

Doppler Study of Uterine Artery and Ultrasonography of Endometrial Thickness in Perimenopausal and Postmenopausal Bleeding

Shaimaa Belal¹, Manal Abdel-Wanees Al-Sayed^{2*}, Hany Mahmoud Abd El Hamid²,
Hesham Mohammed Hamed²

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Helwan University, Helwan, Cairo, Egypt

²Department of Obstetrics and Gynecology, Al-Sahel Teaching Hospital, Cairo, Egypt

Email: *amrh1933@gmail.com

How to cite this paper: Belal, S., Al-Sayed, M.A.-W., El Hamid, H.M.A. and Hamed, H.M. (2022) Doppler Study of Uterine Artery and Ultrasonography of Endometrial Thickness in Perimenopausal and Postmenopausal Bleeding. *Open Journal of Obstetrics and Gynecology*, 12, 309-322.
<https://doi.org/10.4236/ojog.2022.124029>

Received: March 20, 2022

Accepted: April 24, 2022

Published: April 27, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Transvaginal color Doppler sonography of the uterine artery has been reported useful for evaluation of abnormal uterine bleeding in peri-/post-menopausal women. It may differentiate physiological from malignant endometrial changes. **Objective:** Evaluating the endometrial thickness and uterine artery Doppler as an initial diagnostic tool to identify patients with abnormal endometrial pathology. **Methods:** This is a prospective case control study consisted of total 50 women with peri-(n = 35) and post-(n = 15) menopausal bleeding, with 20 women consisting control group (no bleeding) (peri-(n = 10) and post-menopausal (n = 10)). Double layer endometrial thickness and uterine-artery-Doppler waveforms were measured, with the latter being S/D ratio, RI and PI. These were related to histological findings (endometrial biopsy). **Result:** Patients with abnormal uterine bleeding (both peri- and postmenopausal) had a significantly higher mean endometrial thickness than the control women. Study group showed a significantly lower value of all Doppler indices (S/D ratio, RI and PI). In study group, patients with malignant endometrial pathology showed significantly thicker endometrium and significantly lower Doppler indices than those with benign pathology. **Conclusion:** The combination of endometrial thickness and uterine artery color Doppler pattern might predict uterine endometrial malignancy, although whether it can discriminate (screen) patients requiring endometrial biopsy is not evident. Further study is needed.

Keywords

Doppler Study, Uterine Artery, Ultrasonography, Endometrial Thickness

1. Introduction

Diagnostic curettage has long been the method of choice to diagnose cancer of the endometrium in patients with postmenopausal bleeding is a simple but sometimes risky technique with a high incidence of false negative results, In spite of that, it is still considered mandatory to exclude malignant endometrial changes [1]. Transvaginal sonography is less invasive, safe and painless, preferred over uniform endometrial biopsy of postmenopausal women with vaginal bleeding. However, it is not specific and cannot reliably distinguish between benign proliferation, hyperplasia, polyps and cancer. Endometrial sampling is less successful in women with a thin endometrial stripe on ultrasound than in women with the real endometrial pathologic condition [2]. Ultrasonic measurement of endometrial thickness is a sensitive index in detecting cancer and pathological endometrial hyperplasia. By the combined measurement of endometrial thickness and estimation of qualitative features of the endometrial and uterine cavity, TVS image improves results in detecting all types of intrauterine pathology [3]. Transvaginal color Doppler sonography has a significant place in the diagnostic process for evaluation of abnormal uterine bleeding in perimenopausal and postmenopausal women. Doppler sonography can help in differentiating physiological from malignant endometrial changes and in deciding on the most efficient therapeutic regimen [4]. Since unrestricted tumor growth is dependent upon angiogenesis, Doppler has thus been proposed to enhance the ultrasound specificity for gynecologic cancer. However, similar processes of angiogenesis and thus Doppler features, can be observed during normal physiologic events, thus to avoid confusion, morphologic and Doppler features have to be carefully combined [5]. Endovaginally sonographic endometrium examination and Doppler velocimetric study of the uterine artery were found to be clinically useful as a single screening noninvasive tool in discriminating atrophic from abnormal endometrium in women with postmenopausal bleeding [6].

2. Aim of the Work

The aim of this work is to evaluate the value of endometrial thickness measurement and uterine artery doppler waveform analysis as initial diagnostic tool for identifying abnormal endometrial pathology in women with perimenopausal and postmenopausal bleeding and correlate them to histopathological examination of the endometrium.

