

LETTER TO THE EDITOR

Protocol for a national, multicentre prospective study of acute pancreatitis management and outcomes: the PANORAMA study

Abstract

Aim: The primary aim of this study is to determine compliance with key quality performance indicators (QPIs) for the management of acute pancreatitis. The secondary aim is to examine the relationship between compliance to QPIs and clinical outcomes with factors that influence this.

Methods: This prospective cohort study will be conducted via the trainee-led STRATA collaborative network. All public hospitals in Aotearoa New Zealand will be eligible to participate. Data will be collected on all adult patients who are diagnosed with acute pancreatitis over a 3 month period. The primary outcome is compliance with the QPIs for the different domains of acute pancreatitis management. Secondary outcomes include early (30-days from index admission) clinical outcomes including incidence of locoregional complications, interventions, organ failure, and mortality.

Conclusion: This protocol describes the methodology for a nationwide prospective cohort study in Aotearoa New Zealand to evaluate compliance based on QPIs derived from the literature. These data will lay the foundation for future registry studies, clinical trials, and quality improvement initiatives.

Introduction

Acute pancreatitis (AP) is one of the most common gastrointestinal conditions leading to hospital admission. It has an estimated annual incidence of 58 per 100,000 in Aotearoa-New Zealand (AoNZ) adults.¹⁻³ AP is characterised by a local and systemic inflammatory response with variable clinical progression, from mild to severe as defined by the degree of organ dysfunction.⁴ Most patients with AP suffer only mild disease that is self-resolving. However, more than 20 % develop moderate or severe AP, which involves pancreatic or peripancreatic necrosis, organ failure, or both. Severe pancreatitis has a risk of mortality between 20 and 40 %.⁵⁻⁸ Despite the substantial disease burden, there are no effective therapies that alter development of necrosis and/or organ failure and management remains largely supportive.

In the last decade, landmark clinical trials have provided substantial guidance on the management of the AP, particularly with regards to antibiotic use, endoscopic retrograde cholangiopancreatography (ERCP),⁹ nutritional supplementation and management of necrosis.^{10,11} Furthermore, multiple organisations have developed and disseminated evidence-based guidelines for managing AP. However, their adoption of the guidelines into clinical practice remains suboptimal.^{12,13} Recent international cohort studies that assessed compliance with current guidelines in the treatment of patients with acute biliary pancreatitis showed a wide variability of practice.¹⁴ While noncompliance with published guidelines may suggest that recommendations are based on insufficient evidence, limited compliance persists even in areas where high quality evidence

from randomised controlled trials (RCT) is available to guide management.^{14,15} There are no national data for acute pancreatitis management AoNZ.

The primary aim of this study is to determine compliance with key quality performance indicators (QPIs) derived from the literature. The study also aims to examine the relationship between compliance to QPIs and clinical outcomes with factors that may influence this. This study, therefore, aims to provide data that can be used for quality improvement in healthcare services to deliver better outcomes for those diagnosed with AP across AoNZ.

Methods

Study design

PANORAMA is a national multi-centre, prospective observational cohort study of patients with acute pancreatitis. This study adapts the student- and trainee-led collaborative research model as previously used by organisations such as EuroSurg¹⁶ and STARSurg.¹⁷

Teams of collaborators will be formed in each hospital, consisting of medical students, junior doctors, trainees, registrars, and supervising consultants. The local leads of each team will be responsible for securing local ethical approval and providing coordination. Each centre will have a supervising consultant to oversee the ethics applications and to ensure that the study does not interfere with clinical care. The number of data collectors in each centre will be limited to 12. All team members will be credited as PubMed citable authors.

Data will be collected prospectively from eligible patients' medical records and there will be no direct patient interaction. Collaborators will have the responsibility of registering this study at their locality, acquiring appropriate approvals, identifying patients, collecting data and completing 30-day follow-up. Where hospital leads fail to submit complete data collaborators at that hospital will be excluded from the authorship list; if substantially incomplete data is submitted, the writing committee may decide to exclude that hospital from further analysis.

Setting

All publicly-funded secondary or tertiary hospitals in New Zealand within the Health New Zealand Directorate will be eligible to participate in PANORAMA. All participating centres must register the study in accordance with local regulations, and evidence of this registration will be maintained by the coordinating investigator.

In the event of patient transfer from one centre to another, a process has been established to avoid double entry of the patient's records. In this scenario, data collectors will be instructed to inform the site lead who will then inform the coordinating investigator and the site lead of the accepting hospital. The initial record will be transferred on REDCap between the data access

groups (DAGs) to allow for continued data collection. Furthermore, there is a binary datapoint in the data extraction forms inquiring if patients have been transferred to ensure this is not missed.

