

coMpliA nce with evideNce-based cliniCal guidelines in the managemenT of acute biliarY pancreAtitis (MANCTRA-1).

Study Synopsis

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ClinicalTrials.Gov ID Number: NCT04747990

Endorsed by:

World Society of Emergency Surgery (WSES)

Italian Society of Endoscopic Surgery and new technologies (SICE)

American College of Surgeons (ACS) Italy Chapter

Association of Italian Surgeons in Europe (ACIE)

Italian Surgical Research Group (ItSurg)

“Mario Negri” Institute for Pharmacological Research, Milan, Italy.



The World Society of Emergency Surgery



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Study design: international multicenter, retrospective cohort study, observational, no profit

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https://docs.google.com/forms/d/e/1FAIpQLSdzv1VhszFFDIKsIPfD4NKtwCKKcR-MJU2jjN6cWXvF_77QlvA/viewform?usp=sf_link

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TO ACCESS THE ONLINE DATABASE-CRF FORM:

https://docs.google.com/forms/d/e/1FAIpQLSe_SnA3sWQeCG6yad-pEoHeKu0iz-Dav1amQ1r70gGF3Myynrg/viewform?usp=sf_link

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coMpliAnce with evidence-based clinical guidelines in the management of acute biliary pancreatitis (MANCTRA-1).

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Background

Acute pancreatitis (AP) is an inflammatory disease of the pancreas, most commonly caused by gallstones or excessive alcohol use. It represents a management challenge and a significant healthcare burden. The incidence of AP ranges globally from 5 to 30 cases per 100.000 inhabitants/year, and there is evidence that the incidence has been rising in recent years. The overall case-fatality rate for AP is roughly 5%, and it is expectedly higher for more severe stages of the disease. In most cases (80%), the outcome of AP is rapidly favourable. However, acute necrotizing pancreatitis (ANP) may develop in up to 20% of cases and is associated with significant rates of early organ failure (38%), needing some surgical/endoscopic intervention (38%), and death (15%).

In the United States, AP is a leading cause of inpatient care among gastrointestinal conditions: more than 270.000 patients are hospitalized for AP annually, at an aggregate cost of over 2.5 billion dollars per year. In Europe, the UK incidence of AP is estimated as 15-42 cases per 100.000/year and is rising by 2.7% each year.

Despite several scientific societies published their clinical practice guidelines making recommendations on the management of AP, the adherence to them is lacking. Audits about biliary AP have been performed in Italy, Germany, France, and England, with quite disappointing results. Indeed, in these audits, the treatment of biliary AP differed substantially from the recommendations. For example, less than 15% of the responders stated that they strictly followed all recommendations included in the guidelines in Germany, and 25.8% of patients did not receive definitive treatment for biliary AP within one year in the UK.

These findings support the view that publication alone of nationally or internationally developed and approved guidelines is insufficient to modify the practice of non-specialists and raises the question of how best to spread guideline recommendations. Moreover, in 2020, the spread of the virus Covid-19 had represented a pandemic, which also profoundly impacted the surgical community. There are many ways the outbreak of the Covid-19 pandemic could have influenced daily clinical practice for patients with biliary AP, leading to a failure to adhere to the recommendations coming from the guidelines, especially those regarding the early and definitive treatment with cholecystectomy or ERCP and sphincterotomy. First, the recommendation to postpone all non-urgent endoscopic procedures during the peak of the pandemic. Second, the recommendation to conservatively treat inflammatory conditions such as acute cholecystitis and acute appendicitis wherever possible.

Rationale for the study

Despite existing evidence-based practice guidelines for the management of biliary AP, several studies have identified significant discrepancies between evidence-based recommendations and daily clinical practice. It is believed by many that clinical guidelines would help to decrease inappropriate variation in practice, that they provide a rational basis for referral, and that they would help to reduce uncertainty in the management of some conditions. Clinical guidelines also provide a basis for continuing medical education and can improve control of healthcare costs. However, the value of national and/or international guidelines is very much dependent on a strategy for their implementation.

