ESTES
Snapshot Audit 2018

COHORT STUDY PROTOCOL

Acute complicated calculous biliary disease

Study period: 1 October – 31 December 2018

ClinicalTrials.gov Registration: NCT03610308

Table of Contents

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2 Abstract

Background: Acute complications of biliary calculi are common, morbid and complex to manage. Variability exists in the techniques utilised to treat these conditions at a surgeon and unit level. This high-quality pan-European prospective audit will establish current practices and correlate them against outcomes.

Aim: To explore differences in patients, techniques and outcomes across the international cohort to identify areas of practice variability in the presentation and management of acute complicated calculous biliary disease.

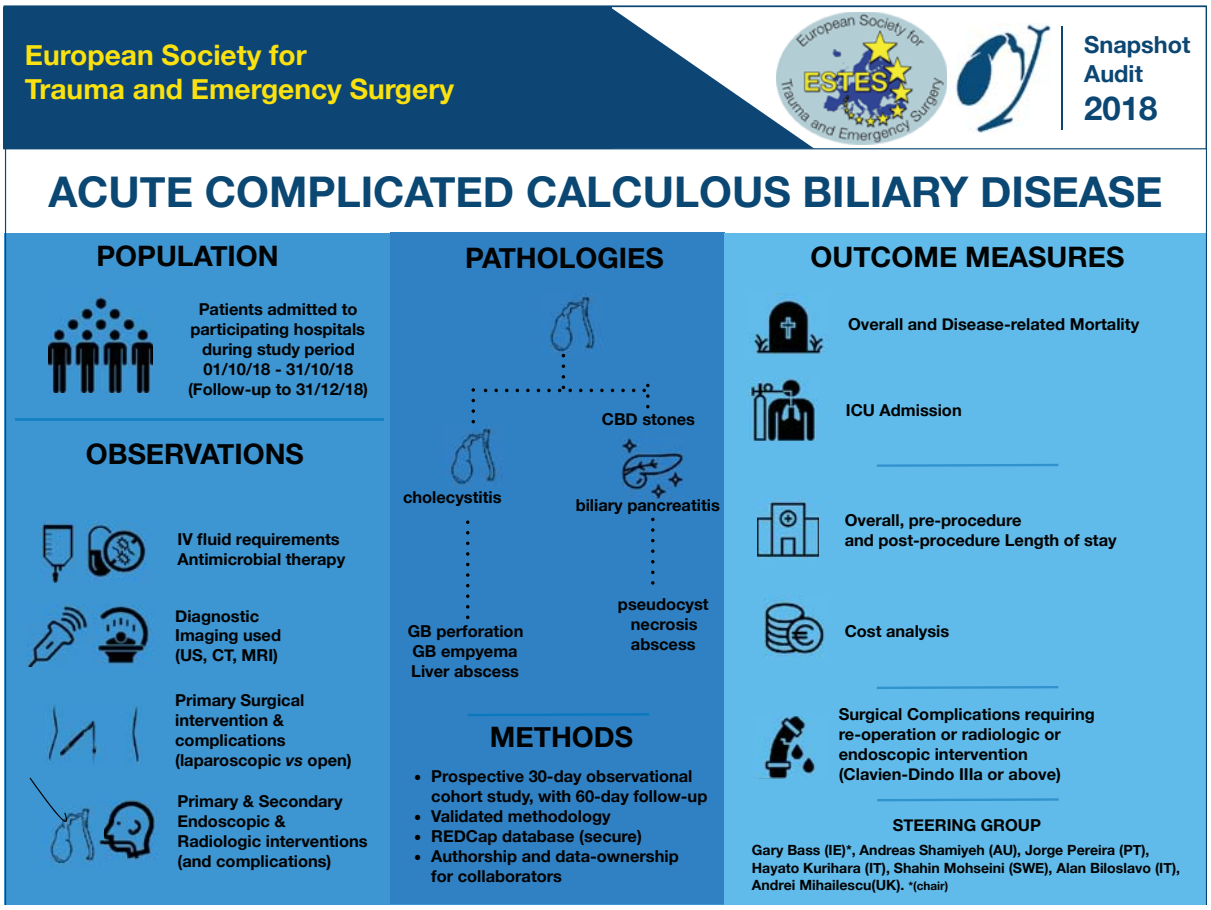
Endpoints: A two-stage data collection strategy collecting patient demographics, details of operative, endocopic and radiologic intervention and outcome metrics. Several outcomes measures will be used including mortality, surgical morbidity (including Clavien-Dindo Grade 3a and above), ICU stay and length of hospital stay.

