# Physiology

## **Characterization of Normal and Polycystic Ovaries Using Three-Dimensional Power Doppler Ultrasonography**

I. Y. Järvelä,<sup>1,2,5</sup> H. D. Mason,<sup>3</sup> P. Sladkevicius,<sup>4</sup> S. Kelly,<sup>2</sup> K. Ojha,<sup>2</sup> S. Campbell,<sup>2</sup> and G. Nargund<sup>2</sup>

Submitted April 9, 2002; accepted June 19, 2002

**Purpose:** To evaluate the characteristics of polycystic compared to normal ovaries using threedimensional (3-D) power Doppler ultrasonography.

*Methods*: We recruited 42 volunteers, all of whom were commencing IVF treatment. Each patient was examined in the cycle preceeding the start of drug therapy during the late follicular phase. If eight or more subcapsular follicles of 2–8 mm in diameter in one two-dimensional (2-D) plane were detected in either of the ovaries, the patient was categorized as having polycystic ovaries (PCO); otherwise the ovaries were considered normal. The parameters examined were volume of the ovary, vascularization index (VI), flow index (FI), vascularization flow index (VFI), and mean greyness (MG). In addition, the ovary was arbitrarily divided into cortex and stroma, and thereafter volume, VI, FI, VFI, and MG were calculated for these two regions. *Results*: Twenty-eight women had normal ovaries and 14 had PCO. The comparison between normal and PCO showed that as a group the PCO were larger, without any differences in VI, FI, VFI, or MG. In patients with PCO, the right ovary was larger than the left one. In patients with normal ovaries, FI was higher on the left side. Division into cortex and stroma revealed that there were no differences in cortical or stromal VI, FI, VFI, or MG between normal and PCO on either side.

**Conclusions:** The ovaries defined as polycystic were larger than normal ovaries, but there was no difference in the echogenicity of the stroma between polycystic and normal ovaries. We were also unable to demonstrate that the polycystic ovarian stroma was more vascularized than the stroma in the normal ovaries.

**KEY WORDS:** Three-dimensional ultrasound; three-dimensional power Doppler; transvaginal color Doppler; transvaginal ultrasound.

## **INTRODUCTION**

The ultrasonographic criterion for polycystic ovaries (PCO) was first defined by Adams *et al.* 

(1) using transabdominal ultrasonography. The typical polycystic pattern described was the presence of either multiple cysts (10 or more) from 2–8 mm in diameter distributed evenly around the ovarian periphery with an increased amount of stroma, or less commonly, multiple small cysts 2–4 mm in diameter distributed throughout abundant stroma (1,2). Polycystic ovaries were also found to be larger than normal ovaries. In addition to these ultrasonographic signs, increased stromal echogenity is often considered typical for PCO (3,4) and even thought to be an extremely specific criterion for making the diagnosis (5). Nevertheless, it has been acknowledged that its recognition is highly subjective (6). Besides these

<sup>&</sup>lt;sup>1</sup> Department of Obstetrics and Gynaecology, Oulu University Hospital, Oulu, Finland.

<sup>&</sup>lt;sup>2</sup> Diana, Princess of Wales Centre for Reproductive Medicine, Academic Department of Obstetrics and Gynaecology,

St George's Hospital Medical School, London, United Kingdom.
<sup>3</sup> Academic Department of Obstetrics and Gynaecology and Department of Physiology, St George's Hospital Medical School, London, United Kingdom.

<sup>&</sup>lt;sup>4</sup> Department of Obstetrics and Gynaecology, Kvinnokliniken, Universitetsjukhuse MAS, Malmö, Sweden.

<sup>&</sup>lt;sup>5</sup> To whom correspondence should be addressed; e-mail: ijarvela@ cc.oulu.fi.

ultrasonographic definitions, stromal blood flow characteristics in PCO seem to differ from those in normal ovaries in studies using transvaginal Doppler ultra-

sonography (7–10). There is still considerable debate as to the definition of polycystic ovary syndrome (PCOS). In the latter, the appearance of PCO on ultrasound is accompanied by one or more clinical or endocrinological disturbances, however the latter may be present in the absence of "typical" PCO (11–13). This suggests that PCOS does not predetermine a single ultrasonographic or Doppler pattern (13).

