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SPECIAL FEATURE

Management Guidelines for Acute Pancreatitis

By James E. McFeely, MD

Medical Director, Critical Care Units, Alta Bates Summit Medical Center, Berkeley, CA

Dr. McFeely reports no financial relationships relevant to this field of study.

There are more than 275,000 hospitalizations for acute pancreatitis per year, with more than $2.6 billion spent on care worldwide. Many of these cases require ICU admission. Mortality rates vary between 2% and 17% depending on illness severity. Despite this burden of illness, questions remain regarding the most basic elements of care. There are some recommended treatment guidelines for the initial management of acute pancreatitis. Many of these recommendations come from a recent guideline issued by the American Gastroenterological Association.[1,2]

There are two categories of pancreatitis: interstitial edematous pancreatitis (acute inflammation without necrosis) and necrotizing pancreatitis with pancreatic or peripancreatic tissue necrosis. Pancreatitis severity is classified as mild (no organ failure), moderate (transient organ failure for less than 48 hours), or severe (organ failure for longer than 48 hours). Many severity scoring systems have been assessed for their utility for pancreatitis, but none are superior to the systemic inflammatory response syndrome (SIRS) criteria or Acute Physiology and Chronic Health Evaluation (APACHE) II score.

Initial patient evaluation should include assessment of organ failure. Laboratory analysis should include chemistries, complete blood count (CBC), triglycerides, calcium, and lactic acid levels. Measurement of lipase and amylase can be useful for initial diagnosis, but they are not useful markers to follow and do not predict severity or prognosis. ICU admission is appropriate for patients with severe acute pancreatitis with significant underlying disease, cardiopulmonary organ failure, coma, or significant electrolyte or acid-base abnormalities. Initial management is supportive with fluids, pain management, and

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[INSIDE]

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nutritional support. Unfortunately, the best practice for some of these elements of care remains unclear. *(See Table 1.)*

IV FLUIDS

There is evidence that aggressive fluid replacement in the initial stages (first 12 to 24 hours) is associated with a reduction in mortality.[3] A small study suggested Ringer's lactate may reduce the incidence of SIRS compared to normal saline.[4] Haydock et al conducted a systematic review to analyze fluid management in pancreatitis. They identified 15 studies that met inclusion critieria. Nine of these compared aggressive vs. nonaggressive resuscitation and were split five to four on the best approach. In two of these studies, researchers tried to use goal-directed therapy (using different goals): one revealed benefit, and one did not.

There is no consensus on which crystalloid to use. Both saline and Ringer's lactate have been used, but have not been compared head to head in a large randomized trial. The exception is in cases of hypercalcemia-induced pancreatitis, where Ringer's lactate is not recommended because it contains 3 mEq/L calcium.[5] Hydroxyethyl starch-containing fluids also are not recommended.

Despite this lack of guidance, many practitioners initially try aggressive fluid resuscitation with a goal of maintaining urine output at least 0.5 mL/kg/hour while watching for signs of volume depletion or overload. Frequent monitoring of vitals, urine output, and labs, including blood urea nitrogen and hemoglobin, can help with adjustments in the rate of administration. Glucose levels should be monitored frequently and treated, as hyperglycemia is associated with an increased frequency of secondary pancreatic infection. If the patient remains oliguric despite aggressive fluid resuscitation, the possibility of abdominal compartment syndrome should be considered and bladder pressures should be transduced.

NUTRITION

Traditionally, bowel rest was recommended to avoid stimulation of pancreatic exocrine function. This is no longer the case. Early (within 24 hours) enteral nutrition is recommended and is thought to help maintain the gut mucosa and decrease bacterial translocation. In a systematic review, Vaughn et al identified nine trials that compared early vs. late feeding.[6] The investigators found no difference in mortality with early feeding, but noted trends toward worsening pancreatic necrosis and multiple organ failure with delayed feeding.

In a meta-analysis of randomized, controlled trials comparing enteral feeding with total parenteral nutrition, Yi et al found clear evidence that enteral feeding is superior, with less mortality, multiple organ failure, infections, and peripancreatic necrosis.[7] For patients who cannot take oral nutrition, nasogastric or nasojejunal feeding should be initiated with a high protein, low-fat, semi-elemental formula that will minimize pancreatic enzyme stimulation.

