Staging stenotic oesophageal tumours: Are CT and/or PET enough? Dilate or not?

J. Meenan
Guy's and St. Thomas' Hospital, London

Introduction

Strictured oesophageal tumours are difficult for patient and physician alike. An inability to use standard equipment freely, concentrates the mind as to what the purpose of staging is: what information is sought and why?

Long-term survival with oesophageal and proximal gastric tumours is poor and treatment options for locally advanced disease, unsatisfactory. The scramble for incremental improvements in survival results in a large variation in practice, particularly in respect of using neoadjuvant chemotherapy. Disagreement over general management strategy is both reflected in and moulds discussion on how the staging of stenotic lesions might be achieved. First, to address some of the important peripheral issues.

General considerations

Surgery confers a survival advantage on those with resectable lesions [1,2]. Neoadjuvant chemotherapy might confer a survival advantage, particularly on those who show a clinical response; equally, those with residual positive nodes fare poorly [3,4]. Although the type of cancer under consideration, adenocarcinoma or squamous cell, does not seem to have much impact on survival, the site of the lesion may; the Siewert classification identifies diseases with different prognoses, junctional (Type II) lesions being more associated with node-positive disease and a poorer prognosis [5,6].

Nodal status is central to the staging of oesophageal cancer, as it predicts survival [1,7]. Three confounding factors to describing nodal status need to be addressed in the setting of stenotic lesions: (a) dispute over the accuracy of endoscopic morphology alone in ascribing involvement [8]; (b) lack of a clear definition of what a coeliac node is or represents [9–11]; and extrapolating from this, (c) deficiency of the TNM staging system in respect of what is truly a local node and what is metastatic [12,13]. The presence of micrometastases in pN0 R0-resections (30% of cases) remains a joker in the pack [14].

To start at the beginning: the purpose of staging is to triage to appropriate therapy. There is an absolute need to know whether the lesion is not resectable for reasons of local spread (i.e T4 or not) or distant disease. There is a qualified need to know whether local lymphatic spread has occurred.

Endosonography

The problem: standard echoendoscopes are stiff and bulky, and tumour dilatation is not without risk. Initial studies reported worryingly high perforation rates [15,16]. More recent figures are considerably better but are not a true reflection of the risks experienced in a wider setting [17–20]. It should be remembered that tumour perforation has a dramatic impact on survival [20].

The combination of sequential dilation and passage of a standard echoendoscope overcomes these difficulties but the risks are higher. The risks associated with oesophageal tumour dilation although less pronounced than previously thought, are not negligible. A prospective audit reported a perforation rate of 6.4% following dilation and/or intubation of malignant strictures compared to 1.1% following dilation of benign strictures [21]. Strict adherence to a graded stepwise dilation protocol (for example, "rule of three") is advocated for safety, but this often means a second or third dilation session [22]. In addition to the risk and inconvenience to the patient, there are also financial implications for this approach both in terms of additional procedures and disposables. Furthermore, even with this approach, complete staging after dilatation might only be achieved in 62% of cases. (23) A final, important point is that the accuracy of EUS staging following dilatation might be poor, though this was reported in an "early" paper (1995) [15].

Approximately 55% of patients present with dysphagia, though this is not a reliable predictor of being unable to pass a standard echoendoscope [24]. There is a wide variation geographically in the proportion of those found to have stenotic lesions ranging from 25% (USA) to 73% (India) [15,25]. Approximately one-third

Correspondence: Dr. John Meenan · Department of Gastroenterology · 1st Floor College House · St. Thomas' Hospital · Lambeth Palace Road · London Se1 7EH · Fax: +44 20 71882484 · E-mail: john.meenan@gstt.nhs.uk

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of patients from Western countries with oesophageal cancer have stenoses at presentation significant enough to prevent the passage of a standard echoendoscope [26,27].