The latest technical achievement in the area of ultrasonography is three-dimensional (3-D) power Doppler sonography, which provides the possibility of systemic analysis of volume, blood flow and vascularization of the whole target organ (14–16). This advance may give additional insight into the function of PCO and enable the morphology to be more precisely defined. The aim of our study was therefore to evaluate the characteristics of polycystic compared to normal ovaries using 3-D power Doppler ultrasonography and, in particular, to compare stromal vascularity and echogenicity using this new method.

## PATIENTS AND METHODS

#### Patients

The patients were volunteers who were commencing IVF treatment in the Assisted Conception Unit at St. George's Hospital Medical School. Ethical approval was obtained from the Ethics Committee of the Medical School, and each subject gave written informed consent before participating in the study. Patients with fibroids, endometriosis or endometrioma, single ovary, salpingectomy, ovarian cystectomy, or known contraindications for the use of GnRH agonists and human menopausal gonadotropin were excluded from the study. Gonadotrophin levels had been measured between days 1–5 of a cycle during the previous 6 months. Only women with FSH level less than 10 IU/l were included.

#### Methods

Each patient was examined in the cycle preceeding commencement of drug therapy, during cycle days 8–16, in order to rule out any pathology preventing the treatment. Where a corpus luteum was visible ultrasonographically the patient was excluded from the study. The ovaries were categorized as either normal or polycystic according to the following criteria: if eight or more (3) subcapsular follicles of 2–8 mm in diameter in one two-dimensional (2-D) plane were detected in either of the ovaries, the patient was considered to have polycystic ovaries (PCO); otherwise the ovaries were considered normal (N). Because ultrasonographically the polycystic ovaries in patients with and without polycystic ovarian syndrome (PCOS) do not seem to differ from each other in terms of volume (17) or stromal color Doppler characteristics (7,9,18), no subdivision according to endocrine or clinical manifestations was performed in PCO group.

All the ultrasound examinations were performed by two of the authors (I.Y.J. and P.S.). The uterus and the ovaries were scanned using Kretz Combison 530D Voluson (Kretztechnik-Medison, Zipf, Austria) with a transvaginal 3–7 MHz volume transducer, which has a 100° field of view. Identical preinstalled instrument settings (color gain 45.6, pulse repetition frequency 0.5, C-PWR 2, wall motion filter 72, frame rate 4–6) were used in all patients.

The region of interest (ROI) was visualized in 2-D B-mode. The "angio mode" was switched on and the mobile sector appeared. The mobile sector was adjusted to cover only the ROI. The 3-D facility was engaged by switching to "volume mode." The volume sector angle was preset to  $90^{\circ}$  and the fast volume acquisition (low resolution) setting was selected to avoid artefacts. The duration of the volume acquisition was between 10 and 20 s, depending on the dimensions. Movements of the vaginal probe were excluded during the volume acquisition. Acquired 3-D volumes were stored on a removable 540 Mb hard disk cartridge (Nomai, Electronique d2, France) for later review. The volumes stored on the hard disk were transferred to PC using DICOM (Digital Imaging and Communications in Medicine) connection for subsequent analysis. No compression of the data was used at any time. The analysis of stored volumes was performed using VOCAL<sup>™</sup>—Imaging program (Virtual Organ Computer-aided AnaLysis) version 4.0, which is integrated in Kretztechnik's Voluson<sup>®</sup> 530D sonography system.

In order to account for any surface irregularity of the ovary, the contour mode in VOCAL-program was set to manual. Longitudinal view was used as a reference image and the rotation step was selected as  $30^{\circ}$ , resulting in the definition of six contours for each ovary. Once a contour was defined in all image planes, the volume of the ovary was obtained. The VOCAL-program then automatically calculated grey-scale and color values for the ovarian volume. The stored volume data obtained using 3-D power Doppler sonography is defined by voxels (smallest unit of volume). Grey-scale voxels contain all 3-D information from black to white, the lowest value (intensity) being 0 and the highest 100 (g0...g100). A similar scale was used for color values (c0...c100). According to these values four indeces were calculated: vascularization index (VI), flow index (FI), vascularization flow index (VFI), and mean greyness (MG).

Vascularization index measures the ratio of color voxels to all the voxels in the ROI, and represents the density of vessels in the tissue expressed as percentage (%). Flow index, the mean value of the color voxels, represents the average intensity of flow. Vascularization flow index is the mean color value in all the voxels in the ROI, and is a feature of both vascularization and flow. Mean greyness, the mean grey value in the grey voxels, represents the mean tissue density or echogenity in the ROI.

