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YUMURTALIQ POLİKİSTOZU SİNDROMU OLAN QADINLARDA YUMURTALIQLARIN QURULUŞUNUN VƏ FUNKSİYASININ SONOQRAFİK XÜSUSİYYƏTLƏRİ

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Xülasə. *Məqalədə yumurtalıq polikistozu sindromu (YPS) olan qadınlarda yumurtalığın struktur-funksional dəyişikliklərinin dupleks-skanlaşdırma yolu ilə tədqiqinin nəticələri əks etdirilmişdir. Bu məqsədlə aparılan tədqiqata yaşı 18-dən 27-yə qədər olan 124 xəstə cəlb edilmişdir. Onlarda yumurtalıqların həcmi 10 sm^3-dən çox və bir sonoqrafik kəsikdə 2-9 mm ölçülü 12-dən artıq follikul olmuşdur. Dinamik müşahidə zamanı yumurtalıqlarda yetişmiş follikul qeydə alınmamış, menstrual tsikl isə qeyri-müntəzəm olmuş 92 qadın **birinci** tədqiqat qrupuna **(YPS)** daxil edilmişdir. **İkinci** (II) tədqiqat qrupuna çox follikullu yumurtalıqlar **(ÇFY)** aşkar edilmiş, follikullarının yetişməsi orta fazada olan və ya dominant follikul qeydə alınan, lakin ovulyasiya baş verməyən 32 qadın daxil edilmişdir. Menstruasiyası normal keçən 28 qadın kontrol qrupunu təmsil etmişdir.*

*Dupleks-skanlaşdırma üsulu ilə aparılmış müayinənin nəticələrinin müqayisəsi göstərmişdi ki, I qrupda **(YPS)** olan qadınlarda II qrupla **(ÇFY)** müqayisədə yumurtalıqların həcmi 14 sm^3-dən çox, bir sonoqrafik kəsikdə follikulların sayı 15-dən çox olmuş yumurtalıq stromasının artan vaskulyarizasiyası əhəmiyyətli dərəcədə daha intensiv olmuşdur. İkinci qrupda yetişmiş və ya dominant follikulların görünüşü yumurtalıqların multifollikulyarlığının funksional xarakter daşıdığını göstərir və bu klassik polikistok əlamət deyil.*

Açar sözlər*: reproduktiv yaş, endoçerviksin dövri dəyişiklikləri, ultrasonoqrafiya*

Ключевые слова*: репродуктивный возраст, циклические изменения эндоцервикса, ультрасонография*

Key words*: reproductive age, cyclic changes of endocervix, ultrasonography*

SONOGRAPHIC FEATURES OF STRUCTURE AND FUNCTION OF OVARIES IN POLYCYSTIC OVARY SYNDROME

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The article presents the results of duplex scanning of structural and functional changes in the ovaries in women with polycystic ovary syndrome (PCOS). For this purpose, 124 patients aged 18 to 27 years were included in the study. Their ovarian volume exceeded 10 cm3, the number of follicles measuring 2-9 mm on one sonographic section was more than 12 pieces. During dynamic observation, 92 women with the absence of a maturing follicle and the presence of an irregular menstrual cycle were included in group I (PCOS). And group II (multifollicular ovaries – MFO) was composed of 32 women who had a maturing or dominant follicle in the middle of the follicular phase, but ovulation did not occur. 28 women with a normal menstrual

cycle made up the control group.

Comparison of duplex scanning results showed that among women of group I (PCOS) compared to group II (MFO), the volume of ovaries is more than 14 cm^3, the number of follicles on one sonographic section is more than 15 pieces, and increased vascularization of the ovarian stroma are found significantly more often. In the second group, the appearance of a maturing or dominant follicle indicates that the multifollicularity of the ovaries is functional in nature, and this is not classic polycystic disease.

Among the women of reproductive age, one of the most common endocrine pathologies is Polycystic Ovary Syndrome (PCOS). Depending on the diagnostic criteria used, the prevalence of PCOS is 5-15%. According to the consensus of many specialized medical societies, the diagnosis of PCOS should be based on the presence of at least 2 of the following 3 criteria: chronic anovulation, hyperandrogenism, and polycystic ovaries. It should be noted that some thyroid disorders, hyperprolactinemia, and non-classic congenital adrenal hyperplasia can mimic the above features of PCOS [1–3]. Accurate diagnosis of PCOS often requires multiple repeated studies, participation of different specialists, and dynamic observation. All this takes a long time and improper treatment can contribute to the progression of the disease [4-6]. PCOS is associated with many diseases, including infertility, metabolic syndrome, obesity, impaired glucose tolerance, type 2 diabetes, cardiovascular risk, depression, endometrial cancer, and non-alcoholic fatty liver disease/non-alcoholic steatohepatitis [7].

