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Original Research Article

To compare trans-vaginal ultrasound colour doppler (TUCD) with hysteroscopy and guided endometrial biopsy in diagnosing abnormal uterine bleeding

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ABSTRACT

Background: To compare trans-vaginal ultrasound Colour Doppler (TUCD) with hysteroscopy and guided endometrial biopsy in diagnosing abnormal uterine bleeding.
Methods: A total of 50 consecutive and haemodynamically stable patients aged more than 40 years with abnormal uterine bleeding (AUB) were included in the study. Patients with pregnancy and probable cervical malignancy were excluded. All the patients were subjected to TUCD followed by hysteroscopic directed endometrial biopsy during the follicular phase of the menstrual cycle between 7th and 11th day to diagnose the underlying pathology. In postmenopausal female both TUCD and hysteroscopy were performed on any day. Results of both the procedures were compared.
Results: The sensitivity and specificity of TUCD as compared to hysteroscopy in diagnosing polyp was found out to be 27.78% and 100%; for fibroid 100% and 84.4%; for endometrial hyperplasia 86.36% and 96.43%; for endometrial carcinoma 71.43% and 100%; and for endometrial atrophy 100% and 100%, respectively. After application of kappa statistics, the degree of agreement between the two diagnostic procedures was found to be 0.599 which was considered to be good.
Conclusions: Conditions like fibroid, endometrial atrophy and cases of A-V malformation are better diagnosed with TUCD, while others like endometrial polyps, endometrial carcinoma are better detected on hysteroscopy. TUCD can diagnose most of the pathologies but not all, so it can be used as an adjunct to hysteroscopy to diagnose endometrial pathology, but can surely not replace hysteroscopy.

Keywords: Abnormal uterine bleeding, Colour doppler, Hysteroscopy

INTRODUCTION

In the women of child bearing age abnormal uterine bleeding (AUB) includes any change in menstrual period frequency, duration or amount of flow and intermenstrual bleeding.[1] In postmenopausal women AUB includes vaginal bleeding of any cause 12 months or more after cessation of menses.[2] Puberty and perimenopause are typically associated with anovulatory menstrual cycles. The immature hypothalamic-pituitary axis during puberty does not develop the necessary hormonal feedback to sustain the endometrium. Likewise, the decline of inhibin levels and rise in follicular stimulating hormone (FSH) levels reflect the loss of follicular activity and

competence as the perimenopausal transition sets in.[3] Broadly AUB has been categorised into ovulatory and anovulatory. Anovulatory bleeding is due to the failure of the development of corpus luteum and hence inadequate progesterone levels to sustain the endometrium whereas ovulatory AUB is due to some associated uterine pathology like polyp, endometrial hyperplasia, cancer, fibroid etc.

Abnormal bleeding is associated with an array of symptoms including heavy or prolonged menstrual flow, intermenstrual bleeding and frequent or delayed cycles. Women also experience social embarrassment, diminished quality of life, sexual compromise and loss of wages due to absence from work. Pain is not a common presenting symptom unless associated with passage of large blood clots.

Besides systemic, iatrogenic or age-related hormonal disharmony, an endometrial pathology (polyps, submucosal myomas, endometrial hyperplasia and endometrial carcinoma) should always be suspected. There is a battery of investigations to evaluate AUB including transvaginal ultrasound (TVUS), saline infusion sonography, hysteroscopy, transvaginal colour Doppler, MRI and endometrial biopsy. This study was intended to compare the diagnostic accuracies of trans-vaginal ultrasound with Colour Doppler (TUCD) and hysteroscopy with guided endometrial biopsy in AUB.

METHODS

This study was carried out in a teaching tertiary care hospital in New Delhi, India. Approval was taken from the Institutional Ethics Committee. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional) and with the Helsinki Declaration of 1975 and revised in 2008. Fifty consecutive patients aged more than 40 years with AUB attending the outpatient clinic and willing for participation in the study were included after informed consent.

Patients with bleeding due to pregnancy complications, known cases of endometrial cancer, pelvic inflammatory diseases, suspected cervical malignancy, adenexal masses and haemodynamic instability were not included in the study cohort. A thorough work-up including historical review, general physical and systemic examination and various investigations to rule out systemic causes of AUB were carried out. All patients were subjected to TUCD during the follicular phase of the menstrual cycle between the 7th and 11th day using a 6.5MHz vaginal transducer (HDI 4000) equipped with colour and pulsed Doppler.

