

# Comparison of uterine, endometrial and ovarian blood flow by transvaginal color Doppler ultrasound in ovulatory and anovulatory cycles

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## ABSTRACT

**Objectives:** Blood flow to uterus and ovaries is demonstrated to be altered during menstruation. Studies has been published stating that blood flow differs also in ovulatory and anovulatory cycles. In this study, using color Doppler ultrasound, we aim to compare uterine, endometrial and ovarian blood flow during ovulatory and anovulatory cycles.

**Material and methods:** Women volunteers who are aged between 18–40 had no endocrinological problem and not receiving exogenous hormone therapy were included to study. Blood levels of FSH, LH, E2, prolactin, DHEAS, free T4 were collected in early follicular phase. Uterine, subendometrial and intraovarian artery blood flow pulsatility and resistance indexes were analysed using Doppler USG technique. Patients were called out to control on 21st of cycle and progesterone levels were analysed. Patients who has ovulation signs in USG and progesterone level above 5 ng/mL were included to ovulatory cycle group. Patient who has no signs of ovulation in ultrasound and has not enough progesterone level were included to anovulatory cycle group.

**Results:** LH and E2 levels were significantly higher in anovulatory patients. No correlation was found between endometrial blood flow resistance and basal E2, prolactin, testosterone levels. However, DHEAS levels were related to endometrial blood flow resistance in anovulatory cycles. No correlation was found between ovarian blood flow resistance/uterine blood flow resistance and basal E2, prolactin, testosterone, DHEAS levels.

**Conclusions:** There is statistically significant difference between endometrial, ovarian, uterine artery blood flow resistance in ovulatory and anovulatory cycles. Blood flow resistance was found to be increased in anovulatory patients. Increased E2 levels in anovulatory cycles were related to endometrial linethickness and endometrial volume

**Key words:** ovulation, Doppler ultrasound, anovulation

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## INTRODUCTION

Body functions are directly influenced by vascularization. The function of the reproductive system varies greatly throughout the menstrual cycle, for follicular development, ovary and endometrium are dependent on blood flow. Blood flow patterns through the ovary and the endometrium can also change by the new blood vessels and microvascularization. The ovarian tissue during the menstrual cycle undergoes cyclic changes and dynamic processes: follicular development, ovulation, luteal growth, regression, and follicular. Similarly, these cyclic changes can also be seen in the uterus and the endometrium.

The vascularization of the dominant follicle was higher than of other follicles on day 9 of the cycle [1]. Being a part of the corpus luteum cells of the endothelial cells is thought to be evidence of changes in vascularization [2].

Since 1970s, color Doppler ultrasonography has been used during the menstrual cycle as a non-invasive method to monitor uterine and ovarian blood flow [3–6]. With the constant change and development of Doppler ultrasound, and a widespread use of this technique, uterine and ovarian arteries as well as endometrial, sub-endometrial, ovarian artery and ovarian stromal blood flow changes during the menstrual cycle have been shown [5–8].

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Various studies showing that the ovarian blood flow changes dramatically during the ovulation have been published [9]. Different authors also claim that a decline in the ovarian artery blood flow resistance, which may be associated with ovarian function, has been demonstrated in cycles with ovulation during the luteal phase [5].

In this study, we aimed to compare uterine, endometrial and ovarian blood flow using color Doppler ultrasound during ovulatory and anovulatory cycles.

## MATERIAL AND METHODS

Our study included 86 patients who were admitted to gynecology policlinics of the Sisli Etfal Research and Training Hospital Gynecology Department due to various reasons, between March 1, 2014 and February 1, 2015. Local Ethics Committee approved of the study.

Women (aged 18–40 years) without endocrine disorders such as diabetes, hyperthyroidism, hypothyroidism, hypertension, hyperprolactinemia, polycystic ovary syndrome, and women not using exogenous hormones were included in the study. All participating volunteers gave their informed consent. Age, smoking, secondary diseases, gravidity, parity, and menstrual patterns, were recorded. Weight and height measurements were used to calculate the body mass index (BMI).

Fasting blood samples were taken between 10:00 and 08:00 in the morning. On day 2 of the menstruation, in the early follicular phase, FSH, LH, E2, prolactin, DHEAS, and free testosterone, TSH, free T4 levels were measured. Hormonal measurements were performed using the enzyme immunoassay method (Roche Elecsys 2010, Roche Diagnostics GmbH, Mannheim, Germany).