Methods: This 30 day prospective audit will be performed across Europe in late autumn 2018, and will be co-ordinated by the Emergency Surgery Cohort Study committee of European Society of Trauma and Emergency Surgery. This will be preceded by a one-week, three-centre pilot. Sites will be asked to pre-register for the audit and will be required to obtain appropriate regional or national approvals in advance of the enrolment date. The ESTES cohort studies committee will assist sites to register where possible.

During the study period, all eligible patients with acute complicated biliary calculous disease will be recorded contemporaneously and followed-up through to 60 days from their admission. The audit will be performed using a standardised pre-determined protocol and a secure online database. The report of this audit will be prepared in accordance with guidelines set by the STROBE (strengthening the reporting of observational studies in epidemiology) statement for observational studies.

Discussion: This multicentre, pan-European audit of acute complicated biliary calculous disease will be delivered by emergency surgeons and trainees in an organised and homogenous manner. The data obtained about areas of variability in provision or practice, and how this may impact upon outcomes, will serve to improve overall patient care as well as being hypothesis generating and inform areas needing future prospective study.

3 Visual Abstract



4 Key Study Dates

Key Dates	
31 July 2018	Draft protocol published; Call for participating centres
1 October 2018 **to 31 October 2018**	Patient inclusion window starts *Sites should collect 30 days of consecutive patient admissions within this window.* *Sites should follow up each patient for 60 days.*
31 October 2018	Last day of admission to include in data collection
31 December 2018	Last day of patient follow up (60 days from patients admitted from 31 October 2018).
30 January 2019	REDCap® database locked *This is the deadline for data submission*
5 May 2019	Data presented at ECTES 2019 Prague *We would aim for near-simultaneous publication of study manuscript*

5 Introduction

Multicentre, 'snapshot' cohort studies or audits have the ability to gather large patient numbers in short time periods from many hospitals. They allow exploration of differences in patients, techniques and management across the cohort to identify areas of practice variability that may result in apparent differences in outcome. As such, whilst not providing true evidence of efficacy or the impact of a particular variable, they can be hypothesis-generating and can identify areas warranting further study in future randomised controlled trials.

The European Society of Trauma and Emergency Surgery has recognised the strengths of this form of research, as well as its power in bringing together surgeons and emergency surgical units across multiple regions or countries for a common research goal, thus strengthening an active network of research participation across Europe.

5.1 Scope

Calculous cholecystitis, choledocholithiasis and their complications are frequently seen in patients admitted through the Emergency Departments of all hospitals where general surgery is performed.

Despite the frequency of presentation of these patients, there remains uncertainty about the optimal timing of diagnostic investigations, the appropriate resuscitation and microbial therapies and the indications and timing of endoscopic, percutaneous interventional radiologic or surgical therapies, which results in significant heterogeneity of approaches and outcomes across Europe. In addition, patient demographics and disease characteristics vary between units and countries, as do unit policies and throughput levels.

This 'ESTES snapshot audit' - a prospective observational cohort study – has a dual purpose. Firstly, as an epidemiologic study, it aims to uncover the burden of disease across Europe. Secondly, it aims to elucidate the current strategies employed to diagnose and treat these patients. These twin aims will serve to provide a 'snapshot' of what we are doing now, but will also be hypothesis-generating while providing a rich source of patient-level data to allow further analysis of particular clinical questions.

6 Methods

6.1 Summary

Pan-European, prospective audit of consecutive patients admitted for the treatment of complicated calculous biliary disease over a 30-day study period. The audit shall include unscheduled admissions from 1 October 2018 to 31 October 2018.

Commencement timeframe: The sites will start within a time window from 1 October to 31 October 2018. Following commencement, the sites will be required to include all eligible consecutive patients for 30 consecutive days.

