

## Transvaginal Ultrasonography of the Endometrium in Women with Postmenopausal Bleeding: Is it Always Necessary to Perform an Endometrial Biopsy?

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The objective of this study was under taken to evaluate whether it was possible to abstain from performing an endometrial biopsy when endometrial thickness according to transvaginal ultrasonography was <4mm in women with post menopausal bleeding. Transvaginal ultrasonography and Papanicolaou smear was performed in 271 cases women aged >50 years with post menopausal bleeding and follow up for one year in BIRDEM hospital September 2006 to August 2011. This was a prospective study. One hundred and seven women had an endometrial thickness  $\leq 4$ mm. In this group one endometrial cancer that was missed by ultrasonography. Endometrial malignancy was diagnosed in 0.9% of women with an endometrial thickness  $\leq 4$  mm. Endometrial biopsy was performed because recurrent bleeding. No cancer or Atypical hyperplasia was subsequently diagnosed among the women with an endometrial thickness  $\leq 4$  mm. But endometrial cancer was diagnosed 20.1% of the women with an endometrial thickness  $\geq 5$  mm. If the false negative rate of endometrial biopsy techniques is taken into Transvaginal Ultrasonography and cervical cytologic examination is an adequate form of management for women with post menopausal bleeding or irregular bleeding during hormone replacement therapy as long as endometrial thickness is  $\leq 4$  mm.

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**Key words:** Biopsy, endometrium, histology, post menopausal, hormone replacement therapy, transvaginal ultrasonography.

### Introduction

Post menopausal bleeding is vaginal bleeding occurring after 12 months of amenorrhoea in a woman at the end of reproductive life. Hence it does not apply to a young woman, who has had amenorrhoea from anorexia nervosa or a pregnancy followed by lactation. It is a common problem representing 5% of all gynaecology out

patient attendance.<sup>1</sup> These are to eliminate endometrial cancer as the cause of the bleeding. Risk factor for endometrial cancer are – Exogenous oestrogen are taken, tamoxifen use for breast cancer, polycystic ovarian disease, hereditary nonpolyposis colorectal carcinoma, obesity with diabetes.<sup>2</sup>

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Management depends upon history and examination by gynaecologist within two weeks.<sup>3</sup> Post menopausal bleeding should be treated as malignant, unless proved otherwise. Transvaginal ultrasound scan is an appropriate first line procedure to identify which woman with P.M.B. are at higher risk of endometrial cancer. The mean endometrial thickness in post menopausal women is much thinner than in premenopausal women. Thickening of the endometrium may indicate the presence of pathology. In general thicker the endometrium, the higher the likelihood of important pathology i.e. endometrial cancer being present. A thickness of  $>5$  mm gives 7.3% likelihood of Endometrial cancer.<sup>4</sup> Thickness of  $<4$  mm has a negative predictive value of 98%.<sup>2</sup> A definitive diagnosis in post menopausal bleeding is made by histology.

### Methods

Two hundred and seventy one women aged  $\geq 50$  years with post menopausal bleeding were taken from Gynae Outpatient department in BIRDEM. The women were requested to complete a questionnaire that included a general medical history, menstrual history, history of gynaecologic operation and menopausal data. The use or non use of hormone replacement therapy was recorded. All women underwent a thorough gynaecologic examination and transvaginal ultrasonographic examination for endometrial thickness and adnexal region to exclude any pelvic masses and also Papanicolaou smear. Women who were found to have an endometrial thickness  $\geq 5$  mm, underwent a curettage for endometrial biopsy or total hysterectomy with bilateral salphingoophorectomy. But women who were found to have an endometrial thickness of  $\leq 4$  mm at first visit and were requested to return after 3 months interval upto 12 months for gynaecologic and transvaginal ultrasonographic examination.

The women were thoroughly informed regarding study and the importance at contacting examining doctor if new bleeding should occur. If there was another episode of vaginal bleeding during follow up period an endometrial biopsy was performed.

