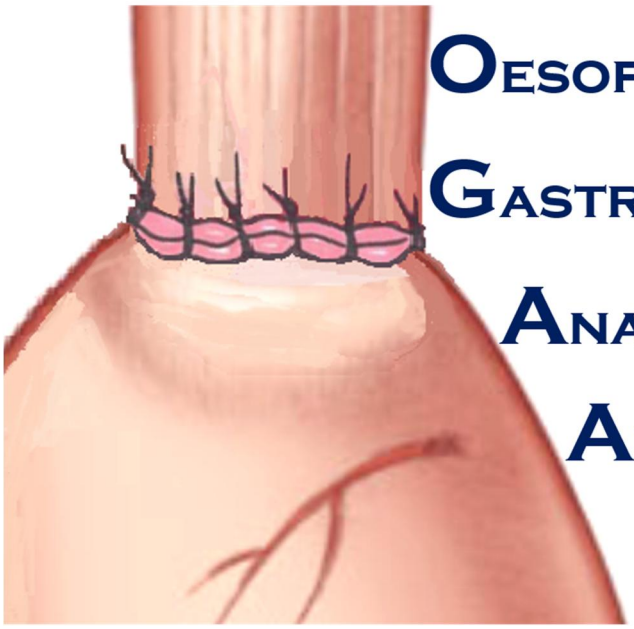


Oesophago-Gastric Anastomosis Audit

Oesophago-Gastric Anastomosis Audit Protocol 2018

www.ogaa.org.uk

Email: OGanastomosisaudit@gmail.com

@OGAAudit

Contents

Steering Group

Name	Organisation	Email
Mr Richard Evans	General Surgery Trainee – West Midlands Deanery	rptevans@doctors.org.uk
Mr Pritam Singh	General Surgery Trainee – West Midlands Deanery	pritam@cantab.net
Mr Sivesh Kamarajah	University of Birmingham	SXK206@student.bham.ac.uk
Mr James Bundred	University of Birmingham	JXB473@student.bham.ac.uk
Dr Dmitri Nepogodiev	University of Birmingham	D.Nepogodiev@bham.ac.uk
Mr Imran Mohamed	General Surgery Trainee – West Midlands Deanery	imranmohamed@doctors.org.uk
Mr Benjamin Jefferies	University of Birmingham	bjj416@student.bham.ac.uk
Mr Kwabena Siaw-Acheampong	University of Birmingham	kxs598@student.bham.ac.uk
Miss Devangi Madani	University of Birmingham	dxm519@student.bham.ac.uk
Ms Siobhan McKay	General Surgery Trainee – West Midlands Deanery	mckay.siobhan@gmail.com
Mr Kasun Wanigsooriya	General Surgery Trainee – West Midlands Deanery	kasun87@live.co.uk
Dr Tony Whitehouse	University Hospitals Birmingham NHS Foundation Trust	Tony.Whitehouse@uhb.nhs.uk
Prof Derek Alderson	Royal College of Surgeons England	dalderson@rcseng.ac.uk
Mr James Gossage	Guy's and St. Thomas' NHS Foundation Trust	james.gossage@gstt.nhs.uk
Prof Richard van Hillegersberg	UMC Utrecht	R.vanHillegersberg@umcutrecht.nl
Mr Ravinder Vohra	Nottingham University Hospitals NHS Trust	Ravinder.Vohra@nuh.nhs.uk
Mr Ewen Griffiths	University Hospitals Birmingham NHS Foundation Trust	ewen.griffiths@uhb.nhs.uk

Supporting organisations

West Midlands Surgical Research Collaborative

Providing REDCap Access

Academic Department of Surgery

Association of Laparoscopic Surgeons GB&I

Lay Summary

Oesophageal cancer is the sixth leading cause of cancer related death affecting up to 450,000 people globally each year. The main surgical treatment for oesophageal cancer is oesophagectomy - an operation to remove part of the oesophagus and stomach followed by a join between the remaining oesophagus and stomach. The techniques used to create this join vary and involve various stitching methods and stapling devices. A proportion of these joins will breakdown and this can result in the patients becoming very unwell with a risk of death. The strategies to manage this complication also vary and include:

- No surgical intervention
- An endoscopic intervention or
- A further surgical procedure.

This international audit will look at the rates of breakdown of these joins, commonly termed a 'leak', how they are managed and the effect on the patient outcomes. The information collected from this audit will help to develop recommendations on how to prevent and manage this serious complication.

Short Summary

Primary Audit Objectives

1- Quantify the incidence of anastomotic leak rate in an international multicentre audit which incorporates data from high and low volume centres and high and low income countries

2- Assess the variation in anastomotic leak rates internationally

3- Assess the relationship between anastomotic technique and optimal patient outcome – discharge home eating and drinking orally

4- Assess the relationship between anastomotic leak therapy and optimal patient outcome

Audit Standard

1- Anastomotic leak and conduit necrosis rate should be less than 13%

2- Major post-operative morbidity (Clavien Dindo Grade III or more) should be less than 35%.

3- 30 day mortality rate should be less than 5% and 90 day mortality rate should be less than 8%.

The audit standards were developed from the AUGIS (Association of Upper Gastrointestinal Surgeons) guidance, but they were modified using up to date evidence of oesophagectomy outcome from the recent publication by the ECCG (Esophagectomy Complications Consensus Group) (16, 21, 25).

A data collection protocol will identify patient demographics, operative and peri-operative details and outcome markers. Key outcome measures will include post-operative mortality, morbidity including grade of leak and length of stay. Management techniques used for anastomotic leaks will also be assessed (e.g. conservative management, oesophageal stent, endo-luminal VAC therapy and re-operation).

Methods

A nine month multicentre prospective audit will be performed globally starting in April 2018 and co-ordinated by University Hospitals Birmingham. This will include patients undergoing oesophagectomy over 6 months and encompassing a 90-day follow up period. A pilot data collection period will occur at University Hospitals Birmingham and 3 other UK hospitals in 2017**.** Sites will be required to pre-register for the audit and obtain local study approval prior to commencement of the study.

During the study sites will be required to record data contemporaneously via a dedicated encrypted server through the Research Electronic Data Capture (REDCap) web application secure online database. The REDCap database will provide a standardised data collection proforma assessing key information to answer the primary audit question. The report of the audit will be prepared in accordance with the guidelines as set by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies and STROCSS (Strengthening the Reporting of Cohort Studies in Surgery)(1,23). All unit results will be anonymised to all but the auditors and the specific unit. Unit results will not be shared with other units or the collaborators as a whole. The study will be defined as audit not research in accordance with the NHS Health research authority recommendations (Appendix 2).

