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ORIGINAL ARTICLE

Quality of Care Indicators in Patients with Acute Pancreatitis

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Abstract

Background Acute pancreatitis (AP) is a common and expensive condition. Improving quality of care in AP is vital to minimizing cost and improving patient outcomes. However, there has been little work accomplished toward developing and validating explicit quality indicators (QIs) in AP.

Aims To define quality of care in patients with AP by developing explicit QIs using standardized techniques.

Methods We used the UCLA/RAND Delphi panel approach to combine a comprehensive literature review with the collective judgment of experts to identify a defined set of process measures for AP.

Results We produced 164 candidate QIs after a comprehensive literature review. After Delphi review, 75 had a median rating ≥ 7. We excluded 11 QIs where the disagreement index exceeded 1.0 and combined indicators overlapping in content to produce a final list of 22 QIs. Overall, 8 QIs related to diagnosis, prevention, or determination of etiology, 2 QIs focused on determination of severity, 3 QIs captured fluid resuscitation, 2 QIs measured nutrition, 1 QI use of antibiotics, and 6 QIs captured endoscopic or surgical management.

Conclusions We have developed 22 QIs spanning the spectrum of AP management including diagnosis, risk stratification, and pharmacological and endoscopic therapy. These QIs will facilitate future quality improvement by practitioners and organizations who treat patients with AP and further identify areas that are amenable to improvement to enhance patient care. We anticipate that this QI set will represent the first step in determining a framework for demonstrating value in the care of patients with AP.

Keywords Acute pancreatitis · Quality improvement · Quality · Delphi

Abbreviations

AP	Acute pancreatitis
Apache	Acute Physiology and Chronic Health Examination
ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
APA	American Pancreatic Association
ASGE	American Society for Gastrointestinal Endoscopy
BISAP	Bedside index for severity in acute pancreatitis
BUN	Blood urea nitrogen
CRP	C-reactive protein
CECT	Contrast-enhanced CT
Cr	Creatinine
DI	Disagreement index
EMR	Electronic medical records
ERCP	Endoscopic retrograde cholangiopancreatography
HCT	Hematocrit
IAP	International Association of Pancreatology
PN	Parenteral nutrition
PEP	Post-ERCP pancreatitis
QIs	Quality indicators
SIRS	Systemic inflammatory response syndrome
WON	Walled-off necrosis

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Introduction

Acute pancreatitis (AP) is a highly prevalent and expensive condition. In the USA, approximately 275,000 patients are discharged from hospitals each year with a principal diagnosis of AP [1]. This number has increased over the past 20 years, with AP being one of the most common gastrointestinal discharge diagnoses in US hospitals [1–5]. The reason for the increasing incidence of AP in the USA is unclear, but may be related to the rising incidence of gallstones (one of the major causes of AP) in association with the obesity epidemic. The overall mortality associated with AP is less than 2% depending on etiology, the development of complications or pancreatic necrosis, and the number and severity of comorbid medical conditions. The cost of care is substantial, with estimates of total direct and indirect costs ranging from $2.6 to $6 billion annually [1, 2, 4].

In light of the high burden of disease, several professional societies have published evidence-based guidelines and consensus statements defining the criteria and standards of care in AP. These include American Gastroenterological Association (AGA), American College of Gastroenterology (ACG), International Association of Pancreatology (IAP), American Pancreatic Association (APA), and American Society for Gastrointestinal Endoscopy (ASGE) [6–9]. These guidelines include recommendations regarding several domains of AP care including prevention, assessment, and treatment of AP.

Despite these well-disseminated guidelines, recent data indicate deficits in the care provided to patients with AP. These deficits span the spectrum of care from diagnosis to treatment. For example, Vlada et al. [10] found that in a cohort of patients with severe AP referred for tertiary level care, only 31% were imaged appropriately with contrast-enhanced CT to evaluate for pancreatic necrosis and other complications. Further, parenteral nutrition (PN) was administered to 60% of patients with available data, with only 17% receiving the preferred enteric feeding, and no nutritional support provided to the remaining 23% [10]. A large survey of physicians performed by Sun et al. [11] also confirmed poor compliance with guidelines for nutrition and antibiotics use in the management of AP. These data also suggest wide variation in the management of AP based on treating physician, with private practitioners much more likely to utilize PN than academic physicians (70.2 vs. 20.5%) [11].

These examples highlight the disconnect between evidence-based guidelines and clinical practice. Resultantly, the quality of care in AP may be sub-optimal across various domains of care. These deficits are particularly concerning because poor quality of care is known to contribute to adverse patient outcomes and increase overall costs [12–14]. For example, Ragnarsson et al. [15] found that 20% of patients with acute biliary pancreatitis in a Swedish cohort did not receive any intervention (cholecystectomy or endoscopic retrograde cholangiopancreatography [ERCP]). These patients were much more likely to be readmitted with pancreatitis, with the mean cost of recurrent pancreatitis $17,000 ± 23,284. While enticing, these data fall short of a comprehensive look at the full spectrum of quality care in AP.

The first step toward measuring and improving the quality of pancreatitis care is to develop an explicit set of quality indicators (QIs) for AP. There has been little work accomplished toward defining QIs in AP, indicating that a structured quality assessment effort is warranted. We sought to identify a set of QIs that could be used to understand and improve the current process of care in AP.

