Assessment of the role of the Edinburgh dysphagia score in referral triage in a national service evaluation of the urgent suspected upper gastrointestinal cancer pathway

Kamran, Umair; King, Dominic; Banks, Matthew; Nylander, David ; Shetty, Sharan ; Hebbar, Srisha; Ransford, Rupert ; Mitchell, David ; Williams, Matthew ; Gupta, Sanjay ; Cheung, Danny; Baker, Graham; Rees, James; Fox, Mark ; Ashall, Barbara ; Barker, Sophie ; Greenaway, John ; Jones, Miriam ; Caffrey, Matthew ; Kadri, Sudarshan

DOI:
10.1111/apt.16811

Assessment of the role of the Edinburgh dysphagia score in referral triage in a national service evaluation of the urgent suspected upper gastrointestinal cancer pathway.

Authors List

[1]Umair Kamran, Gastroenterology Research Fellow, umair.kamran1@nhs.net

[1]Dominic King, Gastroenterology Research Fellow, Dominic.King@nhs.net

[2]Matthew Banks, Consultant Gastroenterologist, matthew.banks2@nhs.net

[3]David Nylander, Consultant Gastroenterologist, david.nylander@nhs.net

[4]Sharan shetty, Consultant Gastroenterologist , sharan.shetty@nhs.net

[5]Srisha Hebbar, Consultant Gastroenterologist , srisha.hebbar@nhs.net

[6]Rupert Ransford, Consultant Gastroenterologist, Rupert.Ransford@wvt.nhs.uk

[7]David Mitchell, Consultant Gastroenterologist, David.Mitchell@chsft.nhs.uk

[8]Matthew Williams, Consultant Gastroenterologist, matthew.williams@jpaget.nhs.uk

[9]Sanjay Gupta, Consultant Gastroenterologist, sanjay.gupta11@nhs.net

[10]Danny Cheung, Consultant Gastroenterologist, danny.cheung@nhs.net

[10]Graham Baker, Consultant Gastroenterologist, graham.baker1@nhs.net

[10]James Rees, Consultant Gastroenterologist, jamesrees@nhs.net

[11]Mark Fox, Consultant Gastroenterologist, Mark.fox@sthk.nhs.uk

[11]Barbara Ashall, Lead Upper Gastrointestinal Cancer Nurse Specialist,

barbara.ashall@sthk.nhs.uk

[12]Sophie Barker, Consultant Gastroenterologist, Sophie.Barker@stgeorges.nhs.uk

[13]John Greenaway, Consultant Gastroenterologist, johngreenaway@nhs.net

[14]Miriam Jones, Macmillan Upper Gastrointestinal Cancer Nurse Specialist, miriam.jones@nhs.net

[15]Matthew Caffrey, Nurse Endoscopist, matthew.caffrey@nhs.net

[16]Sudarshan Kadri, Consultant Gastroenterologist, Sudarshan.Kadri@uhl-tr.nhs.uk

[17]Michael Glynn, Consultant Gastroenterologist, michaelglynn@nhs.net

[18]James Evans, Consultant Gastroenterologist, jamesevans1@nhs.net

[19]Tony C Tham, Consultant Gastroenterologist , tctham1234@gmail.com

[20]Nicola J Adderley, Lecturer in Health Informatics and Epidemiology, N.J.Adderley@bham.ac.uk

[1]Nigel Trudgill, Consultant Gastroenterologist , nigel.trudgill@nhs.net

Affiliations

[1]Department of Gastroenterology, Sandwell and West Birmingham NHS Trust, United Kingdom.

[2]University College London Hospitals NHS Foundation Trust, United Kingdom.

[3]The Newcastle Upon Tyne Hospitals NHS Foundation Trust, United Kingdom.

[4]The Dudley Group NHS Foundation Trust, United Kingdom.

[5]University Hospitals of North Midlands NHS Trust, United Kingdom.

[6]Wye Valley NHS Trust, United Kingdom.

[7]City Hospitals Sunderland NHS Foundation Trust, United Kingdom.

[8]James Paget University Hospitals NHS Foundation Trust, United Kingdom.

[9]Croydon Health Services NHS Trust, United Kingdom.

[10]Worcestershire Acute Hospitals NHS Trust, United Kingdom.

[11]St Helens and Knowsley Teaching Hospitals NHS Trust, United Kingdom.

