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RESEARCH ARTICLE

Features of diagnosing ovarian tumors in women of pre- and postmenopausal age

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Abstract

Currently, one of the main ways to fight cancer, which can improve the results of treatment of ovarian neoplasms, is screening. Presently, the issue of organizing and conducting preventive examinations of women, including those of reproductive age, is one of the most urgent problems of primary health care institutions. The subjects of the study were 168 pre- and postmenopausal patients aged 20 to 60 years with ovarian tumors suspected of oncological pathology, who received treatment on the basis of the Tashkent city branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology for the period from 2018 to 2022, taking into account the selected age interval. An assessment was made of laboratory research methods, such as: General blood count, biochemical blood test, general urinalysis, tumor-associated marker CA-125, HE-4. In the comparative analysis of risk factors, when ovarian tumors develop in pre- and postmenopausal women, malignant and borderline ovarian tumors have complaints, parity, gynecological anamnesis, and the presence of extragenital diseases, which do not have specific characteristics for malignant or borderline tumors. therefore, it does not provide sufficient information in the process of diagnosing ovarian tumors. The sonographic characteristics associated with the degree of ovarian tumor malignancy were examined, and the tumor had a solid component ($p < 0.001$), the presence of obstructions ($p = 0.0005$), and the presence of growth on the inner surface of the capsule ($p < 0.001$), the presence of a significant amount of free fluid in the pelvic cavity ($p < 0.001$), the roughness of the surface of the tumor capsule ($p < 0.001$) were observed to be characteristic of more dangerous processes.

Keywords: Ovarian cancer, Pre-and postmenopausal women, Tumor-associated marker CA-125, HE-4, Screening.

Introduction

Currently, one of the fundamental methods of anticancer control that can improve the results of the treatment of ovarian tumors is screening. Presently, the issue of organizing and conducting preventive examinations of women, including those of reproductive age, is one of the most pressing work of institutions providing primary health care. Screening of women began in the 80s of the last century. At that time, examinations of women included only transabdominal scanning of the pelvic organs. The low efficiency of this screening did not contribute to a decrease in the number of patients with common forms of tumors, including malignant ovarian tumors. The aggressiveness of the course of this pathology remains the reason for the late detection of malignant ovarian tumors. According to various authors, the majority of patients (60–70%) are diagnosed with stages III–IV of the disease (V.L. Vinokurov 2004, E. G. Novikova 2007, N.I. Tursunova 2022). With the support of the Government of the Republic of Uzbekistan, a program was formed for the further development of oncological services and improvement of oncological care to the population of the Republic of Uzbekistan for 2017–2021, approved by this resolution, created with the aim of improving the provision of specialized oncological care, as well as to improve the system of prevention and treatment (M.N. Tillyashayxov 2023, Yu. S. Sidorenko 1992, L. A. Ashrafyan 2015).

The Society of Gynecologic Oncology (SGO) and the American College of Obstetricians and Gynecologists (ACOG) have adopted an algorithm for examining women as an international standard for identifying ovarian cancer, which

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includes a clinical examination and ultrasound examination of organs. small smear and determination of the level of tumor markers in blood serum. Despite the possibilities of preoperative diagnosis, in 0.9 to 4.2% of patients operated on with a diagnosis of benign ovarian tumors, histological examination reveals malignant neoplasms (I. S. Sidorova 2006, M. Canis 2002).

According to modern literature, the frequency of preoperative diagnostic errors for tumor formations is 30.9 to 45.6%, for malignant ovarian tumors – 25 to 51%. The percentage of detection of borderline ovarian tumors at stage I of the disease ranges from 60 to 85%, at stage III it is from 10 to 35% (in contrast to ovarian cancer, in which this figure is from 60 – 70%), and detection of stage IV is recorded very in rare cases (D.A. Bell 2004, I. S. Sidorova 2006). In the United States, research shows that about 20% of all ovarian cancer cases are localized at diagnosis, about 13% are at the regional stage, and the majority are at a distant stage (58%). This distribution differs in histological type. Stromal and germinal tumors are more often diagnosed at localized stages (> 50%) compared with epithelial tumors (19%) (D.L. Clark Pearson 2009, G. Acs 2005).

