FDG PET in oesophagogastric cancer

Introduction

Oesophagogastric cancer is one of the top ten cancers diagnosed worldwide and, despite advancements in therapy, has a relatively poor prognosis compared to other common cancers, with a five-year survival of only 15-20%. This group of cancers includes tumours of the oesophagus and gastro-oesophageal junction, which have similar disease characteristics.

The role of PETCT in oesophagogastric malignancy has become of increasing importance over the last decade. The main role of this technique currently is in the staging of the tumour to plan the most appropriate therapy for each patient, alongside other techniques. However, pathways for investigation of oesophagogastric cancer will vary according to local services, and the timings and order of investigations are not universally transferrable to other regions.

Gastric cancer is a separate entity to oesophagogastric cancer and there is no role for routine use of FDG PET in its management. This will not be considered any further in this article.

Technique

As in other oncology PETCT, the isotope used is fluorine-18-fluorodeoxyglucose (F-18-FDG), which is a glucose analogue. Patients are prepared by fasting for four to six hours prior to the study. Imaging usually commences between 45 and 90 minutes, according to local protocols, after injection of a weight adjusted dose of FDG. The patient empties their bladder prior to the scan. A non-contrast CT from the skull base to upper thighs is acquired followed by the PET image acquisition. Bed position times are guided by injected activity, but are typically between three and five minutes.

Intravenous contrast can be used on the CT component of the PETCT. This can enhance the diagnostic accuracy, mainly with improved detection of nodal and hepatic metastases. However, as patients will have generally already had a contrast enhanced CT, this does not add anything further to the diagnostic pathway. Additionally, there is conflicting data suggesting that the use of intravenous contrast has no additive value in PETCT in some cancers. A further problem in the use of contrast enhanced CT is with attenuation correction, where the use of contrast CT can lead to apparent increased FDG activity on the PET images, although this does not appear clinically significant. Care with interpretation is, however, needed.

Indications

Staging and restaging of patients suitable for radical treatment is the main use for FDG PET, including those who have received neo-adjuvant treatment. It also may be indicated in suspected recurrence when other imaging is equivocal or negative.

Staging

Following diagnosis by endoscopy and staging with contrast enhanced CT, patients who are suitable for radical treatment have an FDG PET scan. The staging of oesophagogastric tumours relies on the TNM classification, which allows standardised assessment of the extent of tumours.

T stage – FDG PET has a limited role in the T staging which is more accurately assessed with other imaging modalities, particularly endoscopic ultrasound (EUS). Early stage tumours are often not visualised, with only 43% of T1 tumours being FDG avid, compared to 95-100% of large tumours. The degree of FDG avidity of the primary tumour can be assessed by the standardised uptake value (SUV), most commonly using the maximum value (max SUV) although the mean can be used. Interestingly, the degree of uptake does not correlate well with the T stage. The max SUV can be used as a prognostic indicator, with increasing value conferring a worse prognosis, but the results are variable.

N stage – FDG uptake in local nodes, adjacent to the tumour, is often hampered by uptake in the primary tumour itself. PET has poor accuracy in detecting involvement of these nodes, which are better assessed with EUS. Likewise regional nodes are better assessed with EUS, but this is not always possible. Where EUS is unable to assess nodes, regional and distant, FDG PET has additive value. Its strength however is in the detection of distant nodes and increased specificity compared to CT. In the overall detection of nodal disease it shows better sensitivity than conventional CT, although this is quite variable (sensitivity 24-82%, specificity 50-95%).

M stage – detection of metastatic disease is the main strength of FDG PET, where it can detect unexpected metastatic disease in up to 28% of patients. This is particularly important as it has major impact on management, as solid organ metastases (liver, lung and bone) have a worse prognosis when compared with lymph node metastases.

Due to the lack of specificity of FDG, synchronous malignant tumours are detected in 5.5% of studies, most commonly in the colon. These are important and may impact on the patient’s management.

Prognostic information

There are several proposed prognostic factors based on FDG PET, such as maxSUV, total lesion glycolysis (meanSUV x tumour volume), metabolic tumour volume and total lymph node count. However, these show inconsistent correlations between studies and are not currently useful in the clinical setting.

Treatment response

The initial treatment for oesophagogastric cancer is neo-adjuvant chemotherapy and radiotherapy. The response of the tumour to this treatment can be assessed on FDG PET...
and the changes between the pre-treatment and post-treatment studies have been shown to correlate well with pathological outcomes.21,22 There is also good correlation with outcomes, with complete responders showing increased, although not sustained, survival times.23-24 Although EUS has similar accuracy in some studies, it is not always feasible.25

One of the main roles for the post-treatment PET scan, especially when surgery is being planned, is the progression of disease which negates surgery. In up to 17% of patients, metastatic disease develops which makes surgery futile.26-28

**Recurrent disease**

Recurrent disease of cancer treatment is unfortunately common and in the majority of cases conventional CT will detect the recurrence. The role of PETCT is somewhat unclear as data is limited, but there is certainly a role when recurrence is suspected but not clearly defined on other imaging. FDG PET has been shown to have good accuracy in identifying recurrent disease, although it is better in detecting distant recurrence compared to local recurrence.29,30 This is because local changes secondary to previous treatments, such as surgery and radiotherapy, distort appearances.