[12]St George's University Hospitals NHS Trust, United Kingdom.

[13]South Tees Hospitals NHS Foundation Trust, United Kingdom.

[14]Hampshire Hospitals NHS Foundation Trust, United Kingdom.

[15]Wirral University Teaching Hospital NHS Foundation Trust, United Kingdom.

[16]University Hospitals of Leicester NHS Trust, United Kingdom.

[17]Barts Health NHS Trust, United Kingdom.

[18]East & North Herts NHS Trust, United Kingdom.

[19]Ulster Hospital, Northern Ireland, United Kingdom.

[20]Institute of Applied Health Research, University of Birmingham, United Kingdom.

Group name

Upper GI cancer two week wait study group

Corresponding author

Dr Nigel Trudgill, Consultant Gastroenterologist, Sandwell and West Birmingham NHS Trust, B17 4HJ. United Kingdom.

nigel.trudgill@nhs.net

Funding declaration

Nothing to declare.

Conflicts of Interests:

No conflict of interest.

Author contributions:

Study concept and design was jointly conceived by UK, DK and NT. All co-authors participated in data collection. UK and NA analysed the data. UK and NT drafted manuscript and it was critically revised and approved by all authors.

Copyright/license for publication

Transparency statement

The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Word count

Main document 2720

Summary

Background

The British Society of Gastroenterology has recommended the Edinburgh Dysphagia Score (EDS) to risk stratify dysphagia referrals during the endoscopy COVID recovery phase.

Aims

External validation of the diagnostic accuracy of EDS and exploration of potential changes to improve its diagnostic performance.

Methods

A prospective multicentre study of consecutive patients referred with dysphagia on an urgent suspected upper gastrointestinal (UGI) cancer pathway between May 2020 and February 2021. The sensitivity and negative predictive value (NPV) of EDS were calculated. Variables associated with UGI cancer were identified by forward stepwise logistic regression and a modified Cancer Dysphagia Score (CDS) developed.

Results

1301 patients were included from 19 endoscopy providers; 43% male; median age 62(IQR 51-73) years. 91(7%) UGI cancers were diagnosed, including 80 oesophageal, 10 gastric and one duodenal cancer. An EDS ≥3.5 had a sensitivity of 96.7(95% CI 90.7-99.3)% and a NPV of 99.3(97.8-99.8)%. Age, male sex, progressive dysphagia and unintentional weight loss >3kg were positively associated and acid reflux and localisation to the neck were negatively associated with UGI cancer. Dysphagia duration <6 months utilised in EDS was replaced with progressive dysphagia in CDS. CDS ≥5.5 had a sensitivity of 97.8(92.3-99.7)% and NPV of 99.5(98.1-99.9)%. Area under receiver operating curve was 0.83 for CDS, compared to 0.81 for EDS.

Conclusions

In a national cohort, the EDS has high sensitivity and NPV as a triage tool for UGI cancer. The CDS offers even higher diagnostic accuracy. The EDS or CDS should be incorporated into urgent suspected UGI cancer pathway.

Introduction

Around 16,000 patients are diagnosed with upper gastrointestinal (UGI) cancer each year in the UK.[1,2] UGI cancer often has a poor prognosis with only 17% and 21% surviving for 5 years after an oesophageal and gastric cancer diagnosis respectively.[3] In the UK, patients suspected of having UGI cancer are referred on an urgent suspected cancer two week wait (2WW) pathway, direct to endoscopy or an outpatient clinic. In 2018/19, 190,000 patients were referred on the UGI 2WW pathway in the UK[4], but only 3% were actually diagnosed with cancer.[5] Dysphagia is an important predictor of UGI cancer[6,7] and the National Institute for Health and Care Excellence (NICE) in the UK recommends that direct, open access UGI endoscopy should be offered to all patients with dysphagia within two weeks.[8] However, it has been reported that up to 15% of patients referred with dysphagia in the UK do not have actual difficulty swallowing and less than 10% are diagnosed with UGI cancer.[9] This results in significant pressures on endoscopy services to achieve these national waiting time targets and may delay UGI cancer diagnosis in patients investigated outside the 2WW pathway.

