Transvaginal Echography in Assessing of Structures and Functional Changes in Polycystic Ovaries

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Abstract

Introduction: Chronic anovulation is the main cause of endocrine infertility. The synthesis of polycystic ovaries syndrome (PCOS) is a classic example of the complete absence of the process of maturation of follicles. The European Society for Reproductive Medicine and Human Embryology/The American Society for Reproductive Medicine, often called Rotterdam, includes a triad: hyperandrogenism, menstrual disorders and polycystic ovaries by ultrasonography. Ultrasonographic parameters used in the diagnosis of PCOS, still cause a lot of controversy.

Objective: To study the echographic semiotics of PCOS in a transvaginal triplex mode.

Materials and Methods: This cross-sectional clinical study was conducted at the Kharkov Medical Academy of Postgraduate Education and Institute of Problems of Endocrine Pathology the name of V. Ya. Danilevsky AMS of Ukraine during the period 2013 - 2016. 216 female with menstrual irregularities, aged 18 - 29 years were recruited in the study. Transvaginal echography (TVE) was performed on the 4th - 6th and 8th - 10th days of the menstrual cycle, and in the absence of menstruation on any day. All women had the ultrasound criteria of PCO: the presence of 12 or more 2 - 9 mm ovarian follicles and ovarian volume of more than 10 cm^3. In all women, the level of anti-Mullerian hormone (AMH), (FSH), luteinizing and follicle stimulating hormones, their ratio (LH/FSH), prolactin (P), 17-OH-progesterone was defined. Based on dynamic TVE and hormonal studies, polycystic ovaries (PCO) was diagnosed in 159 (73.6%) women, multifollicular ovaries (MFO) - in 57 (26.4%) women.

Results: Among the women with PCOS, the peripheral location of the ovaries was noted in 91 (57.2 ± 3.9%) cases, displaced in 78 (42.8 ± 3.9%) cases (P<0.01), in patients with PCO in 23 (40.4 ± 6.5%) and in 34 (59.6 ± 6.5%) cases (P < 0.05), among the healthy women in 27 (79,4 ± 6,9%) and in 7 (20,6 ± 6,9%) cases respectively (P < 0,001). An increase in the echogenicity of the stroma was recorded in 84 (52.8 ± 4.0%) women of the I group (P < 0,001), in 18 (31.6 ± 6.2%) women of the II group and in 3 (8.8 ± 4.9%) of the control group (CG).

The number of follicles within the limits of 13 - 15 was registered in 73 (45.9 ± 4.0%) of women of the I group, 41 (71.9 ± 6.0%) of women of the II group (P < 0.001), and more than 15 follicles - in 86 (54.1 ± 4.0%) and in 16 (28.1 ± 6.0%) women (P < 0.001), respectively.

In the group of PCOS, the average volume of the ovaries was 18.3 ± 3.7 cm^3), in the group of PCO – 12.4 ± 2.9 cm^3, respectively. 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.

The vascularization of the ovary stroma in the patients with PCOS was significantly more than in the PCO and CG. The average value of Vmax in the I group was 48.6 ± 8.9 cm/s, in the II group - 36.5 ± 7.2 cm/s, in reproducibly healthy women - 19.1 ± 4.7 cm/s, respectively (P1-3 < 0.001; P2-3 < 0.05). Parameters of RI in these groups were 0.48 ± 0.03; 0.54 ± 0.03 and 0.54 ± 0.03, respectively (P1-3 <0.05).

Conclusion:

1. Mixed type distribution of follicles, their number is more than 15 on the echographic section, the volume of the ovary is more than 14 cm^3, 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 increases the reliability of ultrasound PCOS criteria.

2. 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.

Keywords: Transvaginal Echography; Structures and Functional Changes in Polycystic Ovaries; Menstrual Irregularities

Introduction

Chronic anovulation is the main cause of endocrine infertility. The synthesis of polycystic ovaries syndrome (PCOS) is a classic example of the complete absence of the process of maturation of follicles.

In 1935, Stein and Leventhal were the first to describe a condition consisting of amenorrhea, obesity, and masculinizing symptoms that is now known as polycystic ovarian syndrome (PCOS) [1]. PCOS has a prevalence of 6.6% in women of reproductive age and affects 4 - 5 million women of reproductive age in the United States [2]. Although this condition is now recognized as the most common endocrine abnormality in women of reproductive age, there is still no universal consensus on diagnostic criteria for PCOS, and its etiology remains incompletely understood.