### Results

Endometrial thickness was  $\geq 5$  mm in 164 of the 271 women (60.51%). With post menopausal bleeding an endometrial biopsy or curettage or total hysterectomy was done. Twenty two women were found to have a primary endometrial cancer (13.4%). Two women had a metastasis in endometrium from primary breast cancer (1.2%). Six Women were found to have atypical endometrial hyperplasia (3.6%).

Three women were found ovarian cancer (stage – I-A) (1.8%), that was diagnosed with transvaginal sonography. In total 33 (20%) of 164 women were found to have some form of cancer. Rest of the women had no gynaecological malignancy.

One hundred and seven women were found to have an endometrial thickness  $\leq 4$  mm were followed up 3 months interval. Three women came with another bleeding episode at the end of 3 months. Transvaginal sonography and endometrial biopsy was done. One woman had endometrial polyp. One had atrophic changes of endometrium (endometrial thickness 3 mm). One had endometrial carcinoma after hysterectomy (endometrial thickness 4-5 mm). So, endometrial carcinoma was 0.9% (1 in 107).

After 6 months, six women came with per vaginal bleeding. Transvaginal ultrasonography and endometrial biopsy was done. Four had atrophic changes of endometrium (endometrium thickness 3 mm, 2 mm, 2 mm, 4 mm). One had endometrial polyp (endometrium 4 mm). One had simple