During the first wave of the COVID-19 pandemic in the UK in April 2019, the British Society of Gastroenterology (BSG) recommended that all 2WW referrals should be triaged by senior clinicians and the Edinburgh dysphagia score (EDS) used to prioritise patients with dysphagia for urgent endoscopy.[5] The EDS was devised in 2010 for risk stratification of patients with symptoms of dysphagia, with those with an EDS ≥3.5 at higher risk of oesophageal cancer.[10] Predictors of oesophageal cancer included age, sex, unintentional weight loss > 3kg, localisation to the neck, duration of symptoms and reflux symptoms. The EDS was further validated in a single centre study of 1775 patients and reported to have a sensitivity of 98.4% and negative predictive value of 98.0%.[11]

We conducted a national service evaluation of the UGI cancer 2WW referral pathway during the recovery phase of COVID-19 and prospectively validated EDS performance in a cohort of patients referred with dysphagia.

Methodology

Study population and data collection

This study included consecutive adult patients referred with symptoms of dysphagia on a 2WW UGI cancer pathway, to the 19 participating providers across the UK, between May 2020 and February 2021. All referrals were triaged on the telephone by consultant gastroenterologists, consultant UGI surgeons, nurse endoscopists or clinical nurse specialists in UGI cancer or endoscopy. A standardised anonymised data collection tool on a Microsoft Excel spreadsheet was used by all providers, which allowed automatic calculation of the EDS and included a decision aid to guide prioritisation of endoscopy or alternate investigations if no endoscopy capacity, based on the BSG recovery document.[5] Data on additional clinically relevant variables identified from a literature search were also collected.[11,12] Variables included patient demographics (age, sex, smoking status), symptoms (dysphagia or odynophagia, duration of dysphagia >6 months, localisation of dysphagia to neck, progressive or intermittent symptoms of dysphagia, unintentional weight loss >3kg and reflux symptoms). Data on triage decision details and investigation results was also recorded.

Referrals were triaged to one of the following pathways: EDS ≥3.5- 2WW endoscopy; EDS < 3.5 and patient age >55 years- urgent (non 2WW) endoscopy; EDS < 3.5 and patient age <55 years- routine endoscopy; and no investigation if no true dysphagia or other indication for investigations. Alternative investigations included CT scan and barium swallow.

Exclusion criteria included: patients not referred with symptoms of dysphagia, if investigations were declined by patients, if patients were not fit for any investigation, if patients did not have true dysphagia or other symptoms worthy investigation, if investigation results not available on 28th February 2021 and if a non-UGI cancer was diagnosed.

Aims

The primary aims of this study were to validate the diagnostic accuracy of EDS and to assess if any amendments could potentially improve its diagnostic performance, using patient variables associated with UGI cancer.

Statistical analysis and development of cancer dysphagia score

Statistical analysis was performed using *Stata Statistical Software Release 16*: StataCorpLLC. Categorical variables were summarised as number and percentages and continuous variables as median and interquartile range (IQR). The $\chi 2$ test was used to compare categorical variables and the t-test or nonparametric test (Mann-Whitney U) were used to compare continuous variables as appropriate. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of EDS at a cut off of ≥3.5 were calculated.

Univariable and multivariable logistic regression models explored the association of study variables with an UGI cancer diagnosis. The dependent variable was the occurrence of UGI cancer and the exploratory variables included age as a continuous variable and sex, unintentional weight loss >3kg, localisation of dysphagia to neck, progressive dysphagia, presence of reflux symptoms, history of smoking and duration of symptoms of <6months as categorical variables. The variables with statistical significance on univariate analysis were included in multivariable analysis. Missing data were treated as complete case analysis and any observation with a missing value for the variable of interest was excluded and only complete observations were included in the logistic regression analysis.

To develop a modified prediction model, candidate variables were selected using a forward stepwise regression approach. Forward stepwise regression is a method of fitting regression models in which the choice of predictive variables is carried out by an automatic procedure. Starting with no variables in the model, the addition of each variable using a chosen model fit criterion ($p<0.1$) is tested, adding the variable whose inclusion gives the most statistically significant improvement of the fit, and repeating this process until none improves the model to a statistically significant extent. The model was internally validated by bootstrap resampling,

which used 1000 random samples drawn with replacement from the original dataset.[13,14] Regression coefficients of the selected variables from multivariable logistic regression analysis were used to develop a scoring system following the methodology described by Sullivan et al.[15] and explained in supplementary material 1.