Already in 2003 in Rotterdam, at a symposium devoted to PCPA, it was decided to include in the diagnosis of PCOS echographic signs of polycystic ovarian changes [3], which caused controversy among researchers, as it expanded the number of patients who met the diagnosis of PCOS and allowed the creation of various phenotypic groups of patients [4,5]. The 2003 joint ESHRE/ASRM meeting in Rotterdam created a consensus definition for the polycystic ovary, which was reaffirmed by the Androgen Excess and PCOS Society in 2009 [2] and subsequently incorporated into American College of Obstetricians and Gynecologists guidelines [6]. According to the consensus definition, polycystic ovaries are present when one or both ovaries demonstrate 12 or more follicles measuring 2 - 9 mm in diameter, or the ovarian volume exceeds 10 cm^3.

In most women, management includes lifestyle modifications towards weight loss. Oral hypoglycaemic agents help to improve insulin sensitivity; some women start to have regular periods with the use of metformin only [7]. The question of what constitutes an abnormally large ovarian volume has been the subject of considerable investigation. Jonard S., *et al.* (2005) selected as the threshold volume for a polycystic ovary volume of 10 cm^3 [8,9]. The diagnosis is made on the combined clinical, biochemical and sonographic grounds. The revised 2003 ASRM/ESHRE Rotterdam consensus criteria require two of the following three criteria for the diagnosis: 1) oligo- or anovulation; 2) hyperandrogenism (clinical or biochemical); 3) follicle count on imaging [10]. The European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine criteria, often called Rotterdam, includes various phenotypes based on a combination of any two of the three findings of hyperandrogenism, menstrual irregularity, and polycystic ovaries on ultrasound [10]. However, a wealth of literature agrees that women may present an appearance of PCO at ultrasound without any sign of androgen excess, although with indicators of ovarian dysfunction [11].

Luteinizing hormone (LH) is usually increased and follicle stimulating hormone (FSH) can be normal or decreased. Normally premenopausal LH:FSH is 1:1. In PCOS it may be > 2:1 or > 3:1. Anti-Müllerian hormone (AMH) levels are generally increased [12]. The estimated prevalence of PCO is ~6% (range 4 - 8%) of women of reproductive age but this varies (up to 20%) depending on the diagnostic criteria used [13].

Transvaginal ultrasound is considered the gold standard in the diagnosis of polycystic ovaries. Features include: 1) presence of > 25 follicles per ovary (superseding the earlier Rotterdam criteria of 12 or more follicles); 2) individual follicles are generally similar in size and measure 2 - 9 mm in diameter; 3) peripheral distribution of follicles; this can give a "string of pearls" appearance; 4) background ovarian enlargement (volume greater than 10 cm^3); 5) central stromal brightness +/-prominence [14]. Only one ovary fitting these criteria is sufficient to define PCO. If there is evidence of a dominant follicle (>10 mm) or a corpus luteum, the scan should be repeated during the next cycle [15].

Most researchers tend to believe that the volume of ovaries and the counting of antral follicles should be necessarily included in the list of diagnostic criteria for PCOS. At present, it has been established that in women with PCOS the serum AMH level increases [16,17].

Materials and Methods

This cross-sectional clinical study was conducted at the Kharkov Medical Academy of Postgraduate Education and Institute of Problems of Endocrine Pathology the name of V. Ya. Danilevsky AMS of Ukraine during the period 2013 - 2016. 216 female with menstrual irregularities, aged 18 - 29 years were recruited in the study. All women had a sexual life, 27 of them were married, 199 - unmarried. Females with diabetes mellitus, thyroid and adrenal disorders and on hormonal replacement therapy (HRT) were excluded from the study. Menstrual irregularities were defined as; chronic anovulation as amenorrhea of 3 months duration or oligomenorrhea as intermenstrual 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 hormone (AMH), (FSH), luteinizing and follicle stimulating hormones, their ratio (LH / FSH), prolactin (P), 17-OH-progesterone was defined.

All women had the ultrasound criteria of PCO: the presence of 12 or more 2-9 mm ovarian follicles and ovarian volume of more than 10 cm^3. Hirsutism was registered in 27 (12.5%) women with polycystic ovaries. The comparative group (CG) consisted of 34 reproductively healthy women aged 19 - 25 years with a regular menstrual cycle, normal ovarian size and cyclic changes in them.

