# Comparing transvaginally defined endometrial thickness with hysteroscopic and histopathologic findings in asyptomatic postmenopausal women

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**Summary**

*Purpose:* To assess the diagnostic value of transvaginal sonography (TVS) measurement of the endometrium compared to hysteroscopic findings and histopathologic reports in order to facilitate clinical management in asymptomatic postmenopausal women with thickened endometrium. *Methods:* During the period between January 2000 and December 2008, a retrospective analysis was performed including cases of women who were preoperatively diagnosed with a sonographically thickened endometrium, while asymptomatic, and therefore underwent hysteroscopic and fractionated dilatation and curettage (D & C) under general anesthesia at the Second Department of Obstetrics and Gynecology at Aretaieion Hospital in Athens, Greece. In the present study we compare US, hysteroscopic and pathologic findings. *Results:* The mean age of the patients ranged between 54-74 years (mean age 65.2 ± 6.8 years). In 108 cases, sonographically measured endometrial thickness ranged between 5 and 10 mm. In 59 cases, endometrial thickness ranged between 11 and 15 mm, whereas in 22 cases, between 16 and 20 mm and finally, in 13 cases endometrial thickness was more than 20 mm. Hysteroscopic examination revealed endometrial polyps in 161 cases, focal hyperplastic lesions in 28 cases, complete hyperplastic lesions in five cases while atrophy was found in five and cancer in three cases, respectively. Pathological results of the samples taken after hysteroscopy are as follows: in 169 cases (83.67%) in women with asymptomatic abnormal endometrial thickness, an endometrial polyp was present. Endometrial thickness in these cases patients was 10.9 ± 7.5 mm. In patients with focal hyperplasia (22 cases), endometrial thickness was 7.2 ± 0.5 mm but in patients with complete hyperplasia (5 cases) endometrial thickness was higher (12.3 ± 5.1 mm). Finally, in three cases with endometrial carcinoma endometrial thickness was 15.5 ± 7.8 mm. Six cases out of 28 described in our study were diagnosed as focal hyperplasia and two out of five cases as complete hyperplasia, whereas histological reports classified these cases as endometrial polyps. The other histological diagnoses confirmed hysteroscopic findings and thus provided the same results. *Conclusions:* We recommend hysteroscopy to follow gynecological TVS when a thickened endometrium is found in asyptomatic postmenopausal women for better diagnostic and, in a later stage, therapeutic efficacy.

*Key words:* Asymptomatic; Postmenopausal; Endometrial thickening; Ultrasound; Hysteroscopy.

## Introduction

Transvaginal sonography (TVS) is a useful method to detect endometrial pathology [1-3]. Different cut-off values for endometrial thickness in symptomatic postmenopausal women have been used in the differential diagnosis of pathologic endometrial lesions and cancer exclusion [4-8]. However, in asymptomatic women, when a thick endometrium is discovered during a routine ultrasound (US) examination, a clinical dilemma is raised as to which therapeutic strategy should be chosen because the diagnostic value of endometrial thickness alone has not been documented till now [9]. Hysteroscopy is commonly used to offer solutions to this dilemma as it is thought to be the "gold standard" for diagnosing endometrial lesions providing close color visualization [10].

The aim of the present study was to assess the diagnostic value of TVS measurement of endometrium compared to hysteroscopic findings and histopathologic reports in order to facilitate clinical management in asymptomatic postmenopausal women with thickened endometrium.

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## Materials and Methods

During the period January 2000 and December 2008, a retrospective analysis was performed including cases which were preoperatively diagnosed with a sonographically thickened endometrium and therefore underwent hysteroscopic and fractionated dilatation and curettage (D&C) under general anesthesia at the Second Department of Obstetrics and Gynecology at Aretaieion Hospital in Athens, Greece.

The study group consisted of 202 postmenopausal asymptomatic women with endometrial thickness of ≥ 5 mm (double layer) on TVS scanning. It should be mentioned that the US scan was performed as a complementary method during their routine gynecological check.

Diagnostic hysteroscopy was performed with a Versapoint bipolar (Johnson and Johnson, USA) or with a Karl Storz resectoscope with the patient being under general anesthesia. Uterine distention was achieved by saline infusion. Following hysteroscopy, a fractional D&C was performed and the specimens were sent for histological examination. All specimens were characterized according to the World Health Organization criteria. Overall, the "gold standard" of diagnosis was the histological report.

Medical records including age, possible hypertension, diabetes mellitus, and body mass index were recorded for all patients of our study. Operation notes and histopathological databases were also thoroughly searched for the same period.

Data was entered into computerized database. The Student's t-test, Fisher's exact test and $X^2$ test were used to statistically compare clinical parameters. ROC curve analysis was performed to display area under the ROC curve, with standard error and 95% confidence interval (CI). When the variable under study could not distinguish between the two groups, i.e., where there is no difference between the two distributions, the area will be equal to 0.5 (the ROC curve will coincide with the diagonal). When there is a perfect separation of the values of the two groups, i.e., there is no overlapping of the distributions, the area under the ROC curve equals 1 (the ROC curve will reach the upper left corner of the plot). The 95% CI is the interval in which the true (population) area under the ROC curve lies with 95% confidence. A probability value of less than 0.05 was considered to be statistically significant. For the statistic analysis, SPSS STATISTIC 17.0 and MedCalc (version 11.4.4.0) were used.