After calculating the indices for the whole ovarian volume, the indices for ovarian cortex and subcortical stroma were compared between polycystic and normal ovaries using the VOCAL programme. The ovarian cortex was designated to be a region just beneath

the ovarian capsule and the remaining spheroid in the center of the ovary was then considered representative of ovarian stroma. The cortex thickness was initially assigned from the fact that the size of subcapsular follicles in PCO is 2-8 mm. In order to include as many follicles as possible in the cortical volume, an optimal shell diameter would have been 8 mm, however, in normal ovaries the maximal measurable thickness was 6 mm. This was then also used as the diameter for the subcapsular region in PCO to allow for valid comparisons (Fig. 1). After defining the shell thickness the volume of the subcapsular region (representing the cortex) and the inside spheroid (representing the stroma) was calculated. In addition, the software enabled recalculation of the individual indices for the cortex, and the indices for the subcortical stroma were then calculated using the Statistical Package for the Social Sciences progamme (Release 10.1 SPSS Inc., Chicago, IL, USA).

All the statistical analyses were performed using the SPSS programme. Departure from a normal distribution was assessed using the Kolmogorov–Smirnov test. Paired t tests were used for normally distributed data and the Wilcoxon test for skewed data. Pearson's correlation coefficient was used as appropriate. p < 0.05 was considered significant. All values given are means (SD).



**Fig. 1.** The ovaries were divided into cortex and medulla in order to compare the greyness and colorness indices between these two volumes. The shell diameter was chosen to be 6 mm. The medulla was thought to be representative for stromal tissue.

#### RESULTS

We examined the ovaries of 42 women using 3-D ultrasonography. The data regarding the requirement for IVF treatment, ovulation frequency, age, menstrual cycle length, number of previous pregnancies, number of previous IVF treatments, pretreatment FSH and LH levels, LH/FSH ratio, and smoking status are presented in Table I. According to the ultrasonographic criteria, 28 women had normal ovaries and 14 had PCO. The dominant follicle could be detected in 27 (64.3%); in 22 out of 28 patients with normal ovaries (78.6%), and in five out of 14 patients with PCO (35.9%). All the patients were menstruating and the length of the menstrual cycle was shorter in the group of patients with normal ovaries. The pretreatment FSH level was lower and the LH/FSH ratio was higher in patients with PCO.

Among the study patients (n = 42) there was a remarkably narrow range of results for those parameters directly determined from grey and color voxels, given that the possible range covers 100 units in each case. For example, the maximum and minimum values for FI across all ovaries were 30 and 53 respectively and for MG, 29 and 54.

Initially, findings from either the left or right side were compared within each group. Although the volume of the left-sided normal ovaries was almost identical to that on the right (8.7 vs. 8.2), the rightsided polycystic ovaries were larger than their leftsided counterparts (14.2 vs. 12.1) (Table II).

 
 Table I. Patients Characteristics in Patients with Normal or Polycystic Ovaries

	Normal	PCO	p value
Number of patients	28	14	
Reason for IVF			0.600
Male factor (%)	9 (32.1)	5 (35.7)	
Ovarian	2 (7.1)	3 (21.4)	
dysfunction (%)			
Tubal factor (%)	6 (21.4)	2 (14.3)	
Unexplained (%)	10 (33.3)	3 (21.4)	
Mixed (%)	1 (3.6)	1 (7.1)	
Dominant follicle	22	5	0.023
Right	11	3	
Left	11	2	
Age (SD)	35.3 (3.4)	33.8 (3.9)	0.202
Cycle length, days	28	33	0.022
Previous pregnancies	0.6(0.8)	0.7(1.2)	0.792
Number of previous IVF	0.4 (0.7)	0.7 (1.0)	0.228
FSH	6.8 (1.5)	5.0 (1.3)	0.001
LH	4.5 (2.7)	5.6 (2.6)	0.272
LH/FSH	0.7 (0.3)	1.1(0.7)	0.041
Smoking	20.8% (8/26)	23.1% (3/13)	0.719