Final date for operation inclusion: The sites can include admissions that occur up to 31 October 2018.

All patients will be followed for 60 days post-admission. Data collection should therefore be completed by 31 December 2018.

As this is an observational cohort audit, no change to normal patient management is required.

6.2 Primary Objective

To explore differences in patients, techniques and outcomes across the entire cohort to identify areas of practice variability resulting in apparent differences in outcome warranting further study.

Examples of the postoperative outcomes that the study will examine are:

- Incidence of complicated acute calculous biliary disease
- Complications (type, grade and rate) related to disease and/or therapies within 30 post-operative days
- Length of post-operative stay in the hospital and cost-analysis
- Re-admission within 30 postoperative days
- Histopathological results

6.3 Primary Research Questions

(should these be required for local approvals process)
What is the local and Europe-wide incidence of complicated calculous biliary disease?
What are the treatment algorithms currently employed in the management of these patients?

6.4 Secondary Research Questions

(should these be required for local approvals process)
What is the prevalence of complications and treatment failure in the management of complicated calculous biliary disease?
How do variations in the approach to these conditions impact on cost and length of hospital stay?

6.5 Inclusion Criteria

Adult patients (over 18 years of age) admitted for:

- Acute gangrenous or perforated calculous cholecystitis (AAST Severity Grade II or above)
- Choledocholithiasis or complications of cholelithiasis and/or choledocholithiasis
- Biliary Pancreatitis

Procedures which should be included:

1. Cholecystectomy (open, laparoscopic or robotic)
2. Choledochotomy/common bile duct exploration (open, laparoscopic or robotic)
3. Pancreatic necrosectomy
4. Gastrojejunostomy
5. Cyst gastrostomy
6. Endoscopic retrograde choledochopancreatography (ERCP) or Endoscopic ultrasound (EUS)
7. Percutaneous cholecystostomy (transhepatic or transperitoneal)
8. Percutaneous transhepatic drainage, stone removal or stent placement

6.6 Exclusion Criteria

- Uncomplicated biliary colic
- Biliary dyskinesia
- Acute calculous cholecystitis (AAST Grade I)

Methods for identifying patients

Multiple methods may be used according to local circumstances/staffing:

1. Daily review of emergency theatre lists, emergency endoscopy lists, Interventional Radiology lists
2. Daily review of team handover sheets / emergency admission lists / ward lists
3. Review of operating room logbooks

6.7 Centre eligibility

All hospitals/units performing gastrointestinal surgery are eligible to join this audit. No unit size or case throughput stipulations are made. Countries outside Europe can also participate in this audit.

All participating centres will be required to register their details with the ESTES cohort study office and will be responsible for their own local approvals process prior to the start of the data collection period.

Centres should ensure that they have appropriate pathways and manpower to include all consecutive eligible patients during the study period and provide >95% completeness of data entry before locking of the study REDCap® database on the 30 January 2019.

6.8 Patient follow-up

The audit is designed so normal patient follow-up pathways can be utilised to obtain outcomes data. No additional visits or changes to normal follow-up should be made.

However, local investigators should be proactive in identifying post-diagnosis events (or lack thereof), within the limits of normal follow-up. These may include reviewing the patient notes (paper and electronic) during admission and before discharge to note in-hospital complications, reviewing hospital systems to check for re-attendances or re-admissions, and reviewing post-operative radiology reports, as well as the notes from the in-person outpatient review which we anticipate will occur between 4 and 6 weeks following discharge in most circumstances.

6.9 Data completion and organisation

REDCap® Data Collection Instruments (DCIs) are reproduced in Appendix B.

This research takes the form of an audit study and no changes to the normal patient pathway need to be instigated for it to be run. Data Collection Instrument (DCIs) have been designed to reflect the normal practice and be completed with minimal extra work from the clinical team. We envisage that most hospitals opening for the study will identify a team of 4-5 members, including one or more Consultant-level members (which most centres require to be the official local 'lead' of the study), and trainee surgeons, or data administrators who will undertake the organisational and logistical roles as well as co-ordinate data entry.