The patients were examined with transvaginal ultrasound B-mode and color Doppler. Uterine artery, sub-endometrial (spiral arteries) and intraovarian artery blood flow Doppler technique pulsatility index (PI) and resistance (RI) index were measured. Right and left basal ovarian follicular assessment was performed with transvaginal ultrasound. Patients were called back on menstruation day 21 for the analysis of progesterone levels. Transvaginal ultrasonographic evaluation was used to determine whether the participants were ovulating. Rupture of the follicle, follicle shrinkage, presence of the corpus luteum, and fluid in the Douglas pouch, etc., were accepted as signs of the ovulation. Ovulation confirmed on ultrasound and progesterone levels of > 5 ng/mL were the inclusion criteria for the ovulatory group. Patients with progesterone levels of < 5 ng/mL and no signs of the ovulation on ultrasound on day 21 of the menstruation constituted the anovulatory group. Volunteers were called back for check-up at the end of the menstruation. Endometrial and ovarian volumes were measured.

Windows SPSS 15.0 was used for statistical analysis. The t-test was used to analyze clinical and biochemical data of the independent groups. The p-value of < 0.05 was considered as statistically significant.

## RESULTS

A total of 86 participants were included in the study and divided into the ovulatory and anovulatory cycle groups. Ovulation was confirmed in the 36 (37.5%) women while 50 (62.5%) had anovulatory cycles. Age, BMI, gravidity, parity, and smoking status were assessed in both groups but no statistically significant differences were detected (Table 1).

Mean FSH, LH, TSH, E2, prolactin, FT4, DHEAS, testosterone levels were calculated in the ovulatory and anovulatory patients. Women with the anovulatory cycles were assessed on day 2 of the menstruation and LH and E2 levels were found to be significantly higher (Table 2).

Uterine, ovarian and endometrial artery PI-R values were lower in the ovulatory patients. Endometrial thickness, endometrial volume, right over volume, and left over volume were also significantly different between the ovulatory and anovulatory groups (Table 3).

No correlation was found between endometrial blood flow resistance, basal E2, prolactin, and testosterone levels. However, DHEAS levels in the anovulatory group were found to be proportional to the endometrial blood flow

**Table 1. Characteristic of the study group**

	Ovulatory cycle (n: 36)	Anovulatory cycle (n: 50)	P result
Age	30.8 ± 8.3	29.8 ± 6.8	0.536
BMI [kg/m <sup>2</sup> ]	25.5 ± 5.5	26.6 ± 5.7	0.369
Gravida	2.4 ± 2.0	2.1 ± 1.8	0.458
Parity	1.6 ± 1.4	1.4 ± 1.4	0.595
Smoke	14 (38%)	19 (38%)	0.933

**Table 2. Hormone levels of the participants**

Hormones	Ovulatory cycle (n: 36)	Anovulatory cycle (n: 50)	P result
FSH	7.6 ± 2.0	7.6 ± 4.1	0.996
LH	5.7 ± 1.6	10.2 ± 3.9	0.003
TSH	1.4 ± 0.9	1.6 ± 0.87	0.140
E2	66.2 ± 19.2	90.1 ± 64.4	0.033
Prolactin	17.0 ± 6.19	17.7 ± 6.4	0.503
FT4	1.23 ± 0.85	1.1 ± 0.19	0.371
DHEAS	235.1 ± 79.3	231.0 ± 55.4	0.779
Testosteron	39.6 ± 17.8	47.7 ± 19.4	0.051

**Table 3.** Transvaginal ultrasound B-mode and color Doppler results

	Ovulatory cycle (n: 36)	Anovulatory cycle (n: 50)	P result
Uterine artery PI	1.78 ± 0.28	1.99 ± 0.38	0,006
Uterine artery RI	0.80 ± 0.12	0.87 ± 0.08	0.003
Ovary artery PI	1.73 ± 1.19	1.90 ± 0.42	0.030
Ovary artery RI	0.79 ± 0.10	0.85 ± 0.10	0.009
Endometrial artery PI	1.69 ± 0.20	1.86 ± 0.39	0.021
Endometrial artery RI	0.78 ± 0.11	0.86 ± 0.10	0.001
Endometrial thickness	3.9 ± 2.5	8.3 ± 2.5	0.001
Endometrial volume	1.8 ± 0.69	2.75 ± 0.65	0.001
Right ovary volume	6.1 ± 1.6	4.6 ± 1.5	0.001
Left ovary volume	6.6 ± 2.6	5.03 ± 1.65	0.001

**Table 4.** The effect of hormones on the endometrial artery resistance index

Hormones	P result
E2	0.209
Prolactin	0.808
DHEAS	0.044
Testosterone	0.082

**Table 5.** The effect of hormones on the ovarian artery resistance index

Hormones	P result
E2	0.069
Prolactin	0.781
DHEAS	0.898
Testosterone	0.816

**Table 6.** The effect of hormones on the uterine artery resistance index

Hormones	P result
E2	0.494
Prolactin	0.870
DHEAS	0.965
Testosterone	0.231

resistance. No correlation was found between ovarian blood flow resistance and E2, prolactin, DHEAS, and testosterone levels. Also, there was no statistically significant correlation between uterine blood flow resistance and basal E2, prolactin, DHEAS, and testosterone levels (Tables 4–6).

