# Polikistik over sendromu olgularında meme terminal duktus çapları ve kan akımında değişiklikler

## Alterations in terminal duct diameter and blood flow in the breasts of subjects with polycystic ovary syndrome

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### ÖZ

**GİRİŞ ve AMAÇ:** *Polikistik over sendromu (PKOS) doğurganlık çağındaki kadınlarda en sık karşılaşılan jinekolojik ve endokrin bozukluktur. Bu çalışmanın amacı PKOS olgularında meme dokusunda terminal duktus çapları ve rezistivite indeks (RI) değerlerinde olan değişiklikleri gri skala ultrasonografi (US) ve renkli Doppler US (RDUS) ile değerlendirmektir.*

**YÖNTEM ve GEREÇLER:** *Çalışmaya 39 PKOS olgusu ile aynı yaşlardaki 22 sağlıklı ve gönüllü kontrol olgusu dahil edildi. Tüm katılımcıların vücut kitle indeksleri ve parite sayıları kaydedildi. Gri skala US ile terminal duktus çapları ve RDUS ile memenin iç, dış ve retroareolar bölgelerinden RI değerleri ölçülerek her olgu için ortalama RI değeri hesaplandı.*

**BULGULAR:** *PKOS olgularında terminal duktus çapları istatistiksel olarak anlamlı şekilde artmıştı (Dağılım; 0,8-4,4mm &1-2,95 mm, Ortalama (Ort) ± Standart Sapma (SS); 2,04 ± 0,73 mm &1,65 ± 0,64 mm; p = 0,04). Bununla birlikte gruplar arasında ortalama RI değerleri arasında istatistiksel anlamlı farklılık saptanmadı (Ort ± SS; 0,68 ± 0,06 & 0,66 ± 0,06; p = 0.432).*

**TARTIŞMA ve SONUÇ:** *PKOS olguları ile kontrol grubu arasında meme dokusunda RI değerleri arasında fark yok iken terminal duktus çapları arasında istatistiksel anlamlı farklılık saptandı.*

**Anahtar Kelimeler:** *Ultrasonografi, renkli Doppler ultrasonografi, polikistik over sendromu, meme, rezistivite indeksi, terminal duktus çapı*

### ABSTRACT

**INTRODUCTION:** *Polycystic ovary syndrome (PCOS) is the most common gynecological and endocrinal disorder amongst women of reproductive age. The aim of this study was to investigate the changes in the diameter of the terminal ducts and resistive index (RI) values of the breasts in subjects with PCOS using gray-scale ultrasonography (US) and Color Doppler Ultrasonography (CDUS).*

**METHODS:** *The study and control groups consisted of 39 subjects with PCOS and 22 age-matched, healthy volunteers, respectively. Body mass index and the parity history of all of the participants were recorded. The diameters of the terminal ducts of the both breasts were measured with gray-scale US and the RI values were evaluated at the medial, lateral, and retroareolar regions of the breasts with CDUS. The mean values of RI were calculated for each participant.*

**RESULTS:** *The diameter of the terminal ducts were statistically significantly increased in subjects with PCOS (range, 0.80-4.4 mm vs. 1-2.95 mm and mean ± standard deviation (SD), 2.04 ± 0.73 mm vs. 1.65 ± 0.64 mm, respectively; p = 0.04). However, there was no statistically significant difference between PCOS and control groups regarding the mean average RI values (mean ± SD, 0.68 ± 0.06 vs. 0.66 ± 0.06, respectively; p = 0.432).*

**DISCUSSION AND CONCLUSION:** *There was no difference regarding the blood flow between two groups, but the diameters of the terminal ducts were increased in PCOS group.*

**Keywords:** *Ultrasonography, Color Doppler Ultrasonography, polycystic ovary syndrome, breast, resistive index, diameter of terminal ducts*

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common gynecological and endocrinal disorder that affects as much as 15% of women (1). Primary features of PCO are hyperandrogenism and ultrasound morphology (2). The accepted long-term health risks of PCOS are obesity, type II diabetes mellitus, cardiovascular diseases, dyslipidemia, and endometrial cancer (3). PCOS also could be a risk factor for other estrogen-dependent tumors such as breast and ovarian cancer (4). However, it has been suggested that unopposed hyperestrogenism can cause benign breast diseases (5). Some reports revealed a higher prevalence of benign breast diseases in patients with PCOS (6,7).

