Objectives: To determine the role of B-mode ultrasonography combined with Doppler ultrasonography in diagnosing uterine intracavitary pathology in perimenopausal and postmenopausal women with abnormal uterine bleeding (AUB). Patients and Methods: This prospective observational study included 150 women aged >40 years with AUB hospitalized at Hue University Hospital and Hue Central Hospital between 6/2016 and 6/2019. All participants were investigated by B-mode transvaginal ultrasound and Doppler transvaginal ultrasound, and the result of sonography was compared to the histopathological endpoint. Results: The morphological features, structure, margin, border line of the endometrial-mass lesion, intracavitary uterine fluid, and Doppler signal clearly differed between benign and malignant intracavitary pathologies ($P < 0.0001$). However, echogenicity had a limited value in distinguishing between uterine intracavitary pathologies ($P = 0.1$). The sensitivity and specificity of the pedicle sign in diagnosing endometrial polyps were 50.0% and 97.6%, respectively; for the circular pattern in subendometrial fibroids were 46.2% and 100.0%, respectively; for the multiple vessel pattern in endometrial cancer were 64.0% and 96.0%, respectively, and for the scattered-vessel pattern in endometrial hyperplasia were 43.96% and 56.43%, respectively. Conclusions: Ultrasound B-mode combined with Doppler as a noninvasive tool was significantly valuable in the diagnostic procedures for uterine intracavitary pathology in perimenopausal and postmenopausal women with AUB. It could also help differentiate malignant diseases from benign endometrial changes.

Keywords: Abnormal uterine bleeding, Doppler ultrasound, intracavitary uterine pathology, perimenopausal women, postmenopausal women
Currently, there are many tools with different advantages and disadvantages such as imaging modalities (sonography, computed scan, and magnetic resonance imaging) and surgical procedures (blind biopsy and hysteroscopy). Interestingly, transvaginal B-mode ultrasound is an easily accessible and safety which investigates the abnormal structure and morphological features of the uterus. Moreover, there have been many studies showing that Doppler ultrasound is probable to detect vascular proliferation feeding gynecological tumors. The dominant vascular proliferative phenotype helps to differentiate between UIPs. Cogendez et al. has shown the value of doppler transvaginal ultrasound in the diagnosis of polyps by pedicle vascular and EF by circle vascular as imagine soft markers. The sensitivity, the positive predictive values (PPV) were 80.0%, 100.0% and 72.0%, 100.0%, respectively.[2] Study of Alcazar et al. suggested that multiple angiogenesis sign was characteristic of EC with sensitivity of 78.8%, specificity of 100.0%, and PPV of 100.0%, while EH is predominantly scattered vascular proliferation.[3] Therefore, we aimed to determine the value of B-mode ultrasound combined with transvaginal Doppler to elucidate this approach method in perimenopausal and postmenopausal women with AUB.

Patients and Methods

This prospective observational study was conducted according to the ethics committee of our institution and was approved by our institutional review board. All females gave us a written informed consent. This study was done at Hue Central Hospital and Hue University Hospital between June 2016 and June 2019.

The inclusion criteria were as follows: all women above 40 years of age complaining with AUB; the patient underwent uterine B-mode ultrasound combined with Doppler and had histopathological results for comparison.

The exclusion criteria included: bleeding related to pregnancy, hormone replacement therapy, tamoxifen, coagulation disorders, bleeding not originating from the uterine cavity, abnormalities associated with the cervix, iatrogenic bleeding, and lack of information on the study protocol.

Overall, a total of 150 women were recruited and participated in this study.

All patients underwent thorough disease history, general examination, gynecological examination, cervical cytology (Pap. smear), and laboratory investigations (complete blood count, liver function tests, kidney function tests, and a coagulation profile). Transvaginal sonography was performed in all patients using a 5–7.5 MHz endovaginal transducer.

All patients underwent interventional procedures such as endometrial biopsy, hysteroscopy, myomectomy, or hysterectomy. These indications were decided according to the following medical protocol applied at our hospital [Figure 1].

Features of morphological ultrasound of intracavitary abnormalities

Intracavitary fluid, structure, echogenicity, border, and endometrium-myometrial boundary of the endometrium/lesion were classified according to the International Endometrial Tumor Analysis (IETA) System when evaluated using B-mode ultrasound [Figure 2]. During the evaluation, the practitioner first determined the image of the uterus, occupying 2/3 of the screen to access the clearest image.[4-6]

Determination of predominant angiogenesis pattern

According to Doppler flow mapping, four different vascular patterns were defined as description in Figure 3.

