A national cross-sectional survey investigating the use of endoscopic ultrasound in the diagnosis and treatment of oesophageal cancer in the UK

C.M. Jones a,b,* A. Lyles a, K.G. Foley c

a Leeds Cancer Centre, The Leeds Teaching Hospitals NHS Trust, Leeds, UK
b Radiotherapy Research Group, Faculty of Medicine & Health, University of Leeds, Leeds, UK
c Department of Clinical Radiology, Velindre Cancer Centre, Cardiff, UK

AIM: To evaluate variation in the pre-pandemic use of endoscopic ultrasound (EUS) for oesophageal cancer diagnosis and treatment planning up to 2019, and which factors contributed to this.

MATERIALS AND METHODS: A UK-wide online survey of oesophagogastric multidisciplinary team lead clinicians was undertaken to determine perceptions towards, and the use of, EUS to aid staging and treatment planning in oesophageal cancer.

RESULTS: Thirty-five responses were received, representing 97 UK National Health Service Trusts/Health Boards. A majority of centres (n=21, 60%) did not have formal written guidance for EUS use. Although all respondents had access to EUS, a perceived lack of utility (n=7) and concerns about delaying treatment start dates (n=8) each restricted EUS use for a fifth of respondents. For most centres (n=24, 68.6%), EUS use is case-specific, whereas for 10 (28.6%) EUS is used for all patients with potentially curable disease. A majority of centres use diagnostic positron-emission tomography for radiotherapy target volume delineation (TVD), whereas 22 (62.9%) use EUS. The factors contributing to decisions to use EUS for staging, TVD and surgical planning varied between centres. The proportion of centre respondents who would request EUS in each of six clinical scenarios varied considerably.

CONCLUSION: There were substantial differences in the patient and disease characteristics that are perceived to be indications for EUS use for both staging and treatment planning. Research to clarify in which patients with oesophageal cancer EUS affords benefit is required, as is urgent standardisation of its role in the diagnostic pathway.

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* Guarantor and correspondent: C. M. Jones, LIGHT Laboratories Level 7, Faculty of Biological Sciences, University of Leeds, LS2 9JT, UK. Tel: +44 113 2068586; fax: +44 113 2068474.
E-mail address: c.jones1@leeds.ac.uk (C.M. Jones).

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Introduction

Oesophageal cancer is a leading cause of cancer-related death worldwide. In the UK, 9,200 cases are diagnosed each year and rates of oesophageal adenocarcinoma (OAC), one of the two predominant histological subtypes, are growing faster than any other malignancy. Prognosis is poor, with only a minority of patients suitable for radical therapy. For patients with potentially curative disease, intensive multi-modal treatment strategies are generally favoured. These include definitive chemoradiotherapy (CRT) as well as neoadjuvant chemotherapy or CRT followed by surgical resection. Earlier disease stages may be amenable to endoscopic mucosal resection (EMR).

Treatment selection for patients without metastatic disease is dependent on the extent of tumour infiltration and nodal involvement. Standard imaging modalities used in the staging and treatment planning of oesophageal cancer include computed tomography (CT) and positron-emission tomography combined with CT (PET-CT). Endoscopic ultrasound (EUS) may also be used for both disease staging and treatment planning, although its use is advocated by the National Institute for Health and Care Excellence (NICE) only when it will help guide management.

The circumstances in which EUS use does effectively guide management are contentious, and there is anecdotal evidence of variation in its use across the country. Between 2016–2018, the National Oesophago-Gastric Cancer Audit reported that around 49% of patients with oesophageal cancer proceeded to EUS; however, it did not provide information on which patients had been selected nor whether EUS was used for staging or to support surgical or radiotherapy treatment planning. The onset of the coronavirus disease 2019 (COVID-19) pandemic has potentially exacerbated this variation, with widespread reports of restrictions in access to EUS due to concerns about resource limitations and its risks as an aerosol-generating procedure (AGP).

It is therefore uncertain to what extent EUS use varies across the UK and there has been no previous formal assessment of which centre-, patient- or disease-specific characteristics favour its utilisation. Understanding this variation is important for ensuring that all patients have access to an optimised and standardised diagnostic pathway. This includes identifying disparities in EUS capacity as well as the factors used to inform patient selection for EUS; in addition to informing research aimed at harmonising these. Understanding the extent to which EUS provision varies may also provide a greater insight into which groups of patients are likely to have been most significantly impacted by reductions in EUS use due to the COVID-19 pandemic.