Before discussing the options for dealing with non-traversable lesions, it is important to consider what information can be gleaned from an incomplete study. Stricturing tumours are rarely less than T3 and positive nodes might be expected in 77%-81% of these [25,28,29]. The lymphatics of the upper two-thirds of the oesophagus drain in a cephalad direction [30]. Sixty percent of involved nodes will be found proximal or level with the tumour, 25% being unreachable distal, yet local, nodes with a further 4.5% being located within 1 cm of the coeliac artery [31]. Applying reductionist logic, the staging problem presented by strictures is limited to relatively few cases, particularly taking into account those unfit for surgery (20%), if neo-adjuvant chemotherapy is given to all operable tumours and if coeliac nodes might be considered local to junctional tumours [32,33].

There are six options for non-traversable malignant strictures: dilation of the stenosis to allow for passage by a standard echoendoscope, use of a catheter ultrasound probe, use of the Olympus MH908 oesophagoprobe, reliance on cross sectional imaging such as CT and positron emission tomography (PET), diagnostic surgery, or, a combination of methods. But, whichever approach is taken, it ought to be done at a specialist centre [34].

Miniprobes (catheter probes) are generally of high frequency (12MHz-30MHz), excepting the Fujinon 7.5MHz back-loaded probe (PL-2226B-7.5). The resulting lack of penetration offsets the advantage of small size; although miniprobe sonography can be as accurate as standard echoendosonography, these instruments are not adequate for the staging of large tumours or distant nodes [25,35].

The Olympus (MH908) 7.9 mm non-optical, wire-guided, 7.5MHz, oesophagoprobe showed promising results in small studies [36–38]. Later, larger series (reported in abstract) show this instrument to be a very powerful tool, permitting the complete staging (by morphology) of 95% of cases without the need for dilatation. (25,31) Questions have been raised over the ability of the MH908 to adequately inspect the coeliac trunk on account of restricted tip-deflection, but this worry is not born out in practice [31,35].

Intuitively, it would be reasonable to reserve the oesophagoprobe for those in whom a standard echoendoscope failed to pass. However, as problematic strictures cannot be predicted with any certainty from prior clinical questioning and as EUS equipment may be limited, the use of oesophagoprobe from the outset will improve the staging success and decrease the need for dilation. It might be suggested that the MH908 is the instrument of choice for all oesophageal tumours.

But, what of coeliac nodes and the need to biopsy? This question can only be answered at a local level. There is probably a great difference in the number of lymph nodes to be found in a "normal" mediastinum between both geographic regions and races. It is likely that endemic diseases whether fungal (USA), tuberculosis (developing world) or sarcoid (Afro-Caribbean) lead to varying numbers of detectable nodes; a point noted in Indians undergoing surgery for oesophageal cancer [40]. Anecdotal evidence from the UK (personal data) suggests that if a rounded node is found in a caucasian, in the presence of a tumour, it will almost certainly be positive. Similarly, our experience is that coeliac nodes (those within 1 cm of the coeliac trunk) are only found in 4.5% of cases, a lower figure than that reported by others [40,41]. Taking local conditions into account, application of modified EUS criteria could be applied to minimize the need for FNA [42]. In re-staging tumours following neoadjuvant chemotherapy, EUS-FNA might certainly offer clinically relevant information as non-biopsy FNA in this setting adds little to the information provided by CT [43]. This issue is dealt with elsewhere in this supplement.

CT and PET

Turning to cross-sectional imaging to help with the predicament of strictured lesions. Improvements in computed tomography and greater experience with positron emission tomography (PET) have opened up the possibility of high resolution, dynamic images with the potential for virtual endoscopy. Unfortunately, this bright bauble of imaging tarnishes rapidly.

Leaving aside structural methods of staging and turning to dynamic imaging. Positron Emission Tomography is not tumour specific as benign tissue may accumulate tracer; the commonly used 18F-fluoro-deoxyglucose (FDG), however, is superior to other substrates [44,45]. Early studies showed PET to identify local disease [46,47] though imperfectly [46,48,49] as well as distant metastases [46–50]. Importantly, the histology of the tumour does not confound PET results [51].