PROPHYLACTIC ANTIBIOTICS

Up to 20% of patients with pancreatitis develop an extrapancreatic infection. In randomized trials of the use of prophylactic antibiotics for severe necrotizing pancreatitis, no difference was observed in mortality nor in pancreatic or peri-pancreatic rates of infection. There was no difference in development of single

Table 1. Quality of Evidence for Interventions in Acute Pancreatitis

Intervention	Recommendation	Quality of Evidence
Intravenous fluids (rate, type, goal)	None	Very low
Early vs. delayed feeding	Early	Low
Total parenteral nutrition vs. enteral feeding	Enteral	Moderate
Early vs delayed cholecystectomy	Early	Moderate
Alcohol avoidance intervention	Yes	Moderate

or multiple organ failures or hospital length of stay. Based on these studies, prophylactic antibiotics should not be used routinely for pancreatitis.[8]

TIMING OF INVASIVE PROCEDURES/SURGERIES

In a systematic review comparing urgent endoscopic retrograde cholangiopancreatography (ERCP) to conservative management in acute gallstone pancreatitis. No difference was observed in mortality, organ failures, infection, or total rates of necrotizing pancreatitis. As a result, urgent ERCP is not recommended routinely for acute pancreatitis. The exception to this is in cases of acute cholangitis, when it is indicated regardless of the presence of pancreatitis, and in cases in which a visible common bile duct obstruction is seen on imaging.

There has been debate regarding timing of cholecystectomy in acute gallstone pancreatitis. van Baal et al conducted a systematic review and found that advocates for early intervention point to fewer late complications from gallstones, while advocates for delayed surgery believe that a delayed approach is safer and perhaps associated with better outcomes because of decreased inflammation in the surgical bed.[9]

A single, good-quality randomized trial included in the review revealed substantial evidence that cholecystectomy performed during initial admission is associated with significant reductions in a composite outcome of mortality and gallstone-related complications, with no increase in surgical difficulty or conversion from a laparoscopic to an open procedure. Based on these findings, early cholecystectomy is recommended.[9]

ALCOHOL AVOIDANCE INTERVENTION

There are few studies evaluating the role of alcohol counseling in patients with alcohol-induced pancreatitis. The results of one randomized trial showed a trend toward lower overall readmission rates, but no change in the rate of recurrent pancreatitis. A Cochrane Review of a brief alcohol intervention in a primary care setting showed a significant reduction in consumption, a finding that persisted in a follow-up meta-analysis. Thus, a brief alcohol intervention is recommended in cases of alcohol-induced acute pancreatitis.[10]

SUMMARY

Acute pancreatitis continues to be a disease in need of more research to define the best management practices. Current recommendations include avoiding prophylactic antibiotics, and TPN. Early enteral feedings, performing a cholecystectomy if indicated during the index hospitalization, and providing alcohol avoidance counseling are recommended. Less certain is how to provide initial fluid resuscitation (including which fluid to use), what rate to administer, and what goal to aim for. Hopefully, these questions will be answered by good quality trials in the near future. ■

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ABSTRACT & COMMENTARY

Maintaining Oxygenation Without Increasing Aspiration Risk During Induction

By Vibhu Sharma, MD, MS

Attending Physician, Division of Pulmonary and Critical Care Medicine, John H. Stroger Hospital of Cook County; Assistant Professor of Medicine, Rush University Medical Center, Chicago

Dr. Sharma reports no financial relationships relevant to this field of study.

SYNOPSIS: In this multicenter, randomized, unblinded trial, bag-mask ventilation from time of induction to laryngoscopy was associated with higher oxygen saturations and lower incidence of severe hypoxemia compared to those not "bagged."

SOURCE: Casey JD, Janz DR, Russell DW, et al. Bag-mask ventilation during tracheal intubation of critically ill adults. *N Engl J Med* 2019;380:811-821.

Casey et al designed a trial to determine whether bag-mask ventilation (BMV) starting at induction prevents a drop in oxygen saturation (SpO_2). Further, the authors wanted to know whether BMV increased the risk for aspiration. The primary outcome was the lowest SpO_2 documented between induction and two minutes after endotracheal intubation. The secondary outcome was the incidence of severe hypoxemia (SpO_2 < 80%). Other prespecified outcomes included operator-visualized aspiration (oropharyngeal or gastric) and the presence of a new opacity on chest X-ray. Exploratory SpO_2 outcomes also were compared (lowest SpO_2 < 90%; lowest SpO_2 < 70%; and decrease in SpO_2). Seven academic medical center ICUs in the United States participated; 266 of 667 patients enrolled were excluded (those with emesis, hematemesis, hemoptysis, and those with a full stomach. Patients who needed urgent intubation also were excluded, as were those with severe acidemia or severe hypoxemia in whom ventilation was deemed indicated during induction.

Thus, 401 patients undergoing tracheal intubation were randomized to receive either ventilation with a bag-mask device or no ventilation between induction and laryngoscopy. Overall, 60% of enrolled patients experienced hypoxemic respiratory failure, and half had sepsis or septic shock. All patients received preoxygenation. The technique was not mandated and left to the operator, with an equivalent proportion in each group receiving positive pressure oxygenation (defined as either bi-level positive airway pressure [BiPAP], high-flow nasal cannula [HFNC] oxygen, or BMV). BiPAP and HFNC settings were not standardized.