Cyclical hormonal variations cause changes in blood flow and angiogenesis in the ovaries and endometrium (8,9). Gorins and Denis showed that growth of the mammary glands was affected by the critical balance between estrogen and progesterone (10). Furthermore, the hormones that affect ovaries also affect other areas like endometrium, breast, thyroid, and pancreas. In addition, it is a common knowledge that all benign or malignant tumors are formed via vascularization.

There are many reports that have focused on the blood flow changes in breast diseases (11-15). The breast blood flow is different in the pre- and postmenopausal women (16). Questions have risen regarding whether or not hormones could affect vascular structures.

The aim of this study was to investigate the breast blood flow and the diameters of terminal ducts in patients with PCOS using gray-scale ultrasonography (US) and color Doppler ultrasonography (CDUS).

## MATERIALS AND METHODS

This study was designed as a prospective case-controlled study. The University of Tokat Gaziosmanpasa School of Medicine local Human Research Ethics Comittee gave their approval, and all participants provided their written informed consent for participation prior to the investigation. The study group consisted of 39 consecutive cases with PCOS patients who were diagnosed at the Department of Obstetrics & Gynecology of Gaziosmanpasa University Faculty of Medicine, from January 2012 to March 2013. The diagnoses of PCOS was made according to the criteria of the Rotterdam European Society for Human Reproduction and Embryology (ESHRE)/American Society for Reproductive Medicine (ASRM)–sponsored PCOS Consensus Workshop Group (2004), with two out of the following three criteria being a requirement: oligomenorrhea (<6 menstrual periods in the preceding year) and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, and the presence of 12 follicles in each ovary measuring from 2–9 mm in diameter and/or an increased ovarian volume (>10 ml) (17). The control group consisted of 22 age-matched, healthy volunteers who were recruited from the hospital staff that had neither clinical nor US findings of PCOS. The subjects who were using oral contraceptives and had atherosclerotic risk factors were excluded.

Body mass indexes (BMI) of all cases were calculated. The parity histories of all participants were recorded.

US examinations were performed by the a radiologist experienced in this field, using the ACUSON Antares™ US system (Siemens AG, Erlangen, Germany) with a 13-5 MHz linear array transducer in dorsal decubitus position. The transmitted Doppler frequency ranged from 5-10 MHz, the pulse repetition frequency varied between 488 and 1563 Hz, and the wall filter was always set at its lowest setting. The Doppler gain was also adjusted to maximize sensitivity without producing color noise, and the angle correct cursor was manually aligned parallel to the flow direction with Doppler angles of approximately 60 degrees. The diameters of the terminal ducts of both breasts were measured with gray scale US (Fig. 1).

*Figure 1. The largest diameter of the terminal duct of the left breast of a 26-year-old patient with PCOS was 2.5 mm.*

The resistive index (RI) values were measured from the branches of the lateral and internal thoracic arteries at the horizontal line that crosses the nipple and at the medial, lateral, and retroareolar regions of the breasts. The retroareolar region was defined as the breast tissue at the posterior of the areola, and the other regions were designated by the contiguity regions located at the medial or lateral part of the areola. In addition, the mean of the three measured RI values for each of the subjects was calculated (Fig. 2).
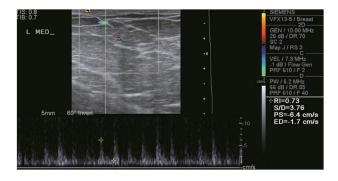


*Figure 2. The blood flow parameters of a branch of internal thoracic artery at the medial portion of the left breast of a 32-year-old patient with PCOS.*

All statistical analyses were performed using the SPSS version 11.01 for Windows software program (SPSS Inc, Chicago, IL, USA). Continuous data was expressed as mean ± standard deviation (SD), and categorical data was given as numbers with the related percentages (n, %). The differences in the categorical data were analyzed using a chi-square test, and the continuous variables between the groups were compared via Student's t test. A p-value of < 0.05 was considered to be statistically significant.

**RESULTS**

There was no statistically significantly difference in terms of age, parity, and BMI (p>0.05) between both groups (Table 1). The diameters of the terminal ducts were statistically significantly higher in PCOS group than control group [range, 0.80-4.4 mm vs. 1.0-2.95 mm and mean ± standard deviation (SD), 2.04 ± 0.73 mm vs. 1.65 ± 0.64 mm, respectively; p = 0.04]. Furthermore, the two groups demonstrated no significant difference with regard to the mean RI values (mean ± SD, 0.68 ± 0.06 vs. 0.66 ± 0.06, respectively; p = 0.432) (Table 2).

