

## ORIGINAL RESEARCH

# Study to evaluate uterine blood flow measurements in spiral arteries by transvaginal colour doppler sonography in predicting endometrial tumors at a tertiary care centre, South India

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### ABSTRACT

**Aim:** The aim of the present study is to evaluate the diagnostic value of blood flow measurements in spiral artery by transvaginal Colour Doppler Sonography (CDS) in predicting endometrial tumors. **Material & Methods:** A prospective observational study was carried out at Department of radiology and secondary data of patients is collected from the Obstetrics and Gynaecology department. 200 patients presenting with abnormal uterine bleeding and requiring endometrial assessment were included. **Results:** Mean age, parity, and endometrial thickness of the participants were  $45.15 \pm 2.58$  years,  $3.2 \pm 2.14$  and  $12.46 \pm 6.34$  mm respectively. The histopathological diagnoses were as follows; 84 cases (42%) endometrial polyp, 18 cases (8%) endometrial hyperplasia, 24 cases (12%) submucous myoma, 16 cases (8%) endometrium cancer, and 60 cases (30%) nonspecific findings. There were significant correlations between spiral artery PI and different endometrial histopathological pictures. There were significant correlations between spiral artery RI and different endometrial disease conditions (tumors). **Conclusion:** Endometrial spiral artery Doppler changes were strongly associated with the existing endometrial tumors and diseases among the study participants.

**Key words:** Spiral artery, doppler ultrasonography, endometrium

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### INTRODUCTION

Endometrial cancer (EC) ranks as the sixth most prevalent cancer among women globally and is the most frequent malignant gynaecological condition in postmenopausal women due to the rise in life expectancy. According to GLOBOCAN's estimation for the year 2020, there were approximately 417,000 new cases and 97,000 fatalities. Furthermore, the number of cases has risen in numerous countries <sup>1</sup>. There is a direct correlation between the age of a woman experiencing postmenopausal bleeding (PMB) and her chance of developing endometrial cancer (EC). <sup>2</sup> Fortunately, surgical intervention can cure 95% of EC stage I cases, resulting in a 5-year survival rate of 85-91%. Additionally, vaginal bleeding is a common symptom in around 90% of EC cases. PMB, or postmenopausal bleeding, is characterized by

vaginal bleeding that occurs after a woman has gone without menstruation for more than 12 months <sup>2, 3</sup>. Postmenopausal bleeding (PMB) is an initial indication of endometrial cancer (EC), with around 10% of cases of PMB being associated with EC. Overall, the occurrence of malignant endometrial pathology is four times higher in women who have bleeding compared to those who do not <sup>4</sup>. Presently, a variety of modalities for examining the uterus have been utilized, encompassing both invasive and non-invasive techniques. Nevertheless, invasive procedures and costly methods are not appropriate for healthcare centers in low to middle-income nations. Ultrasound has gained widespread acceptance as the primary method for addressing gynaecologic issues due to its dependable nature and widespread availability. Specifically, the Doppler ultrasound can

precisely identify the blood flow within a tumor<sup>5</sup>. The low values of the resistance index (RI), pulsatility index (PI), and peak systolic velocity (PSV) of the uterine artery (UtA) are linked to the presence of malignancy<sup>6, 7</sup>. The utilization of Grey scale ultrasound in conjunction with transvaginal colour Doppler ultrasound (TV-CDU) is valuable in differentiating between benign endometrium and endometrial malignancy. Additionally, this technique can assist in distinguishing between low-grade and high-grade cancers, as well as assessing the extent of tumor invasion prior to surgery<sup>8</sup>. Nevertheless, the use of this combination continues to be a subject of debate and disagreement among various research investigations<sup>9</sup>.

Colour Doppler sonography, a non-invasive and straight forward technique, is valuable in differentiating endometrial lesions, aiding in determining the need for intrusive tests, and strategizing the appropriate invasive approach to be utilized. Endometrial carcinoma is the predominant tumor affecting the female reproductive system<sup>10</sup>. Endometrial thickening is an indeterminate indication of endometrial cancer<sup>11</sup>. Therefore, using colour Doppler sonography (CDS) on the genital vasculature can enhance the accuracy of transvaginal sonography (TVS) in detecting and predicting endometrial cancers<sup>12</sup>.

The study aimed to evaluate the diagnostic significance of sub endometrial spiral artery blood flow parameters in predicting underlying endometrial tumors and diseases.

