Contribution of real-time elastography in diagnosis of polycystic ovary syndrome

Saliha Çıracı, Sinan Tan, Aysenur Şirin Özcan, Ahmet Aslan, Hüseyin Levent Keskin, Ömer Faruk Ateş, Yıldız Akçay, Halil Arslan

PURPOSE
We aimed to assess the feasibility and reproducibility of real-time elastography (RTE) for displaying the effects of morphological changes in the ovary in polycystic ovary syndrome (PCOS).

METHODS
Forty-eight patients diagnosed with PCOS and 48 healthy women were enrolled in the study. Ultrasonography and RTE were performed on the 3rd day of the menstrual cycle. Evaluations were performed independently by two radiologists. Ovarian volume, number of follicles, elasticity pattern, and strain ratio were measured. Elasticity patterns were assessed as hard (type 1: blue or blue-green), moderate (type 2: green or green-yellow) or soft (type 3: red or orange-red).

RESULTS
Both radiologists determined the elasticity pattern as mostly type 1 in the PCOS group and type 3 in the control group (\( P < 0.01 \)). The mean strain ratios obtained by the first and second radiologist were 6.1±1.8 (2.7–10.1) and 6.0±1.5 (3.0–9.0) in PCOS and 3.3±1.2 (1.7–7.2) and 3.2±0.9 (1.7–6.8) in the control group, respectively (\( P < 0.001 \)). Interobserver agreement was moderate for the elasticity pattern (κ=0.48) and good for the strain ratio (intraclass correlation coefficient, 0.77). A strain ratio of 3.8 was determined as the optimized cutoff point by receiver operating curve analysis. Strain ratio was correlated with the ovarian volume and the number of detected follicles (\( P < 0.001 \)).

CONCLUSION
Elasticity pattern and strain ratio can help identify morphological changes that make PCOS ovaries stiffer than normal ovaries.

methods

Patients

This observational study was approved by the institutional review board and informed written consent was obtained from all reviewed subjects. Forty-eight patients who were diagnosed as PCOS by the Gynecology Department and 48 healthy women from consecutive patients who were referred to the Gynecology Department for routine control were included in the study. PCOS diagnoses were made according to the Rotterdam (ESHRE/ASRM) criteria (1, 12). The patients who had a diagnosis of Cushing syndrome, congenital adrenal hyperplasia, hyperprolactinemia, thyroid dysfunction, virilizing tumors, type 2 diabetes mellitus, or patients on medication such as oral contraceptives, glucocorticoids, antiandrogens, insulin sensitizers, or drugs that may cause hirsutism were excluded from the study. Patients who had follicles larger than 9 mm or corpus luteum cysts were also excluded because these features could potentially alter the results.
Scanning and equipment

The gray-scale US and RTE studies were done using a 6.5 MHz vaginal probe (Logiq E9, GE Healthcare, Milwaukee, Wisconsin, USA) on the 3rd day of the menstrual cycle by one of two radiologists having 3–5 years of experience with sonography and one year of experience in elastography, who were blinded to the patients’ diagnosis, clinical features, or complaints. All transvaginal US studies were performed in a gynecologic position, when the bladder was empty.

The ovaries were examined by gray-scale US and maximum diameters in three planes (longitudinal, antero-posterior and transverse) were measured to calculate the ovarian volume by the prolate ellipsoid formula \( V = D_1 \times D_2 \times D_3 \times 0.523 \; \text{cm}^3 \). The number and maximum diameter of detected follicles were noted. Scanning of ovaries was completed when each ovary was scanned from medial to lateral aspects.

RTE was performed with the same probe used in gray-scale US evaluation. Manual light compression and decompression of the ovaries by the transducer was performed attentively to achieve an optimal and consistent color coding. The quality factor of compression applied to the ovary, represented on a bar scale of 1–7, was used to select the optimal image, and images having an adequate compression (bar scale of 5–7) were evaluated. The scanning protocol was completed after the ovarian stroma was imaged adequately. RTE and B-mode US images were simultaneously displayed as a two-panel image. The elastographic box contained the ovary, the fallopian tube, and the surrounding tissue for all patients. The elastogram was visualized on a color scale with type 1 appearing as blue or blue-green (hardest tissue, no strain), type 2 as green or green-yellow (intermediate tissue, average strain), and type 3 as red or orange-red (softest tissue, greatest strain) over the B-mode US image (Fig. 1) (13). Cine RTE images (at least five seconds per ovary) were recorded by the sonography device digitally for later evaluation.