Methods

Development of a Quality Assessment Tool in AP

We used the UCLA/RAND Delphi panel approach to identify an explicit set of process measures for AP. This approach combines the best available scientific evidence with the collective judgment of experts to determine the appropriateness of aspects of care at the level of patient-specific medical history, symptoms, and test results [16]. This approach has been widely used to develop QIs across several areas of medicine, including cirrhosis, inflammatory bowel disease, and Barrett's esophagus [17–23]. Selecting QIs following this methodology has been shown to be highly reliable with content, construct, and predictive validity [16, 18, 24]. In developing our QI set, we utilized a standardized 3-step method. This included a comprehensive review of the literature, which in turn informed an expert panel of 7 key opinion leaders to determine the appropriateness of candidate QIs, and conversion of these guidelines into measurable QIs.

Development of Quality Indicators

Our QI review process was based on an initial review of existing clinical guidelines related to AP: including IAP, APA, AGA, ACG, and ASGE [6–9]. This review generated the initial cohort of candidate QIs for evaluation. These QIs were further categorized into those measuring care related to diagnosis, determination of etiology, prognosis and management (including fluid resuscitation, nutrition, use of antibiotics, endoscopy, surgery, and management of complications).

For each candidate QI, we defined the population to which it applies and the process of care that it measures. That is, based on RAND/UCLA methodology, we operationalized

candidate QIs by using "IF and THEN" statements, where "IF" describes eligible patient population and "THEN" defines the process of care that should be performed [18, 25]. For example, IF a patient has acute gallstone pancreatitis AND concurrent acute cholangitis and is hemodynamically stable, THEN he/she should undergo ERCP within 48 h of admission.

Review of the Scientific Literature

To transform a process of care into a QI, it must be associated with a clinically important outcome. To assess the strength of evidence and the process–outcome link for each guideline, two investigators (G.K. and R.S.) performed a comprehensive review of all available clinical practice guidelines with the accompanying referenced literature. We also reviewed the published literature that followed the preparation of clinical guidelines to update the data supporting each candidate QI. Literature searches included MEDLINE and EMBASE and identified English language publications up to January 2017. We performed manual searches of bibliographies of key articles and, where available, prioritized data from randomized clinical trials and meta-analyses.

We graded the quality of evidence with a classification system that reflects the size as well as the precision of the treatment effect as depicted in Table 2 [18]. Briefly, class I indicated that the benefit associated with a process outweighs the risk by a wide margin, whereas class III indicated that the risk significantly outweighs the benefit. Class II indicated that although the benefit is greater than the risk, additional data are needed to confirm this advantage. Within each class, level A indicated that the recommendation is based on evidence from multiple randomized trials or meta-analyses, level B that the recommendation is based on a single randomized trial or several nonrandomized studies, and level C that the recommendation is based on expert opinion or case series. We prepared a comprehensive report summarizing the results of our literature review. Refer to Supplementary Technical Appendix 1 for a summary of our literature review report, including the level of evidence supporting the candidate QIs. In addition to levels of evidence, the report sought to clarify issues that might be relevant to implementation of QI measurement; these include eligibility criteria, the time frame during which a process is expected to occur, and the health care delivery setting (inpatient vs. outpatient setting) for the candidate QIs.

Selection of Expert Panel Members

RAND/UCLA Style Expert Panel of Health Care Providers

A multidisciplinary group of 7 gastroenterologists specializing in AP care participated in the QI development initiative. We selected the expert panel members on the basis of their publication records during the past 5 years, membership in the practice guidelines committees, and participation in the Advisory Councils for AGA, APA, ASGE, and ACG. The selection process was designed to maintain geographic, clinical, and research interest diversity among the group, as suggested by the RAND/UCLA methodology [25]. Thus, the final panel included 7 members from across the USA and included academicians with varied clinical and research interests. The panel members met in a one-day face-to-face meeting and one subsequent teleconference.

Expert Panel Ratings

Overview of RAND/UCLA Rating Process

We used the modified RAND/UCLA process to rate the appropriateness of each candidate QI [25]. The method uses a formal group process in which an expert panel discusses and iteratively rates the appropriateness of candidate quality measures and processes of care by using a 2-round process. In the first round, the experts rated the proposed measures individually (via a Web-based survey) without any interaction among the members. Ratings were based on review of an evidence report disseminated to the panel in advance. These preliminary ratings were analyzed in advance of the second round—a face-to-face meeting—during which all QIs and their preliminary ratings were discussed. Then, each of the indicators was re-rated. All ratings were anonymous, and the ratings of each panelist received equal weight. Unlike the guideline development panel, consensus was not required to establish the panel rating.

Rating System

Before the first round of ratings, we provided the panel with the report summarizing the literature review (summary included in Supplementary Technical Appendix 1) with the list of candidate QIs. By using the best available data contained in the report, the panelists rated the appropriateness of each candidate QI by using a standard RAND/UCLA 9-point appropriateness scale (RAS) where 1–3 indicated "definitely not appropriate," 4–6 indicated "uncertain or equivocal appropriateness," and 7–9 indicated "definitely appropriate." The scale was anchored with "1" indicating "extremely inappropriate" and "9" indicating "extremely appropriate" [25]. We instructed the panel to use standardized definitions of "appropriate" and "inappropriate" when rating the QI on the 9-point scale. Specifically, the RAND/UCLA method defines an appropriate process as one in which "the expected health benefits (e.g., increased life expectancy, reduction in anxiety, or improved functional capacity) exceed the expected negative consequences (e.g., mortality, morbidity, or time lost from

work) by a sufficiently wide margin that the process is worth doing, exclusive of cost" [25]. A process is inappropriate when "the expected negative consequences for the patient exceed the expected benefit by a sufficiently wide margin that the process should not be done." An uncertain process is one in which the net result of expected negative consequences and benefits is equivocal and highlights the need for further work to clarify the evidence [25].