## Results

The mean age of the patients ranged between 54-74 years (mean age 65.2 ± 6.8 years). The main characteristics of the female patients are presented in Table 1. More specifically, 5.4% of the patients were nulliparous and 19.3% multiparous, while 75% of the patients had one or two children. Over 50% of the patients were obese, whereas 55% and 16% of the patients had hypertension and diabetes mellitus, respectively.

Results of endometrial thickness and hysteroscopic diagnoses of the patients are shown in Table 2. More specifically, in 108 cases, sonographically measured endometrial thickness ranged between 5 and 10 mm. In 59 cases, endometrial thickness ranged between 11 and 15 mm, whereas in 22 cases, between 16 and 20 mm and finally, in 13 cases endometrial thickness was more than 20 mm. Hysteroscopic examination revealed endometrial polyps in 161 cases, focal hyperplastic lesions in 28 cases, complete hyperplastic lesions in five cases while atrophy was found in five and cancer in three cases, respectively.

Statistically significant findings were identified after analysis. More specifically, sensitivity, specificity, positive [PPV) and negative predictive value (NPV) were estimated. Sensitivity and specificity for polyps were 95.27% and 100%, respectively while PPV and NPV were 100% and 80.5% respectively ($p < 0.0001$). The respective estimates for focal hyperplasia were 100.0%, 96.67%, 78.6% and 100.0% ($p < 0.0001$), while those for complete hyperplasia were 100%, 100%, 60.0% and 100.0%, respectively ($p < 0.0001$). The respective estimates of sensitivity, specificity, PPV and NPV for atrophy were 60.0%, 100%, 100% and 99.9% ($p < 0.0143$), while those for cancer were 100%, 98.99%, 100% and 100%, respectively ($p < 0.0001$).

A subgroup analysis was performed according to endometrial thickness which ranged between 5-10, 11-15, and 16-20 mm in the different sugroups. Regarding focal hyperplasia, the estimates of sensitivity and specificity for 5-10 mm were 72.3 and 100, respectively and PPV and NPV were 100 and 50, with a $p$-value < 0.0001, while the estimates of sensitivity and specificity for 11-15 mm were 27.27 and 100, respectively and PPV and NPV were 100 and 27.3, with a $p$-value < 0.0001. The estimates of sensitivity and specificity for 16-20 mm were 18.18 and 100, respectively and PPV and NPV were 100 and 25, with a $p$-value < 0.0001, while the estimates of sensitivity and specificity for > 20 mm were 9.09 and 100, respectively and PPV and NPV were 100.0 and 23.1, but there was not statistical significance ($p < 0.1473$). Regarding polyps, the findings were not statistically significant in the performed sub-analysis, however the estimate of sensitivity for 5-10 mm was 51.5 and for PPV and NPV 100 and 0. The estimate of sensitivity for 11-15 mm was 29 and for PPV and NPV 100 and 0. The estimate of sensitivity for 16-20 mm was 8.88 and for PPV and NPV 100 and 0. The estimate of sensitivity for > 20 mm was 5.59 and for PPV and NPV 100 and 0. Regarding cancer, there were no significant differences in our outcomes.

In Table 3, we present the histopathological results of the samples taken after hysteroscopy. Thus, in 169 cases (83.67%) of women with asymptomatic abnormal endometrial thickness, an endometrial polyp was present. Endometrial thickness in these patients was 10.9 ± 7.5 mm. In patients with focal hyperplasia (22 cases), endometrial thickness was 7.2 ± 0.5 mm but in patients

Table 1. — *Patient clinical characteristics*.

| Characteristcs | n | % |
|---|---|---|
| *Parity* | | |
| 0 | 11 | 5.4% |
| 1-2 | 152 | 75.3% |
| 3+ | 39 | 19.3% |
| *Body mass index (BMI)* | | |
| < 25 | 30 | 14.9% |
| 25-29.9 | 62 | 30.7% |
| > 30 | 110 | 54.4% |
| Past hormone therapy | 26 | 12.8% |
| Arterial hypertension (systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg) | 111 | 55% |
| Diabetes mellitus | 32 | 15.84% |
| Past use of oral contraceptives | 10 | 5% |

Table 2. — *Hysteroscopic diagnosis of uterine cavity pathology*.

| Endometrial thickness (mm) | Polyps | Focus hyperplasia | Complete hyperplasia | Atrophia | Cancer |
|---|---|---|---|---|---|
| 5-10 | 87 | 16 | 0 | 4 | 1 |
| 11-15 | 49 | 6 | 2 | 1 | 1 |
| 16-20 | 15 | 4 | 2 | 0 | 1 |
| > 20 | 10 | 2 | 1 | 0 | 0 |
| | 161 | 28 | 5 | 5 | 3 |