Quality performance indicators

Multiple practice guidelines have been published for the management of AP.^{13,18–22} The recommendations in these guidelines are usually based on a systematic review of the relevant literature and the best available evidence, which is usually graded. 'Quality performance indicators' (QPIs) were drawn from a detailed review of published evidence-based recommendations and relevant randomised controlled trials for each of the nominated management domains (*Supplementary Appendix*). Any differences in the recommendations from the source guidelines were resolved by discussion amongst the Scientific Advisory Group and consensus established for the QPIs. Furthermore, the QPIs were reviewed by an independent academic pancreatic surgeon not involved in the conduct or analysis of the study to ensure concordance with the current guidelines. The QPIs are largely relevant to the first 72 h of admission in hospital.

The QPIs were developed for the following management domains are defined in [Table 1](#).

Table 1 The quality performance indicators for the management of acute pancreatitis, drawn from the evidence-based guidelines in the literature

Management Domain	Quality performance indicator
Aetiology	All patients are appropriately investigated for aetiological factors that may alter management in the early (<72 h) phase. 1. Radiological imaging of the biliary tree. 2. Hypertriglyceridaemia investigated.
Prediction of severity	All patients have a prediction of disease severity on admission.
Radiology	Initial CT assessment performed after 72 h if poor response to initial management or clinical deterioration, unless there is diagnostic uncertainty. Not required for severity prediction.
Fluid resuscitation	1. All patients commenced on IV balanced salt solution within 1 h of admission to the emergency department by a clinician and at an initial rate of 7.5–12.5 ml/kg in response to hypovolemia until resuscitation goals were reached. 2. Then a rate of 1–2 ml/kg/hour for patients not tolerating PO in the first 72 h.
Antibiotics	Antibiotic prophylaxis is not prescribed for the prevention of infectious complications in AP.
Nutrition	1. No patients made 'nil-by-mouth' and no food withheld unless there was a clear clinical indication. 2. Patients with 'mild' disease allowed an ad libitum low fat diet when from admission and at least within 72 h of admission. 3. Patients with moderately severe/severe disease are first commenced on enteral nutrition if they do not tolerate sufficient oral intake by 72 h. Parenteral nutrition is avoided unless intolerance to enteral nutrition.
ERCP/ES	In patients with biliary pancreatitis, early ERCP is only performed within the first 72 h in those presenting evidence of acute cholangitis (Charcot's triad).
Cholecystectomy	Laparoscopic cholecystectomy performed in the same admission for mild biliary pancreatitis.
Anticoagulation^a	All patients with predicted severe AP started on prophylactic anticoagulation within 24 h of admission or continued on their regular anticoagulation therapy if applicable.
Analgesia^a	All patients given narcotic analgesia within 1 h of admission, unless AP is mild and simple analgesics provide optimal pain relief.

^a The lack of sufficient evidence for these two domains means that these QPIs are based on the management of other acute inflammatory conditions.

Patient eligibility

Patients must fulfil the following criteria to be considered eligible for inclusion in this study.

Inclusion criteria

- All patients ≥ 16 years old who present with AP, as defined by the revised Atlanta criteria (*Supplementary Appendix*).
- Presenting to a public hospital that admits and manages acute patients in AoNZ.

Exclusion criteria

- Age less than 16.
- Chronic pancreatitis (*Supplementary Appendix*).
- Postoperative pancreatitis following upper gastrointestinal surgery (not including endoscopic retrograde cholangiopancreatography [ERCP]).

Required data and study outcomes

Specific data points are detailed in the case report forms and data dictionary outlined in *Supplementary Appendix*. Centre-level, de-identified data from each centre will be requested including: the presence of a hepatobiliary-pancreatic (HPB) surgeon at the hospital (if yes, the number of HPB surgeons), the number of available intensive care unit (ICU) beds, the availability of a high-dependency unit (HDU - and if there is, the number of HDU beds available), the availability of endoscopic retrograde cholangiopancreatography (ERCP) service and number of endoscopists, the availability of an interventional radiology service and number of interventionists.

Study outcomes will include the proportion of patients compliant with the QPI for each domain of management. Variation will also be examined at hospital level. Further outcomes of interest include respiratory failure requiring high-flow oxygen, non-invasive ventilation, or mechanical ventilation; renal failure requiring new renal replacement therapy; requirement for inotropic or vasopressor support; locoregional complications (pancreatic and peripancreatic necrosis \pm infection); alive and discharged at 30-days from index admission. and centre level variation.

Statistical analysis

The study will be reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.²³ The primary analyses will be descriptive assessments of compliance with QPIs in the selected management domains. Descriptive statistical analysis will be performed where normal continuous variables will be compared with Student's t test, and non-normal continuous variables will be compared with Mann-Whitney U test, if > 2 categories a one-way ANOVA or Kruskal-Wallis test will be used for normal and non-normal variables respectively. Chi-square tests will be

used to detect differences between categorical variables. All analyses will be conducted under a two-tailed hypothesis. Multiple imputation may be used in the case of missing data.