Reviewing comparative studies with CT, PET does not identify all primary tumours [52–59]; it does not identify all involved nodes [sensitivity: 30%-80%, median 45%; specificity 82%-100%, median 90% and accuracy 48%-93%, median 80%] [47,48,52,46,65,53,54,62,63,61,60,51,64,58] and nor does it identify all distant metstases [sensitivity 38%-88%, median 64%; specificity 89%-93%, median 90% and accuracy 74%-91%] [47,48,50,52,54,57,58,61–64,66]. But, PET certainly yields additional useful information to that provided by CT [47,48,51,52,54,58,64,66,67]. As one might expect with a dynamic modality, PET demonstrates superior specificity but lower sensitivity than EUS for the identification of loco-regional nodes [54,57,64,68].

Technology gets better. Combined PET/CT holds promise for incremental improvement in staging accuracy. [69–71] But, initial reports evaluating multi-detector CT (with virtual endoscopy) show a persisting inferiority in accuracy to that obtained with PET [72].

The major drawbacks, impairing the accuracy of PET include: a halo effect from the primary tumour hotspot obscuring local nodes [46], a high rate of false-positive hilar node interpretations [63], a tendency to lower sensitivity for nodes in the mid/lower thorax as compared with those in the upper chest, neck or abdomen [55] and spatial/breathing artefact [70]. A false-positive rate of 15% is worrying yet, PET still outperforms EUS-FNA [73,74].

In addition to staging information, the data yielded by PET such as degree of tracer uptake (standardized uptake value, SUV), has been shaken, poked and prodded to reveal prognostic information: an SUV greater than 3 – 4.5 may predict a less good outcome [55,75] but, this is not universally reported [76,77].

In the setting of neo-adjuvant chemo(radio)therapy, the dynamic nature of PET holds promise for guiding treatment. As might be expected, the burden of disease identified by PET (tumour length and number of positive nodes) and resultant upstaging correlate poorly with survival [66,78]. Early change in tumour 18F-FDG uptake predicts a reduction in tumour size following completion of therapy [79]. In respect of pathological response, a drop in SUV, possibly from a high baseline (> 4) may correlate with favourable post-operative findings [55,80 – 82] and/or survival [83,84]. Again, not all authors are so positive [85,86]. A meta-analysis of the accuracy of PET, CT and EUS in assessing response to chemotherapy shows equivalence between PET and EUS, both being superior to CT [87].

Overall assessment of the clinical value of PET in the setting of oesophageal cancer shows benefit in terms of useful additional information and the prevention of unnecessary surgery [51,52,60,60,88 – 90] although a medium sized trial (n = 56) rains somewhat on this parade [61]. In terms of cost, although the best approach might be PET combined with EUS-FNA, limiting investigations to CT and EUS-FNA might be the most cost effective [91]. Such models however, cannot address the difficulties presented by strictured lesions. So, where does that leave us? PET holds promise in the staging and re-staging of oesophageal tumours but, not as a free standing test.

Other techniques

Other methods to detect lymphatic spread of disease include the search for sentinel lymph nodes whether by cross-sectional or intra-operative lymphangiography [92,93,84]. It is not possible to place this approach in any algorithm from the information available.

Towards an algorithm

So, what to do with a stricturing tumour of the oesophagus or oesophago-gastric junction? There are three issues to addressed before imaging: firstly, ascertain the local disease "profile" of this carcinoma (might the majority of nodes, particularly those at the coeliac axis, be considered positive?); secondly, decide whether the patient is fit for surgery and thirdly, decide the criteria for offering neo-adjuvant chemotherapy and subsequent operability ("once T4, always T4"?, what if a coeliac node disappears with therapy? etc). Initial imaging triage should be with CT, or ideally PET/CT. If no disease spread is seen, then EUS using the Olympus oesophagoprobe followed by either acceptance of morphological evidence or graded-dilatation followed by EUS-FNA. In respect of residual strictures following neo-adjuvant chemotherapy, EUS-FNA is required if positive cytology will lead to a non-operable status.

Competing interests: None

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