Accuracy of doppler ultrasound in diagnosis of endometrial carcinoma

Saima Batool,[1] Shahid Manzur,[2] Saleem Raza[3]

Abstract

Objective: To determine the accuracy of Doppler ultrasound in the diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding while taking histopathological findings as the gold standard.

Methods: The cross-sectional study was done at the Department of Radiology, Bahawal Victoria Hospital, Bahawalpur, from April 1 to September 30, 2009, and comprised 128 patients above 50 years of age having history of post-menopausal bleeding and who were referred to the department. Name, age and hospital registration number were recorded on a proforma. Doppler ultrasound was performed and endometrial thickness and uterine artery resistive index were recorded on transabdominal ultrasonography. Patients with endometrial thickness of more than 5mm and uterine artery resistive index of less than 0.7 were considered to be having endometrial carcinoma. Histopathology findings were also recorded using the hospital registration number of the patient. The findings of Doppler ultrasound scan were validated with the findings of histopathology.

Results: Of the 128 patients, 48 (37.5%) were between the ages of 51 and 55 years; 46 (35.93%) were in the 56-60 age group; and 34 (26.57%) were over 65 years. On the basis of Doppler ultrasound findings, 106 (82.8%) patients were diagnosed as having endometrial carcinoma, while 22 (17.19%) were declared negative. Ultrasonography results were compared with histopathology findings. The percentages of true positive, true negative, false positive and false negative were calculated. There were 103 (80.47%) true positive; 12 (9.37%) false positive; 10 (7.81%) true negative; and 3 (2.35%) false negative. Specificity, sensitivity, positive predictive value and negative predictive value were found to be 97.16%, 76%, 89.56% and 76.92% respectively.

Conclusion: The use of Doppler ultrasonography in non-invasive diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding was quite useful with good sensitivity, specificity, as well as positive and negative predictive values. There were no procedural complications.

Keywords: Post-menopausal bleeding, Endometrial carcinoma, Doppler ultrasonography, Resistive index, Endometrial thickness. (JPMA 63: 28; 2013)

Introduction

Post-menopausal bleeding is a common clinical problem accounting for approximately 5% of visits to a general gynaecologist.[1] Post-menopausal bleeding has been defined as vaginal bleeding occurring at least 6 months after complete cessation of periods in women not taking hormonal replacement therapy (HRT), or non-cyclic vaginal bleeding occurring in post-menopausal women who are receiving HRT.[2]

Abnormal vaginal bleeding may be caused by a number of gynaecologic or non-gynaecologic disorders. Endometrial atrophy is reported to be the most common cause of post-menopausal bleeding.[3] Other causes include endometrial hyperplasia, endometrial polyps, endometrial carcinoma, and

....

Department of Radiology, CMH, Lahore,[1,3] Department of Radiology, Bahawal Victoria Hospital, Bahwalpur.[2]

Correspondence: Saima Batool. Email: saima4me29@hotmail.com

submucosal leiomyomas. Though most studies indicate that endometrial atrophy is the most common cause of post-menopausal bleeding, the results of recent studies with hysterosonography indicate that anatomic abnormalities, such as leiomyomata and polyps, are much more common than has been generally believed.[4]

A diagnosis of endometrial carcinoma should be excluded in all women of peri-menopausal or post-menopausal age presenting with abnormal vaginal bleeding.[2] Intermenstrual and post-menopausal bleeding is the initial symptom in 75% to 90% of patients with endometrial carcinoma.[5] Early diagnosis and treatment are important because the 5-year survival of patients varies from 90% to 100% in patients with little or no myometrial involvement, to 40% to 60% in patients with deep myometrial invasion.[6] Early diagnosis of invasive carcinoma is also desirable, which allows for appropriate treatment,

while surgical cure is still possible. Unfortunately, screening tests for endometrial carcinoma are not available, because the endometrium is not as accessible as the cervix, which is successfully screened by the Pap smear test. Historically, dilation and curettage has been considered the gold standard for the diagnosis and often the treatment of endometrial disease, but that requires general anaesthesia.