Given this, and in order to inform future research priorities and post-pandemic service recovery, the aim of the present study was to evaluate variations in the pre-pandemic use of EUS for oesophageal cancer diagnosis and treatment planning up to 2019, and which factors contributed to this.

Materials and methods

Study design

A national cross-sectional survey was undertaken to determine perceptions towards, and the use of, both EUS and EUS–fine-needle aspiration (FNA) in the UK prior to the COVID-19 pandemic.

Survey instrument

An online survey was developed by the authors and hosted by the cloud-based software provider SurveyMonkey (SVMK, CA, USA). This was piloted prior to dissemination by eight UK-based clinicians who are routinely involved in the care of patients with oesophagogastric cancers. An overview of the survey instrument is provided in the Electronic Supplementary Material. Case study exemplars designed with assistance from experts in the relevant speciality were also used to explore the variations in indication for EUS, and which factors underlie these decisions. The information routinely provided in local EUS reports was also requested. (Electronic Supplementary Material).

Study population and survey dissemination

Clinicians involved in the care of patients with oesophagogastric malignancies in NHS Trusts/Health Boards across the UK were invited to participate in the survey between 1 July 2020 and 1 October 2020 using an upper gastrointestinal contact list curated by one of the authors (C.M.J.). A reminder email was sent within 6 weeks of initial contact. Survey respondents were asked to report their centre’s usual practice prior to the onset of the COVID-19 pandemic.

Data analysis and representation

Descriptive analyses were undertaken, and graphs generated, using GraphPad Prism 9.0.0 (GraphPad Software, CA, USA).

Results

Respondents

Thirty-five responses were received, representing the pre-COVID-19 practice of 86 English NHS Trusts, six Welsh Health Boards and five Scottish Health Boards (Electronic Supplementary Material Table S1). No response was received from respondents representing Northern Ireland, three regions in England or nine Scottish Health Boards, although a number of these are unlikely to have their own oesophagogastric cancer service.

Access to EUS

A majority of respondents (n=21, 60%) reported that their multidisciplinary team (MDT) did not have formal
written guidance for the use of EUS. All respondents reported that they had access to EUS; 30 (85.7%) within the same NHS Trust/Board as the MDT. Similarly, all respondents had access to EUS-FNA, with 32 (91.4%) respondents reporting access within the same NHS Trust/Board as the MDT; however, a minority of respondents (n=4, 11.4%) reported that difficulty obtaining EUS limited their use (Table 1).

The median reported number of EUS and EUS-FNA operators per centre was two (range 1–7 for EUS and 1–6 for EUS-FNA). Gastroenterologists were most frequently reported to be delivering both EUS and EUS-FNA (Fig 1a and b). Other professional groups involved in the delivery of EUS were radiologists and surgeons, with only one centre reporting a role for non-medical endoscopists. Two centres did not provide data for the number of EUS or EUS-FNA operators. As summarised in Fig 1c, the most commonly reported EUS measurements were tumour location, tumour length, clinical T-stage and N-stage, and both the proximal and distal tumour extent, though variation in reported parameters was seen with, for instance, tumour thickness reported for only 11 (31.4%) respondents.

**Use of EUS**

Overall, EUS was recommended for use in all patients with potentially curable oesophageal cancer in just over a quarter of respondents (n=10, 28.6%), although for one (2.9%), EUS was never recommended. Therefore, a majority (n=24, 68.6%) reported the use of EUS in select cases. No centres use EUS solely for fulfilling trial inclusion/exclusion criteria. One fifth (n=7) of respondents reported that a perceived lack of utility restricted EUS use in the NHS Trust/Boards they represent (Table 1). A similar proportion (n=8,
reported that concerns about delaying treatment start dates limited EUS use.

The routine use of EUS was considered more commonly after MDT discussion in order to inform treatment planning (n=29, 82.9%) than prior to MDT in order to inform disease staging (n=13, 37.1%); however, considerable differences were seen in the sequencing and timing of EUS and PET-CT when EUS was used as a component of the oesophageal cancer diagnostic pathway (Fig 2a). A similar proportion of respondents would request EUS at the same time as PET-CT (n=14, 40%) or routinely following PET-CT (n=2, 5.7%) as would request EUS on a case-specific basis dependent on PET-CT results (n=16, 45.7%).