1. Multiple-vessel pattern (Pattern A): Multiple vessels were found within the endometrium and in the myometrial–endometrial interface. This pattern is considered a characteristic of EC as it has been demonstrated that important neoangiogenic phenomena occur in EC within the tumor tissue and the surrounding area.

2. Pedicle-vessel pattern (Pattern B): A single vessel was identified penetrating the endometrium from the myometrium. This pattern was considered as

Women above 40 years old with AUB

- Taking patient’s history, clinical examination, and laboratory tests
- Consent’s patient
- Ultrasound B-Mode and Doppler

Excluded:
- Bleeding not originated from uterine cavity
- Previous endometrial biopsy or medical treatment

Surgical procedures
Endometrial biopsy, hysteroscopy, or hysterectomy

Excluded:
- No indication for intervention
- Contraindicated for surgery

Histological results as "gold standard" consideration

Excluded:
- Result obtained was unsatisfactory
- Retained tissue after checked-up by ultrasound.

Data collection and analysis

Figure 1: Study flowchart. AUB: Abnormal uterine bleeding
characteristic of EP as this vessel is thought to correspond to the vascularized polyp’s pedicle
3. Scattered-vessel pattern (Pattern C): Disseminated vasculature within the endometrium. This pattern is considered characteristic of EH[3]
4. Ring-shaped-vessel pattern (Pattern D): Increased vascularity in the peripheral surrounding of the tumor, common in uterine fibroids.

All morphological and structural features of endometrium, lesion mass, and intracavitary uterine abnormalities were evaluated on B-mode ultrasound following the standards of IETA.

Phenotype of vascular angiogenesis such as single-vessel, scattered-vessel, multiple-vessel, rim-like vessel (ring-shaped vessel and circle vessel), no vascular flow were determined by sonographer with 5-year experience.

EH, EP, EF, and EC was collected from histopathological result.

All of them were coded in categorical variables.

Statistical analysis
Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM Corp., Armonk, NY, USA).and $P < 0.05$ was considered to be statistically significant.

RESULTS

Regarding the structure of the endometrium/ lesion mass, most EFs and malignant lesions had heterogeneous-mixed echogenicity, while other benign pathologies were predominantly homogenous. Most lesions had hyperechogenic echogenicity, however, in fibroids, hypoechoic form was predominant (7/13 cases). Regarding to endometrial-myometrium junction, almost all malignant lesions of cases were irregular, the boundary was not clear, and discontinuous, whereas, the benign lesions had regular margins, and the boundaries were clearly observed. According to the intracavitary lesion, the majority of cases of benign lesions were not identified with fluid (88.0%), different from EC, 56.0% of cases presented with fluid.

In the malignant group, detectable Doppler signals were present in 24/25 (99.0%) cases, more than those in the benign group, 73/125 (58.4%) cases. In the benign group, only 48.4% of cases of EH were detected with Doppler signal, but 81.2% of polyps and 100.0% of EFs had Doppler signal.

In the EC group, multiple vessel pattern occupied to 64.0% of cases. In the cases of polyp, the single-vessel form accounted for 50.0%. In the group of EF group, rim-like vessel accounted for 46.2% of the lesions. However, in the cases of EH, all cases did not have vascular proliferation, however, if there was Doppler signal, most of them had a scattered vessel pattern (44.0%). Most of the dominant vascular phenotypes had low diagnostic sensitivity for intracavitary pathology (<80.0%), but high specificity (over 80.0%), with the exception of scattered-vessel patterns that could be seen in many
different pathologies. The rim-likely form was a specific feature of fibroids that was not appeared in others pathologies (Sp: 100.0%, PPV: 100.0%). In 150 cases, there were 25 cases with histopathological endpoint in EC, and Doppler ultrasound identified accurately 21/25 cases. Similarly, regardless of EH, there were 76/91 cases diagnosed by ultrasound compatible with histopathological results, polyps in 13/16 cases and EFs in 12/13 cases [Table 1].

