European Journal of Radiology 97 (2017) 71–75

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Loco-regional staging accuracy in oesophageal cancer—How good are we in the modern era?

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ARTICLE INFO

Keywords:
Oesophageal cancer
Chemotherapy
Chemoradiotherapy
Neoadjuvant therapy
Staging

ABSTRACT

Introduction: Accuracy of locoregional staging in patients with oesophageal cancer is critical in determining operability and the need for neoadjuvant treatment. Imaging technology has advanced significantly in recent years but it is not known whether this translates to improved staging accuracy. This study investigates staging accuracy in relation to CT, EUS, PET-CT and final pre-operative stage. It specifically addresses the accuracy of staging with respect to the threshold for administering neoadjuvant therapies.

Materials and methods: Pre-operative staging according to CT, EUS, PET-CT and final pre-operative stage were compared to the postoperative histological staging in 133 patients undergoing potentially curative surgery (without neoadjuvant therapy) for oesophageal cancer between January 2010 and January 2015. T and N stage accuracies were reported separately for each imaging modality. Patients were also divided into two groups depending on whether the final pre-operative stage was below ($\leq$T2, N0, early tumours) or above ($\geq$T3 and/or $\geq$N1, locally advanced tumours) the threshold for offering neoadjuvant therapy. Accuracy of pre-operative staging was then analysed with respect to identification of patients below/above this threshold. The additional benefit offered by EUS for this purpose was investigated.

Results: T stage accuracies were 72.6%, 76.7% and 79.3% for CT, EUS and final pre-operative stage respectively. N stage accuracies were 75.6%, 77.2%, 74.5% and 78.6% for CT, EUS, PET-CT and final pre-operative stage respectively. Staging accuracy with respect to threshold for neoadjuvant treatment showed 62.0% early tumours were correctly staged and 80.5% advanced tumours were correctly staged. Whether or not patients underwent EUS did not affect the staging accuracy with respect to neoadjuvant treatment threshold.

Conclusions: Staging accuracy with respect to the threshold for treatment with neoadjuvant therapy is poor, leading to potential over/under treatment. Predicting individual response to neoadjuvant therapy would provide a better way to determine which patients should receive this additional treatment.

1. Introduction

Clinical staging of oesophageal cancer is used not only to determine operability, but also, the need for neoadjuvant treatment. Loco-regional staging accuracy is therefore of critical importance in modern multi-modality treatment.

A number of imaging techniques are used in clinical staging of oesophageal cancer. These including computed tomography (CT), PET-CT, endoscopic ultrasound (EUS) +/− fine needle aspiration (FNA), endobronchial ultrasound (EBUS) +/− FNA, staging laparoscopy and focussed ultrasound with FNA/biopsy. Some are used routinely and others selectively, the most frequently used being CT, EUS and PET-CT. The gold-standard, to which all radiological staging methods are compared is histopathological staging. The most widely used system is the Union for International Cancer Control (UICC) tumour, node, metastasis (TNM) staging system. Currently the 7th edition manual is in use; the 8th edition has been published but will not be adopted until 2018. Imaging technology continues to improve such that published literature on staging accuracy is often based on out-of-date techniques. It is hoped that these technological advances will translate to improved rates of staging accuracy. Whilst staging accuracies of individual staging modalities are reported in the literature, there is little consideration given to the accuracy of final pre-operative stage, on which treatment decisions are based. In an era of increasing neoadjuvant therapy use, determining the accuracy of radiological staging is challenging due to the therapeutic effect of downstaging.

This paper aims to provide a pragmatic update of staging accuracy in relation to CT, EUS, PET-CT and final pre-operative stage. It also specifically addresses the accuracy of staging with respect to the threshold for administering neoadjuvant therapies.

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http://dx.doi.org/10.1016/j.ejrad.2017.10.015
Received 8 August 2017; Received in revised form 5 October 2017; Accepted 20 October 2017

2. Materials and methods

2.1. Patients and data

All patients planned to undergo surgical resection for malignant oesophageal cancer and starting treatment between January 2010 and January 2015 were identified retrospectively from a prospectively kept database. Patients undergoing any form of neoadjuvant therapy were excluded. Data were collected on patients' demographics, tumour characteristics, preoperative staging, neoadjuvant treatment, surgical treatment and final pathological stage. Advice was taken from the regional ethics committee recommending use of the Health Research Authority decision tool. On the basis that treatment was not being changed in patients whose data were used for the study and there was no randomisation/intervention, formal ethics approval was not required.