## DISCUSSION

In our study, we detected significant differences between the uterine artery, the ovarian artery, and the endometrial artery blood flow resistance in ovulatory and anovulatory cycles. Blood flow resistance parameters in the anovulatory group were significantly higher as compared to the ovulatory group. The literature offers a number of reports on transvaginal Doppler examination of the uterine, ovarian, and endometrial arteries during a normal menstrual cycle [2, 6, 8–10]. Kutlesic et al., found that ovarian artery stromal blood flow resistance and sub-endometrial artery blood flow resistance in the ovulatory group is lower as compared to the anovulatory group. These authors were not able to find any differences in arcuate artery blood flow resistance. They found that uterine and ovarian artery Doppler ultrasound PI and RI levels, blood flow resistance in the ovulatory groups was lower as compared to the anovulatory groups. In our study, we found that anovulatory group blood flow resistance was higher as compared to the ovulatory group. The same results have been found in IVF patients who had no ovulation and had undergone controlled ovarian hyperstimulation. In the same study by Kutlesic et al., in the ovulatory group, ovarian stromal artery blood flow resistance was proportionate to the E2 levels and inversely correlated with gonadotropin levels. Also, no correlation was found between basal hormone levels and blood flow resistance in the anovulatory group. It has been attributed to several other factors which also affect the ovulation. Nevertheless, blood flow to the uterus and the ovaries was concluded to be influenced by local factors more than hormone levels in circulation. In our study, there was also no correlation between blood flow resistance and basal FSH, LH, E2, and prolactin levels but in anovulatory cycles, DHEAS levels were proportionate to the endometrial blood flow resistance. Dal et al., showed that during the mid-luteal phase of ovulatory cycles, uterine, arcuate, radial and spiral arteries blood flow resistance index is lower than in the anovulatory cycles [11–13]. Merce et al., also investigated intraovarian Doppler velocimetry in ovulatory, dysovulatory, and anovulatory cycles, and found that the luteal phase dominant follicle had lower blood flow resistance, the intraovarian resistance index has not changed in anovulatory cycles, and it is obvious that the absence of the ovulation prevents the change of intraovarian spiral artery network. Blood flow changes in the luteal phase have to be determined by ultrasound to detect the ovulation [14]. In our study, we found the ovulatory cycle blood flow resistance to be lower as compared to the anovulatory cycles.

Estrogen shows its effect on the uterine blood vessels and the endometrium through beta-2E2 receptors. E2 recep-

tors are found on the walls of the uterine artery, so estrogen has as a direct vasodilator effect on the uterine vessels [15]. In patients with premature ovarian failure, low estrogen levels decrease PI values in the uterine artery [16]. The effect of progesterone on the uterine artery blood flow has been less studied. In cases of luteal insufficiency, using exogenous progesterone levels increases uterine blood flow in the presence of normal estrogen levels [17]. In our study, we found increased endometrial thickness and endometrial volume with elevated E2 levels in the anovulatory group. However, no correlation was found between E2 levels and blood flow resistance in the ovulatory and anovulatory groups.

In various studies, color Doppler ultrasound examination, especially on the side of the dominant follicle, revealed lower blood flow resistance between uterine and ovarian arteries. This is directly related to the fact that local factors of the dominant follicle affect the blood flow [18]. There is no dominant follicle in anovulatory cycles, so the absence of the dominant follicle and local factors is related to increased blood flow resistance. However, in patients with PCOS, who have no ovulation, local factors are related with increased stromal vascularization [19]. Our study demonstrated that local factors can change the blood flow. In this regard, there is a need for a further study.

Numerous reports in the literature state that deficiency of physiological changes of blood flow during the menstrual cycle can cause infertility. Steer et al., showed that increased uterine artery blood flow resistance can cause unexplained infertility [20]. In another study, Taylor et al., found that patients undergoing controlled ovarian hyperstimulation have increased ovarian artery blood flow resistance and low response to in vitro fertilization [21]. Temizkan et al., demonstrated that hyperprolactinemia had a vasoconstrictor effect and was related to increased blood flow resistance [22]. However, in our study there was no correlation between prolactin levels in both groups.

## CONCLUSIONS

There is a statistically significant difference between endometrial, ovarian, uterine artery blood flow resistance in ovulatory and anovulatory cycles. Increased E2 levels in anovulatory cycles were related to endometrial line thickness and endometrial volume. Increased DHEAS levels in anovulatory patients were related to endometrial artery blood flow resistance.

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