Pulsed Doppler indices and colour Doppler vascularity of the endometrium have been used to differentiate between benign and malignant endometrial pathology. Resistive index (RI) ranging from 0.40 to 0.70 has been reported to differentiate benign from malignant endometria accurately, with most authors recommending a threshold value of 0.40.[7] Proposed values for the pulsatility index (PI) range from 1.00 to 2.00.[8]

In these studies, the values of RI and PI obtained below the given threshold indicated malignant disease.[8] Other investigators, however, found endometrial thickness to be a better predictor of endometrial pathology than any of the Doppler indices evaluated to date.[9] The present study was carried out to assess the accuracy of Doppler ultrasound in the diagnosis of endometrial carcinoma in Pakistani women presenting with post-menopausal bleeding while taking histopathological findings as the gold standard.

Patients and Methods

The cross-sectional study comprised 128 patients above 50 years of age having history of post-menopausal bleeding. Who had been referred to the Radiology Department of Bahawal Victoria Hospital, Bahawalpur, Pakistan, by consulting gynaecologists from April 1 to September 30, 2009. Non-probability purposive sampling technique was used. Only those patients were included in the study who had an endometrial thickness of more than 5mm on ultrasonography (US). Patients having an endometrial thickness of less than 5mm and uterine artery resistive index of more than 0.7 on Doppler ultrasound were not included in the study.

Name, age and hospital registration number were recorded on a proforma. Patients were informed that the data collected would be used in a study and that issues related to confidentiality and anonymity would be taken due care of. After taking informed consent, Doppler ultrasound was performed, by using Logiq P-5 General Electric Ultrasound machine equipped with multiple probes of varying frequencies. Endometrial thickness and uterine artery resistive index were

recorded. Patients having endometrial thickness more than 5mm and uterine artery resistive index less than 0.7 were labelled as endometrial carcinoma.

Endometrial biopsy of these patients was carried out in the Gynaecology Department and sent to the Pathology Department of the Bahawal Victoria Hospital. Their results were also recorded using hospital registration number almost after 1 week. These results were compared with ultrasound findings. All data was entered into SPSS 10 for statistical analysis. Endometrial thickness greater than 5mm and uterine artery resistive index less than 0.7 was considered positive for endometrial carcinoma. Histopathology findings were compared with those of Doppler ultrasound. A 2x2 table was generated to calculate the sensitivity, specificity as well as positive and negative predictive values as well as accuracy of the Doppler ultrasound.

Results

The age of the 128 patients ranged from 51 to over 65 years, with 48 (37.5%) being in the 51-55 age group; 46 (35.93%) within 56-60 years; and 34 (26.57%) over 65 years. The mean age was 57.93±4.07 years (Table-1). A total of 106 (82.81%) patients were found to have endometrial carcinoma, while 22 (17.19%) were negative (Table-2). These results were compared with histopathology findings. The incidence of true positive, true negative, false positive and false negative were calculated. Of all the patients, 103 (80.47%) were found to be true positive; 12 (9.37%) false positive; 10 (7.81%) true negative; and 3 (2.35%) were false negative. Specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) were found to be 97.16%, 76%, 89.56% and 76.92% respectively (Table-3).

Table-1: Age-wise distribution.

Age (in years)	No of Patients	Percentage
51 to 55 years	48	37.5
56 to 60 years	46	35.93
> 60 years	34	26.57
Total	128	100
	Mean 57.93 ± 4.073	

Table-2: Endometrial carcinoma.

Endometrial Carcinoma	No of Patients	Percentage
Yes	106	82.81
No	22	17.19

Table-3: Incidence of false positive and false negative tests.

Result	Endometrial carcinoma	
	No. of Patients	Percentage
True positive	103	80.47
False positive	12	9.37
True negative	10	7.81
False negative	03	2.35
Total	128	100

Sensitivity= True +ve/True+ve+False-veX100=97.16%
Specificity= True -ve/True-ve+False-veX100=76%
Positive Predictive Value= True +ve/True+ve+False+veX100= 89.56%
Negative Predictive Value= True -ve/True+ve+False-veX100= 76.92%.