Discussion

Data for this multicentre international audit will be collected by both surgeons and trainees to provide greater insight into the complexities of oesophagectomy and outcome. This audit may highlight trends in improved survival associated with specific operative techniques or specific management strategies to deal with leaks that can be further assessed and analysed through research to improve outcomes in oesophageal cancer.

Introduction

Oesophageal cancer is the sixth leading cause of cancer related mortality affecting up to 450,000 people globally each year. There are 2 histological types – squamous cell carcinoma and adenocarcinoma. While the incidence of squamous cell cancer is stable worldwide, the incidence of adenocarcinoma has risen dramatically in the western world in parallel with obesity over the last 30 years. Despite advances in modern treatment, 5-year survival remains at around 15 to 20%. Oesophagectomy is a mainstay in curative treatment for those with oesophageal cancer however the technique, particularly regarding operative technique and methods of reconstruction, and outcome varies greatly.

Anastomotic leakage following oesophagectomy is associated with high rates of morbidity and mortality. 30 day mortality in patients with a demonstrable leak can be as high as 17-35% whereas the 30 day mortality of patients with an intact anastomosis is 2-3% (2, 3). In addition, anastomotic leakage is known to increase length of hospital stay, reduced quality of life and be economically costly for the health service(4). There is also evidence that anastomotic leakage affects long term prognosis and is associated with reduced long term survival and increased recurrence rates (5).

Anastomotic leak rates are variable between surgeons, units and countries. Current practices demonstrate anastomotic leak rates between 1.8% and 18.2% (6-15). The largest of the recent studies by Kassis *et al* identified 7,595 oesophagectomies with a leak rate of 10.6% and Ryan *et al* identified 7,167 oesophagectomies with a trans-thoracic oesophagectomy leak rate of 9.8% and a trans-hiatal oesophagectomy leak rate of 12% (6, 7). However, until recently the definition of anastomotic leakage and gastric conduit necrosis have not be standardised across the surgical literature.

In 2015, the Esophagectomy Complications Consensus Group (ECCG) defined anastomotic leaks as *full-thickness defects involving the oesophagus, anastomosis, staple line or conduit, irrespective of the presentation or method of identification (21)*. In this classification, leaks were divided into three

types based on management strategy: type 1 leaks requiring no change in therapy, treated medically or with dietary modification; type 2 leaks requiring interventional but not surgical therapy (interventional radiology drain, stent, etc.); and type 3 leaks requiring surgical intervention.

Gastric conduit necrosis has also been classified by the ECCG Group, as when the gastric conduit becomes ischaemic and necrotic. Gastric conduit necrosis was further subclassified as: type 1 with focal gastric conduit necrosis , identified endoscopically and managed with increased monitoring and non-surgical therapy; type 2 as focal gastric conduit necrosis, identified endoscopically and not associated with a free anastomotic leak or conduit leak and treated surgically, but not requiring oesophageal diversion; and type 3 as extensive gastric conduit necrosis, treated with re-operation and resection of the necrotic stomach together with oesophageal diversion via cervical oesophagostomy.

The ECCG Group published data on 2,704 oesophageal resections between January 2015 and December 2016 (16), with data from 24 high volume oesophageal units in 14 countries. The indication for resection was malignancy in 95.6%, and neoadjuvant chemoradiation or neoadjuvant chemotherapy was given in 46.1% and 29.5% of cases respectively. The anastomotic leak rate was 11.4% (95% CI 10.2-12.6) with a rate of conduit necrosis of 1.3% (95% CI 0.7-1.7) (16). There was a high rate of open oesophagectomies n this study (52.1% cases), and a significant major complication rate with the upper limit of the 95% confidence interval being 35.6% (Clavien Dindo grade 3 or above).In a similar benchmark study from Schmidt *et al* including 13 high volume units over a 5 year period, outcomes from totally minimally invasive oesophagectomy (43.7% were 3 stage procedures) in low risk patients were reported. Anastomotic leakage in this cohort was 15.9% (24).

To date, no one technique for oesophageal anastomosis has been shown to be robustly beneficial, with numerous studies advocating varying techniques, comparing handsewn and mechanical options for anastomoses (17, 18). There is some evidence that a mechanical anastomosis using a linear stapler has a reduced leak rate and reduced stricture rate compared to a handsewn anastomosis.

However, results vary markedly between surgeons and units (19). Furthermore, there is evidence to suggest cervical anastomoses are associated with an increased leak rate compared to thoracic anastomoses (7, 20).

Prompt recognition of anastomotic leakage is critical and can expedite clinical intervention and potentially improve patient outcome. Early signs of anastomotic leakage include: tachycardia; pyrexia; raised white cell count; raised CRP; delirium; and cardiac arrhythmias, particularly atrial fibrillation. Late signs of anastomotic leakage include: bilious output from chest drain; acidosis; hypotension; and septic shock. The clinical management of leaks are controversial and depend on the site of the leak, size of the defect, perfusion of the gastric conduit and the clinical status of the patient. Small contained anastomotic leaks can be managed conservatively without surgery, where patients are kept nil by mouth, and given antibiotics and nasogastric drainage. Leaks that are not localised or that cause greater systemic upset are generally considered to be those that require some form of active intervention such as radiological drainage or treatment with either endoluminal VAC therapy, covered oesophageal stenting or re-thoracotomy, although there is little evidence of superiority of one technique over another. Large anastomotic leaks, especially if associated with severe sepsis or gastric conduit necrosis may require re-thoracotomy resection of the anastomosis and oesophageal diversion with cervical oesophagostomy. The main purpose of this international audit is to identify the incidence of leaks, identify when they are diagnosed and how they are specifically managed.

An international multicentre audit will enable a large volume of patient data to be obtained over a short time period when changes in unit policies are likely to be minimised. It will potentially obtain a more general overview of the variations in practice across units and countries. Surgical access and anastomosis technique have been continued areas of disagreement amongst oesophago-gastric surgeons and their influence on mortality and morbidity has long been disputed. This audit seeks to provide up to date information in the international variations in practice.

Aim

Primary Audit Question

1- Quantify the incidence of oesophago-gastric anastomotic leak rate in an international multicentre audit which incorporates data from high and low volume centres and high and low income countries.

2- Assess the variation in anastomotic leak rates internationally.

3- Assess the relationship between anastomotic technique and optimal patient outcome (defined as discharge home eating and drinking orally).

4- Assess the relationship between anastomotic leak therapy and optimal patient outcome.

Audit Standard

1- Anastomotic leak and conduit necrosis rate should be less than 13%.

2- Major post-operative morbidity (Clavien Dindo Grade III or more) should be less than 35%.