**Radiotherapy planning**

FDG PET has been shown to improve tumour volume delineation, correlating well with pathological extent of tumours. Consequently it can alter the planned tumour volumes in radiotherapy planning, both increasing and reducing them.31 However, the effect of this on recurrence-free survival and overall survival is unknown.

**Novel technologies**

There is limited published work on PET tracers other than FDG. So far, there has been no tracers shown to be better than FDG, with fluorine-18-fluorothymidine (FLT)32 and carbon-11-choline33 showing lower accuracies when compared with FDG PET. A different type of acquisition technique called dual time point imaging, where two PET acquisitions usually at one and four hours after injection of FDG, is well known in PET imaging. This exploits the continued accumulation of isotope by malignant cells compared to washout in benign cells. In oesophageal cancer, a small study has shown limited value in this technique, with some improvement in detection of the primary tumour and metastases, but no improvement in nodal metastases.34

PETMRI is a developing technology, with early data showing promise in oesophageal cancer, with improved T and N staging compared to PETCT, but further work is needed.35

**Overall impact and conclusion**

FDG PET has significant impact on the management of oesophagogastric cancer, improving staging accuracy and detecting synchronous tumours, with consequent change in management in up to 40% of patients.36-38 Its value in early stage disease appears less dramatic and some advocate that it should not be routinely used in this group.39 It may also provide useful prognostic stratification, although the direct clinical value of this remains uncertain.

Surprisingly, despite the improvements FDG PET has made in the management, it has not had any significant impact on recurrence rates and overall survival.31

**References**

1. Pennathur A, Gibson S M, Johe B A, Luehchte J D. Oesophageal carci-
2. Wong R, Walker-Delis C, Rajaf A. Evidence-based guideline recommen-
3. Allam W H, Blazey J M, Grünfin S M et al. Guidelines for the manage-
15. Heeren P A M, Jager P L, Boogaerts F et al. Detection of distant meta-
17. Chan D S Y, Fielding P, Roberts S A et al. Prognostic significance of 18F-
deoxyglucose-to-position emission tomography (18F-FDG PET/CT) in the iden-
25. Westerterp M, Van Westreenen H L, Reitsma J B et al. Esophageal Cancer: CT, endoscopic US and FDG PET for assessment of response to neoadju-
29. Guo H, Zhu H, Xi Y et al. Diagnostic and prognostic value of 18F-FDG PET/CT for patients with suspected recurrence from squamous cell carci-
30. Kato H, Miyazaki T, Nakajima M et al. Value of positron emission tomo-
32. Van Westreenen H L, Cohen D C, Jager P L et al. Comparison of 18F-

Figure 1
Fused axial PETCT image (top left) and axial PET image (top right) showing a highly metabolically active oesophageal malignancy, with invasion into adjacent structures (aorta and left main bronchus). Fused axial PETCT image (bottom left) and axial PET image (bottom right) showing a metabolically active regional mediastinal lymph node. Stage T4 N1 M0.

Figure 2
MIP (maximum intensity projection) PET image (top left) showing a metabolically active lesion in the lower oesophagus, which is also demonstrated on the axial PET image (top right) and fused coronal PETCT image (bottom right). A small lung nodule is seen in the right lung on the fused axial PETCT image (bottom left) which is not metabolically active but, due to its size, cannot be accurately characterised and is equivocal. Stage T3 N0 Mx.

Figure 3
Fused PETCT axial (top left) and sagittal (top right) images showing a large metabolically active malignancy in the lower oesophagus. The bottom two images are equivalent slices from a PETCT scan performed after neoadjuvant chemotherapy, which show marked reduction in metabolic activity indicating good response to treatment. The ill-defined activity in the lower lobe of the left lung is inflammatory.

Figure 4
Fused PETCT image (top left) showing a small metabolically active oesophageal malignancy. The MIP image (bottom right) shows multiple areas of abnormal activity throughout the skeleton, the largest being in the proximal left humerus (top right), in keeping with widespread bone metastases. Stage T3 N0 M1.
Figure 5
Axial PETCT image (top left) and axial PET image (top right) showing a highly metabolically active mass at the thoracic inlet, shown to be recurrent oesophageal cancer. The patient had had a previous oesophagectomy and axial fused PETCT images show the gastric pull up (bottom left) and anastomosis (bottom right) to be free from recurrence.