DCI A (patient demographics) and DCI C (follow-up information) can be completed by any suitably qualified member of the local team.

We do stipulate the DCI B (operative details) must be completed by, or in direct conjunction with, a surgeon who was present during the operation itself. It should ideally be completed immediately after surgery, at the same time as the operation notes are written, to ensure data accuracy and completeness.

6.10 Missing data and retrospective patient entry

The online database has been designed to allow sites to securely access an individual patient's data for all DCIs throughout the study period. This means that any missing or erroneous data can be altered by the local investigators whilst the data collection period is ongoing. In order to maximise data completion and emphasise its importance to collaborators, participating centres with >5% missing data in **mandatory fields** (i.e. less than 95% data completeness) will be excluded from the study.

The study design means that sites may retrospectively identify eligible patients that were missed primarily and for whom contemporaneous patient and operation data was not entered. We are happy for these patients to be entered during the study period providing that DCI B (operative details) is completed by, or in direct conjunction with, a surgeon who was present during the operation itself.

6.11 Data collection system and information governance

Data will be recorded contemporaneously on a dedicated, secure server running the Research Electronic Data Capture (REDCap®) web application. REDCap® allows collaborators to enter and store data in a secure system. To ensure , in strict compliance with European Union General Data Protection Regulation 2018 (GDPR) legislation, **no patient identifiable data** (name, date of birth, address, etc) will be recorded on REDCap®.

Registered local investigators will have individual password-protected access to their unit's data entered on to REDCap®. During the running of the audit, only local data will be visible to individual investigators; other sites' data will not be accessible.

In order to facilitate entry of follow-up data, investigators will need a way to cross-reference REDCap® records to local patient records at their study centre. This can be achieved, for example, by keeping an offline password-protected spreadsheet containing a look-up table. This should cross-reference the automatically generated REDCap® ID. It is the responsibility of each participating centre to ensure their own records comply with local data governance legislation and with European Union General Data Protection Regulation 2018 (GDPR).

ESTES will not provide administrative support to participating centres for the project or for the REDCap® system. The REDCap® system used will be hosted by ESTES. Many hospitals already use these validated secure data collection tools to measure clinical practice and drive improvements in healthcare in multiple disease settings.

Data will be stored securely on encrypted and certified servers for a minimum of five years under the governorship of the European Society of Trauma and Emergency Surgery (ESTES). The full database may be used for future research, upon request, by collaborating centres, although it should be noted that the anonymised nature of the database means individual patients will not be reverse-identifiable in the future.

6.12 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. Participating centres will be asked to confirm that they have gained formal approval at their site.

6.13 Authorship

A maximum of six (6) investigators from each individual site will be included as formal co-investigators in this research, and will be PubMed searchable and citable. The output from this research will be published under a single corporate authorship – e.g "**ESTES Cohort Studies Group**" or similar.

6.14 Pilot

A one-week pilot across five hospitals across Europe will be performed to test the data collection tool. Adjustments to the REDCap® Data Collection Instruments based on these experiences may be made before rolling out the main audit.

6.15 Publication of data

Data will be published as a pool from all participating units. Subgroup analyses by disease, technique or outcome variables may be presented, but no hospital-level or surgeon-level data will be published whereby an individual patient, unit or surgeon could be identified. If local investigators would like a breakdown of their own unit's data for benchmarking purposes and local presentation/discussion, this can be made be available after the end of the study; however, it will not be possible or permissible to de-anonymise patient data stored in REDCap®, in strict compliance with European Union General Data Protection Regulation 2018 (GDPR).

6.16 Data governance

The ESTES Cohort Studies Committee welcomes the use of the data for further research that benefits patients. Requests can be submitted to the ESTES Cohort Studies Committee. Data sharing is subject to ESTES approval and the appropriate safeguarding as determined by the ESTES. Any future sub-projects should also comply with our policy of a single corporate authorship e.g. "**ESTES Cohort Studies Group**" or similar. However, authors' contributions will be highlighted in accordance with the recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals (commonly referred to as the Vancouver Convention) by the International Committee of Medical Journal Editors (ICMJE).