3- 30 day mortality rate should be less than 5% and 90 day mortality rate should be less than 8%.

The audit standards were developed from the AUGIS (Association of Upper Gastrointestinal Surgeons) guidance, but they were modified using up to date evidence of oesophagectomy outcome from the recent publication by the ECCG (Esophagectomy Complications Consensus Group) (16, 21, 25).

Primary Objective

The audit aims to identify trends in patient factors and differences in operative technique that influence outcome. This in turn will allow for the formulation of more detailed research.

Key outcomes will include:

- Anastomotic Leak rate as defined by the ECCG group

- All cause 30-day mortality

- All cause 90-day mortality

- 30-day complication rate defined by the ECCG group (21)

- Length of stay

- 30 day readmission

Methods

A global prospective audit of patients undergoing oesophagectomy over a 6 month period from April 2018 to October 2018. Patients will be followed up for 90 days after the date of surgical resection.

Registered units must include all patients undergoing oesophagectomy during the study period.

A 2 month pilot of 4 centres within the UK will be undertaken to finalise the detailed online case report forms. This will ensure that all relevant data is collected to achieve the goals of the audit.

Study Population

Inclusion Criteria

- All adult patients undergoing oesophagectomy for malignancy with an oesophagogastric anastomosis performed during the study period.
- Any approach (2 stage Ivor Lewis, 3 stage McKeown, thoracoabdominal, trans-hiatal) using any combination of open, robotic or standard minimal access approaches.
- Elective (planned) resections.
- Thoracic and cervical anastomotic locations.

Exclusion criteria

- Extended Total Gastrectomy.
- Pharyngolaryngoesophagectomy.
- Colonic interposition and small bowel jejunal interposition reconstructions.
- Emergency resection.
- Resections for benign disease.

Patient identification

- Multidisciplinary team meetings.
- Coordination with lead surgeon for oesophago-gastric cancer resections.
- Coordination with Upper GI Cancer Specialist nursing services.
- Review of theatre scheduling systems.

Centre Eligibility

Any centre routinely performing elective oesophagectomies is eligible to join the audit. No restriction will be placed on global location or number of surgeons involved.

No restriction will be placed on the minimum number of oesophagectomies required to be enrolled in the audit.

Each unit will be required to register prior to the start date for data collection.

Each unit will be responsible for obtaining local hospital approval before commencement of the audit.

Each unit must ensure they have appropriate staff that will be able to ensure a >95% completeness of data entry before the closing date of the study.

Patient Follow Up

The study design aims to ensure that no additional patient follow up or intervention is required that would deviate from the normal patient journey.

For the purposes of accurate data entry, investigators will be required to follow up post operative patients to collate accurate outcome. Information could be gained from electronic and paper records and consultation with operating surgeons and medical teams.

The data collection period will be for 90 days after the index operation involving the patient's first reconstruction.

Data Completion and Organisation

Data input will be via a dedicated encrypted server through the Research Electronic Data Capture (REDCap) web application. No patient identifiable information will be inputted into the database. REDCap will provide an ID number for each patient entered. Locally held records containing

corresponding REDCap ID numbers and local patient identifiers must be stored securely. This will facilitate patient data entry at different time points by different team members and enable cross checking of data entry by different team members to ensure accuracy of data collection.

An electronic REDCap "App" will be available for smart phones to enable data collection. Data can be entered offline, and will be held securely on the "App" and information can be uploaded to the central database when internet access is available. Printable data collection proformas will be made available to enable participants to record data as required that can be uploaded to REDCap when a computer/device is available.

Patient data will be entered into case report forms (CRFs) which are designed not to deviate from safe patient care. CRFs will only record patient events and not instigate any form of intervention.

Each unit will be able to register a maximum of 5 members who will be granted access to input unit data. Each unit will be required to have a lead auditor of Consultant grade (or equivalent, country dependent). Units may apply on an individual basis if they require additional team member registration.

Intra-operative detail must be entered by a surgeon present at the time of the operation. However, if a nominated member of the audit is not present at the operation he/she must take instruction from a surgeon who was present at the time of the operation. This will minimise error and ensure accurate operative data recording that may be absent in operation note records. All other data such as demographics or outcomes may be inputted by any member of the audit team.

Missing data may be entered any time during the study period. Units with >5% missing data will be excluded from the study.

The Birmingham Surgical Trials Consortium, University of Birmingham, will host the REDCap system. All data will be stored securely on encrypted and certified servers for a minimum of 5 years.

Data Collection Form

Please see appendix 1 for our detailed Data Collection / Case Report Form

Pre-operative variables, including patient demographics, age, gender, smoking and alcohol history, pre-operative blood results (Albumin, Haemoglobin, Creatinine) and co-morbidities will be collected. These can be completed prior to the date of the operation if desired. Data will also be collected on neoadjuvant therapy and pre-operative tumour stage.

Intra-operative variables, including the operation type, technique of the operation (open / laparoscopic / robotic), location of the anastomosis, type of anastomosis performed and any techniques to assess the anastomosis during the surgery. Techniques to try to reduce anastomotic leakage, including wrapping the anastomosis in omentum or burying the anastomosis in the pleural will be collected.

Anaesthetic variables, including information on single lung ventilation (double lumen tube / bronchial blocker), intra-operative infusion of fluids and blood and administration of vasopressors by bolus or infusion in the intra-operative period. We would also like to know the post procedure lactate level and whether the patient was extubated on the same day as the operation.

Post-operative / complications variables. These will mainly focus on the ECCG definitions of anastomotic leak and conduit necrosis (Appendix 3) and complications according to other organ systems (respiratory, cardiac, renal, chyle leak, etc). We will be assessing whether the anastomosis was formally assessed for integrity (by endoscopy / CT or contrast study) during the post-operative period. In addition, if an anastomotic leak or conduit necrosis does occur we will document the management strategy for the patient. This could change between the primary (first), secondary (second) and tertiary (third) management options – for example non-operative, operative (re-thoracotomy), radiological and endoscopic (stenting or endoVAC therapy) – in any order depending

on what actually occurs to the patient. Final outcome data such as whether the patient was discharged eating and drinking normally, total length of stay, 30 and 90 day mortality and readmission will also be collected.

Local Approvals

All data collected will measure current practice, with no changes made to normal treatment. As such, this study should be registered as an audit of current practice at each participating centre. It is the responsibility of the local team at each site to ensure that local audit approval (or equivalent) is completed for their centre. For example, surgeons and teams from other countries will have to abide by their local hospital / country approval process. Participating centres will be asked to confirm that they have gained formal approval at their site. Some international centres may require formal ethical approval to be obtained and some units may require individual patient consent. In the UK we have had confirmation that the project should be registered as an Audit (Appendix 2).

