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ADVANCING SURGICAL CARE

HEARTBURN CANCER UK

ARROW

AUDIT & REVIEW OF ANTI - REFLUX OPERATIONS & WORK-UP

AUGIS
Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland

Roux Group
Training | Education | Research

STUDY PROTOCOL

Full Title

A multicentre prospective cohort study to investigate the current management of patients undergoing anti-reflux surgery in the United Kingdom: ARROW (Audit & Review of Anti-Reflux Operations & Workup)

The ARROW study team

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Design: Multicentre, prospective audit of current clinical practice.

Abstract

Background

There are a variety of surgical and endoscopic interventions available to treat gastroesophageal reflux disease. There is, however, no consensus on which approach is best.

The aim of this national audit is to describe the current variation in United Kingdom (UK) clinical practice in relation to anti-reflux surgery and to report adherence to available clinical guidelines.

Method

This national audit will be conducted at centres across the UK using the secure online web platform ALEA. The study will comprise two parts: a registration questionnaire and a prospective multi-centre audit of anti-reflux surgery. All participating centres will be required to complete the registration questionnaire comprising details regarding pre-, peri- and post-operative care pathways and whether or not these are standardised within each centre. Following this, a 12-month multi-centre prospective audit will be undertaken to capture data including patient demographics, predominant symptoms, pre-operative investigations, surgery indication, intra-operative details and post-operative outcomes within the first 90 days.

Conclusion

Variation in surgical practice and outcomes after elective surgical intervention are an important quality metric within healthcare. This study will identify and explore variation in the processes and outcomes following anti-reflux surgery within the UK using a collaborative cohort methodology. The results generated by this audit will facilitate local and national quality

improvement initiatives and generate new possibilities for future research in anti-reflux interventions.

Introduction

Gastroesophageal reflux disease (GORD) is a common condition, affecting 10-20% of the Western population[1,2]. In addition to having a detrimental effect on quality of life, GORD is a risk factor for the development of Barrett's metaplasia[3,4] and oesophageal adenocarcinoma[5]. Primary treatments include lifestyle modification and proton pump inhibitors (PPIs) which are generally well tolerated. Some patients continue to have refractory symptoms and others cannot tolerate, or do not wish to take, long-term medication. In these cases anti-reflux surgery (ARS) may be a therapeutic option[6–8]. Current guidelines from the National Institute of Health and Care Excellence (NICE) reflect this, with consideration of laparoscopic fundoplication recommended for patients with a confirmed diagnosis of acid reflux and who are not suitable for long term acid suppression therapy[9].

Despite national guidelines and published evidence from randomised controlled trials (RCTs)[13–15], there is a lack of consensus regarding the most effective ARS technique, and whether procedures should be tailored to a particular patient's symptomology, nature of reflux disease or oesophageal motility. Technical uncertainties in fundoplication (the most common procedure) include the extent of dissection (i.e. hiatal dissection and division of short gastric vessels[14]), wrap formation (i.e. partial, full, anterior or posterior[15–17]), whether gastropexy is required[18,19], and the method of crural repair[20] (including whether this should be undertaken or mesh utilised to reinforce the repair[21]). In addition to fundoplication, other minimally invasive techniques such as LINX™[10], Stretta™[11] and EsophyX™[12] are available, although the precise role of these novel treatments remains to be clearly defined (Appendix 1). There is also anecdotal inconsistency in selection of patients for surgery and in the use of preoperative assessment investigations, despite recommendations from the Association of Upper GI Surgeons (AUGIS)[22], British Society of Gastroenterology (BSG)[23], and the recent International

Consensus Regarding Preoperative Examinations and Clinical Characteristics Assessment to Select Adult Patients for Antireflux Surgery (ICARUS) guidelines[24].