6.17 Financial arrangements

This study is undertaken voluntarily by participating institutions under the co-ordination of the Emergency Surgery Cohort Study Steering Committee by the European Society of Trauma and Emergency Surgery. It is not anticipated that participating centres would bear any costs. Similarly, no financial reimbursement will be made to units or investigators for their involvement in the project.

7 Key steps for successful inclusion of your centre

1. Contact a member of the **Emergency Surgery Cohort Studies Steering Group** (see contact details earlier in this Protocol Document) about participation in the study at the centre of your choice. They will connect you to any other interested medical students and doctors at your centre or country.

2. Form a **team** of **up to six collaborators**. If possible, it is encouraged that a **medical student** should co-ordinate the team and lead audit registration/data collection. They must be supported by at least one motivated doctor. This can be a doctor of any grade but should preferably a trainee/resident. A consultant/attending surgeon should be involved at each centre.

3. The data collection period will be 1st October 2018 to 31st October 2018. Your team must ensure its availability to collect the data during the entire study period.

4. Ensure that you secure **formal ethics committee approval** from your hospital according to local regulations. This must be done prior to commencing data collection. **It is essential that you begin this process immediately; approval can take up to 2-3 month. If you have any difficulties or are unsure what is required contact the Emergency Surgery Cohort Studies Steering Group or your supervising surgeon, or your local ethics committee chairperson.**

5. Once the local ethics committee approval is received, please forward evidence of this to the **Emergency Surgery Cohort Studies Steering Group.** REDCap® accounts will not be issued until proof of approval is received.

6. Arrange to **meet** with the other members of your team, including the trainee/resident and supervising consultant/attending. Agree in advance who will be responsible for each stage of the project, e.g. identifying patients, collecting baseline data, completing follow-up, data entry to REDCap®. Talk through how you will identify patients and collect required data; it will be particularly helpful if the consultant/attending is present to offer guidance regarding this.

7. **Identify** all patients meeting **inclusion criteria** within the study window.

8. Regularly **follow-up** for information on complications over the **60-day post-operative period.** This study is **prospective,** so you should not wait until the end of the post-operative period to follow-up patients. Discuss the best way to follow up patients with the consultant/attending supervising your audit, as this will vary from centre to centre.

9. Ensure all data has been uploaded to the **REDCap®** system and you have completed all fields, avoiding **missing data points**. If more than 5% of patients at your centre are missing data, your centre cannot be included and your name will be withdrawn from the author list.

8 APPENDIX A - American Association for the Surgery of Trauma (AAST) Disease Severity Grading

8.1 Acute Cholecystitis

AAST Grade	Description	Clinical Criteria	Imaging Criteria (CT/US/HIDA findings)	Operative Criteria	Pathologic Criteria
I	Acute cholecystitis	Right upper quadrant (RUQ) or epigastric pain; Murphy's Sign; leukocytosis	Wall thickening; distention; gallstones or sludge; pericholecystic fluid; non-visualization of gallbladder (GB) on hepatobiliary iminodiacetic acid (HIDA) scan	Inflammatory changes localized to GB; wall thickening; distention; gallstones	Acute inflammatory changes in the GB wall without necrosis or pus
II	GB empyema or gangrenous cholecystitis or emphysematous cholecystitis	RUQ or epigastric pain; Murphy's Sign; leukocytosis	Above, plus air in GB lumen, wall or in the biliary tree; focal mucosal defects without frank perforation	Distended GB with pus or hydrops; necrosis or gangrene of wall; not perforated	Above, plus pus in the GB lumen; necrosis of GB wall; intramural abscess; epithelial sloughing; no perforation
III	GB perforation with local contamination	Localized peritonitis in RUQ	HIDA with focal transmural defect, extraluminal fluid collection or radiotracer but limited to RUQ	Perforated GB wall (non-iatrogenic) with bile outside the GB but limited to RUQ	Necrosis with perforation of the GB wall (non-iatrogenic)
IV	GB perforation with perichole-cystic abscess or gastrointestinal fistula	Localized peritonitis at multiple locations; abdominal distention with symptoms of bowel obstruction	Abscess in RUQ outside GB; bilio-enteric fistula; gallstone ileus	Pericholecystic abscess; bilio-enteric fistula; gallstone ileus	Necrosis with perforation of the GB wall (non-iatrogenic)
V	GB perforation with generalized peritonitis	Above, with generalized peritonitis	Free intra-peritoneal bile	Above, plus generalized peritonitis	Necrosis with perforation of the GB wall (non-iatrogenic)