Authorship

A maximum of five investigators from each individual unit will be incorporated in this study as co-investigators. Investigators will be PubMed searchable and citable. The output form the study will be published under a single corporate authorship “Oesophagogastric Anastomosis Study Group, West Midlands Research Collaborative”.

Data Publication and Governance

Data will be published as pooled data. It is important to emphasise that no surgeon or unit specific data will be published. Local units may request their own specific data at the end of the study.

The “Oesophagogastric Anastomosis Study Group, West Midlands Research Collaborative” welcome the use of the data for further research. All requests will be assessed on an individual basis with a strong emphasis on safeguarding of data.

All subsequent publications using the dataset must recognise OAI and be published under the principals of shared authorship with a single corporate author.

International centres may require a data transfer agreement and this can be provided if required.

Funding

The Oesophagogastric Anastomosis Study Group currently has no specific funding, however the funding of the website (www.ogaa.org.uk) was kindly provided by funding from the Birmingham Oesophageal Cancer Patients Group which meets on a regular basis at the Queen Elizabeth Hospital, Birmingham.

Cohort size

We have estimated the number of eligible operations performed across Europe. Hospital Episode Statistics (HES) is a data warehouse containing details of all admissions at NHS hospitals in England. A HES database publication showed that over a ten year period between 2000 – 2010, an average of 1,657 oesophagectomies were performed per year (22). The population of England is approximately 53 million. The population of Europe is approximately 739.2 million. Therefore, if we accept the same rate ((1657/53,000,000) x 739,200,000) there will be around 23,110 operations performed across Europe per year.

This prospective study will only pick-up a proportion of these patients, and this depends upon three factors: Penetration - the proportion of hospitals who sign up to recruit patients to the study across

Europe; Pick-up - the proportion of the eligible patients at each centre are entered into the study; Study duration.

The following projection models have been estimated using various combinations of these three factors:

5% penetration; 80% pick-up 6 month recruitment = 924 cases

8% penetration; 90% pick-up 6 months recruitment = 1663 cases

10% penetration; 80% pick-up 6 month recruitment = 1848 cases

10% penetration; 90% pick-up 6 months recruitment = 2079 cases

20% penetration; 90% pick-up 6 month recruitment = 4159 cases

Caveats to these calculations include the variation in rates of oesophageal cancer and oesophagectomy in Europe and the intention that centres in other continents will also contribute to the study

Statistical analysis

The report of the audit will be prepared in accordance with the guidelines as set by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies and STROCSS (Strengthening the Reporting of Cohort Studies in Surgery). (1). Data will be collected and analysed in clinically relevant categories, and the Chi squared tests used to detect differences between groups. Missing data for predictor values will be replaced using the multiple imputation method to create five imputed datasets; all predictor and outcome variables will be entered into the predictive models for imputation.

Binary logistic regression modelling will be used. Multivariable models will be built to produce odds ratios (OR) to account for the impact of predictive variables when assessing outcomes (anastomotic leak). Variable selection will be based upon those which are statistically significant at univariable analysis, and those which are clinically significant but not statistically. Fixed, forced entry will be used to adjust the main outcome measure. The effect of interaction, and sequential removal of non-significant variables will be assessed using changes in Akaike information criterion for multilevel models, and p-values for multiply imputed fixed models. Finally, risk adjusted funnel plots will be produced to test the performance of individual (anonymised) centres for rates of anastomotic leak and other factors.

References

1- Agha, R. A., Borrelli, M. R., Vella-Baldacchino, M., Thavayogan, R., Orgill, D. P., Pagano, D., Pidgeon, T. E. (2017). The STROCSS statement: Strengthening the Reporting of Cohort Studies in Surgery. International Journal of Surgery, 46, 198–202.

2- Turrentine, Florence E., et al. "Morbidity, mortality, cost, and survival estimates of gastrointestinal anastomotic leaks." Journal of the American College of Surgeons 220.2 (2015): 195-206.

3- Low, Donald E. "Diagnosis and management of anastomotic leaks after esophagectomy." Journal of Gastrointestinal Surgery 15.8 (2011): 1319-1322.

4- Goense, L., van Dijk, W. A., Govaert, J. A., van Rossum, P. S. N., Ruurda, J. P., & van Hillegersberg, R. (2017). Hospital costs of complications after esophagectomy for cancer. European Journal of Surgical Oncology, 43(4), 696–702.

5- Markar, S., Gronnier, C., Duhamel, A., Mabrut, J.-Y., Bail, J.-P., Carrere, N., Mariette, C. (2015). The Impact of Severe Anastomotic Leak on Long-term Survival and Cancer Recurrence After Surgical Resection for Esophageal Malignancy. Annals of Surgery, 262(6), 972–980.

6- Ryan, Carrie E., et al. "Transthoracic anastomotic leak after esophagectomy: Current trends." Annals of Surgical Oncology 24.1 (2017): 281-290.

7- Kassis, Edmund S., et al. "Predictors of anastomotic leak after esophagectomy: an analysis of the society of thoracic surgeons general thoracic database." The Annals of thoracic surgery 96.6 (2013): 1919-1926.

8- Dent, B., et al. "Management and outcomes of anastomotic leaks after oesophagectomy." British Journal of Surgery 103.8 (2016): 1033-1038

9- Hu, Zhongwu, et al. "The diagnostic value of routine contrast esophagram in anastomotic leaks after esophagectomy." World Journal of Surgery (2017): 1-6.

10- Zehetner, Jörg, et al. "Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy." Annals of surgery 262.1 (2015): 74.

11- Bolton, John S., William C. Conway, and Abbas E. Abbas. "Planned delay of oral intake after esophagectomy reduces the cervical anastomotic leak rate and hospital length of stay." Journal of Gastrointestinal Surgery 18.2 (2014): 304-309.

12- Kanamori, J., et al. "Leak grading and percutaneous transanastomotic drainage for the treatment of cervical anastomotic leakage after esophagectomy." Diseases of the Esophagus 30.5 (2017): 1-7.

13- Roh, Simon, et al. "Role of Barium Swallow in Diagnosing Clinically Significant Anastomotic Leak following Esophagectomy." The Korean journal of thoracic and cardiovascular surgery 49.2 (2016): 99.

14- Guo, Juntang, et al. "Choice of therapeutic strategies in intrathoracic anastomotic leak following esophagectomy." World journal of surgical oncology 12.1 (2014): 402.

15- Perry, Yaron, et al. "Serial drain amylase can accurately detect anastomotic leak after esophagectomy and may facilitate early discharge." The Annals of thoracic surgery 100.6 (2015): 2041-2047.