We determined the median panel rating to quantify the level of agreement and calculated the RAND disagreement index (DI) for each candidate QI. The DI is based on the distribution and symmetry of the scores across the 9-point RAS and has been externally validated as a measure of variation in provider beliefs. A higher DI indicates wider spread across the 9-point scale, and lower values indicate increasing consensus. If the DI exceeds 1.0, then the distribution meets criteria for extreme variation in ratings. If the DI is $\leq$1.0, then there is no extreme variation. The DI is calculated by using a standard published equation [25].

Meeting Procedures

The panel face-to-face and teleconference meetings were moderated by F.K. (nonvoting member). During these meetings, each panelist received a copy of the tables generated from the pre-meeting ratings to view his or her own score and to compare it with the median score generated from the other panelists. The panel members specifically focused on areas of disagreement. They were also asked to identify additional QIs not on the original list, modify existing QIs that were imprecisely worded, and delete QIs that were perceived to be problematic or irrelevant. After an updated list of QIs was developed, the panelists re-rated the appropriateness of each QI again using the 9-point RAND scale.

We used similar analyses for the final round ratings as detailed above for the first round. We considered a QI as an appropriate measure of quality care if the median rating was 7–9 without any disagreement between the ratings, defined as a corresponding DI $\leq$1.0 [25].

Post Meeting Procedures

After the meeting, a separate group of 11 experts reviewed the final generated list of QIs for face and content validity. This expanded expert panel, which included those participating in the Delphi process, all agreed with the final list of QIs presented.

Results

Our literature review identified 164 candidate QIs that were subjected to review by the expert panel. The complete set of QIs with voting results is included in Supplementary Table S1. Of these 164 candidate indicators, 75 ultimately had a median rating $\geq$ 7. We then excluded 11 QIs where the DI exceeded 1.0, and combined selected indicators which overlapped in content to produce a final list of 22 QIs (Table 1). For example, some QIs were associated with multiple timelines for a process to be completed, of which several were deemed appropriate by the expert panel and hence combined.

We also further characterized QIs based on the class and level of evidence (Table 2). Two-thirds of the QIs had a Class 1 rating (the benefit associated with a process outweighs the risk by a wide margin). The level of evidence also varied with the majority level B or C. Overall, there were 8 QIs related to diagnosis, etiology, and prevention, 2 regarding determination of severity, 3 capturing fluid resuscitation, 2 concerning nutrition, and 1 related to use of antibiotics. The additional 6 QIs were related to endoscopic or surgical management, including ERCP and cholecystectomy.

The selected QIs are reproduced below with summary of the evidence used by the expert panel in choosing these QIs.

1. IF a patient presents with upper abdominal pain, lipase > 3 × upper limit of normal, and/or radiological evidence of pancreatic/peri-pancreatic inflammation or pancreatic necrosis, THEN a diagnosis of AP must be documented within 12 h of presentation.

ACG guidelines specify these clinical criteria for diagnosis of AP. The expert panel agreed with a 12-h window as reasonable for making the diagnosis as this would account for variations in laboratory testing and assessments in routine clinical care.

2. IF a patient is diagnosed with AP, THEN he/she should receive liver function tests within 24 h of diagnosis.
3. IF a patient is diagnosed with AP and has elevated alanine aminotransferase, THEN he/she should receive a transabdominal ultrasound within 48 h of diagnosis.

In a prospective study on the epidemiology of AP, the most common etiology was gallstones in women and alcohol in men [26]. In a large retrospective study of 1068 patients, cholelithiasis and alcohol accounted for 37.1% and 41% of cases, respectively [27]. A sensitivity of 94% and a specificity of 100% were obtained for the detection

