Significance of Doppler ultrasonography in the diagnosis of polycystic ovary syndrome

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Summary

Objective: To investigate the importance of transvaginal color Doppler ultrasonography of uterine and intraovarian arteries in the clinical diagnosis of polycystic ovary syndrome (PCOS).

Material & Method: This study was planned as a cohort, controlled, prospective study. A total of 80 participants (40 with PCOS and 40 as a control group) were enrolled in the study. A Doppler system with a 6.0 MHz transvaginal probe was used when performing ultrasonography (USG) and Doppler examinations. Ovarian size and volume, number of follicles and stromal echogenity were evaluated by USG. Doppler flow studies were targeted to uterine and intraovarian arteries and the pulsatility index (PI) was assessed. The concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (T) and dihydroepiandrostenedione sulphate (DHEAS) were measured by immunometric methods.

Results: The mean values of the number of follicles and the ovarian volume of both the right and left ovaries were higher in the group with PCOS than the control group ($p < 0.05$). The mean PI values of the right and left ovaries, respectively, were 0.84 ± 0.23 and 1.09 ± 1.17 in the group with PCOS, and 0.88 ± 0.14 and 0.92 ± 0.15 in the control group. The mean PI values of the right and left uterine arteries, respectively, were 3.25 ± 0.98 and 3.33 ± 1.12 in the group with PCOS, and 3.17 ± 0.93 and 3.2 ± 1.38 in the control group ($p > 0.05$). The correlation analysis of the ovarian volume, the number of follicles and Doppler parameters revealed that there was a positive correlation and statistically significant difference between the right ovarian volume and right uterine artery PI in the group with PCOS and the left ovarian volume and left uterine artery PI in the control group ($p > 0.05$).

The mean stromal PI of the ovarian and uterine arteries were 0.96 ± 0.61 and 3.29 ± 1.02 in the group with PCOS and 0.9 ± 0.12 and 3.19 ± 1.14 in the control group, respectively ($p > 0.05$). In the group with PCOS, the mean ovarian volume and the mean number of follicles were 11.46 ± 4.43 and 13.91 ± 4.11, respectively, whereas they were 7.63 ± 2.44 and 5.55 ± 2.34 in the control group ($p < 0.05$).

Conclusion: It is not beneficial to use color Doppler transvaginal ultrasonography in the clinical diagnosis of patients with PCOS.

Key words:

Introduction

PCOS is known as the most common cause of anovulation in women admitted with irregular ovulation and subfertility. It was first described by Stein and Leventhal in 1935 [1]. All patients with only a history of oligomenorrhea, hirsutism, enlarged and polycystic ovaries were accepted as having PCOS for years. It is useful to not be limited with the terminology: polycystic ovary syndrome or disorder. This problem should be considered as a continuous anovulation status exhibiting different clinical symptoms due to different etiologies [2].

After the introduction of USG to gynecology, the characteristic appearance of PCOS was revealed [3]. In clinical practice, ultrasonographic evaluation has become the first choice to make a diagnosis of PCOS instead of laparoscopy which has been thought to be the most important diagnostic procedure for years. Developments in transvaginal endosonography have led us monitor the size and shape of the ovaries together with the follicles and the stroma. Color Doppler examination enables us to detect stromal vascularization of the ovaries [1].

The goal of this study was to investigate the importance of color Doppler transvaginal examination of the uterine and intraovarian arteries in diagnosing patients with PCOS.

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Material and Method

This study was planned as a cohort controlled prospective study and was conducted between August 2001 and August 2002 at Zeynep Kamil Gynecologic and Pediatric Training and Research Hospital. A total of 80 subjects (40 with PCOS and 40 as the control group) were enrolled to the study.

In making the diagnosis of PCOS; clinical history (irregular menstruation, hirsutism and infertility), hormonal evaluation and typical ultrasonographic findings (> 5 follicles, all follicles less than 10 mm, peripheral spread of the follicles, increased stromal echogenity and volume > 8 ml) were used. Patients in the control group were randomly chosen; they had normal values of FSH and LH, and menstruated regularly.

Patients who had not received any hormonal medication in the previous three months, smoked less than ten cigarettes per day and who had blood pressure below 140/90 were found eligible. Subjects who had a menstrual cycle more than 35 days were accepted as oligomenorrheic. Oligomenorrheic and control patients were evaluated in the early follicular phase (3-5 days of the cycle), whereas amenorrheic patients were randomly assessed. The Ferriman-Gallwey scoring system was used to assess hirsutism. Patients who had a score above 8 were considered to have hirsutism.