16- Low, D. E., Kuppusamy, M. K., Alderson, D., Cecconello, I., Chang, A. C., Darling, G., Wijnhoven, B. P. L. (2017). Benchmarking Complications Associated with Esophagectomy. Annals of Surgery, 1.
17- Price, Theolyn N., et al. "A comprehensive review of anastomotic technique in 432 esophagectomies." The Annals of thoracic surgery 95.4 (2013): 1154-1161.
18- Markar, Sheraz R., et al. "Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis." Annals of surgical oncology 20.13 (2013): 4274-4281.
19- Deng, Xu-Feng, et al. "Hand-sewn vs linearly stapled esophagogastric anastomosis for esophageal cancer: a meta-analysis." World Journal of Gastroenterology: WJG 21.15 (2015): 4757.
20- Biere, S. S. A. Y., et al. "Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis." Digestive surgery 28.1 (2011): 29-35.
21- Low, Donald E., et al. "International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG)." Annals of surgery 262.2 (2015): 286-294.
22- Mamidanna, Ravikrishna, et al. "Surgeon volume and Cancer esophagectomy, gastrectomy, and pancreatectomy: a population-based study in England." Annals of surgery 263.4 (2016): 727-732.
23- von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., & Vandenbroucke, J. P. (2014). The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. International Journal of Surgery, 12(12), 1495–1499.
24- Schmidt, H. M., Gisbertz, S. S., Moons, J., Rouvelas, I., Kauppi, J., Brown, A., Gutschow, C. A. (2017). Defining Benchmarks for Transthoracic Esophagectomy: A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients. Annals of Surgery, 266(5), 814–821.
25- Association of Upper GI Surgeons- Provision of Service Document 2016 (www.augis.org/wp-content/uploads/2016/06/Provision-of-Services-June-2016.pdf)
26- Oken, M., Creech, R., Tormey, D., Horton, J., Davis, T., McFadden, E., & Carbone, P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. American Journal of Clinical Oncology
27- Sundararajan, V., Henderson, T., Perry, C., Muggivan, A., Quan, H., & Ghali, W. A. (2004). New ICD-10 version of the Charlson comorbidity index predicted in-hospital mortality. Journal of Clinical Epidemiology, 57(12), 1288–1294.
28- Clavien, P. A., Barkun, J., De Oliveira, M. L., Vauthey, J. N., Dindo, D., Schulick, R. D., … Makuuchi, M. (2009). The clavien-dindo classification of surgical complications: Five-year experience. Annals of Surgery.

Appendix 1: Pre-Operative Data Collection

Gender	Male / Female
Age (in Years)	
ASA	1/2/3/4
Eastern Cooperative Oncology Group (ECOG)/WHO/Zubrod Score (26)	0- Fully active, able to carry on all pre-disease performance without restriction 1- Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature 2- Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of working hours 3- Capable of only limited self-care; confined to bed or chair >50% of waking hours 4- Completely disabled ; cannot carry on any self-care; totally confined to bed or chair
Charlson Comorbidity Index (27)	
Myocardial infarction	Yes/No
Congestive Heart Failure	Yes/No
Peripheral vascular disease (includes aortic aneurysm >6cm)	Yes/No
Cerebrovascular disease: CVA with mild or no residual weakness or TIA	Yes/No
Dementia	Yes/No
Chronic pulmonary disease	Yes/No
Connective tissue disease	Yes/No
Peptic ulcer disease	Yes/No
Mild liver disease (without portal hypertension, includes chronic hepatitis)	Yes/No
Diabetes without end organ damage (excludes diet controlled alone)	Yes/No
Hemiplegia	Yes/No
Moderate or severe renal disease	Yes/No
Diabetes with end organ damage (retinopathy, neuropathy, or brittle diabetes)	Yes/No
Tumour without metastasis (exclude if > 5 years from diagnosis)	Yes/No
Leukaemia (acute or chronic)	Yes/No

Lymphoma Moderate or severe liver disease Metastatic solid tumour AIDS (not just HIV +ve)	Yes/No Yes/No Yes/No Yes/No
Smoking History	Never, Current, ex >6/52, ex <6/52
Height (cm) **Weight** (kg)	Automatic BMI Calculation
Pre-op bloods at start of surgery (or last recorded level, within previous 2 weeks) Albumin Haemoglobin Serum Creatinine Micromol/L Mg/dl	 _____ g/L **or** mmol/L Absolute value in g/L to one decimal place [with pop-up converter to change from g/dL to mmol/L]
Malignancy details Tumour type Location of tumour Overall Pre-operative staging Neo-adjuvant therapy Chemotherapy regimen Cycles of chemotherapy - Intended Cycles of chemotherapy - Completed If Radiotherapy give pre-op	 Adeno / SCC / Other Upper / Mid / Siewert 1 / 2 / 3 TNM 7th None / Chemotherapy / Chemoradiotherapy None/Chemotherapy/Chemoradiotherapy CF – Cisplatin, 5FU/ ECF – Epirubicin, Cisplatin, 5FU / ECX - Epirubicin, Cisplatin, Capecitabine /EOX - Epirubicin, Oxaliplatin, Capecitabine /FLOT - 5FU, Oxaliplatin, Leucoverin, Docetaxel/ MIC - Mitomycin, Ifosfamide, Cisplatin / CROSS - Carboplatin, Paclitaxel / Other - Please specify Total Gy _____ Did the radiotherapy field include the gastric fundus – yes / no
Pre-operative nutritional support	None Oral Supplements Enteral Nutrition via NJ/NG/PEG/Jej etc TPN
Pre-operative gastric ischaemic preconditioning performed *	Yes / No

* This is when laparoscopy and division of the left gastric vessels +- short gastric vessels are performed prior to oesophagectomy under a separate anaesthetic

Intra Operative Data Collection

Training operation Trainee performed abdominal phase Trainee performed chest dissection Trainee performed anastomosis	Yes / No Yes / No Yes / No Yes / No
Abdominal phase	Lap / Open / Lap Converted to open / Robotic
Thoracic phase	Thorascopic / Open Right Chest / Open Left chest or thoracoabdominal / Thorascopic converted to open / Trans-hiatal / Robotic
Lympadenectomy	Abdominal only Abdominal and Thoracic (2 field) Abdominal / Thoracic / Neck (3 field)
Gastric Tube	Whole Stomach, Wide Gastric Tube > 5cm, Thin Gastric Tube < 5cm
Anastomosis level	Neck / Chest above Azygous / At Azygous / Below Azygous / Anastomosis not performed
Anastomotic configuration	End to End Side to End Side to Side
Anastomosis technique Handsewn Circular stapler Linear stapler Orringer style anastomosis (linear stapled and sutured)	 Single layer / Two layer Interrupted / Continuous CDH (Ethicon)/ CEEA (Covidien)/ ECS (Ethicon) EEA (Covidien)/ SDH (Ethicon)/ OrVil/ Other - please specify (size in mm) Endopath (Ethicon)/ GIA (Covidien)/ NTLC (Ethicon)/ TA (Covidien)/ TCT (Ethicon)/ TL (Covidien)/ TLC (Ethicon)/ TX (Ethicon)/ Other - please specify Yes / No
Was the anastomosis wraped or covered in omentum	Yes / No
Was the anastomosis buried in mediastinal pleura	Yes / No