3. Patients and Methods

This study was carried out in Obstetrics and Gynecology Department in Al-Sahel Teaching Hospital, Cairo, Egypt, from January, 2019 till June, 2020. It is one of the main referral hospitals in Egypt.

Our study is prospective case control study. Pretesting questionnaire was done to facilitate cases selection. Seventy female patients attending the hospitals were recruited for the study; they were divided into two main groups; study and con-

trol groups.

1) Study group includes 50 women complaining of abnormal vaginal bleeding subsequently divided into two age groups:

a) Perimenopausal patients; 35 cases with mean age 46.5 ± 3.59 years. Those patients are in the perimenopausal period, after the age of forty but not passed more than 12 months after the last menstrual period.

b) Postmenopausal patients; 15 cases with mean age 58.2 ± 7.44 years. These patients are in the postmenopausal period which is at least 12 months after the last menstrual period.

2) Control group includes 20 women, 10 of them in the perimenopausal age group, and 10 in the postmenopausal age group. These patients were attending the outpatient clinic for complaints other than abnormal vaginal bleeding and their complaints were considered as to have no effect on the pelvic vasculature. The perimenopausal control cases were examined in the luteal phases of their cycles for the sake of standardization.

Selection criteria of the patients: All the patients in the perimenopausal and postmenopausal age groups were selected on the basis of the following criteria:

a) The patients were complaining of abnormal vaginal bleeding in any form as menorrhagia, metrorrhagia, menometrorrhagia or polymenorrhagia.

b) The patients were not under the effect of any hormonal treatment as injectable contraception, contraceptive pills or HRT.

c) The patients not using mechanical contraception methods as I.U.C.D., no recent gynecological surgery was done, and patients not recently exposed to pelvic irradiation.

d) Exclusion of local vulval, vaginal, cervical lesions and uterine fibroids by examination and ultrasound.

e) Exclusion of pregnancy by urine pregnancy test in perimenopausal patients.

All the patients were subjected to the following.

1) History taking.

2) Examination: general condition, manifestation of anemia, vital signs, chest and heart examination, abdominal examination to detect masses, tenderness, ascites, organomegaly or scar of previous surgery.

3) Laboratory investigations: Complete blood count/Fasting and two hours postprandial blood sugar level/urea & creatinine/Liver function tests/coagulation profile/Thyroid function.

4) Transvaginal ultrasonographic examination of the pelvis for determination of:

- Uterine position, measurements, uterine cavity contents and any organic or focal lesions as fibroids.
- Endometrial thickness measured in two layers in the longitudinal scan of the uterus, and if there were any masses in the uterine cavity or distortion of the endometrium with possibility of myometrial infiltration, the sub-endometrial halo and myometrial echogenicity were observed.
- Ovarian measurement to exclude ovarian lesions as cysts or tumors and any

pelvic masses or fluid collection or excessive varicosities especially in the broad ligament was noticed.

5) Pulsed Doppler scanning of the uterine artery was performed.

6) Endometrial sampling by full curettage under general anesthesia.

Analytical statistics: Analysis of the data was done by comparing between groups where variables were calculated as mean, standard deviation, median and minimum-maximum values for quantitative variables and absolute frequency and percentage for qualitative variables were estimated, qualitative variables were analyzed using the Chi square test while Student t-test was used in comparing quantitative data. We used commercially available software (SPSS for windows version 21.0; SPSS, Inc., Chicago, IL), with significance level set at 5%.