Table 1 Acute pancreatitis quality indicators

Quality Indicator	Score (DI)	Level of evidence
Diagnosis		
1. IF a patient presents with upper abdominal pain, lipase > 3 × upper limit of normal, and/or radiological evidence of pancreatic/peri-pancreatic inflammation or pancreatic necrosis, THEN a diagnosis of AP must be documented within 12 h of presentation	8(0.6)	IC
Determination of etiology		
2. IF a patient is diagnosed with AP, THEN he/she should receive liver function tests within 24 h of diagnosis	9(0.2)	IB
3. IF a patient is diagnosed with AP and has elevated alanine aminotransferase, THEN he/she should receive a transabdominal ultrasound within 48 h of diagnosis	9(0.2)	IB
4. IF a patient presents with AP, THEN alcohol history should be documented in the medical records prior to discharge	9(0.2)	IB
5. IF a patient presents with AP, THEN he/she should have serologic measurement of triglycerides within 24 h of diagnosis of AP	8(0.3)	IC
6. IF a patient has unexplained AP and is > 60 years old, THEN cross-sectional imaging should be performed to assess for underlying malignancy within 2 months of initial presentation	8(0.6)	IC
7. IF a patient, < 40 years old, has recurrent idiopathic AP and EUS and s-MRCP are negative, THEN he/she can be considered for genetic testing after two or more attacks	7(0)	IIaC
Determination of severity		
8. IF a patient presents with AP, THEN a severity score should be calculated at admission and at 48 h and documented in the medical records.	8(0)	IIaB
9. IF a patient has AP and does not show clinical improvement (defined as persistent pain, fever, nausea, unable to begin oral feeding) or has clinical deterioration (defined as worsening pain, worsening nausea, hemodynamic instability or signs of infection), THEN a CT or MRI should be performed	8(0.2)	IC
Fluid resuscitation		
10. IF a patient presents with AP, THEN he/she should receive Lactated Ringer's solution for initial fluid resuscitation	8(0)	IIaB
11. IF a patient presents with AP, THEN aggressive hydration (defined as at least 3 ml/kg/h) should be initiated unless cardiovascular, renal, or other related comorbid factors exist	8(0.2)	IB
12. IF a patient with AP is undergoing aggressive initial hydration, THEN he/she should receive tests for BUN, HCT, Cr every 8–12 h for the first 24–48 h	9(0)	IB
Nutrition		
13. IF a patient has mild AP (absence of organ failure or local and systemic complications), THEN oral feeding should be initiated within 24 h of control of symptoms	8(0.3)	IIaB
14. IF patient has severe AP (defined as persistent organ failure or presence of pancreatic necrosis) and cannot tolerate an oral diet, THEN he/she should receive enteral nutrition using nasojejunal feeding within 3–5 days of presentation	8(0.3)	IB
Antibiotic therapy		
15. IF a patent has AP with sterile necrosis (defined as necrosis seen on imaging but no fever, leukocytosis, or other indicators for infection), THEN he/she should not receive antibiotics to prevent the development of infected necrosis	9(0.2)	IB
Endoscopic and surgical management		
16. IF a patient has acute gallstone pancreatitis AND concurrent acute cholangitis and is hemodynamically stable, THEN he/she should undergo ERCP within 48 h of admission	7(0.5)	IB
17. IF a patient has acute gallstone pancreatitis AND concurrent acute cholangitis and is hemodynamically unstable, THEN he/she should undergo ERCP within 24 h of admission after stabilizing the hemodynamic status with hydration and antibiotics	9(0)	IB
18. IF a patient has acute gallstone pancreatitis AND evidence of biliary obstruction by clinical or imaging criteria but no evidence of cholangitis, THEN he/she should undergo ERCP prior to cholecystectomy	8(0.7)	IC
19. IF a patient has mild AP attributed to known gallstones, THEN a cholecystectomy or ERCP with sphincterotomy (if cholecystectomy is not possible) should be performed within 2 weeks to prevent recurrent AP	9(0.2)	IB
20. IF a patient with AP has symptomatic sterile or infected walled-off necrosis, THEN this should be drained	8(0.8)	IB
21. IF a patient with AP develops infected necrosis or fluid collection that meets criteria for drainage, THEN this should be performed through minimally invasive methods with a step-up approach using endoscopic drainage, or percutaneous drainage as the first minimally invasive step, based on available expertise	8(0.5)	IC
Prevention of AP		
22. IF a patient is high risk of post-ERCP pancreatitis, THEN he/she should receive rectal indomethacin **	9(0.15)	IA

** High risk of AP is defined as any one of the following major criteria: suspected sphincter of Oddi dysfunction, a history of post-ERCP pancreatitis, pancreatic sphincterotomy, precut sphincterotomy, more than eight cannulation attempts (as determined by the endoscopist), pneumatic dilatation of an intact biliary sphincter, or ampullectomy. Patients are also considered high risk if they have two or more of the following minor criteria: an age of less than 50 years and female sex, a history of recurrent pancreatitis (≥ 2 episodes), three or more injections of contrast agent into the pancreatic duct with at least one injection to the tail of the pancreas, excessive injection of contrast agent into the pancreatic duct resulting in opacification of pancreatic acini, or the acquisition of a cytologic specimen from the pancreatic duct with the use of a brush

EUS endoscopic ultrasound, *s-MRCP* secretin-magnetic resonance cholangiopancreatography, *CT* computed tomography, *MRI* magnetic resonance imaging, *BUN* blood urea nitrogen, *HCT* hematocrit; *Cr* creatinine, *ERCP* endoscopic retrograde cholangiopancreatography

Table 2 Definition of class and level of evidence. Kanwal et al. [18]

	Class I Benefit >> > Risk Procedure/Treatment should be performed	Class IIa Benefit >> Risk. It is reasonable to perform procedure or administer treatment	Class IIb Benefit ≥ Risk Procedure/Treatment might be considered	Class III Risk ≥ Benefit Procedure/Treatment should not be performed because it is not helpful and might be harmful
Level A	Sufficient evidence from multiple randomized trials or meta-analyses	Some conflicting evidence from multiple randomized trials or meta-analyses	Greater conflicting evidence from multiple randomized trials or meta-analyses	Sufficient evidence from multiple randomized trials or meta-analyses
Level B	Limited evidence from single randomized trial or nonrandomized studies	Some conflicting evidence from single randomized trial or nonrandomized studies	Greater conflicting evidence from single randomized trial or nonrandomized studies	Limited evidence from single randomized trial or nonrandomized studies
Level C	Only expert opinion, case studies, or standard of care	Only diverging expert opinion, case studies, or standard of care	Only diverging expert opinion, case studies, or standard of care	Only expert opinion, case studies, or standard of care

of gallstones in patients with AP when a combination of abnormal liver biochemical tests and transabdominal ultrasound was used [28]. The panel felt that it was appropriate to assess for gallstone pancreatitis using liver biochemical tests within 24 h of diagnosis of AP and to obtain an ultrasound based on this initial screen within the first 48 h.

4. IF a patient presents with AP, THEN alcohol history should be documented in the medical records prior to discharge.

Alcohol is one of the most common causes of AP accounting for 35% of cases [29]. Alcoholic pancreatitis can present as recurrent AP with short attacks separated by long asymptomatic periods [30]. The diagnosis should be considered if a person has a history of over 5 years of heavy alcohol consumption defined by greater than 50gm of alcohol per day [9]. The expert panel felt that identifying alcohol as an etiology provided a means to offer timely interventions and counseling for alcohol cessation in order to improve patient outcome (i.e., prevent recurrent attacks).