**Discussion**

**Morphological features of uterine intracavitary pathologies on B-mode ultrasound**

Table 2 showed the echogenic structure of the endometrial lesions in the malignant group accounted for 88.0% was mixed-heterogeneous, compared with 37.6% in the benign group. The main echogenic structure of the benign group was 62.4% homogeneous (P < 0.0001). Similar to the study by Ashour et al., in the malignant group, 100.0% of the echogenic structures were heterogeneous and in the benign group, 51.0% of the cases were homogenous. In a study by Madkour 90.0% of the malignant group had mixed echogenic, whereas, 92.0% of the benign group had homogeneous echogenicity.

Regardless of echogenicity, it was found that the majority of echogenicity in the EC group was hyperechogenic (76.0%) compared with the hypoechoic form (24.0%), similar to that of Razik et al.[8] In the benign group, 88.2% was hyperechoic, 10.2% were hypoechoic and 1.6% were homogenous with the myometrium. According to Madkour et al. in the group of benign pathologies, regardless of the echogenicity of polyps, hyperechogenicity accounted for 96.9% (31/32) cases, hypoechoic only accounted for 3.1% (1/10 cases).[8] Similarly, the echogenic level of polyps was mostly hyperechogenicity, accounting for 91.2% (31/45) cases, and three cases of hypoechoic (8.8%) were observed in the study by Talaat et al.[10] In our study, respectively, those cases were 87.5% and 12.5%, respectively, and none of them were homoechogenic.

In contrast, in EF, echogenicity accounted for only 5.9% (1/17 cases), hypoechoic for 47.1% (8/17 cases) and homoechogenicity for 47.1% (8/17 cases), P < 0.001. According to Cil et al.
Thus, the presence of fluid can help in the differential diagnosis of EP from fibroids.\cite{14}

**Presence of Doppler signal in uterine intracavitary pathologies**

Figure 4 shows that most of the malignancy group had a Doppler signal (96.0%), in contrast, in the benign group, this was detected only 58.4%. This feature is consistent with the vascular proliferative properties of malignancies. In a study by Alcazar et al., signs of vascular proliferation were found in 32/33 cases of EC, and only 1/33 cases had no Doppler signal.\cite{3}

Similarly, in a recent study by author Li and Li, 66.7% of EC cases had Doppler signal, whereas, only 11.1% of cases were detected with Doppler sign in the benign group. Therefore, the presence of Doppler signal in endometrial lesions is strongly associated with the risk of malignancy, odds ratios: 16.0, 95% confidence interval: 1.3–192.8.\cite{15,16} However, we also found that in the benign group, Doppler signal was present in 13/16 cases of polyps (81.2%) and 13/13 cases of EFs (100.0%).

**Distribution characteristics and diagnostic value of dominant vascular phenotypes**

**Diagnostic value of endometrial cancer by signs of multiple angiogenesis**

In the present study, the predominant pattern in EC was multiple vessel: 16/25 cases (64.0%), and a scattered-vessel pattern accounted for 32.0%, similar to result of El Kady et al. in Egypt.\cite{17} In a study by Madkour signs of multiple angiogenesis were found in 7/10 cancer cases, remaining 1 case of disseminated vascular proliferation and 2 cases of no Doppler signal.\cite{8} The LR (+) index was 16.0, showing signs of multiple vascular proliferations that were valuable for diagnosing EC in our study [Table 3].

**Valuable diagnosis of pedicle vessel pattern**

Table 4 shows that in the polyp group, the predominant pattern was pedicle vascular in 8/16 (50.0%) cases,
scattered vessels in 3/16 cases (18.8%) and multiple vessel in 1/16 (5.9%) cases. In the study of Amreena et al. the vascular peduncle sign was found in 13/16 cases, accounting for 76.5% and this author found that the polyp size was related to the pedunculated vascular sign, the more common vascular peduncle sign with the larger size of polyp, the average size of polyps in this study was 17.77 mm with $P = 0.044$. This assessment differs from that of Medina et al. who found no relationship between polyp size and pedunculated vessel sign. The LR (+) index of 22.32 showed the value of the pedicle vessel sign to diagnose polyps in our study [Table 3].