4. Results

The perimenopausal cases had a mean age of 46.5 ± 3.59 , a mean parity of 3.5 ± 2.4 and a mean BMI of 26.5 ± 3.3 . The postmenopausal cases had a mean age of 58.2 ± 7.44 , a mean parity of 3.66 ± 3.45 and a mean BMI of 26.2 ± 3 . The perimenopausal control cases had a mean age of 45 ± 3.55 , a mean parity of 2.9 ± 2.02 and a mean BMI of 28.1 ± 3.1 . The postmenopausal control cases had a mean age of 55.9 ± 5.2 , a mean parity of 2.6 ± 1.8 and a mean BMI of 26.1 ± 3.5 . According to histopathological examination of the endometrium in the study groups, most patients had a normal pattern followed by hyperplasia then uterine polyps and cancers and lastly endometritis and adenomyosis. The frequency of distribution of the various medical disorders among perimenopausal patients with normal and abnormal endometrial histopathology was statistically insignificant. The frequency of distribution of the various medical disorders among postmenopausal patients with normal and abnormal endometrial histopathology was statistically insignificant. The mean uterine artery S/D ratio and PI were found to be significantly lower in cases with perimenopausal bleeding (4.6 ± 0.9 & 2.08 ± 0.44) respectively when compared with perimenopausal control women (5.38 ± 1.12 & 2.41 ± 0.5) respectively. Also, the mean uterine artery RI was highly significantly lower in cases with perimenopausal bleeding (0.82 ± 0.06) than in perimenopausal control women (0.93 ± 0.08). It was found that 62.9% of perimenopausal patients with bleeding had endometrial thickness ≥ 8.5 mm but 30% of perimenopausal control women had endometrial thickness ≥ 8.5 mm. The mean uterine artery S/D ratio and PI were found to be highly significantly lower in cases with postmenopausal bleeding (4.53 ± 1.1 & 2.5 ± 0.36) respectively when compared with postmenopausal control women (6.2 ± 1.2 & 3.2 ± 0.87) respectively. Also, the mean uterine artery RI was significantly lower in cases with postmenopausal bleeding (0.85 ± 0.8) than in postmenopausal control women (0.92 ± 0.02). 86.6% of postmenopausal patients with bleeding had endometrial thickness ≥ 5 mm but 10% of postmenopausal control women had endometrial thickness ≥ 5 mm. 100% of perimenopausal patients with malignant endometrium had endometrial thickness ≥ 8.5 mm and 60.6% of patients with

benign endometrium had endometrial thickness ≥ 8.5 mm. 100% of postmenopausal patients with malignant endometrium had endometrial thickness ≥ 5 mm and 85.7% of patients with benign endometrium had endometrial thickness ≥ 5 mm. The three cut off limits of endometrial thickness in perimenopausal study group where, the cut off limit of (8 mm) showed the highest sensitivity (74.3%) and negative predictive values (40%), whereas the cut off limit off (8.5 mm) showed the highest specificity (70%) and positive predictive values (88%).

As regard Doppler indices, for the S/D ratio, the cut off limit of (5.5) showed the highest sensitivity (91.4%), positive predictive value (88.9%) and negative predictive value (66.7), whereas the cut off limit of (5) showed the highest specificity (60%).

For the RI, the cut off limit of (0.89) showed the highest sensitivity (94%) and negative predictive value (80%), whereas cut off limit of (0.86) showed highest specificity (90%) and positive predictive values (96.4%).

For the PI, the cut off limit of (2.4) showed the highest sensitivity (82.9%), positive predictive value (87.9%) and negative predictive value (50%), whereas cut off limit of (2) showed the highest specificity (80%).

The three cut off limits of endometrial thickness in postmenopausal study group where, the cut off limit of (4.5 mm) showed the highest sensitivity (93.3%) and negative predictive values (83.3%), whereas the cut off limit off (5 mm) showed the highest specificity (90%) and positive predictive values (92.9%). As regard Doppler indices, for the S/D ratio, the cut off limit of (5.5) showed the highest sensitivity (86.7%) and negative predictive value (77.8), whereas the cut off limit of (4.5 and 5) both showed the highest specificity (80%) and positive predictive value (81.8%).

For the RI, the cut off limit of (0.90) showed the highest sensitivity (86.7%) and negative predictive value (77%), whereas cut off limit of (0.88 and 0.85) both showed highest specificity (100%) and positive predictive values (100%).

For the PI, both the cut off limit of (2.4 and 2.6) showed the highest sensitivity (93.3%), positive predictive value (82.4%) and negative predictive value (87.5%), whereas all the 3 cut off limit of (2.2, 2.4 and 2.6) all showed the same specificity (70%). A positive correlation between uterine artery S/D ratio & RI and PI in the study group and this correlation were found to be statistically significant (**Tables 1-9**).

5. Discussion

This study included the examination of 50 patients with abnormal vaginal bleeding, 35 patients with perimenopausal bleeding and 15 patients with postmenopausal bleeding and 20 control women not complaining from abnormal uterine bleeding, 10 of them in the perimenopausal age group and another 10 control women in the postmenopausal age group. Sixteen patients in the perimenopausal study group (45.7%) and 7 patients in the postmenopausal study group (46.7%) were found to have abnormal pathology. The abnormal pathological

Table 1. Clinical characteristics of the study and control groups.

