SMART Medical Review

Acute Pancreatitis: Assessment and Management in the First 24 Hours

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Abstract: Acute pancreatitis (AP) is an inflammatory reaction of the pancreas caused by inappropriate trypsin activation and an injury / innate inflammatory response. The many etiologies and potentially life-threatening consequences of AP in adults require that clinicians initiate prompt and individualized treatment upon diagnosis. Application of new advances in the management of AP are required at the point of care. To facilitate care, a group of clinical experts have developed a set of recommendations for the evaluation and management of AP during the first 24 hours based on current evidence and evolving concepts. Ten areas of care are addressed where expert recommendations may be useful: (1) physical examination, (2) laboratory tests, (3) diagnosis, (4) early treatment, (5) severity determination, (6) etiology-based management, (7) recommended orders sets, (8) determining of appropriate level of care, (9) quality of care, and (10) quality improvement recommendations. Conclusion: These recommendations should become available as clinical decision support tools that are accessible at the point of care, in real time.

Key Words: Acute pancreatitis, multiple organ failure, capillary leak syndrome, numerical analysis, abdominal pain.

Outline

Abbreviations used in this paper. ABG, arterial blood gas; AKI, acute kidney injury; ALA, alpha-linolenic acid; ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; AP, acute pancreatitis; ARDS, adult respiratory distress syndrome; AWS, alcohol withdrawal syndrome; BISAP, severity score including BUN, Impaired mental status, SIRS, Age and Pleural effusion; BMI, body mass index; BUN, blood urea nitrogen CP, chronic pancreatitis,
(continued on the next page)

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Abbreviations used in this paper (Continued). CECT, contrast-enhanced CT scan; CKD, chronic kidney disease; CLS, capillary leak syndrome; Cr, creatinine; CRP, C-reactive protein; CT, computed tomography; DBili, direct (conjugated) bilirubin; DKA, diabetic ketoacidosis; DHA, docosahexaenoic acid; DM, diabetes mellitus; EPA, eicosapentaenoic acid; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; FA, fatty acid; FCS, familial chylomicronemia syndrome; HAPS, Harmless Acute Pancreatitis Score; HbA1c, Hemoglobin A1C; HCT, hematocrit; HR, heart rate; HTG, hypertriglyceridemia; ICU, intensive care unit; IgG4-RD, IgG4-related disease; JSS, Japanese Severity Score, LDH, lactate dehydrogenase; LFT, liver function (injury) test; MCS, multifactorial chylomicronemia syndrome; MMS, modified Marshall score; MODS, multi-organ dysfunction syndrome, MOF, multi-organ failure; MRI, magnetic resonance imaging; MUFA, monounsaturated fatty acids OF, organ failure; PHPT, primary hyperparathyroidism; POP, Pancreatitis Outcome Prediction score; PNPLIP, pancreatic lipase; PNec, pancreatic necrosis; PQRST, pain assessment of Precipitating and relieving factors, Quality, Radiation, Severity [0 to 10] and Timing; PRSS1, Serine Protease 1 (cationic trypsinogen gene); PUFA, polyunsaturated fatty acids; RAC, Revised Atlanta Criteria; RAP, recurrent acute pancreatitis; RR, respiratory rate; SIRS, systemic inflammatory response syndrome; SOF, single organ failure; TBili, total bilirubin; TUS, transabdominal ultrasound; WBC, white blood cell count; ULN, upper limits of normal

1. Introduction.

Acute pancreatitis (AP) is inflammation of the pancreas with an acute onset, variable clinical course and increasing incidence over the last several decades [1-3]. Among gastrointestinal diseases, AP represents one of the leading causes of hospital admission in the United States[4, 5]. The majority of patients with AP experience a mild clinical course, while 10-20% of patients develop more severe AP defined by the development of local complications, systemic inflammatory response syndrome (SIRS)[6], persistent SIRS (lasting ≥48 hours)[7], capillary leak syndrome (CLS), multi-organ dysfunction syndrome (MODS), and single- or multi-organ failure (SOF, MOF).[2, 8] Mortality may approach 30% in patients with organ failure.[2] Additionally, patients with severe AP may suffer long-term sequelae[9, 10] with a significant financial burden on health care systems.

A severe systemic inflammatory response developing in a subset of AP patients is similar in presentation to other conditions triggering SIRS such as polytrauma, extensive burns, sepsis and COVID-19[11-14]. Most of the early morbidity and mortality in AP comes from the SIRS to MOF pathway. Development of cardiovascular shock from loss of intravascular fluid leads to severe tissue damage and organ dysfunction. Experience with polytrauma and sepsis patients has taught us that early intervention and stabilization improves outcomes (i.e., during the "golden first hour").[15-18]. The Surviving Sepsis Campaign [13, 14, 19, 20] has demonstrated that avoiding delays in treatment (e.g., antibiotic initiation) result in better outcomes[18, 21]. In a primarily sterile inflammatory disorder like AP, early fluid resuscitation[22, 23] (and not antibiotics) and use of lactated Ringer's solution[24, 25] appears to improve outcomes[26, 27], while over hydration is deleterious[28] especially in patients who present with euvolemia or limited cardiovascular reserve.[29-32] Thus, the early assessment of patients with AP must focus on identifying patients who may develop, or are developing SIRS and hypovolemic shock and/or are at risk of other potentially severe complications that must be addressed within the first hours of AP onset to optimize outcomes (see Supplemental Information).

Health care professionals who evaluate and initiate treatment on AP patients may benefit from expert recommendations on a complete and adequate early evaluation, initiating appropriate treatment and anticipating the monitoring needed to manage complex AP patients with an evolving, more severe inflammatory process. To fulfill this need, we developed a series of questions to be addressed by an *ad hoc* panel of expert physician-scientists, offering guidance in ten critical areas of care.

2. Methods.

A group of experienced physicians and surgeons with clinical expertise and academic acumen in AP was assembled to develop consensus "best practice" guidance on the management of AP during the first 24 hours of care. The goal was to define the state-of-the-art care through literature review and clinical experiences, and then to define evidence-based best practices. To help guide and direct future research, we also considered gaps in knowledge and opportunities to address management challenges.

The working group conducted videoconference calls and exchanged emails until 10 questions were identified as fundamental for optimizing care. The questions were divided among the working group members based on interest and expertise, with all authors reviewing and modifying the responses until consensus (>90%) was reached.

3. Results.

The following ten questions were posed, and resultant ten recommendations were compiled by consensus.

Question 1. *What are the most important features of the physical examination and vital signs that should be carefully assessed in a patient suspected of having AP?*

The life-threatening complications of AP are respiratory failure and cardiovascular collapse. The abdominal examination is important in determining the severity and extent of (peri)pancreatic inflammation and the evolution of major complications such as peritonitis and/or ileus.

Recommendation 1: We recommend a complete physical examination with special attention toward features linked to risk factors and indicators of organ dysfunction. A checklist of key exam features and physiological monitoring is listed in **List 1**.

List 1. Physical features that should be documented during the initial examination of an AP patient.