In the context of treatment planning, EUS was most commonly (n=27, 77%) used for selecting between surgery and CRT for more advanced but potentially resectable disease (Fig 2b). Over two thirds of centres used EUS for treatment planning in patients selected for surgery, EMR, and CRT. Fourteen (52%) use EUS for single-modality radiotherapy planning.

A majority (n=22, 62.9%) of centres use the diagnostic PET-CT for radiotherapy planning (Fig 2c). Twenty-two (62.9%) respondents routinely use EUS for radiotherapy planning, though only two (5.7%) solely use EUS to aid target volume delineation (TVD). The factors underlying the use of EUS for planning both radiotherapy (Fig 2d) and surgery (Fig 2e) varied between centres. For radiotherapy, the most commonly cited indications for EUS use included uncertainty regarding nodal involvement (n=15, 42.9%), or non-avidity on PET-CT (n=14, 40%). Only 11 (31.4%) would use EUS to determine disease length for maximum gross tumour volume (GTV). For surgical planning, EUS is most commonly requested to establish suspected T4 disease (n=22, 62.9%) or to FNA an out-of-field node (n=21, 60%). It is less frequently used to determine the upper extent of a cancer (n=9, 25.7%) or to help decide on a specific operative procedure (n=9, 25.7%).

When planning radiotherapy, EUS-guided fiducial placement was not used by a majority of centres (n=23, 65.7%). The remainder would use fiducials selectively; four reported that fiducial placement was used to aid TVD where tumour was not visible on imaging, two specifically for treatment post-EMR and three when requested specifically by an oncologist or surgeon.

Significant differences in practices relating to the use of EUS for the diagnosis and treatment-planning of oesophageal cancer were seen in the case scenarios presented in Fig 3. For all scenarios, between 31.4–45.7% would routinely request EUS, whereas between 14.3–37.1% would never...
request EUS. EUS was least likely to be used for a junctional adenocarcinoma planned for surgical resection and most likely to be routinely used in an early OAC planned for EMR or where nodal involvement was present on PET-CT for a T3N1 OAC. Small differences in the reported use of EUS were also recognisable between histological subtypes in cancers with identical stages. In particular, EUS was more likely to be considered for oesophageal squamous cell carcinoma (OSCC) than OAC.

Discussion

The present study demonstrated that prior to the COVID-19 pandemic, there was considerable variation across the UK in EUS use for the diagnosis and treatment planning of oesophageal cancer. A significant contributor to this was substantial differences in the patient and disease characteristics that centres use to decide on whether or not to utilise EUS, as well as variation in the sequencing of EUS and other imaging modalities such as PET-CT, and disparities in reported EUS measurements.

For patients with oesophageal cancer, EUS has typically been advocated for tumour staging and treatment planning, including guiding surgical approaches and for delineating radiation fields. The reported benefits of EUS include superior evaluation of tumour invasion (T-stage), with overall accuracy of 80%, and definition of disease length, which is an important factor for defining the GTV during radiotherapy planning; however, the accuracy of lymph node staging (N-stage) is lower at between 55–80%, and EUS is an invasive procedure with risks to the patient that include bleeding, perforation, and infection as well as risks relating to sedation. Consequently, the overall benefit of EUS in comparison to its associated risks has been questioned.

Cognisant of these factors, NICE stipulates that EUS should be offered to patients with oesophageal cancer only when it will help guide management. Between 2016–2018, the National Oesophago-Gastric Cancer Audit (NOGCA) found that this translated to 49% of patients with oesophageal cancer in England and Wales receiving EUS; however, the rationale for its use in these cases was unclear. Although EUS is considered by most centres, it is predominantly used on a case-specific basis with the factors that centres cite as contributing to decisions regarding its use varying significantly. This apparent lack of consensus means that current NICE guidance introduces such inherent variation in EUS use that for many of the case scenarios outlined.

Figure 3 The proportion of centres reporting that they would routinely request EUS, request EUS on a case-by-case basis, or in no cases request EUS for specific clinical scenarios relating to the diagnosis and treatment planning of oesophageal cancer. OAC; oesophageal adenocarcinoma; OSCC, oesophageal squamous cell carcinoma.
in Fig 3, similar numbers of patients would be offered EUS as would not, whilst two identical patients managed at different centres would feasibly receive entirely different diagnostic work-up.