Study group	Perimenopausal cases (N = 35)	Postmenopausal cases (N = 15)
Age Mean \pm SD	46.5 \pm 3.59	58.2 \pm 7.44
Range	40 - 52	48 - 72
Parity Mean \pm SD	3.5 \pm 2.4	3.66 \pm 3.45
Range	0 - 8	0 - 14
BMI Mean \pm SD	26.5 \pm 3.3	26.2 \pm 3.2
Range	21.5 - 32.2	21.3 - 31.2
Control group	Perimenopausal control group (N = 10)	Postmenopausal control group (N = 10)
Age Mean \pm SD	45 \pm 3.55	55.9 \pm 5.2
Range	40 - 51	49 - 65
Parity Mean \pm SD	2.9 \pm 2.02	2.6 \pm 1.8
Range	0 - 6	0 - 6
BMI Mean \pm SD	28.1 \pm 3.1	26.1 \pm 3.5
Range	21.3 - 32.9	20.2 - 30.8

Table 2. Frequency of histopathological finding in perimenopausal and postmenopausal women with bleeding.

Endometrium	Perimenopausal cases		Postmenopausal cases	
	N = 35	%	N = 15	%
Normal Proliferative	11	31.4	0	0.0
Secretory	8	22.9	0	0.0
atrophic	0	0.0	8	53.3
Hyperplasia Simple	4	11.4	1	6.7
Glandular	3	8.6	2	13.3
Adenomatous	3	8.6	0	0.0
With atypia	1	2.9	1	6.7
Adenocarcinoma	2	5.7	1	6.7
Polyp	3	5.7	1	6.7
Endometritis	0	0.0	1	6.7
Adenomyosis	1	2.9	0	0.0

$X^2 = 3.31$, $P = 0.65$ (NS).

finding in perimenopausal patients included hyperplasia (31.4%), endometrial cancer (5.7%), endometrial polyps (5.7%), and finally adenomyosis (2.9%). In postmenopausal patients the abnormal pathological finding were hyperplasia (26.7%), endometrial cancer (6.7%), endometrial polyps (6.7%), and finally endometritis (6.7%).

This study showed a mean body mass index of (26.5 \pm 3.3 and 26.2 \pm 3.2) for perimenopausal and postmenopausal patients respectively compared to (28.1 \pm

Table 3. Medical disorders according to type of pathology in perimenopausal study group.

Perimenopausal study group	Normal		Hyperplasia		Cancer		Polyp		Total	X ²	P
	No	%	No	%	No	%	No	%			
Hypertension	2	40	1	100	0	0.0	0	0.0	3	3.6	0.3
D.M	1	20	0	0.0	1	50	1	100	3	3.15	0.36
Hypertension +D.M	1	20	0	0.0	1	50	0	0.0	2	1.48	0.68
Hypothyroid	1	20	0	0.0	0	0.0	0	0.0	1	0.9	0.82
Total	5		1		2		1		9		

Postmenopausal study group	Normal		Hyperplasia		Cancer		Polyp		Total	X ²	P
	No	%	No	%	No	%	No	%			
Hypertension	2	66.7	1	50	1	100	0	0.0	4	2.29	0.52
D.M	0	0.0	0	0.0	0	0.0	1	100	1	7.0	0.07
Hypertension +D.M	0	0.0	1	50	0	0.0	0	0.0	1	2.92	0.4
Hepatic	1	33.3	0	0.0	0	0.0	0	0.0	1	1.56	0.66
Total	3		2		1		1		7		

Table 4. Comparison of S/D Ratio, RI and PI and Endometrial thickness cut off (8.5 mm) between cases with perimenopausal bleeding and perimenopausal control women.

Doppler indices	Perimenopausal study group (N = 35)	Perimenopausal control group (N = 10)	t	p
S/D Mean ± SD	4.6 ± 0.9	5.38 ± 1.12	2.46	0.016 sig.
Range	2.2 - 7	4.16 - 7.12		
RI Mean ± SD	0.82 ± 0.06	0.93 ± 0.08	5.13	<0.001 sig.
Range	0.65 - 0.93	0.81 - 1.1		
PI Mean ± SD	2.08 ± 0.44	2.41 ± 0.50	2.01	0.04 sig.
Range	1.2 - 3.15	1.88 - 3.22		

Endometrial Thickness (mm)	Perimenop.	study group (35)	Perimenop.	control group (10)
≥8.5	22	62.9%	3	30%
<8.5	13	37.1	7	70

3.1 and 26.1 ± 3.5) in perimenopausal and postmenopausal control women respectively and this was similar to that of a study that found a mean BMI of 27.1 kg/m² for postmenopausal women with pathologic conditions compared to 25.7 kg/m² for those without pathologic conditions [7].

Although the relationship of diabetes mellitus and hypertension to endometrial carcinoma is well known and documented in another study, our study showed that there was no statistically significant relationship between them and the type of endometrial pathology. This may be due to the small number of patients in this study [8].

