Ovarian stromal echogenicity in women with normal and polycystic ovaries

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Since the widespread use of transvaginal ultrasound to diagnose polycystic ovary syndrome (PCOS), a cardinal feature has been shown to be the presence of a bright, highly echogenic stroma. This is usually assessed subjectively. The objective of this study was to determine whether ovarian stromal echogenicity when measured objectively actually differed between women with polycystic ovaries and those with normal ovaries. A total of 67 women underwent a detailed ultrasound assessment before considering assisted conception treatment. Ovarian morphology was assessed and total ovarian volume, stromal volume, peak stromal blood flow velocity and mean stromal echogenicity were measured. The stromal index (ratio of mean stromal echogenicity to mean echogenicity of the entire ovary) and total stromal echogenicity were also calculated. Ovarian volume, stromal volume, and stromal peak blood flow velocity were all significantly higher in ovaries from women with PCOS. There was no difference in the mean stromal echogenicity, although the stromal index was significantly greater in women with polycystic ovaries. The apparent subjective increase in stromal echogenicity in women with polycystic ovaries, as exemplified by the greater stromal index, is due to a combination of the increased volume of ovarian stroma and the significantly lower mean echogenicity of the entire ovary in these women.

Key words: echogenicity/ovary/polycystic ovary syndrome/stroma/ultrasound

Introduction

Polycystic ovary syndrome (PCOS) is the most frequent disorder of ovarian function in women of reproductive age (Franks, 1989). Diagnosis of the syndrome is generally based clinically on the presence of amenorrhoea/oligomenorrhoea or symptoms of hyperandrogenism, and biochemically on the presence of elevated serum luteinizing hormone (LH) and androgen concentrations. More recently, transvaginal ultrasound examination of ovarian morphology has been used to help make the diagnosis.

Swanson et al. (1981) were the first to describe the ultrasound findings associated with PCOS. The classical image is that of enlarged ovaries containing an increased number of small follicles (2–10 mm) encircling the ovarian cortex like a string of pearls, although this is sometimes incomplete, and the presence of an increased bright echogenic stroma (Adams et al., 1985). The presence of hypertrophic ovarian stroma has been used by many groups to distinguish between PCOS and normal ovaries (Conway et al., 1989; Dewaill et al., 1993).

The degree of echogenicity of the ovarian stroma is usually assessed subjectively but this is open to observer bias where other features of PCOS are already seen. Methods of quantitatively measuring ultrasound image data, often termed textural feature analysis, have been useful in identifying diffuse diseases of the liver (Raeth et al., 1985) and brain (Barr et al., 1995). Using these recent advances in ultrasound software, the brightness, or echogenicity, of the ovarian stroma can be determined objectively by measuring the intensity level of the ultrasound pixels within the stroma displayed on an ultrasonic image. The mean echogenicity of a given area can then be calculated.

The objective of this study was to determine whether the ovarian stromal echogenicity measured objectively differed significantly between women with PCOS and those with normal ovaries.

Materials and methods

Transvaginal pelvic ultrasound and Doppler examination were performed during the early follicular phase of the menstrual cycle (days 2–4) on 67 consecutive patients who were not taking any medication as part of routine assessment prior to undergoing in-vitro fertilization for a variety of indications at the McGill Reproductive Center.

All ultrasound examinations were performed firstly using a 5 MHz endovaginal probe with colour and pulsed Doppler facilities (Acuson XP 128/10®; Acuson Corp., Mountain View, CA, USA), and then using a 7.5 MHz endovaginal probe with histogram measurement of echogenicity (Aloka SSD 2000®; Aloka Co., Tokyo, Japan). All ultrasound examinations were performed by one of the authors (W.B.).

A systematic examination of the morphology of the uterus and ovaries was performed using previously described criteria (Zaidi et al., 1995a; Tan et al., 1996). An ultrasound diagnosis of PCOS was made when there were greater than 10 small cysts/follicles (2–8 mm diameter) around a dense core of stroma. These ultrasound findings were invariably accompanied with an increased ovarian volume. Any ovaries which contained ovarian cysts (over 12 mm mean diameter) or ultrasound evidence of endometriomas were excluded from the analysis.