1. Patient height, weight, body mass index (BMI)
2. Heart rate (continuous measure using pulse oximeter)
3. Blood pressure (include systolic and diastolic pressure, and orthostatic blood pressure)
4. Temperature
5. Respiratory rate (tachypnea or respiratory distress)
6. Oxygen saturation (e.g., pulse oximetry or arterial blood gas ABG) with documentation of the rate and route of supplemental oxygen during the reading.
7. Pain assessment (e.g., PQRST: Precipitating and relieving factors, Quality, Radiation, Severity [0 to 10] and Timing)
8. Mental status (e.g., Glasgow coma scale)
9. Pulmonary exam (wheezing, rales, dullness to percussion)
10. Cardiovascular exam (pulses, capillary refill, lower extremity edema)
11. Abdominal exam (visceral obesity, distention, absence of bowel sounds [ileus], local tenderness, rebound tenderness, guarding)
12. Skin exam (clammy, skin turgor, dry mucus membranes, jaundice, periumbilical/flank discoloration, xanthomas/xanthelasmas)

Discussion 1: Older patients or those taking cardiovascular medications may have inconsistent examinations; furthermore, the examination should be tailored on medication use (i.e. beta-blockers) and comorbidities. Confusion in an older patient can be a sign of impending severe AP. Documentation of key physical examination features (e.g., abdominal guarding or peritonism) is also important for calculating severity scores and tracking patient responses to treatment. Obesity (especially in male patients) is a major risk factor for SIRS, local complications, MOF and hypertriglyceridemic AP (HTG-AP). Height (if feasible) and weight are needed to calculate body mass index (BMI); hip-to-waist ratio is useful in documenting central obesity. Pain assessment is important in determining the mechanism and severity of pain and treatment effectiveness. Ileus is an ominous sign and may precede abdominal compartment syndrome.[33]

List 2. Initial laboratory tests in a patient with AP

A. **Pre-pancreatitis** / Base-line Reference Values (From 7 to 365 days prior to arrival)
   1. Lipase (amylase may be added)
   2. Hematocrit
   3. Blood urea nitrogen (BUN), Creatinine (Cr)
   4. Albumin / total protein
   5. Glucose / Hemoglobin A1C
   6. Triglycerides
   7. Ionized calcium
   8. LFTs

B. Pancreatitis Severity Measures and Predictors
   1. White blood cell count (WBC)
   2. Hematocrit (HCT)
   3. Comprehensive Metabolic Panel (this includes BMP / chem 7 plus albumin, total protein, ALP, ALT, AST, Bilirubin)
   4. Hemoglobin A1C
   5. Triglycerides
   6. Ionized calcium (if total calcium, albumin / total protein levels are needed)
   7. CRP (high sensitivity)
   8. Procalcitonin
   9. Lactate
   10. Chest X-ray
   11. LDH (optional)
   12. Arterial blood gas (optional)

Question 2. *Which laboratory tests should be included in the initial evaluation of a patient suspected of having AP?*

A battery of laboratory tests should be ordered to help determine the etiology, current level of severity and baseline biomarkers to track the trajectory of AP over time.

Recommendation 2*:*
We recommend that the following panel of biomarker tests be ordered as initial AP measures (**List 2**) with Pre-pancreatitis biomarker values (**2A**) collected from the medical records, when available, to be compared with baseline AP values (**2B**).

Discussion 2. Laboratory tests are objectively measured biomarkers used as indicators of normal physiological processes, pathologic changes, or pharmacologic responses to therapeutic interventions.[34, 35] During the course of AP many of these biomarkers will be repeatedly measured to determine the patient's condition and disease trajectory.

Biomarkers of disease severity. The list of pancreatitis severity measures in this recommended list (List (2B) provides laboratory tests of acute inflammation (WBC, C-reactive protein (CRP), Procalcitonin / presepsin).[36-39] vascular dysfunction (albumin & total protein [CLS], hemoconcentration, BUN/Cr [pre-renal azotemia], lactate [inadequate tissue perfusion]) [40], metabolic (calcium, electrolytes, glucose, ion gap) and other organ dysfunctions (arterial blood gas and pulse oximetry for lung dysfunction, Cr for kidney dysfunction). These laboratory measures are also used to calculate severity scores including APACHE-II, BISAP, Glasgow, HAPS, JSS, Mounzer Scores, Panc 3, POP, Ranson, SIRS (summarized in Mounzer et. al.[41]) and to track organ function over time, as some biomarkers (e.g. CRP) may initially be normal. [39]

Pre-acute pancreatitis reference values. Accurate biomarker trajectory analysis requires the inclusion of pre-acute pancreatitis baseline values.[32, 40] These values include baseline hematocrit, blood urea nitrogen (BUN), creatinine, total protein and albumin.[40] Hemoglobin A1C (HbA1c) provides an estimate of glucose control prior to the onset of AP. AP may lead to new onset DM and post-AP DM may have a different mechanism and prognosis from pre-AP DM [42-45] Since serum glucose is typically elevated during the stress of AP (transient hyperglycemia), obtaining an HbA1c at admission to establish baseline levels is important as AP predisposes to or causes DM.

Hemoconcentration. One of the most important determinations in AP management is to evaluate for presence of a capillary leak syndrome (CLS). One simple clinical measure linked to CLS is hemoconcentration. A recent study showed that use of a patient's own pre-AP hematocrit level was far more accurate in detecting hemoconcentration than using population-based cutoff values, even when stratified for patient sex.[40] Comparing pre-AP hematocrit levels with measures taken within 24 hours of pain onset showed that the MOF patients had incremental increases in hematocrit from baseline by 5.00% [3.70, 8.70], which was significantly higher than incremental changes in non-MOF patients of -0.20% [-1.55, 1.40] ($p<0.002$). Using a rise in HCT >3% from baseline in individual patients using pre-AP HCT significantly distinguishes MOF from non-MOF (OR 17.7, $p=0.014$). A rise in creatinine and BUN, a drop in albumin, or an initial rise in non-albumin serum protein (day 1) followed by a drop (> day 1) are additional biomarkers of the same process.[40]

Imaging in early AP. An upright chest X-ray is useful for detecting pulmonary edema and pleural effusions; this information is also used in several severity calculations. CT imaging is seldom required to make the diagnosis of AP[2] and performance of CT scan in patients with persistent SIRS does not result in any change of management.[47] Contrast enhanced CT (CECT) should be delayed as pancreatic edema and abnormal fluid collections or pancreatic necrosis (PNec) require time to evolve and fully develop (1-2 days, or longer). Secondly, moderate fluid resuscitation in the setting of CLS and hypovolemia must be among the top priorities of management and giving intravenous contrast for a CECT in a hypovolemic patient carries a risk of inducing (or worsening) acute kidney injury (AKI) and may worsen PNec. Transabdominal ultrasound (TUS) is indicated in patients with suspected biliary (gallstone) pancreatitis, typically suspected when abnormal liver tests and/or cholangitis are concomitantly present with AP.