Table 5. Comparison of S/D ratio, RI and PI and Endometrial thickness cut off (5 mm) between cases with postmenopausal bleeding and postmenopausal control women.

Doppler indices	Perimenopausal study group (N = 15)	Perimenopausal control group (N = 10)	t	p
S/D Mean \pm SD	4.53 \pm 1.1	6.2 \pm 1.2	3.64	<0.001 (sig.)
Range	2.9 - 6.5	4.25 - 7.21		
RI Mean \pm SD	0.85 \pm 0.80	0.92 \pm 0.02	2.66	0.013 (sig.)
Range	0.6 - 0.94	0.89 - 0.96		
PI Mean \pm SD	2.5 \pm 0.36	3.2 \pm 0.87	4.6	<0.001 (sig.)
Range	1.17 - 2.81	2.15 - 4.38		
Endometrial Thickness (mm)	Postmenopausal	study group	Postmenopausal	control group
	N = 15	%	N = 10	%
\geq 5	13	86.6	1	10
<5	2	13.4	9	90

Table 6. Comparison of endometrial thickness cut off (8.5 mm) between cases with benign lesions and those with malignant lesions in perimenopausal and post menopausal cut off (5 mm) study group.

Perimenopausal cases	Benign endometrium		Malignant endometrium	
Endometrial Thickness (mm)	N = 33	%	N = 2	%
\geq 8.5	20	60.6	2	100
<8.5	13	39.4	0	0.0
Postmenopausal cases	Benign endometrium		Malignant endometrium	
	N = 14	%	N = 1	%

Table 7. Sensitivity, specificity, positive predictivity and negative predictivity of measuring endometrial thickness & S/D & RI and PI in diagnosing normal endometrium among perimenopausal study group.

	Sensitivity %	Specificity %	+ve predictive value %	-ve predictive value %
Endometrial thickness (mm) cut off				
8	74.3	60	86.7	40
8.5	62.9	70	88	35
9	54.3	70	86.4	30
S/D cut off				
4.5	45.7	60	72.7	17.4
5	71.4	60	80.6	28.6
5.5	91.4	40	88.9	66.7
RI cut off				
0.83	60	90	95.5	39.1
0.86	77	90	96.4	52.9
0.89	94	80	94.3	80
PI cut off				
2	31.4	80	84.6	25
2.2	71.4	60	86.3	37.5
2.4	82.9	60	87.9	50

Table 8. Sensitivity, specificity, positive predictivity and negative predictivity of measuring endometrial thickness & S/D & RI and PI in diagnosing normal endometrium among postmenopausal study group.

	Sensitivity %	Specificity %	+ve predictive value %	-ve predictive value %
Endometrial thickness (mm) cut off				
4.5	93.3	50	73.7	83.3
5	86.6	90	92.9	81.8
5.5	66.6	90	90.9	64.3
S/D cut off				
4.5	60	80	81.8	57.1
5	60	80	81.8	57.1
5.5	86.7	70	55.3	77.8
RI cut off				
0.85	46.7	100	100	55.6
0.88	60	100	100	62.5
0.90	86.7	70	81.3	77
PI cut off				
2.2	77.3	70	78.6	63.6
2.4	93.3	70	82.4	87.5
2.6	93.3	70	82.4	87.5

Table 9. Correlation between uterine artery S/D & RI and PI in the study group.

	S/D	RI	PI
No	50	50	50
Mean \pm SD	4.6 \pm 1.76	0.82 \pm 0.061	2.08 \pm 0.45

$r = 0.33$, $p < 0.05$ (sig.).

The results of the study of endometrial thickness in perimenopausal patients showed that the mean endometrial thickness was found to be significantly higher than in the control group (10.2 ± 3.7 mm and 7.6 ± 2.4 mm respectively). The same was found when comparing postmenopausal cases with postmenopausal controls (8.9 ± 6.1 mm and 4.6 ± 1.1 mm respectively).

As regarding the effect of the pathology on the endometrial thickness, cases with benign endometrium had a mean endometrial thickness which were less than those with malignant endometrium (9.1 ± 3.3 mm for benign endometrium compared to 21.3 ± 6.1 mm for malignant cases). This observation was found to be statistically highly significant.

These finding are in accordance with the study that found a mean double layer endometrial thickness of (3.6 ± 3.3 mm in control postmenopausal patients, compared to 10.8 ± 7 mm and 22.5 ± 8.9 mm for cases with benign and malignant pathology respectively) [9].