Specific aspects of these guidelines include the need for oesophageal manometry to be performed prior to consideration of anti-reflux surgery which was a strongly endorsed recommendation in the ICARUS and BSG guidelines[23,24]. The primary purpose of oesophageal manometry in the setting of anti-reflux surgery is to identify any major oesophageal motility disorder, gastro-oesophageal outflow obstruction or absence of contractility in order to prevent anti-reflux surgery being performed in patients with a primary motility disorder such as achalasia or diffuse oesophageal spasm[23,24]. Other recommendations include the need for pre-operative oesophagogastroduodenoscopy (OGD) within 12-months of anti-reflux surgery in order to identify the presence of Barrett's oesophagus (and grade dysplasia where present) and assess the size and configuration of any hiatal hernia[24]. These factors can provide important information for operative planning, and although precise timing of OGD prior to anti-reflux surgery has not been specifically studied, a timeframe of having been performed within 12-months of surgery has been selected based on expert opinion[24].

A previous study has highlighted significant variation in England in relation to the provision of ARS, although clinical outcomes were comparable[25]. Variations included the rate of conversion to open procedures, 30-day reintervention or readmission and rates of other adverse events. Unplanned re-admission or re-operation have both been demonstrated as useful quality measures within general surgery, as these issues may be representative of problems relating to the primary procedure itself[26,27]. AUGIS have provided specific recommendations that all units performing ARS should have a rate of conversion to open surgery of under five percent, 30-

day readmission rate of under ten percent, and rate of unplanned return to theatre within 30-days of less than five percent[22].

The aim of this national audit is to describe the current variation in United Kingdom (UK) clinical practice in relation to ARS, to compare adherence to current guidelines and report short-term outcome measures (readmission and re-operation rate). The study will focus on patient selection, pre-operative investigations, operative procedure and techniques, post-operative care and short-term outcomes. This variation will be compared to recommendations from national and international guidelines[22–24].

Rationale of ARROW study and hypothesis

It is known that there is considerable variation in the provision of ARS in England[25]. We aim to undertake a UK wide multicentre study to determine the extent of the variation in practice of anti-reflux surgery. During this analysis, current UK practice will be compared against a number of reported quality standards (Table 1).

Table 1: Details of audit standards utilised for the purposes of the current study.

Source	Measure	Evidence	Expectation
British Society of Gastroenterology (BSG) Guidelines[23] ICARUS Guidelines[24]	Oesophageal manometry is mandatory in the work-up of patients for anti-reflux surgery	Documentation in patient care record	100%
ICARUS Guidelines[24]	In patients with non-erosive GORD Reflux monitoring is mandatory in the work-up of patients for anti-reflux surgery	Documentation in patient care record	100%
ICARUS Guidelines[24]	Endoscopy is mandatory in the work-up of patients for anti-reflux surgery and has to be carried out in the last year prior to anti-reflux surgery	Documentation in patient care record	100%
The Provision Of Services For Upper Gastrointestinal Surgery Association of Upper GI Surgeons (AUGIS)[22]	Patients undergoing anti-reflux surgery should have this procedure completed laparoscopically (Unit level:<5% open conversion rate)	Documentation in patient care record	95%
The Provision Of Services For Upper Gastrointestinal Surgery AUGIS[22]	Patients undergoing anti-reflux surgery should not have an unplanned readmission (Unit level <10% readmission rate at 30 days postoperatively)	Documentation in patient care record	90% (unit level)
The Provision Of Services For Upper Gastrointestinal Surgery AUGIS[22]	Patients undergoing anti-reflux surgery should not have an unplanned reoperation (Unit level <5% reoperation rate at 30 days postoperatively)	Documentation in patient care record	95%

Although other recommendations are available within each of these clinical guidelines, these audit standards have been specifically chosen pragmatically as each can be objectively measured as part of the current audit and were strongly endorsed by the reporting guidelines as listed above[22–24]. Other recommendations within these guidelines were not selected for measurement within the present audit as they may have related to patient selection (and therefore not possible to capture data from those patients not selected for ARS based on the current methodology), or were considered to be potentially subjective and therefore difficult to define as a specific audit standard. Full details of all standards reported within these guidelines are provided in Appendix 2 alongside details of the rationale for excluding those which were not included as specific audit standards for the current study.