PCOS is a multifactorial disease. Two popular hypotheses postulate that individuals with a genetic predisposition exposed to certain factors exhibit features of PCOS. The most common of these are obesity and insulin resistance [8]. Among all the pathophysiological mechanisms of PCOS, functional hyperandrogenism predominates. Two thirds of PCOS manifestations have typical functional ovarian hyperandrogenism, characterized by dysregulation of androgen secretion with an excessive response of 17-hydroxyprogesterone to gonadotropin stimulation [9]. 3]. Accurate diagnosis of PCOS often requires multiple repeated tests, participation of different specialists, and dynamic observation. All this takes a long time, and incorrect treatment can contribute to the progression of the disease [4-6]. Many diseases are associated with PCOS, including infertility, metabolic syndrome, obesity, impaired glucose tolerance, type 2 diabetes, cardiovascular risk, depression, endometrial cancer, and non-alcoholic fatty liver disease/non-alcoholic steatohepatitis [7].

Functional ovarian hyperandrogenism PCOS presents with the primary features: hyperandrogenism, oligo anovulation, and polycystic ovary morphology. Functional ovarian hyperandrogenism is multifactorial, with a combination of hereditable and environmental factors. Causes for this dysregulation include insulin excess, which is known to sensitize the ovary to luteinizing hormone (LH) by interfering with the process of homologous desensitization to LH in the normal ovulation cycle as well as an intrinsic imbalance among intraovarian regulatory systems [8-10].

A cycle length of more than 35 days suggests chronic anovulation, but a cycle length beween 32 to 35-36 days needs to be assessed for ovulatory dysfunction. The threshold for oligomenorrhea is 35 days cycles in adults and 40 days in adolescents. A patient with cycles shorter than 35 days can be assessed by measuring progesterone levels in the mid-luteal phase [11].

Ovarian morphology assessment is more accurate when done by transvaginal ultrasound. New ultrasound machines allow the diagnosis of PCOM in patients having at least 25 small follicles (2 mm to 9 mm) in the whole ovary. Ovarian size at 10 ml remains the normal size cutoff. 2004 Rotterdam criteria indicate PCOM by at least 12 follicles measuring 2 mm to 9 mm in the ovary or increased ovarian size more than 10 ml. Ultrasound technology has advanced and can improve the diagnosis of PCOS. Androgen Excess and PCOS Society have reviewed current data and published updated guidelines for PCOM diagnosis, increasing follicle count to 25. Ovary size has not been modified. Recent studies have shown that measurement of anti-Müllerian hormone levels may be useful in determining the diagnosis of PCOS when accurate ovarian ultrasound is not available [12].

The purpose of the study is to study the features of structural and functional changes in the ovaries in polycystic ovary syndrome using

duplex scanning.

Material and methods. 124 female with menstrual irregularities, aged 18-27 years were recruited in the study. All women had a sexual life, 26 of them were married, 98 – unmarried. Females with diabetes mellitus, thyroid and adrenal disorders and on hormonal replacement therapy were excluded from the study. Menstrual irregularities were defined as; chronic anovulation as amenorrhea of 3 months duration or oligomenorrhea as inter-menstrual interval > 35 days. Regular menstruation was defined as a 21-35 days and no more than a 4-day difference in duration between cycles.

In all women, the level of anti-Mullerian, follicle stimulating and luteinizing hormones, their ratio, prolactin, 17-OH-progesterone was defined. All women had the ultrasound criteria of PCO: the presence of 12 or more 2-9 mm ovarian follicles on the longitudinal section and ovarian volume of more than 10 cm^3. Hirsutism was registered in 15 (12.1%) women with polycystic ovaries. The comparative group (CG) consisted of 28 reproductively healthy women aged 19 - 25 years with a regular menstrual cycle, normal ovarian size and cyclic changes in them.

Duplex scanning was performed transvaginally on the 4th-6th and 8th-10th days of the menstrual cycle, and in the absence of menstruation on any day. In order to study the cyclic changes in the ovaries, each woman was examined 2 to 5 times, depending on the presence or absence of menstruation. Based on three measurements (length, thickness and width), the volume of the ovaries was calculated, and the number of follicles in one ultrasound section was determined. Follicles measuring 2-9 mm were included in the calculation.