Endometrium was classified as normal or abnormal based on the endometrial thickness, average values of the pulsatility and resistivity indices of bilateral uterine arteries and the various lesions identified. After bleeding stopped, patients were subjected to hysteroscopic directed endometrial biopsy on 7th to 11th day of menstrual cycle using 8mm operative hysteroscope. In postmenopausal females, both TUCD and hysteroscopy were performed on any planned day after bleeding stopped. Endometrial biopsy was taken with a biopsy needle. Endometrium was classified as normal or abnormal depending upon hysteroscopic findings and confirmed by histopathology.

Statistical analysis

Statistical measures like sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), false positive rate (FPR), false negative rate (FNR) were used. Kappa statistics was used to calculate the degree of agreement between the two diagnostic tools. [k< 0.4: poor agreement; k=0.4-0.75: good agreement; k>0.75: excellent agreement

RESULTS

The mean age of study population was 47.04 years. The most common presenting complaint with which patients presented was found to be heavy menstrual bleeding (42%), followed by frequent heavy bleeding (18%). TUCD diagnosed endometrial pathology in 80% patients. (Figure 1).

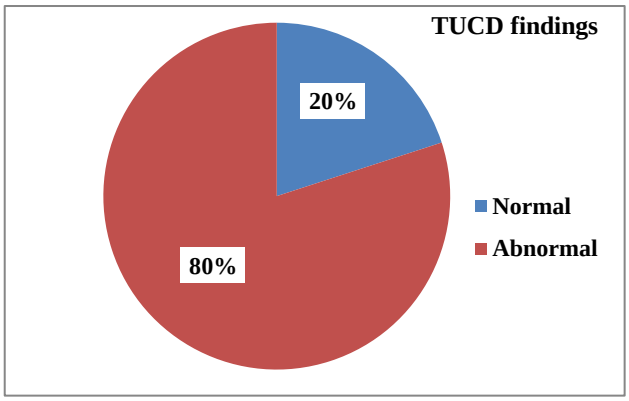


Figure 1: Pie diagram showing relative percentage of cases with some endometrial pathology as diagnosed by TUCD.

Endometrial hyperplasia was the most common endometrial pathology detected by TUCD. Other findings that were found by Doppler are listed in Table 1.

The mean PI (pulsatility index) value was found out to be 1.433 ± 0.293 while the mean RI (resistivity index) was found out to be 0.534 ± 0.0262. The mean endometrial thickness was 12.792 ± 5.9119 mm (Table 2).

Hysteroscopic findings: Endometrial hyperplasia was the most common abnormality detected by hysteroscopic evaluation (24% of cases), followed by polyp alone and polyp along with hyperplasia. Two cases each of fibroid with endometrial hyperplasia, and polyp with suspected carcinoma endometrium were detected.

Table 1: TUCD findings in the study group.

Colour Doppler finding	Frequency (n)	%
Normal (1)	10	20
Polyp (2a)	4	8
Fibroid (2b)	6	12
Endometrial hyperplasia (2c)	13	26
Endometrial carcinoma (2d)	5	10
Atrophic endometrium (2e)	4	8
A-V malformation (2f)	1	2
2a+2c	1	2
2b+2c	6	12
Total	50	100

Table 2: Pulsatility index, resistivity index and endometrial thickness as calculated by TUCD.

	Pulsatility Index (PI)	Resistivity Index (RI)	Endometrial Thickness (ET)
Frequency (n)	50	50	50
Minimum value	1.09	0.47	2.0
Maximum value	2.66	0.58	26.0
Mean	1.4334	0.5344	12.792
S.D.	0.29335	0.0262	5.9119
Median	1.3550	0.54	12.8

Hysteroscopy could recognise some endometrial abnormality in 88% patients with AUB (Table 3). Colour Doppler indices associated with various hysteroscopic findings is shown in Table 4. As can be inferred from the table that fibroid and polyp exhibit a high resistance flow while as carcinoma endometrium shows a low resistance flow. Histopathology revealed simple endometrial hyperplasia as the commonest finding (38%) followed by secretory endometrium (34%). Endometrial carcinoma was diagnosed in 8% patients on histopathology (Figure 2).

Doppler results were compared to hysteroscopy, keeping hysteroscopic findings as gold standard. The sensitivity of TUCD in diagnosing endometrial polyp was almost 27% while its specificity was 100% with a positive predictive value (PPV) of 100% and negative predictive value (NPV) of 71.1%. The false positive rate (FPR) was 0%, while the false negative rate (FNR) 72.2%.