Study group

The study has been devised following a research development meeting held under the oversight of Royal College of Surgeons and AUGIS into unmet research need in upper gastrointestinal (UGI) Surgery. The study group has been formed of UGI surgeons and trainees who have expressed interest in this project and is operating under the umbrella of AUGIS.

Study approach

The study will comprise two parts: a registration questionnaire and a prospective multi-centre audit of laparoscopic anti-reflux surgery.

All participating centres will be required to complete the registration questionnaire (Appendix 3), comprising specific details about pre-, peri- and post-operative care pathways and whether or not these are standardised within each centre. Following this, a 12-month multicentre prospective audit will be undertaken.

Local registration with institution audit department / Caldicott guardian

Each centre will be responsible for registering the ARROW study with their local audit department and Caldicott guardian. Research ethics approval is not required for this study and this has been confirmed by the use of the online National Research Ethics Service (NRES) decision tool (http://www.hra-decisiontools.org.uk/research/, accessed 13/12/2019, Appendix 4). Inclusion in this study will not have any effect upon an individual patient's clinical pathway. Once ARROW has been registered with a local audit department, confirmation of this should be submitted to the ARROW steering committee by email to arrowsurgerystudy@gmail.com.

Eligible patients

All patients aged 18 and over, undergoing primary or revisional ARS (and/or para-oesophageal hernia repair for reflux symptoms) of any type will be eligible for inclusion. As well as fundoplication, patients undergoing LINX™, Stretta™ or EsophyX™ for reflux symptoms will be eligible for inclusion. Patients undergoing gastric bypass surgery following a primary referral for management of reflux symptoms will also be eligible for inclusion. Those referred initially as part of a weight-management pathway will be excluded, as will individuals undergoing conversion to gastric bypass for reflux following previous bariatric surgery. Patients undergoing ARS as part of treatment of a non-reflux related upper gastrointestinal condition (such as during treatment for achalasia or upper gastrointestinal cancer) will be excluded. Patients undergoing para-oesophageal hernia repair for non-reflux related symptoms will also be excluded.

Patients will be identified from theatre scheduling systems, multi-disciplinary team meetings and co-ordination with the lead upper gastrointestinal (UGI) surgeon in each centre.

Eligible centres and surgeons

All centres and surgeons undertaking ARS will be eligible to take part. There will be no restrictions on volume of practice. Centres within the National Health Service and private healthcare sector will be eligible for inclusion. Eligible centres will be identified through the National Research Collaborative network, individual surgical trainee research collaboratives (which encompass hospitals from most areas of the UK) and AUGIS. Regions without collaboratives will be identified and specific trainees targeted in order to ensure coverage from all areas of the UK.

Previous studies estimated that 2,400 anti-reflux procedures are completed in England per year[25]. We hope to capture a minimum of 25% of procedures over a 12-month period (with the additional benefit of collecting data from centres in the rest of the United Kingdom not included in previous Hospital Episode Statistics databases). We anticipate a minimum of 600 procedures to be recorded in this dataset. The number of cases recorded will not be capped.

Each centre will have a nominated lead surgeon who will be assisted by other team members to undertake patient identification, collection of a full dataset and entry into the study registry. Prior to publication, each lead surgeon will be responsible for collating a list of contributors from their site.

Data collection

Details of the data collection form are provided in Appendix 5. Data will be collected in the following categories:

- Demographic details
- Referral details
- Predominant symptoms
- Pre-operative investigations
- Indications for surgery
- Intra-operative details
- Post-operative details
- Details of any readmission
- Post-operative patient outcomes at last follow up point

Data management

ARROW will use ALEA Clinical (www.aleaclinical.eu) to host electronic records. Collaborators will be granted online access to the survey section of the study and on completion of the survey and evidence that they have registered ARROW with their local audit department they will be provided access to the prospective patient entry section. Collaborators will be asked to complete electronic Case Report Forms (eCRFs) for each patient in a timely manner using source documents from each individual case.

