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Oesophageal cancer: assessment of response and follow up

S.C. Rankin

Guy's & St. Thomas Foundation Trust, London, UK

Corresponding address: Dr S.C. Rankin, Department of Radiology, Guy's Hospital, St Thomas Street, London, SE1 9RT, UK.
Email: sheila.rankin@gstt.nhs.uk

Abstract

The prognosis for oesophageal cancer is poor with a median survival of 3–5 months and recurrences are frequent. The best chance of cure is successful surgery and pre-operative chemoradiotherapy is used to try and improve outcomes. However, patients may either not respond or may progress during therapy and it is important to differentiate the responders from non-responders. Clinical parameters such as weight gain and improvement in swallowing can be assessed but imaging is used in an attempt to improve outcomes.

Keywords: *Oesphageal cancer; recurrence; response; endoscopic ultrasound; CT; positron emission tomography.*

Introduction

The prognosis for oesophageal cancer is poor with a median survival of 3–5 months and recurrences are frequent. The best chance of cure is successful surgery and pre-operative chemo-radiotherapy is used to try and improve outcomes with the aim of eradicating lymphatic and haematogenous metastases, not only to improve survival and decrease recurrences, but also to shrink the primary tumour. Patients who achieve a complete response with the chemo-radiotherapy have a 5-year survival of 63% compared to 23% in the non-responders.

However patients may either not respond or may progress during therapy and these groups may benefit from early surgical intervention and so it is important to differentiate the responders from the non-responders. Clinical parameters such as weight gain and improvement in swallowing can be assessed but imaging is used in an attempt to improve outcomes but has rather variable results.

Response assessment

Endoscopic ultrasound (EUS) is the most accurate method for staging the primary tumour and local lymph nodes at diagnosis, but has limitations following chemo-radiotherapy as EUS cannot differentiate between fibrosis and residual disease with over staging being reported in up to 69% of patients. However, using a reduction of 50% or greater in the maximum cross sectional area is relatively accurate in both predicting response (PPV 80%) and survival[1,2].

The use of computed tomography (CT) has produced conflicting results. Walker *et al.*[3] found a wide discrepancy between the reported CT response and the pathological correlation (48% responding on CT with a 90% pathological response) and these authors suggested CT could predict a response, but lack of CT response did not preclude a pathological response. However, more recent studies found no correlation between the CT and the pathological response[4,5] although a recent study by Beer *et al.*[6] using multidetector CT suggested that a CT scan performed 14 days after the initiation of chemotherapy could predict the final response (sensitivity 100%, specificity 53%) but using a volumetric method of measurement, rather than the tumour diameter.

FDG-positron emission tomography (FDG-PET) is used to assess response in other tumours and appears to be the best method for identifying responders in oesophageal cancer. Studies by Ott *et al.*[7] in assessing early response to therapy (within 14 days of commencement of chemo-radiotherapy) found a decrease in uptake (SUV) of greater than 35% indicated a major pathological

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response with a 3-year survival of 70%, compared to a 3-year survival of only 35% in the non responders. FDG-PET can also be used at the end of treatment to predict response in both adenocarcinoma and squamous cell carcinoma. Flamen *et al*.[8] found FDG-PET was both sensitive and specific (71% and 82%) in identifying a major response, although in this study the response was both over and under estimated in 11% of patients. Swisher *et al*.[9] compared EUS, CT and FDG-PET and found FDG-PET was more accurate (70%) than EUS (68%) or CT (62%). In this study an SUV of greater than 4 was an independent predictor of survival with a 2-year survival of 34%, compared to a 2-year survival of 64% with a SUV of less than 4.

However, none of the imaging modalities can differentiate a complete response (0% viable cells) from microscopic residual disease (1–10% viable cells) so patients with a complete metabolic response may still need further intervention. Duong *et al*.[4] found patients with a complete response on FDG-PET who did not undergo surgery had a comparable survival to those that did, perhaps therefore allowing a more conservative approach in selected patients.

Recurrent disease

The recurrence rate after resection is high (34–79%) with more than 50% occurring in the first year and most presenting within 2 years of surgery.

Recurrences may be either local (30%) or distant, with local or distant nodal deposits and haematogenous spread to the lungs common. Local recurrence is usually extragastric in the mediastinum or upper abdominal lymph nodes[10]. There is no correlation between the site of the primary tumour and that of the recurrence presumably because of extensive lymphatic spread prior to the surgery[11]. Distant spread may occur without any local recurrence in 40% of patients and is commonest, in descending order to nodes, lung, liver, pleura and adrenals. A recent autopsy study[12] found tumour in 63% of patients following 'curative' surgery and in this study 43% of patients whose death was unrelated to cancer had tumour recurrence.

Flamen *et al*.[13] in a study of patients with clinical or radiological suspected recurrence compared FDG-PET with the conventional work up of CT and EUS. In this study all equivocal lesions on any modality were called positive. The sensitivity for FDG-PET for peri-oesophageal recurrence was 100% with a specificity of 57% and accuracy of 74%, whereas the conventional work up was 100% sensitive, 93% specific and 96% accurate. A false positive result may occur with FDG-PET in patients who have undergone dilatations. The majority of recurrences were distant metastases and the sensitivity, specificity and accuracy of FDG-PET compared to conventional imaging was 94%, 82% and 87% vs 81%, 82% and 81%, respectively. Although in this study there was no significant difference in the results between the methods of investigation, on a patient basis FDG-PET did provide additional information in 11 out of 41 patients (27%), identifying unsuspected recurrence in 5 and upstaging a further 5 patients.

Kato *et al*.[14] looked at a group of post surgical patients, only 8% of whom were symptomatic, but 35% had recurrent disease. FDG-PET was 100% sensitive but only 75% specific for local recurrence compared to CT (84% and 86%, respectively). The false positives for FDG-PET were in physiological uptake in the gastric tube and in mediastinal lymph nodes probably related to chronic lung disease. For distant recurrence the diagnostic accuracy for FDG-PET and CT were similar for liver metastases, whereas FDG-PET was less sensitive than CT (50% vs 100%) for lung metastases. FDG-PET was more sensitive for bone metastases (100% vs 17% respectively).

Conclusions

Imaging provides important information for assessing response to therapy, predicting survival and identifying recurrent disease in oesophageal cancer. FDG-PET/CT would appear to be the most appropriate method for assessing response to therapy but all methods have limitations in identifying small volume disease. Local recurrence is equally well demonstrated by conventional and functional imaging, although there are some advantages in using FDG-PET for distant recurrences. At the present time most institutions do not undertake routine follow up but only investigate symptomatic patients.

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