Table 3: Hysteroscopic examination findings in the study population.

	Frequency (n)	%
Normal (1)	6	12
Polyp (2a)	8	16
Fibroid (2b)	3	6
Endometrial hyperplasia (2c)	12	24
Carcinoma endometrium (2d)	5	10
Atrophic endometrium (2e)	4	8
A-V malformation (2f)	0	0
2a+2c	8	16
2a+2d	2	4
2b+2c	2	4
Total	50	100

These observations showed that Colour Doppler could be used as a diagnostic tool for diagnosing polyps, but not as a screening tool. Sensitivity of Colour Doppler for diagnosing fibroids was 100%. Specificity, PPV and NPV were found out to be 84.4%, 41.67% and 100% respectively.

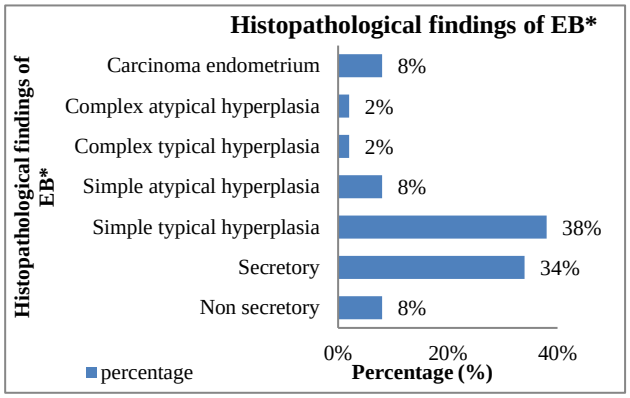
Table 4: Colour doppler indices associated with various hysteroscopic findings.

TUCD Indices	Patients with normal hysteroscopy	Polyp	Fibroid	Endometrial hyperplasia	Carcinoma endometrium	Endometrial atrophy
PI*	1.25± 1.09	1.39±0.22	1.45±0.07	1.27±0.18	1.29±0.06	2.16±0.36
RI*	0.54±0.02	0.55±0.01	0.56±0.01	0.54±0.01	0.48±0.01	0.51±0.01
ET*	8.89±2.74	10.34±3.26	7.63±0.85	16.5±2.19	23.2±3.11	2.3±0.47

*PI: Pulsatility index, RI: Resistivity index, ET: Endometrial thickness

FPR and FNR were 15.6%, and 0% respectively. Extrapolation of these findings suggested that Colour Doppler could be used as a fairly good tool to diagnose as well as screen fibroids. The sensitivity and specificity found in case of endometrial hyperplasia were 86.36% and 96.43%, respectively. PPV and NPV were found out to be 95% and 90%, respectively. For detecting endometrial carcinoma, the sensitivity was found to be 71.43%, while, specificity was 100%. PPV was 100% and NPV was 95.5%. FPR was 0% and FNR 28.57%. From this it could be inferred that TUCD was a better technique to diagnose endometrial carcinoma but not that good a technique to screen for carcinoma, as many cases of carcinoma could go undetected by TUCD alone. The sensitivity, specificity, PPV and NPV of TUCD to diagnose endometrial atrophy were 100% each making it

as good a diagnostic and screening tool as hysteroscopy. FPR and FNR were 0% each in these cases.



*EB: endometrial biopsy

Figure 2: Histopathological findings of the endometrial biopsy.

This value of kappa (k) came out to be 0.559 which signified a good agreement between the results of TUCD and hysteroscopy.

DISCUSSION

TUCD imaging facilitates the visualisation of small vessels in the utero-ovarian circulation and measurement of impedance to blood flow in this vascular tree. Hysteroscopy is considered as the gold standard technique for the evaluation of endometrial pathology for long.

In present study, the mean age of the participants was 47.0±6.2 years with only one third being literate. Majority of the participants were of 3rd or more parity with only 2 nulliparous patients both of whom presented as post-menopausal bleeding and were eventually diagnosed as endometrial cancer which high lightened the fact that nulliparous women are at high risk for endometrial cancer.

