: detection of a malignant pathological process in the organs of the reproductive system or other localization; the presence of hormone-synthesizing ovarian tumors; pregnancy and lactation; patients under 30 years of age and over 50 years of age; refusal to participate in the study.

The clinical characteristics of the examined women were based on the study of complaints, obstetric-gynecological and somatic anamnesis. All patients were examined for general and gynecological anamnesis and features of menstrual function. Particular attention was paid to previous inflammatory diseases of the genital organs, a history of spontaneous abortions, premature pregnancies, antenatal fetal death, the course of pregnancy, as well as their results. The examination of patients included a routine general examination, gynecological examination, ultrasound examination (ultrasound) with determination of the location and size of nodes, determination of the presence and degree of adenomyosis. At the same time, a Doppler study of blood flow in the uterine arteries and vessels around and inside the myomatous node was carried out to determine the resistance index. All patients first underwent 2D (two-dimensional) transvaginal ultrasound examination. Then, according to indications, 3D transvaginal echography (3D TVE) of the pelvic organs was performed. Ultrasound examination of the pelvic organs was carried out with transabdominal and transvaginal sensors on a digital stationary ultrasound diagnostic device Accuvix XQ-EXP, an expert class company from Madison Co. Ltd (Korea). Statistical processing of the obtained data was carried out by analyzing the results using Microsoft Excel spreadsheet programs, generated in accordance with the objectives of the research.

Results of the study and their discussion. The conducted studies found that the largest group consists of patients aged 36–40 years – in the main group – 92 women, 41.1±3.3 %, and in the control group – 37 women, 44.0±5.4 %. The percentages of patients aged 30–35 years old were 26.4±4.3 % in Group I and 27.1±4.1 % in Group II. The distribution of other age subgroups was as following: 36–40 years old – 42.5±4.8 % and 39.8±4.5 %; 41–50 years old – 31.1±4.5 % and 33.1±4.3 % (in Group I and in Group II, respectively).

When dividing patients into the main group in the age group of 30–35 years, 28 women of the Group I (6.4±4.3 %) and 32 women of the Group II (27.1±4.1 %) were identified. In the main groups, it was found that in Group I there were 60 women of reproductive age, which is 26.8±2.9 %, in Group II – 92 women (41.1±3.3 %). A total of 152 patients (67.9±3.1 %) of the main group were of reproductive age, and 72 patients (32.1±3.1 %) were of perimenopausal age.

In patients with adenomyosis, menstrual irregularities such as hyperpolymenorrhea occur in almost every third patient, and algodysmenorrhea – in almost every second patient (Table 1).

Table 1

Age of onset of menarche, duration and type of menstrual irregularities in the examined patients

Indices			Group I (n=106)		Group II (n=118)		Control group (n=84)	
The mean age of the onset of menarche (age)			10.628±2.074		11.401±1.14		13.124±1.022	
The mean duration of the menstrual cycle (days)			24.453±1.530		25.348±1.489		29.722±1.632	
Types of menstrual disorders								
	Abs.	%	Abs.	%	Abs.	%	$\chi 2$ 1 – 2	p
Hyperpolymenorrhea	37	34.9±4.6	28	23.7±3.9	9	10.7±3.4	3.39	0.0657
Algodismenorrhea	52	49.1±4.8	33	27.9±4.1	6	7.1±2.8	10.55	0.0012

From the data presented it is clear that hyperpolymenorrhea occurred in 34.9±4.6 % of patients in the Group I (37 women), in the Group II (28 women) – in 23.7±3.9 %, and in the control group (9 women) was detected in 10.7±3.4 %. Algodysmenorrhea was observed in groups accordingly: 49.1±4.8 % (52 women), 27.9±4.1 % (33 women) and 7.1±2.8 % (6 women). The duration of the disease is of great importance when conducting research on a particular nosology. From the moment of diagnosis, adenomyosis was observed from 3 to 8 years, the average period of diagnosis was 6.2±1.4 years. It should

be noted that, as a rule, the duration of diagnosis increases in parallel with the prevalence of adenomyosis. It was also found that the lack of criteria for early diagnosis of adenomyosis also leads to delays and difficulties in diagnosis. Analysis of the reproductive history revealed the following features: the absence of frozen pregnancies in 99 patients of Group I (93.39±2.3 %), in 106 patients of Group II (89.83±2.9 %), 1 frozen pregnancy was noted in 7 patients of Group I (6.61±2.4 %), in 12 patients there were Group II (10.17±2.8 %). When studying the frequency of births in the study groups, it was found that there were no births in 10 patients of Group I (9.4±2.9 %), in 7 patients of Group II (5.93 ± 2.1 %), only one birth was observed in 33 patients of Group I (31.13±4.5 %), 28 patients of Group II (23.72±3.9 %), three or more births in 28 patients of Group I (26.41±4.3 %), in 30 patients of Group II (25.43±3.9 %) (Table 2).