Table II. Comparison of All Normal and Polycystic Ovaries

	Right	Left	p value
Normal ovaries $(n = 28)$			
Volume $(cm^3)$ (SD)	8.7 (4.5)	8.2 (3.0)	0.519
VI (SD)	6.1 (4.6)	7.6 (5.9)	0.334
FI (SD)	43.1 (4.7)	46.6 (6.7)	0.014
VFI (SD)	2.7 (2.2)	3.8 (3.6)	0.222
MG (SD)	45.7 (5.2)	45.9 (4.6)	0.829
Polycystic ovaries $(n = 14)$			
Volume $(cm^3)$ (SD)	14.2 (3.3)	12.1 (3.6)	0.001
VI (SD)	5.3 (3.3)	7.5 (5.5)	0.120
FI (SD)	44.0 (4.4)	44.9 (6.4)	0.491
VFI (SD)	2.4 (1.6)	3.6 (2.9)	0.109
MG (SD)	44.5 (6.1)	45.7 (5.3)	0.119

The presence of a dominant follicle did not significantly change the volume in PCO, but normal ovaries without a dominant follicle were smaller than those with (p = 0.001). Even when those polycystic ovaries containing a dominant follicle were excluded, the right ovary was still larger than the left (Table III).

Because of this difference in volume, the other parameters were also compared between right and left sides. Surprisingly, the FI was significantly higher on the left side in normal ovaries with no difference in any other parameter. In fact, the mean values for the other parameters were remarkably similar in each case (Table II).

A comparison of indices between normal and polycystic ovaries showed that there was again very little difference in VI, FI, VFI, and MG between ovaries on the same side (Table IV). Indeed, the mean VI, FI, and VFI were virtually identical throughtout, as was MG. The dominant ovaries did not show any differences between normal and polycystic ovaries (data not shown).

The images were reanalyzed after division of each ovary into cortex and subcortical medulla, the latter representing the stroma. In both the normal and polycystic ovary groups there were a few ovaries which were too small in volume to use a 6-mm cortical diameter for division. In these cases the maximum achievable diameter was used. Ovaries containing a dominant follicle were excluded. As expected,

**Table III.** Patients (n = 9) PCO, No Dominant Follicle Detected

	Right	Left	p value
Volume (cm <sup>3</sup> ) (SD)	14.8 (3.3)	13.2 (3.6)	0.030
VI (SD)	6.2 (3.1)	9.9 (5.4)	0.079
FI (SD)	44.6 (4.3)	47.0 (5.5)	0.166
VFI (SD)	2.8 (1.6)	4.9 (2.9)	0.071
MG (SD)	44.8 (4.8)	44.9 (4.6)	0.947

	Normal $(n = 28)$	PCO ( <i>n</i> = 14)	p value
All the ovaries			
Right ovary			
Vol in $cm^3$ (SD)	8.7 (4.5)	14.2 (3.3)	0.000
VI (SD)	6.1 (4.6)	5.3 (3.3)	0.547
FI (SD)	43.1 (4.7)	44.0 (4.4)	0.546
VFI (SD)	2.7 (2.2)	2.4 (1.6)	0.635
MG (SD)	45.7 (5.2)	44.5 (6.1)	0.521
Left ovary			
Vol in cm <sup>3</sup> (SD)	8.2 (3.0)	12.1 (3.6)	0.000
VI (SD)	7.6 (5.9)	7.5 (5.5)	0.966
FI (SD)	46.6 (6.7)	44.9 (6.4)	0.420
VFI (SD)	3.8 (3.6)	3.6 (2.9)	0.881
MG (SD)	45.9 (4.6)	45.7 (5.3)	0.917
	Normal $(n = 17)$	PCO ( $n = 11$ )	
Ovaries without a dominant follicle Right ovary			
Vol in $cm^3$ (SD)	7.5 (4.0)	14.6 (3.1)	0.000
VI (SD)	6.5 (5.5)	5.6 (3.0)	0.649
FI (SD)	41.5 (4.6)	44.4 (3.8)	0.097
VFI (SD)	2.9 (2.7)	2.6 (1.5)	0.745
MG (SD)	47.5 (3.6)	45.4 (4.5)	0.199
	Normal $(n = 17)$	PCO ( $n = 12$ )	
Left ovary	-		
Vol in cm <sup>3</sup> (SD)	7.2 (2.2)	12.2 (3.8)	0.000
VI (SD)	9.2 (7.1)	8.1 (5.7)	0.654
FI (SD)	48.8 (7.4)	45.5 (6.8)	0.218
VFI (SD)	4.8 (4.3)	4.0 (3.0)	0.562
MG (SD)	47.3 (4.4)	45.1 (5.4)	0.244

Table IV. Comparison Between Normal and Polycystic Ovaries

the stroma and cortex volumes were larger in PCO, however neither showed any differences in VI, FI, VFI, or MG between normal and PCO on each side (Tables V).