Data analysis

After obtaining all elastograms, static images and video sequences of patients and the control group were evaluated individually by two radiologists who were blinded to the clinical and biochemical findings and final diagnoses. Elasticity patterns were assessed as hard (type 1), moderate (type 2) or soft (type 3). The strain ratio for the ovarian stroma was then calculated by comparing the stroma (A) to the adjacent soft tissue outside the ovary that was clearly not bowel or blood vessel (B). The first region-of-interest (ROI) was placed on the adjacent soft tissue (B) and the second ROI was placed on the ovary containing ovarian stroma (A) entirely (Fig. 2). The strain ratio (B/A), represented graphically, indicating the stiffness of the ovarian stroma was then calculated automatically by the sonoelastography device. A minimum of three measurements were derived for each ovary and the mean value of six measurements was used to assess the strain ratio of the ovarian stroma for each patient.

Statistical analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS version 15.0, Chicago, Illinois, USA). Categorical variables are
Real-time elastography in polycystic ovary syndrome

Table 1. Strain ratios and elasticity pattern of ovaries in PCOS and control groups by two radiologists

<table>
<thead>
<tr>
<th>Elasticity pattern</th>
<th>Strain ratio</th>
<th>Observer 1</th>
<th></th>
<th></th>
<th></th>
<th>Observer 2</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1</td>
<td>Type 2</td>
<td>Type 3</td>
<td>(P)</td>
<td>Mean±SD</td>
<td>Type 1</td>
<td>Type 2</td>
<td>Type 3</td>
</tr>
<tr>
<td>PCOS group</td>
<td>61 (63.5)</td>
<td>12 (12.5)</td>
<td>23 (23.9)</td>
<td>&lt;0.001</td>
<td>6.1±1.8</td>
<td>&lt;0.001</td>
<td>38 (39.6)</td>
<td>31 (32.3)</td>
</tr>
<tr>
<td>Control group</td>
<td>9 (9.3)</td>
<td>16 (16.6)</td>
<td>71 (73.9)</td>
<td></td>
<td>3.3±1.2</td>
<td></td>
<td>2 (2.1)</td>
<td>34 (35.4)</td>
</tr>
</tbody>
</table>

Unless otherwise noted, data are presented as \(n\) (\%).

PCOS, polycystic ovary syndrome; SD, standard deviation.

Discussion

In this study we assessed the use of RTE for differentiating ovaries in patients with PCOS and healthy women. We determined that elasticity pattern and strain ratio parameter could be used to show the morphological changes in PCOS with moderate and good interobserver agreement, respectively.

Insulin resistance and hyperinsulinemia, exaggerated frequency and amplitude of serum luteinizing hormone secretion, increased production of ovarian and/or adrenal androgens, changes of cortisol metabolism and genetic transition can be seen in patients with PCOS (3, 15). Hyperinsulinemia, elevated serum luteinizing hormone/follicle stimulating hormone ratio,
ratio is a semiquantitative measure of relative tissue hardness (18). The strain pattern, because it showed images of the ovaries in PCOS, which we thought to be more objective than the elasticity pattern on elastographic images requires experience and may lead to false-negative diagnoses by elasticity (19).

There are different classifications of elasticity patterns with RTE. In the current study we used three types of elasticity patterns for assessing ovarian stiffness, which we thought easy to use (13). The type 1 pattern indicates a soft tissue with no or little elasticity, whereas type 3 indicates a hard tissue with no or little elasticity. Both observers agreed that ovaries in PCOS were significantly harder than normal, which can be demonstrated by RTE (17).

There are different classifications of elasticity patterns with RTE. In the current study we used three types of elasticity patterns for assessing ovarian stiffness, which we thought easy to use (13). The type 1 pattern indicates a soft tissue with no or little elasticity, whereas type 3 indicates a hard tissue with no or little elasticity. Both observers agreed that ovaries in PCOS were significantly harder than normal, which can be demonstrated by RTE (17).