A color Doppler system (TOSHIBA Powervision 7000) with a 6.0 MHz transvaginal probe was used in the ultrasonographic and Doppler examinations: the size and the volume of the ovaries, the number of follicles and stromal echogenity (0: normal, 1: moderately increased, 2: severely increased) were assessed [4].

Doppler flow indices were examined in the uterine and intraovarian arteries after at least 15 minutes of rest and full emptiness of the bladder to minimize external impacts on pelvic blood flow. A 50 Hz filter was used to get rid off the low frequency signals arising from the venous walls. The stromal region far from the surface of the ovary was examined. Color flow examination of the rising branch of the uterine artery was performed at the longitudinal axis, lateral to the cervix at the level of the internal os. The pulsalility index (PI: maximum systolic velocity – diastolic velocity/mean velocity) was used to assess uterine and intraovarian arteries by transvaginal color Doppler USG. There was no significant difference between the right and left uterine artery PI or the right and left intraovarian artery PI, hence mean PI was used for both uterine and intraovarian arteries.

Ultrasonographic examination and Doppler analysis were performed by a single observer. Hormonal status of the patients was not known by the observer. Peripheral blood samples were drawn on the same day as ultrasonographic and Doppler examinations between 9 and 11 am.

LH, FSH, total testosterone (T), free androgenic index (FAI) and DHEAS concentrations were studied by immunometric methods (chemiluminescent, Immulite One). The LH/FSH ratio was also calculated.

The SPSS (Statistical Package for Social Sciences) version 10.0 was used for statistical analysis. The Student's t-test was used to compare the general demographic characteristics: number of follicles, volume of the ovaries, Doppler indices. Homogenization was assessed with Levene's test. Pearson's correlation coefficient was calculated to show the correlation between ovarian volume and the number of follicles with uterine and ovarian artery Doppler indices. A p value below 0.05 was considered statistically significant.

Results

There was no statistical significant difference in terms of age, gravida and parity. The mean age of the patients was 25.4 ± 5.16 years in the group with PCOS and 25.5 ± 4.11 in the control group (Table 1).

The mean Ferriman Gallwey score, used to classify hirsutism, was 10.15 ± 4.38 in the group with PCOS and 1.1 ± 2.35 in the control group ($p < 0.05$). The mean length of the cycles was 60.23 ± 28.63 days and 30.45 ± 4.02 days in the group with PCOS and in the control group, respectively ($p < 0.05$). The mean body mass index (BMI) was 25.96 ± 4.16 kg/m^2 in the group with PCOS, whereas it was 23.94 ± 3.61 kg/m^2 in the control group ($p < 0.05$) (Table 1).

The FSH (mIU/ml) and PRL (ng/ml) levels were similar between the groups ($p > 0.05$), however other hormonal parameters, LH (mIU/ml), testosterone (nmol/l), the FAI and LH/FSH ratio showed a statistically significant difference. The mean levels of these parameters were 7.6 ± 2.13, 3.33 ± 1.41, 6.71 ± 4.01 and 2.01 ± 0.73 in the group with PCOS and 4.84 ± 2.86, 2.57 ± 0.86, 4.67 ± 1.17 and 1.06 ± 0.45 in the control group, respectively ($p < 0.05$) (Table 1).

The mean number of follicles of the right and left ovary, respectively, was 13.87 ± 4.35 and 13.95 ± 4.39 in the group with PCOS and 5.5 ± 2.53 and 5.6 ± 2.44 in the control group ($p < 0.05$). The mean volume of the right and left ovary respectively was, 11.75 ± 5.3 and 11.16 ± 4.03 in the PCOS group and 8.33 ± 3.7 and 6.93 ± 2.68 in the control group ($p < 0.05$) (Table 2).

PIs of the right and left intraovarian artery were 0.84 ± 0.23 and 1.09 ± 1.17 in the group with PCOS and 0.88 ± 0.14 and 0.92 ± 0.15 in the control group, respectively. The mean PI of the right and left uterine artery, respectively, was 3.25 ± 0.98 and 3.33 ± 1.12 in the group with PCOS and 3.17 ± 0.93 and 3.2 ± 1.38 in the control group. There was no statistically significant difference found in terms of PI between the two groups (Table 2).

In the PCOS group, there was statistical significance and a positive correlation between the right ovarian volume with the right uterine PI. There was also a positive correlation between the number of follicles and volume of the right ovary with the right uterine artery PI and between the left ovarian volume with the left uterine artery PI ($p < 0.05$) (Table 3).