Data will be collected and retained in accordance with local laws and regulations, for example the General Data Protection Regulation (2018) in the UK. The Lead Surgeon at each site is responsible for ensuring the accuracy, completeness, and timeliness of the data. Any study documents will be retained in a secure central location at the University of Southampton during and after the study has finished. During the study, all data will be reported in pseudo-anonymised form and identified by the assigned participant number. Individual sites will only have access on ALEA to data collected via their specific site, including that which links a

participant to their assigned participant number. The administrative centre (University of Southampton) will have access via ALEA to all data except that which links a participant to their assigned participant number, from all investigation sites. Ultimate responsibility for security and safety of data submitted to ALEA rests with the Professor Tim Underwood and the University of Southampton Clinical Informatics Research Unit.

Only the Lead Surgeon at each site and authorised personnel should enter or change data in the electronic Case Report Forms (eCRFs) in ALEA. An audit trail will be incorporated into the eCRFs whereby any changes to the data originally entered will be documented. A table of all changes including the original value, new value, field, relevant visit details, individual responsible for changes and why the changes were made, will be stored in a table in the study database. Further details regarding data collection and storage via the ALEA online platform are provided in Appendix 6.

Quality of the data entered into the eCRF data fields will be controlled by limiting free text fields, drop down options and predefined data formats. Range checks for chosen fields will automatically appear where data points are outside of a pre-specified range. Verification and explanation for unexplained data point will be required and will subsequently appear in a query log for the study team to check.

Data validation

Data completeness from individual centres for all study fields should be 95% or greater. If data completeness is less than 95% then the local study team will be required to investigate. Failure to do so will be considered by the steering committee, and data from that centre may not be

included in the final analysis. Individual units will be asked to nominate an independent data validator as part of the study team who will review 10% of submitting patient files and 25% of data points within these submissions. The overall responsibility for data completeness and accuracy will rest with the lead Consultant for that institution.

Data analysis

Results 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[28]. Data will be collated and analysed in clinically relevant categories, and chi-square tests used, where appropriate, to detect differences in proportions between groups. Procedures performed for missing data, if identified, will include multiple imputation.

Results will be analysed to compare adherence to the established audit standards as detailed in Table 1.

An initial pilot data collection period will occur at five UK hospitals (Musgrove Park, North Bristol, University Hospital Bristol, Southampton, and Brighton) prior to commencement of the study in order to test the feasibility of the collection of proposed data points using the ALEA eCRF. Sites will be required to pre- register for the audit and obtain local study approval as per institution policy prior to commencement of the study.

Proposed Study Timeline

Data collection and analysis will be completed along the following timeline:

- 1st February 2020 to 29th February 2020 – Pilot study period within five United Kingdom centres.
- 1st April 2020 to 31st March 2021 – Main study data collection period.

- 29th June 2021 – Main study 90-day follow up ends.
- 2nd Sept 2021 – Central data submission anticipated to be complete.
- 30th Dec 2021 – Anticipated that independent data validation completed.
- 28th March 2022 – Initial data analysis anticipated to be complete.

Discussion

Variation in surgical practice and outcomes after elective surgical intervention are an important quality metric within healthcare. This study will identify and explore variation in process and outcome after anti-reflux surgery within the United Kingdom using a collaborative cohort methodology. The results generated by this audit will facilitate local and national quality improvement initiatives and generate new possibilities for future research in anti-reflux interventions.

Dissemination of results

This study will follow the previously reported approach for dissemination amongst surgical research collaboratives. Local teams will retain access to their own data to facilitate local quality improvement. The full dataset will be reported at national and international scientific congresses and will contribute to peer-reviewed publications and national quality improvement initiatives.

Authorship

Manuscript preparation following data analysis will be undertaken by a writing committee. All members of the ARROW protocol writing group, steering committee, lead surgeons and team members for individual centres will be Pubmed citable collaborators as part of the ARROW study group. Units who fail to submit data, or whose data is incomplete (as outlined above)

will be excluded from the authorship list. Prior to publication, each lead surgeon will be responsible for collating a list of authors from their site.

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