Was the anastomosis tested for integrity	Not performed / NG Air Leak Test / Intra-op Endoscopy / Methylene Blue / Indigocyanine green (IGC) assessment / Other method
Nutritional Feeding Access	None / Feeding Jejunostomy / Nasojejunal tube
Procedures on the Pylorus	None/ Pyloromyotomy / Pyloroplasty / Botox / Dilatation / other
Intra-op complications	Yes / No Major vessel injury Unable to perform anastomosis Unplanned splenectomy Enteric injury Airway injury Non-viable gastric conduit Gastric conduit unable to reach planned anastomosis site.
Total Operative duration (mins)(skin incision to skin closure) Please specify in minutes e.g. 210 minutes not 3.5 hours	

Anaesthetic Data Collection

Single Lung Ventilation	Yes / No If Yes – Double Lumen Tube or Bronchial Blocker If Yes - Duration of One Lung Ventilation (mins)
Intra-operative vasopressor support required (For example Noradrenaline, Metaraminol, Ephredrine or phenylephredrine etc)	Yes – bolus Yes – continuous infusion No
Total IV Fluid (mls) given intra-operatively	_____mls crystalloid _____mls colloid
Intra-operative blood transfusion	Yes / No If Yes - Number of units transfused_____
Analgesia technique	Epidural Thoracic paravertebral block Intra-thecal Morphine Patient Controlled Analgesia (PCA) Ketamine Abdominal pain catheter
Lactate Level immediately postoperative	_____mmol/L
Was the patient extubated the same day as resectional surgery?	Yes / No

Post Operative Data Collection

Was assessment of anastomosis performed in the post op period? Endoscopy Plain Film Contrast Swallow CT Contrast Swallow Other What day post operatively did this occur	 Yes / No Yes / No Yes / No Please specify Post-op Day_____
Post Operative Complications Anastomotic leak No. of days after surgery leak was diagnosed Conduit Necrosis No. of days after surgery conduit necrosis was diagnosed	 Yes / No / Grade 1 / 2 / 3 No days _____ Yes / No / Grade 1 / 2 / 3 No days _____
Primary Treatment of leak/conduit necrosis Post-operative day of start of treatment _____ Primary treatment strategy of leak/conduit necrosis operative Operative technique Conservative (non-interventional) strategy (This means radiological drains/ endoscopically placed stents/ EndoVac/sponge were not used Conservative Management Strategy	 Yes/No Minimal access procedure / Minimal access converted to open procedure / Open thoracotomy. Washout only / Anastomotic Repair / Reformation of the Anastomosis / T-Tube / Opening of Neck Wound / Intercostal or muscle flap repair / Disconnection and cervical oesophagostomy Yes/No Nil by mouth Antibiotics Antifungals Parenteral nutrition Enteral nutrition(NG/NJ/feeding jejunostomy) Non-operative management – Yes / No

Radiological drainage Number of radiologically sited drains at initial intervention Was and oesophageal stent used to treat the leak Oesophageal stent type Complications from oesophageal stenting Total no of stents used EndoVac/ Endosponge placed Total number of vac changes Failure of primary leak/conduit necrosis management If failed but no secondary strategy commenced please select no.	Yes / No Yes / No Covered Plastic / Covered Metal / Covered biodegradable / other Displacement / Erosion / Failure to Occlude Leak / Other Endoluminal VAC therapy – Yes / No Total no of EndoSponge changes Yes/ No Yes/ No
Secondary Leak Treatment of leak/conduit necrosis Post-operative day of start of treatment _____ Secondary treatment strategy of leak/conduit necrosis operative Operative technique Conservative (non-interventional) strategy (This means radiological drains/ endoscopically placed stents/ EndoVac/sponge were not used Conservative Management Strategy	 Yes/No Minimal access procedure / Minimal access converted to open procedure / Open thoracotomy. Washout only / Anastomotic Repair / Reformation of the Anastomosis / T-Tube / Opening of Neck Wound / Intercostal or muscle flap repair / Disconnection and cervical oesophagostomy Yes/No Nil by mouth

	Antibiotics Antifungals Parenteral nutrition Enteral nutrition(NG/NJ/feeding jejunostomy) Non-operative management – Yes / No
Radiological drainage Number of radiologically sited drains at initial intervention Was and oesophageal stent used to treat the leak Oesophageal stent type Complications from oesophageal stenting Total no of stents used EndoVac/ Endosponge placed Total number of vac changes Failure of primary leak/conduit necrosis management If failed but no tertiary strategy commenced please select no.	Yes / No Yes / No Covered Plastic / Covered Metal / Covered biodegradable / other Displacement / Erosion / Failure to Occlude Leak / Other Endoluminal VAC therapy – Yes / No Total no of EndoSponge changes Yes/ No Yes/ No
Gastrointestinal Complication	Nil Oesophagoenteric leak from anastomosis Conduit necrosis/failure. Ileus defined as small bowel dysfunction preventing or delaying enteral feeding Small bowel obstruction Feeding J-tube complication Pyloromyotomy/pyloroplasty complication Clostridium difficile Infection Gastrointestinal bleeding requiring intervention or transfusion Delayed conduit emptying requiring intervention or delaying discharge or requiring maintenance of NG drainage >7d postoperatively Pancreatitis

	Liver dysfunction
Chyle leak grade **Chyle leak volume**	Nil Grade 1/2/3 Type A (< 1 Litre in 24 hours) Type B (>1 Litre in 24 hours)
Vocal Cord Injury/Palsy	Nil Type 1: Transient injury requiring no therapy Type 2: Injury requiring elective surgical procedure Type 3: Injury requiring acute surgical intervention (due to aspiration or respiratory issues Unilateral /Bilateral
Pneumonia	Nil Pneumonia Pleural effusion requiring additional drainage procedure Pneumothorax requiring treatment Atelectasis mucous plugging requiring bronchoscopy Respiratory failure requiring reintubation Acute respiratory distress syndrome (Berlin Definition) Acute aspiration Tracheobronchial injury Chest tube maintenance for air leak for >10 d postoperative
Cardiac complication	Nil Cardiac arrest requiring CPR Myocardial infarction (Definition: World Health Organization) Dysrhythmia atrial requiring treatment Dysrhythmia ventricular requiring treatment Congestive heart failure requiring treatment Pericarditis requiring treatment
Wound/Diaphragmatic complication	Nil Thoracic wound dehiscence Acute abdominal wall dehiscence/hernia Acute diaphragmatic hernia
Urologic complication	Nil Acute renal insufficiency (defined as doubling of baseline creatinine) Acute renal failure requiring dialysis Urinary tract infection