## MATERIAL & METHODS

This is a Hospital based prospective observational study which is carried out at Department radiology with the help of secondary data from obstetrics and Gynaecology department over a period of one year since January 2023 to January 2024. 200 patients presenting with abnormal uterine bleeding and requiring endometrial assessment were included.

## EXCLUSION CRITERIA

Pregnancy, Pelvic inflammatory disease, Cervicitis,

## RESULTS

**Table 1: Demographic and clinical variables among the study participants**

Variables	Mean $\pm$ SD
Age (years)	45.15 $\pm$ 2.58
Gravity	4.3 $\pm$ 3.57
Parity	3.2 $\pm$ 2.14
Hemoglobin concentration (g/dl)	12.52 $\pm$ 1.86
Endometrial thickness (mm)	12.46 $\pm$ 6.34

Mean age, parity, and endometrial thickness of the participants were 45.15 $\pm$ 2.58 years, 3.2  $\pm$  2.14 and 12.46 $\pm$ 6.34 mm respectively.

**Table 2: Histological diagnosis of all study participants**

Histological diagnosis	N%
Endometrial polyp	84 (42)
Endometrial hyperplasia	16 (8)

Genital tumor, Systemic diseases causing abnormal uterine bleeding, Intrauterine device use and Use of drugs affecting uterine vasculature such as hormonal therapy, oral contraceptives or tamoxifen during the previous 3 months.

## METHODOLOGY

This study is conducted according to the guidelines for clinical studies described in the Declaration of Helsinki. All patients gave oral and written informed consent prior to the examination. The patients were examined prospectively by standard B-mode TVS and CDS in the mid-follicular phase. Histopathologic examination was performed in the pathology laboratory of our hospital. All ultrasound scans were performed by the same examiner to avoid interobserver variability. All women were examined firstly using conventional gray-scale TVS with a 5.0-MHz transvaginal probe in the lithotomy position with an empty bladder. The uterus was thoroughly assessed in coronal and sagittal planes using a esaote 2D machine. Endometrial double layer thickness, structure and echogenicity were noted. Endometrial double layer width is measured at the thickest portion of the longitudinal section. Then, vascularization of the uterus is visualized with colour Doppler technique. Blood flow velocity waveforms were evaluated in the spiral arteries at the sub endometrial region that is within 1 mm of the originally defined myometrial-endometrial contour<sup>13</sup>. The results of the examinations were compared with the histologic diagnosis of the endometrial specimen. The primary outcome measures were spiral artery Pulsatility index (PI) and spiral artery resistive index (RI).

## STATISTICAL ANALYSIS

Statistical calculations were undertaken using SPSS version 22. Categorical data were compared using the chi-square test. Kruskal Wallis test was used to compare the parameters with abnormal dissociation between the groups for descriptive statistical methods as well as quantitative data. Result assumed to be statistically significant if the P value of each respective test was  $\leq$  0.05.

Submucous fibroid	24 (12)
Endometrium cancer	16 (8)
Nonspecific findings	60 (30)

The histopathological diagnoses were as follows; 84 cases (42%) endometrial polyp, 18 cases (8%) endometrial hyperplasia, 24 cases (12%) submucous myoma, 16 cases (8%) endometrium cancer, and 60 cases (30%) nonspecific findings.