Although different guidelines for the management of biliary AP have been published, they have not been adequately investigated, and compliance has generally been unsatisfactory.

Deficiencies and lack of standardization of the management of AP worldwide have been reported.

The most commonly reported gaps between clinical practice and AP guidelines include the indications for CT scan, need and timing of artificial nutritional support, indications for antibiotics, and surgical/endoscopic management of biliary AP.

MANCTRA-1 study can identify a number of areas for quality improvement that will require new implementation strategies. We aim to summarize the main areas of sub-optimal care due to the lack of compliance with current guidelines to provide the basis for introducing a number of bundles in AP patients' management to be implemented during the next years.

Aim of the study

Since the clinical compliance with recommendations about AP is poor and the impact of implementing guideline recommendations in biliary AP has not been well studied globally, we launched the MANCTRA-1 study intending to demonstrate areas where there is currently a sub-optimal implementation of current guidelines on biliary AP.

Moreover, we argue that during the Covid-19 pandemic, the tendency to disregard the guidelines recommendations has been more marked than usual, and we will try to find out if AP patients' care during the Covid-19 pandemic resulted in a higher rate of adverse outcomes compared to non-pandemic times due to the lack in the compliance of the guidelines.

Primary objective

- 1. To evaluate which items of the current AP guidelines, if disregarded, correlate with negative clinical outcomes according to the different clinical presentations of the disease**

Secondary objectives

- 1. To assess the compliance of surgeons worldwide to the most up-to-date international guidelines on biliary AP**
- 2. To evaluate the medical and surgical practice in the management of biliary AP during the non-pandemic (2019) and pandemic Covid-19 periods (2020)**
- 3. To investigate outcomes of patients with biliary AP treatment during the two study periods**

Primary outcomes

- 1. 30-day mortality: assessed by the number of AP patients with biliary etiology deceased during the non-pandemic period (2019) and the Covid-19 pandemic period (2020)**
- 2. 30-day morbidity: assessed by the number of AP patients with biliary etiology who experienced any type of AP-related complication within 30-days from the hospital admission during the non-pandemic period (2019) and the Covid-19 pandemic period (2020)**

Secondary outcomes

- 1. Early definitive treatment rate in 2019 vs. 2020: defined as treatment in accordance with the current guidelines (cholecystectomy or ERCP with endoscopic sphincterotomy during the same hospital admission or within 2 weeks of discharge)**
- 2. 30-day hospital readmission rate in 2019 vs. 2020: defined as hospital readmission within 30-days from discharge for recurrent biliary AP while awaiting interval cholecystectomy, or due to post-cholecystectomy complications**
- 3. Predictive factors of morbidity and mortality in patients with biliary AP**

The compliance of surgeons to the most up-to-date international guidelines on biliary AP will be assessed through the analysis of the following attitudes:

Use of scoring systems for the diagnosis and severity grading of biliary AP

Use of lipase dosage (for the diagnosis) and CRP (for the severity grading) during the diagnostic workup

Use of Ultrasound scan, CT scan, MRCP, and endoscopic Ultrasound scan (EUS) in the correct way and timing

Use of early ERCP and sphincterotomy in case of cholangitis and/or choledocholithiasis

Use of percutaneous and/or endoscopic drainage in case of infected pseudocyst or necrosis

Timing of surgical necrosectomy

Timing of re-laparotomy in case of open abdomen strategies

Use of prophylactic antibiotics/antifungals

Use of somatostatin analogs

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Use of early enteral feeding

Use of early definitive treatment strategies, including cholecystectomy and/or ERCP and sphincterotomy

Study design

The MANCTRA-1 study (coMpliA nce with evideNce-based cliniCal guidelines in the managemenT of acute biliaRy pancreAtitis) is an international multicenter, retrospective cohort study to assess the outcomes of patients admitted to hospital with a diagnosis of biliary AP and the compliance of surgeons worldwide to the most up-to-dated international guidelines on biliary AP. The study compares data collected in 2019 (pre-pandemic period) with those of 2020 (Covid-19 pandemic period).