Table 2

Reproductive history in the studied groups of women

Indices	Group II (n=106)		Group II (n=118)		Total (n=224)		Control group (n=84)	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Birth rate in study groups								
There was no birth	10	9.4±2.9	7	5,93±2.1	17	7.59±1.8	0	0
1 birth	33	31.13±4.5	28	23.72±3.9	61	27.23±3.0	17	20.24±4.4
2 births	35	33.06±4.6	53	44.92±4.6	88	39.29±3.3	43	51.19±5.4
3 births and more	28	26.41±4.3	30	25.43±3.9	58	25.89±2.9	24	28.57±4.8
Frequency of artificial abortions in study groups								
No abortions	48	42.28±4.8	52	44.07±4.6	100	44.64±3.3	21	25.0±4.7
One abortion	25	23.58±4.1	29	24.58±3.9	54	21.11±2.7	24	28.57±4.8
Two abortions	33	34.14±4.6	37	31.35±4.3	70	34.25±3.2	39	46.43±5.4
Frequency of spontaneous abortions								
No abortions	94	88.67±3.0	107	90.67±2.6	201	89.73±2.0	84	100
One abortion	8	7.54±2.6	6	5.08±2.2	14	6.25±1.7	-	-
Two abortions	4	3.79±1.9	5	4.25±2.0	9	4.02±1.3	-	-
Frequency of frozen pregnancies								
There were no frozen pregnancies	99	93.39±2.3	106	89.83±2.9	205	91.52±1.8	84	100
One frozen pregnancy	7	6.61±2.4	12	10.17±2.8	19	8.48±1.8	-	-
Prevalence of infertility in study groups								
Absent	96	90.57±2.8	111	94.07±2.2	207	92.41±1.7	84	100
Primary	6	5.66±2.3	3	2.55±1.6	9	4.02±1.3	-	-
Secondary	4	3.77±1.9	4	3.38±1.8	8	3.57±1.3	-	-

When studying the analysis of gynecological morbidity and extragenital pathology in the examined patients, it was found that a history of gynecological diseases was observed in all examined women with various forms of adenomyosis. The distribution of gynecological morbidity by nosology was as following: pathology of the cervix 54.71±4.8 % and 47.45±4.6 % in Group I and Group II, respectively; uterine fibroids – 56.60±4.8 % and 44.93±4.6 %, respectively; inflammatory diseases of the pelvic organs – 44.33±4.8 % and 55.13±4.6 %, respectively; polycystic ovary syndrome – 36.79±4.6 % and 28.81±4.2 %, respectively; external genital endometriosis – 34.9±4.6 % and 27.9±4.1 %, respectively; bacterial vaginosis – 31.94±4.5 % and 27.1±4.1 %, respectively; vaginitis – 26.4±4.3 % and 23.7±3.9 %, respectively; tumor-like formations (cysts) ovaries – 16.24±3.6 % and 10.16±2.8 %, respectively; prolapse of the walls of the vagina and uterus – 8.49±2.7 % and 6.78±3.3 %, respectively; chronic inflammatory diseases of the uterine appendages – 13.20±3.3 % and 5.93±2.1 %, respectively; genitourinary infections – 22.64±4.1 % and 17.79±3.5 %, respectively.

These data show that patients with various forms of the disease had the most common pathology of the cervix (114 women, 50.89±3.3 %), uterine fibroids (113 women, 50.45±3.4 %) and inflammatory diseases of the pelvic organs (113 women, 50.45±3.4 %). These diseases occurred in almost every second patient. Gynecological morbidity was detected in all patients with adenomyosis (100 %) and in 19 patients of the comparison group (22.61±4.6 %). In the history of surgical interventions, every tenth patient had a cystectomy, less often a tubectomy. In women with diffuse adenomyosis, cystectomy was performed in 13.20±3.3 % of cases (14 women), and tubectomy was performed in 8.49±2.7 % of patients (9 women). In women with nodular adenomyosis, cystectomy was performed in 10.16±2.8 % of cases (12 women), and tubectomy – in 6.78±2.3 % of patients (8 women).

Of the extragenital pathologies, chronic diseases of the gastrointestinal tract (gastritis, cholecystitis) were most often recorded – in 40.62±3.3 % of cases (91 women), diseases of the nervous system – in 35.71±3.2 % of cases (88 women), chronic diseases of the nasopharynx – 35.29±3.2 % of cases (79 women). Less common were endocrine diseases (24.55±2.8 %, 55 women) and diseases of the cardiovascular system (22.32±2.8 %, 50 women). Diseases of the skin (20.98±2.7 %, 47 women) and genitourinary system (14.73±2.4 %, 33 women) were also encountered. Mastopathy was detected in 25 patients with various forms of adenomyosis, which amounted to 11.16±2.2 %; there was no mastopathy among patients in the control group. There were no statistically significant differences among groups with various forms of adenomyosis in extragenital pathology.