**Table 3: Comparison of the pulsatility indices (PI) of spiral artery between endometrial tumor and other pathologies**

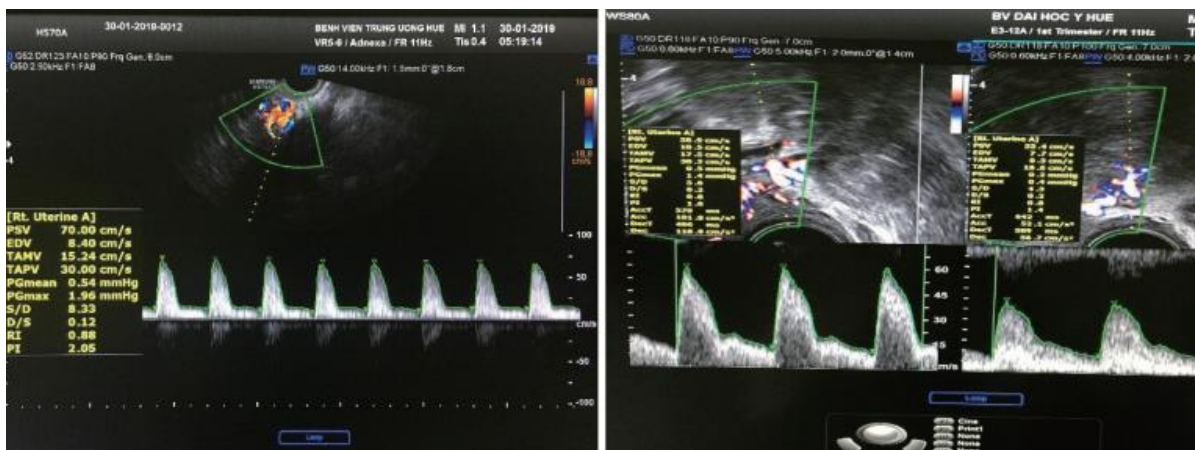
Endometrial histology	Spiral Artery PI Mean ± SD	P Value
Endometrial polyp	0.55±0.05	0.001
Endometrial hyperplasia	1.36±0.34	0.001
Submucous fibroid	1.06±0.44	0.001
Endometrium tumors	1.16±0.46	0.001
Nonspecific findings	1.12±0.56	0.005

There were significant correlations between spiral artery PI and different endometrial histopathological pictures.

**Table 4: Comparison of the spiral artery resistive indices between endometrial tumor and other pathologies**

Endometrial histology	Spiral Artery RI Mean±SD	P Value
Endometrial polyp	0.46±0.04	0.001
Endometrial hyperplasia	0.72±0.18	0.001
Submucous fibroid	0.55±0.17	0.001
Endometrial tumor	0.57±0.14	0.005
Nonspecific findings	0.54±0.15	0.055

There were significant correlations between spiral artery RI and different endometrial histopathological pictures.



Determination of bilateral uterine arteries the Doppler window was opened from 1.5–2.0 mm. The Doppler angle between the ultrasound beam and the vascular direction was <20 degree. RI, PI, and PSV index were automatically calculated from three consecutive waveforms. RI, resistance index; PI, pulsatility index; PSV, peak systolic velocity.

**DISCUSSION**

Transvaginal sonography has demonstrated high

accuracy in excluding endometrial cancer in women who experience postmenopausal bleeding. A recent meta-analysis has shown that the risk of endometrial cancer is minimal when the double-layer endometrial thickness, as determined by transvaginal sonography, is less than 5 mm. Fourteen Nevertheless, endometrial thickening is a nonspecific observation that can arise from various causes, including cancer, polyps, hyperplasia, or even endometrial cystic atrophy. Transvaginal color Doppler allows for a direct

evaluation of the blood flow in the uterus and endometrium<sup>15</sup>. Endometrial carcinoma is the most prevalent type of cancer, but malignant tumors of the myometrium are seldom. Endovaginal ultrasonography (EVU) is the preferred imaging technique for the initial assessment of women experiencing uterine bleeding during the post or perimenopausal period, as well as intermenstrual bleeding. Endometrial cancer can be effectively ruled out in postmenopausal women with irregular bleeding if the endometrial thickness is less than 4 mm. This method has a sensitivity rate of 94.8% and a specificity rate of 46.7%<sup>16,17</sup>.

The average age, number of previous pregnancies, and thickness of the endometrium in the individuals were 45.15±2.58 years, 3.2 ± 2.14, and 12.46±6.34 mm, respectively. The histological diagnosis were as follows: 84 cases (42%) were diagnosed as endometrial polyp, 18 cases (8%) as endometrial hyperplasia, 24 cases (12%) as submucous myoma, 16 cases (8%) as endometrium tumors, and 60 cases (30%) had nonspecific features. There were strong associations observed between the pulsatility index (PI) and resistance index (RI) of spiral arteries and various types of endometrial histologies. Recently, numerous researches have been conducted on the evaluation of the uterine cavity using gynaecologic Doppler ultrasound. Ernest et colleagues conducted a study to examine the correlation between uterine blood flow and blood flows in the endometrium and sub endometrium, both in stimulated and spontaneous menstrual cycles<sup>18</sup>. Several researchers have also investigated the impact of various drugs on the blood flow in the uterine artery and endometrium<sup>19-21</sup>.