Study population

All consecutive adult patients admitted to the participating surgical departments with a clinical and radiological diagnosis of biliary AP (with and without concomitant cholecystitis) between 01/01/2019 and 31/12/2020. Patient data will be retrospectively analyzed and demographic characteristics, comorbidity status, clinical and radiological findings, treatment strategies, 30-day morbidity and mortality will be evaluated.

Inclusion criteria

Patients of both sexes, ≥ 16 years old, admitted to any of the participating surgical departments and/or internal medicine or gastroenterology departments for biliary AP in 2019 and 2020.

Exclusion criteria

Patients with AP of etiology other than gallstones; Pregnant patients.

Study periods

The pre-pandemic period runs from 01/01/2019 to 31/12/2019. The Covid-19 pandemic period runs from 01/01/2020 to 31/12/2020. Data will be entered in the database from 01/03/2021 to 31/08/2021.

Data collection (see also the “Analyzed Data” - CRF - paragraph below)

All epidemiological, clinical and surgical data will be collected on a CFR that will be completed by accessing to a protected data system. The link for accessing the completion of the CFR will be sent via email to only one contact person (Local Lead) of each participating center.

Sample size

Studies on biliary AP found a mortality rate of approximately 10%. Patients with biliary AP tend to have a higher mortality than patients with alcoholic pancreatitis. However, this rate has been falling over the last 2 decades as improvements in supportive care have been initiated. In patients with severe disease (organ failure), who account for about 20% of presentations, mortality is approximately 30%. This rate has not decreased in the past 10 years.

We estimate that a minimum of 200 patients per group (2019 vs. 2020) would yield a power of 0.80 ($1-\beta$) to establish whether changes in clinical care for patients with biliary AP during the Covid-19 pandemic has impacted on overall mortality using a one-sided significance α level of 0.05 (5%) with power sample size calculator (sealedenvelope.com).

Statistical analysis

The dichotomous variables will be expressed as numbers and percentages, while continuous variables will be expressed as mean and SD, or median and IQR (minimum and maximum values). Student's t test or ANOVA will be used for comparisons of continuous variables between groups. Chi-squared test or Fisher's exact test, as appropriate, will be used for analysis of categorical data. Multilogistic regression models will be used to investigate clinical attitudes, physical, laboratory, and radiologic variables predictive of morbidity and mortality. A value of $P < 0.05$ will be considered statistically significant.

Ethical aspects

This is an international observational study, it will not attempt to change or modify the clinical practice of the participating physicians. The study will meet and conform to the standards outlined in the Declaration of Helsinki and Good Epidemiological Practices. Every clinical center attending the study is responsible for Ethics Committee approval depending on the local policy for observational and non-interventional studies. All surgeons involved in the patients' recruitment will be included in the research authorship.

Publication policy

The Local Lead and two Collaborators from each center will be listed as Co-authors in the final publications. Data will be published as a pool from all participating surgical units. Data emerged from the MANCTRA-1 study will be published irrespective of findings. Results will be published on ClinicalTrials.Gov and each manuscript that is generated based on the registry will be disseminated to all participating centers before final publication.

Safety issues

None.

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Data collection

In each centre, the coordinator will collect and compile data in an online case report system. Data will be recorded contemporaneously on a dedicated, secure server that allows collaborators to enter and store data in a secure system. No patient identifiable data (name, date of birth, address, telephone number, etc.) will be recorded.

Informed consent

Due to its retrospective design, this observational study will not attempt to change or modify the laboratory or clinical practices of the participating physicians. Consequently, informed consent will not be required.

Data management

Every local investigator is responsible for entering data on an on line case report form for every patient included in the study.

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Financial and Insurance

Not applicable.