8.2 Acute Pancreatitis

AAST Grade	Description	Clinical Criteria	Imaging Criteria (CT findings)	Operative Criteria	Pathologic Criteria
I	Acute edematous pancreatitis	Midepigastric abdominal pain and tenderness; elevated amylase and/or lipase	Pancreatitis without phlegmon, necrosis, peripancreatic fluid collection or abscess	Edematous pancreas	N/A
II	Pancreatic phlegmon or peripancreatic fluid collection or hemorrhage	Midepigastric abdominal pain and tenderness; elevated amylase and/or lipase	Phlegmon or peripancreatic fluid collection or hemorrhage	Pancreatic phlegmon or peripancreatic fluid collection	N/A
III	Sterile pancreatic necrosis	Midepigastric abdominal pain and tenderness; elevated amylase and/or lipase	Pancreatic necrosis without extraluminal air or abscess	Pancreatic necrosis without purulence or abscess	Gram stain and culture of necrosis negative for organisms
IV	Infected pancreatic necrosis or abscess	Severe midepigastric abdominal pain and tenderness; elevated amylase and/or lipase	Pancreatic necrosis with extraluminal air or abscess	Pancreatic necrosis with purulence or abscess	Gram stain and culture of necrosis or abscess positive for organisms
V	Extra-pancreatic extension of pancreatic necrosis involving adjacent organs, such as colonic necrosis	Severe diffuse midepigastric abdominal pain and tenderness; elevated amylase and/or lipase	Extra-pancreatic extension of necrosis involving adjacent organs, such as colonic necrosis	Involvement or necrosis of adjacent organs	Involvement or necrosis of resected adjacent organs

9 APPENDIX B – Clavien-Dindo Classification of Complications

Grade	Definition (examples listed in italics)
I	Any deviation from the normal postoperative course without the need for pharmacological (other than the "allowed therapeutic regimens"), surgical, endoscopic or radiological intervention. Allowed therapeutic regimens are: selected drugs (antiemetics, antipyretics, analgesics, diuretics and electrolyte replacement), physiotherapy and wound infections opened at the bedside but **not** treated with antibiotics. *Examples: Ileus (deviation from the norm); hypokalaemia treated with K; nausea treated with cyclizine; acute kidney injury treated with intravenous fluids.*
II	Requiring pharmacological treatment with drugs beyond those allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included. *Examples: Surgical site infection treated with antibiotics; myocardial infarction treated medically; deep venous thrombosis treated with enoxaparin; pneumonia or urinary tract infection treated with antibiotics; blood transfusion for anaemia.*
IIIa	Requiring surgical, endoscopic or radiological intervention, **not under** general anaesthetic. *Examples: Therapeutic endoscopic therapy (do not include diagnostic procedures); interventional radiology procedures.*
IIIb	Requiring surgical, endoscopic or radiological intervention, **under** general anaesthetic. *Examples: Return to theatre for any reason.*
IVa	Life-threatening complications requiring critical care management – **single organ** dysfunction, or neurological complications including brain haemorrhage and ischemic stroke (excluding TIA). *Examples: Single organ dysfunction requiring critical care management, e.g. pneumonia with ventilator support, renal failure with filtration; SAH; stroke.*
IVb	Life-threatening complications requiring critical care management – **multi-organ** dysfunction.
V	Death of a patient