Transvaginal echography (TVE) was performed 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, follicles counting 2 - 9 mm.

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.

Results

In 159 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 - with polycystic ovary syndrome (PCOS). In 57 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 23 of them there were disorders of the menstrual cycle. Dynamic observation in 41 cases recorded a ripening follicle, in 13 cases - the dominant follicle, in three - the yellow body. In 11 women, luteinization of the neovulatory follicle was noted and in 3 - insufficiency of the luteal phase. These women made up the II group - multifollicular ovaries (MFO). The control group (CG) consisted of 34 healthy women with the number of 2 - 9 mm follicles less than 10 pieces on the ultrasonographic section, the ovary volume less than 10 cm3, the normal menstrual cycle and physiological changes (Table 1).

Ultrasonographic parameters	PCOS (n = 159) Group I	MFO (n = 57) Group II	The healthy women (n = 34) CG
Peripheral arrangement of follicles	91 (57,2 ± 3,9%)	23 (40,4 ± 6,5%)	27 (79,4 ± 6,9%)
Displaced arrangement of follicles	78 (42,8 ± 3,9%)	34 (59,6 ± 6,5%)	7 (20,6 ± 6,9%)
Increased echogenicity of the stroma	84 (52,8 ± 4,0%)	18 (31,6 ± 6,2%)	3 (8,8 ± 4,9%)
Number of follicles 13-15	73 (45,9 ± 4,0%)	41 (71,9 ± 6,0%)	-
Number of follicles > 15	86 (54,1 ± 4,0%)	16 (28,1 ± 6,0%)	-
Ovaries volume < 10 cm^3	-	17 (29,8 ± 6,1%)	34 (100,0 ± 2,9%)
Ovaries volume 11 - 14 cm^3	85 (53,5 ± 4,0%)	29 (50,9 ± 5,9%)	-
Ovaries volume > 14 cm^3	74 (46,5 ± 4,0%)	11 (19,3 ± 5,2%)	-
Average volume of ovary (cm^3)	18,3 ± 3,7 P1-3 < 0,01	12,4 ± 2,9 P2-3 < 0,01	6,1 ± 1,8
Enhanced vascularization of ovarian stroma	63 (39,6 ± 3,9%) P1-2 < 0,01 P1-3 < 0,001	12 (21,1 ± 5,4%) P2-3 < 0,05	-
Vmax, cm/c	48,6 ± 8,9 P1-3 < 0,001	36,5 ± 7,2 P2-3 < 0,05	19,1 ± 4,7
IR	0,48 ± 0,03 P1-3 < 0,05	0,54 ± 0,03	0,59 ± 0,04

Table 1: *Ultrasonographic parameters of ovaries in 4-6th days of the menstrual cycle in the range of follicles 2-9 mm.*

As can be seen from the table, among the women with polycystic ovaries, the peripheral location of the ovaries was noted in 91 (57.2 ± 3.9%) cases, displaced in 78 (42.8 ± 3.9%) cases (P < 0.01), in patients with MFO, on the contrary, in 23 (40.4 ± 6.5%) and in 34 (59.6 ± 6.5%) cases, (P < 0.05), among the healthy women in 27 (79,4 ± 6,9%) and in 7 (20,6 ± 6,9%) cases respectively (P < 0,001).

An increase in the echogenicity of the stroma was recorded in 84 (52.8 ± 4.0%) women of the I group (P < 0,001), in 18 (31.6 ± 6.2%) women of the II group and in 3 (8.8 ± 4.9%) of the control group.

The number of follicles within the limits of 13-15 was registered in 73 (45.9 ± 4.0%) of women of the I group, 41 (71.9 ± 6.0%) of women of the II group (P < 0.001), and more than 15 follicles - in 86 (54.1 ± 4.0%) and in 16 (28.1 ± 6.0%) women (P < 0.001), respectively.

The volume of the ovary less than 10 cm^3 in the II group was noted in 17 (29.8 ± 6.1%) 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 85 (53.5 ± 4.0%), more than 14 cm^3 in 74 (46.5 ± 4.0%) cases, in 29 (50.9 ± 5.9%) cases of II group respectively.

Enhanced vascularization of ovarian stroma was recorded in 63 (39,6 ± 3,9%) cases of I group, in 12 (21,1 ± 5,4%) cases of II group respectively.