### DISCUSSION

The hypothesis in the present study was that 3-D power Doppler ultrasonography provides the possibility of systemic analysis of volume, blood flow, vascularization, and echogenity of the whole ovary (14). According to our results, there was very little variation in each parameter between patients. Secondly, when normal ovaries were compared to PCO, there were surprisingly few differences in the indices representing blood flow, vascularity, and tissue echogenity.

In this study polycystic ovarian morphology was determined by the presence of eight or more subcapsular follicles of 2–8 mm in diameter in one plane alone. Ovarian volume, stromal volume or stromal hyperechogenity were not used as criteria, since neither the Adams *et al.* (2) study nor any of the other available definitions (19) provide objective criteria or precise cut-off values to determine them (20). Despite of using only the number of ovarian follicles in one 2-D plane for categorizing, those patients with polycystic ovaries had less ovulatory cycles, longer menstrual cycle and higher LH/FSH ratio, all of which are typical characteristics of polycystic ovary syndrome (3). According to this division, the PCO group consisted of 14 women and the normal ovary group of 28 women. Because the number of PCO patients is limited, it may have an impact on the statistical power of the study.

Ovarian stromal echogenity has been assessed earlier using 2-D ultrasonography (4,21), and this is the first study to use 3-D technology to assess echogenity throughout the entire ovary. Mean greyness (MG) was the parameter used to evaluate the echogenicity in the ovary. Surprisingly, we did not find any difference in the MG between normal and polycystic ovaries, when comparing the total volume of the ovaries. In the study by Buckett *et al.* (21), the mean total ovarian echogenicity was lower in the polycystic ovary in comparison with the normal ovaries. This maybe true in one optimally selected plane using 2-D ultrasonography, but our study reveals that even

	Normal $(n = 17)$	PCO ( $n = 11$ )	p value
Right ovary			
Stroma			
Vol in cm <sup>3</sup> (SD)	0.5 (0.4)	2.2 (1.1)	0.000
VI (SD)	8.2 (11.6)	8.0 (8.6)	0.974
FI (SD)	41.2 (6.0)	44.6 (5.7)	0.154
VFI (SD)	3.8 (5.9)	3.9 (4.9)	0.939
MG (SD)	46.8 (3.4)	45.9 (4.2)	0.560
Cortex			
Thickness of the cortex in mm (SD)	5.6 (1.5)	5.9 (0.3)	0.504
Vol in cm <sup>3</sup> (SD)	7.0 (3.8)	12.4 (2.2)	0.000
VI (SD)	6.3 (5.1)	5.5 (2.7)	0.600
FI (SD)	41.5 (4.5)	44.2 (3.9)	0.117
VFI (SD)	2.8 (2.4)	2.5 (1.4)	0.694
MG (SD)	47.5 (3.6)	45.4 (4.6)	0.177
	Normal $(n = 17)$	PCO ( <i>n</i> = 12)	
Left ovary			
Stroma			
Vol in cm <sup>3</sup> (SD)	0.6 (0.5)	1.7 (1.1)	0.007
VI (SD)	11.8 (14.0)	15.3 (12.2)	0.489
FI (SD)	47.7 (7.8)	47.1 (9.0)	0.851
VFI (SD)	6.2 (8.2)	8.0 (7.2)	0.555
MG (SD)	46.3 (4.6)	45.7 (5.6)	0.755
Cortex			
Thickness of the cortex in mm (SD)	5.6 (1.2)	6.0(0.0)	0.186
Vol in cm <sup>3</sup> (SD)	6.5 (2.2)	10.5 (2.8)	0.000
VI (SD)	9.1 (6.5)	7.1 (5.2)	0.389
FI (SD)	48.7 (7.4)	44.7 (6.9)	0.147
VFI (SD)	4.7 (4.0)	3.4 (2.7)	0.337
MG (SD)	47.4 (4.4)	45.0 (5.5)	0.211

 Table V. Comparison of Ovarian Cortex and Stroma Between Normal and PCO (Ovaries Containing a Dominant Follicle Were Excluded)

when using the mean echogenity from the total volume of the ovaries, no differences in the echogenity can be found between polycystic and normal ovaries.

