Diagnostic precision of nanoparticle-enhanced MRI for lymph-node metastases: a meta-analysis

CRD summary
The review assessed the diagnostic precision of ferumoxtran-10-enhanced magnetic resonance imaging (MRI). The authors concluded that the technique is sensitive and specific in the detection of lymph-node metastases for various tumours, and is superior to unenhanced MRI. The conclusions appear reliable.

Authors’ objectives
To assess the diagnostic precision of ferumoxtran-10 magnetic resonance imaging (MRI) compared with unenhanced MRI for the diagnosis of lymph-node metastases.

Searching
EMBASE, the Cochrane Library, PubMed and other databases (via Ovid) were searched to May 2005; the keywords were provided. In addition, articles were identified using the ‘related-articles function’ in PubMed and the references of identified articles were screened. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
The review did not specify any inclusion criteria for study design. All of the included studies were prospective studies. Some studies provided diagnostic accuracy data for contrast-enhanced and unenhanced MRI, while the majority of included studies provided only data for contrast-enhanced MRI.

Specific interventions included in the review
Studies using MRI with or without ferumoxtran-10 for the detection of lymph-node metastases were eligible for inclusion. Where reported, the compared detected lymph nodes in the included studies ranged from 18 to 1,029, the contrast dose ranged from 1.7 to 2.6 mg Fe/kg, the type of MRI magnet ranged from 0.2 to 1.5 tesla, and the post-contrast MRI timing ranged from 10 to 48 hours.

Reference standard test against which the new test was compared
The studies had to compare the MRI results with the histological diagnosis to be eligible for inclusion.

Participants included in the review
Studies of participants undergoing investigations for lymph-node metastases were eligible for inclusion. The inclusion criteria for patients in the included studies varied: patients in some studies had to have a confirmed primary cancer, have no previous chemotherapy or radiotherapy, or have at least one lymph node visible on pre-contrast MRI to be eligible in the primary study. All of the studies were of adults.

Outcomes assessed in the review
To be eligible for inclusion, the studies had to report sufficient information for the calculation of the sensitivity and specificity. The review presented these measures in addition to 95% confidence intervals (CIs), summary receiver operating characteristic curves, area under the curve (AUC) and standard error of measurement (SE), and diagnostic odds ratio (DOR) with corresponding CI.

How were decisions on the relevance of primary studies made?
The authors did not state how all the papers were selected for the review, or how many reviewers performed the selection. However, for publications with possible overlap, three reviewers discussed the studies and selected the best-quality study.
Assessment of study quality

The primary studies were assessed using the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) guidelines and the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool.

The authors did not state how many reviewers performed the validity assessment.

Data extraction

Two authors extracted the data independently and any discrepancies were resolved by consensus. The diagnostic accuracy data were taken from the primary publication or computed from the reported data. The diagnostic accuracy calculations were performed either on a per-patient or per-node basis.

Methods of synthesis

How were the studies combined?

Pooled sensitivity and specificity measures were obtained by applying a random-effects model, and were presented together with the 95% CI. Summary receiver operating characteristic curves were presented for the unenhanced and the ferumoxtran-10 enhanced MRI. The AUC and corresponding SE were presented, and the presence of contrast enhancement was included as a covariate in a univariate meta-regression. The relative DOR and corresponding 95% CI were calculated for the comparison of unenhanced and enhanced MRI.

How were differences between studies investigated?

Detailed study characteristics and results were presented for each individual study. The Q statistic was used to calculate statistical heterogeneity. The influence on the DOR of study quality, whether more than 100 nodes were assessed, body region, use of 1.5 tesla MRI scanners, dose, and a combination of scanner and dose was also assessed.

Results of the review

Nineteen studies (n=631) were included in the review.

The study quality ranged from STARD values of 15 to 22 (maximum score 25) and QUADAS values of 7 to 13 (maximum score 14).

Seventeen identified studies with ferumoxtran-10-enhanced MRI showed a pooled sensitivity of 0.88 (95% CI: 0.85, 0.91) and a specificity of 0.96 (95% CI: 0.95, 0.97) for detecting lymph-node metastases. The pooled DOR was 123.05 (95% CI: 5.93, 256.93) and the weighted AUC was 0.96 (SE=0.01). All analyses showed statistically significant heterogeneity.

The pooled sensitivity for the six studies providing data on unenhanced MRI was 0.63 (95% CI: 0.57, 0.69) and the specificity was 0.93 (95% CI: 0.91, 0.94). The weighted AUC value was 0.84 (SE=0.11) and the DOR was 26.75 (95% CI: 8.48, 84.42). Statistically significant heterogeneity was detected.

The meta-regression analysis showed a significant effect of ferumoxtran-10 on the diagnostic precision of MRI.

Authors’ conclusions

Ferumoxtran-10-enhanced MRI is sensitive and specific in detecting lymph-node metastases for various tumours. It offers higher diagnostic precision than unenhanced MRI and allows functional and anatomical definition when used as an imaging modality.

CRD commentary

This was a fairly well-conducted and very well-documented review. It addressed a clear question and used overall clear inclusion criteria. The search for published studies was of an adequate standard, but no attempts were made to locate unpublished studies; this can introduce publication bias in the review. Many details of the included studies were given.
and these allowed a clear overview of the existing primary studies. The quality of the included studies was assessed in detail and used in sensitivity analyses.

The statistical analyses were thorough. The pooled estimates were based on studies that differed in many aspects and showed statistically significant heterogeneity. Although sources of differences were followed up not all were detected, making it unclear whether a pooled result is clinically meaningful. Many more studies were found that investigated enhanced MRI rather than unenhanced MRI. Only very few studies compared both methods in the same patient sample. Overall, the conclusions appear reliable.

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

**Practice:** The authors did not state any specific implications for practice other than their statement of the superiority of enhanced MRI.

**Research:** The authors made recommendations for future research. They stated that further studies should assess the following: the use of ferumoxtran-10-enhanced MRI for axillary lymph-node metastases in breast cancer and for non-operable tumours; the diagnostic accuracy of positron emission tomography and computed tomography and ferumoxtran-10-enhanced MRI in a direct comparison; the usefulness of the technique in children, in the monitoring of tumour recurrence or in the downstaging of tumours after neoadjuvant treatment, and in patients with granulomatous disease; and generally, the safety, tolerance, cost-effectiveness and application of ferumoxtran-10-enhanced MRI in clinical practice.

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