Question 3. *How is AP diagnosed?*

Acute pancreatitis can present as sudden onset of severe abdominal pain, as gradually increasing pain, or with no clear pain.

Recommendation 3. The diagnosis of AP can be made based on presence of **2 of 3** features listed in **List 3**.[2]

List 3. Diagnosis of Acute Pancreatitis

1. **Abdominal pain** consistent with AP (acute onset of a persistent, severe, upper abdominal pain often radiating to the back),
2. **Serum lipase or amylase** levels at least three times greater than the upper limit of normal (ULN), and/or
3. **Imaging**. Characteristic AP findings of pancreatic edema or peripancreatic stranding/fluid on contrast-enhanced computed tomography (CECT) or other imaging modalities [transabdominal ultrasound (TUS) or abdominal magnetic resonance imaging (MRI)].

Discussion 3*:* In most cases, AP can be diagnosed with the first two criteria alone, and CT or other imaging modalities are *not* needed nor recommended. (Use of CT in the first 24 hours of AP is discussed in Q2., **supplemental information** and below). Once the diagnosis of AP has been established, then additional tests and interventions may be required within the first 4 to 24 hours.

Question 4. *What is the initial treatment of AP?*

Patients who present with AP are typically dehydrated because of reduced fluid intake and/or vomiting or may have hypovolemia from evolving capillary leak syndrome (CLS). Patients who are dehydrated or with evolving hypovolemia should be given a bolus of crystalloid fluid as initial therapy and, with normal renal and cardiac function, these fluids are unlikely to be detrimental to the patient but may be very helpful in minimizing impending hypovolemic shock.

Recommendation 4*:* In patients with a high likelihood of AP on presentation, or with a confirmed diagnosis, we recommend that clinicians initiate the following treatments for all patients (List 4).

List 4. Initial treatment of AP.

1. Supplemental oxygen
2. One liter of lactated Ringer's solution given IV over 30 minutes unless contraindicated
3. If hypercalcemia is present, consider judicious normal saline (0.9% NaCl) (see Q6)
4. Pain medication intravenously, avoiding morphine
5. Antibiotics are *NOT* indicated

Discussion 4: Supplemental oxygen and fluid bolus should be given early in the event that the patient is developing cardiovascular and pulmonary dysfunction. A recent high-profile paper, the WATERFALL Trial,[28] highlighted the dangers of overhydration, but did *not* address underhydration (i.e. adequate fluid resuscitation and management in patients with impending hypovolemic shock).[48] Lactated Ringer's solution is the preferred crystalloid solution, although it is high in calcium chloride (concentrations may differ by manufacturer) and can be incompatible with some other intravenous medications. Normal saline is high in chloride and may worsen acidosis. As noted above (List 4), morphine should be avoided as it constricts the sphincter of Oddi, and may theoretically exacerbate pancreatitis. Plasmalyte should be considered for patients with cirrhosis.

Question 5. How should severity be determined and predicted in an AP patient?

The best outcomes for a patient with an early diagnosis of AP (Day 1) follows good management with the detection of confounding disorders and metabolic derangements that require immediate intervention, rapid stabilization of cardiovascular and pulmonary dysfunction, and anticipating MOF early in the evolution of the inflammatory process. Multiple approaches have been advocated.

Recommendation 5. We recommend early identification of risks for organ failure and the use of prognostic scores to track the development and severity of SIRS and early indicators of MODS. Confounding factors, risks and indicators of poor outcomes are summarized in **List 5**.

List 5. Severity factors and predictors.

1. **Risk factors for progression to MOF**.
    a. Age, sex and ancestry (i.e., race)
    b. (Visceral) obesity and BMI>30 kg/m^2
    c. Recent and historical excessive alcoholic use
    d. Underlying comorbidities: pulmonary, cardiovascular and kidney diseases, diabetes.
2. **Useful prognostic biomarkers and clinical scores**:
    a. Biomarkers: BUN, CRP, hematocrit (sequential assessment)
    b. Clinical scores: BISAP, SIRS
    c. ADAPT (https://adapt-demo.arielmedicine.com/): this web-based tool helps classify AP patients at risk of severe AP (up to 95% probability) using 13 existing prognostic models.
3. **Confounding disorders requiring targeted treatment: (See Question 6)**
    a. Ascending cholangitis
    b. Diabetic ketoacidosis
    c. Lactic acidosis
    d. Hypercalcemia
    e. Hypertriglyceridemia
    f. Alcohol withdrawal syndrome

Discussion 5. Optimal outcomes require systematically and repeatedly assessing the AP patient as the inflammatory process and organ dysfunction evolve differently among the spectrum of patients.

Multiorgan failure. The initial severity determination is focused on detecting and tracking the systemic inflammatory response (clinically defined as SIRS), a prerequisite to multi-organ dysfunction syndrome (MODS) and multi-organ failure (MOF).[40, 49] The risk of SIRS is higher with more severe pancreatic injury (~etiology dependent), obesity and underlying genetic factors that cause an exaggerated immune response[50-52] The risk of MODS and MOF following SIRS is higher in patients with limited physiologic reserve (e.g. older, those with preexisting organ dysfunction), with hypertriglyceridemia, and/or pancreatic lipase-dependent lipotoxicity.[53-55]

In many cases, signs and symptoms of MODS and MOF are present at initial assessment due to patient delay in seeking medical attention for their conditions and/or systems associated delays. In contrast, others present early in the course before these signs and symptoms develop resulting in underestimation of the severity of the evolving clinical course since MODS and MOF may take up to 24 hours or longer to develop. Alcohol withdrawal syndrome may also confound the interpretation of severity measures and requires specific treatment.

Scoring systems. Numerous scoring systems have been developed for early identification of patients who will develop more severe disease, but the practical utility of these tests is limited (see Mounzer et.al.[56]). The Revised Atlanta Criteria (RAC) is the gold standard for research studies, but is best suited for retrospective studies as it focuses on documenting organ dysfunction rather than preventing them (i.e. the Modified Marshall Score).[2] Newer methods, such as the Ariel Dynamic Acute Pancreatitis Tracker (ADAPT, Ariel Precision Medicine, Pittsburgh, PA) represent advances based on machine learning and sophisticated modeling techniques linked to therapy. Further discussion of the RAC, SIRS, MODS, MOF, and ADAPT is presented in **Supplemental Information**.

Metabolic derangements. Acidosis can cause pancreatitis (i.e. DKA) and AP can cause acidosis (e.g. cardiogenic shock / lipotoxicity affecting mitochondrial function).[53, 57] An anion gap on serum electrolyte results or a respiratory rate >20 (suggesting acidosis with respiratory compensation) may require an arterial blood gas and additional laboratory testing may be needed to resolve this question. Hypercalcemia and hypertriglyceridemia complicate the course of acute pancreatitis and will require specific treatment depending on their levels and associated complications (**List 5.3**).