	Urinary retention requiring reinsertion of urinary catheter, delaying discharge, or discharge with urinary catheter
Thromboembolic complication	Nil Deep venous thrombosis Pulmonary embolus Stroke (CVA) Peripheral thrombophlebitis
Infection	Nil Wound infection requiring opening wound or antibiotics Central IV line infection requiring removal or antibiotics Intrathoracic/intra-abdominal abscess Generalized sepsis (Definition: CDC) Other infections requiring antibiotic
Complication not otherwise specified	
Final Histology (23-24) T stage No Nodes examined No Nodes positive for malignancy Surgical Margins M stage	 Complete path response / HGD / 1 / 2 / 3 / 4 No nodes_____ No nodes_____ Proximal – clear / involved (<1mm) Distal – clear / involved (<1mm) CRM – clear / involved (<1mm) 0/1
Outcomes Overall Clavien-Dindo Classification (at the time of discharge)(28) *Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. Grade 1 also includes wound infections opened at the bedside.	 Grade 1- Any deviation from the normal post operative course* without need for pharmacological treatments or surgical, endoscopic and radiological interventions. Grade 2- Requiring pharmacological therapy with drugs other than such allowed for grade 1 complications. Blood transfusions and total parenteral nutrition are also included. Grade 3a- Requiring surgical, endoscopic or radiological intervention NOT under general anaesthesia 3b- Requiring surgical, endoscopic or radiological intervention UNDER general anaesthesia Grade 4a- Life threatening complication (including CNS complications) requiring ICU management: SINGLE organ dysfunction

	Grade 4b- Life threatening complication (including CNS complications) requiring ICU management: MULTI organ dysfunction Grade 5- Death of a patient
Did the patient require re-intubation in the post-operative period	Yes / No
Did the patient get re-admitted to the intensive care unit in the post-operative period	Yes / No
Did the patient return to theatre for a general anaesthetic and surgical procedure (Local anaesthetic procedures and endoscopic procedures i.e. tracheostomy and lines are excluded)	Yes / No
Did the patient require a tracheostomy in the post-operative period	Yes / No
Total length of ITU/HDU stay (non ward based care)(in days)	
Was the patient eating and drinking on discharge	Yes / No
Destination on discharge	Home Other medical facility e.g. secondary hospital, rehabilitation centre, nursing facility
Re-admission within 30 days of discharge	Yes / No
Number of days after discharge the patient was re-admitted	
Location of readmission	Primary / secondary hospital
Cause for re-admission	
90 day mortality	Yes / No
How many days post op did the patient die	
Location of death	In hospital Out of hospital

Unit Questionnaire

Number of consultant surgeons performing oesophagectomy	Total No.
Number of oesophagectomies performed between Jan 2015 and Dec 2016	
Speciality of Surgeons	Thoracic / Oesophagogastric / General Surgeon / Surgical Oncologist
Size of institution	Total number of beds Total number of ICU beds
24 hour on call rota for oesophageal emergencies	24hour / 9-5 / none
24 hour on call availability for interventional radiology	24hour / 9-5 / none
24 hour access to emergency theatre	24hour / 9-5 / none
Where do oesophagectomy patients routinely go post-operatively	Ward HDU ICU Dedicated GI HDU
ERAS protocol for oesophagectomy patients ERAS nurse Physio input	Yes / No Yes / No Nil dedicated / Daily / Twice daily
Does your unit perform gastric ischaemic preconditioning?	Yes – Routinely Yes – Selectively No If Yes – how many days prior to surgery
Does your unit have an agreed approach to oesophagectomy for lower 1/3 adenocarcinoma?	No Yes Open Right Transthoracic Oesophagectomy Open Left thoracoabdominal oesophagectomy Open Transhiatal Oesophagectomy Hybrid Transthoracic Oesophagectomy (Lap abdominal mobilisation) 2 stage Minimal Access Oesophagectomy 3 stage Minimal Access Oesophagectomy Robotic Oesophagectomy Other
Does you unit have an agreed technique to perform intra-thoracic anastomosis?	No Yes Handsew

	Circular Stapled OrVil Stapled side to side with suturing (Orringer style) Other
Does your unit have access to Indigo-Cynanine Green assessment of the anastomosis or gastric conduit?	Yes / No
Does your unit have a policy of performing routine post-operative assessment of the anastomosis?	No Yes – Barium or Water Soluble Contrast Swallow Yes – Endoscopy Yes – CT If your unit routinely assess the anastomosis in the post-operative period, what day is this generally performed? Postop Day_____
Does your unit have access to following for the treatment of oesophageal anastomotic leak?	TPN – Yes / No Endoscopic Clips – Yes / No Endoscopic or radiologically placed covered oesophageal stents – Yes / No EndoVAC / Endosponge therapy – Yes / No Interventional guided drainage of abdominal or thoracic collections – Yes / No

Appendix 2- How to register this audit

Every hospital has an audit department which should be able to advise on the information required to register the project. Please contact them well in advance to ensure all the paper work is correct (we would recommend at least one month prior to the study commencing).

At Trust level:

1. Identify a PI (Primary Investigator) at each trust – this is a Consultant who agrees to support the study.

2. Create a team of Consultants/ surgical registrars.

3. Contact your hospital's Clinical Audit Department preferably by email

    a. They will provide you with a standard audit form to complete, via email or from the intranet

    b. You can copy and paste from this protocol

    c. Ensure that the audit department know that this is part of a larger project and that you will send anonymised data for central collation via secure nhs.net email addresses. This will involve gaining permission from the Trust's Caldicott Guardian if based in the UK.