This study focused on examining the vascularization of the endometrium and myometrium using Doppler sonography. Endometrial polyps, fibroids, and endometrial cancer have been associated with several discriminatory vascular patterns<sup>22-24</sup>. Epstein *et al.*<sup>25</sup> discovered that power Doppler can aid in accurately diagnosing endometrial cancer in women experiencing postmenopausal haemorrhage who have an endometrial thickness more than 5 mm. Samulak *et al.* conducted a study to assess the maximum end-diastolic velocity of blood flow in the uterine artery, the time-averaged maximum velocity of blood flow (TAMXV), and the peak systolic velocity of blood flow in women experiencing postmenopausal haemorrhage. Despite being statistically insignificant, the values were observed to be the greatest in the carcinoma group and the lowest in the control group<sup>26</sup>. This indicates reduced resistance to the flow of blood in malignant growths. Englert-Golon *et al.* found that patients with endometrial cancer had considerably lower pulsatility index (PI) and resistance index (RI) in the endometrial vasculature and uterine arteries compared to patients with endometrial hyperplasia. Additionally, patients with endometrial cancer had significantly greater time-averaged maximum velocity (TAMXV) in the

endometrial vessels and uterine arteries. This was reported in a study by Englert-Golon *et al.*<sup>27</sup>.

The current investigation demonstrated an association between the pulsatility index (PI) and resistance index (RI) of the spiral artery and the presence of endometrial tumor. Patients diagnosed with endometrial tumor had significantly reduced spiral artery pulsatility index (PI) and resistance index (RI) compared to those without malignant histology. Patient with endometrial tumor and hyperplasia exhibited a notably increased endometrial thickness.

## CONCLUSION

To summarize, there is a strong association observed between endometrial tumors and diseases in relation with alterations in the endometrial spiral arteries. Currently, the use of Doppler ultrasound as a diagnostic test is not approved, despite the fact that patients with malignant endometrial lesions show decreased impedance in the blood flow of the spiral arteries. Nevertheless, as technology progresses, colour Doppler sonography has the potential to supplement invasive diagnostic techniques for diagnosing endometrial tumors and diseases.

## REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021 May;71(3):209-249.
2. Bengtson MB, Veres K, Nørgaard M. First-time postmenopausal bleeding as a clinical marker of long-term cancer risk: A Danish Nationwide Cohort Study. *Br J Cancer.* 2020 Feb;122(3):445-451.
3. Jones ER, O'Flynn H, Njoku K, Crosbie EJ. Detecting endometrial cancer. *The Obstetrician & Gynaecologist.* 2021 Apr;23(2):103-12.
4. Menzies R, Wallace S, Ennis M, Bennett A, Jacobson M, Yip G, Wolfman W. Significance of abnormal sonographic findings in postmenopausal women with and without bleeding. *J Obstet Gynaecol Can.* 2011 Sep;33(9):944-51.
5. Emoto M, Tamura R, Shiota K, Hachisuga T, Kawarabayashi T. Clinical usefulness of color Doppler ultrasound in patients with endometrial hyperplasia and carcinoma. *Cancer.* 2002 Feb 1;94(3):700-6.
6. Khurana I, Satia MN. Preoperative evaluation of ovarian masses with color Doppler and its correlation with pathological finding. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology.* 2016 Jul 1;5(7):2084-93.
7. Nasheeha N, Gk P. Diagnostic accuracy of uterine artery and spiral artery Doppler for evaluation of endometrial pathology in