Receiver operating characteristic (ROC) curves were produced for both the EDS and the modified prediction model and the discriminative ability of both models was compared using the area under receiver operating curve (AUC), equivalent to *c*-statistics. Calibration plots were produced to examine the performance of the models, displaying observed probability by deciles of predicted probability. LOWESS (Locally weighted scatterplot smoothing) function was used to create a smooth line through the scatter plot to display relationship between expected and observed probabilities and foresee trends. Calibration slope gradient and calibration in the large (CITL) were reported. Calibration slope close to 1 and CITL close to 0 represent good calibration.

Subgroup analyses were performed to compare the sensitivity of both scoring systems at age cut offs of 70 and 60 years.

Patient and public involvement

There was no patient and public involvement in this study.

Ethics

As determined by the national decision-making tool of the NHS Health Research Authority and the Medical Research Council, this study was part of a service evaluation and did not require ethics committee approval. Each participating provider attained local institutional approval prior to data collection.

Results

Study subjects

A total of 1301 patients were included from 19 providers across the UK. A flow chart of the patients included in the study is shown in Figure 1. 69% (n=910) of patients were triaged to 2WW endoscopy, 20% (n=257) to urgent (non 2WW) endoscopy, 5% (n=66) to routine endoscopy, 2% (n=25) to CT scan and 3% (n=43) to barium swallow.

91 (7%) patients were diagnosed with UGI cancer, including 80 oesophageal, 10 gastric and one duodenal cancer. Prevalence of UGI cancer in the patients triaged to 2WW endoscopy and urgent (non 2WW) endoscopy was 9.2% and 2.3% respectively. One cancer was diagnosed in patients triaged to Barium swallow (2.3%) and no UGI cancer was diagnosed in patients triaged to routine endoscopy or CT scan. The baseline characteristics and the symptoms of patients with and without an UGI cancer diagnosis are shown in Table 1. Patients with UGI cancer were more commonly male and reported more often progressive symptoms, a history of unintentional weight loss, less commonly had symptoms localised to the neck or reflux symptoms and had a higher median EDS.

The diagnostic accuracy of the Edinburgh Dysphagia Score

An EDS ≥3.5 had a sensitivity of 96.7(95% CI 90.7-99.3)%, a specificity of 32.6(30.0-35.4)%, a PPV of 9.7(7.9-11.9)% and a NPV of 99.3(97.8-99.8)%. 3(3%) UGI cancers were diagnosed in patients with an EDS <3.5 (one gastric cancer with EDS 2.5, two oesophageal cancers with EDS 1.5). The AUC for EDS was 0.81(0.76-0.85).

Univariable and multivariable logistic regression analysis of factors associated with UGI cancer and development of a new Cancer Dysphagia Score

The results of univariable and multivariable regression analysis of factors associated with UGI cancer are shown in Table 2. Increasing age, sex, unintentional weight loss > 3kg, localisation of dysphagia to neck, progressive symptoms and reflux symptoms were associated with UGI cancer and retained in the prediction model. However, duration of dysphagia <6 months and history of smoking were excluded in forward stepwise selection regression analysis. Weighted points were

assigned proportional to the regression coefficient values of selected variables to develop the cancer dysphagia score (CDS), as explained in supplementary material 1. This had strong discriminative ability on internal validation, as measured by AUC (0.83(95% CI 0.79-0.87)).

A CDS cut off of ≥5.5 had a sensitivity of 97.8(92.3-99.7)%, a specificity of 31.2(28.7-34.0)%, a PPV of 9.7(7.8-11.8)% and NPV of 99.5(98.1-99.9)%. Two (2.2%) oesophageal cancers were diagnosed in patients with a CDS <5.5. Both patients were female (age <50 years) and presented with more than 6 months history of dysphagia without weight loss (CDS 2.0). One patient had associated symptoms of chest pain. Both were triaged to urgent endoscopy which was performed within a month of triage.

Comparison between the Edinburgh Dysphagia Score and the Cancer Dysphagia Score

The variables and points allocated to each of the risk categories for both EDS and CDS are presented in Table 3 and a comparison of the ROC curves and AUC is shown in Figure 2. The AUC for the CDS (0.829) is higher than the AUC for EDS (0.805). Calibration plots are presented in Figure 3. Slope gradients of 1.00 and CITL of 0.00 represent excellent performance for both models. When applied to the overall cohort, the prevalence of UGI cancer in high and low risk categories based on the CDS and EDS is shown in Table 4. The CDS is more sensitive than the EDS with less cancers in the low risk group, but this difference is only based on one UGI cancer that is high risk on the CDS but low risk on the EDS.