In 27 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 7 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 (Figures 1, 2).
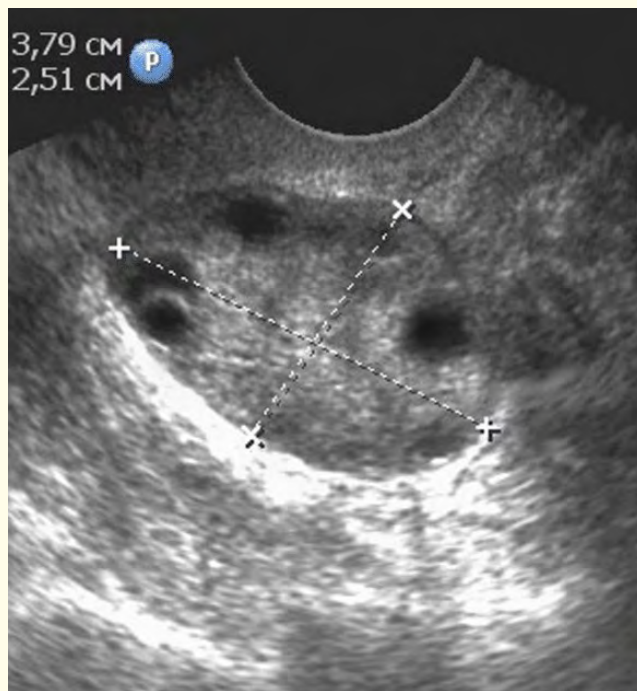
Figure 1: Normal ovary of the healthy women aged 21 years in the early proliferative phase. Several follicles of 4-6 mm are located along its perimeter.
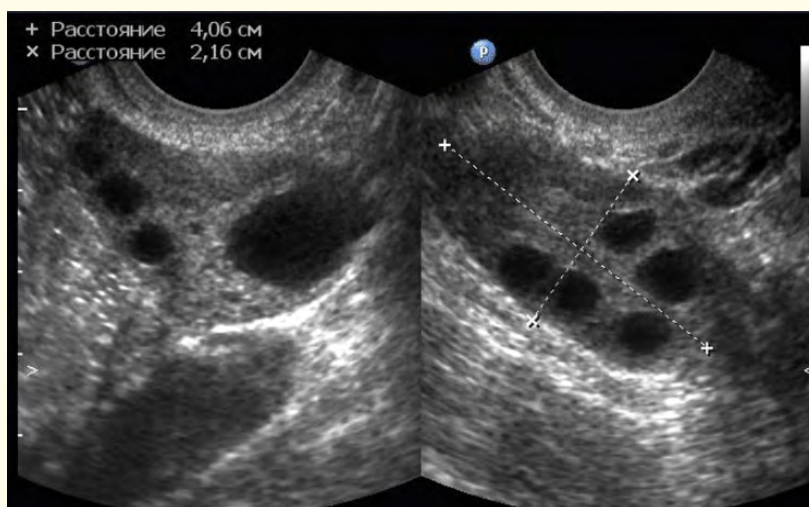

Figure 2: Normal ovaries. In the middle proliferative phase, the ripening follicle is visualized in the right ovary.

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 (Figure 3-5). 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 (Figure 6). In the II group of patients, in contrast to group I, the ripening or dominant follicle in the ovary was recorded (Figures 3-7).

Figure 3: 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.