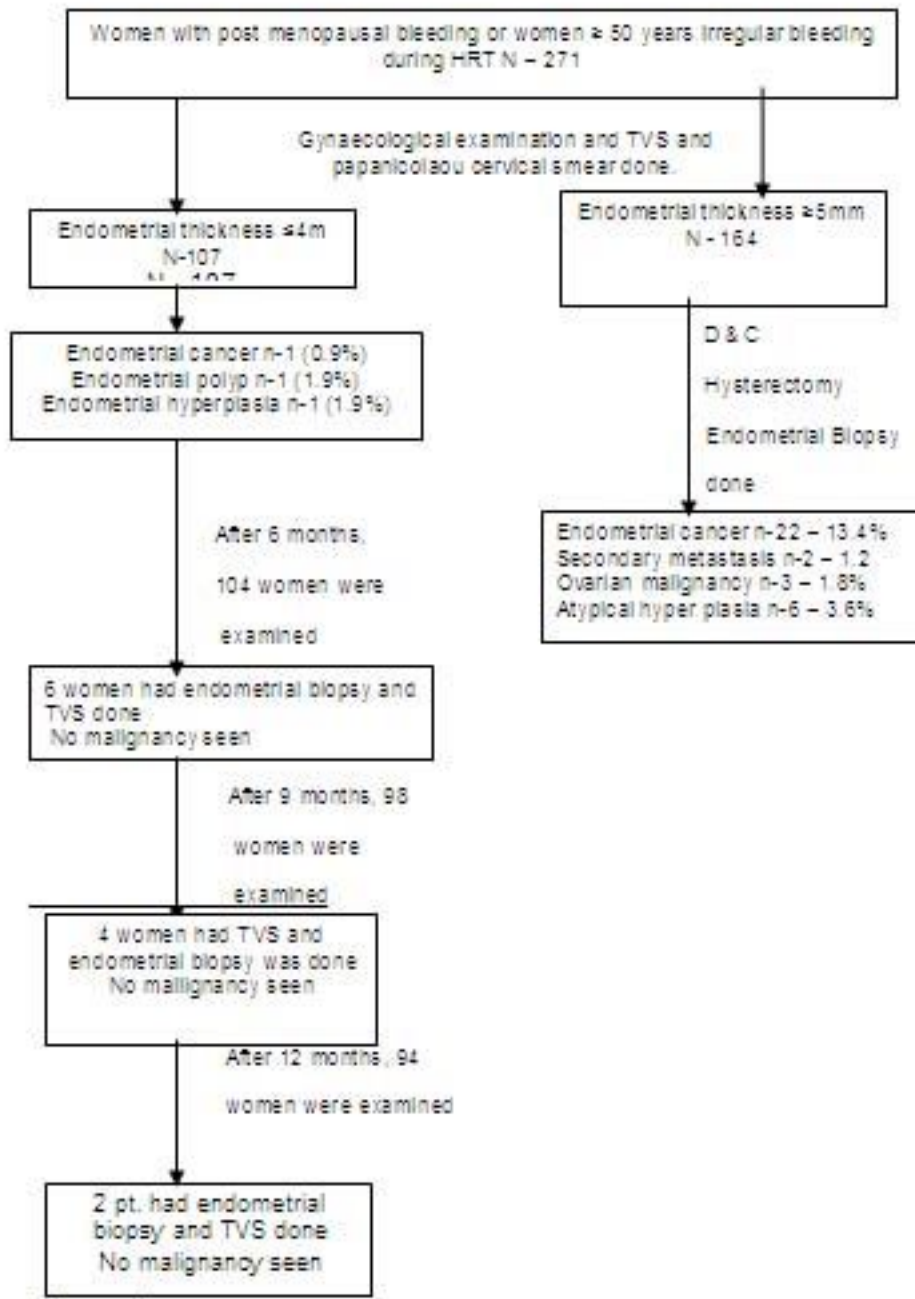


Figure 1. Schematic description of study design and main results. TVS - Transvaginal ultrasonography.

In total, 179(66%) of 271 women underwent biopsy during the study.

hyperplasia without atypia (6 of the 104 women 5.7%).

After 9 months 4 women underwent endometrial biopsy and transvaginal sonography with episode of pervaginal bleeding. One had atrophic changes of endometrium. Two had adenomyosis after hysterectomy. One had simple endometrial hyperplasia (4 of the 98 women 4.0% at 9 month visit).

After 12 months visit 2 women came with episode of pervaginal bleeding. Endometrial biopsy and transvaginal sonography was done. One had atrophic changes and one had simple endometrial hyperplasia (2 women of the 94 is 2.1%).

Two women were not available in this study period. One woman died of cardiac failure and one woman had not been available because she had emigrated were not still available. During the follow up period at 1 year endometrial biopsy was performed 15 (14%) of 107 women for the indication of repeated bleeding.

## Discussion

In this study endometrial cancer was diagnosed in 0.9% of woman who had an endometrial thickness <4 mm, versus 20.1% among women who had an endometrial thickness >5 mm. No endometrial cancer was subsequently diagnosed 104 of 107 women with an endometrial thickness  $\leq$ 4 mm who were followed up for 1 year after the initial transvaginal ultrasonographic examination. This study confirms earlier reports<sup>5-25</sup> that endometrial cancer is uncommon finding among women with a thin endometrium as measured by transvaginal ultrasonography.

Traditionally curettage procedure and in more recent years, other simpler endometrial biopsy techniques have been used in the diagnosis of

post menopausal bleeding or irregular bleeding during hormone replacement therapy. It has been reported that a curettage procedure carries a false negative rate of between 2% and 6% for diagnosis of endometrial cancer and hyperplasia.<sup>26-27</sup> This is perhaps not an unreasonable finding, because curettage is a blind procedure and in approximately 60% of curettage procedures less than half of the uterine cavity is actually curatted.<sup>26</sup>

Hysteroscopy has been shown to be very accurate for diagnosis of endometrial disorder.<sup>29</sup> Technical improvements and videos techniques have made this method more suitable for office use. It is, however, still a rather invasive method that carries a false negative rate of 3% and complication may occur.<sup>29</sup> In this study the false negative rate for transvaginal ultrasonography alone was only 0.9%.

This analysis illustrates two important points. First endometrial cancer will occasionally be missed when a cut off 4mm is used as shown in some studies.<sup>20,21</sup> However the number of missed cancer does not appear to be greater than that reported for curettage or endometrial biopsy techniques. Second this study also illustrates the value of performing a Papanicolaou cervical smear not only for diagnosis of cervical cancer but also for diagnosis of endometrial abnormalities.

Most women with endometrial cancer have post menopausal bleeding as the first symptom and there generally are repeated bleeding episodes. It has been estimated that about 10% of women with post menopausal bleeding are subsequently found to have an endometrial carcinoma<sup>19,20</sup> and a further 20% to 40% have hyperplasia and endometrial Polyp or some other endometrial pathologic condition as the cause of the bleeding.

