Positron emission tomography (FDG) for soft tissue sarcoma (STS)
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Authors' objectives
To assess the performance of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) in the
diagnosis, grading and management of soft tissue sarcoma (STS).

Searching
MEDLINE and EMBASE were searched for English language articles; the search terms were reported. The reference
lists from retrieved articles were checked for additional studies.

Study selection
Study designs of evaluations included in the review
There were no stated inclusion criteria for the study design. However, single case reports were excluded and the
included studies were required to evaluate at least three patients, at least one of whom had STS. The study design was
unclear for half of the included studies; the remaining studies were a mixture of prospective and retrospective designs.
Only 3 studies stated that consecutive patients were used.

Specific interventions included in the review
Studies of FDG-PET were eligible for inclusion in the review. PET was evaluated in the included studies using four
diagnostic criteria: qualitative visualisation; standard uptake value with cut-offs of 2.0 and 3.0; and metabolic rate of
glucose with a cut-off value of 6.0 micromol/100 g per minute. Studies were also included if PET was compared with
magnetic resonance imaging (MRI) or computed tomography (CT). Compared against the reference standard. The reference standards used by studies included in the review were mainly biopsy, in addition to operative histological diagnosis, other imaging, clinical (surgical excision) or other (unspecified) methods.

Reference standard test against which the new test was compared
There were no specific inclusion criteria for the reference standard. The reference standards used by studies included in the review were mainly biopsy, in addition to operative histological diagnosis, other imaging, clinical (surgical excision) or other (unspecified) methods.

Participants included in the review
There were no specific inclusion criteria for the participants. The included studies comprised men and women with
primary or recurrent soft tissue lesions, as demonstrated by a variety of tumour types and diagnostic pathways upon
entry. The mean or median age of the patients was between 11 and 54 years (range: 1 to 89).

Outcomes assessed in the review
There were no stated inclusion criteria for the outcomes. Studies that enabled the calculation of sensitivity and
specificity as markers of FDG-PET test performance for diagnosis and grading were included in the review. Studies
that reported changes in patient management, improved patient outcomes, or tumour response to therapy were also
included.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The data collection for this review included a validity assessment in terms of whether the evaluators were blinded and
whether there was potential for verification (work-up) bias. The authors did not state how the papers were assessed for
validity, or how many reviewers performed the validity assessment.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

In order to calculate the sensitivity and specificity (diagnostic performance), data were collected on the number of true positives, false positives, true negatives and false negatives for FDG-PET (plus CT or MRI where applicable) in diagnosing malignant or benign lesions using the four diagnostic criteria. In addition, the type of lesion and tumour grade were also recorded. In studies of patient management, information was extracted on the diagnostic accuracy and impact of FDG-PET.

Methods of synthesis
How were the studies combined?
The results of the studies were summarised narratively according to predefined research questions, as follows.

What is the diagnostic test performance of FDG-PET for distinguishing benign lesions from malignant STS, and in distinguishing low-grade from high-grade STS?

How does the test performance of FDG-PET compare with conventional anatomic imaging (CT, MRI, etc.) among patients with STS in terms of primary diagnosis, and in diagnosing locoregional recurrence and distant metastasis.

How were differences between studies investigated?
Differences between the studies were investigated and described narratively, according to the predefined research questions.

Results of the review
Twenty studies were included in the review. There were 4 prospective studies (and a possible 5th) with 205 evaluated participants; 4 retrospective studies (and a possible 5th) with 135 evaluated participants; and 10 studies of unclear design with 373 evaluated participants.

The results of the review were presented according to the predefined research questions.

What is the diagnostic test performance of FDG-PET for distinguishing benign lesions from malignant STS, and in distinguishing low-grade from high-grade STS?