High risk etiologies. Some etiologies have a higher risk for a severe course if not addressed early, including gallstone pancreatitis with ascending cholangitis, HTG-AP, diabetic ketoacidosis and a few others (see above **List 5.3**). Identifying these risk factors early and providing appropriate management can potentially reduce the overall morbidity and mortality of AP. Some patients may have sepsis on top of acute pancreatitis from ascending cholangitis, requiring immediate attention (Question 6, below). Severity assessments should, therefore, include pre-existing conditions, etiology, current state of the patient and their future likelihood of developing MODS and MOF.

Question 6. *What are the etiology-specific treatments recommended within the first 24 hours?*

Establishing etiology (or etiologies) requires careful review of the patient's history, selected laboratory and imaging studies. This knowledge directs treatment to minimize severity, improve outcomes, and reduce recurrence.

Recommendation 6. We recommend that the etiology of AP and associated complications be determined as soon as possible and linked to specific treatments. Both urgent (first 24 hours) and prompt (during hospitalization) management planning is indicated. Specific methods of determining the underlying etiology of AP are listed in **List 6A** and managing individual by AP etiology in **List 6B**.

Discussion 6*:* Several AP etiologies require urgent interventions or therapies to diminish drivers of injury, inflammation, or sepsis. These etiologies include biliary (gallstone) pancreatitis with evidence of ascending cholangitis, hypertriglyceridemic AP, hypercalcemia and diabetic ketoacidosis.[3] These are discussed in more detailed in **Supplemental Information**.

Hypercalcemia. One of the most effective treatments of hypercalcemia is rigorous IV hydration with normal saline to dilute the serum calcium concentrations. In AP, aggressive hydration is contraindicated [28], especially with existing organ dysfunction and CLS. In addition to calcitonin (**List 6**) an IV bisphosphonate should also be considered.[61, 62] Fluid resuscitation should be given using 0.9% NaCl or 0.45% NaCl (and avoid lactated Ringer's solution) with continued cardiac and pulmonary monitoring as fluid overload leads to organ dysfunction.[28] Initiate investigations for the underlying etiology as this determines longer term treatment[61-63] (see Supplemental Information).

Genetic factors. Genetic analysis is indicated for idiopathic pancreatitis, including *suspected* biliary pancreatitis (no gallstones seen) to determine if the patient is at risk of gallstones before the gallbladder is removed to prevent recurrence. Many patients have received previous genetic testing, and this information may be helpful in developing ongoing management plans. A review of the family history, including pancreatitis-associated syndromes (i.e. hereditary pancreatitis, cystic fibrosis, CFTR related disorders [CFTR-RD]), is important in determining the priority of new genetic testing (if not previously done with adequate coverage). A pancreatitis screening test (including common genetic risk factors for acinar or duct cell dysfunction,

gallstones, hypertriglyceridemia, and immune response genes) is of low risk and genetic counseling is not needed. If cystic fibrosis or autosomal hereditary pancreatitis is suspected, provide genetic counseling and informed consent before ordering genetic test and arrange for follow-up of results. Genetics can also be useful in determining key contributing factors to hypertriglyceridemia that may respond to specific therapies.[64-66]

List 6A. Determination of the etiology of a patient with AP

1. **History and physical examination:**
    a. Present illness: onset of symptoms in relation to food, duration of symptoms, severity and location of pain, associated symptoms (e.g., patients with biliary pancreatitis often endorse a history of biliary colic and post-prandial symptoms leading up to acute onset abdominal pain), recent alcohol intake and quantity, and any recent history of abdominal trauma
    b. Previous history of acute pancreatitis: How many hospitalizations, any ICU admissions, and endoscopic or surgical interventions including Post-ERCP AP, cholecystectomy, and etiology assigned previously
    c. Concurrent features of IgG4-associated disease: e.g. sialadenitis, tubulointerstitial nephritis, visual disturbance, skin rashes, retroperitoneal fibrosis, jaundice, etc.
    d. Risk factors: Sex, age, BMI, ancestry, family history, genetics, pre-existing conditions & co-morbidities
    e. Recently started medications (over the last 3 months)
    f. Family history: pancreatitis, pancreatic cancer, HTG, cystic fibrosis, hereditary pancreatitis
    g. Social history: Alcohol consumption history (lifetime consumption estimation can help distinguish if alcohol is the main contributor or associated risk factor), smoking (lifetime use), and marijuana use. Note that many patients diagnosed with alcohol-associated pancreatitis have an underlying genetic risk, justifying genetic testing to guide future management)[58]
    h. Procedural/Surgical history: ERCP, EUS-FNA, pancreatic surgery, cholecystectomy
    i. Physical examination: jaundice, evidence of blunt trauma, xanthelasma/xanthomas
2. **Fasting Lipid panel** (focus on triglyceride level)
3. **Blood glucose** / Hemoglobin A1C* (add ketones and ABG if glucose is high or DKA suspected)
4. **Ionized serum calcium level**
5. **Liver injury tests** (focusing on ALT, AST/ALT ratio, total and direct bilirubin, albumin and total protein): ALT level > 3x UL strongly indicate biliary etiology, AST/ALT >2 in appropriate clinical context may suggest alcoholic etiology, cholestatic jaundice may indicate choledocholithiasis or head of the pancreas malignancy. Albumin and total protein levels are useful in trajectory analysis.[40]
6. **Phosphatidylethanol** or carbohydrate deficient transferrin to evaluate for recent alcohol consumption.
7. **Imaging** (when gallstones are suspected start with right upper abdominal ultrasound, defer CT unless clinically indicated (see Recommendations 8 & 9, List 6A and Supplemental Information)

If no clear etiology identified, then the following etiologies should be considered during hospitalization.

8. **Genetic testing** is generally useful for pancreatitis of unclear etiology or patients with a positive family history. A broad genetic screening panel should be used to include pancreatitis risk genes, risk of gallstone formation and genetic risks of hypertriglyceridemia (avoid delays in obtaining results).
9. If the patient is > 40 years old and this is their first attack of AP, then they are at increased risk of cancer-related AP and CT imaging and/or including Endoscopic Ultrasound (EUS) and other evaluations of pancreatic cancer risks and early signs should be considered after the acute phase.
10. If the patient has recurrent idiopathic AP, serum IgG4 levels and CT imaging with contrast may be considered after acute inflammation has subsided to rule out autoimmune pancreatitis or anatomic factors.