We analyzed the strain ratio of the ovarian stroma, which we thought to be more objective than the elasticity pattern, because it showed images of relative tissue hardness (18). The strain ratio is a semiquantitative measurement of hardness of the lesion with respect to the adjacent soft tissues, where higher ratios point to harder tissues (9). We displayed the adjacent soft tissue in elastographic images and used it for comparison, to achieve a strain ratio. We detected high strain ratios in PCOS, representing the hard ovarian stroma, and found substantial interobserver agreement (ICC=0.77), which supports our theory. We chose a cutoff value of 3.8 for discrimination between the PCOS and control groups by strain ratio, which was closer to the mean strain ratio of the control group than the mean strain ratio of the PCOS group. We obtained sensitivity, specificity, PPV, and NPV values similar to those obtained from US findings of PCOS, such as detected number of follicles and ovarian volume. Although we did not compare patients with polycystic ovaries and PCOS patients without polycystic ovary appearance, this may imply that RTE, by providing the quality factor of compression, can be a useful diagnostic tool compared to the time consuming counting of ovarian follicles or ovarian volume by grayscale US (10). Also RTE displays ovarian stiffness as a result of histopathological changes in ovaries due to PCOS.

Both observers had false-positive or false-negative diagnoses by elasticity pattern or strain ratio, which could be related to previous diseases that affected the ovaries, such as infections, gonadal hormonal imbalances, or medications. Such previous diseases can change the elasticity properties of the ovaries and can make ovarian stroma harder or softer than normal, thus altering the RTE appearance or strain ratio of the ovaries. Also, duration of PCOS may affect the elasticity properties of the ovaries. With prolonged disease, older follicles regress, convert into stroma, and increase the subcortical stroma (15). Further studies comparing RTE with histopathological findings of the ovary and disease duration will be beneficial for solidifying this theory. Additionally, medications for PCOS may affect the ovaries, and thus, the ovarian stroma stiffness.

In this study the strain ratio showed moderate positive correlations with ovarian volume and the number of detected follicles which may be explained by a mechanism related with hyperandrogenism.

In our study, we had several limitations. First, polycystic ovary appearance can be seen in many healthy women under certain situations, such as taking combined contraceptive drugs, anovulation, and obesity (19). We did not have patients with polycystic ovary appearance in the control group and could not compare our results with them. Second, we excluded patients having cysts exceeding 9 mm, but small cysts around the ovarian stroma may affect the compression of the ovarian stroma due to the absence of strain of the fluid in them (20). Also RTE by transvaginal probe necessitates experience to evaluate the stiffness of the ovarian stroma because it requires lighter pressure rather than strong compression (10). Finally, we did not compare the strain ratio of the ovarian stromas in PCOS after various treatments, which could confirm that ovarian stiffness remains the same with PCOS.

In conclusion, this study highlights the possibility of PCOS evaluation by RTE, a relatively new, available, and dynamic imaging modality that can help to show morphological changes in PCOS. Elastographic features of ovarian stroma may have a role in the diagnosis of PCOS, like gray-scale US, especially using the strain ratio. However, further studies comparing women with polycystic ovaries with or without clinical symptoms or hormonal parameters of PCOS are needed to understand and appreciate the value of RTE in the diagnosis of PCOS.

Table 2. Comparison of strain ratio and gray-scale US findings to determine the presence of PCOS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Strain ratio</th>
<th>US findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observer 1</td>
<td>Observer 2</td>
</tr>
<tr>
<td>AUC</td>
<td>0.888</td>
<td>0.939</td>
</tr>
<tr>
<td>Optimal cutoff</td>
<td>&gt;3.8</td>
<td>&gt;3.8</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>87.5</td>
<td>89.5</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>85.4</td>
<td>83.3</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>85.7</td>
<td>84.3</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>87.2</td>
<td>88.8</td>
</tr>
</tbody>
</table>

US, ultrasonography; PCOS, polycystic ovary syndrome; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value.
Conflict of interest disclosure
The authors declared no conflicts of interest.

References
5. Fraser IS, Kovacs G. Current recommendations for the diagnostic evaluation and follow-up of patients presenting with symptomatic polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol 2004; 18:813–823. [CrossRef]