Thus, a comparative analysis did not reveal a clear relationship between gynecological and extragenital diseases observed in patients with various forms of adenomyosis. All women examined had concomitant somatic pathology. However, it is important to note that all women had a combination of several concomitant diseases. When studying body mass index, a strong connection was noted between the presence of obesity and the development of various forms of adenomyosis. When analyzing body mass index indicators in the examined women, attention is drawn to the increase in the incidence of various forms of adenomyosis in the presence of overweight and obesity in patients. Body mass index is a leading risk factor for endometrial hyperplasia or adenomyosis in perimenopausal women. It is important to note that the triad - endocrine morbidity, cardiovascular diseases, obesity is a risk factor for the occurrence of hyperplastic and malignant processes of the endometrium. Our results showed that the high frequency of endocrine and metabolic disorders indicates the pathogenetic basis of the occurrence of endometrial hyperplasia and adenomyosis in women of reproductive age and perimenopause.

During ultrasound, attention was paid to the presence of adenomyotic foci and myomatous nodes in the uterus, determining their number, size, type and topography. Color Doppler scanning determined the nature of the vessel feeding the node, the resistance index (RI) and the speed of blood flow around and inside the adenomyotic nodes, as well as in the uterine arteries in various forms of adenomyosis. In all patients with adenomyosis of Groups I and II and in patients of the control group, parameters characterizing blood flow were assessed on days 3 – 5 and 20 – 23 of the menstrual cycle, and in patients of the control group – on days 5 – 7 of the menstrual cycle. As a result of the research, it was possible to differentiate different types of adenomyosis, establishing the type of nodes. Blood flow parameters determined by color Doppler scanning in the examined patients were as following: SDR (systole-diastolic ratio systole-diastolic ratio) – 4.76±0.02 in Group I and 3.52±0.01 in Group II ($p<0.05$); PI (pulsation index) – 1.91±0.02 in Group I and 1.42±0.01 in Group II ($p<0.05$).

Resistance index (RI) values (in follicular phase, days 3 – 5 of the cycle) at uterine artery were 0.84±0.02 and 0.43±0.01 in Group I and Group II, respectively ($p<0.05$); at arcuate arteries – 0.81±0.02 and 0.72±0.02, respectively ($p<0.05$); at radial arteries – 0.64±0.01 and 0.68±0.02, respectively ($p<0.05$).

The same indicator in luteal phase (days 12 – 14 of the cycle) has the statistical significant differences between groups. At uterine artery resistance index values was 0.46±0.02 and 0.37±0.01 in Group I and Group II, respectively ($p<0.05$); at arcuate arteries – 0.53±0.02 and 0.42±0.02, respectively ($p<0.05$); at radial arteries – 0.39±0.01 and 0.34±0.02, respectively ($p<0.05$).

Color Doppler scanning revealed that in patients of Group I compared with patients of Group II, values of RI in the follicular phase of the menstrual cycle were significantly higher only in the uterine and arcuate arteries. Compared to patients of the control group, all values of blood flow parameters were significantly lower. This can be explained by the fact that in the follicular phase of the menstrual cycle, angiogenesis processes in the endometrium increase and with an increase in the total volume of the vascular bed, peripheral vascular resistance to blood flow decreases, leading to a decrease in RI parameters.

When analyzing dopplerometric indicators of blood flow in the uterine arteries in patients with various forms of adenomyosis, depending on the phase of the menstrual cycle, it was revealed that the final diastolic blood flow rate in the second phase of the menstrual cycle exceeded this indicator by almost 2 times, compared with the first phase; in the second phase, lower blood flow resistance was revealed, which was manifested by a significant decrease SDR, RI and PI.

In our work the incidence of adenomyosis was highest in the ae subgroup of 36–40 years old. This data was close to the results of other authors. Thus, Yu O, et al (2020), reported that the incidence of adenomyosis in their study was highest among patients 41 to 45 years of age [14].

Doppler ultrasound examination is one of the important diagnostic methods that used before surgery, so, according to the imaging manifestations, the surgeon can preliminarily judge the location, size, and invasion depth of adenomyosis lesions before surgery to formulate individualized surgical plan [11, 15].

According to our data, Color Doppler scanning showed significant differences between of study groups, which are important to understand the features of blood flow in the uterine arteries in patients with various forms of adenomyosis, depending on the phase of the menstrual cycle. Zhu J, et al (2022), in their study revealed that the coincidence rate, sensitivity, and specificity of color Doppler ultrasonography were higher than those of abdominal ultrasonography, and the differences were statistically significant ($p<0.05$) [15]. So, we used this method for deeply analyzed the conditions of arteries to prepared the optimal treatment plan.