The mean ovarian stromal artery PI and mean uterine artery PI were detected as 0.96 ± 0.61 and 3.29 ± 1.02 in the group with PCOS and 0.9 ± 0.12 and 3.19 ± 1.14 in the control group, respectively ($p > 0.05$) (Table 4).

There was a statistically significant difference in terms of ovarian volume and number of follicles between the two groups ($p < 0.05$) (Table 4); 11.46 ± 4.43 and 13.91 ± 4.11 in the PCOS group and 7.63 ± 2.44 and 5.55 ± 2.34 in the control group, respectively.

Table 1. — *Comparison of demographic and hormonal data of the groups.*

	PCOS (no. 40)		Control (no. 40)		p	Normal valves
	Ort.	SD	Ort.	SD		
Age (year)	25.4	5.16	25.5	4.11	0.924	
Gravidity	1.15	1.46	1.5	1.3	0.261	
Parity	0.85	1.14	1.1	0.96	0.292	
Ferriman Gallwey score	10.15	4.38	1.1	2.35	0.0005*	
Length of the cycle (gün)	60.23	28.63	30.45	4.02	0.0005*	28 ± 7
BMI (kg/m^2)	25.96	4.16	23.94	3.61	0.023*	20-25
FSH (mIU/ml)	4.11	1.42	4.66	2.01	0.164	2.8-11.3
LH (mIU/ml)	7.6	2.13	4.84	2.86	0.0005*	1.1-11.6
Testosterone (nmol/l)	3.33	1.41	2.57	0.86	0.005*	2.2-4.2
FAI	6.71	4.01	4.67	1.17	0.003*	< 8.5
Prolaktin (ng/ml)	14.46	4.16	12.21	6.71	0.076	2.7-14.6
LH/FSH	2.01	0.73	1.06	0.45	0.0005*	1.2-2

*Statistically significant: $p < 0.05$; FAI: free androgenic index.

Table 2. — *Comparison of the two groups in terms of ovarian volume, number of follicles and color Doppler parameters.*

	PCOS (no. 40)		Control (no. 40)		p
	Ort.	SD	Ort.	SD	
Right ovary follicles (no.)	13.87	4.35	5.5	2.53	0.0005*
Left ovary follicles (no.)	13.95	4.39	5.6	2.44	0.0005*
Right ovary volume	11.75	5.3	8.33	3.7	0.001*
Left ovary volume	11.16	4.03	6.93	2.68	0.0005*
Right ovary PI	0.84	0.23	0.88	0.14	0.347
Left ovary PI	1.09	1.17	0.92	0.15	0.372
Right uterine artery PI	3.25	0.98	3.17	0.93	0.732
Left uterine artery PI	3.33	1.12	3.2	1.38	0.640

*Statistically significant: $p < 0.05$

Table 3. — *Correlation analysis of ovarian volume, number of follicles and Doppler parameters of the right and left ovaries.*

	PCOS (no. 40)		Control (no. 40)	
	r	p	r	p
Right ovary volume/ Right ovary PI	0.055	0.734	-0.258	0.108
Right ovary volume/ Right uterine artery PI	0.353	0.025*	0.005	0.973
Right ovary follicles/ Right ovary PI	0.141	0.385	-0.111	0.496
Right ovary follicles/ Right uterine artery PI	0.281	0.079	0.350	0.027*
Left ovary volume/ Left ovary PI	-0.159	0.327	0.061	0.710
Left ovary volume/ Left uterine artery PI	0.221	0.170	0.421	0.007*
Left ovary follicles/ Left ovary PI	-0.110	0.499	-0.183	0.259
Left ovary follicles/ Left uterine artery PI	0.200	0.216	0.242	0.132

*Statistically significant: $p < 0.05$

Table 4. — *Comparison of the mean OV, OS-PI, UA-PI and number of OF of the two groups.*

	PCOS (no. 40)		Control (no. 40)		p
	Ort.	SD	Ort.	SD	
OS-PI	0.96	0.61	0.9	0.12	0.523
UA-PI	3.29	1.02	3.19	1.14	0.672
OV-cm^3	11.46	4.43	7.63	2.44	0.0005*
OF	13.91	4.11	5.55	2.34	0.0005*

*Statistically significant: $p < 0.05$; OV: Ovarian volume; OS-PI: Ovarian stromal artery pulsatility indices; UA-PI: Uterine artery pulsatility indices; OF: Ovarian follicles.