These broad disparities in the use of EUS arise despite all centres reporting that they have access to this imaging modality, although this did appear restricted for around 10% of respondents. In addition, there were considerable discrepancies in the information made available to clinicians within EUS reports, with only three of 17 possible measurements reported across all centres. This variation may reflect a lack of specific guidance relating to EUS use in oesophageal cancer, as well as the previously reported haphazard development of UK EUS services and inconsistencies in training for its operators. One impact visible in the data presented here is that parameters useful for radiotherapy planning, such as tumour length, are not being made available to clinicians in every centre, despite the reported differences in EUS measurements compared to PET-CT.

Surprisingly, a greater number (n=32) of respondents reported that they have local access to EUS-FNA than reported local access to EUS (n=30). It is unclear why this might be the case but it may reflect nuances in local pathways or differences in the availability of radial (R-EUS) and linear array EUS (L-EUS). R-EUS provides circumferential images in a plane perpendicular to the scope axis and is therefore used for staging. In contrast, L-EUS provides good resolution to a depth of 3–5 cm in a plane parallel to the scope axis so is not used for staging but instead incorporates a working channel through, which a needle can be passed for FNA.

The present data also demonstrate considerable variation in both diagnostic and treatment-planning pathways for oesophageal cancer. It is generally accepted that the most appropriate order of investigations is PET-CT followed by EUS to assist treatment planning. 20 Despite this, a most appropriate order of investigations is PET-CT followed for oesophageal cancer. It is generally accepted that the diagnostic work-up. 20

Furthermore, EUS has good accuracy for differentiating T1a from T1b disease, 12 hence the use of EUS to plan endoscopic versus surgical treatment approaches was the third most commonly cited indication.

Finally, despite featuring as a requirement in the inclusion criteria for the recent SCOPE, NEOSCOPE, and SCOPE2 trials in oesophageal cancer, no centres indicated that EUS was undertaken solely for the purpose of fulfilling trial criteria. 23–25

Together, these important clinical aspects point to widespread variation in EUS practice and the interpretation of evidence for its use. As demonstrated in both the recent NOGCA report and the clinical scenarios outlined here, there is the potential for considerable variation in EUS use even for identical clinical cases in different centres. As services recover from COVID-19, urgent standardisation of EUS use and its role in the broader oesophageal cancer diagnostic pathway is required, as well as research to determine in which patients EUS affords benefit. It is clear that once an optimal role for EUS is identified, standardised diagnostic pathways and both training for and oversight of healthcare providers involved in them will be required.

**Limitations**

This survey demonstrates that there are clear differences in the factors that MDT leads cite as contributing to their utilisation of EUS; however, it does not provide patient-level data relating to EUS use, though the present findings are in keeping with rates of EUS utilisation reported in the recent NOGCA publication. It is also important to note that COVID-19 has placed significant restrictions on EUS use and the extent to which the rates of EUS use reported here have been impacted by COVID-19 is unclear.

In addition to the reported EUS variables outlined here, the extent to which MDTs perceive that the quality of EUS data are sufficient for clinical decision making is unclear. This requires well-planned prospective studies to determine. Similarly, the present analysis is not sufficient to determine which of the factors cited for EUS use, if any, impact on disease and treatment outcomes; however, the present findings clearly indicate this to be an area in which
further formal research is urgently required. Finally, differences in L-EUS versus R-EUS availability were not assessed. The nature of the survey means that the reason more respondents had local access to EUS-FNA compared with EUS alone cannot be explained. It would be of interest to collate and analyse annual L-EUS and R-EUS usage, including per operator and centre, as a proportion of cancer cases in order to further evaluate differences in service usage.

In conclusion, there is considerable widespread variation in the use of EUS for oesophageal cancer patients across the UK. Furthermore, many different patient and disease characteristics are used by clinicians when deciding upon EUS use during diagnosis and treatment planning. There is a lack of standardisation for EUS reporting, and a lack of standardised oesophageal cancer diagnostic pathways and clinical indications for EUS. Further research is required to determine the optimal role of EUS in oesophageal cancer, and to standardise the diagnostic and treatment pathways in which EUS is used.

**Conflict of interest**

The authors declare no conflict of interest.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrad.2021.02.021.

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