Under the control of color Doppler, blood flow was recorded in the stroma of the ovaries. The number of vessels to be visualized was more than 5 mm in length, more than 1.5 mm in width, to assess the degree of vascularization. Vascularization of the strengthened was considered, if the number of imaged large vessels was more than 6 pieces. Measurement of blood flow parameters was carried out in pulsed Doppler mode 3-5 times in different parts of the stroma. The highest systolic blood flow velocity and resistance index, their averaged value were taken into account.

Duplex scanning was carried out using a Philips HD-11 ultrasound machine with a transvaginal sensor in a frequency mode of 4-9 MHz. Statistical analysis was carried out using the nonparametric Mann-Whitney method. If the p value <0.05, the difference between the compared groups was considered statistically significant.

Results and discussion. In 92 examined women, the number of follicles 2-9 mm in size on the longitudinal echographic section was more than 12 pieces, the volume of the ovary (DxLxWx0.52) exceeded 10 cm3, all had irregularities in the menstrual cycle in the form of oligo- or amenorrhoea, and under dynamic observation the diameter of the follicles did not exceeded 9 mm. These women made up the I group - polycystic ovary syndrome (PCOS). In 32 women, also the number of follicles 2-9 mm in size exceeded 12 pieces, the volume of the ovary more than 10 cm^3, in 13 of them there were disorders of the menstrual cycle. Dynamic observation in 23 cases recorded a ripening follicle, in 7 cases – the dominant follicle, in 2 – the yellow body. In 7 women, luteinization of the neovulatory follicle was noted and in 2 – insufficiency of the luteal phase. These women made up the II group – multifollicular ovaries (MFO). The control group (CG) consisted of 28 healthy women with the number of 2-9 mm follicles less than 10 pieces on the ultrasonographic slices, the ovary volume less than 10 cm^3, the normal menstrual cycle and physiological changes (Table 1). As can be seen from the table, among the women with polycystic ovaries, the peripheral location of the ovaries was noted in 53 (57,6±5,1%) cases, displaced in 39 (42,4±5,1%) cases ($p < 0,01$), in patients with MFO, on the contrary, in 13 (40,6±8,7%) and in 19 (59,4±6,5%) cases ($p<0,05$), among the women of control group – in 23 (82,1±7,2%) and in 5 (17,9±7,2%) cases respectively ($p<0,001$). An increase in the echogenicity of the stroma was recorded in 48 (52,2±5,2%) women of the I group ($p < 0,001$), in 11 (34,4±8,4%) women of the II group and in 2 (7,1±4,8%) of the control group.

The number of follicles within the limits of 13-15 was registered in 42 (45,6±5,1%) of women of the I group, 23 (71,9±7,9%) of women of the II group ($p<0,01$), and more than 15 follicles – in 49 (53,3±5,2%) and in 9 (28,1±7,9%) women ($p<0,001$), respectively. The volume of the ovary less than 10 cm3 in the II group was noted in 10 (31,2±8,2%) cases, in all patients of control group ($p<0,001$), respectively. In all women with PCOS, the ovary volume exceeded 10 cm3, within 11-14 cm^3 it was recorded in 51 (55,4±5,2%), more than 14 cm^3 in 41 (44,6±5,2%) cases, in 17 (53,2±8,8%) cases of II group respectively.

Table 1. Ultrasound parameters of ovaries in the 4th-6th days of the menstrual cycle with follicle sizes of 2-9 mm