Discussion

There have been many evaluations in various populations to find out the true prevalence of PCOS since the development of ultrasonographic examination [5, 6]. Nevertheless, it has been shown that 42% of the cases could not be sufficiently monitored anatomically by transabdominal USG in recent years [6].

Development of transvaginal probes has led to the examination of ovarian structures in a detailed way. The correlation between histologic findings and laparoscopic measurements with the transvaginal approach of USG is well established, hence, transvaginal ultrasonography has become the most sensitive method in diagnosing patients with PCOS when compared to clinical and endocrinologic findings [7-9]. What is beyond, as has been shown in recent years, is that Doppler analysis is a useful additional diagnostic method in PCOS [10-12].

In order not to affect Doppler flow studies, patients with no previous medication, nonsmokers or patients smoking less than ten cigarettes per day and normotensive patients were enrolled in our study. We aimed to minimize the variables to obtain healthy results i.e., patients menstruating were evaluated in the early follicular phase, blood samples were drawn at the same time of day for hormonal assessment and consequent Doppler studies were performed by the same observer.

There was no statistically significant difference between the two groups of patients in terms of age, gravida and parity. Ages of all patients were similar and within the midreproductive period, thus with this randomization the affect of age over ovarian function was minimized.

The hallmarks of PCOS are chronic anovulation and hyperandrogenism leading to increased duration of the menstrual cycle and hirsutism (rise in Ferriman Gallwey score). Our findings on these parameters show similarities with the studies in the literature [10, 13].

When BMI was compared between the two groups, the mean BMI of patients with PCOS was significantly higher ($p < 0.05$). In the literature, there are similar studies with some detecting no difference in BMI between two groups [14, 15] and some supporting [16] the present study.

FSH levels were found to be similar in both groups. There have not been any contrary results in the literature [10, 13, 14, 16]. In patients with PCOS, we detected higher levels of LH, testosterone, FAI and LH/FSH ratio than for the control group ($p < 0.05$). Elevation of these parameters is due to hyperplasia of teca and stromal cells and accompanying LH hypersecretion in the follicular phase of patients with PCOS. There are many studies supporting these findings [10, 13, 15, 16].

In patients with PCOS, the mean number of follicles of both ovaries and the mean ovarian volume were noted to be higher than for the control group. In the present study, there were approximately five to six follicles (no more than 8 follicles) in the control group. When making the diagnosis of PCOS, more than ten follicular cysts of less than 10 mm in diameter is a diagnostic criterion. Also increased stromal echogenity supports the diagnosis [9].

In general, the ovaries are bilaterally enlarged due to an increased number of follicles and stromal cell hyperplasia. Measurements of ovarian volume may reveal different results when included as a diagnostic criterion considering the difficulties of exposing three different orthogonal planes of the ovaries. In our study, the mean ovarian volumes were 11.46 ± 4.43 cm^3 in the group with PCOS and 7.63 ± 2.44 cm^2 in the control group. Since there were measurements up to 12 cm^3 in the control group, our opinion is that 10 cm^3 should be used as the cutoff value as a diagnostic criteria instead of 8 cm^3 [9, 17]. Otherwise, the rate of false positivity will increase and the sensitivity will decrease. For all participants, we investigated if there was any correlation among Doppler parameters, number of follicles and ovarian volume. We found that in the group with PCOS there was only one positive and significant correlation – between right ovarian volume and PI of the right uterine artery. However, PI of the left uterine artery and left ovarian volume in the control group also demonstrated the same correlation suggesting that this finding was not specific to PCOS. There was also no correlation between Doppler analysis and number of follicles ($p > 0.05$).

When we compared the two groups in terms of mean ovarian volume (OV), PI of the ovarian stroma (OS-PI), PI of the uterine artery (UA-PI) and the number of ovarian follicles (OF), there was no significant difference between OS-PI and UA-PI values ($p > 0.05$). Parallel with our previous results, there was a significant difference between the mean OV and OF. Although there are many studies noting high values of UA-PI in patients with PCOS [10, 14, 15], opposite results have been reported in recent years [18]. The mean OV was noted as 12-13 cm^2 in studies supporting an increase in OV in PCOS, which is similar to our study.

In 1995, Battaglia *et al.* [10] observed a high UA-PI with a low resistance flow (RI: 0.55 ± 0.05) in the stromal veins of ovaries in patients with PCOS and reported that these two parameters were negatively correlated with each other. In the same study, PI was positively and RI was negatively correlated with the LH/FSH ratio; androstenedione and UA-PI was also correlated. They concluded that uterine and intraovarian artery transvaginal color Doppler examination, in addition to traditional endocrinologic and ultrasonographic assessments, is useful in making a diagnosis of PCOS.