- postmenopausal bleeding. *J Gynecol Obstet Hum Reprod.* 2021 Dec;50(10):102209.
8. Ahmadzade A, Gharibvand MM, Azhine S. Correlation of color Doppler ultrasound and pathological grading in endometrial carcinoma. *J Family Med Prim Care.* 2020 Oct 30;9(10):5188-5192.
  9. Kumari P, Gaikwad HS, Nath B. Endometrial Cut Off Thickness as Predictor of Endometrial Pathology in Perimenopausal Women with Abnormal Uterine Bleeding: A Cross-Sectional Study. *Obstet Gynecol Int.* 2022 Jan 4;2022:5073944.
  10. Epstein E, Skoog L, Isberg PE, *et al.* An algorithm including results of gray-scale and power Doppler ultrasound examination to predict endometrial malignancy in women with postmenopausal bleeding. *Ultrasound Obstet Gynecol* 2002;20:370–376.
  11. Develioglu OH, Bilgin T, Yalcin OT, Ozalp S. Transvaginal ultrasonography and uterine artery Doppler in diagnosis endometrial pathologies and carcinoma in postmenopausal bleeding. *Arch Gynecol Obstet* 2003;268:175-180.
  12. Wilailak S, Jirapinyo M, Theppisai U. Transvaginal Doppler sonography: is there a role for this modality in the evaluation of women with postmenopausal bleeding? *Maturita* 2005;50:111-116.
  13. Ng EH, Chan CC, Tang OS, Yeung WS, Ho PC. Endometrial and subendometrial blood flow measured during early luteal phase by three-dimensional power Doppler ultrasound in excessive ovarian responders. *Human Reproduction.* 2004 Apr 1;19(4):924-31.
  14. Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, Brand R, Grady D. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. *Jama.* 1998 Nov 4;280(17):1510-7.
  15. Kanat-Pektas M, Gungor T, Mollamahmutoglu L. The evaluation of endometrial tumors by transvaginal and Doppler ultrasonography. *Arch Gynecol Obstet* 2008;277:495-499
  16. Karlsson B, Gransberg S, Wikland M, Ylostalo P, Torvid K, Marsal K, Valentin L. Transvaginal Ultrasonography of the Endometrium in Women With Postmenopausal Bleeding--A Nordic Multicenter Study. *Obstetrical & gynecological survey.* 1996 Feb 1;51(2):100-1.
  17. Gull B, Karlsson B, Milsom I, Wikland M, Granberg S. Transvaginal sonography of the endometrium in a representative sample of postmenopausal women. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 1996 May;7(5):322-7.
  18. Ng EH, Chan CC, Tang OS, Yeung WS, Ho PC. Relationship between uterine blood flow and endometrial and subendometrial blood flows during stimulated and natural cycles. *Fertility and sterility.* 2006 Mar 1;85(3):721-7.
  19. Haliloglu B, Celik A, Ilter E, Bozkurt S, Ozekici U. Comparison of uterine artery blood flow with levonorgestrel intrauterine system and copper intrauterine device. *Contraception.* 2011 Jun 1;83(6):578-81.
  20. Dane B, Akca A, Dane C, Evcimen S, Cetin A. Comparison of the effects of the levonorgestrel-releasing intrauterine system (Mirena®) and depot-medroxyprogesterone acetate (Depo-Provera®) on subendometrial microvascularisation and uterine artery blood flow. *The European Journal of Contraception & Reproductive Health Care.* 2009 Jan 1;14(3):240-4.
  21. Jiménez MF, Arbo E, Vettori D, de Freitas FM, Cunha-Filho JS. The effect of the levonorgestrel-releasing intrauterine system and the copper intrauterine device on subendometrial microvascularization and uterine artery blood flow. *Fertility and sterility.* 2008 Nov 1;90(5):1574-8.
  22. Alcazar JL, Castillo G, Minguez JA, Galan MJ. Endometrial blood flow mapping using transvaginal power Doppler sonography in women with postmenopausal bleeding and thickened endometrium. *Ultrasound in obstetrics & gynecology.* 2003 Jun;21(6):583-8.
  23. Opolskiene G, Sladkevicius P, Valentin L. Ultrasound assessment of endometrial morphology and vascularity to predict endometrial malignancy in women with postmenopausal bleeding and sonographic endometrial thickness  $\geq 4.5$  mm. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 2007 Sep;30(3):332-40.
  24. Cil AP, Tulunay G, Kose MF, Haberal A. Power Doppler properties of endometrial polyps and submucosal fibroids: a preliminary observational study in women with known intracavitary lesions. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 2010 Feb;35(2):233-7.
  25. Epstein E, Skoog L, Isberg PE, De Smet F, De Moor B, Olofsson PÅ, Gudmundsson S, Valentin L. An algorithm including results of gray-scale and power Doppler ultrasound examination to predict endometrial malignancy in women with postmenopausal bleeding. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology.* 2002 Oct 1;20(4):370-6.
  26. Samulak D, Wilczak M, Englert-Golon M, Michalska MM. The diagnostic value of evaluating the maximum velocity of blood flow

- in the uterine arteries of women with postmenopausal bleeding. Archives of gynecology and obstetrics. 2011 Nov;284:1175-8.
27. Englert-Golon M, Szpurek D, Moszyński R, Pawlak M, Sajdak S. Clinical value of the measurement of blood flow in uterine arteries and endometrial vessels in women with postmenopausal bleeding using "power" angio Doppler technique. Ginekologia polska. 2006 Oct 1;77(10):759-63.