18F-fluoro-deoxyglucose positron emission tomography in assessment of myeloma-related bone disease: a systematic review

van Lammeren-Venema D, Regelink JC, Riphagen II, Zweegman S, Hoekstra OS, Zijlstra JM

CRD summary
This review concluded that $^{18}$F-fluoro-deoxyglucose positron emission tomography (FDG-PET) had a superior sensitivity for myeloma bone lesions compared with whole body X-ray, and that response monitoring with FDG-PET computed tomography during treatment was promising. Given the limitations of the review and the included studies, the conclusions seem overly strong.

Authors' objectives
To evaluate whole body X-ray and $^{18}$F-fluoro-deoxyglucose positron emission tomography (FDG-PET) for staging and response assessment of multiple myeloma.

Searching
PubMed and EMBASE were searched, without language restrictions, up to December 2010; articles published in languages other than English were subsequently excluded. The database searches were supplemented by cross-referencing; no further details were reported. Unpublished studies and conference abstracts were excluded.

Study selection
Studies of patients diagnosed with multiple myeloma or plasmacytoma according to Salmon-Durie criteria that used FDG-PET or PET computed tomography (PET-CT) in addition to standard diagnostic tools were eligible for inclusion. The index tests were compared with whole body X-ray or (if performed) T1- or T2-weighted magnetic resonance imaging (MRI) of the spine and pelvis with and without fat suppression and short inversion recovery. Biopsies were performed when plasmacytoma was diagnosed. Case reports were excluded.

The age of participants ranged from 23 to 85 years across the studies. Most of the included studies recruited only patients with multiple myeloma; the others studies also included patients with plasmacytoma. The definition of a positive PET scan varied across studies.

Two independent reviewers selected studies for the review; disagreements were resolved by discussion.

Assessment of study quality
Two independent reviewers assessed study quality using the 14-point QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool. Each item was scored as positive or negative; if the information on a specific item was lacking, it was scored as negative.

Data extraction
The number of lesions located by each technology was extracted. The concordance of FDG-PET changes with clinical outcome for response monitoring, and the detection of non-secreting and extramedullary multiple myeloma, were also extracted.

The authors did not report the number of reviewers performing the data extraction.

Methods of synthesis
Studies were combined in a narrative synthesis. The level of concordance between the tests being conducted was reported. Differences between studies were discussed in the text. Study details and results were tabulated.

Results of the review
Eighteen studies (798 patients; range 6 to 303) were included in the review. Seven of the studies were retrospective and 11 were prospective. The mean QUADAS score (percentage of the maximum score achievable) was 61% (range 29% to 86%). All studies had a representative patient cohort and a valid reference test that was independent of the index test.
Of the 18 studies, 11 described the inclusion criteria. Seven studies described the execution of the reference test. Seven studies did not give a clear definition of a positive PET scan. Seven studies provided insufficient information on image reconstruction methods. Nine studies reported blinding interpreters of the index test.

**FDG-PET versus whole body X-ray** (seven studies; 242 patients): In six studies, FDG-PET (with or without CT) showed more lytic lesions than conventional whole body X-ray with the exception of lytic lesions located in the skull.

**FDG-PET versus MRI** (five studies): Four studies reported that MRI was superior to FDG-PET. The fifth study reported that there was no difference between the tests. FDG-PET was inferior to MRI in detecting myeloma bone disease, especially in the case of diffuse bone infiltration.

The results of studies that compared FDG-PET or PET-CT individually with whole body X-ray or their use for response monitoring during and after treatment were discussed individually.

**Authors’ conclusions**

In general, FDG-PET had a superior sensitivity for myeloma bone lesions compared with whole body X-ray. Response monitoring with the use of FDG-PET-CT during treatment was promising and allowed more precise prediction of prognosis compared with the standard response monitoring.

**CRD commentary**

The authors addressed a clear review question and applied reproducible inclusion criteria. Relevant sources were searched, but inclusion was restricted to papers published in full and in English, so bias may be present. Specific search terms were not reported, but it appeared that diagnostic filters were used which could have resulted in missed studies. Study selection and the quality assessment were conducted in duplicate; it was unclear whether similar methods to reduce error and bias were employed during the data extraction process.

Study quality was assessed using appropriate criteria; the results were presented in full. Results were not presented in a standard diagnostic format and the synthesis was minimal. The included studies were generally small, heterogeneous and prone to bias of some kind.

Given the limitations of the review and the included studies, the conclusions seem overly strong.

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

**Practice:** The authors stated that in view of the expanding treatment options for multiple myeloma, the promising results for response monitoring with PET-CT during treatment may provide important information for treatment decisions. The authors also stated that because of the disperse variability in methodology of acquisition, image reconstruction, and data analysis, standardised uptake values values were difficult to generalise, but implementation of guidelines such as the Netherlands Society of Nuclear Medicine or European guidelines for standardisation of the acquisition and interpretation would overcome these difficulties in the future.

**Research:** The authors stated that future studies would have to validate the additive value of myeloma-related bone disease detected on FDG-PET in predicting outcome. The authors also stated that guidelines were essential for the use of PET-CT in staging and response monitoring of multiple myeloma in multi-centre trials and meta-analyses.

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