5. IF a patient presents with AP, THEN he/she should have serologic measurement of triglycerides within 24 h of diagnosis of AP.

In a retrospective review of patients with AP over a 12 year period, Fortson et al. [31] found hypertriglyceridemia was the etiology in 1.3–3.8%. In patients with hypertriglyceridemia-associated AP, the mean triglyceride level was 4587 mg/dl (±3616). A predisposition to hypertriglyceridemia is often found alongside a secondary cause in the same patient [32]. While serum triglyceride levels can rise as a consequence of AP, a serum triglyceride level > 1000 mg/dL is generally considered to be the cause of AP. Given these data, the expert panel felt it was appropriate to assess for this etiology within 24 h of diagnosis.

6. IF a patient has unexplained AP and is > 60 years old, THEN cross-sectional imaging should be performed to assess for underlying malignancy within 2 months of the initial presentation.

Pancreaticobiliary tumors can present as acute recurrent pancreatitis in 5–7% of cases [33]. In a retrospective study, Kohler et al. [34] found 13.8% of 174 patients presenting with AP had pancreatic cancer. However, in a larger series of 302 patients with AP, only 10 patients (3.0%) were found to have pancreatic cancer [35]. Mujica et al. [36] conducted a physician survey and identified 45 patients with AP preceding pancreatic cancer diagnosis—the majority of whom were men > 50 years old with mild AP. In a retrospective review of patients with idiopathic AP undergoing ERCP,

the incidence of pancreatic cancer was low in those under 40 years of age (3%) compared to ages 40–60 (21%) and those older than 60 years (25%) [37]. Based on these data, the expert panel deemed appropriateness of evaluating older patients (> 60 years) with idiopathic AP for underlying malignancy as high.

7. IF a patient, < 40 years old, has recurrent idiopathic AP and EUS and s-MRCP are negative, THEN he/she can be considered for genetic testing after two or more attacks.

Genetic defects may contribute to the development of AP in patients with anatomic anomalies, such as pancreas divisum [38]. In 221 patients with AP, mutations in *SPINK1, CFTR,* and *CTRC* were detected in 6.3%, 2.3%, and 1.8% versus 3.2%, 3.8%, and 1.2% of healthy volunteers [39]. Based on these data and their collective clinical experience, the panel felt that genetic testing is an important measure of quality in a subset of young patients (< 40 years) with recurrent AP without known structural abnormalities.

8. IF a patient presents with AP, THEN a severity score should be calculated at admission and at 48 h and documented in the medical records.

In a retrospective study of 259 patients with AP (28% with severe disease), assessing organ failure correctly predicted outcome in 67% of patients [40]. Overall, there are several scoring systems of varying degrees of complexity that can be used to predict severity including systemic inflammatory response syndrome (SIRS), Acute Physiology and Chronic Health Examination (Apache) II, Ranson's and bedside index for severity in acute pancreatitis (BISAP). These scores performed similarly in predicting organ failure, complications, and mortality in a prospective study of 185 AP patients [41].

9. IF a patient has AP and does not show clinical improvement (defined as persistent pain, fever, nausea, unable to begin oral feeding) or has clinical deterioration (defined as worsening pain, worsening nausea, hemodynamic instability, or signs of infection), THEN a CT or MRI should be performed.

In AP, the finding of pancreatic necrosis on a contrast-enhanced CT (CECT) is associated with a worse prognosis [42]. In a study of 88 patients with AP, those who had developed pancreatic necrosis had a mortality of 23% compared with 0% for those without necrosis [43]. Necrosis predicted a severe outcome (death, major hospitalization, or prolonged hospital stay) with a sensitivity of 83% and a specificity of 65% in another study of 73 patients [44]. It may take up to 3 days after onset of AP for pancreatic necrosis to be apparent on CT; hence, early CECT may underestimate the severity of pancreatitis [6]. Given the correlation of pancreatic necrosis with worse outcomes, evaluation for this may be reasonable; however, it is not clear that routinely identifying presence of necrosis affects such outcomes. Given this, the panel felt that it was more appropriate to perform such imaging if there is a failure to improve or worsening of clinical status instead of imaging all comers with AP.

10. IF a patient presents with AP, THEN he/she should receive lactated Ringer's solution for initial fluid resuscitation.
11. IF a patient presents with AP, THEN aggressive hydration (defined as at least 3 ml/kg/h) should be initiated unless cardiovascular, renal, or other related comorbid factors exist.

There are high-quality data supporting the use of aggressive hydration in patients with AP [9]. In a small randomized controlled trial by Buxbaum et al., a higher proportion of patients treated with aggressive versus standard hydration showed clinical improvement at 36 h: 70 versus 42% (adjusted hazard ratio = 2.32, 95% confidence interval 1.21–4.45). In a multicenter randomized controlled trial of 40 patients with AP, those who received lactated Ringer's solution had a significant reduction in the SIRS at 24 h [45]. Given these data, the expert panel rated aggressive resuscitation with Lactated Ringers as an important measure of quality in AP care.

12. IF a patient with AP is undergoing aggressive initial hydration, THEN he/she should receive tests for blood urea nitrogen (BUN), hematocrit (HCT), and creatinine (Cr) every 8–12 h for the first 24–48 h.