10 APPENDIX D – NCEPOD Procedure Classification

Code	Category	Description	Target time to theatre	Expected location	Example Scenarios	Typical procedures
1	Immediate	Immediate (A) lifesaving or (B) limb or organ-saving intervention. Resuscitation simultaneous with surgical treatment.	Within minutes of decision to operate	Next available operating theatre – "break-in" to existing lists if required	• Ruptured aortic aneurysm • Major trauma to abdomen or thorax • Fracture with major neurovascular deficit • Compartment syndrome • Acute myocardial infraction (AMI)	• Repair of ruptured aortic aneurysm • Laparotomy/ thoracotomy for control of haemorrhage • Fasciotomy • Coronary angioplasty
2	Urgent	Acute onset or deterioration of conditions that threaten life, limb or organ survival; fixation of fractures; relief of distressing symptoms.	Within hours of decision to operate and normally once resuscitation completed	Day time "emergency" list or Out-of-hours emergency theatre (including at night)	• Compound fracture • Perforated bowel with peritonitis • Critical organ or limb ischaemia • Acute coronary syndromes (ACS) • Perforating eye injuries	• Debridement plus fixation of fracture • Laparotomy for perforation • Coronary angioplasty
3	Expedited	Stable patient requiring early intervention for	Within days of decision to operate	Elective list which has "spare" capacity or Day	• Tendon and nerve injuries	• Repair of tendon and nerve injuries • Excision of tumour with potential to bleed or obstruct

		a condition that is not an immediate threat to life, limb or organ survival		time “emergency” list (not at night)	• Stable & non-septic patients for wide range of surgical procedures • Retinal detachment	• Coronary angioplasty
4	Elective	Surgical procedure planned or booked in advance of routine admission to hospital	Planned	Elective theatre list booked & planned prior to admission	• Encompasses all conditions not classified as immediate, urgent or expedited.	• Elective AAA repair • Laparoscopic cholecystectomy • Varicose vein surgery • Joint replacement • Coronary angioplasty

11 APPENDIX C - STROBE Statement—Checklist of items included in reports of *cohort studies*

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders

		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org

APPENDIX E – REDCap® Data Collection Instruments (DCIs)

E.1 Data Collection Instrument 1 – Patient and Centre Demographics

Demographics	Data Type	Values
Country ID	List	*List of included countries*
Centre ID	List	*List of study centres*
Age (years)	Integer	*18-99*
Sex	List	*Male, Female*
Body Mass Index	Integer	*Calculated from weight and height*
Date of Admission	Date	*Date of index admission*
Date of Discharge	Date	*Date of discharge from hospital*
Length of Stay	Integer	*Calculated from input dates (above)*
Disposition	List	*Home, Convalescence in Nursing Facility,Discharge to another Hospital, Death*
Diagnosis	**Data Type**	**Values**
Primary Diagnosis	List	*Acute cholecystitis; Acute cholangitis; Acute pancreatitis; Obstructive jaundice*
AAST Severity	List	*See Protocol Appendix A*
Histopathologic findings	List	*Histopathology reports*

Medical History	Data Type	Values
Date of Index Admission	Date	
Surgical intervention	Yes/No	
ASA Grade	I-V	*(Anaesthetic chart)* *See the American Society of Anaesthesiologists website for definitions and examples:* *https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system*
Charlson comorbidity index	1-...	*See Medcalc https://www.mdcalc.com/charlson-comorbidity-index-cci*
History of previous abdominal surgery	Yes/No	*(Admission clerking, clinical notes, clinic letters).* *Include any abdominal surgery for any indication – e.g. include appendicectomy, cholecystectomy, right hemicolectomy, nephrectomy, caesarian section, etc.*
History of ischemic heart disease		*(Admission clerking, clinical notes, clinic letters). Required to calculate pre-operative Revised Cardiac Risk Index (RCRI).*
Histroy of congestive heart failure		*(Admission clerking, clinical notes, clinic letters). Required to calculate pre-operative Revised Cardiac Risk Index (RCRI).*
History of cerebrovascular disease		*(Admission clerking, clinical notes, clinic letters). Required to calculate pre-operative Revised Cardiac Risk Index (RCRI).*
History of insulin-dependant diabetes		*(Admission clerking, clinical notes, clinic letters). Required to calculate pre-operative Revised Cardiac Risk Index (RCRI).*
History of chronic renal disease		(Admission clerking, clinical notes, clinic letters). Required to calculate RCRI. CKD is defined as a baseline (pre-operative) creatinine >177 umol/L, or >2 mg/dL.
Smoking history	Never smoked Current smoker Ex-smoker (<6 weeks) Ex-smoker (≥6 weeks) Unknown	*(Admission clerking, clinical notes).* *Record smoking status as at time of admission.* *For ex-smokers: record when they stopped smoking: <6 or ≥6 weeks ago.* *For current and ex-smokers: Record their total pack year history. Pack year history can be calculated online at:* *http://smokingpackyears.com*
Immunosuppressant drugs	Steroids – low or high dose	*(Admission clerking, clinical notes, drug chart)* *Steroids: Low dose <20mg, high dose ≥20mg prednisolone or equivalent. Only include patients who were on steroids within a week*