Ultrasonographic parameters	PCOS (n = 92)	MFO (n = 32)	The healthy women (n = 28)
	1	**2**	**3**
Peripheral arrangement of follicles	53 (57,6 ± 5,1%)	13 (40,6 ± 8,7%)	23 (82,1±7,2%) $P_{3-1} < 0,01$ $P_{3-2} < 0,001$
Displaced arrangement of follicles	39 (42,4 ± 5,1%) $P_{1-3} < 0,01$	19 (59,4 ± 8,7%) $P_{2-3} < 0,001$	5 (17,9±7,2%)
Increased echogenicity of the stroma	48 (52,2 ± 5,2%) $P_{1-3} < 0,001$	11 (34,4 ± 8,4%) $P_{2-3} < 0,01$	2 (7,1 ± 4,8%)
Number of follicles 13-15	42 (45,6 ± 5,1%)	23 (71,9 ± 7,9%) $P_{2-1} < 0,01$	-
Number of follicles > 15	49 (53,3 ± 5,2%) $P_{1-2} < 0,01$	9 (28,1 ± 7,9%)	
Ovaries volume < 10 cm^3	-	10 (31,2 ± 8,2%)	34 (100,0 ± 1,9%)
Ovaries volume 11-14 cm^3	51 (55,4 ± 5,2%)	17 (53,2 ± 8,8%)	
Ovaries volume > 14 cm^3	41 (44,6 ± 5,2%) $P_{1-2} < 0,001$	5 (15,6 ± 6,4%)	
Average volume of ovary (cm^3)	18,9 ± 3,6 $P_{1-3} < 0,01$	11,8 ± 2,7 $P_{2-3} < 0,01$	6,1 ± 1,8
Enhanced vascularization of ovarian stroma	36 (39,1 ± 5,1%) $P_{1-2} < 0,01$ $P_{1-3} < 0,001$	6 (18,9 ± 6,9%) $P_{2-3} < 0,05$	
Vmax, cm/c	49,3 ± 8,6 $P_{1-3} < 0,001$	35,7 ± 7,2 $P_{2-3} < 0,05$	21,2 ± 4,6
IR	0,48 ± 0,03 $P_{1-3} < 0,05$	0,54 ± 0,03	0,59 ± 0,04

The number of follicles within the limits of 13-15 was registered in 42 (45,6±5,1%) of women of the I group, 23 (71,9±7,9%) of women of the II group ($p<0,01$), and more than 15 follicles – in 49 (53,3±5,2%) and in 9 (28,1±7,9%) women ($p<0,001$), respectively. The volume of the ovary less than 10 cm^3 in the II group was noted in 10 (31,2±8,2%) cases, in all patients of control group ($p<0,001$), respectively. In all women with PCOS, the ovary volume exceeded 10 cm^3, within 11-14 cm^3 it was recorded in 51 (55,4±5,2%), more than 14 cm^3 in 41 (44,6±5,2%) cases, in 17 (53,2±8,8%) cases of II group respectively.

In 23 healthy women in the early proliferative phase of the menstrual cycle along the periphery of the ovary several follicles with dimensions of 4-8 mm are visualized. In 5 cases, the follicles are also located in the central zone of the stroma. In the middle proliferative phase appears ripening follicle, and in the periovulatory period - the dominant follicle.

In more than half of cases of polycystic ovary syndrome, antral follicles of 2-9 mm were located along the periphery, an increase in stromal echogenicity was noted. Follicles can be located in one ovary along the periphery, in another mixed type (Fig. 1-3). Regardless of the localization of the follicles, the main difference of PCOS was the absence of a ripening follicle under dynamic observation. In the presence of a follicle more than 10 mm, a dynamic observation was carried out. In the II group of patients, in contrast to group I, the ripening or dominant follicle in the ovary was recorded (Fig. 4).

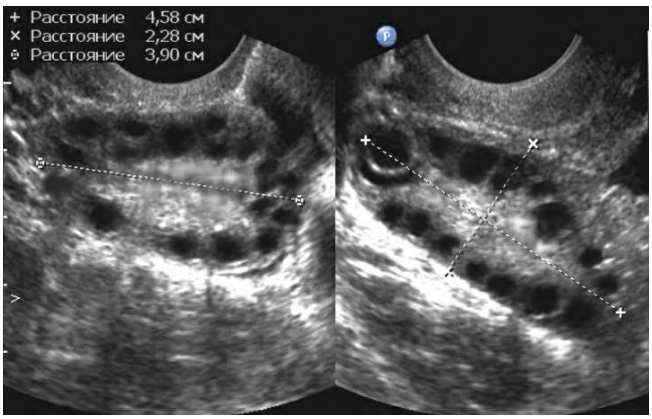

Fig. 1. The main echographic type of PCOS. On the periphery of the ovary are more than 16 follicles 2-6 mm. Echogenicity of the ovary stroma is increased.

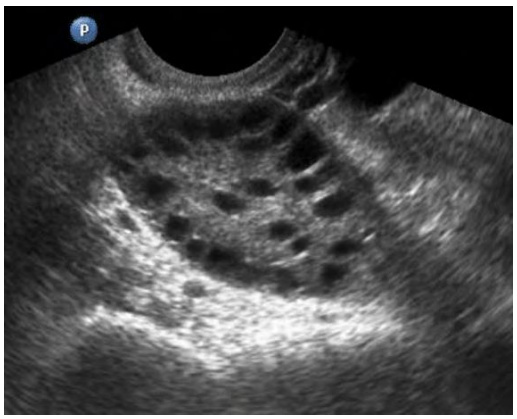

Fig. 2. Mixed type of location of antral follicles in a woman with PCOS. Antral follicles 2-7 mm are located in the stroma and along the periphery of the ovary.