One clear finding in our study is that in the polycystic ovary group the right ovary was larger than the left one. A similar finding has been made by Wu et al. (22), who also used 3-D ultrasonography. Interestingly, a recent study (5) in PCOS patients also showed that the presence of 10 or more follicles in the ovary and the peripheral distribution of follicles was more common in the right than in the left ovary. In addition, Griffin et al. have earlier observed that prepubertal girls have a significantly larger right ovary compared to the left (23). The causality underlying these differences is obscure. The only known difference between the right and left ovary lies in the anatomy of the venous drainage. The left ovarian vein drains to the left renal vein and the right ovarian vein to the inferior vena cava. We did not find any difference in the colorness indices between the right and left polycystic ovary, but there was a tendency in the nondominant polycystic ovaries, for VI and VFI to be higher on the

left side. Within normal ovaries FI was higher on the left side. Whether or not the difference of the size in polycystic ovaries and the difference in the flow indices in normal ovaries between the sides are due to the anatomical difference in the venous drainage remains obscure.

When analyzing data from whole ovaries there were no differences between normal and polycystic ovaries in either echogenicity or flow and this was also the case when comparing parameters between those normal or PCO containing a dominant follicle. When comparing the nondominant ovaries both right and left PCO were larger than their normal counterparts, but surprisingly no other differences were detected. The finding of increased ovarian volume was expected as it is a typical feature of polycystic ovaries (1,3).

The lack of differences cannot be ascribed to the technique. Pairleitner *et al.* (14) used this technique in the examination of adnexal masses and reported that it gave reproducible information. In our own reproducibility study (submitted) the results concerning the intraobserver and interobserver reproducibility were good in most of the parameters.

Our results are not entirely in accordance with those recently presented by Pan et al. (24). They used a similar 3-D power Doppler method to compare ovarian volume, VI, FI and VFI between normal and PCOS patients (24). They discovered that the polycystic ovaries were larger than the normal ones, like in the current study. No difference was detected between right and left ovarian volume in the PCOS group, which disagrees with our results and also with the previous finding by the same group (22). Ovarian VI, FI, and VFI values were observed to be higher in PCOS patients than in patients with normal ovaries (24). The ultrasonographic measurements took place on cycle days 2-3, which was earlier in the cycle than in our study. Patients with normal ovaries were significantly older than PCOS patients, which may have affected the ovarian blood flow characteristics. Differences in MG were not evaluated.

Because it was considered that the differences between N + PCO may be localized 3-D images were reanalyzed, in order to compare the stromal greyness and colorness indices. The ideal ultrasonographic image of a polycystic ovary is subcapsularly arranged, equal sized follicles with a diameter of 2-8 mm lying in the ovarian cortex, which surrounds the medulla, consisting mainly of stroma. We decided to divide the ovary into two regions, a subcapsular shell corresponding to the cortex (containing most of the follicles) and inside this the medulla, which mainly contains stroma without follicles. An arbitrary value of 6 mm for the thickness of the cortex was used. It is obvious that the division is artificial, but it enabled valid comparisons to be made between normal and polycystic ovarian cortex. The authors realize that the medullar volumes achieved using this method do not actually correspond to the true stromal volumes. The aim was however not to compare the medullar volumes, but the greyness and colorness indices in a representative sample of stroma.

We did not find any difference in the stromal MG between polycystic and normal ovaries. The latter finding coincides with those achieved using 2-D ultrasonography (4,21). According to our results both cortical and medullar volumes were higher in polycystic vs. normal ovaries, but this was to be expected since the total volume of the PCO was larger.

Even when analyzed separately, however, the stromal VI, FI, and VFI values were not different between normal and polycystic ovaries. Although these parameters have not previously been assessed, earlier studies using 2-D color Doppler facilities found that the peak systolic velocity (PSV) and time-averaged maximum velocities (TAMX) were higher in stromal arteries during the early days of the follicular phase in patients with PCO compared to those in patients with normal ovaries (7,9,25); nevertheless not all studies have confirmed this finding (8). The indices for blood flow impedance, pulsatility index (PI) and resistance index (RI), have been either at the same level or lower in PCO (8–10,25,26). The findings concerning the increased blood flow velocities are thought to be representative for highly vascularized stroma typical of PCO (9). However, we did not find any differences in the mean vascularization or flow indices between polycystic and normal ovaries, either while comparing the values obtained from the whole ovarian volume or only those from the medulla representing the stroma. The discrepancy between results obtained with the two methods may be caused by the fact that the 3-D method used in this study measures combined mean arterial and venous vascularization and flow in the whole ovary, whereas 2-D color Doppler measures arterial flow in one 2-D plane. In addition, the scanning in our study took place in the late follicular phase as opposed to in the early follicular phase in the 2-D studies in the late follicular phase. According to earlier 2-D color Doppler studies, the blood flow changes during the normal or stimulated menstrual cycle in the dominant ovary (27-29), whereas in the nondominant ovary it remains constant throughout the menstrual cycle (27–29), without any correlation to serum LH, FSH, progesterone or estradiol concentrations (28). We excluded the effect of leading follicle on the ovarian blood flow by analyzing separately only nondominant ovaries, and the stromal VI, FI, and VFI values were not different between normal and polycystic ovaries. Our results suggest that in general, the blood flow in the stroma of polycystic ovaries does not differ from that in normal ovaries during late follicular phase.