2.2. Staging protocol

Staging was reported according to the UICC 7th edition manuals for oesophageal cancer. After histological confirmation of oesophageal cancer via endoscopic biopsy, patients underwent staging with CT of thorax, abdomen and pelvis using 64-slice multi-detector scanners using the same oesophageal staging protocol (0.625–1.25 mm slices, oral water as negative contrast and intravenous contrast with portal venous phase imaging). All CT scans were reviewed by at least one of four specialist upper gastrointestinal CT radiologists at a specialist MDT meeting. Tumours were staged according to the criteria described by Ba-Ssalamah et al. [1]. Specifically, T2 tumours were characterised as having thickening of the oesophageal wall of less than 15 mm with slight/mild stenosis and outer borders which are smooth or show stranding for less than one third of the tumour extension. T3 lesions were represented by thickening of greater than 15 mm with mild to severe stenosis and marked stranding for over one third of the tumour extension or extensive blurring of the outer border. T4 lesions required invasion into adjacent structures such as pericardium, diaphragm, pleura, tracheobronchial tree or aorta. Lymph nodes were considered to be involved on CT if the short-axis diameter was 1 cm or greater.

PET-CT was performed for N and M staging in cancers with the potential for radical treatment and curative intent in accordance with current guidelines [2]. Nodes or distant lesions demonstrating avidity significantly greater than background were deemed involved; although the pattern of nodal uptake was also evaluated to exclude nodal avidity from alternative causes such as sarcoid like reaction to malignancy.

EUS was used in selected traversable tumours to further assess T and N stage which helped to determine resectability and the need for neoadjuvant therapy. Involvement of lymph nodes was defined according to criteria published but the British Society of Gastroenterology [3]. Specifically, nodes were considered involved if greater than 1 cm in short-axis, hypoechoic, well demarcated or round-shaped.

Staging laparoscopy was undertaken in all potentially resectable lower oesophageal/gastro-oesophageal junction cancers with a component below the level of the diaphragm or in those with significant regional intra-abdominal lymphadenopathy to exclude extracapsular spread.

Ultrasound, EUS or EBUS (all +/− FNA/biopsy) were used in selected cases where positive nodal involvement would change management.

On the basis of all available staging modalities, the final pre-operative stage was then decided by the MDT and recorded on the database.

2.3. Analysis

Pre-operative staging according to CT, EUS, PET-CT and final pre-operative stage were compared to the postoperative histological staging. T and N stage accuracies were reported separately for each imaging modality.

Patients were also divided into two groups depending on whether the final pre-operative stage was below (≤T2, N0, early tumours) or above (≥T3 and/or ≥N1), locally advanced tumours the threshold for offering neoadjuvant therapy used in our institution. Patients with locally advanced tumours in this cohort of patients not undergoing neoadjuvant therapy were either unfit for chemotherapy or declined neoadjuvant treatment. The accuracy of pre-operative staging was then analysed with respect to identification of patients below/above this threshold. The positive predictive value (PPV) and negative predictive value (NPV) of identifying early stage tumours was reported. Patients were divided into two groups according to whether or not they had EUS performed. Data from these groups were also analysed with regards to accuracy in predicting stage above or below the threshold for neoadjuvant therapy.

2.4. Surgery

Patients with resectable tumours who were still fit for operation underwent resection. Ivor-Lewis gastro-oesophagectomy was performed for lower oesophageal and gastro-oesophageal junction tumours, with either laparoscopic or open abdominal components.

2.5. Pathological reporting

Histopathological reporting followed the minimum dataset for oesophageal cancer. Routine histopathological reporting included recording the Mandard score (TRG) and pathological TNM staging according to the UICC 6th or 7th Edition manual and was performed by a specialist gastrointestinal pathologist.

2.6. Adjuvant therapy

Adjuvant therapy was used in a minority of patients with the decision based on a number of individual factors including post-operative pathological stage, response to therapy and the patient's clinical condition.

3. Results

3.1. Patient characteristics

Of the 463 patients who were identified from the database, 137 patients were planned to have surgical resection without neoadjuvant therapy, either because they had early tumours or were not fit enough to undergo multimodality therapy. 4 patients were inoperable leaving 133 patients with resected cancers included in the analysis (Fig. 1). Patient characteristics are shown in Table 1. Median age was 72.3 years and 67.2% were male. The majority of patients were staged pre-operatively as T2 or less (64.7%) and the majority of patients were staged as N0 (82.8%).

3.2. Loco-regional staging

Accuracy of T staging is shown in Table 2. Accuracy of N staging is shown in Table 3.

3.3. Staging according to neoadjuvant therapy threshold

92 patients were staged as early tumours (≤T2 and N0) and of these, 57 were correctly staged (NPV 62.0%), see Table 4. 41 patients were staged as locally advanced (≥T3 or ≥N1) and of these, 33 were correctly staged (PPV 80.5%).

Of the 133 patients in the dataset, 63 had undergone EUS and 70 had not undergone EUS. Of those undergoing EUS, all had CT and 61/