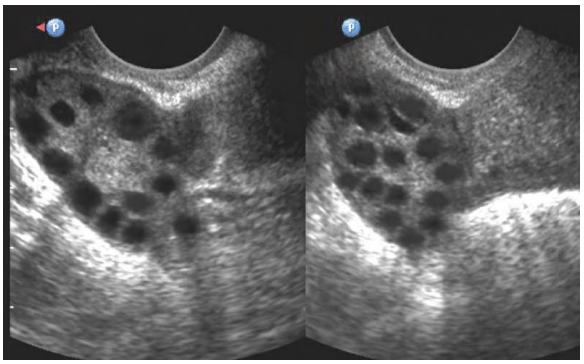

Fig. 3. PCOS. Peripheral type of localization of the follicles in the right ovary, mixed type – in left ovary.

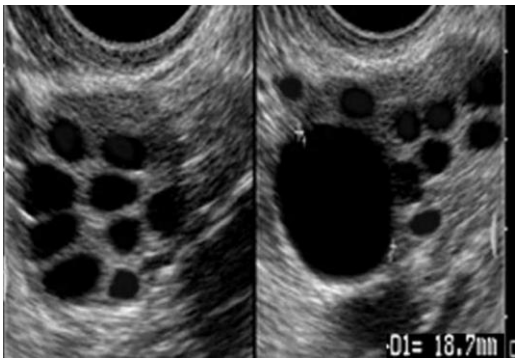

Fig. 4. Multifollicular ovaries. In the left ovary, the dominant follicle is visualized.

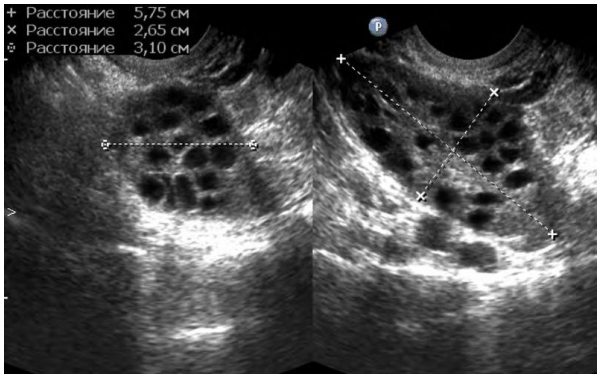

Fig. 5. Polycystic ovary syndrome. The mixed type of follicles localization. The volume of the ovary is 24.6 cm^3 (5.75 x 2.65 x 3.1 cm x 0.52)

In the I group of women, the volume of the ovaries varied within 11.5-24.3 cm^3 (an average of 18.9±3.6 cm^3), and in the II group – 8.7-14.9 cm^3 (an average of 11.8±2.7 cm^3), respectively. The greatest increase in the volume of the ovaries was noted at women with a mixed type of localization of the follicles (Fig. 5). There were no statistically significant differences in the volumes between these groups. However, in the I and II groups the volume of the ovaries was significantly ($P<0.01$) higher than the parameters of the control group.

When studying the degree of vascularization in the ovarian stroma, we took into account the number of color linear tubular structures more than 2 mm wide, the maximum systolic velocity (Vmax) and the index of peripheral resistance (RI) to the blood flow. The presence of color reflections in the stroma less than 5 was considered weak, 5-8 – moderate and more than 8 – enhanced vascularization. In the group with PCOS in 37 women, the number of such color reflections in the ovary stroma was more than 10 and, on the whole, significantly more than in the second and control groups.

