Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: a systematic review and meta-analysis


CRD summary
This individual patient data review concluded that a cut-off level of 3mm rather than 4mm to 5mm using transvaginal ultrasonography has greater diagnostic accuracy for exclusion of endometrial cancer in women with postmenopausal bleeding. The conclusion reflects the evidence but potential quality and availability biases mean there was uncertainty regarding the reliability of the conclusions.

Authors' objectives
To estimate the accuracy of endometrial thickness measurement in the detection of endometrial cancer amongst women with postmenopausal bleeding.

Searching
Studies were identified from three previous reviews augmented with a search of MEDLINE to identify any subsequently published studies (January 2000 to December 2006). Search terms were reported and references were checked for additional studies.

Study selection
Eligible studies reported on endometrial thickness measurement by transvaginal ultrasonography in women with postmenopausal bleeding and subsequent histological assessment of endometrial carcinoma. Studies restricted to asymptomatic, premenopausal or perimenopausal patients were excluded. Authors of eligible studies were contacted and asked to provide individual patient data.

Included studies were published between 1992 and 2007. Most patients had complete histological verification of endometrial carcinoma (patients without cancer - median endothelial thickness 2 to 7mm; patients with cancer - median endothelial thickness 6 to 21mm). The mean age of patients was 62; 58% had diabetes, 60% had hypertension and 92% were using hormone replacement therapy .

Two independent reviewers assessed eligibility.

Assessment of study quality
Validity assessment of publications with QUADAS was not reported. Likewise, comparison of individual patient data and aggregate data or checks on the consistency, integrity and completeness of the individual patient data were not reported.

Data extraction
The distribution of endometrial thickness was calculated per study for patients with and without endometrial carcinoma. Subsequently, different methods were used to estimate diagnostic accuracy of endometrial thickness.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Receiver operating characteristic curves (ROC) were calculated for each study with a summary area under the curve generated by weighting study specific area under the curve by sample size. Individual patient data were pooled and analysed as i) ROC analyses combined with random-effects logistic regression without stratification ii) ROC analysis with endometrial thickness expressed as multiples of the overall median value within each study (a form of centring) iii) ROC analysis based on a random-effects logistic regression with different odds ratios per study iv) random cut-off values between 2 and 8mm were used to facilitate use of the Moses-Littenberg method to construct a ROC for comparison with a previous analysis. Finally 2x2 tables were constructed for each cut-off level and study to calculate sensitivity and specificity which were analysed with a nonlinear random-effects model. Summary estimates of
sensitivity and 1-specificity were presented along with ROC curves from the previous analyses.

**Results of the review**

Thirteen authors provided data on 2,896 patients (sample sizes of studies 40 to 913) of whom 259 had endothelial cancer. Individual patient data was unavailable from a further 66 authors.

All methods of synthesis resulted in similar receiver operating characteristic curves with mean area under the curve varying from 0.82 to 0.84. For the bivariate model with cut-off levels between 1mm to 7mm, sensitivity ranged from 99.8% (95% CI 99.0 to 99.9%) to 83.9% (95% CI 72.7 to 91.0%), and specificity ranged from 5.4% (95% CI 3.1 to 9.1%) to 68.7% (95% CI 62.4 to 74.3%). Sensitivity was higher at 3mm than 4mm and 5mm while specificity was lower. At 3mm sensitivity was 97.9% (95% CI 90.1 to 99.6%) for a specificity of 35.4% (95% CI 29.3 to 41.9%).

Heterogeneity was not quantified although differences in prevalence of cancer across studies were statistically significant (p<0.01) in a random-effects model.

**Authors’ conclusions**

A cut-off level of 3mm rather than 4mm or 5mm using transvaginal ultrasonography has greater diagnostic accuracy for exclusion of endometrial cancer in women with postmenopausal bleeding.

**CRD commentary**

The review addressed a clearly defined question with clear inclusion criteria and employed appropriate methods to identify and screen eligible studies but only one database was searched and it was unclear whether any language restrictions were applied. Individual patient data was obtained from a subset of eligible studies but the use of the QUADAS tool or exploration of data quality individual patient data individual patient data was not reported. A range of analytical techniques were utilised drawing broadly consistent conclusions suggesting that analytical approach was not critical. Analysis of different thresholds was an integral part of the approach to this synthesis but further sources of heterogeneity were not explored despite the use of individual patient data.

The authors’ conclusions were supported by the results, but should be interpreted with caution because reporting, publication and availability biases limit generalisability and the methodological limitations of the included studies were unclear.

**Implications of the review for practice and research**

**Practice:** The author's stated that transvaginal ultrasonography measurement of endometrial thickness in women with postmenopausal bleeding with a cut-off value of 3mm was clinically useful and reliably excludes endometrial carcinoma in women with postmenopausal bleeding.

**Research:** The author's stated that high quality primary accuracy studies synthesised using individual patient data were necessary to guide clinical decision-making.

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