Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment

Niekel MC, Bipat S, Stoker J

CRD summary
This review concluded that magnetic resonance was the preferred first-line imaging modality for evaluating liver metastases in previously untreated patients with colorectal cancer; 18F-fluorodeoxyglucose positron emission tomography could be used as the second-line modality. Limitations in the available data and analyses mean that these conclusions should be interpreted cautiously.

Authors' objectives
To assess the diagnostic accuracy of computed tomography (CT), magnetic resonance imaging (MRI), 18F-fluorodeoxyglucose positron emission tomography (18FDG-PET) and 18FDG-PET/CT for the detection of liver metastases in patients with previously untreated colorectal cancer.

Searching
MEDLINE, EMBASE, CINAHL, Web of Science and the Cochrane Database of Systematic Reviews were searched from January 1990 to January 2010. Search strategies were reported in an appendix.

Study selection
Prospective studies that assessed the accuracy of CT, MRI, 18FDG-PET, or 18FDG-PET/CT for identifying liver metastases in patients with histologically proven primary colorectal cancer were eligible for inclusion. Included studies had to have at least 10 participants, use intra-operative findings, histological examination, or follow-up as the reference standard, and report sufficient data to calculate sensitivity and specificity. Studies were excluded if they reported combined data for different imaging modalities or if the data for the individual modalities could not be extracted separately.

Studies evaluated both patients with suspected and known metastases. The mean age of study participants was 61.4 years (range 20 to 93 years); just over half were male. Histological examination was the most frequent reference standard, used in all but two studies; studies also used intra-operative palpitation, intra-operative ultrasound and follow-up. Full technical details of imaging modalities used were reported in a supplementary online appendix (see URL for Additional Data). CT studies used single-section or multi-section helical scanning. All but one of the MRI studies used contrast-enhanced techniques. All 18FDG-PET studies used whole-body scanners.

Two reviewers independently selected studies for the review. Any disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality, using a modified, ten-item version of QUADAS (Quality Assessment of Diagnostic Accuracy Studies); any disagreements were resolved by consensus. Items assessed were: use of an appropriate patient spectrum; selection of participants; execution of the index test and reference standard; evaluation of the index test and reference standard; availability of clinical information; differential and partial verification biases; and independence of the reference standard.

Data extraction
Two reviewers extracted data to populate 2x2 contingency tables (numbers of true positive, false negative, false positive, and true negative imaging test results), on a per-lesion and per-patient basis. Any disagreements were resolved by consensus. Data were used to calculate per-lesion sensitivity and per-patient sensitivity and specificity.

Methods of synthesis
Studies were grouped by imaging modality. Summary estimates of per-patient sensitivity and specificity and per-lesion
sensitivity, with 95% confidence intervals (CIs), were calculated for each modality. Between-study heterogeneity was quantified using $I^2$. Where $I^2$ was below 25%, a fixed-effect model was used to generate summary estimates; where $I^2$ was 25% or over, a random-effects model was used. The z-test was used to assess differences between imaging modalities.

The following subgroup analyses were conducted for per-lesion data: comparisons between CT and MRI for the detection of lesions under 10mm versus 10mm or more (head-to-head comparisons only); studies performed before and after January 2004; studies using single-section CT versus studies using multi-section CT; CT performed in the portal phase alone versus CT performed in both arterial and portal phases; comparisons between un-enhanced MRI versus MRI using different contrast agents.

Publication bias was assessed using funnel plots and the Egger regression test, for per-lesion data.

**Results of the review**

Thirty-nine studies (n=3,391 patients) were included in the review. Study quality was variable; the most frequently failed QUADAS criteria were avoidance of differential verification bias, and adequate execution and evaluation of the reference standard. The availability of clinical data was poorly reported.

**Computed tomography (CT):** The per-lesion estimate of diagnostic sensitivity (38 data sets) for liver metastases was 74.4% (95% CI 68.7 to 79.3; $I^2$=70.9%). The per-patient estimate (nine data sets) of sensitivity was 83.6% (95% CI 66.9 to 92.8; $I^2$=92.9%) and specificity was 94.9% (95% CI 92.9 to 96.3; $I^2$=52.5%).

**Magnetic resonance imaging (MRI):** The per-lesion estimate of sensitivity (61 data sets) was 80.3% (95% CI 74.6 to 85.0; $I^2$=83.4%). The per-patient estimate (six data sets) of sensitivity was 88.2% (95% CI 64.8 to 96.8; $I^2$=43.3%) and specificity was 92.5% (95% CI 89.5 to 94.6; $I^2$=61.8%).

**$^{18}$Fluorodeoxyglucose positron emission tomography (**$^{18}$FDG-PET):** The per-lesion estimate of sensitivity (eight data sets) was 81.4% (95% CI 66.5 to 90.6; $I^2$=86.4%). The per-patient estimate (six data sets) of sensitivity was 94.1% (95% CI 91.6 to 95.9; $I^2$=0%) and specificity was 95.7% (95% CI 92.7 to 97.6; $I^2$=0%).

**$^{18}$FDG-PET/CT:** The per-lesion estimate of sensitivity (one data set) was 66.2% (95% CI 54.5 to 76.2). The per-patient estimate (three data sets) of sensitivity was 96.5% (95% CI 94.2 to 97.9) and specificity was 97.2% (95% CI 92.8 to 99.0).

**Comparisons between imaging modalities:** The per-patient sensitivity of CT was lower than that of $^{18}$FDG-PET; all other estimates were comparable.

**Subgroup analyses:** For lesions smaller than 10mm, the sensitivity of MRI was higher than that of CT. The sensitivity of MRI increased significantly after January 2004. No other subgroup analyses showed significant differences between groups.

There was no evidence of publication bias.

**Authors' conclusions**

MRI was the preferred first-line imaging modality for evaluating liver metastases in previously untreated patients with colorectal cancer. $^{18}$FDG-PET could be used as the second-line modality. The role of $^{18}$FDG-PET/CT was unclear due to the small number of studies.

**CRD commentary**

The review reported a clear research question. Inclusion criteria were defined for participants, index test, reference standard, outcomes and study design. A number of sources were searched for relevant studies; search strategies were reported in full. Measures to minimise error and/or bias were applied throughout the review process.

The methodological quality of included studies was assessed and findings reported. The calculation of pooled estimates
of sensitivity and specificity was questionable, given the apparent between-study heterogeneity. The authors' conclusions broadly reflected the data presented. However, the overall performance of MRI and $^{18}$FDG-PET appeared equivalent and no assessment was made of the performance of $^{18}$FDG-PET for the detection of smaller lesions (the basis for the authors' differentiation between the two modalities).

The limited data on $^{18}$FDG-PET and weaknesses in the analysis mean that the authors' conclusions should be interpreted cautiously.

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

*Practice*: The authors did not specify any recommendations for practice.

*Research*: The authors provided detailed recommendations for the reporting of study design characteristics and presentation of data in future studies, in an on-line appendix.

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