Table 3. — *Pathological findings*.

| | |
|---|---|
| Endometrial polyps | 169 |
| Simple hyperplasia | 22 |
| Complex hyperplasia | 3 |
| Endometrial cancer | 3 |
| Atrophy | 5 |

with complete hyperplasia (5 cases) endometrial thickness was higher (12.3 ± 5.1 mm). Finally, in three cases with endometrial carcinoma endometrial thickness was 15.5 ± 7.8 mm. Six cases out of 28 described in our study were diagnosed as focal hyperplasia and two out of five cases as complete hyperplasia whereas the histological report classified these cases as endometrial polyps. The other histological diagnoses confirmed hysteroscopic findings and thus provided the same results.

No major events complicated the hysteroscopic process. Complications included three uterine perforations resulting in ending of the operative procedures, which were repeated in a later period.

## Discussion

To our knowledge, this is one of the first studies used to evaluate TVS, hysteroscopy and histolopathological reports of asymptomatic postmenopausal women with a sonographically thickened endometrium. Other researchers have compared the value of diagnostic hysteroscopy with TVS in different populations [11, 12]. According to Kasraeian *et al*. TVS is a moderately accurate test in asymptomatic postmenopausal women with sensitivity, specificity, PPV and NPV being 62.2%, 93.9%, 68.3% and 92.2%, respectively [13].

As is already known, TVS is a useful modality to detect endometrial lesions [1-3]. Increasing use of sonohysterography improves diagnostic performance of TVS [11]. However, hysteroscopy is highly accurate and so it can be used as a diagnostic tool for diagnosing endometrial lesions by evaluating the specimens of dilatation and curettage [14]. It is known that an endometrial thickness of 4-5 mm in postmenopausal symptomatic women is generally used as a limit for excluding endometrial malignancy, and if found in a range between 5 and 8 mm further investigation of the lesion is required [1-3]. This limit is not applicable to women without postmenopausal bleeding. US measurement of endometrial thickness alone is not a useful test for diagnosing focal intrauterine pathologies in these women [15-18].

In asymptomatic postmenopausal women benign focal lesions such as endometrial polyps, are the most common findings [19, 20].

In our department US scans are generally performed in symptomatic or asymptomatic women as a complementary method during their standard gynecological examination. The next diagnostic step in our clinical protocols depends on US findings and if we find an abnormally thickened endometrium (that is, thickness > 5 mm) we perform D&C and hysteroscopy. In our study, we certified that endometrial polyps were the most common findings among postmenopausal women with thickened endometrium. To be more specific, 169 out of 202 women (83.66%) were found to have an endometrial polyp, which is probably the reason for the endometrial thickness. This result is in accordance with that of Schmidt *et al*. [21], who reported a polyp incidence of 78.5% of their patient group, consisting of women who presented with thickened endometrium in their US examination, and with that of Dreisler *et al*. [22] who reported a 11.8% prevalence of uterine polyps in a large Danish population between 20 and 74 years old, in the postmenopausal women of this population.

An interesting finding of our study is that we discovered eight cases of endometrial polyps [6 were hysteroscopically considered to be focal hyperplastic lesions and 2 complete hyperplastic lesions) that were missed by hysteroscopic examination and the final diagnosis was made after histological examination of the tissue specimens. This reveals that despite the high accuracy rates of hysteroscopy, some cases (4.7%) may be missed. On the other hand, it highlights the fact that endometrial polyps, although not considered as genuine precancerous lesions, have a hyperplastic potential (as shown elsewhere) [22], and thus should be removed.

The sensitivity and specifity rates of hysteroscopy are high, and are 95.26%-100% for the diagnosis of endometrial polyps, respectively, 100%-96.67% for focal hyperplasia, 100%-98.99% for complete hyperplasia, 60%-100% for atrophic lesions and 100%-100% for the diagnosis of endometrial cancer (despite the fact that there was no statistical significance for the cases of endometrial cancer due to the small number of such cases). Those findings are similar to those described by Dreisler *et al*. [22], who reported sensitivity and specifity rates at the levels of 56% and 88%, respectively for a cut-off level of 5 mm for TVS, as was also used in our study.

Another finding of our study is that we discovered five cases of atrophic endometrium, in which the thickness measurement was more than 5 mm (4 cases between 5 and 10 mm, and 1 case between 11 and 20 mm). In all three cases of cancer, endometrial thickness was more than 5 mm, and further investigation was performed including a hysteroscopy and hysteroscopic-guided D&C, due to the high sensitivity and specifity rates for endometrial cancer dignosis [23].

## Conclusion

Encouraged by the results of our study, we recommend hysteroscopy to follow gynecological TVS when a thickened endometrium is found in asyptomatic postmenopausal women for better diagnostic and, in a later stage, therapeutic efficacy.

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