In summary, we have utilized both 3-D ultrasonography and power Doppler to evaluate the differences in the volume, the total vascularization and blood flow, and in the mean greyness between normal and polycystic ovaries. Not surprisingly, those ovaries defined as polycystic were found to be larger than normal ones, but there was no difference in the echogenicity of the stroma between polycystic and normal ovaries. We also demonstrated that, by this new technique, the stroma of PCO does not appear to be more vascularized that that of normal ovaries. Three-dimensional power Doppler ultrasonography offers us a new tool to assess the size of the target organ, to quantify tissue blood perfusion and echogenity, which may expand our knowledge concerning the physiology in the organs.

## ACKNOWLEDGMENTS

This research (I.Y.J.) has been supported by a Marie Curie Fellowship of the European Community Programme "Quality of Life and Management of Living Resources" under contract number QLRI-CT-1999-51230.

#### REFERENCES

- Adams J, Franks S, Polson DW, Mason HD, Abdulwahid N, Tucker M, Morris DV, Price J, Jacobs HS: Multifollicular ovaries: Clinical and endocrine features and response to pulsatile gonadotropin releasing hormone. Lancet 1985;2:1375– 1379
- Adams J, Polson DW, Franks S: Prevalence of polycystic ovaries in women with anovulation and idiopathic hirsutism. Br Med J (Clin Res Ed) 1986;293:355–359
- Homburg R: Polycystic ovary syndrome—From gynaecological curiosity to multisystem endocrinopathy. Hum Reprod 1996;11:29–39
- Al-Took S, Watkin K, Tulandi T, Tan SL: Ovarian stromal echogenicity in women with clomiphene citrate-sensitive and clomiphene citrate-resistant polycystic ovary syndrome. Fertil Steril 1999;71:952–954
- Atiomo WU, Pearson S, Shaw S, Prentice A, Dubbins P: Ultrasound criteria in the diagnosis of polycystic ovary syndrome (PCOS). Ultrasound Med Biol 2000;26:977–980
- Kyei-Mensah A, Zaidi J, Campbell S: Ultrasound diagnosis of polycystic ovary syndrome. Baillieres Clin Endocrinol Metab 1996;10:249–262
- Zaidi J, Campbell S, Pittrof R, Kyei-Mensah A, Shaker A, Jacobs HS, Tan SL: Ovarian stromal blood flow in women with polycystic ovaries—A possible new marker for diagnosis? Hum Reprod 1995;10:1992–1996
- Aleem F, Predanic M: Transvaginal color Doppler determination of the ovarian and uterine blood flow characteristics in polycystic ovary disease. Fertil Steril 1996;65:510–516
- Agrawal R, Sladkevicius P, Engmann L, Conway GS, Payne NN, Bekis J, Tan SL, Campbell S, Jacobs HS: Serum vascular endothelial growth factor concentrations and ovarian stromal blood flow are increased in women with polycystic ovaries. Hum Reprod 1998;13:651–655
- Pinkas H, Mashiach R, Rabinerson D, Avrech OM, Royburt M, Rufas O, Meizner I, Ben-Rafael Z, Fisch B: Doppler parameters of uterine and ovarian stromal blood flow in women with polycystic ovary syndrome and normally ovulating women undergoing controlled ovarian stimulation. Ultrasound Obstet Gynecol 1998;12:197–200
- 11. Takahashi K, Okada M, Ozaki T, Uchida A, Yamasaki H, Kitao M: Transvaginal ultrasonographic morphology in poly-