**Table 1. Demographic and baseline characteristics of the study and control groups.**

|  | PCOS (n =29) n(%) Mean ±SD | Control (n =22) n ( %) Mean±SD | P |
|---|---|---|---|
| *Age (years)* | 25.03 ± 5.79 | 26.59 ± 6.48 | 0.432 |
| *BMI (kg/m²)* | 25.79 ± 5.27 | 25.06 ± 3.42 | 0.624 |
| *Parity history* | 14 (48.3) | 9 (40.9) | 0.138 |

PCOS: Polycystic ovary syndrome; SD: Standard deviation; BMI: Body mass index

**Table 2. Mean resistive index values and mean terminal duct diameters of the study and control groups.**

|  | PCOS (n =29) Mean ±SD | Control (n =22) Mean ±SD | P |
|---|---|---|---|
| *RI values* | 0.68 ± 0.06 | 0.66 ± 0.06 | 0.432 |
| *Diameters of the terminal ducts (mm)* | 2.04 ± 0.73 | 1.65 ± 0.64 | 0.04 |

*PCOS: Polycystic ovary syndrome; SD: Standard deviation; RI: Resistive index*

## DISCUSSION

PCOS is a common and complex ovarian dysfunction in women of childbearing age. It occurs when the cyclic secretion of hormones from the pituitary gland and ovaries is disturbed. In patients with PCOS a disproportionally high lutein hormone (LH) secretion with relatively low or normal follicular-stimulating hormone secretion is observed (12). Moreover, the estrogen levels are increased because of the conversion in the peripheral body. The androgen levels are also increased and the progesterone levels are decreased (13).

Ovarian and adrenal steroids as well as the pituitary, thyroid, and pancreatic hormones contribute to the growth, secretory differentiation, lactogenesis, and galactopoiesis of the mammary glands (18,19). The formation of duct is mainly dependent on estrogen whereas structural growth, secretory differentiation, initiation, and the maintenance of milk secretion are dependent on prolactin (14,18). During the menstrual cycle, structural and functional changes occur in breasts which are related to hormones, and these hormones are carried to the breast via vessels. Dogliatti et al. suggested that dynamic hormonal changes and chronobiological rhythms (i.e., daily, menstrual, and seasonal changes) play important roles in the development of benign breast disorders (20).

Our data indicated that the mean diameters of the terminal ducts were statistically significantly higher in the PCOS patients than the control subjects. Panaritis et al. also suggested a relationship between the diameters of terminal ducts and PCOS like the results of our study (21). Furthermore, in another study by Milliken et al. that involved transgenic mice they reported that the increased LH levels were the cause of gland hyperplasia (22).

Rettenbacher et al. reported that the mean RI of breasts is lower in premenopausal women than postmenopausal women and explained that this is the result of a loss in metabolic activity (16). We know that this loss of activity in postmenopausal women is caused by hormonal changes; hence, it is possible that diseases characterized by hormonal changes could affect the breasts. Many hormonal changes occur in patients with PCOS, but it is unclear how these changes affect the breasts. One theory is that this occurs via the changes in blood flow. In fact, there are many reports regarding the blood flow changes in malignant and benign tumors of the breast (13-15,21,22). PCOS-related breast disorders have been examined by some authors (4-7,11). However, to our knowledge, this is the first study that has evaluated blood flow changes in the breasts of patients with PCOS. We suggested that the hormonal changes which were caused by PCOS could change the blood flow of breasts. But we found no statistical difference in the RI values between the PCOS and control groups. Other pathways should also be taken into consideration, such as increased receptor activities and higher growth factor levels. Thus, more research studies might be helpful on this topic.

The RI values of our study groups similar to the Rettenbacher et al. study. They reported statistically significantly higher RI values in the breasts of postmenopausal women than premenopausal women (16). Their mean RI value for premenopausal women was 0.64 while it was 0.70 for postmenopausal women. The mean RI values of our subjects with PCOS (0.68 ± 0.06) were close to those of the postmenopausal women in their study group. Whereas, the mean RI values of the control subjects (0.66 ± 0.06) in our study were close to those found in their premenopausal women.

There are some limitations of the present study. Because of the ethical, legal, and financial reasons, it was not possible to obtain the hormone levels in both groups. Besides, the sample sizes of both groups were small.

## CONLUSIONS

Our study demonstrated increased diameter in terminal ducts of the patients with PCOS. Further studies should be conducted to evaluate the changes in blood flow of the breasts of patients with PCOS.

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Nil

**Conflicts of interest**

There are no conflcts of interest.

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