The ACG guidelines advocate a goal of decreasing hematocrit and BUN and maintaining a normal creatinine during the first day of hospitalization, as markers of adequate hydration [9]. Other clinical guidelines agree with HCT and suggest additional markers of organ failure [8]. Brown et al. [46] showed that in a cohort study of 128 patients admitted with AP, admission hematocrit ≥ 44% and a failure of admission hematocrit to decrease at 24 h were associated with the development of necrotizing pancreatitis and organ failure. The negative predictive value was 96% for necrotizing pancreatitis and 97% for organ failure. Hemoconcentration had a high negative predictive value of 88% in a prospective study of 316 AP patients [47].

In a large cohort study, BUN levels were higher among non-survivors than survivors during the first 48 h of presentation. Of note, a post hoc analysis of 1612 patients with AP found that admission hematocrit ≥ 44% and rise in BUN

at 24 h were associated with persistent organ failure and pancreatic necrosis [48]. In addition, when both admission hematocrit was ≥ 44% and BUN levels increased at 24 h, the rates of persistent organ failure and pancreatic necrosis reached 53.6% and 60.3%, respectively. The expert panel felt it was reasonable to expand this period of monitoring to 24–48 h.

13. IF a patient has mild AP (absence of organ failure or local and systemic complications), THEN oral feeding should be initiated within 24 h of control of symptoms.

Recent data suggest that earlier initiation of feeding is safe in patients with AP. In a small study, 60 patients with mild AP were randomized to either fasting or immediate oral feeding; there were no significant differences in the groups with respect to inflammatory markers or abdominal pain, though the length of stay was significantly shorter in the oral feeding group (4 vs. 6 days, $P < 0.05$) [49]. Likewise, a non-liquid diet appeared to significantly decrease the length of hospitalization compared to a liquid diet, in a subsequent meta-analysis [50]. Given these data, the expert panel rated early oral feeding as an important measure of quality in AP. They felt that a period within 24 h of control of symptoms was reasonable based on their clinical experience.

14. IF patient has severe AP (defined as persistent organ failure or presence of pancreatic necrosis) and cannot tolerate an oral diet, THEN he/she should receive enteral nutrition using nasojejunal feeding within 3–5 days of presentation.

A meta-analysis and a Cochrane systematic review found a significant decrease in infectious complications, organ failure, and mortality in patients with AP who were provided enteral nutrition as compared with total parenteral nutrition [51, 52]. Allied with a trend toward reduction in the length of hospital stay, these data argue for enteral nutrition as the preferred means of providing nutritional support in patients with AP.

In a meta-analysis by Li et al. [53] that included 11 studies and 775 patients, enteral nutrition within 48 h of admission improved clinical outcomes—with reductions in infections, hyperglycemia, the length of hospitalization, and mortality. In a large randomized controlled trial, 208 AP patients were randomized to nasoenteric tube feeding within 24 h after randomization (early group) or to an oral diet initiated 72 h after presentation (on-demand group). There were no significant differences between these groups in the rate of major infection (25% and 26%, respectively; $P = 0.87$) or death (11% and 7%, respectively; $P = 0.33$) [54].

The expert panel felt that these data supported nasoenteric feeding in patients with severe AP; they rated the appropriateness of nasojejunal feeding as high based on their clinical experience. The timing of initiating such feeding was not fully clear, but they felt that within 3–5 days of the initial presentation was appropriate.

15. IF a patent has AP with sterile necrosis (defined as necrosis seen on imaging but no fever, leukocytosis, or other indicators for infection), THEN he/she should not receive antibiotics to prevent the development of infected necrosis.

In a meta-analysis of 14 randomized controlled trials (841 patients), the use of antibiotic prophylaxis was not associated with a mortality benefit, incidence of infected pancreatic necrosis, non-pancreatic infections, or surgical interventions [55]. Given this consistent evidence, the expert panel rated this measure as an appropriate indicator of quality care in AP.

16. IF a patient has acute gallstone pancreatitis AND concurrent acute cholangitis and is hemodynamically stable, THEN he/she should undergo ERCP within 48 h of admission.
17. IF a patient has acute gallstone pancreatitis AND concurrent acute cholangitis and is hemodynamically unstable, THEN he/she should undergo ERCP within 24 h of admission after stabilizing the hemodynamic status with hydration and antibiotics.
18. IF a patient has acute gallstone pancreatitis AND evidence of biliary obstruction by clinical or imaging criteria but no evidence of cholangitis, THEN he/she should undergo ERCP prior to cholecystectomy.

In a Cochrane review of patients with acute gallstone pancreatitis and concurrent cholangitis, early ERCP significantly reduced mortality (RR 0.20, 95% CI 0.06–0.68) as well as local and systemic complications (RR 0.45, 95% CI 0.20–0.99; and RR 0.37, 95% CI 0.18–0.78, respectively) [56]. ERCP was also associated with a significant reduction in local complications in patients with biliary obstruction. A meta-analysis of randomized controlled trials also found that ERCP within 24–72 h of admission decreased morbidity and mortality in patients with AP complicated by biliary sepsis [57].

Based on these data, the expert panel rated the use of early ERCP in the setting of biliary obstruction and cholangitis as an important measure. Based on their clinical experience, they chose a 24-h window for hemodynamically unstable patients and a maximum of 48-h window for hemodynamically stable patients.

19. IF a patient has mild AP attributed to known gallstones, THEN a cholecystectomy or ERCP with sphincter-

otomy (if cholecystectomy is not possible) should be performed within 2 weeks to prevent recurrent AP.