Intra-ovarian blood flow was assessed by pulsed Doppler examina-
Ovarian stromal echogenicity

Figure 1. The outline of, and histogram displaying the echogenicity within, the entire ovary (A) and the ovarian stroma (B) in a woman with normal ovaries.

Figure 2. The outline of, and histogram displaying the echogenicity within, the entire ovary (A) and the ovarian stroma (B) in a woman with polycystic ovaries.

tion of blood vessels in the ovarian stroma, as previously described (Zaidi et al., 1995b, 1996).

The mean echogenicity was defined as the sum of the product of each intensity level (varying from 0–63) and the number of pixels for that intensity concentration divided by the total number of pixels in the measured area, as follows:

\[
\text{mean} = \frac{\sum x_i f_i}{n}
\]

where \( n \) = total number of pixels in the measured area
\( x \) = intensity level (from 0 to 63)
\( f \) = number of pixels corresponding to that level.

The mean echogenicity of the entire ovary and of the ovarian stroma were separately calculated. The spread of intensities was also displayed by histogram, where the horizontal axis indicated the different intensity concentrations and the vertical axis the number of pixels at each intensity level (Figures 1 and 2).

The total stromal echogenicity was calculated as the product of the mean stromal intensity and the total number of pixels measured in the same two-dimensional ultrasound image of the stroma.

The stromal index was then calculated by dividing the mean stromal echogenicity by the mean echogenicity of the entire ovary in order to correct for cases where the gain was adjusted to allow optimal image definition. The stromal index was therefore more than one if the mean stromal echogenicity was greater than the mean echogenicity of the entire ovary.

Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and dihydroepiandrosterone sulphate (DHEAS) were also measured in the early follicular phase on the day of the baseline ultrasound scan.

Normally distributed data were expressed as means with 95% confidence limits and compared using Student’s unpaired two-tailed t-test. Non-parametric data were expressed as medians with inter-quartile range and compared using the Mann–Whitney rank sum test.

Results

Of a total of 67 patients who underwent ultrasound assessment (one of whom had had a previous oophorectomy), five patients were excluded. Reasons were the presence of endometrioma (3) or of a simple ovarian cyst >15 mm mean diameter (2). Of the 123 ovaries included in the study, 46 (37%) had an ultrasound diagnosis of PCOS.

The total ovarian volume, stromal volume, and peak stromal blood flow (as assessed by colour Doppler) were all significantly higher \( (P < 0.0001; P < 0.05; \text{and } P < 0.001 \text{ respectively}) \) in the women with PCOS compared with those with normal ovaries (Table I).

There was no significant difference in the mean stromal echogenicity between the two groups, and although the total
Ovarian volume, stromal volume, and peak stromal blood flow velocity in normal and polycystic ovaries. Values are means with 95% confidence intervals (CI) or medians with interquartile ranges (IQR).

<table>
<thead>
<tr>
<th></th>
<th>Normal ovaries</th>
<th>Polycystic ovaries</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total ovarian volume (ml)</td>
<td>6.31 (5.60–7.02)</td>
<td>9.94 (8.29–11.59)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stromal volume (ml)</td>
<td>1.90 (1.18–2.78)</td>
<td>2.41 (2.15–3.22)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Peak stromal blood flow velocity (cm/s)</td>
<td>5.98 (4.84–7.12)</td>
<td>10.45 (8.73–12.17)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean stromal echogenicity, mean echogenicity of the entire ovary, stromal index, and total stromal echogenicity in women with normal ovaries and PCOS. Values expressed as medians with interquartile ranges (IQR).

<table>
<thead>
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<th>Polycystic ovaries</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Mean stromal echogenicity</td>
<td>20.0 (17.9–24.3)</td>
<td>19.6 (17.8–23.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean total ovarian echogenicity</td>
<td>17.6 (15.8–22.4)</td>
<td>16.7 (14.6–18.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Total stromal echogenicity</td>
<td>5844 (4574–9559)</td>
<td>6717 (4718–11004)</td>
<td>NS</td>
</tr>
<tr>
<td>Stromal index</td>
<td>1.10 (1.06–1.21)</td>
<td>1.20 (1.12–1.31)</td>
<td>&lt;0.0001</td>
</tr>
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NS = not significant.
PCOS = polycystic ovary syndrome.

Concentrations of serum follicle stimulating hormone (FSH), serum luteinizing hormone (LH), serum testosterone and serum dihydroepiandrosterone sulphate (DHEAS) and LH:FSH ratio in women with PCOS and normal ovaries.