The complexity of this situation lies in the asymptomatic course of the tumor process in the ovaries and the untimely detection of the neoplastic process, which is especially important for young women. The reasons for the ease of tumor transition from one category to another are varied. According to literature reviews, these include the absence of specific symptoms, features of tumor spread (implantation, hematogenous, lymphogenous), and initially aggressive tumor growth. This multifactorial nature leads to the difficulty of differential diagnosis of benign tumors of the uterine appendages. Sometimes it is difficult to distinguish what type of neoplasm the identified process is classified as initial forms of cancer or borderline tumors. Diagnostic errors contribute to an increase in the number of inadequate surgical interventions and treatment, more often leading to an unfavorable prognosis (J.S. Berek 1995, E. A. Borisova 2015).

At the same time, extended observation periods for patients with small ovarian cysts, long-term unsuccessful anti-inflammatory treatment for ovarian enlargement, observation of patients with a presumptive diagnosis of uterine fibroids, and with neoplasms in the pelvis of unknown localization become the reason for late surgical treatment. One of the saving ones was the use of ultrasound diagnostic method, introduced since 1970. Ultrasound examination (ultrasound) is a non-invasive, inexpensive, most accessible and easily reproducible research method. Sonography is one of the most important methods for diagnosing tumors and tumor-like formations of the ovaries due to its high information content, as well as the ability to assess signs of malignancy using color Doppler sonography and three-dimensional power Doppler (D.A. Bell 2004, I. Boger-Megiddo 2005, I. N. Ozhiganova 2013). When assessing ultrasound parameters, the first step is to analyze the types of echostructure of pelvic formations, thanks to which tumors of the uterine appendages that are prone to malignancy are differentiated. The advent of Dopplerography has made it possible to achieve greater accuracy in differentiating malignant and benign ovarian tumors. The basis of the method is the phenomenon of neovascularization, in which the tumor itself induces the growth of its capillaries, and the latter contributes to its growth, while malignant tumors have their own characteristics of blood flow, which are formed due to the lack of smooth muscle tissue in the walls of malignant vessels and the presence of multiple shunts that promote high-speed intratumoral blood flow. However, a number of authors do not recommend using this method as a screening method to identify a tumor process in the ovaries (I. I. Baranov 2018, E. A. Borisova 2018).

Materials and Methods

The subjects of the study were 168 pre- and postmenopausal patients aged 20 to 60 years with ovarian tumors suspected of oncological pathology. The patients compiled a retrospective continuous sample of inpatient medical records of patients of reproductive and postmenopausal age according to codes D27 and C56 according to the ICD-10 classification, who received treatment on the basis of the Tashkent city branch of the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology for the period from 2018 to 2022, taking into account the selected age interval.

To implement the goals and objectives of this work, the patients were grouped in accordance with the WHO morphological classification of 2013: 101 (60.1%) patients with benign tumors, 24 (14.3%) patients with borderline tumors and 43 (25.6%) women with malignant tumors.

Patients ranged in age from 30 to 81 years with a mean age of 55 ± 11.9 years.

A thorough collection and analysis of obstetric and gynecological history was carried out: age at menarche, number of abortions, number of births, characteristics of the ovarian-menstrual cycle, the presence of dyspareunia, metrorrhagia, the presence of infertility and its causes, chronic endometritis, endometrial polyps and hyperplasia, uterine fibroids, endometriosis, pathologies of the cervix, the presence of concomitant or previously existing malignant formations of the reproductive system (cancer of the body, cervix, cancer of the fallopian tube), chronic adnexitis and salpingitis, a history of ovarian apoplexy, pre-existing ovarian tumors, types of previously performed gynecological operations.

An assessment was made of laboratory research methods, such as general blood count, biochemical blood test, general urinalysis, tumor-associated marker CA-125, HE-4.