List 6B. Etiology-based management:

1. **Etiology-specific treatments to reduce severity**.

    a) **Triglycerides** >1,000, lipase> 3x ULN, SIRS, and organ dysfunction: Consider ICU management of fluids and insulin therapy and close monitoring for MOF. Include endocrinologist for urgent and long-term management. Avoid heparin treatment. Urgent plasma exchange is currently of unproven benefit. Consider keeping patient NPO until triglycerides <1,000mg/dL.
    b) **Diabetic ketoacidosis**: If diagnosis confirmed, follow ADA guidelines for initial management. Initiate fluids (Initially 1L of 0.9% NaCl/hr., insulin therapy (IV: 0.1 units/kg bolus followed by 0.1 units/kg/hour infusion), assess the need for bicarbonate (i.e., bicarbonate replacement for pH <7.0), and K replacement (if urine output ≥50 mL/hr.)[59]. Consider endocrine consult (DKA, DM +/- HTG) and ICU management of DKA.
    c) **Hypercalcemia:** Very high calcium levels (>14 mg/dL or 3.5 mmol/L) are treated by judicious IV fluids to dilute the calcium, diuretics to prevent fluid overload and subcutaneous calcitonin (4 units/kg) to increase renal calcium excretion and decrease bone resorption (see Supplemental Information)
    d) **Retained common bile duct stone** with rising serum bilirubin or suspected ascending cholangitis: Stabilize the patient and start antibiotics when cholangitis is suspected (e.g., Charcot's triad) and proceed with urgent ERCP (</= 48 hours). [60]
    e) **Alcoholic pancreatitis**: Determine if the patient is having AWS that may interfere with cardiovascular assessment and/or require targeted treatment.

2. **Etiology-specific assessments and treatments to prevent recurrence**.

    f) **Medication Review**: Review cardiovascular medications that may interfere with interpretation of heart rate or blood pressure, medications causing metabolic [lactic] acidosis (e.g. metformin). Consider stopping medications suspected to cause AP.
    g) **Toxins**: exposure to pesticides causing hyperstimulation AP, exposure to toxins causing metabolic acidosis.
    h) **Alcohol**. Counseling and treatment of alcohol use disorder. Smoking cessation is also warranted.
    i) **Genetic etiologies**: provides insights into possible hereditary pancreatitis (including in alcohol-associated pancreatitis), CFTR-related disorders, gallstone risk, HTG risk and others. Knowledge may reduce future un-necessary testing/procedure related morbidity
    j) **Obstruction/ mass**. (may need to be reassessed after the acute phase)
    k) **Gallstone pancreatitis** - cholecystectomy prior to discharge.
    l) **Trauma**: Consult both surgical, endoscopic, and interventional radiology specialties for guidance on evaluation and treatment

Question 7: *What are typical orders that are prescribed for patients with acute pancreatitis?*

Physician orders for the care of individual patients must be personalized. Nevertheless, examples and templates remain useful to expedite care and ensure completeness in acute care settings.

Recommendation 7. We recommend early support of vital systems, continuous or repeated measures of physiologic state, symptom-directed therapy and organizing specialist management teams when necessary. An example is given in **List 7.**

Discussion 7. During the initial evaluation of patients with AP it is important to monitor the biological systems that are at highest risk of dysfunction as well assessing overall disease severity, patient disposition and patient comfort. As noted above (List 4) we recommend one liter of Ringer's lactate solution given over 30 minutes as soon as AP is suspected. The goal is to treat dehydration and possible impending hypovolemic shock, which is difficult to detect early. Compensated shock occurs with a blood volume loss of less than 1000 ml and there are no (or only slight)changes in clinical signs. [67] With > 1000 ml volume loss, there are substantial changes in heart rate and blood pressure with hypotension, tachycardia and increased respiratory rates developing after a loss of 25–35% of intravascular volume loss.[67] Younger patients may be able to compensate vital organ dysfunction and impeding shock to a greater degree and for greater duration than older patients, then suddenly deteriorate when they can no longer compensate. Early signs of CLS and impending shock include hemoconcentration, falling albumin and non-albumin total protein and increased BUN and creatinine.[40]

List 7. Consensus order set for acute pancreatitis (modified for each patient).

1. **Oxygen**: (multiple options on delivery), notify attending physician if oxygen saturation is < 95%.
2. **Pulse oximetry**. Record oxygen saturation and supplemental oxygen delivery method and rate (e.g., 4 L/m per nasal canula);track levels every 15 minutes
3. **Blood pressure**: Record and track blood pressure every 15 minutes.
4. **Fluid orders** (maintenance + resuscitation)
    a. With suspected AP give 10mL/kg bolus followed by 1.5mL/kg, watching for signs of fluid overload (e.g., desaturation on pulse oximeter, increased respiratory rate, and tense abdomen)
    b. If HR > 90 BPM or systolic BP <100 mmHG or lactate ≥ 3 mmol/L or metabolic acidosis, consider repeating the fluid bolus (being careful not to administer >4,000mL in 24 hours period) and notify attending physician, specialists and/or ICU for ongoing goal-directed therapy.
    c. Record fluid *inputs* including content and route.
    d. Measure fluid *outputs* (including urine, NG, vomiting) every 6-8 hours.
5. **Pain management**: Record pain level using a 0 to 10 scale (10=worst pain ever) every 15 minutes. IF pain is >7 and patient is post fluid resuscitation [for ischemic pain] give, (for example) NSAIDs or hydromorphone 0.5-2 mg IV, repeat every 15 min. as needed with ECG/blood pressure/oximetry/LOC assessment. Hold if RR<10 systolic BP <90 mmHG.
6. **Nausea**: (for example) ondansetron 4-8 mb IV and repeat q hr as needed or metoclopramide 10 mg IV q 2-4 hours as needed (maximum dose 40 mg/12 hours, monitor for dystonia)
7. **Etiology – driven orders**: (see list 6A)
8. **Antibiotics**: antibiotics administration is discouraged unless there is objective evidence of a concurrent infection. Fevers and elevated laboratory markers of inflammation are very common in patients with sterile acute pancreatitis and should not be used to determine the need for antibiotics usage. Procalcitonin level greater than 1 ng/mL WITHIN appropriate clinical context is better guide for antibiotics prescription.
9. **Consultation requests**: For examples: ICU, surgery, gastroenterology/therapeutic endoscopy, Interventional Radiology (IR), endocrinology, referral center
10. Notify**: RESEARCH team** if eligible for ongoing AP studies

The current standard of care for fluid resuscitation is Ringer's lactate solution with some evidence of better outcomes than with normal saline[24, 25, 68], although the mechanism of benefit is not clear and the beneficial effect may be transient.[69-71] Furthermore, well designed studies on adding albumin or fresh frozen plasma to compensate for loss of intravascular oncotic pressure in humans are lacking; however, use of dextran may be harmful.[40, 72] The current IAP/APA guideline suggests goal-directed infusion of Ringer's lactate solution at a moderate infusion rate of 5–10 ml/kg/h since higher infusion rates and rapid hemodilution to a hematocrit of <35% in 48 h has been found to be associated with worse outcome.[32, 72] However, the volume distribution of aqueous solutions in fat is different than other tissues and adjusted body weight, e.g. ideal body weight, plus 40% of the difference of actual and ideal body weights, should be used. Goal-directed therapy is now recommended to prevent under- or over-resuscitation [18, 69], but consensus is lacking on the measures and goals.[73-75]

Over-resuscitation with large volumes of crystalloids can contribute to the development of interstitial edema and abdominal compartment syndrome.[31, 32] For example, in a recent randomized trial comparing aggressive vs moderate resuscitation with lactated Ringer's solution, aggressive fluid resuscitation (median volume administered in 24 hours: 5.4L) was associated with higher incidence of fluid overload without improving clinical outcomes compared to moderate resuscitation (median volume administered in 24 hours: 3.3L).[28] Given accumulating evidence for the benefit of assessing fluid responsiveness, patients who do not respond adequately to initial boluses of fluid may need to be managed in a higher level of care capable of assessing dynamic assessment of fluid responsiveness to guide further resuscitation.[76]

Symptomatic management of pain as well as nausea is often necessary. Narcotics should be used judicially[77, 78], as they can prolong ileus but are frequently required early in the management of severe pain. Morphine should be avoided.[79, 80]

Recommendations in **List 7** is an example of an order set that provides general guidance for managing AP patients in the acute phase and anticipating the need for repeated measures of key laboratory biomarkers of physiological measures (see previous recommendations). The caregiver will need to modify these general recommendations based on the needs of the individual patient, especially when they have pre-existing medical conditions such as congestive heart failure, CKD, or COPD that require special attention when administering intravenous fluid.