On subgroup analyses, sensitivity and NPV of CDS ≥5.5 and EDS ≥3.5 were 100% at the age cut off ≥70 years. However, CDS was more sensitive than EDS in identifying UGI cancer patients in those less than 70 years of age (CDS 94.59% vs EDS 91.89%) and in those less than 60 years of age (CDS 86.67% vs EDS 80%).

Discussion

Given the relatively low diagnostic yield (3%) of the current 2WW UGI cancer referral pathway in the UK and the pressures on endoscopy units given the COVID 19 pandemic and addressing consequent waiting issues, the availability of an effective triage tool will be of great value in prioritising patients for endoscopy. In this multicentre, prospective study, we have shown that the EDS and the updated CDS are just such triage tools with very high sensitivities and negative predictive values. Applying the CDS to the 2WW referral population studied, up to 30% of dysphagia referrals could have been safely investigated more routinely.

The EDS was initially developed to triage patients with dysphagia into high and low risk groups.[10] The prevalence of cancer in this study was 10% and 14% in the derivation and validation cohorts, respectively, and the AUC for the EDS was reported to be 0.70 in the validation cohort. However, this study had a number of limitations including a relatively small sample size, being from a single provider and retrospective. Finally, data were extracted from the primary care referral forms for both the derivation and validation of the EDS rather than from direct contact with the patient. An audit of dysphagia referrals to a district general hospital reported that up to 15% of patients referred on a cancer pathway did not have true dysphagia and relying on data from referral forms may therefore have limitations.[9] The present study is the largest prospective multicentre study of the EDS in 2WW referrals. Senior clinicians collected information directly from patients using a structured data collection tool during telephone triage. 5% of patients referred on the 2WW pathway did not have true swallowing difficulties or had a brief episode with spontaneous resolution of symptoms and hence did not require any investigation. Unlike the study that developed EDS[10], in the present study the duration of symptoms was not found to be associated with UGI cancer, and a strong positive association was found between UGI and progressive dysphagia. A single provider study of 2000 patients with dysphagia has also reported a positive association of progressive symptoms with UGI cancer [11]. Progressive dysphagia increased the odds of having UGI cancer more than two-fold and was therefore selected as a predictor in the updated CDS. The AUC for the CDS was 0.83 (compared to 0.81 for the EDS), with small improvements in sensitivity and NPV compared with EDS.

According to NICE recommendations in the UK, 2WW endoscopy should be offered to patients of any age over 18 referred with dysphagia to exclude cancer.[8] However, dysphagia is a common symptom in the community with a prevalence of up to 16% in the general population[16,17], and despite it being considered an important "alarm" feature, only 2%-8% of those referred with dysphagia for investigation are diagnosed with UGI cancer.[18–20] We found that the CDS, at a threshold of ≥5.5, clearly identified a much higher risk group of patients with dysphagia with a prevalence of UGI cancer of 9.7%. Although both CDS and EDS were highly sensitive to detect UGI cancers in elderly patients over 70 years of age, the sensitivity of CDS was higher in identifying the higher risk patients in younger age groups. However, two female patients (age <50 years) were mis-categorised as low risk by both CDS and EDS and were found to have oesophageal cancer. It is important that although high risk patients with EDS ≥3.5 (or CDS ≥5.5) as a smaller cohort with a higher prevalence of cancer can be investigated more urgently within two weeks, as recommended by the BSG and NHS England, patients at lower risk (but not zero risk) of UGI cancer are safety netted in primary care and their investigation pathway should be reviewed if their symptoms and CDS get worse.[21]

Although urgent investigation pathways for dysphagia are focused on cancer detection, there are important non-malignant causes of dysphagia including eosinophilic oesophagitis, benign oesophageal strictures and achalasia, which can have a major impact on patients' quality of life. Although effective treatments are available for these conditions, such patients may not be categorised as higher risk on risk stratification systems and there is a risk of delayed diagnoses for those not investigated on an urgent pathway.