An analysis was made of ultrasound, CT and MRI indicators in the study group, such as: the size and volume of the uterine body, the presence of free fluid in the pelvis, the type of tumor structure and the size of the collateral ovary, the structure of the cervix. When assessing the tumor process in the ovaries, the following criteria were assessed: Type of structure (solid, cystic or cystic-solid), unilateral or bilateral ovarian lesions, size of formations, presence of septa in the structure of the formation, assessment of the structure of the tumor capsule (namely the presence of growths along the internal or external the surface of the capsule, the surface of the capsule itself), the presence of blood flow in the formation, the speed of blood flow and the resistance index of blood flow in the tumor.

The statistical analyses presented in our work were carried out in Microsoft Excel. Before starting the analysis, quantitative and qualitative characteristics were collected for a selected group of patients. To determine the characteristics measured on a nominal scale, contingency tables were analyzed with the calculation of χ^2 and, in some cases, Fisher's exact method.

Research Results

Complaints of abdominal enlargement (p = 0.688) occurred in 17.8% of patients with benign ovarian tumors (18), in 12.5% of patients with borderline tumors (3) and in 20.9% of patients (9) with malignant tumors, ovarian tumors.

Complaints of dyspareunia were made by 2 patients (2.0%) with benign ovarian tumors and 1 patient (2.3%) with a malignant ovarian tumor; p = 0.767.

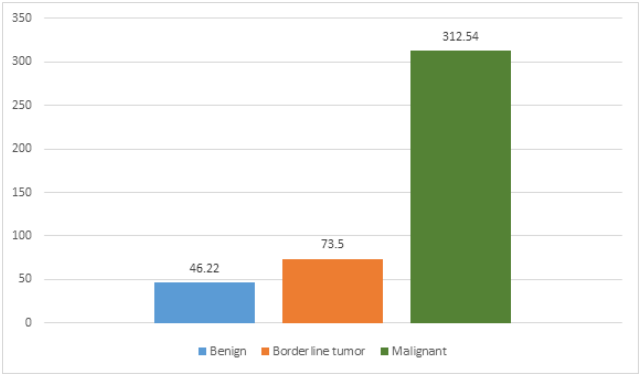

Figure 1: Average CA-125 titers in patients of reproductive age with ovarian

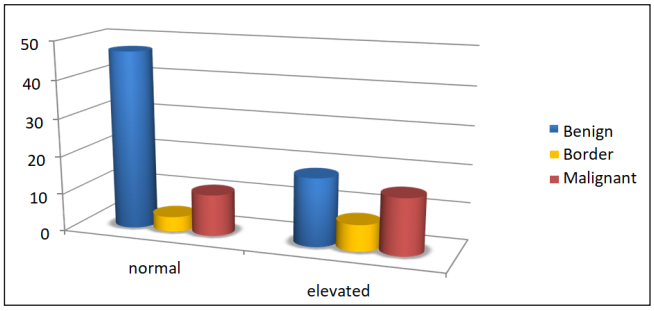

Figure 2: Analysis of qualitative results (normal – increased) of CA-125 titer in patients of reproductive age with ovarian tumors

The titers of tumor markers were assessed; as a result, the indicators were divided as follows (Figure 1): benign tumors - 46.22 ± 12.73 units/mL, borderline tumors - 73.50 ± 25.26 units/mL and malignant tumors – 312.54 ± 115.83 with a titer

Table 1: Complaints of patients of reproductive age in the group with tumors and tumor-like formations of the ovaries