Infection during the early phase of AP is uncommon. Fevers, elevated WBC, CRP in a patient diagnosed with AP are

often due to acute inflammation and therefore do not necessarily indicate presence of a superimposed infection unless there is clinical evidence for concurrent cholangitis (Charcot's triad). Overuse of antibiotics in the early phase of AP remains a significant issue[81], when considering that there is very limited evidence of its benefit even among patients with necrotizing pancreatitis. [82] The decision for their prescription is often guided by non-specific markers of inflammation or pancreatic injury (e.g., WBC, CRP, lipase and amylase level).[81] Administration of antibiotics based on procalcitonin level appears to reduce overuse of antibiotics. [83]

Question 8: *How should the patient's appropriate level of ongoing care be determined?*

Determining appropriate level of care for AP patients in the first 24 hours is determined by projected severity, organ failure status, confounding coexisting complications and the expertise of consultants at the initial facility.

Recommendation 8. We recommend that the decision to transfer a patient to another level of care should only occur after the patient is fluid resuscitated and urgent metabolic or severe confounding disorders have been addressed and stabilized (if needed). Patients with current or impending organ failure, hemodynamic instability or those who require specialized resources and nursing care (such as insulin infusion for HTG or DKA) should be sent to an ICU. Triage to lower levels of care should be at facilities that will allow rapid increase in care level if needed and quick access to subspecialties skilled in specific procedures such as therapeutic endoscopy, surgery, plasma exchange or endocrinology.

The working group recognizes that criteria for admission to stepdown unit or ICU may vary widely depending on the institution. We recommend assigning the following level of care in AP patients. Some example criteria for triaging a patient to an ICU, a monitored step-down unit, to an observation unit or to a hospital medical or surgical floor are given in **List 8.**

Discussion 8: Levels of care:

Intensive care unit. Patients with established organ failure or predicted severe AP. Once a patient is predicted to develop severe AP (using prognostic models) or is in organ failure (using Revised Atlanta Classification), appropriate level of care needs to be determined for the patient. In an international cohort of well-phenotyped AP, when progressed to severe AP, 82% of patients needed an ICU admission with mortality rate of 21%.[84] This mortality is likely driven by development of CLS leading to MOF which includes acute respiratory distress syndrome and circulatory failure and, less commonly, early infected necrosis that require timely evidence-driven management for improved outcomes.[76, 85-88]

List 8. Considerations in triaging patient to ongoing care units.

A. Stepdown unit or ICU:

1. Patients with organ failure using Modified Marshall Scoring System
    a. Respiratory failure: patients whose respiratory: $Pa0_2/Fi0_2$: <300 mmHg or worse (calculation can be easily done given widely available online tools like Oxygen Calculator); alternatively, patients requiring 2L through nasal cannula or higher to keep oxygen saturation ≥92% translates to respiratory failure as defined by Modified Marshall Scoring System.
    b. Systolic blood pressure <90 mmHg not responsive to fluid bolus (e.g., 2L over 2-4 hours), or signs of tissue hypoperfusion evidenced by decreasing pH <7.3 and/or lactate level >4mmol/L
    c. Acute kidney failure with uremia or other indications for urgent dialysis
2. Patients with advanced comorbid conditions: in these patients, even initial support for respiratory or circulatory system may be complex and require intensive monitoring. For example, patients with systolic blood pressure <90 mmHg with history of advanced chronic kidney disease, congestive heart failure (risk of rapid fluid overload) or oxygen desaturation in patients with history of advanced COPD (risk of acute on chronic respiratory failure).
3. Patients who have a score of 3 or greater on BISAP or classified by the ADAPT tool to be at high risk of severe AP.
4. Impaired mental status/ confusion

C. Observation unit:

1. Patients not in organ failure AND without signs of progression to moderate or severe AP (i.e., no SIRS, no concerning trend in HCT compared to baseline, normal BUN and creatinine, and no rebound tenderness). Examples of these patients include mild (recurrent) alcoholic pancreatitis, idiopathic acute pancreatitis, uncomplicated hypertriglyceridemic pancreatitis, and drug-induced pancreatitis are ideal phenotypes for observation.

D. Floor:

1. Mild biliary pancreatitis who will benefit from index hospitalization cholecystectomy.
2. Predicted mild/moderate severity with intractable symptom burden (uncontrolled pain despite IV pain medication and/or nausea/vomiting with oral intolerance)
3. Mild/moderate severity with cholestasis that may require an inpatient procedure.

While infected necrosis is relatively uncommon in the early phase of AP (i.e., first 2 weeks of disease), it can still occur.[88] Distinguishing between sterile and infected necrosis can be extremely challenging, so multidisciplinary discussion in a high-volume expert center is critical to inform management strategies and to potentially avoid unnecessary invasive interventions to the detriment of the patient.. Therefore, providers caring for patients with organ failure or predicted severe AP in a community-based hospital setting should strongly consider transferring the patient to a tertiary referral center that has a high-volume multidisciplinary pancreaticobiliary service (comprises interventional endoscopy, interventional radiology, abdominal radiology, and pancreatic surgery) and specialized intensive care units.[76, 85-87, 89]

Stepdown unit/Intensive care unit: If a patient with predicted severe AP or with organ failure is already at a tertiary referral center, then the decision whether to increase the level of care (i.e., admission to the intensive care unit) is highly dependent on institution-specific polices and ICU admission criteria, so it should be contextualized to the local institution.[87] Nevertheless, there are several principles that can guide providers to consult the intensivist. Higher level of care should be strongly considered in patients who are in organ failure especially in the respiratory and circulatory system. Revised Atlanta Classification uses the Modified Marshall Scoring System to define organ failure (renal: serum creatinine >1.9 mg/dL, respiratory: $Pa0_2/Fi0_2$: <300 mmHg, cardiovascular: systolic blood pressure <90 mmHg not responsive to fluid bolus). Among AP patients in organ failure, respiratory and circulatory failure status may be particularly specific for impending progression to MOF as elevation of creatinine, especially when isolated, may indicate pre-renal azotemia responsive to fluids.[90]

Observation: Observation level of care may be appropriate in patients who are predicted to have mild AP (i.e., no organ failure, no SIRS, no concerning trend in HCT compared to baseline, normal BUN and creatinine, and no rebound tenderness). Focus on these patients need to be hydration to hasten recovery with lactated Ringers and resumption of a solid diet[91] and a systematic approach to ascertaining reversible causes. Patients suspected to have mild (recurrent) alcoholic pancreatitis, idiopathic acute pancreatitis, uncomplicated hypertriglyceridemic pancreatitis, and drug-induced pancreatitis are ideal phenotypes for observation. At discharge every effort should be made to bridge them to appropriate outpatient care to reduce readmissions and/or recurrences in the future. For example, inpatient counseling before discharge, followed by repeated outpatient intervention reduces recurrence in alcoholic pancreatitis[92]; unfortunately even inpatient counseling is administered infrequently.[93] Idiopathic AP patients should be discharged with scheduled follow-up at a center with EUS expertise to promptly eliminate important causes of AP.