	6-mercaptopurine Methotrexate Azathioprine	*of admission.* *Other drugs: Only include patients who were on 6-MP, MTX or azathioprine within one month of admission.*

E.2Data Collection Instrument 2 – Index admission

Presentation data	**Data Type**	**Values**
Clinical appearance		*Pain, pruritus, skin color, nausea/vomiting, anorexia, fever, rigors*
Lab data	List	*Bilirubin level, Liver enzymes level, cholestasis enzymes level, CRP*
US data	List	*Cholelithiasis is **mandatory**. IHD and/or CBD dilation, GB wall thickening, Pericholecystic fluid, GB perforation*
CT data	List	*Gallbladder perforation, abscess, biloma, ductal dilatation, Balthazar pancreatitis score*
MRCP data	List	*Gallbladder perforation, abscess, biloma, ductal dilatation*
Surgical Intervention	**Data Type**	**Values**
Date of Surgery	Date	
Laparoscopic or Open	Drop-down	Laparoscopic, open, robotic
NCEPOD Classification	Drop-down	***IMMEDIATE** – Immediate life, limb or organ-saving intervention – resuscitation simultaneous with intervention. Normally within minutes of decision to operate. **URGENT** – Intervention for acute onset or clinical deterioration of potentially life-threatening conditions, for those conditions that may threaten the survival of limb or organ, for fixation of many fractures and for relief of pain or other distressing symptoms. Normally within hours of decision to operate. **EXPEDITED** – Patient requiring early treatment where the condition is not an immediate threat to life, limb or organ survival. Normally within days of decision to operate. **ELECTIVE** – Intervention planned or booked in advance of routine admission to hospital. Timing to suit patient, hospital and staff.*
Procedure Performed	List	ICD-10 codes
Complications	List	*None, Wound infection, Abscess, Wound dehiscence, Damage to bile ducts (Strasberg classification), Enterotomy, Haemorrhage*
Complication Severity	Drop-down	See Appendix B, Clavien-Dindo Classification of Complications

Pharmacology	Data Type	
Antibiotics	List - all relevant	
Bacteria identified on culture	List - all relevant	
Thrombopropylaxis	List - all relevant	None, TEDS, LMWH, UFH, other
Stress ulcer prophylaxis	List - all relevant	*None, ranitidine, PPI(oral), PPI (IV)*
Radiologic Intervention	**Data Type**	**Values**
Date of Procedure	Date	*Pain, pruritus, skin color,*
Procedure Performed	List	*ICD-10 codes*
Complications	List	*None, Infection, Pancreatitis, Bleeding, Perforation*
Complication Severity	Drop-down	*See Appendix B, Clavien-Dindo Classification of Complications*
Endoscopic Intervention	**Data Type**	**Values**
Date of Procedure	Date	*Pain, pruritus, skin color,*
Procedure Performed	List	*ICD-10 codes*
Complications	List	*None, Infection, Pancreatitis, Bleeding, Perforation*
Complication Severity	Drop-down	*See Appendix B, Clavien-Dindo Classification of Complications*

E.3 Data Collection Instrument 3 – Follow-up data

Critical Care	Data Type	Values
ICU admission?	Yes/No	
Date of ICU admission	Date	
Date of ICU discharge	Date	
APACHE-II		Calculated APACHE-II score
Post-operative length of stay	Integer	Calculated from Date of Surgery and Date of Admission
Re-admission	Yes/No	
Ongoing morbidity	Yes/No	