The results from 18 studies revealed marked variations in terms of the prevalence of malignant disease in the study population (13 to 88%). There were other notable variations within all included studies, such as those relating to country of origin, diagnostic pathways and procedures for carrying out the tests. When a positive FDG-PET result was defined by visualisation, the sensitivity ranged from 91% (specificity 88%) to 100% (specificity 26% and 86%) in diagnosing primary lesions and from 50% (specificity 93%) to 100% (specificity 66%) in studies of recurrent lesions. The specificity varied between 26% (sensitivity 100%) and 88% (sensitivity 91%) for primary lesions but was higher, 92% (sensitivity 88%) to 94% (sensitivity 74%), for recurrences. All grade II/III tumours were visualised, along with most low-grade tumours. Variable proportions of benign tumours and almost all inflammatory lesions were visualised. When the test result was based on standard uptake values, the sensitivity and specificity differed according to the cut-off value used. At a cut-off value of greater than or equal to 2.0, the sensitivity for evaluating primary lesions ranged from 64% (specificity 71%) to 100% (specificity 73% and 100%). The largest study of recurrences showed a sensitivity of 58% (specificity 92%). All high/intermediate (but only half of low-grade) tumours were identified at this cut-off point. False-positive results and misclassifications were noted for benign inflammatory and non-inflammatory lesions. The results were not markedly improved (in terms of grading or lesion type) when the cut-off value was raised to 3.0. When a positive FDG-PET result was defined by glucose metabolic rate (4 studies), the sensitivity ranged from 73% (specificity 75%) to 100% (specificity 0%). The only study of recurrences showed a sensitivity of 58% (specificity 100%). This suggested only a modest diagnostic test performance. Further data revealed only limited discriminatory ability in terms of low-grade malignant and benign lesions.

How does the test performance of FDG-PET compare with conventional anatomic imaging (CT, MRI, etc.) among
patients with STS in terms of primary diagnosis, and in diagnosing locoregional recurrence and distant metastasis.

There were no data to answer this question in terms of primary diagnosis, owing to most studies being carried out on selected patients following indicative CT or MRI results. This limitation also applied to the results that follow. The results from 2 studies suggested similar diagnostic performance of MRI and FDG-PET in terms of locoregional recurrence, but this conclusion was based on small studies with some design flaws. The results from one of 3 studies looking at the diagnosis of distant metastases suggested equal diagnostic performance for FDG-PET (sensitivity 87%; specificity 100%) to CT scan (sensitivity 100%; specificity 96%) in the diagnosis of lung metastasis, but this study (along with all others) was hindered by methodological limitations.

A lack of control group data meant that changes in patient management or improved outcomes could not be adequately assessed in the 4 studies that addressed this topic. Despite one promising result regarding tumour response to hyperthermic isolated limb perfusion, the available data to address this topic were largely insufficient and inconclusive.

Authors' conclusions
FDG-PET had good discriminating ability in the evaluation of primary and recurrent soft tissue lesions. Although potentially helpful in terms of tumour grading, the test was poor in terms of discriminating low-grade tumors and benign lesions. A lack of data meant that it was not possible to comment on the impact of the test on clinical outcomes, in assessing response to therapy, or on its comparative effectiveness against CT or MRI.

CRD commentary
The review objective was clearly defined in terms of the intervention under investigation, but failure to specify inclusion criteria for the reference standard, participants, outcomes and study design meant that there was substantial variation in the retrieved studies. The fact that the design of half of the included studies was reported as unclear potentially limits the reliability of the findings. The validity assessment (although limited) addressed verification bias, which was appropriate in this diagnostic review. However, the results of validity assessment were not reported and were not apparently used in the interpretation of the data. The literature search was based largely on two electronic databases (with no search dates given) and was restricted to English language articles, thus relevant studies might have been missed. The lack of reporting on how the papers were selected, validity assessed and data extracted presents a substantial threat to the internal strength of the review.

A narrative synthesis of the studies was appropriate, but substantial variation in the results means that the generalisability of the findings is likely to be limited. The authors' main conclusion that FDG-PET has good discriminating ability in the evaluation of primary and recurrent soft tissue lesions appears to be dependent upon the diagnostic criteria applied. Other conclusions are reliably based upon the strength of the evidence presented.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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