Floor: Patients appropriate for regular nursing floor level of care include predicted mild biliary pancreatitis who will benefit from index hospitalization cholecystectomy, predicted mild/moderate severity with intractable symptom burden (uncontrolled pain despite IV pain medication and/or nausea/vomiting with oral intolerance), or mild/moderate severity with cholestasis that may require an inpatient procedure.

Question 9: *How should patients with AP be monitored in the first 24 hours?*

Acute pancreatitis is a dynamic inflammatory process that evolves over the first 48 hours beginning with an innate local, and sometimes systemic inflammatory immune response (e.g. SIRS, cytokine storm) and then transitioning into a compensatory anti-inflammatory response syndrome (CARS) with increased susceptibility to secondary infections.[94] During the first 24 hours the trajectory of the immune response, as well as confounding conditions generally present themselves. The human body has a variable reserve to tolerate organ dysfunction, but when the compensatory mechanism can no longer compensate for organ dysfunction the patient will suddenly "crash". Thus, evaluation of the patient's status, and tracking trajectory over the first 24-48 hours is critical to prevent sudden death – or a "code" with significant organ damage and lasting morbidity.

Recommendations 9. We recommend that patients with AP should be closely monitored over the first 24 hours and that the managing team is required to adjust their treatment approach, especially in regards to the volume and rate of intravenous fluids administered based on patients' response to resuscitation. An example of some key parameters that should be considered for monitoring are given in **Table 9.**

Discussion 9. These recommendations are based on the evidence that showed that 70-90% of severe AP occurs within the first week of disease onset and early signs of impending organ failure often manifest in the first 24 hours.[8, 84] In patients exhibiting signs of hypovolemia (e.g., elevations in serum creatinine or BUN, hematocrit >44% or increased trend compared with baseline value (if available), urine output <0.75mL/kg/hr, systolic blood pressure <90mmHg or physical examination findings of hypovolemia) initial fluid resuscitation with an intravenous fluid bolus of 10mL/kg should be administered. Patient's vital signs should be rechecked. In those who continue to be tachycardic (HR>90 beats/min) and/or hypotensive (mean arterial pressure <60 mmHg) another bolus of 10mL/kg can be administered at the 12 hour checkpoint but not to exceed 4,000mL in a 24 hours period. In contrast, those patients who have stable vital signs, may continue to receive a moderate infusion rate of approximately 1.5 ml/kg/hour over the next 12 hours.

List 9. Reassessment recommendations during the first 24 hours.

1. Physical examination: AP patients should be frequently (q 4 hours) re-examined for signs of impending decompensation (e.g., impaired mental status, tachypnea with oxygen desaturation, and signs of hypovolemia).

2. The following laboratory parameters can be useful to trend over time (i.e., more than once in the first 24-hour period, e.g at 6 hour and 12 hours if severe or moderately severe)
    a. CBC (focus on Hematocrit as early sign of CLS)
    b. Comprehensive Metabolic Panel (focus on BUN, Creatinine, anion gap, electrolytes; albumin & total protein – trend decreasing levels for vascular leak, LFTs)
    c. Triglycerides (if initially >500 to 1000 mg/dL and therapy is to be monitored)
    d. Lactate (especially if previously elevated or becomes hypotensive)

At 12 hours from presentation, the managing team should reassess all AP patients and adjust their IVFs accordingly. Those patients who continue to have a low mean arterial pressure of <60 mmHg or low urine output of <0.5 mL/kg/hr, in whom 4,000mL has already been administered, assigning a higher level of care should be strongly considered (see List 7.4). They should also have blood work repeated to include a CBC and a basic metabolic panel focusing on bicarbonate level, BUN, and hematocrit. In contrast, those patients who are found to have normal vital signs and urine output should receive a slower infusion rate of approximately 1.5 ml/kg/hour between 12 and 24 hours. Our recommended approach is based on the moderate fluid resuscitation recommendation by the WATERFALL investigators.[28]

Repeating laboratory work at 4, 12 and 24 hours is also of importance in assessing the patients' response to the initial treatment. A multicenter prospective study comparing admission BUN, hematocrit, and creatinine, as well as changes in their levels over 24 hours, found that an admission hematocrit ≥44% and rise in BUN at 24 hours were the most accurate laboratory tests in predicting persistent organ failure (AUC: 0.67 and 0.71, respectively), outperforming the other laboratory parameters and the acute physiology and chronic health evaluation-II (APACHE-II) score.[95] Therefore, a rise in BUN at 24 hours represents a helpful prognostic marker following the first 24-hour fluid resuscitation indicating a poor outcome and need of a higher level of care.

Question 10: *How should health care systems and hospitals modify systems and processes for the continual improvement of care for patients with AP?*

The presentation of patients with AP can happen at any healthcare entry point, at any stage of disease with evaluation by healthcare providers having variable experience and training in managing AP. Therefore, a facility and system quality improvement program is required to provide measurable improvement in patient outcomes and to minimize gaps in the acute care of AP patients across diverse clinical settings.

***Recommendation 10*:** We recommend policy makers and hospital leaders consult report of the *Acute Pancreatitis Task Force on Quality: Development of Quality Indicators for Acute Pancreatitis Management*[89] to design locally contextualized systems of care to measure important indicators of quality for early management of AP with the aim to improve patient outcomes.

The following domains and quality indicators are taken from the document, and these should be referenced to evaluate the quality of early management of AP in a particular system. Four important domains for quality improvement are given in **List 10**.

***Discussion 10*:** It is well established in other acute diseases such as sepsis and myocardial infarction that constructing a system comprising evidence based high-quality processes of care improves outcomes.[96-98] Similar focus on constructing high-quality systems of care is needed to improve outcomes in AP patients. To this end, the ACG Institute's Acute Pancreatitis Task Force on Quality recently developed and published 40 quality indicators across 10 clinical domains.[89] The project was the result of a consensus process from an expert panel's assessment of evidence-based standards of care related to acute pancreatitis. Quality indicators assess process, appropriateness, efficiency, as well as outcomes. As there is an emphasis on outcomes to measure performance, quality indicators serve as objective metrics that can be used for benchmarking. The clinical domains pertinent to the first 24 hr. Of acute pancreatitis management are: diagnosis, initial assessment/risk stratification, early moderate fluid resuscitation, appropriate imaging (e.g., avoid unnecessary CT scans), pharmacotherapy, antibiotic stewardship, early enteral nutrition as tolerated, and urgent ERCP in the setting of cholangitis. Additionally, a quality indicator within the "structure of care" domain specifies that institutions that manage patients with AP should have EUS and ERCP services available or a transfer agreement with a facility that does.