Complaints	Result	Benign		Borderline tumor		Malignant		хи^2	p
		Abs.	%	Abs.	%	Abs.	%		
	No complaints	32	31,7	7	29,2	16	37,2	0,58	0,748
	There are complaints	69	68,3	17	70,8	27	62,8		
Dyspareunia	no	99	98,0	24	100,0	42	97,7	0,53	0,767
	yes	2	2,0	–	–	1	2,3		
Pain in the lower abdomen	no	40	39,6	6	25,0	21	48,8	3,66	0,161
	Yes	61	60,4	18	75,0	22	51,2		
Increase in abdominal volume	no	83	82,2	21	87,5	34	79,1	0,75	0,688
	yes	18	17,8	3	12,5	9	20,9		
Infertility	Primary	10	9,9	2	8,3	9	20,9		
	Secondary	8	7,9	3	12,5	2	4,7	4,79	0,310
	No	83	82,2	19	79,2	32	74,4		
Cause of infertility	No infertility	76	75,2	18	75,0	34	79,1		
	Pipe factor	11	10,9	2	8,3	3	7,0		
	Ovulation disorders	4	4,0	1	4,2	3	7,0	6,77	0,562
	Male factor	8	7,9	2	8,3				
	Mixed factor	2	2,0	1	4,2	3	7,0		

Table 2: Ultrasound assessment of the tumor process in the ovaries in patients of reproductive age with tumors and tumor-like formations of the ovaries

Result	*Benign*		*Borderline*		*Malignant*		xu^2	*p*
Ovarian lesion								
One ovary is affected	82	81,2 %	13	54,2 %	37	86,0 %	14,56	0,006
Both ovaries are affected	14	13,9 %	5	20,8 %	2	4,7 %		
appendages from the side of the tumor were removed	5	5,0 %	6	25,0 %	4	9,3 %		
Free fluid in the pelvis								
No	85	84,2 %	16	66,7 %	37	86,0 %	17,80	0,007
Minor amount	16	15,8 %	4	16,7 %	2	4,7 %		
Moderate quantity	–	–	3	12,5 %	3	7,0 %		
Large quantity	–	–	1	4,2 %	1	2,3 %		
Type of tumor structure								
Solid	1	1,0 %	2	8,3 %	5	11,6 %	28,26	<0,001
Cystic-solid	12	11,9 %	9	37,5 %	17	39,5 %		
Cystic	88	87,1 %	13	54,2 %	21	48,8 %		
The presence of growths on the inner surface of the capsule								
No	60	59,4 %	5	20,8 %	15	34,9 %	15,33	<0,001
Yes	41	40,6 %	19	79,2 %	28	65,1 %		
The presence of growths on the outer surface of the capsule								
No	97	96,0 %	24	100,0 %	39	90,7 %	3,30	0,192
Yes	4	4,0 %	–	–	4	9,3 %		
Presence of septa in the tumor								
No	56	55,4 %	14	58,3 %	14	32,6 %	7,10	0,029
Yes	45	44,6 %	10	41,7 %	29	67,4 %		
Surface of tumor								
smooth	80	79,2 %	17	70,8 %	23	53,5 %	9,78	0,008
lumpy	21	20,8 %	7	29,2 %	20	46,5 %		
Presence of blood flow in the tumor								
No	56	55,4 %	6	25,0 %	5	11,6 %	30,66	<0,001
Yes	18	17,8 %	9	37,5 %	23	53,5 %		

Note. p – comparisons using two-way analysis of variance by Kruskal–Wallis.

rate of up to 35 units/mL. When assessing the quantitative indicators of the CA-125 titer in benign tumors, the indicators are significantly lower. In the future, to determine the significance of this sign in a given group of patients from a diagnostic point of view, we evaluate the titers of tumor markers as a qualitative indicator (Figure 2). As a result, we obtained a significant increase in the CA-125 titer ($p = 0.006$), which indicates to us the significance of this diagnostic sign and the possibility of its use for the early diagnosis of a tumor process in the ovaries (Table 1).

There may be many cases of elevated CA-125 levels, and its diagnostic sensitivity is relatively low, especially when it comes to early diagnosis of ovarian cancer, which is not ideal, just vulnerable to the effects of benign diseases. In addition, the specificity is also poor. HE-4 is not expressed normally from the ovary, but it was highly expressed in ovarian cancer but not or low expressed in most non-malignant ovarian tumors. Thus, for the diagnosis of ovarian cancer, HE4 has been shown to have better specificity. It is the difference in sensitivity and specificity between CA125 and HE4 that results in a more efficient dual-performance detection method. Few scientists have proposed the concept of the ROMA index to estimate the risk of developing ovarian cancer using study results and associated statistical analysis. An assessment of ultrasound parameters in the study group was carried out, such as: the size and volume of ovarian formation, the presence of free fluid in the pelvis, the type of tumor structure. When assessing the tumor process in the ovaries, the following criteria were assessed (Table 2): type of structure (solid, cystic or cystic-solid), unilateral or

bilateral ovarian lesions, size of formations, presence of septa in the structure of the formation, assessment of the structure of the tumor capsule (namely the presence of growths on the inner or outer surface of the capsule, the surface of the capsule itself), the presence of blood flow in the formation.