This study has a number of limitations. The absence of long term follow up data limited the ability to assess the outcomes for a small number of patients (5%) who were triaged to no investigations due to the absence of true dysphagia or a brief episode of symptoms which had spontaneously resolved. During the pandemic it was not possible to endoscope such patients with clinically an extremely low risk of UGI cancer. These patients were consequently excluded from the analysis but it is possible that some might have re-presented with similar symptoms at a later date and

been diagnosed with UGI cancer. Although a standardised data collection tool was used to prospectively collect information, clinical judgment was required to interpret the information provided on the telephone by the patient bringing a risk of information or measurement bias. Progressive dysphagia was found to be a predictor of UGI cancer and was used in the development of the CDS, but this information was based on a patient's perception of worsening in their swallowing since the start of their symptoms, rather than a functional grading system to assess the severity of dysphagia. We suggest that future studies should consider using a validated dysphagia grading system for consistency in the interpretation of progressive dysphagia. The data for this study was collected directly from the patients by experienced clinicians over the telephone. This was an important process to prioritise scarce endoscopy resources during the first wave of the COVID 19 pandemic in the UK.[5] It has not been possible in UK hospitals to continue to provide the clinical time for telephone triage of all 2WW referrals, given the partial recovery of endoscopy services and competing demands on clinical time. There are still considerable endoscopy diagnostic backlogs due to COVID throughout the UK and resource prioritisation is still important. It has been proposed that the EDS is used by primary care practitioners in England to prioritise referrals with dysphagia [21]. However, as previously noted, primary care practitioners may be less able to accurately recognise dysphagia and other symptoms as experienced gastroenterological clinicians [9] and the EDS or CDS should be studied when utilised in primary care prior to referral for endoscopy to ensure it performs as well in this setting as it does in secondary care telephone triage. This study was carried out during the COVID19 pandemic and it is possible that primary care practitioners had a lower threshold for referral on the 2WW pathway, given difficulty accessing secondary care opinions through other routes. However, the overall cancer rate was 7% and this is similar to historic cancer rates for 2WW UGI cancer referrals.[22] Finally, although the CDS showed a high sensitivity and discriminative ability on internal validation, it has not been externally validated.

Conclusion

In a multi-centre prospective evaluation of patients referred on an urgent cancer pathway from primary care with dysphagia, the EDS had a high sensitivity and NPV as a triage tool for UGI

cancer. The sensitivity and NPV can be improved further in the CDS. The CDS or EDS should be incorporated into the 2WW UGI cancer pathway to prioritise those at highest risk of cancer.

Acknowledgement

We are grateful to the Clinical Services and Standards Committee of the BSG for their support and help promoting this service evaluation. We are also grateful to Sara Brogden (Lead Non-medical Endoscopist, University College London Hospitals NHS Foundation Trust, United Kingdom), Samantha Horley (Endoscopy Nurse Practitioner, The Dudley Group NHS Foundation Trust, United Kingdom), Suzanne Friday (Advanced Nurse Practitioner, Upper Gastrointestinal Cancer Nurse, Croydon Health Services NHS Trust, United Kingdom) and Tracey Noakes (Upper Gastrointestinal Cancer Nurse Specialist, James Paget University Hospitals NHS Foundation Trust, United Kingdom) for their help in data collection.

Funding declaration

Nothing to declare.

References

1 Stomach cancer statistics. 2015.https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/stomach-cancer (accessed 22 Jun 2021).

2 Oesophageal cancer statistics. 2015.https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/oesophageal-cancer (accessed 22 Jun 2021).

3 OFFICE FOR NATIONAL STATISTICS. *CANCER SURVIVAL IN ENGLAND: Adult, Stage at Diagnosis and Childhood - Patients Followed Up... to 2018*. 2019.

4 Freedman J , Ubaldo AR , Dai D , et al . Waiting times for suspected and diagnosed cancer patients 2018-19 annual report. NHS England, 2019. https://www.england.nhs.uk/statistics/wp-content/uploads/sites/2/2019/07/Cancer-Waiting-Times-Annual-Report-201819-Final-1.pdf (accessed 23 Jun 2021).

5 Penman I , Edwards C , Coleman M , et al . GI Endoscopy Activity and COVID-19: Next steps [Internet]. British Society of Gastroenterology, 2020. Available: https://www.bsg.org.uk/covid-19-advice/gi-endoscopy-activity-and-covid-19-next-steps/ (accessed 23 Jun 2021).

6 Kapoor N. Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. Gut. 2005;**54**:40–5. doi:10.1136/gut.2004.039438

7 Astin MP, Martins T, Welton N, *et al.* Diagnostic value of symptoms of oesophagogastric cancers in primary care: a systematic review and meta-analysis. *Br J Gen Pract* 2015;**65**:e677–91.