Figure 4: 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.
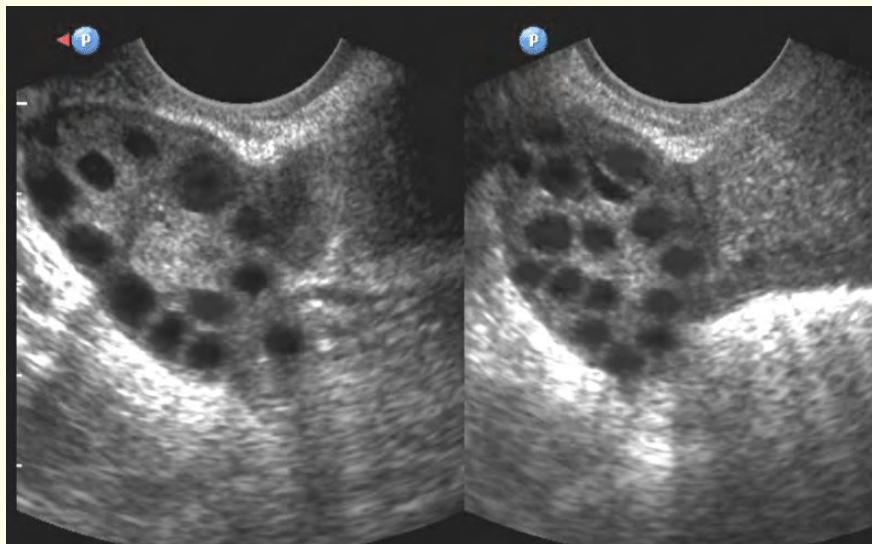
Figure 5: PCOS. Peripheral type of localization of the follicles in the right ovary, mixed type – in left ovary.
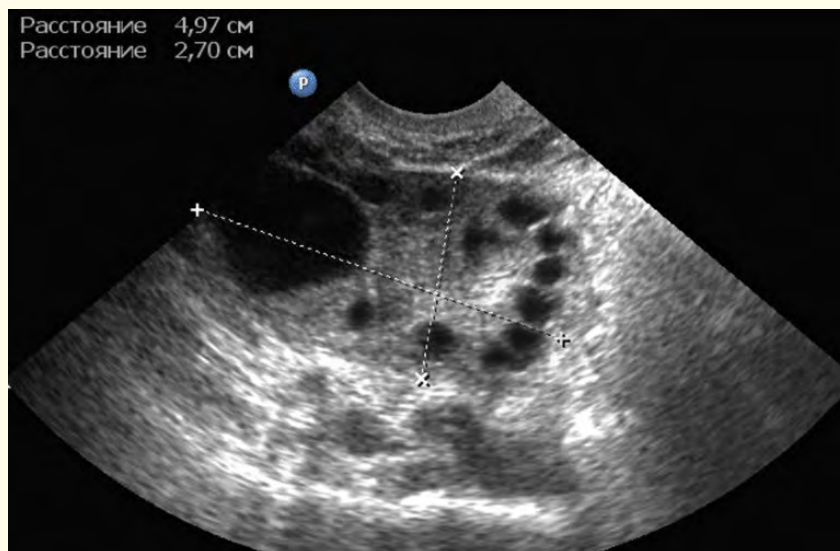

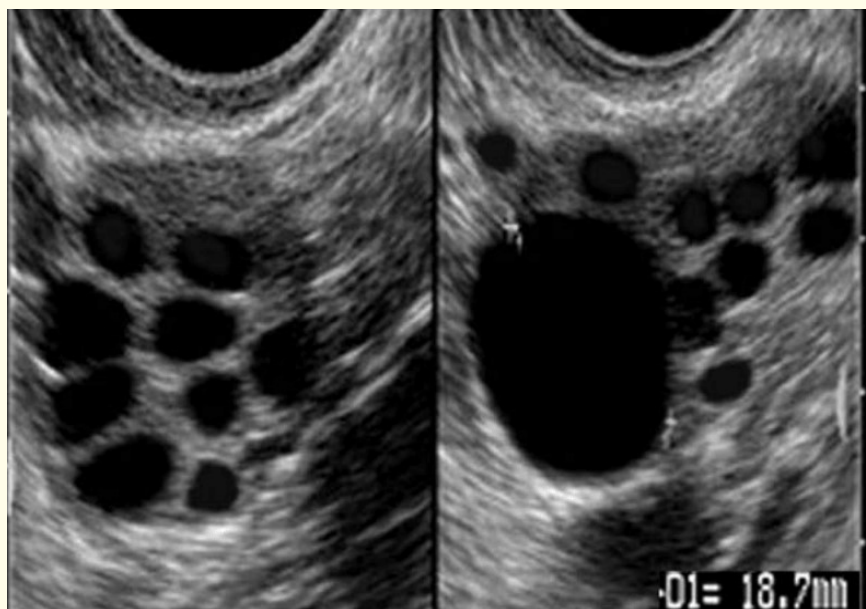*Figure 6: Polycystic ovaries. The ripening follicle is visualized.*

Figure 7: Multifollicular ovaries. In the left ovary, the dominant follicle is visualized.

