Detection of lymph node metastases by gadolinium-enhanced magnetic resonance imaging: systematic review and meta-analysis

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CRD summary
This well-conducted review concluded that the overall accuracy of gadolinium enhanced magnetic resonance imaging for detection of nodal metastases was moderate. Incorporating contrast enhancement in the malignancy criteria substantially improved the accuracy of this test. These conclusions are likely to be reliable.

Authors’ objectives
To determine the accuracy of gadolinium enhanced magnetic resonance imaging (MRI) for staging lymph node metastases.

Searching
MEDLINE, EMBASE, CANCERLIT and The Cochrane Library were searched from 1988 to January 2008. Search terms were reported. Reference lists of retrieved papers were screened. The review was restricted to studies in English and German.

Study selection
Studies of at least 10 patients with histologically proven primary carcinoma that evaluated gadolinium enhanced MRI (index test) compared to histopathology of lymph nodes obtained by surgery, autopsy or biopsy (reference standard) were eligible for inclusion if they reported sufficient data to construct a 2x2 table of test performance. Studies of health volunteers only or patients with non-lymphatic metastases were excluded.

Included studies evaluated patients with colon/rectal, cervical, breast, lung, head and neck, oesophageal, pancreatic, renal cell, urinary bladder, gall bladder, endometrial, ovarian and gastric cancers. Mean age at diagnosis was 58 years.

One reviewer screened the results of the searches and two reviewers independently assessed full-text studies for inclusion. Disagreements were resolved through referral to a third reviewer.

Assessment of study quality
Two reviewers independently assessed study quality using the QUADAS criteria.

Data extraction
Two reviewers independently extracted data as 2x2 tables of test performance and used these to calculate sensitivity and specificity, together with 95% confidence intervals (CI). If data were not available at the patient level, these were requested from the author. When data were reported as 3x3 or 4x4 tables these were reconstructed to form 2x2 tables by considering N1 and higher stages as metastasis-positive lymph nodes and N0 as metastasis negative. If studies reported data for multiple malignancy criteria, data with the highest sensitivity were extracted. Sensitivity analysis based on the data with the lowest sensitivity were performed.

Methods of synthesis
Summary estimates of sensitivity and specificity together with their 95% CIs were calculated using the bivariate random-effects model. A summary receiver operating characteristic (SROC) curve was constructed. Heterogeneity was assessed using the Q and I² statistics. Sensitivity analysis was carried out by pooling data separately for different criteria used to define malignancy on MRI: single criterion, multiple criteria without incorporating contrast agent and multiple criteria including contrast highlighting. Heterogeneity was investigated by including covariates in the bivariate model: lymph node region; prevalence of lymphatic metastases; language; complete versus incomplete verification; and blinding of reviewers to index test/reference standard results. Due to the small number of studies included, covariates were included individually in the model and these analyses were considered exploratory.
Results of the review
Forty-three studies met inclusion criteria, but only the 32 (n=1,402) studies that reported data at the patient level were included in the meta-analysis. All studies fulfilled QUADAS criteria for completeness of verification, reporting of uninterpretable results and explanation of withdrawals. More than 80% of studies included an appropriate patient spectrum. Differential verification bias was present in 35% of studies. Blinding of index test and reference standard, availability of clinical information, time period between index test and reference standard, avoidance of differential verification bias and uninterpretable test results were poorly reported.

Based on all 32 studies, summary sensitivity was 72% (95% CI 66% to 79%) and summary specificity was 87% (95% CI 82% to 91%). There was substantial heterogeneity for both sensitivity ($I^2=62\%$) and specificity ($I^2=84\%$). Summary estimates of sensitivity and specificity were similar for studies that used a single malignancy criterion and studies that used multiple malignancy criteria without contrast enhancement. Summary sensitivity was increased (84%, 95% CI 70% to 92%) and specificity decreased (82%, 95% CI 72% to 89%) in the nine studies that used multiple criteria including contrast highlighting.

Regression analysis showed that sensitivity was lower when para-aortic and pelvic lymph node evaluation were combined compared to studies that evaluated the pelvic lymph nodes alone. Increased prevalence of disease resulted in increased sensitivity, but decreased specificity. Sensitivity was higher when no differential or partial verification bias was present. German studies had higher estimates of both sensitivity and specificity than English studies.

Authors' conclusions
The overall accuracy of gadolinium enhanced magnetic resonance imaging for detection of nodal metastases was moderate. Incorporating contrast enhancement in the malignancy criteria substantially improved the accuracy of this test.

CRD commentary
The review addressed a clear question supported by defined inclusion criteria. The literature search was adequate for published studies, but no specific attempts were made to locate unpublished data and the review was restricted to studies in English and German. The possibility of a small-study effect was considered in the review, but the authors acknowledged that these methods had limitations when applied to diagnostic data. Appropriate steps were taken to minimise bias and errors during the review process. Study quality was formally assessed using appropriate criteria and the results were clearly presented and incorporated into the synthesis. Methods used to pool data were appropriate and included assessment and investigation of heterogeneity. This was generally a well-conducted review and the authors' conclusions are likely to be reliable.

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