In another study, conducted in 1999, Battaglia *et al.* [13] established two groups according to the number of follicles in patients with PCOS (5-10 and > 10 follicles), and performed Doppler studies to obtain hormonal parameters. In the group with more follicles, they reported that the levels of LH, LH/FSH ratio, androstenedione and ovarian volume were higher. Doppler studies showed high UA-PI values which positively correlated with androstenedione levels. According to the number of follicles UA-PI increased, whereas on the contrary OS-PI values decreased and showed a negative correlation with LH/FSH ratio. Although the method of the study was different from ours, results showing that hormonal parameters were positively correlated with an increased number of follicles and ovarian volume are similar. Another conclusion arising from this study was that clinical abnormalities were more obvious when the number of microcysts and ovarian volume increased.

Ajossa *et al.* [14] evaluated a total of 88 cases and detected that the levels of LH, total T, free T and androstenedione were significantly different in patients with PCOS (63 cases). The mean UA-PI of the patients with PCOS (2.97 ± 0.9) was significantly higher than the control group (1.89 ± 0.2) ($p < 0.05$). They divided the patients into three groups ($PI < 2$, $2 < PI < 3$ and $PI > 3$). The rates of the patients with PCOS and the control group were 7% and 40%, respectively, when the PI value was below 2 ($PI < 2$). When PI was between 2 and 3 ($2 < PI < 3$) the rates were 59% and 40%, respectively, and in the last group the rates were 34% and 20%, respectively, when the PI value was over 3 ($PI > 3$). In patients with PI values over 3, BMI and DHEAS levels were found to be higher and it was noted that there was a direct correlation between UA-PI and DHEAS levels [14]. The authors concluded that high BMI and DHEAS levels may affect UA-PI values.

In a study conducted in 1999, Dolz *et al.* [15] compared patients with PCOS (65 cases) with a control group (25 cases) in terms of hormonal/clinical parameters and ultrasonographic findings. In patients with PCOS, the levels of testosterone, LH, DHEAS, androstenedione and LH/FSH were found to be higher ($p < 0.001$). The ovarian area, stromal thickness, number of follicles, UA-PI and RI values were also higher in the group with PCOS than in the control group ($p < 0.001$). In the same study, subjects were divided in two groups (according to the presence of obesity) and the levels of LH, LH/FSH, insulin, UA-PI and RI were detected to be significantly different between the two groups ($p < 0.05$). However, ovarian stromal vascularization showed no difference ($p > 0.05$).

In 2001, Resende *et al.* [18] compared 24 patients with PCOS with 22 ovulatory women and similar to our study they reported that although there was an increase in ovarian stromal vascularization, OS-PI values were not statistically different between patients with PCOS and the control group ($p < 0.001$). There was no correlation between UA-PI values with testosterone and androstenedione levels. Unlike the study by Dolz *et al.*, the authors showed that the mean UA-PI value did not change when obesity was a factor ($p > 0.05$).

One hypothesis on this subject is that the increased vascular appearance and blood flow in ovarian stroma may be responsible for the increased risk of ovarian hyperstimulation syndrome. Since stromal hyperechogenity is a subjective parameter, investigators should be directed to find out an objective and confident method for stromal analysis [16]. As ultrasonographic monitorization develops, the stromal characteristics will be more important than the follicular patterns in making a diagnosis of PCOS [4, 9, 19]. Newly developed computerized USG systems are useful in making objective comparisons on ovarian area and volume measurements. It has been thought that three-dimensional USG will be used in many clinical areas of gynecology and obstetrics in the near future [16].

The increase in the number of follicles and stromal hyperplasia seen in patients with PCOS, leads to an enlargement of the ovaries and higher ovarian volume. This finding was also evaluated in our study, and yet there is not any common concept on the cutoff value for ovarian volume.

Conclusion

When the prevalence and the heterogenicity of PCOS are taken into consideration, future studies should be conducted with a sufficient number of participants, and careful attention should be paid to the varying clinical findings when making a diagnosis of PCOS.

Even though there are concepts that color Doppler studies are beneficial in making a diagnosis of PCOS in the literature, there are different results in various patient groups due to the heterogenity of this syndrome. In our opinion, the use of color Doppler USG has no significant value in the clinical diagnosis of PCOS unless further studies provide strict data on this syndrome.

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