Enhanced vascularization of ovarian stroma was recorded in 36 (39,1±5,1%) cases of I group, in 6 (18,9±6,9%) cases of II group, respectively (Fig. 6). The average systolic velocity of blood flow in ovary in I group was

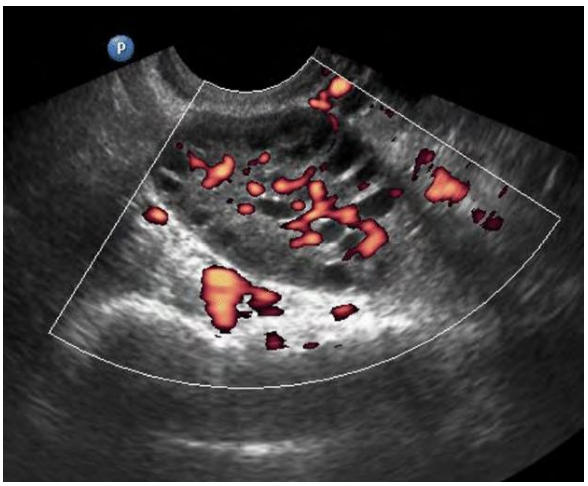

Fig. 6. Polycystic ovary syndrome. Enhanced vascularization of the ovary stroma

49,3±8,6 cm/c, in II group – 35,7±7,2 cm/c, in control group – 21,3±4,6 cm/c, respectively. The average resistive index (RI) of blood flow in ovary in I group was 0,48±0,03, in II group – 0,54±0,03, in control group – 0,59±0,04, respectively (P1-3 < 0.05).

Discussion

Transvaginal ultrasound examination allows obtaining higher quality images of the structures of the body and cervix of the uterus, the follicular apparatus, both in fertile women and in women with suspected polycystic disease [13, 14]. The ultrasound criteria for polycystic ovary syndrome, created in 2003 in the Rotterdam European Society of Reproductive Medicine and Human Embryology/American Society of Reproductive Medicine, are controversial because they expand the number of women who meet the criteria of PCOS and allow the creation of two phenotypic types [15]. These criteria assume that if a follicle with a diameter greater than 10 mm appears in the ovaries, it is necessary to repeat the studies to exclude PCOS. Among our patients, in 32 cases appeared ripening or dominant follicles. With further dynamic ultrasound observation, none of these women had ovulation. The peripheral distribution of follicles in "string of pearls" and hyperechogenicity of the stroma are classical ultrasound features [16]. Among our patients with PCOS, peripheral distribution of follicles was noted only in 57.2% of cases, and in 42.8% – a mixed distribution.

We further studied the features of vascularization of the stroma of the polycystic ovaries. Intensified vascularization of the stroma in PCOS is observed significantly more often than with PCO and in fertile women, which indicates the presence of stromal hyperplasia in PCOS. The maximum systolic blood flow velocity in the stroma in PCOS was significantly higher than in women with PCO, and the peripheral resistance index was vice versa.

Conclusion

1. The most characteristic structural changes in the polycystic ovary syndrome include: a mixed type of distribution of follicles, their number is more than 15 on the echographic section, and the ovary volume is more than 14 cm^3.

2. The characteristic functional indicators of the syndrome of polycystic ovaries include: the absence of a ripening follicle during the menstrual cycle, an increase in the number of color vascular signals, an increase in the maximum systolic velocity of more than 50 cm/s, a decrease in peripheral resistance to blood flow of less than 0.51.

3. Only a combination of elevated levels of AMH, the presence of menstrual irregularities and ultrasound criteria will allow to establish a phenotypic variant of PCOS and determine the tactics of treatment.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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СОНОГРАФИЧЕСКАЯ ХАРАКТЕРИСТИКА СТРУКТУРНО-ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ ЯИЧНИКОВ ПРИ СИНДРОМЕ ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ

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Резюме. В статье представлены результаты дуплексного сканирования структурно-функциональных изменений яичников у женщин с синдромом поликистозных яичников (СПКЯ). С этой целью в исследование включены 124 пациенток в возрасте от 18 до 27 лет. У них объем яичников превышал 10 см^3, количество фолликулов размерами 2-9 мм на одном сонографическом срезе было более 12 штуки. При динамическом наблюдении 92 женщин с отсутствием зреющего фолликула и наличием нерегулярного менструального цикла были включены в I группу (СПКЯ). А II группа (мультифолликулярные яичники – МФЯ) была составлена из 32 женщин, у которых в середине фолликулярной фазы отмечался зреющий или доминантный фолликул, однако овуляция не происходила. 28 женщин с нормальным менструальным циклом составили контрольную группу.

Сравнение результатов дуплексного сканирования показали, что среди женщин I группы (СПКЯ) по сравнению со II группой (МФЯ) объем яичников более 14 см^3, количество фолликулов на одном

сонографическом срезе более 15 штуки, усиленная васкуляризация стромы яичников встречаются достоверно чаще. Во второй группе появление зреющего или доминантного фолликула указывает на то, что мультифолликулярность яичников носит функциональный характер, а это не есть классический поликистоз.

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