The sizes of ovarian tumors in patients differed in a fairly significant range - the maximum sizes ranged from 77.26 ± 6.94 to 97.06 ± 15.29 mm. A direct relationship between the size of the tumor formation and the stage of the tumor process was not established during the study. The volume of tumors of the uterine appendages was 599.06 ± 128.18 mL in the group of patients with benign tumors, 814.54 ± 358.32 mL in the group of patients with borderline tumors and 579.17 ± 196.37 mL in the group of patients with malignant tumors ($p = 0.941$ by one-way analysis of variance Kruskal-Wallis).

Discussion

Epithelial malignant tumors produce the glycoprotein CA-125, which has become the leading one in the diagnosis of ovarian cancer. It has been shown that the level of CA-125 increases only in 55% of patients with tumor size < 1 cm, in 80% of patients with tumors measuring 1 to 5 cm and in 92% of patients with tumors measuring >5 cm (I. I. Baranov 2018, E. A. Borisova 2018). The sensitivity of CA-125 in the early stages of OC is 50%, in late stages - 85–96% This means that in half of the cases with early-stage OC, the level of CA-125 does not exceed the norm and, therefore, cannot become a significant screening factor (D.L. Clark Pearson 2009, E. A. Borisova 2018). It is noteworthy that not all morphological variants of ovarian malignancies express the CA-125 marker equally. For example, an increase in the level of CA-125 in the blood is most often observed in epithelial ovarian tumors: in 90% of patients with serous adenocarcinoma and in 82% of patients with poorly differentiated cancer (D.L. Clark Pearson 2009, E. G. Novikova 2007). Relatively less frequently, increased concentrations of CA-125 in the blood are observed in endometrioid and mucinous carcinomas: 30 to 60 and 30% of cases, respectively. Thus, the absence of tumor marker expression in a patient does not mean the absence of the tumor itself. An increase in the level of CA-125 does not always mean the presence of a tumor; therefore, an increased level of the marker has also been described in non-oncological diseases: tuberculosis, pneumonia, pancreatitis, endometriosis, uterine fibroids, as well as during menstruation and pregnancy. For this reason, the study of tumor markers alone will not be sufficient to establish an accurate diagnosis or exclude a malignant neoplasm.

Conclusion

In the comparative analysis of risk factors, when ovarian tumors develop in pre-and postmenopausal women, malignant and borderline ovarian tumors have complaints, parity, gynecological anamnesis, and the presence of extragenital diseases, which do not have specific characteristics for malignant or borderline tumors. therefore, it does not provide sufficient information in the process of diagnosing ovarian tumors. The sonographic characteristics associated with the degree of ovarian tumor malignancy were examined, and the tumor had a solid component ($p < 0.001$), the presence of obstructions ($p = 0.0005$), and the presence of growth on the inner surface of the capsule. ($p < 0.001$), the presence of a significant amount of free fluid in the pelvic cavity ($p < 0.001$), and the roughness of the surface of the tumor capsule ($p < 0.001$) were observed to be characteristic of more dangerous processes. The relationship between the size and size of the tumor in the ovary and the morphological structure of the tumor was not determined. Since CA-125 and HE-4 onco-markers and index ROMA indicators are observed to increase in pre- and postmenopause peripheral blood mainly in malignant tumor processes, these tests are important in the modern diagnosis of ovarian malignant and borderline tumors. Therefore, we can accept these indicators as a specific indicator of early diagnosis of ovarian malignant tumors.

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