Computer tomography, magnetic resonance imaging, and positron emission tomography or positron emission tomography/computer tomography for detection of metastatic lymph nodes in patients with ovarian cancer: a meta-analysis

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CRD summary
This review concluded that positron emission tomography with or without computed tomography was more accurate than computed tomography alone or magnetic resonance imaging in the detection of lymph node metastasis in patients with ovarian cancer. Given the limitations of the review and the included studies, the results and conclusions should be treated with caution.

Authors' objectives
To compare the diagnostic performance of computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) with or without CT, for detecting metastatic lymph nodes in patients with ovarian cancer.

Searching
MEDLINE and EMBASE were searched for articles published in English between 1990 and July 2010. Search terms were reported, including diagnostic filters. Reference lists of the selected studies were searched.

Study selection
Studies with at least 10 patients with ovarian cancer, assessed using CT, PET with or without CT, or MRI to identify metastatic lymph nodes were eligible for inclusion. Studies had to use histopathology or clinical follow-up for at least six months to confirm diagnosis, and to provide sufficient data to construct 2x2 tables of test performance. Both CT and MRI had to use a contrast agent, and studies of PET had to use $^{18}$F-fluoro-2-deoxyglucose (FDG) as the tracer.

The proportion of patients with a primary diagnosis to those who had received prior treatment seemed equal, over the included studies. Where reported, the mean age ranged from 50.8 to 67 years; the percentage with serous cancer ranged from 35.4 to 93.8; the percentage with International Federation of Gynaecology and Obstetrics (FIGO) criteria stage III or IV disease ranged from 37.5 to 100; and the prevalence of metastases ranged from 6.5% to 100%. Where MRI was used, the magnet strength was 1.5 tesla. Most CT studies did not use multi-detectors and most PET studies were not contrast enhanced.

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
The authors did not report any systematic assessment of study quality, but prospective or retrospective data collection, patient recruitment method, and blinding status were assessed.

Data extraction
Data were extracted to produce 2x2 tables of test performance. Where a cell contained zero, 0.5 was added to all four cells. Sensitivity, specificity, and the diagnostic odds ratio were calculated. The authors did not report how many reviewers extracted the data.

Methods of synthesis
Pooled estimates of sensitivity, specificity and the diagnostic odds ratio were calculated with 95% confidence intervals; the method was not reported. Data for PET alone and PET with CT were combined. Heterogeneity was assessed using Cochran Q and $I^2$; a probability of less than 0.05 or $I^2$ greater than 50% indicated heterogeneity.

Summary receiver operating characteristic curves were produced, from which the area under the curve was calculated; the model used was not reported. The authors stated that meta-regression and subgroup analyses were used to investigate heterogeneity, but the potential sources were not predefined. Publication bias was investigated using funnel...
Results of the review
Eighteen studies met the inclusion criteria, with 882 patients (range 13 to 132). Nine studies reported collecting data prospectively, seven recruited participants consecutively, and 14 reported blinding to allocation for interpreters of the tests.

For CT, the pooled sensitivity was 42.6% (95% CI 36 to 50; I²=68%), specificity was 95% (95% CI 93 to 96; I²=84.2%), and the diagnostic odds ratio was 19.87 (95% CI 6.18 to 63.91; I²=69.3%). For MRI, the pooled sensitivity was 54.7% (95% CI 44 to 65; I²=45%), specificity was 88.3% (95% CI 85 to 91; I²=77.6%), and the diagnostic odds ratio was 12.38 (95% CI 3.94 to 38.9; I²=64.8%). For PET, with or without CT, the pooled sensitivity was 73.2% (95% CI 68 to 78; I²=86.2%), specificity was 96.7% (95% CI 96 to 98; I²=72.4%), and the diagnostic odds ratio was 90.32 (95% CI 36.42 to 224.01; I²=70.2%).

Meta-regression was used to investigate sample size, year of publication, mean age, percentage of serous cancer, percentage of advanced ovarian cancer, and prevalence of metastatic lymph node; no statistically significant relationships were identified. Subgroup analyses were used to investigate the type of patient population, reference standard used, type of CT scanner, and the addition of enhanced or non-enhanced CT to PET; none were statistically significant. Funnel plots suggested the presence of publication bias.

Authors' conclusions
FDG PET with or without CT was more accurate than CT alone or MRI in the detection of lymph node metastasis in patients with ovarian cancer.

CRD commentary
The review addressed a clear research question, with reproducible inclusion criteria. The authors searched relevant sources, but restricted selection to studies that were published in English. Diagnostic filter terms were used and studies could have been missed. It was not reported whether two reviewers independently conducted the review to reduce error and bias. Relevant criteria for study quality were reported, but it was not fully assessed, and it remains unclear whether studies were prone to important bias. From the limited quality assessment, it appears that several studies were at a high risk of bias.

The models used to produce the summary estimates were not reported. It appears that summary diagnostic estimates were produced using standard frequentist meta-analysis, and the Moses-Littenberg model was used to produce the summary receiver operating characteristic curves. Given the clinical variation between studies, one of the more robust summary receiver operating characteristic models that maintain the within-study relationship between sensitivity and specificity would have been more appropriate. Despite some studies evaluating more than one of the index tests, these direct comparisons were not used to assess the within-study comparative accuracy. Relevant potential sources of heterogeneity were investigated.

Given the limitations of the review and the included studies, the conclusions on the relative accuracy of the three diagnostic methods seem too firm, and the results and conclusions of the review should be treated with caution.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that further research was required to determine whether small studies affected the results of their analysis.

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