When searching for a cut off limit for the endometrial thickness in this study, it was kept in mind the main aim of this work to evaluate the usefulness of en-

ometrial thickness measurement only as an initial diagnostic tool. Accordingly an optimal cut off point for diagnosis of a normal endometrium would be the one that give the highest sensitivity and specificity and hence the least false negative and false positive results. A cut off point that give a low sensitivity would lead to the unnecessary submission of patients with normal pathology to endometrial biopsy, only to be proven normal later by pathological examination. On the other hand a cut off point that show a low specificity would lead to high false positive results, and consequently patients with abnormal pathology who are initially screened by this method would be improperly dismissed on the basis of having no endometrial abnormality.

In this study different cut off points of endometrial thickness measurement in cases of perimenopausal bleeding were tested for their sensitivity and specificity, accordingly a cut off point of (8 mm) was associated with a sensitivity of (74.3%), and specificity (60%) and cut off point of (9 mm) although associated with increased specificity (70%) it was associated with a much lower sensitivity (54.3%), but cut off limit of (8.5 mm) was associated with a sensitivity of (62.9%), and a specificity of (70%), so it was preferred over the other two values, but still there was no acceptable cut off value which possess both higher sensitivity and specificity to exclude endometrial pathology in cases of perimenopausal bleeding.

Paraskevaidis *et al.*, (2012), used a 13 mm cut-off limit for endometrial thickness measurement in cases with perimenopausal bleeding, they showed that the sensitivity, specificity and positive predictive values were (100%, 71.64% and 40.62%, respectively), they concluded that TVS can identify women with perimenopausal bleeding in which the likelihood of endometrial pathology is high and in which tissue sampling should be performed [10].

The summarized data from the study of Zlatkov *et al.*, (2011), as regard endometrial thickness measurement in cases with perimenopausal bleeding, showed that in the limit of 8 mm, the diagnostic accuracy of the method sensitivity (75%) specificity (73.8%) and efficacy (74%) gave them the cause to recommend the transvaginal sonography of the endometrium in women in the perimenopausal period as a screening tool in the diagnostic protocol for endometrial cancer [11].

On the other hand, in patients with postmenopausal bleeding a cut off limit of (5 mm) seems to be appropriate as it was associated with a (86.6%) sensitivity and (90%) specificity and hence low false positive and false negative results, when compared with other cut off point (4.5 mm) although associated with a higher sensitivity (93.3%), it showed much lowered specificity (50%). Also a cut off limit of (5.5 mm) was associated with the same specificity (90%) yet, it showed lowered sensitivity (66.6%).

Gull *et al.*, (2003) stated that the reliability of double layer endometrial thickness cut off value of (4 mm) as a diagnostic test for endometrial cancer was as follow (sensitivity 100%, specificity 60%, positive predictive value 25% and nega-

tive predictive value 100%) [12].

Ciatto *et al.*, (2002) stated that the best cut off for clinical purposes was (4 mm half layer), with (a sensitivity of 91.1%, a specificity of 79.8%, a positive predictive value of 14.8% and a negative predictive value of 99.6%) [13].

This study suggests that the endometrial thickness measurement is of great value in postmenopausal patients than in perimenopausal patients. This may be due to the wide range of normal endometrium patterns that may be found in the perimenopausal patients due to the cyclic effect of estrogen and progesterone on the endometrium. In the opinion of Tabor *et al.*, (2012), stated that Endometrial thickness measurement in symptomatic postmenopausal women does not reduce the need for invasive diagnostic testing because (4%) of the endometrial cancers would still be missed with a false-positive rate as high as (50%) [14].

The first Doppler index to be studied was the S/D ratio. This study showed that the mean S/D ratio was significantly lower in perimenopausal cases with bleeding relative to those of the control group (4.6 ± 0.9) compared to 5.38 ± 1.12 for controls). The same was true for postmenopausal cases that showed a mean S/D ratio of (4.5 ± 1.1), which was highly significantly lower than controls (6.2 ± 1.2). The study also showed that cases with malignant endometrium had a significantly lower value than those with benign endometrium (3.25 ± 0.4 for malignant cases and 4.6 ± 0.9 for benign cases).

The RI showed the same finding, where the mean RI in perimenopausal patients was highly significantly lower than the control group (0.82 ± 0.06 compared to 0.93 ± 0.08). Postmenopausal patients had a mean value of (0.85 ± 0.8 compared to 0.92 ± 0.02 for controls).

Also, the mean value was significantly lower in malignant cases compared to benign cases (0.75 ± 0.03 compared to 0.84 ± 0.06).

