Radiologic staging in patients with endometrial cancer: a meta-analysis

Authors' objectives
To compare the utility of computed tomography (CT), ultrasonography (US), and magnetic resonance imaging (MRI) in staging endometrial cancer.

Searching
MEDLINE was searched from January 1980 to September 1997 for US and CT, and from January 1985 to September 1997 for MRI, for publications in the English language. The keywords used were 'uterine neoplasms' or 'endometrial carcinoma' with 'CT', 'MR imaging' or 'US'. In addition, the reference lists of the retrieved articles were checked. Studies published in English, Japanese, French, Italian and German were included. Unpublished data were excluded.

Study selection
Study designs of evaluations included in the review
There were no explicit inclusion criteria relating to study design, but the included studies had to specify that the observers were blinded to the pathologic results.

Specific interventions included in the review
Studies which investigated the radiologic staging of endometrial cancer were eligible for inclusion. The specific tests used included CT, US (with or without endovaginal probe) and MRI (with or without contrast-enhanced imaging). The frequencies of the endovaginal US transducers ranged from 5.0 to 7.5 MHz, and the magnetic field strengths for MRI ranged from 0.02 to 1.5 T.

Reference standard test against which the new test was compared
Studies comparing CT, US or MRI to surgical staging with histopathologic results were eligible for inclusion.

Participants included in the review
Studies investigating patients with a histologic diagnosis of endometrial carcinoma were eligible for inclusion.

Outcomes assessed in the review
Studies that allowed for the calculation of true-positive, true-negative, false-positive and false-negative results for imaging tests were eligible for inclusion. Review articles, letters, comments, and articles that did not present raw data were excluded.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The methodological quality of the studies was rated on the basis of four criteria: adequate description of the study group; adequate description of the diagnostic criteria; no potential work-up bias; and congruence of the presented data. The studies were classified as 'high quality' if they met all of the methodologic requirements; 'medium quality' if they met 3 of the requirements; 'fair quality' if they met 2 of the requirements; and 'not acceptable' if they met only one of the requirements. The authors do not state the number of reviewers who performed the quality assessment.

Data extraction
Two reviewers extracted the following data: sample size; stage distribution, using International Federation of Gynecology and Obstetrics stage guidelines; imaging modality and technique; design of imaging interpretation; the
diagnostic criteria used for imaging interpretation; and true-positive, true-negative, false-positive, false-negative study results for the staging elements of myometrial invasion, cervical invasion, presence of extraterine disease, and presence of lymph node metastasis. Any disagreements were resolved through consensus and consultation with a third reviewer. The reviewers were not blinded to the authors, journal or year of publication.

Methods of synthesis
How were the studies combined?
Sensitivity and specificity were recalculated for each included study using the conventional corrections for zero counts (see Other Publications of Related Interest no.1). To compare the three imaging modalities, summary receiver operating characteristic (ROC) curves were constructed (see Other Publications of Related Interest nos.2-3), and the authors obtained corresponding Q* values (points on the summary curve where sensitivity and specificity are equal).

How were differences between studies investigated?
Summary ROC curves were constructed in all cases. In addition, the transformed data of all the included studies were combined through a robust regression (Huber M-regression) analysis (see Other Publications of Related Interest no.4) in a regression line.

Covariate adjustment analysis was also undertaken (see Other Publications of Related Interest no.2) using the following covariates: severity of disease, year of publication, results of methodologic quality rating, and subtype of imaging technique.

Results of the review
Forty-seven studies were included. Of these, one study compared CT with US and MRI, 2 studies compared MRI with US, and 2 studies compared MRI with CT. Subsets of data were obtained for the assessment of myometrial invasion in 42 studies (n=1,556), cervical invasion in 14 studies (n=536), extraterine disease in 6 studies, and lymph node metastasis in 1 study. Due to the limited data, the studies investigating extraterine disease and lymph node metastasis were excluded from the analysis.

Overall performance.

The summary ROC analysis revealed no statistically-significant differences in the performance of CT, US and MRI. The Q* values were 0.80 (95% confidence interval, CI: 0.62, 0.98) for CT, 0.86 (95% CI: 0.81, 0.91) for US, and 0.87 (95% CI: 0.85, 0.89) for MRI. The covariate analysis showed that the imaging results were not influenced by the year of publication, stage distribution, or methodologic quality rating.

Myometrial invasion.

Six CT studies (n=203), 16 US studies (n=611) and 20 MRI studies (n=742) were included. The Q* values were 0.79 (95% CI: 0.61, 0.96) for CT, 0.85 (95% CI: 0.81, 0.88) for US, 0.86 (95% CI: 0.83, 0.89) for MRI, 0.83 (95% CI: 0.79, 0.87) for non-enhanced MRI, and 0.91 (95% CI: 0.89, 0.92) for contrast-enhanced MRI. For the comparison of CT, US and MRI, the summary ROC curves showed no significant differences in performance. The comparison between MRI techniques showed significantly better results for contrast-enhanced versus non-enhanced MRI (p<0.001). Differences in the Q* values did reach statistical significance when contrast-enhanced imaging was compared with US (p=0.002). There was also a trend towards a higher diagnostic accuracy for contrast-enhanced MRI than for CT (p=0.18).

Cervical involvement.

The Q* values could only be calculated for MRI (0.92, 95% CI: 0.87, 0.95).

Authors’ conclusions
Although US, CT or MRI can be used in the pre-treatment evaluation of endometrial cancer, contrast-enhanced MRI offers ‘one-stop’ examination with the highest efficacy.
CRD commentary

Overall, the methodological quality of this review was fair. The authors posed a suitable review question and the inclusion and exclusion criteria were well described. The literature search could have been more comprehensive, and by restricting the search to one database, the likelihood that important studies were missed was increased. The quality assessment was carried out appropriately but the number of reviewers who carried out the assessment was not reported. The process used to select the studies was also not described. The data extraction process was described, but the data were not well presented. Only data from the trials assessing myometrial invasion were tabulated and a number of details, including the patients' characteristics, were missing. The methods used for the statistical analysis were appropriate.

The authors' conclusions appear over-optimistic in light of the data presented and should be viewed with caution given the methodological flaws outlined.

Implications of the review for practice and research

Practice: The authors state a number of implications for practice.

1. No imaging is required for patients with grade 1 tumours and a non-enlarged uterus at physical examination, because the pre-test probability of myometrial, cervical or nodal involvement is low. If results from the physical examination are inconclusive or if there is concomitant pelvic disease, US, CT or MRI can be used at the initial radiologic investigation.

2. Patients with high-grade papillary or clear cell tumours should undergo CT or MRI because there is a high pre-test probability of nodal involvement.

3. Patients with possible cervical involvement at physical examination, or with positive or inconclusive results from endocervical curettage, should undergo MRI since this is the only modality that has been shown to accurately depict cervical invasion.

4. For in-patients who require multifactorial assessment, contrast-enhanced MRI is the only modality that can be used to accurately evaluate myometrial, cervical and nodal involvement.

Research: The authors did not state any implications for further research.

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