Conclusions

1. The largest number of adenomyosis are registered in patients aged 36–40 years – 92 women, 41.1±3.3 %.

2. The most common pathologies in patients with various forms of adenomyosis were diseases of the cervix (114 women, 50.89±3.3 %), uterine fibroids (113 women, 50.45±3.4 %), and inflammatory diseases of the pelvic organs (113 women, 50.45±3.4 %).

3. Resistance index values in the follicular and luteal phases have statistically significant differences between groups of patients with adenomyosis ($p<0.05$).

References

1. Abrão MS, Andres MP, Barbosa RN, Bassi MA, Kho RM. Optimizing Perioperative Outcomes with Selective Bowel Resection Following an Algorithm Based on Preoperative Imaging for Bowel Endometriosis. J Minim Invasive Gynecol. 2020 May-Jun;27(4):883–891. doi: 10.1016/j.jmig.2019.06.010.

2. Artymuk N, Zotova O, Gulyaeva L. Adenomyosis: genetics of estrogen metabolism. Horm Mol Biol Clin Investig. 2019 Mar 15;37(2). doi: 10.1515/hmbci-2018-0069.

3. Dessouky R, Gamil SA, Nada MG, Mousa R, Libda Y. Management of uterine adenomyosis: current trends and uterine artery embolization as a potential alternative to hysterectomy. Insights Imaging. 2019 Apr 27;10(1):48. doi: 10.1186/s13244-019-0732-8.

4. Donnez O, Donnez J. Gonadotropin-releasing hormone antagonist (linzagolix): a new therapy for uterine adenomyosis. Fertil Steril. 2020 Sep;114(3):640–645. doi: 10.1016/j.fertnstert.2020.04.017.

5. Dueholm M. Minimally invasive treatment of adenomyosis. Best Pract Res Clin Obstet Gynaecol. 2018 Aug;51:119-137. doi: 10.1016/j.bpobgyn.2018.01.016.

6. Harada T, Khine YM, Kaponis A, Nikellis T, Decavalas G, Taniguchi F. The Impact of Adenomyosis on Women's Fertility. Obstet Gynecol Surv. 2016 Sep;71(9):557-68. doi: 10.1097/OGX.0000000000000346.

7. Hashimoto A, Iriyama T, Sayama S, Nakayama T, Komatsu A, Miyauchi A, et al. Adenomyosis and adverse perinatal outcomes: increased risk of second trimester miscarriage, preeclampsia, and placental malposition. J Matern Fetal Neonatal Med. 2018 Feb;31(3):364–369. doi: 10.1080/14767058.2017.1285895.

8.Khalifa MA, Atri M, Klein ME, Ghatak S, Murugan P. Adenomyosis As a Confounder to Accurate Endometrial Cancer Staging. Semin Ultrasound CT MR. 2019 Aug;40(4):358–363. doi: 10.1053/j.sult.2019.04.004.

9. Lazzeri L, Morosetti G, Centini G, Monti G, Zupi E, Piccione E, et al. A sonographic classification of adenomyosis: interobserver reproducibility in the evaluation of type and degree of the myometrial involvement. Fertil Steril. 2018 Nov;110(6):1154–1161.e3. doi: 10.1016/j.fertnstert.2018.06.031.

10.Orlova YuA, Hromova AM, Ketova OM, Liakhovska TYu, Martynenko VB, Krutikova EI. Aseptic inflammation as the essential link in the pathogenesis of endometrioid disease. Medicni perspektivi. 2023;28(3):55–61. https://doi.org/10.26641/2307-0404.2023.3.288961

11. Osada H. Uterine adenomyosis and adenomyoma: the surgical approach. Fertil Steril. 2018 Mar;109(3):406-417. doi: 10.1016/j.fertnstert.2018.01.032. 12.Schrager S, Yogendran L, Marquez CM, Sadowski EA. Adenomyosis: Diagnosis and Management. Am Fam Physician. 2022 Jan 1;105(1):33–38.

13. Szubert M, Koziróg E, Olszak O, Krygier-Kurz K, Kazmierczak J, Wilczynski J. Adenomyosis and Infertility-Review of Medical and Surgical Approaches. Int J Environ Res Public Health. 2021 Jan 30;18(3):1235. doi: 10.3390/ijerph18031235.

14.Yu O, Schulze-Rath R, Grafton J, et al.; Adenomyosis incidence, prevalence and treatment: United States population-based study 2006 – 2015. Am J Obstet Gynecol. 2020;223(1):94.e1–94.e10.

15.Zhu J, Liu S, Gao D. Application of Color Doppler Ultrasound in Microscopic Imaging Diagnosis of Adenomyosis. Scanning. 2022 May 31;2022:2366871. doi: 10.1155/2022/2366871.

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