Secondary analyses will evaluate the differences in results according to the hospital. Risk-adjusted funnel plots will be produced to test the performance of individual, anonymised centres for normal rates of primary and selected secondary outcomes. Funnel plots' Y-axes will demonstrate QPI of a management domain and X-axis will show the number of patients admitted in each hospital. Furthermore, differences in clinical outcomes between patients that are managed according to best available evidence (QPI) and those that were not will be explored through mixed effects multivariable logistic models. These models will use the patient at the fixed effect level 1 and the hospital as the random effect level 2 (using the R lmer package) will be performed. A one level, fixed effect binary logistic regression model using a pooled dataset from 5 multiply imputed datasets will also be used in the event of substantial missing data.

Variable selection will be based on statistically significant univariable analysis, and those variables deemed clinically significant. 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 criteria for multilevel models, and p-values for multiple imputed fixed models.

Ethical considerations and data storage

Data will be collected and stored online via the Research Electronic Data Capture (REDCap) web application,^{24,25} hosted and managed by the University of Auckland, New Zealand. No patient identifiable data will be uploaded or stored on the REDCap database.

Locality approval will be sought and obtained at all centres prior to study commencement. An encrypted excel spreadsheet will be kept alongside the REDCap database at each hospital. This will be stored on a password protected hospital computer at each hospital. A unique REDCap number will be created for each patient. This number will allow re-identification of patients by the local hospital lead if required. After data has been uploaded into REDCap the local hospital copy of the data will be destroyed to protect patient privacy. An Excel spreadsheet containing the REDCap key and the relevant patients NHI will be kept allowing future patient re-identification if required. During REDCap data upload there will be no data fields where identifiable data (e.g., names or national number) can be uploaded. Local Excel files will be securely stored at each hospital for 10 years and destroyed following this. The central de-identified data set will be stored for 10 years using REDCap electronic data capture tools.

Publication and authorship rules

The manuscript will be prepared by a writing committee. Prior to publication all hospital leads will be invited to review drafts of the manuscripts, abstracts, social media posts, press releases and any

other publications arising from the study. All investigators and collaborators in the hospital teams including supervising consultant(s) will be acknowledged as PubMed-citable co-authors using a corporate authorship model.²⁶ Authors will acknowledge the study funding sources and other contributors.

Discussion

Acute pancreatitis continues to be a clinical and economic challenge with variable outcomes.^{14,27} There are several reasons for this variation. While it may reflect differences in resources and expertise available in the hospitals, it might also indicate delays in adopting the latest evidence-based guidelines. It might also reflect a lack of standardisation and compliance around best practice guidelines based on high level evidence. This national prospective study will define the level of compliance with a set of QPIs covering key management domains derived from the current literature. It will also evaluate the relationship between the variation and clinical outcomes with the factors that may influence this.

Variation in clinical practice can create inequitable outcomes.²⁸ This is particularly relevant in Aotearoa New Zealand with the indigenous Māori population. Existing evidence demonstrates inequity in outcome already exists, as Māori have higher rates of AP and of post pancreatitis diabetes mellitus when compared to non-Māori.³ This national prospective study will allow for a better understanding of the basis for inequity.

The QPIs have been developed by consensus from current published recommendations. Data will be collected prospectively over 3 months by teams in all public hospitals in Aotearoa New Zealand. Patients will be followed for one month. Data will be collected in relation to each management domain and in emerging areas for improvement, such as the analgesic strategy and the role of prophylactic anticoagulation, where relatively little evidence exists. For example, preclinical models and clinical evidence suggest opiate analgesia may impact the prognosis of pancreatitis.^{27,29} Similarly, as pancreatitis is considered a prothrombotic state, there is emerging evidence to suggest therapeutic anticoagulation could limit failure of the microcirculation and the extent of pancreatic necrosis.³⁰

While there is no specific and effective drug treatment for AP and high-quality care relies on a comprehensive management protocol. This includes early prediction of severity, fluid resuscitation, nutritional support, symptom alleviation, judicious antibiotic administration, and endoscopic retrograde cholangiopancreatography when indicated.¹³ Accumulating evidence and guidelines have defined how supportive management measures can influence the disease course.^{18–22} Conversely, some outdated management measures are ineffective and may even harm the patient.^{4,14}

In summary the PANORAMA study will document the early management of AP in relation to QPIs derived from the current literature. While it is expected to demonstrate variable suboptimal

compliance and outcomes, the benefit will be the identification of areas where quality improvement initiatives and research should be targeted.

Funding source

None.

Declaration of competing interest

None to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.hpb.2024.09.008>.

Steering group

Expert advisory group

STRATA collaborative group

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