Discussion

Endometrial carcinoma is the most common malignancy of the female genital tract. According to the Surveillance Epidemiology and End Results (SEER) database[10] the incidence of endometrial carcinoma in women aged 30 to 34 years is 2.3/100,000; increases to 6.1/100,000 between ages 35 and 40 years; and rises dramatically to 36.2/100,000 in women aged 40 to 49 years. In post-menopausal women not having HRT, any bleeding is considered ''cancer until proven otherwise,'' although the incidence of malignancy in such patients ranges from 2% to 10% depending on the risk factors.[11] Endometrial curettage, first described in 1843,[12] is the most common operation performed on women across the world. As early as the 1950s, a review of 6907 curettage procedures[13] found that the technique missed endometrial lesions in 10% of cases. Of these, 80% were polyps. In the 1970s, vacuum-suction curettage devices allowed sampling without anaesthesia in clinical setting. The most popular was the Vabra aspirator (Berkeley Medevices, Berkeley, California). This device was found to be 86% accurate in diagnosing cancer.[14] Lately, less expensive, smaller, less painful plastic catheters with their own internal pistons to generate suction have become popular. One of these, the Pipelle device (Unimar, Wilton, Connecticut), was found to have similar efficacy but better patient acceptance compared with the Vabra aspirator.[15]

In an important study, Guido et al[16] studied the Pipelle biopsy in patients who had known carcinoma undergoing hysterectomy. Out of a total of 65 patients, a Pipelle biopsy provided adequate tissue for analysis in 63 (97%), but malignancy was detected in only 54 patients (83%). Of the 11 with false-negative results, 5 (8%) had disease confined to endometrial polyps and 3 (5%) had tumour localised to less than 5% of the surface area of the cavity. The surface area of the endometrial involvement in that study was 5% or less of the cavity in 3 of 65 (5%); 5% to 25% of the cavity in 12 of 65 (18%), of which the Pipelle missed four cases; 26% to 50% of the cavity in 20 of 65 (31%), of which the Pipelle missed four; and greater than 50% of the cavity in 30 of 65 patients (46%), of which the Pipelle missed none.

These results provide an insight into the way endometrial carcinoma can be distributed over the endometrial surface or confined to a polyp, because tumours localised in a polyp or a small area of endometrium may go undetected. The investigators in that study concluded that the ''Pipelle is excellent for detecting global processes in the endometrium''. It seems that undirected sampling, whether through curettage or various types of suction aspiration, is often fraught with error, especially in cases in which the abnormality is not global, but focal (polyps, focal hyperplasia, or carcinoma involving small areas of the uterine cavity).

Ultrasonography (US), especially a transvaginal approach, is the initial imaging modality in patients with suspected endometrial cancer. Endometrial cancer most often appears as thickened endometrium that is more than 5mm in a post-menopausal woman or 15mm in a pre-menopausal woman. Echogenecity varies, but alteration of endometrial texture or focal increased echogenecity may be seen.[17] These appearances are not specific and can be observed in endometrial hyperplasia and polyps.[18] Saline infusion sonohysterography improves diagnosis for endometrial cancer with reported 89% sensitivity, 46% specificity, 16% PPV, and 97% NPV.[19] Risk of disseminating malignant cells by saline infusion sonohysterography is small (approximately 7%).[20] Colour Doppler US often reveals increased vascularity with a multivessel pattern, in contrast to the pedicle artery sign seen in endometrial polyps.[21] Spectral Doppler indices may have low impedance flow, but there is significant overlap in Doppler indices of benign and malignant conditions of the endometrium.[22]

Myometrial invasion is depicted as irregularity of the endometrium — myometrium border and disruption of the subendometrial halo. The accuracy of US in diagnosing the depth of invasion is approximately 73% to 93%, but US is better for grade 2-3 tumours and should not be used as the sole criterion for the decision to perform extensive surgery.[21] Although US can be used to estimate the depth of invasion, a recent meta-analysis has shown that contrast-enhanced

magnetic resonance imaging has better overall performance.[22]

Conclusion

The use of Doppler ultrasonography in the diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding is useful with good sensitivity, specificity, PPV and NPV. Besides, there are no procedural complications.

