The use of 18F-FDG PET in the diagnosis of cardiac sarcoidosis: a systematic review and metaanalysis including the Ontario experience

CRD summary
This review concluded that 18F-fluro-2-deoxyglucose positron emission tomography had high accuracy for the diagnosis of cardiac sarcoidosis. There were limitations in the search strategy, review methods and analysis. The conclusion appears optimistic given the wide range of sensitivity and specificity estimates reported and the small number of participants upon which these were based.

Authors' objectives
To evaluate the accuracy of 18F-fluro-2-deoxyglucose positron emission tomography (18F-FDG-PET) in diagnosing cardiac sarcoidosis.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched. The search strategy was published in an online appendix. Only studies in English were included.

Study selection
Studies were eligible for inclusion if they assessed the accuracy of 18F-FDG-PET for the diagnosis of cardiac sarcoidosis and used Ministry of Health Labour and Welfare of Japan guidelines as the reference standard to confirm diagnosis.

The modified Ministry of Health Labour and Welfare criteria required histological or clinical diagnosis of extra-cardiac sarcoidosis with a diagnosis of complete right bundle branch block, left axis deviation, atrio-ventricular block, ventricular tachycardia, premature ventricular contractions or Q or ST-T abnormalities on echocardiograph plus one of the diagnoses: abnormal regional wall motion, wall thinning or dilation of the left ventricle; a perfusion defect; elevated intra-cardiac pressures, low cardiac output or abnormal wall motion or depressed left ventricular ejection fraction on contrast-enhanced left ventriculography.

Most of the included studies included patients already diagnosed with cardiac sarcoidosis or with a strong clinical suspicion of cardiac sarcoidosis; the overall prevalence of cardiac sarcoidosis was 50%. Included studies used various qualitative and/or quantitative 18F-FDG-PET diagnostic criteria (details reported in an online appendix).

Two reviewers independently assessed studies for inclusion.

Assessment of study quality
The methodological quality of included studies was assessed using the 14-item QUADAS tool.

Two independent reviewers performed the quality assessment.

Data extraction
Data were extracted to calculate sensitivity, specificity and positive and negative likelihood ratios and diagnostic odds ratios, with 95% confidence intervals (CIs) of 18F-FDG-PET for the diagnosis of cardiac sarcoidosis for each included study.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled estimates of sensitivity, specificity, positive and negative likelihood ratios and diagnostic odds ratio, with 95% CIs were calculated using a DerSimonian and Laird random-effects model weighted by sample size. A summary receiver operating characteristic (SROC) curve was constructed (Moses and Littenberg model).
Between-study heterogeneity was assessed using the Cochran Q test and $I^2$ statistic.

**Results of the review**

Seven studies (164 participants) were included in the review. Three studies did not include a representative spectrum of patients (diagnostic case-control studies), two studies interpreted index test results with access to the results of the reference standard and all studies were rated as unclear on whether or not the reference standard used was likely to correctly classify the target condition (all studies used diagnostic guidelines which cannot provide a definitive pathologic diagnosis).

The ranges of reported sensitivities and specificities of $^{18}$F-FDG-PET for the diagnosis of cardiac sarcoidosis were 79% to 100% (sensitivity) and 38% to 100% (specificity). The pooled estimate of sensitivity was 89% (95% CI 79% to 96%) and the pooled estimate of specificity was 78% (95% CI 68% to 86%). $I^2$ values indicated low between-study heterogeneity for sensitivity and moderate to high heterogeneity for specificity.

Pooled estimates of likelihood ratios and a pooled diagnostic odds ratio were reported.

**Authors’ conclusions**

$^{18}$F-FDG-PET had high accuracy for the diagnosis of cardiac sarcoidosis when evaluated against Ministry of Health Labour and Welfare criteria.

**CRD commentary**

The article reported a clear research objective. Broad inclusion criteria were specified for the index test, reference standard and target condition. The search strategy was limited to three bibliographic databases and only studies in English were included, which raised the possibility of language bias and potential omission of relevant studies. Study selection and quality assessment included measures to minimise error and bias; it was not clear whether similar measures were applied to data extraction. The methodological quality of included studies was assessed and the results of this assessment were reported in full in an online appendix. The generation of pooled estimates of sensitivity and specificity was of questionable value given the reported variation in diagnostic thresholds across studies; a bivariate or hierarchical SROC model is generally recommended for this type of data.

The authors’ conclusions appear optimistic given the variation in $^{18}$F-FDG-PET diagnostic criteria, the wide range of sensitivity and specificity estimates reported and the small number of participants upon which these were based.

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

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

**Research:** The authors stated that large multicentre studies were required to further evaluate the role of $^{18}$F-FDG-PET in the diagnosis of cardiac sarcoidosis. The authors stated that cost-effectiveness studies should be considered.

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