The PI also showed similar finding. In perimenopausal patients with bleeding it showed a mean of (2.08 ± 0.44 compared to 2.4 ± 0.5 for controls). In postmenopausal cases the mean value was (2.05 ± 0.36 compared to 3.2 ± 0.87 for controls). The mean value was also found to be significantly lower in patients with malignant pathology than in patients with benign pathology (1.32 ± 0.2 and 2.1 ± 0.38 and respectively).

It is clear from all the above that all Doppler indices are significantly lower in cases with bleeding compared to control cases, and in malignant compared to benign cases. These results agree with the studies suggested that there is a significant decrease in the vascular resistance associated with endometrial pathology.

Arslam *et al.*, (2013) proved that Doppler velocity waveforms of uterine vessels coupled with transvaginal ultrasonography are not valuable enough to replace histopathological examination in the diagnosis of a neoplastic endometrial pathology. However, it may be helpful in cases in which invasive techniques are difficult to perform and in the differentiation of a certain group of patients at little risk of endometrial carcinoma [15].

As in the case of endometrial thickness, this study has tested different cut off limits for the various measured Doppler indices. The value giving the highest

sensitivity and specificity and hence the least false negative and false positive results was preferred.

At cut off limit of (5) for S/D ratio in perimenopausal patients showed a sensitivity of (71.4%) and specificity (60%) but at cut off limit of (5.5) although there was an increase in sensitivity to (91.4%) the specificity decreased to (40%) which increase the incidence of false positive results. So, cut off value of (5) was more considered in postmenopausal patients. A cut off limit of (5 or 4.5) for the S/D ratio was associated with a sensitivity of (60%) and specificity of (80%) for both, but at cut off limit of (5.5) although there was an increase in the sensitivity to (86.7), the specificity was decreased to (70%) so at cut off limit of (4.5 or 5) the number of patients with abnormal pathology who will be missed is slightly less than with the other value, but we consider the higher value of (5).

As regard the RI, in perimenopausal patients the selected cut off value was (0.86) as it was associated with a specificity of (90%) and sensitivity (77%). At cut off limit of (0.89) there was a higher sensitivity of (94%) but lower specificity of (80%). In postmenopausal patients the selected cut off value for RI was (0.88) as it was associated with a specificity of (100%) and hence no false positive results, although its specificity was (60%).

The last index to be examined was the PI. In perimenopausal patients a cut off limit of (2) was found to be associated with the highest specificity (80%), however, this figure was associated with a very low sensitivity of (31.4%) but cut off limit of (2.4%) although associated with a decrease in the specificity to (60%) there was increased sensitivity to (82.9%) so it was considered. In postmenopausal patients using a cut off limit of (2.6 or 2.4) both was associated with (93.3%) sensitivity and (70%) specificity. It would however seem safer to take the higher value as cases with neovascularization are associated with lower values due to diminished resistance.

When comparing the cut off values for the three Doppler indices in perimenopausal patients the RI showed the highest specificity (90%) and sensitivity (94%), so the preferred Doppler index is the RI followed by the PI and the least is the S/D ratio as it is affected not only by diminished resistance and increased diastolic blood flow but also, by changes in the systolic blood flow. In postmenopausal patients the RI showed the highest specificity (100%), while the PI showed the highest sensitivity (93.3%).

It is evident from all the above that all the Doppler indices are more accurate in postmenopausal cases than in perimenopausal cases. It is also evident that none of the parameters tested in this study, whether Doppler indices or endometrial thickness could guarantee a 100% specificity alone in all cases with peri and postmenopausal bleeding. It is possible however that the combined use of more than one parameter would improve the efficacy of these tests as initial screening methods.

Finally, the Doppler parameters were correlated with each other and the results showed a positive correlation between all Doppler indices and each other. The correlation between the (S/D ratio and the RI), and (the S/D ratio and the

PI) was found to be statistically significant and between (the RI and the PI) was statistically highly significant, accordingly one may expect a similar change in all Doppler indices in the same condition. Evaluating the value of endometrial thickness measurement and uterine artery Doppler study as an initial diagnostic tool to identify patients with abnormal endometrial pathology needs further investigations and endometrial biopsy.