Thus most women with post menopausal bleeding (50% - 60%) will have bleeding related to a benign condition which will be confirmed as such on examination of the biopsy specimen.<sup>19,20,31</sup> Once cervical lesion has been excluded, the cause of the bleeding is usually considered to be fragility of blood vessels in the thin atrophic mucosa of the endometrium or vaginal skin.<sup>7,32</sup> Previous studies have indicated that endometrial cancer and other endometrial pathologic conditions are extremely uncommon among women in whom the endometrial thickness  $\leq 5$  mm.<sup>5-25</sup> The result of this study support the argument that trans vaginal ultrasonography is at least as effective as endometrial biopsy techniques as a means of excluding serious pathologic conditions among with post menopausal bleeding in whom endometrial thickness is  $\leq 4$  mm.

### Conclusion

This is to our knowledge, the first study to demonstrate the result of expectant management for women with post menopausal bleeding or bleeding during hormone replacement therapy in whom endometrial thickness was found to be  $\leq 4$  mm. The question thus arises as to whether endometrial biopsy is necessary for women with post menopausal bleeding as bleeding during hormone replacement therapy, when endometrial thickness is  $\leq 4$  mm.

### References

- Moodley M, Roberts C; Clinical pathway for the evaluation of postmenopausal bleeding with an emphasis on endometrial cancer detection. *J Obstet Gynaecol.* 2004 Oct;24(7):736-41. [abstract]
- Sahdev A; Imaging the endometrium in postmenopausal bleeding. *BMJ.* 2007 Mar 24; and 334(7594):635-6.
- Referral for suspected cancer, NICE Clinical Guideline (2005)
- Smith-Bindman R, Weiss E, Feldstein V; How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding. *Ultrasound Obstet Gynecol.* 2004 Oct;24(5):558-65. [abstract]
- Fleischer AC, Kalemeries GC, Machin JE, Entmann SS, James AF. Jr. Sonographic depiction of normal and abnormal endometrium with histopathological correlation. *J Ultrasound Med* 1986;5:445-52.
- Goldstein S, Nachtigall M, Snyder J, Nachtigall I. Endometrial assessment by vaginal ultrasonography before endometrial sampling in patients postmenopausal bleeding. *Am J Obstet Gynecol* 1990;163:119-23.
- Malpani A, Singer J, Wolverson M, Merenda G. Endometrial hyperplasia: value of endometrial thickness in ultrasonographic diagnosis and clinical significance. *J Clin Ultrasound* 1990;18:173-7.
- Osmers R, Vollson M, Schaner A. Vaginosonography for early detection of endometrial carcinoma. *Lancet* 1990;335:1569-71.
- Rudelstorfer R, Nanz S, Bernaschek G. Vaginography and its diagnostic value in patients with postmenopausal bleeding. *Arch Gynecol Obstet* 1990;248:37-44.
- Granberg S, Wikland M, Kulsson B, Norstrom A, Friberg I. G. Endometrial thickness as measured by endovaginal ultrasonography for identifying endometrial abnormalities. *Am J Obstet Gynecol* 1991;164:17-32.
- Nasri MN, Shepherd JII, Setchell MF, Lowe DG, Chard T. Sonographic depiction of postmenopausal endometrium with transabdominal and transvaginal scanning. *Ultrasound Obstet Gynecol.* 1991;1:279-83.
- Bourne TH, Grayford T, Hampson J, Collins WP, Campbell S. The detection of