**Valuable diagnosis of rim-likely vessel pattern**

In our study, the predominant vascular pattern of EF was rim-likely vascularity in 6/13 cases (46.2%), followed by scattered-vessel in 4/13 cases (30.8%), multiple vessel occupied 2/13 cases (15.4%) and pedicle vessel pattern in 1/13 cases (7.7%). According to Cogendez et al., among fibroids, 72.2% had signs of rim-likely vascularity, and there were 27.8% had multiple angiogenesis and there was no case with single vascular pattern. Thus, in EF, circular flow may be present or absent, but if the circular vessel pattern was present, the diagnostic value for the fibroid was 100.0%, so this was an extremely specified phenotype for fibroid [Table 3].

**Diagnostic value of endometrial hyperplasia by signs of disseminated vascular proliferation**

According to our study, in EH group, 47/91 cases were diagnosed without vascular proliferation, accounting for 51.6%, 40/91 cases with scattered vascular proliferation accounting for 44.0%, 2/91 cases with multiple vessel patterns, and 2/91 cases had pedicle vessel pattern. According to Cogendez et al., signs of disseminated vascular proliferation were found in 72.7% of EH cases, however, this sign was also observed in 66.7% cases of endometrial atrophy cases. The signs of disseminated vascular proliferation were common but uncommon in EH, it could be seen in other UIP. The diagnostic value of scattered vascular sign in EH was low, with the sensitivity, specificity, PPV, negative predictive value, and accuracy of 43.96%, 56.43, 68.97%, 34.51%, and 54.0%, respectively, and the positive likelihood index LR (+) was 1.0 [Table 3].

**Conclusions**

The morphological, structural, border, endometrium-myrometrium junction, fluid, and Doppler signal are clearly different among uterine pathologies, between benign and malignant groups, whereas, the level of echogenicity was less useful. Using Doppler ultrasound, we found a difference in the proportion of dominant vessel patterns among UIP.

**Author’s contributions**

Phuc Nhon Nguyen was responsible for data analysis, contributed to writing and editing the manuscript. Van Tuan Nguyen supervised the study. Both authors read and approved the final manuscript.

**Acknowledgment**

We thank the patients, who agreed to allow us to participate in our research and to publish their clinical data. The authors are also grateful to all teachers and colleagues working at the Department of Gynecology, the Department of Image Diagnostic, and the Department of Histopathology at Hue Central Hospital and at Hue University Hospital. We are thankful directly

---

**Table 3: Value of dominant vascular pattern**

| Vascular pattern | Se (%) | Sp (%) | PPV (%) | NPV (%) | AC (%) | LR + | LR − |
|-----------------|--------|--------|---------|---------|--------|------|------|
| Scattered-vessel | 43.96  | 56.43  | 68.97   | 30.51   | 54.0   | 1.00 | 0.99 |
| Ring-shaped vessel | 46.2   | 100.0  | 100.0   | 95.14   | 95.33  | -    | 0.54 |
| Multiple vessel  | 64.0   | 96.0   | 76.19   | 93.02   | 90.67  | 16.0 | 0.38 |
| Pedicle vessel   | 50.0   | 97.76  | 72.73   | 94.24   | 92.67  | 22.32| 0.51 |

PPV: Positive predictive value, NPV: Negative predictive value, Se: Sensitivity, Sp: Specificity, LR+: Positive likelihood ratio, LR−: Negative likelihood ratio, AC: Accuracy

**Table 4: Distribution of dominant vascular pattern followed by uterine intracavitary pathologies**

| Vascular pattern | EC, n (%) | EP, n (%) | EF, n (%) | EH, n (%) | Other, n (%) | Total |
|------------------|-----------|-----------|-----------|-----------|--------------|-------|
| No vascular presence | 1 (4.0) | 4 (25.0) | 0 | 47 (51.6) | 2 (40.0) | 54 |
| Scattered-vessel | 8 (32.0) | 3 (18.8) | 4 (30.8) | 40 (44.0) | 3 (60.0) | 58 |
| Ring-shaped vessel | 0 | 0 | 6 (46.2) | 0 | 0 | 6 |
| Multiple vessel | 16 (64.0) | 1 (6.2) | 2 (15.4) | 2 (2.2) | 0 | 21 |
| Pedicle vessel | 0 | 8 (50.0) | 1 (7.7) | 2 (2.2) | 0 | 11 |
| Total | 25 (100.0) | 16 (100.0) | 13 (100.0) | 91 (100.0) | 5 (100.0) | 150 |