In present study, most common symptom was heavy menstrual bleeding (42%) which was comparable to the study by Jaiswar et al in 2006 (40%).[4]

TUCD could diagnose endometrial polyp in 4 (8%) cases while on hysteroscopy polyp was demonstrated in 8 (16%) patients. The basic principle that leads to the diagnosis of polyp by TUCD is demonstration of a vascular pedicle. The use of power Doppler with better resolution may improve the diagnostic accuracy of TUCD for polyps.[5] Although our study demonstrated low resistance flow in malignant lesions but neither hysteroscopy nor TUCD can establish the benign or malignant nature of these polypoidal lesions. Our study results revealed that TUCD was a good diagnostic tool for polyps with 100% specificity but lacks the sensitivity to be used as a screening device as supported by the studies of Pascual A et al and Yela DA et al.[6,7]

TUCD picked up fibroid uterus in 12 cases out of which 6 patients had both fibroid and endometrial hyperplasia. Hysteroscopy could demonstrate only 5 cases of fibroid uterus out of which two cases were complicated by endometrial hyperplasia as well. It was found that hysteroscopy readily picked up the submucous myomas but could not diagnose intra-mural myomas except the large ones which distorted uterine cavity where their presence could be suspected. In a study by Farquhar C et al the diagnostic accuracy for submucous uterine fibroids was better by hysteroscopy and saline hystero-sonography as compared to transvaginal ultrasonography.[8]

Hysteroscopy comes with the added advantage of resection of the submucous fibroids in the same sitting.[9,10] While studying the blood flow patterns of the fibroids by TUCD a decrease in the impedance to the flow was observed in addition to a constant diastolic flow to the myoma. These findings were similar to the study by Kurjak A et al.[11]

TUCD demonstrated endometrial hyperplasia in 26% patients. The mean endometrial thickness recorded was 16.5±2.19. Hysteroscopy could prompt presence of hyperplastic endometrium in 24% patients. However, on histopathological examination endometrial hyperplasia was diagnosed in 50% patients. Ten percent patients were diagnosed to have atypical hyperplasia while the rest had simple hyperplastic endometrium. These findings suggested that although TUCD and hysteroscopy could diagnose endometrial hyperplasia, both lack accuracy and histopathology is necessary specially to diagnose the cases with atypical changes because of the associated risks of malignant transformation. As per the previous studies too it seems logical that a patient with AUB be subjected to non-invasive TUCD to know the endometrial thickness and colour flow patterns following which the patient can undergo hysteroscopy and directed biopsy, shall the need be felt.[6,12]

Present study found that TUCD was as good a screening and diagnostic tool for endometrial atrophy as hysteroscopy with a sensitivity, specificity, PPV, NPV of 100% each. Other international studies also show that endo-vaginal ultrasound is a fairly good tool for diagnosis of atrophic endometrium and that below a cut off limit of 5mm thick endometrium, the risk of malignancy being very low, endo-vaginal ultrasound may be the lone investigation needed.[13]

Uterine arteriovenous malformation constitutes a rare cause of refractory AUB. In our study, we came across one such case which was diagnosed by TUCD but hysteroscopy couldn't detect any abnormality. There are case reports in literature which highlight Colour Doppler

as the primary non-invasive diagnostic test for arteriovenous malformations.[14-16]

Five cases of endometrial carcinoma were predicted by TUCD. All the cases exhibited a low resistance flow. The mean endometrial thickness in these cases was 23.2±3.11mm. Hysteroscopy also predicted the same number of cases but histopathology confirmed the diagnosis in only 4 cases. The fifth cases were diagnosed as complex hyperplasia with atypia. Although TUCD can diagnose endometrial carcinoma with a fair degree of accuracy, it can't be relied upon completely and can't be used as the sole screening tool keeping in mind the seriousness of the condition. Also, the study parameters like thickened endometrium and low resistance flow can also be seen in patients on hormone therapy or tamoxifen therapy for breast cancer. There have been research studies in the past which show that Colour Doppler ultrasound can predict malignant endometrial disease.[5,17] However, hysteroscopy and directed biopsy form the gold standard diagnostic modality in contemporary medicine.[18,19] Although there were concerns regarding the spread of endometrial cancer by hysteroscopy, the ideology has been refuted by current research.[20]

CONCLUSION

Hysteroscopy is considered as the gold standard for the evaluation of endometrial pathology. On comparing Transvaginal Colour Doppler findings with those of hysteroscopy, it was observed that there was a good agreement between the results of the two techniques. Transvaginal Colour Doppler can also be used as fairly good investigation technique for the diagnosis endometrial pathology.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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