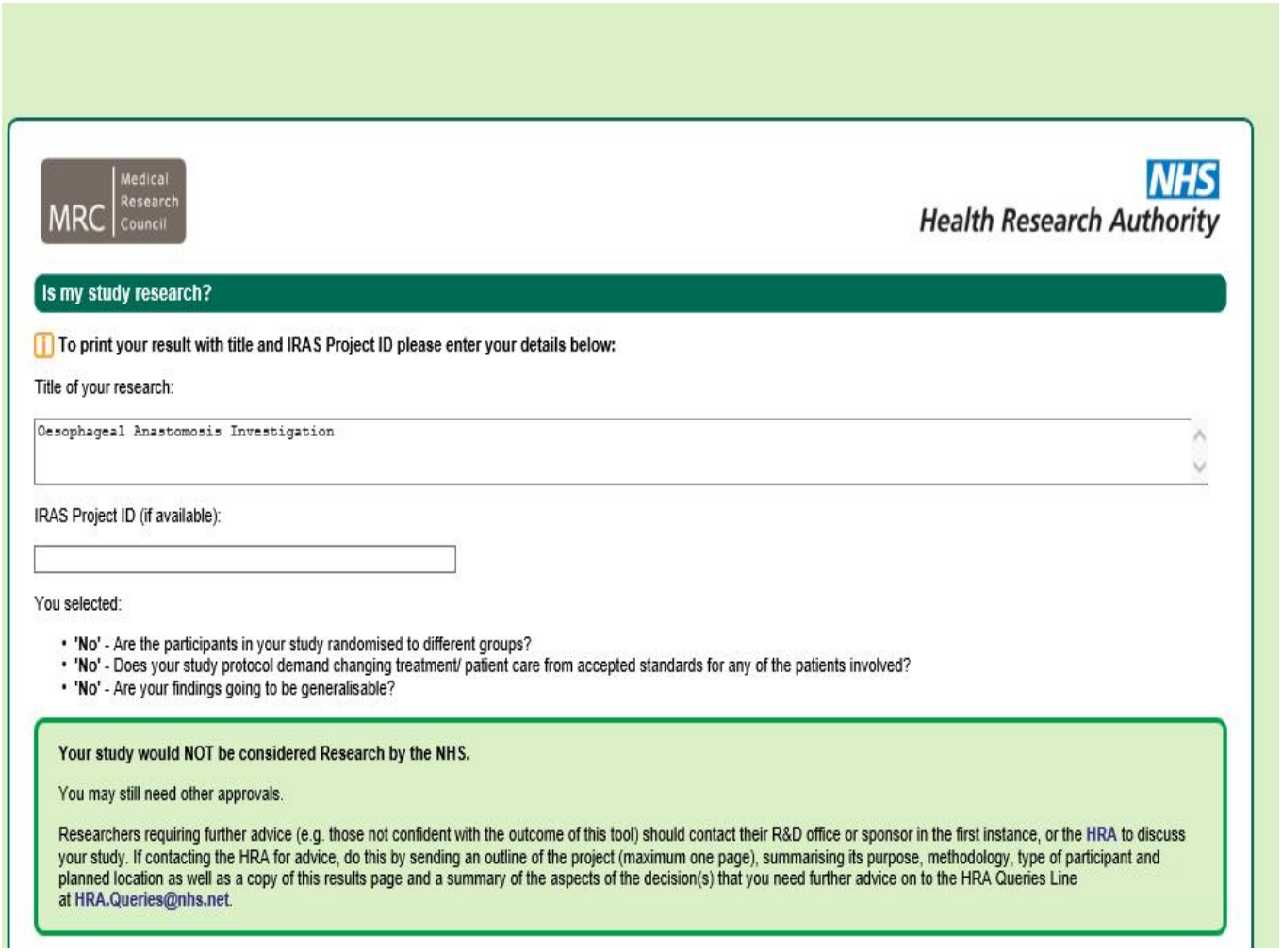
4. Once the form is completed, you may need to ask your supervising consultant to sign it.

5. Form submission

a. Submit the form and protocol to the Audit Department as soon as possible.

6. Email form to OGanastomosisaudit@gmail.com to register your interest.

Appendix 3 - Health Research Authority Tool UK



MRC Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Oesophageal Anastomosis Investigation

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at HRA.Queries@nhs.net.

Appendix 4 - Grading Oesophageal Complications

Anastomotic Leak

Defined as: Full thickness GI defect involving oesophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification

Type I: Local defect requiring no change in therapy or treated medically or with dietary modification

Type II: Localized defect requiring interventional but not surgical therapy, for example, interventional radiology drain, stent or bedside opening, and packing of incision

Type III: Localized defect requiring surgical therapy

Conduit Necrosis

Type I: Conduit necrosis focal Identified endoscopically

Treatment — Additional monitoring or non-surgical therapy

Type II: Conduit necrosis focal Identified endoscopically and not associated with free anastomotic or conduit leak

Treatment — Surgical therapy not involving esophageal diversion

Type III: Conduit necrosis extensive

Treatment — Treated with conduit resection with diversion

Low, Donald E., et al. "International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG)." *Annals of surgery* 262.2 (2015): 286-294

Appendix 5 - Definitions

Gastric ischaemic preconditioning: This is when laparoscopy and division of the left gastric vessels +- short gastric vessels are performed prior to oesophagectomy under a separate anaesthetic. This is usually performed 1 – 3 weeks prior to oesophagectomy.

Anastomotic leak: Full thickness GI defect involving oesophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification

Gastric conduit necrosis: When the gastric conduit becomes ischaemic and necrotic. This can be limited or extensive.

Endoluminal VAC therapy: is negative pressure therapy, or vacuum-assisted closure (VAC), where a piece of sponge is placed in to cavity associated with an anastomotic leak or defect and connected to a naso-gastric tube for continuous suction. The sponge is usually replaced with endoscopic assistance every 48-72 hours.

Indigocyanine green (IGC) assessment: Using fluorescence angiography to assess the perfusion of the gastric conduit and anastomosis with the intra-venous injection of indigocyanine green and assessing the perfusion with special laparoscopic or open video monitoring technology and software (For example those developed by Karl Storz, *FireFly*™ or PINPOINT from Novadaq®). Also known as near-infrared perfusion.

Appendix 6 – TNM Staging (7th Edition, 23-24)

Primary Tumour (T)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis High-grade dysplasia

T1 Tumour invades lamina propria, muscularis mucosae, or submucosa

T1a Tumour invades lamina propria or muscularis mucosae

T1b Tumour invades submucosa

T2 Tumour invades muscularis propria

T3 Tumour invades adventitia

T4 Tumour invades adjacent structures

T4a Resectable tumour invading pleura, pericardium, or diaphragm

T4b Unresectable tumour invading other adjacent structures, such as the aorta, vertebral body, and trachea

Regional lymph nodes (N)

NX Regional lymph node(s) cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in 1-2 regional lymph nodes

N2 Metastasis in 3-6 regional lymph nodes

N3 Metastasis in 7 or more regional lymph nodes

Distant metastasis (M)

M0 No distant metastasis

M1 Distant metastasis