Radiological evaluation of lymph node metastases in patients with cervical cancer: a meta-analysis

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Authors' objectives
To compare the utility of lymphangiography, computed tomography (CT) and magnetic resonance imaging (MRI) for the diagnosis of lymph node metastasis in patients with cervical cancer.

Searching
MEDLINE was searched using the keywords 'cervical cancer' and 'lymph node metastasis' with 'lymphadenopathy', 'lymphangiography', 'computed tomography', or 'magnetic resonance imaging'. The database was searched over different dates for the different modalities: from January 1970 to June 1996 for LAG, from January 1980 to June 1996 for CT, and from January 1985 to June 1996 for MRI. The reference lists of all the retrieved articles were checked manually and experts were consulted. Review articles, letters, comments and articles not presenting raw data were excluded.

Study selection
Study designs of evaluations included in the review
All study designs with a minimum sample size of 20 patients were eligible for inclusion.

Specific interventions included in the review
No inclusion criteria were specified with respect to the intervention. The index tests studied were lymphangiography (LAG), CT and MRI. An intravenous contrast medium was used for CT.

Reference standard test against which the new test was compared
Studies were eligible for inclusion if they used histologic or cytologic specimens obtained by surgery or lymph node biopsy as the reference standard.

Participants included in the review
Patients with a diagnosis of cervical cancer, who were having an evaluation of lymph node metastasis, were eligible for inclusion. The patients included were those with early-stage cancer, defined as International Federation of Gynaecology and Obstetrics (FIGO) stages I to IIa, and those with late-stage cancer (FIGO IIb or higher).

Outcomes assessed in the review
Studies were eligible for inclusion if there were sufficient data to allow the calculation of true positive, false positive, false negative and true positive results. The sensitivity, specificity, and positive and negative likelihood ratios were calculated for each included study.

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 authors do not state that they assessed validity.

Data extraction
Two authors extracted the true positive, true negative, false positive and false negative study results for the presence of lymph node metastasis. The sensitivity and specificity, and positive and negative likelihood ratios were calculated for each study. The abstractors were not blinded to the journal, year of publication, or the authors. Any disagreements were
resolved by consultation with a third reviewer.

**Methods of synthesis**

How were the studies combined?

The studies were combined using meta-analytic methods to produce summary receiver operating characteristic (SROC) curves. Single number summaries (Q* values), which correspond to the point on the SROC curve at which the sensitivity and specificity are equal, were calculated. Testing for differences between LAG, CT and MRI was based on Q* values and their associated standard errors. The positive and negative likelihood ratios calculated from the Q* values were used to characterise the utility of the tests, and to estimate the post-test probability of disease by means of a Bayesian analysis. The method used to assess the pre-test likelihood of lymph node metastases in cervical cancer was provided.

How were differences between studies investigated?

The threshold effect was investigated using Pearson correlation coefficients.

**Results of the review**

There were 17 studies (1,408 patients) on LAG, 17 studies (1,042 patients) on CT and 10 studies (837 patients) on MRI.

Patients with early-stage cervical carcinoma (clinical FIGO stages I to IIa) were assessed using LAG in 12 studies (911 patients), CT in 7 studies (431 patients), and MRI in 7 studies (714 patients). Patients with late-stage cervical carcinoma (clinical FIGO stages IIb or higher) were assessed using LAG in 5 studies (398 patients) and CT in one study (253 patients).

Patients with pelvic adenopathy were assessed using LAG in 6 studies (563 patients), CT in 11 studies (508 patients) and MRI in 9 studies (791 patients). Patients with para-aortic adenopathy were assessed using LAG in 5 studies (422 patients) and CT in 7 studies (487 patients).

Overall: the Pearson correlation coefficient between sensitivity and specificity was -0.08 for LAG, -0.43 for CT and -0.05 for MRI. SROC analysis demonstrated no significant differences in the performance among modalities. The Q* value was 0.74 (95% confidence interval, CI: 0.67, 0.81) for LAG, 0.80 (95% CI: 0.74, 0.86) for CT and 0.85 (95% CI: 0.77, 0.93) for MRI.

Clinical FIGO stages I to IIa: the SROC curves were of a similar shape. The Q* value was 0.75 (95% CI: 0.64, 0.85) for LAG, 0.78 (95% CI: 0.55, 1.00) for CT and 0.80 (95% CI: 0.63, 0.97) for MRI. There were no statistically-significant differences between the imaging techniques.

Clinical FIGO stages IIb or higher: Q* could be calculated only for LAG (0.79, 95% CI: 0.72, 0.85).

Pelvic adenopathy: the Q* value was 0.75 (95% CI: 0.69, 0.82) for LAG, 0.78 (95% CI: 0.73, 0.83) for CT and 0.87 (95% CI: 0.81, 0.93) for MRI. There were no statistically-significant differences between the imaging techniques.

Para-aortic adenopathy: the Q* value was 0.72 (95% CI: 0.66, 0.78) for LAG and 0.81 (95% CI: 0.69, 0.93) for CT. There were no statistically-significant differences between the imaging techniques.

Clinical utility: the literature review showed over 27% prior probability of lymph node metastasis in cervical cancer. The positive post-test probability was 0.68 (95% CI: 0.55, 0.83) for MRI, 0.60 (95% CI: 0.51, 0.69) for CT and 0.51 (95% CI: 0.43, 0.61) for LAG. There were no statistically-significant differences between the imaging techniques.

**Authors' conclusions**

LAG, CT and MRI perform similarly in the detection of lymph node metastasis from cervical cancer. CT and MRI should be considered the preferred adjuncts to clinical evaluation of invasive cervical cancer, as they are less invasive than LAG and also assess local tumour extent.
CRD commentary
Generally, this was a reasonably well-conducted and clearly presented review. The inclusion criteria were clearly defined and incorporated a uniform reference standard. The reasons why some studies were excluded were given, and the methods used to extract the data were rigorous and clearly described. The results of the individual included studies were clearly reported. The search strategy was very limited, and was further constrained by its restriction to English language studies. It therefore seems unlikely that all relevant studies were retrieved. In addition, no attempt was made to identify unpublished studies, and publication bias was not formally assessed. The significance of publication bias cannot, therefore, be assessed. The methods used to combine the results of the included studies were appropriate and clearly reported. An assessment of threshold effect was included, and this was appropriately used to guide the choice of the meta-analytic technique.

The review included an assessment of the imaging results for different stages of the disease, while the discussion mentions factors limiting the diagnostic accuracy of the imaging techniques. Unfortunately, only the results from LAG were available for nodal disease (FIGO greater than IIb), and there were no MRI scanning results for aortic node metastasis, thus limiting the evidence offered for these stages of disease. A comparison of the incidence of side-effects may have provided useful information to aid decision-making.

The authors’ conclusions of the equivalence of LAG, MRI and CT for all stages of nodal disease and pelvic node metastasis are supported by the evidence given.

Implications of the review for practice and research
Practice: The authors state that CT or MRI, rather than LAG, should be considered as the preferred adjunct to the clinical evaluation for treatment planning in cervical cancer.

Research: The authors state that a prospective, cross-sectional study comparing LAG, CT and MRI in the same patient population would be methodologically ideal. However, such a study would be difficult to carry out because of prevailing patterns of care, ethical considerations and cost.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.