18F-fluorodeoxiglucose positron emission tomography for the evaluation of neoadjuvant therapy response in esophageal cancer: systematic review of the literature

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CRD summary
The review assessed 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for evaluating neoadjuvant therapy response in oesophageal cancer and concluded that FDG-PET appeared the best available imaging modality. The review had a number of methodological weaknesses. Overall, the conclusions were not supported; data on FDG-PET were sparse and heterogeneous, and comparison with other imaging modalities was not the stated objective.

Authors’ objectives
To assess the utility of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) in evaluating neoadjuvant therapy response in oesophageal cancer.

Searching
MEDLINE, EMBASE, The Cochrane Library, DARE, NHS EED, HTA database, NRR, ClinicalTrials.gov and topic-relevant articles and websites were searched from January 1999 to August 2006. Search terms were reported and the detailed search strategy provided on-line. Bibliographies of selected articles were screened for additional studies. No language restrictions were applied. Studies published only as conference abstracts were excluded.

Study selection
Prospective studies that compared FDG-PET or PET/computed tomography (CT) with the reference standard of pathological confirmation, other imaging techniques or clinical follow-up over one year in patients with confirmed oesophageal cancer suitable for neoadjuvant therapy were eligible for inclusion. Studies with less than 10 participants were excluded. Mean age of study participants ranged from 54 to 68 years. Most participants were male. Participants with all stages of oesophageal cancer (I to IVB) were included; most patients had stage II or III oesophageal cancer. Previous therapies varied (reported in paper); most studies used chemotherapy plus radiotherapy as neoadjuvant treatments. Most included studies were of whole body imaging using FDG-PET; FDG doses range from 250MBq to 740MBq. Acquisition times ranged from five minutes to 20 minutes. Diagnostic cut-off values used for PET standardised uptake value (SUV) varied across studies.

The authors stated neither how studies were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Methodological quality of included studies was independently assessed by two reviewers who used the 14-item QUADAS tool. Studies were assigned an overall quality score (maximum 14). Disagreements were resolved by consensus.

Both reviewers were nuclear medicine specialists. They also evaluated the technical specifications and quality of PET procedures.

Data extraction
Data were extracted on the sensitivity, specificity, accuracy and positive and negative predictive values, with 95% confidence intervals (CIs), of FDG-PET for primary tumour response assessment and for restaging oesophageal cancer after neoadjuvant therapy. Data comparing SUV in responders and non responders were also extracted.

Data were extracted by one reviewer.

Methods of synthesis
Studies were summarised using a narrative synthesis and structured tables.

**Results of the review**

Seven studies with a total of 248 participants were included in the review. All studies performed at least two FDG-PET scans (before and after neoadjuvant treatment) per patient. Time from end of therapy to final FDG-PET scan ranged from 2.7 weeks to four weeks. Methodological quality scores ranged from 8 to 11 points; the main areas of weakness were in participant selection criteria, blinded interpretation of test results and handling of indeterminate test results.

Sensitivity of FDG-PET for primary tumour response assessment ranged from 27.3% to 97.3% and specificity ranged from 41.7% to 95.2%.

Sensitivity of FDG-PET for N restaging after neoadjuvant therapy ranged from 16.0% to 67.5% and specificity ranged from 85.7% to 100%.

Differences in SUV measures between responders and non-responders were mostly non-significant; only one study reported a significant difference in post-treatment SUV.

Results were reported for two primary studies and a systematic review that compared FDG-PET and cross-sectional imaging for evaluation of the primary tumour, lymph nodes and distant metastases.

**Authors' conclusions**

The authors concluded that FDG-PET appeared to be the best available imaging modality for assessment of neoadjuvant therapy response in oesophageal cancer.

**CRD commentary**

The stated objective of the review was to assess the utility of FDG-PET in evaluating neoadjuvant therapy response in oesophageal cancer. Appropriate inclusion criteria were defined and a wide range of sources were searched without language restrictions for relevant studies. The exclusion of studies not published in full left open the possibility of publication bias (not assessed) and may have resulted in the loss of some relevant data. The methodological quality of included studies was assessed using a validated tool and measures were taken to avoid error/bias in this process. It was unclear how studies were selected for the review and data extraction was undertaken by one reviewer alone, which left these processes open to error/bias. The decision to present a narrative synthesis was appropriate given the apparent heterogeneity of the included studies, but the synthesis presented could have been clearer. The reference standards used by each included study were not reported. Data for direct comparisons between FDG-PET and other imaging modalities not specified in the objective and inclusion criteria were included in the results; as the authors did not set out to make a comparison between FDG-PET and other imaging modalities, it seemed unlikely that they included all available comparative data. Overall, data presented were insufficient to support the authors' conclusion that FDG-PET appeared to be the best available imaging modality for the assessment of neoadjuvant therapy response in oesophageal cancer; data on the performance of FDG-PET were sparse and heterogeneous and comparison with other imaging modalities was not the stated objective of the review.

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

**Practice**: The authors made no recommendations for practice.

**Research**: The authors stated that more larger prospective studies were needed to confirm the power of this imaging tool in the evaluation of treatment response and determine the best analytical method and threshold to differentiate between responders and non-responders.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.