There is growing evidence for early cholecystectomy in patients with mild pancreatitis attributed to gallstones [9]. In several cohort studies and one randomized trial incorporating 998 patients with biliary pancreatitis, there was a high readmission rate for recurrent biliary events in those who did not have cholecystectomy (0% in patients who underwent cholecystectomy vs. 18% who did not, $P < 0.0001$) [9, 58]. A Cochrane review identified one trial of 50 patients with mild AP, comparing early (within 48 h of admission) versus delayed laparoscopic cholecystectomy [59]. The total hospital stay was significantly shorter in the early group than in the delayed cohort (MD -2.30 days; 95% CI −4.40 to −0.20), while there was no significant difference in the development of serious adverse events (RR 0.33; 95% CI 0.01–7.81).

In patients who cannot undergo surgery, endoscopic sphincterotomy is protective of recurrent acute biliary pancreatitis, although attacks of cholecystitis may still occur [60]. The AGA guidelines summarized 8 case series comprising 320 patients with gallstone pancreatitis or choledocholithiasis and gallbladder in situ managed by ERCP and sphincterotomy alone, with only 3 (1%) developing recurrent biliary pancreatitis but 56 (17%) developing other biliary symptoms or complications (such as acute cholecystitis or biliary colic) [6]. In a more recent, albeit small, retrospective review of 80 patients who underwent endoscopic sphincterotomy for acute biliary pancreatitis, time to cholecystectomy was 3.3 days (range 0.5–10) in the early and 141.6 days (range 18–757) in the delayed group. Of the 35 patients in the delayed group, 21 (60%) experienced biliary complications compared with 1 of 45 (2%) in the early group ($P < 0.001$). Based on these cumulative data, the expert panel felt that a 2-week timeline for intervention was appropriate in clinical practice.

20. IF a patient with AP has symptomatic sterile or infected walled-off necrosis, THEN this should be drained.

Asymptomatic pancreatic necrosis should not require intervention as they often resolve over time, regardless of size, location, or extension [61]. Drainage of walled-off necrosis (WON) is usually indicated for gastric outlet or biliary obstruction, refractory abdominal pain, ongoing systemic illness, anorexia, or protracted weight loss [8, 62]. The expert panel agreed that given the availability of many options for drainage (especially endoscopic), WON should be drained if symptomatic or infected.

21. IF a patient with AP develops infected necrosis or fluid collection that meets criteria for drainage, THEN this should be performed through minimally invasive methods with a step-up approach using endoscopic drainage, or percutaneous drainage as the first minimally invasive step, based on available expertise.

The ASGE guidelines recommend minimally invasive necrosectomy or surgery be performed only after the necrosis is walled off [62]. A multicenter randomized control trial showed that using a step-up approach (percutaneous catheter drainage followed by video-assisted retroperitoneal debridement) reduced the rate of major complications or death among patients with necrotizing AP and infected necrotic tissue [63]. A Cochrane review, incorporating 306 participants, also found that a minimally invasive step-up approach was associated with fewer adverse events, less organ failure, and lower costs compared to open necrosectomy, although the quality of the evidence was low [64]. The review also suggested that an endoscopic minimally invasive step-up approach resulted in fewer adverse events than the video-assisted minimally invasive step-up, though the quality of evidence was very low. Given these data, the experts rated the use of a minimally invasive approach as an important process of care for patients with AP who develop infected necrosis or fluid collection that meets criteria for drainage. They felt that locally available expertise could best determine the initial approach—endoscopic or percutaneous.

22. IF a patient is high risk of post-ERCP pancreatitis, THEN he/she should receive rectal indomethacin.

There is ample evidence for rectal indomethacin in preventing post-ERCP pancreatitis (PEP). In a landmark study, 602 patients considered high risk of PEP were randomized to either 100 mg rectal indomethacin or placebo immediately after ERCP [65]. PEP occurred in 9.2% of the indomethacin group versus 16.9% of the placebo group ($P = 0.005$). In a subsequent, prospective, double-blind, placebo-controlled trial of 449 consecutive patients, rectal indomethacin did not appear to reduce the risk of PEP [66]. In this study, 70% of patients were average risk of PEP, and thus, the authors suggested that rectal indomethacin may be of benefit only in those at high risk of PEP. However, a multicenter randomized controlled trial of 2600 patients showed a significant reduction in PEP in those who universally received rectal indomethacin before the procedure, compared with those who received it after the procedure based on risk stratification (4 vs. 8%, RR 0.47; 95% CI 0.34–0.66; $P < 0.0001$) [67]. Additionally, a large retrospective study of 4017 patients found a 65% reduction in the rate of PEP with the use rectal indomethacin [68]. Based on the review of the literature, the panel agreed that the best quality data supported the use of rectal indomethacin in those at high risk of post-ERCP pancreatitis.

Discussion

Several evidence-based guidelines have specified recommendations for the management of patients with AP. The link between the indicated process and desirable patient outcomes is clearly proved for some recommendations. For example, the prophylactic use of rectal indomethacin has been shown in a large multicenter randomized control trial to decrease the incidence of post-ERCP pancreatitis in high-risk patients [65]. Likewise, there is ample direct and indirect clinical evidence that early aggressive hydration improves outcomes in patients with AP [69–71].

In contrast to the above-mentioned examples, high-quality data linking the indicated process and outcome are not available for several of the guidelines' recommendations. For example, these include preference for a specific type of intravenous hydration (lactated ringers), recommendation that all patients with AP receive transabdominal ultrasound, and consideration of genetic testing in young patients with a family history of pancreatic disease and no evident etiology, among others [9]. Given these limitations, we subjected our QI draft to further scrutiny by an expert panel using the modified Delphi approach.