In the I group of women, the volume of the ovaries varied within 11.5 - 24.3 cm^3 (an average of 18.3 ± 3.7 cm^3), and in the II group - 8.9 - 15.2 cm^3 (an average of 12.4 ± 2.9 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 (Figure 8). 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 (V_{max}) 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 63 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 (Figures 9, 10).
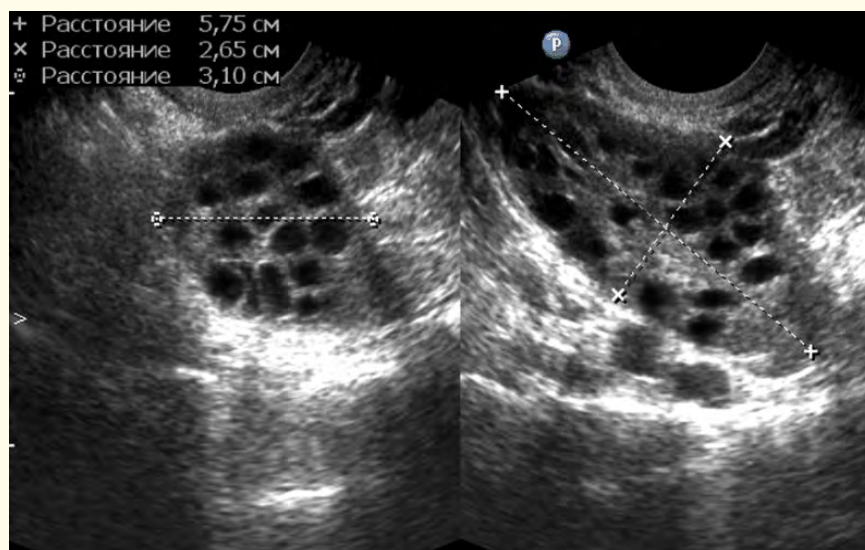

Figure 8: PCOS. The mixed type of follicles localization. The volume of the ovary is 24.6 cm3 (5.75 x 2.65 x 3.1 cm x 0.52).

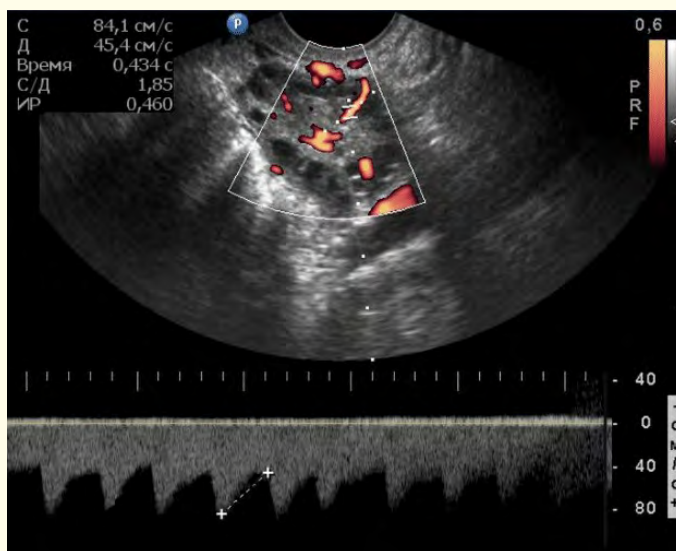*Figure 9: PCOS. Enhanced vascularization of the ovary stroma.*

Figure 10: PCOS. The maximum systolic blood flow velocity in the stroma is 84 cm/s, RI – 0,46.

The average value of Vmax in the I group was 48.6 ± 8.9 cm/s, in the II group - 36.5 ± 7.2 cm/s, in reproducibly healthy women - 19.1 ± 4.7 cm/s, respectively (P1-3 < 0.001; P2-3 < 0.05). Parameters of RI in these groups were 0.48 ± 0.03; 0.54 ± 0.03 and 0.54 ± 0.03, respectively (P1-3 < 0.05).

Discussion

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 [4,5]. 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 57 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 [18]. Among our patients with PCOS, peripheral distribution of follicles was noted only in 57.2% of cases, and in 42.8% - a mixed distribution.

According to the results of Azziz R., *et al.* (2006), hirsutism was observed in 29% of cases. Among our patients this clinical sign was noted no more than 12% of cases.

An increase in the level of anti-Mullerian hormone was noted in no more than 70% of women with ultrasound PCOS criteria [19].

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 declare that they have no conflicts of interest.

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