8 Recommendations organised by site of cancer | Suspected cancer: recognition and referral | Guidance | NICE. https://www.nice.org.uk/guidance/ng12/chapter/1-Recommendations-organised-by-site-of-cancer#upper-gastrointestinal-tract-cancers (accessed 23 Jun 2021).

9 Melleney EM-A, Subhani JM, Willoughby CP. Dysphagia referrals to a district general hospital gastroenterology unit: hard to swallow. *Dysphagia* 2004;**19**:78–82.

10 Rhatigan E, Tyrmpas I, Murray G, *et al.* Scoring system to identify patients at high risk of oesophageal cancer. *Br J Surg* 2010;**97**:1831–7.

11 Murray IA, Palmer J, Waters C, *et al.* Predictive value of symptoms and demographics in diagnosing malignancy or peptic stricture. *World J Gastroenterol* 2012;**18**:4357–62.

12 Lee C-H, Lee J-M, Wu D-C, *et al.* Independent and combined effects of alcohol intake, tobacco smoking and betel quid chewing on the risk of esophageal cancer in Taiwan. *Int J*

Cancer 2005;**113**:475–82.

13 Steyerberg EW, Harrell FE Jr, Borsboom GJ, *et al.* Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *J Clin Epidemiol* 2001;**54**:774–81.

14 Steyerberg EW, Bleeker SE, Moll HA, *et al.* Internal and external validation of predictive models: a simulation study of bias and precision in small samples. *J Clin Epidemiol* 2003;**56**:441–7.

15 Sullivan LM, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: The Framingham Study risk score functions. *Stat Med* 2004;**23**:1631–60.

16 Eslick GD, Talley NJ. Dysphagia: epidemiology, risk factors and impact on quality of life--a population-based study. *Aliment Pharmacol Ther* 2008;**27**:971–9.

17 Cho Y-S, Choi M-G, Jeong J-J, *et al.* Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Asan-si, Korea. *Am J Gastroenterol* 2005;**100**:747–53.

18 Qureshi NA, Hallissey MT, Fielding JW. Outcome of index upper gastrointestinal endoscopy in patients presenting with dysphagia in a tertiary care hospital-A 10 years review. BMC Gastroenterology. 2007;**7**. doi:10.1186/1471-230x-7-43

19 Vakil N, Moayyedi P, Brian Fennerty M, *et al.* Limited Value of Alarm Features in the Diagnosis of Upper Gastrointestinal Malignancy: Systematic Review and Meta-analysis. Gastroenterology. 2006;**131**:390–401. doi:10.1053/j.gastro.2006.04.029

20 Kapoor N, Bassi A, Sturgess R, *et al.* Predictive value of alarm features in patients referred to a rapid access upper gastrointestinal cancer service (RAUGICS). Gastroenterology. 2003;**124**:A181. doi:10.1016/s0016-5085(03)80901-0

21 Urgent cancer diagnostic services during COVID-19 V2.0 January 2021. https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/01/C0789-Urgent-cancer-diagnostic-services-pathways-160221-.pdf(accessed 9 Sep 2021).

22 Thorne K, Hutchings HA, Elwyn G. The Two-Week Rule for NHS Gastrointestinal Cancer Referrals: A Systematic Review of Diagnostic Effectiveness. The Open Colorectal Cancer Journal. 2009;2:27–33. doi:10.2174/1876820200902010027

Tables

Table 1 The demographic details and symptoms at triage of study patients, stratified by a diagnosis of upper gastrointestinal cancer

Variables	Total	Non-UGI cancer cohort	UGI cancer cohort	P-value
Number	1301	1210	91	
Age, median (IQR)	62 (51, 73)	62 (51, 73)	71 (61, 76)	<0.001
Male	554 (42.7%)	488 (40.4%)	66 (72.5%)	<0.001
History of smoking*	437 (34.9%)	399 (34.3%)	38 (42.7%)	0.11
Duration of dysphagia <6 months	908 (69.8%)	843 (69.7%)	65 (71.4%)	0.72
Dysphagia localised to neck	314 (24.1%)	305 (25.2%)	9 (9.9%)	<0.001
Progressive dysphagia**	577 (45.6%)	519 (44.1%)	58 (66.7%)	<0.001
Unintentional weight loss >3kg	377 (29.0%)	323 (26.8%)	54 (59.3%)	<0.001
Reflux symptoms	407 (31.3%)	391 (32.3%)	16 (17.6%)	0.003
Other associated symptoms				
Abdominal mass	2 (0.2%)	2 (0.2%)	0 (0.0%)	0.12