References

1. Fazio SB, Ship AN. Abnormal Uterine bleeding. South Med J 2006; 100: 376-82.
2. Choudry A, Javaid M. Clinical usefulness of pipelle endometrial sampling. J R Army Med Corp 2005; 2: 35-7.
3. Ghazi A, Jabbar S, Siddiqi N. Frequency of Endometrial carcinoma in patients with post-menopausal bleeding. Pak J Surg 2005; 21: 41-4.
4. Cullinan JA, Fleischer AC, Kepple DM, Arnold AL. Sonohysterography: a technique for endometrial evaluation. Radiographics 1995; 15: 501-14.
5. Chen SS, Lee L. Retroperitoneal lymph node metastases in stage 1 carcinoma of the endometrium: correlation with risk factors. Gynecol Oncol 1983; 16: 319-25.
6. Figge DC, Otto PM, Tamimi HK, Greer BE. Treatment variables in the management of endometrial cancer. Am J Obstet Gynecol 1983; 146: 495-500.
7. Qureshi IA, Hidayat Ullah, Akram H, Ashfaq S, Nayyar S. Transvaginal versus Transabdominal Sonography in the evaluation of pelvic pathology. J Coll Physicians Surg Pak 2004; 14: 390-3.
8. Weaver J, McHugo JM, Clark TJ. Accuracy of transvaginal ultrasound in diagnosing endometrial pathology in women with post-menopausal bleeding on tamoxifen. Br J Radiol 2005; 78: 394-7.
9. Davidson KG, Dubinsky TJ. Ultrasonographic evaluation of the endometrium in postmenopausal vaginal bleeding. Radiol Clin North Am 2003; 41: 769-80.
10. Vuopala S. Diagnostic accuracy and clinical applicability of cytological and histological methods for investigating endometrial carcinoma. Acta Obstet Gyneocl Scand Suppl 1977; 70: 1-72.
11. Kaunitz AM, Masciello AS, Ostrowsky M. Comparison of endometrial Pipelle and Vabra aspirator. J Reprod Med 1988; 33: 427-31.
12. Guido RS, Kanbour A, Ruhn M. Pipelle endometrial sampling sensitivity in the detection of endometrial cancer. J Reprod Med 1995; 40: 553-5.
13. Sheikh M, Sawhney S, Khurana A, Al Yatoma M. Alteration of sonographic texture of the endometrium in post-menopausal bleeding: a guide to further management. Acta Obstet Gynecol Scand 2000; 79: 1006-10.
14. Nalaboff KM, Pellerito JS, Ben-Levi E. Imaging the endometrium: disease and normal variants. Radiographics 2001; 21: 1409-24.
15. Bree RL, Bowerman RA, Bohm-Velez M, Benson CB, Doubilet PM, De Dreu S, et al. US evaluation of the uterus in patients with postmenopausal bleeding: a positive effect on diagnostic decision making. Radiology 2000; 216: 260-4.
16. Dubinsky TJ, Stroehlein K, Abu-Ghazzeh Y, Parvey HR, Makland N. Prediction of benign and malignant endometrial disease: hysterosonographic-pathologic correlation. Radiology 1999; 210: 393-7.
17. Alcazar JL, Errasti T, Zornoza A. Saline infusion sonohysterography in endometrial cancer: assessment of malignant cells dissemination risk. Acta Obstet Gynecol Scand 2000; 79: 321-2.
18. Sawicki V, Spiewankiewicz B, Stelmachow J, Cendrowski K. Color Doppler assessment of blood flow in endometrial cancer. Eur J Gynaecol Oncol 2005; 26: 279-84.
19. Alcazar JL, Ajossa S, Floris S, Bargellini R, Gerada M, Guerino S. Reproducibility of endometrial vascular patterns in endometrial disease as assessed by transvaginal power Doppler sonography in women with postmenopausal bleeding. J Ultrasound Med 2006; 25: 159-63.
20. Timmerman D, Verguts J, Konstantinovic ML. The pedicle artery sign based on sonography with color Doppler imaging can replace second stage tests in women with abnormal vaginal bleeding. Ultrasound Obstet Gynecol 2003; 22: 166-77.
21. Teefey SA, Stahl JA, Middleton WD, Huettner PC, Bernhard LM, Brown JJ, et al. Local staging of endometrial carcinoma: comparison of transvaginal and intraoperative sonography and gross visual inspection. AJR Am J Roentgenol 1996; 166: 547-52.
22. Kinkel K, Yasushi K, Yu KK, Segal MR, Lu Y, Powell CB, et al. Radiologic staging in patients with endometrial cancer: a metaanalysis. Radiology 1999; 212: 711-8.