<table>
<thead>
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<th>Normal ovaries</th>
<th>Polycystic ovaries</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum FSH (IU/l)</td>
<td>8.89 (7.46–10.32)</td>
<td>6.85 (6.10–7.60)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum LH (IU/l)</td>
<td>5.19 (4.29–6.09)</td>
<td>6.78 (5.51–8.05)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LH:FSH ratio</td>
<td>0.59 (0.51–0.67)</td>
<td>1.01 (0.80–1.22)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Serum testosterone (nmol/l)</td>
<td>1.09 (0.95–1.23)</td>
<td>1.37 (1.20–1.54)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum DHEAS (nmol/l)</td>
<td>3.70 (3.23–4.17)</td>
<td>5.27 (3.77–6.77)</td>
<td>&lt;0.05</td>
</tr>
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</table>

The mean stromal echogenicity was higher in the PCOS group this did not reach statistical significance (Table II).

The stromal index (ratio of mean stromal echogenicity to mean echogenicity of the entire ovary) was higher in the PCOS group (P < 0.0001), partly as a result of the reduced mean echogenicity of the entire ovary in the PCOS group (P < 0.05).

The endocrine parameters of PCOS were all significantly raised in the PCOS group (Table III), although the serum FSH was lower than in the control group.

Discussion

This study confirms the results of previous studies that there is a high incidence of ultrasound diagnosed PCOS in women undergoing in-vitro fertilization (IVF) for a variety of indications (Polson et al., 1988; MacDougall et al., 1992). We found that the total ovarian volume and the stromal volume are increased in women with PCOS. We also confirmed that the peak ovarian stromal blood flow velocity is significantly higher in polycystic ovaries than in normal ovaries (Zaidi et al., 1995b; Battaglia et al., 1997).

Interestingly, the mean stromal echogenicity was no higher in women with PCOS compared with women with normal ovaries which suggests that there is no intrinsic difference in the nature of the stroma itself. This is an important finding as a highly echogenic stroma is a cardinal feature in the ultrasound diagnosis of PCOS (Conway et al., 1989; MacDougall et al., 1992; Dewailly et al., 1993). The significant difference in the stromal index would suggest that the impression of a highly echogenic stroma in PCOS is primarily due to a visual perception of the difference in echogenicities between the stroma and the ovary as a whole with its multiple small cysts. Clearly the greater the number and the larger the size of the cysts the greater the stromal index would be since the mean total ovarian echogenicity would be lower.

The greater total stromal echogenicity would also suggest that the subjective impression of highly echogenic stroma in women with PCOS may be partly due to the increased stromal volume. The reason that statistical significance was not reached is probably because of the small sample size.

Histological examination of ovaries from women with PCOS has shown a five-fold increase in the sub-cortical (medulla) stroma (Hugheson, 1982). The findings of the present study that the mean stromal echogenicity is comparable in the two groups of women are consistent with the histological evidence that although the stromal volume is increased, there is no other change which could account for an increased echogenicity per se.

It has been suggested that vascular endothelial growth factor (VEGF) has a role in the maintenance of perifollicular blood flow (Van Blerkom et al., 1997) and recent evidence shows a positive correlation between VEGF and ovarian stromal blood flow velocities in women with ultrasound diagnosed polycystic ovaries and PCOS (Agrawal et al., 1998). This increased vascularity, possibly mediated by VEGF, is therefore probably responsible for the formation of increased stroma and the ultimate phenotype associated with PCOS.

In conclusion, the ultrasonic measurement of mean ovarian stromal echogenicity adds little to the ultrasound diagnosis of PCOS and cannot be recommended in the routine ultrasound assessment of the pelvis. Although the stromal echogenicity appears subjectively brighter, this is primarily a reflection of the difference between the echogenicity of the stroma compared with that of the entire ovary. There was an increased stromal index as well as an increased stromal volume in women with polycystic ovaries. Although the measurement of ovarian and stromal volume and intra-ovarian blood flow were not primary outcomes in this study, we recommend their routine measurement in women undergoing induction of ovulation because of their predictive value in the responsiveness of the ovary to hormonal stimulation (MacDougall et al., 1992; Zaidi et al., 1996b).

References


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