- endometrial cancer by transvaginal ultrasonography colour Doppler. *Ultrasound Obstet Gynecol*. 1992; 2:75.
13. Abu Hmeidan F, Bilek K, Baier D, Nuwayhid M, Kade R. Das sonographische bild des endometrium – karzinoms. *Ultraschall Med* 1992; 13:178-82.
  14. Botsis D, Kassamos D, Pyrgitis E, Zomlas PA. Vaginal sonography of endometrium in postmenopausal women. *Clin Exp Obstet Gynecol*. 1992;19:189-92.
  15. Auslender R, Bornstein J, Dirnfeld M, Kogan O, Atad J, Abramovici H. Vaginal ultrasonography in patients with post menopausal bleeding. *Ultrasound Obstet Gynecol* 1993;30: 126-8.
  16. Dorum A, Kristensen GB, Langebrette A, Sornes T, Skarr O. Evaluation of endometrial thickness measured by endovaginal ultrasound in women with postmenopausal bleeding. *Acta Obstet Gynecol Scand*. 1993;72:116-9.
  17. Bakos O, Smith P, Heimer G. Transvaginal ultrasonography for identifying endometrial pathology in postmenopausal women. *Maturitas* 1994;20:181-9.
  18. Sladcevins P, Valentin I, Marsal K. Endometrial thickness and Doppler velocimetry of the uterine arteries as discriminators of endometrial status in women with postmenopausal bleeding: a comparative study. *Am J Obstet Gynecol* 1994; 171:722-8.
  19. Karlsson B, Granberg S, Wikland M, Ylostalo P, Kisernd T, Marsal K, et al. Transvaginal ultrasonography of the endometrium in women with postmenopausal bleeding—a Nordic multicenter study. *Am J Obstet Gynecol* 1995;172:1488-94.
  20. Ferrazzi E, Torri V, Trio D, Zannoni F, Filiberto S, Dordoni D. Sonographic endometrial thickness a useful test predict atrophy in patient postmeno bleeding: an Italian multicenter study. *Ultrasound Obstet Gynecol*. 1996;7:31521.
  21. Kufahl J, Pedersen I, Sindberg Eriksen P, Helkjaer PE, Larsen LG, Jensen KL, et al. Transvaginal ultrasound, endometrial evology sampled by Gynoscann and histology obtained by Uterine Explora Curette compared to the histology of the uterine specimen: a prospective study in pre and postmenopausal women undergoing elective hysterectomy. *Acta Obstet Gynecol Scand* 1997;76:790-6.
  22. Mateos F, Zarauz R, Seco C, Rayward JR, del Barrio P, Aguirre J, et al. Assessment with transvaginal ultrasonography of endometrial thickness in women with postmenopausal bleeding. *Eur J Gynaecol Oncol* 1997;18:501-7.
  23. Briley M, Lindsell D. The role of transvaginal ultrasound in the investigation of women with postmenopausal bleeding. *Clin Radiol* 1998;53:502-5.
  24. Weber G, Merz F, Bahhmann E, Roseh B. Evaluation of different transvaginal sonographic diagnostic parameters in women with postmenopausal bleeding. *Ultrasound Obstet Gynecol* 1998;12:265-70.
  25. Granberg S, Friberg LG, Norstorm A, Wikland M. Endovaginal ultrasound scanning of women with postmenopausal bleeding. *J Ultrasound Med* 1998;7:283.
  26. Stock RJ, Kanbour A. Prehysterectomy curettage. *Obstet Gynecol* 1975;15:53711.
  27. Mackenzie IZ, Bibby JG. Critical assessment of dilatation and curettage 1029 women. *Lancet* 1978;2:566-8.
  28. Stowall TG, Solomon SK, Ling FW. Enometrial sampling prior hysterectomy. *Obstet Gynecol* 1989;73:105-9.
  29. Gampleson RJ, Rappold HO. A comparative study between panoramic hysteroscopy with directed biopsies and dilatation and curettage. *Am J Obstet Gynecol* 1988;158:189-92.

30. Parsons A, Lens II. Sonography for endometrial abnormalities preliminary results. J Clin Ultrasound 1993;21:87-95.
31. Hoist J, Koskela O, Von Schonltz B. Endometrial findings following curettage in 2018 women according to age and indications. Ann Chin Gynecol 1983;72:271-7.
32. Choo YG, Mak KG, Iisu G, Wong TS, Ma HK. Postmenopausal uterine bleeding of nonorganic cause. Obstet Gynecol 1986;66:225-8.