We present a set of candidate QIs generated using a comprehensive literature search and refined by a multidisciplinary panel of experts. Using the RAND/UCLA modified Delphi method, we have identified 22 explicit QIs in AP care. While several of these QIs may appear obvious, collectively they define the quality of care to be expected for AP. Indeed, these QIs span the spectrum of AP management including diagnosis, risk stratification, and pharmacological and endoscopic therapy. Our study adds to the evolving literature on continuous QI improvement in gastroenterology, by identifying the explicit QIs that represent the first step in this process [17–19].

These QIs were based on existing guidelines and are not meant to replace them, but to provide more specific means for evaluating quality improvement. The QIs generated by this process enable physicians to measure quality of care and identify opportunities for improvement [17]. That is, these QIs operationalize the guidelines, by specifying the population and conditions needed for their application. This allows the consensus guidelines to be more easily translated into clinical practice. Indeed, in an era of markedly rising costs, QI metrics are critical in both assessing value and identifying areas for improvement. We expect these explicit QIs to facilitate quality improvement projects at both practitioner and institutional levels.

It is important to note that the majority of the QIs either relate to determination of the etiology of AP or the role of endoscopy in AP. Indeed, quickly and accurately defining the cause of AP should prevent recurrent attacks through interventions including appropriate cholecystectomy, alcohol cessation counseling, and triglyceride management. Likewise, appropriate endoscopic therapy (e.g., early ERCP for gallstone pancreatitis with cholangitis, minimally invasive endoscopy instead of open necrosectomy, and sphincterotomy or cholecystectomy for gallstone pancreatitis prior to discharge) would be expected to reduce complications. Thus, we expect that adhering to these QIs in medical practice would support good clinical management of patients with AP and likely improve outcomes.

Although the measure set can allow reliable assessment of AP quality care, we believe that it would be premature to use the measure set to benchmark provider performance without further research. Specifically, implementation of these measures for accountability, in contrast to quality improvement efforts, will require further testing to address a variety of issues pertaining to the identification of a subset that not only is important but also meets the criteria for necessary care (i.e., the expected benefits not only outweigh the expected harms, but they do so by such a margin that the provider must offer the service); other issues include methods of data collection, frequency of implementation, comparability among practices, audit requirements, the system of public reporting, and more importantly, the input from stakeholder groups, including third-party payers and policy makers. We believe that future work can use our measurement set to identify whether some of the measures can be applied for tracking quality for purposes of accountability in AP.

The QIs generated by this process have several limitations. First, not all processes in the management of AP are equally important (e.g., early aggressive fluid resuscitation may be more important than documenting alcohol history). Future research should help identify the relative impact of different QIs. Second, not all QIs are equally generalizable. QIs related to cyst drainage and necrosis debridement are more applicable to therapeutic endoscopists, for instance. Likewise, there will be variations in available resources depending on clinical practice. However, many of the remaining QIs apply to a wide range of practitioners and situations including emergency room physicians, intensive care physicians, and general gastroenterologists. Hence, this tool is intended to be applicable in any setting in which care for patients with AP is provided.

Further, there will be exceptions to their application. For instance, there may be infected necrosis in a location technically challenging for debridement; hence, antibiotics alone may be tried. Indeed, QIs have a sensitivity and specificity and can have false negatives and false positives, but remain applicable when exceptions are rare and randomly distributed [17]. Fourth, a significant number of indicators without strong evidence were deemed by the expert panel to be appropriate QIs. This also highlights the paucity of randomized controlled trials in the study of patients with AP and emphasizes the importance of the expert panel in this review and selection of QIs.

Additionally, while many of these QIs permeate the current clinical spectrum and may already be standard of care in many institutions, evidence suggests that they are not performed or followed as often as expected. For instance, in a retrospective cohort study of patients with acute gallstone pancreatitis, only 37.4% received early definitive therapy (cholecystectomy or endoscopic sphincterotomy) [72].

We recognize that a major barrier to implementing AP measures in clinical practice is the challenge of collecting data to successfully track and record performance. Because the movement in the quality measurement field is to track quality metrics that are readily obtainable from electronic medical records (EMR), further work around the performance characteristics of the selected set is an important next step in our research. Successful implementation of some measures that are not readily extractable from the existing EMR may require adaptations in technical infrastructure to allow data collection. Major electronic medical record vendors are creating structured data fields within specialty-specific templates that can allow collection of structured data for consistent and reliable quality assessments in future efforts.

In summary, we have developed a set of 22 QIs that span the domains of care in the prevention, diagnosis, and management of AP. These QIs should facilitate continuous quality improvement by practitioners and organizations that treat patients with AP and further identify areas that are amenable to improvement to enhance patient care. Within the current era focused on high value care, these metrics will aid in the development of strategies to improve the quality of patient care and reduce costs to provide this care. This is especially important for AP, which is one of the leading gastrointestinal discharge diagnoses, and associated with significant costs and morbidity. We believe this QI set represents the first step in determining a framework for demonstrating high value for the care of patients with AP.

Author's contributions Gyanprakash Ketwaroo MD involved in study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis. Robert Jay Sealock MD took part in study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis. Steven Freedman MD PhD contributed to acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Phil A. Hart MD took part in acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Mohamed Othman MD involved in acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Wahid Wassef MD took part in acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Peter Banks MD contributed to acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Santhi Swaroop Vege MD contributed to acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Timothy Gardner MD MS involved in acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Dhiraj Yadav MD contributed to acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Sunil Sheth MD involved in acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content. Fasiha Kanwal MD, MSHS took part in study concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; statistical analysis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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