Chest pain	45 (3.5%)	38 (3.1%)	7 (7.7%)	
Dyspepsia	643 (49.4%)	603 (49.8%)	40 (43.4%)	
Globus	38 (2.9%)	38 (3.1%)	0 (0.0%)	
Haematemesis/melaena	4 (0.3%)	4 (0.3%)	0 (0.0%)	
Throat clearing/cough	17 (1.3%)	15 (1.2%)	2 (2.2%)	
EDS score	5 (3-6)	4 (2.5-6)	7 (6-8)	<0.001

*Data not available for 49 patients.

**Data not available for 30 patients.

UGI: upper gastrointestinal cancer, EDS: Edinburgh Dysphagia Score, IQR: Interquartile range.

480 **Table 2 Univariable and multivariable logistic regression analysis of factors**
481 **associated with a diagnosis of upper gastrointestinal cancer.**
482

Variables	**Unadjusted** **OR (95% CI)**	**Adjusted** **OR (95% CI)**	**P-value***	**Regression coefficients**
Age	1.05 (1.03-1.06)	1.05 (1.03-1.06)	<0.001	0.04
Male	3.89 (2.42-6.25)	3.95 (2.36-6.58)	<0.001	1.40
History of smoking	1.43 (0.92-2.20)			
Unintentional weight loss >3kg	3.99 (2.58-6.19)	3.28 (2.02-5.31)	<0.001	1.22
Dysphagia localised to neck	0.33 (0.16-0.66)	0.26 (0.12-0.57)	0.001	-1.40
Duration of dysphagia <6 months	1.09 (0.68-1.75)			
Progressive dysphagia	2.54 (1.60-4.02)	2.30 (1.39-3.79)	0.001	0.83
Reflux	0.45 (0.26-0.78)	0.47 (0.25-0.88)	0.018	-0.73

483

484 49 subjects were excluded from the regression analyses due to missing data.

485 *p value of adjusted odds ratio.

486 OR: odds ratio; CI: confidence interval.

487

Table 3 Variables and the points allocated to each of the risk category in Edinburgh Dysphagia Score and Cancer Dysphagia Score.

Variables	Edinburgh Dysphagia Score	Cancer Dysphagia Score
Age (years)		
<39	0	0
40-49	4	2
50-59	5	4
60-69	6	6
70-79	7	8
80-89	8	10
90-99	9	12
Sex		
Female	-1	0
Male	0	6
Unintentional weight loss >3kg		
No	0	0
Yes	2	5.5
Duration of symptoms ≥ 6 months		
No	0	Not included
Yes	-1.5	
Localisation of dysphagia to neck		
No	0	0
Yes	-2	-6
Acid reflux symptoms		
No	0	0
Yes	-1	-3
Progressive dysphagia		
No	Not included	0
Yes		3.5

Table 4 The prevalence of upper gastrointestinal cancer in the high and low risk categories of the Cancer Dysphagia Score and the Edinburgh Dysphagia Score.

Scoring system	Risk category	Number of patients	Number of cancers	Prevalence (95% Confidence interval)
Cancer dysphagia score (CDS)	High risk (CDS ≥5.5)	920	89	9.7% (7.9-11.8)
	Low risk (CDS <5.5)	381	2	0.5% (0.1-1.8)
Edinburgh dysphagia score (EDS)	High risk (EDS ≥3.5)	903	88	9.8% (7.9-11.9)
	Low risk (EDS <3.5)	398	3	0.8% (0.2-2.2)

Figures

Figure 1 Flow chart of patients in the study.

2WW: two week wait; UGI: upper gastrointestinal.

Figure 2 Comparison between receiver operating curves for the Edinburgh Dysphagia Score and the Cancer Dysphagia Score.

AUC: area under the curve, EDS: Edinburgh Dysphagia Score, CDS: Cancer Dysphagia Score

Figure 3 Calibration plots for the Edinburgh Dysphagia Score and the Cancer Dysphagia Score.

CITL: Calibration in the large, LOWESS: Locally weighted scatterplot smoothing

Supplementary material 1

Development of a new cancer dysphagia scoring system from the multivariable logistic regression model

527