cystic ovarian syndrome. Gynecol Obstet Invest 1995;39:201–206

- 12. Fox R: Transvaginal ultrasound appearances of the ovary in normal women and hirsute women with oligomenorrhoea. Aust N Z J Obstet Gynaecol 1999;39:63–68
- Battaglia C, Regnani G, Artini PG, Giulini S, Genazzani AD, Genazzani AR, Volpe A: Polycystic ovary syndrome: A new ultrasonographic and color Doppler pattern. Gynecol Endocrinol 2000;14:417–424
- Pairleitner H, Steiner H, Hasenoehrl G, Staudach A: Threedimensional power Doppler sonography: Imaging and quantifying blood flow and vascularization. Ultrasound Obstet Gynecol 1999;14:139–143
- Cohen LS, Escobar PF, Scharm C, Glimco B, Fishman DA: Three-dimensional power Doppler ultrasound improves the diagnostic accuracy for ovarian cancer prediction. Gynecol Oncol 2001;82:40–48
- Keberle M, Jenett M, Hahn D: Clinical trial on the accuracy of a freehand and sensor-independent three-dimensional power Doppler ultrasound system measuring diameters, volumes and vascularity of malignant primaries of the neck. Ultraschall Med 2001;22:91–95
- Norman RJ, Hague WM, Masters SC, Wang XJ: Subjects with polycystic ovaries without hyperandrogenaemia exhibit similar disturbances in insulin and lipid profiles as those with polycystic ovary syndrome. Hum Reprod 1995;10:2258–2261
- Agrawal R, Conway G, Sladkevicius P, Tan SL, Engmann L, Payne N, Bekir J, Campbell S, Jacobs H: Serum vascular endothelial growth factor and Doppler blood flow velocities in in vitro fertilization: Relevance to ovarian hyperstimulation syndrome and polycystic ovaries. Fertil Steril 1998;70:651– 658
- Pache TD, Hop WC, Wladimiroff JW, Schipper J, Fauser BC: Transvaginal sonography and abnormal ovarian appearance in menstrual cycle disturbances. Ultrasound Med Biol 1991;17:589–593
- van Hooff MH, Voorhorst FJ, Kaptein MB, Hirasing RA, Koppenaal C, Schoemaker J: Polycystic ovaries in adolescents and the relationship with menstrual cycle patterns, luteinizing hormone, androgens, and insulin. Fertil Steril 2000;74: 49–58
- Buckett WM, Bouzayen R, Watkin KL, Tulandi T, Tan SL: Ovarian stromal echogenicity in women with normal and polycystic ovaries. Hum Reprod 1999;14:618–621
- Wu MH, Tang HH, Hsu CC, Wang ST, Huang KE: The role of three-dimensional ultrasonographic images in ovarian measurement. Fertil Steril 1998;69:1152–1155
- Griffin IJ, Cole TJ, Duncan KA, Hollman AS, Donaldson MD: Pelvic ultrasound measurements in normal girls. Acta Paediatr 1995;84:536–543
- 24. Pan HA, Wu MH, Cheng YC, Li CH, Chang FM. Quantification of Doppler signal in polycystic ovary syndrome using three-dimensional power Doppler ultrasonography: A possible new marker for diagnosis. Hum Reprod 2002;17:201– 206
- 25. Engmann L, Sladkevicius P, Agrawal R, Bekir J, Campbell S, Tan SL: The pattern of changes in ovarian stromal and uterine artery blood flow velocities during in vitro fertilization treatment and its relationship with outcome of the cycle. Ultrasound Obstet Gynecol 1999;13:26–33
- 26. Battaglia C, Artini P, D'Ambrogio G, Genazzani A, Genazzani A: The role of color Doppler imaging in the diagnosis of

polycystic ovary syndrome. Am J Obstet Gynecol 1995;172:108–113

- 27. Sladkevicius P, Valentin L, Marsal K: Blood flow velocities in the uterine and ovarian arteries during normal menstrual cycle. Ultrasound Obstet Gynecol 1993;3:199–208
- 28. Tan S, Zaidi J, Campbell S, Doyle P, Collins W: Blood flow changes in the ovarian and uterine arteries during the

normal menstrual cycle. Am J Obstet Gynecol 1996;175:625-631

29. Zaidi J, Jacobs H, Campbell S, Tan SL: Blood flow changes in the ovarian and uterine arteries in women with polycystic ovary syndrome who respond to clomiphene citrate: Correlation with serum hormone concentrations. Ultrasound Obstet Gynecol 1998;12:188–196