Figure 1 Flow Diagram of Patient Management

(next page)

Q1: What are the most important features of the physical examination and vital signs that should be carefully assessed in a patient suspected of having AP?	•Look for signs of locoregional and/or systemic complications •SIRS, altered mental status (GCS <13/15), hypoxia and/or hypotension Abdominal distension, absent bowel sounds, rebound tenderness
Q2: Which laboratory tests should be included in the initial evaluation of a patient suspected of having AP?	•A battery of laboratory and/or simple radiologic tests to help determine the etiology, level of severity, and to track trajectory of AP over time •Etiology relevant: baseline triglyceride, ionized calcium, LFTs Severity relevant: hematocrit, BUN/Creatinine, triglycerides, ionized calcium, CRP, procalcitonin, lactate, CXR
Q3: How is AP diagnosed?	•Diagnosis of AP: 2 out of 3 criteria including elevated amylase/lipase >3xUL, imaging evidence (CT, US, or MRI) of pancreatic inflammation, abdominal pain
Q4: What is the early treatment of AP?	•In high likelihood of AP or confirmed diagnosis: oxygenation, hydration, pain medication, and avoid antibiotics •Lactated Ringer's is preferred solution (Except in hypercalcemia or hyperkalemia), avoid morphine for analgesia, early SIRS in AP is driven by sterile inflammation (i.e., infection prevalence is low in early AP)
Q5: How should severity be predicted or determined in an AP patient?	•Prognostic scores may predict development of organ dysfunction. •Host-related: advanced age, male sex, visceral obesity, diabetes, recent alcohol excess and underlying cardiopulmonary and renal conditions •Scores and laboratory tests: BUN, CRP, HCT, BISAP, SIRS, and ADAPT tool •Confounders that require targeted treatment: cholangitis, DKA, lactic acidosis, hypercalcemia, HTG, and alcohol withdrawal syndrome
Q6: What are etiology-specific treatments recommended for AP within the first 24 hours?	•Determination of etiology in a patient with AP: List 6A •Etiology-based management: TG >1,000 insulin and avoid heparin; DKA: fluids, IV insulin +/- bicarbonate and K replacement, endocrine consult; hypercalcemia: IV fluids, diuretics, and SC calcitonin (4 units/kg); suspected retained stone with cholangitis: urgent ERCP; alcoholic pancreatitis: assess for alcohol withdrawal syndrome
Q7: What are the recommended orders that are prescribed for patients with AP?	•Nursing: Oxygen, HR/RR, pulse oximetry, BP, strict I/O •Fluids: 10mL/kg bolus followed by 1.5mL/kg, look for fluid overload •Pain : NSAIDs or hydromorphone 0.5-2mg IV (hold RR <10, SBP <90mmHg) •Nausea: ondansetron 4-8mg IV or metoclopramide 10mg (max 40mg/12 h) •Antibiotics: avoid unless objective evidence of infection
Q8: How should the patient's appropriate level of ongoing care be determined?	•Stepdown or ICU: patients with evidence of respiratory ($Pa0_2/Fi0_2$: <300 mmHg or patients requiring 2L through nasal cannula or higher to keep oxygen saturation ≥92%), cardiovascular (SBP <90mmHg not responsive to fluid bolus or uremic renal failure, BISAP or 3 ore more or high risk of severe AP by ADAPT •Observation: no organ failure/SIRS, normal laboratory tests
Q9: How should patients with AP be monitored in the first 24 hours?	•Q4h physical examination focusing on parameters in Q1. •Trend laboratory parameters relevant to severity: HCT, BUN, Cr, anion gap, albumin&total protein, LFTs, triglycerides and lactate
Q10: How should health care systems and hospitals modify systems and processes for the continual improvement of care for patients with AP?	•Diagnosis: appropriate use of CT scans (limit for diagnosis, later for complications) •Documentation: history for etiology determination, severity indicators •Etiology and severity: obtain relevant history and laboratory •Management: fluid resuscitation (volume, type, approach), CCY before discharge for mild biliary pancreatitis, ERCP for cholangitis, early PO feeding

List 10. Quality domains in acute pancreatitis management.

A. Diagnosis domain

Appropriate use of CT scans (limited for diagnosis, later for complications)

B. Etiology domain:

1. History records should include alcohol intake, smoking, and medications
2. Document prior episodes of pancreatitis and family history of pancreatic disease
3. Obtain liver chemistry, triglyceride levels, and calcium levels on presentation
4. Referral to pancreatic center of excellence in cases of mild idiopathic pancreatitis if discharged from the ER or observation unit

C. Initial Assessment and Risk stratification domain

1. Assessment and documentation of orthostatic vital signs, hematocrit, BUN and creatinine
2. Severity indicators should be assessed and documented: organ failure, SIRS, age, impaired mental status, and pleural effusion
3. Documentation to indicate who is at risk of severe AP

D. Initial management domain

1. Adherence to fluid resuscitation strategy
2. Lactated Ringer's as preferred solution
3. Need for fluid resuscitation to be goal-directed
4. Cholecystectomy before discharge in uncomplicated biliary pancreatitis with short length of stay
5. ERCP within 24-48 hrs. for cholangitis associated with biliary pancreatitis
6. Early initiation of PO feeding (as tolerated)

Conclusions

Acute pancreatitis is a commonly encountered challenge in clinical practice. Multiple potential etiologies, varying degrees of clinical severity, and lack of a specific treatment for impeding SIRS/MOF/MODS make management difficult, especially in severe cases and/or in low resource environments.

It is now well recognized that early decisions and interventions within the first 24 hours have a significant potential impact on the outcome of patients with AP. The overarching goal in treating AP patients is to prevent persistent SIRS, pancreatic necrosis, and MOF. Specific, treatable etiological factors need to be addressed in a timely fashion while minimizing redundant tests and delays in appropriate care.

In this collaborative manuscript we have reviewed the latest literature and expert opinion (consensus) based recommendations that currently exist for managing patients with AP, with a unique focus on the evaluation and management in the first 24 hours. The authors have strived to present this information in a practical, highly clinical context with an eye toward simplifying the management algorithm for "point of care" providers in the emergency and general internal medicine fields who are typically the "first responders" taking care of the patient with acute pancreatitis. It is our hope that more widespread adoption of these best practice recommendations will help further reduce the morbidity and mortality associated with AP.

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Conflicts of Interest

DCW is a cofounder and consultants to Ariel Precision Medicine., He serves as CSO and Chair, Medical Advisory Board at Ariel Precision Medicine and has equity,

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