EH: Endometrial hyperplasia, EP: Endometrial polyps, EF: Subendometrial fibroids, EC: Endometrial cancer
to PhD. M.D Van Duc Vo, Ph. D. M.D Thao Nguyen Nguyen Tran, M.D. Ngoc Ty Nguyen Thi, M.D. Diem Thu Nguyen Thi, M.D. Phuong Minh Nguyen Thi, M.D. Thanh Thuy Tran Thi. All of them attributed to provide us the pictures, take care for patient and shared their precious experiences related to manage this clinical course with us.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Committee on Practice Bulletins—Gynecology. Practice bulletin no. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. Obstet Gynecol 2012;120:197-206.
2. Cogendez E, Eken MK, Bakal N, Gun I, Kaygusuz EI, Karateke A. The role of transvaginal power Doppler ultrasound in the differential diagnosis of benign intrauterine focal lesions. J Med Ultrasound (2001) 2015;42:533-40.
3. 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 Obstet Gynecol 2003;21:583-8.
4. Van Den Bosch T, Verbakel JY, Valentin L, Wynants L, De Cock B, Pascual MA, et al. Typical ultrasound features of various endometrial pathologies described using IETA terminology in women with abnormal uterine bleeding. Ultrasound Obstet Gynecol 2021;57:164-72.
5. Sladkevicius P, Installé A, Van Den Bosch T, Timmerman D, Benacerraf B, Jokubkiene L, et al. IETA terminology in women with postmenopausal bleeding and sonographic endometrial thickness ≥4.5 mm: Agreement and reliability study. Ultrasound Obstet Gynecol 2018;51:259-68.
6. Furau A, Toma M, Ionescu C, Furau C, Bungau S, Dimitriu M, et al. The correlation of the IETA ultrasound score with the histopathology results for women with abnormal bleeding in West. Diagnostics 2021;11:1342.
7. Ashour AS, Fawzy T, Faisal MA. The relationship between transvaginal ultrasound endometrial thickness and body mass index and endometrial pathology in women with postmenopausal bleeding. Med J Cairo Univ 2017;85:2017-23.
8. Madkour NM. An ultrasound risk-scoring model for prediction of endometrial cancer in post-menopausal women (using IETA terminology). Middle East Fertility Society Journal 2017;22:201-5.
9. Razik MA, Walid A, Maksoud MA. Transvaginal and color doppler ultrasound assessment of endometrial pathology in patients with postmenopausal bleeding. Egypt Soc Gynaecol Obstet 2012;38:709-14.
10. Talaat S, Mostafa N, Alrauof MA. Diagnostic value of ultrasound and colour doppler in endometrial and cervical polyps. Med J Cairo Univ 2009;77:397-403.
11. 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 Obstet Gynecol 2010;35:233-7.
12. Badawy AM, Abu-Elata M. Can colour Doppler ultrasonography predict the prognosis of endometrial hyperplasia?. J Obstet Gynaecol Res 2003;23:282-4.
13. Epstein E, Valentin L. Gray-scale ultrasound morphology in the presence or absence of intruterine fluid and vascularity as assessed by color Doppler for discrimination between benign and malignant endometrium in women with postmenopausal bleeding. Ultrasound Obstet Gynecol 2006;28:89-95.
14. Azmy OM, Haitham B. Ultrasound Imaging of Endometrial Cancer. Gynecologic Neoplasia. Ultrasonography in Gynecology. Cambridge: Cambridge University Press; 2014. p. 224-32.
15. AbdelMaboud NM, Elsaid HH. Role of transvaginal ultrasonography and colour Doppler in the evaluation of postmenopausal bleeding. Egypt J Radiol Nucl Med 2015;46:235-43.
16. Li Z, Li L. Risk of malignancies among asymptomatic postmenopausal women with thickened endometrium: A cohort study. Medicine (Baltimore) 2019;98:e14464.
17. El Kady SR, EA, Abd El Fatah AA, Mohamed IH, Salem SM. Correlation between endometrial histopathology in postmenopausal uterine bleeding and transvaginal colour Doppler. AJMJ 2020;1:249-52.
18. Amreena S, Singh M, Choh NA, Saldanhab C, Gojwaria TA. Doppler evaluation of endometrial polyps. Egypt J Radiol Nucl Med 2018;49:850-3.
19. Medina T, Bajo J, Huertas MA, Rubio A. Predicting atypia inside endometrial polyps. J Ultrasound Med 2002;21:125-8.