6. Conclusion

Doppler indices are more accurate in postmenopausal than perimenopausal cases. The combination of endometrial thickness and uterine artery color Doppler pattern (rather than each of them alone) might predict uterine endometrial malignancy, although whether it can discriminate (screen) patients requiring endometrial biopsy is not evident. Further study is needed.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] Gupta, J.K., Chien, P.F., Voit, D. *et al.* (2012) Ultrasonographic Endometrial Thickness for Diagnosing Endometrial Pathology in Women with Postmenopausal Bleeding: A Meta-Analysis. *Acta Obstetrica et Gynecologica Scandinavica*, **81**, 799-816. <https://doi.org/10.1034/j.1600-0412.2001.810902.x>
- [2] Davidson, K.G. and Dubinsky, J.J. (2013) Ultrasonographic Evaluation of the Endometrium in Postmenopausal Vaginal Bleeding. *Radiologic Clinics of North America*, **41**, 769-780. [https://doi.org/10.1016/S0033-8389\(03\)00060-5](https://doi.org/10.1016/S0033-8389(03)00060-5)
- [3] Bender, R. and Rzepka, G.I. (2012) Transvaginal Ultrasonography in the Diagnosis of Endometrial and Uterine Cavity Changes in Perimenopausal Women. *Ginekologia Polska*, **73**, 985-990.
- [4] Svetlana, D.D., Atanasije, M., Misa, D. *et al.* (2008) Evaluation of Abnormal Uterine Bleeding by Transvaginal Color Doppler Sonography. *Archive of Oncology*, **6**, 167-169.
- [5] Goes, E. and Osteaux, M. (2005) Transvaginal Duplex Ultrasound in Oncologic Gynaecology. *Journal of the Belgian Society of Radiology*, **78**, 347-349.
- [6] Maher, M. and Ahmad, A. (2008) The Value of Vaginal Endosonography of Endometrium and Doppler Vlocimetry of the Uterine Artery as Discriminators of Endometrial Status in Women with Postmenopausal Bleeding. *The Medical Journal of Cairo University*, **66**, 121-30.
- [7] Gull, B., Carlsson, S.A. and Ylostalo, P. (2009) Transvaginal Ultrasonography of the Endometrium in Women with Postmenopausal Bleeding: Is It always Necessary to Perform an Endometrial Biopsy. *American Journal of Obstetrics & Gynecology*, **182**, 509-515. <https://doi.org/10.1067/mob.2000.103092>
- [8] Lurain, J. (2016) Uterine Cancer. In: Berek, J., Adashi, E. and Hillard, Eds., *Novak's gyn.*, 12th Edition, Williams ad Wilkins, Baltimore, 1057-1110.
- [9] Van Den Bosch, T., Van Schoubroek, D. and Lombared, C. (2006) Age, Weight, Body Mass Index and Endometrial Thickness in Postmenopausal Women. *Acta*

Obstetricia et Gynecologica Scandinavica, **85**, 181-182.

<https://doi.org/10.3109/00016349609033315>

- [10] Paraskevaïdis, E., Kalantaridon, S.N., Papadimitrion, D. *et al.* (2012) Transvaginal Uterine Ultrasonography Compared with Endometrial Biopsy for the Detection of Endometrial Disease in Perimenopausal Women with Uterine Bleeding. *Anticancer Research*, **22**, 1829-1832.
- [11] Zlatkov, V., Nikolov, M., Mikhlova, A. *et al.* (2011) Diagnostic Modalities of Endometrial Ultrasonography in Women with Irregular Bleeding in Menopause. *Akush-Ginekol*, **41**, 17-29.
- [12] Gull, B., Karlsson, B., Milsom, I. *et al.* (2003) Can Ultrasound Replace Dilation and Curettage? A Longitudinal Evaluation of Postmenopausal Bleeding and Transvaginal Sonographic Measurement of the Endometrium as a Predictors of Endometrial Cancer. *American Journal of Obstetrics & Gynecology*, **188**, 401-408.
<https://doi.org/10.1067/mob.2003.154>
- [13] Ciatto, S., Cecchinic, S., Gervasi, G. *et al.* (2002) Association of Endometrial Thickness at Transvaginal Ultrasonography to Detect Endometrial Cancer in Postmenopausal Women a Symptomatic or with Abnormal Uterine Bleeding. *La radiologia medica*, **104**, 437-442.
- [14] Tabor, A., Watt, H.C., Wald, N.J., *et al.* (2012) Endometrial Thickness as a Test for Endometrial Cancer in Women with Postmenopausal Bleeding. *Obstetrics and Gynaecology* **99**, 663-670. <https://doi.org/10.1097/00006250-200204000-00029>
- [15] Arslam, M.A., Erdem, M.G., Yazicio, O. *et al.* (2003) Transvaginal Color Doppler Ultrasonography for Prediction of Precancerous Endometrial Lesions. *International Journal of Gynecology & Obstetrics*, **80**, 299-306.
[https://doi.org/10.1016/S0020-7292\(02\)00374-0](https://doi.org/10.1016/S0020-7292(02)00374-0)