One group (BMV group) was randomized to receive BMV with 5-10 cm H_2O positive end-expiratory pressure (PEEP) and 15 L/minute oxygen at 10 breaths per minute starting from the time of induction until laryngoscopy was performed. The other group (no BMV group) received no ventilation. Oral airways and jaw thrust chin lift maneuvers were allowed as needed. Apneic oxygenation (Apox) was not mandated post-induction in the no BMV group, but was allowed per intubator preference (78% chose to provide Apox with a 100% non-rebreather mask or nasal cannula). BMV was not allowed per the protocol in patients randomized to the no BMV group unless first laryngoscopy failed (n = 44) or SpO_2 < 90% necessitated BMV (n = 5). This latter group was analyzed with their initial assigned group (i.e., no BMV).

All patients underwent rapid sequence intubation with etomidate/ketamine as the induction agent and neuromuscular blockade. Almost all patients in each group were intubated by trainees (critical care fellows or anesthesia residents composed approximately 96% in each group). The intubators in each group had intubated a median of 50 patients (range, 32-100), and the first-pass success rate was about 80% in each group.

The authors found that BMV starting at induction compared to no BMV was associated with a median lowest oxygen saturation of 96% compared to 93%, a statistically significant difference (P = 0.01). Those patients with the lowest SpO_2 at the time of induction benefited the most from BMV. If BMV was used, the lowest SpO_2 for the sickest patients (with SpO_2 < 97% at induction), after all preoxygenation interventions had ceased and induction medications were administered, was higher (89%) compared to the lowest SpO_2 for those who did not receive BMV (82%). Severe

hypoxia (SpO_2 < 80%) occurred less frequently in the BMV group (relative risk [RR], 0.48; 95% confidence interval [CI], 0.30-0.77). Similarly, the lowest SpO_2 also was higher in those "bagged" with $SpO_2 \geq 97\%$ at induction. Overall, the median decrease in SpO_2 from induction to two minutes after intubation was lower in the BMV group compared to the no BMV group (median decrease of 1% vs. 5%; mean difference, 4.5%; 95% CI, 2.2-6.8). The incidence of lowest SpO_2 < 90% and < 70% also was lower in the BMV group. Visualized aspiration during intubation and new opacities on chest X-ray within the 24 hours following intubation were not higher among those receiving BMV.

■ COMMENTARY

Casey et al concluded that "bagging" patients during induction is safe and allows for higher SpO_2 during a critical period of airway management. There are several caveats to the findings.

Patients who needed urgent intubation were excluded. In essence, the authors assessed the effect of study interventions in those patients in whom intubation could proceed with adequate procedures to preoxygenate. Indeed, median SpO_2 in each group at the start of induction was 99%, a relative luxury in the setting of airway management in the ICU. Only a small number of patients in each group (27 in the BMV group and 17 in the no ventilation group) had SpO_2 < 92% at start of induction. The exclusion criteria necessarily introduced selection bias, and the number of patients excluded was substantial. While this was appropriate to maintain safety, the study population skewed toward patients with relatively preserved ventilation/perfusion (V/Q) matching (those who could be "bagged up").

Second, the preoxygenation technique was not standardized. HFNC, BiPAP, and BMV as techniques for preoxygenation were grouped as "preoxygenation with positive pressure." In a post-hoc analysis, while the preoxygenation device did not seem to modify between-group differences in terms of lowest SpO_2, preoxygenation device settings may have been selected intuitively to be more aggressive in patients perceived to be sicker. For example, noninvasive ventilation with higher pressure settings may have been selected for those patients perceived to have worse V/Q mismatch or a higher HFNC oxygen flow rate may have been selected for patients perceived to be sicker. Intubators were not blinded to any patient characteristics, including clinical diagnosis or SpO_2 at start of preoxygenation, given the pragmatic nature of the study.

Third, the majority of patients were intubated by critical care fellows and anesthesia residents with approximately 50 intubations under their belt on average (range, 30-100). A survey of pulmonary/critical care fellowship programs in the United States revealed that 67% of fellows graduated with ≤ 50 laryngoscopies performed.[1] Although Casey et al did not find that operator experience modified the effect of BMV on the lowest SpO_2, the results of other studies have shown that the level of experience matters.[2,3] Given the absence of harm and evidence of benefit, BMV during induction ought to be the standard, especially with trainees as intubators.

Fourth, while the proportion of patients with one or more difficult airway characteristics was no different between groups, those with obstructive sleep apnea were overrepresented in the no BMV group (26 vs. 15). This may have skewed toward lower SpO_2 with a longer time to intubation and (potentially) a failed first laryngoscopy, especially with neuromuscular blockade. The mean difference between groups with respect to the lowest SpO_2 was driven by two of seven sites (and mostly by a single center that recruited the largest number of patients). The authors offered no details with respect to characteristics of patients or preoxygenation techniques analyzed by institution.

Finally, none of the institutions performed preinduction gastric antral ultrasound. This technique has been well described and may prevent clinically relevant aspiration events around the time

of intubation.[4] If the stomach is empty, the effect of BMV on gastric aspiration events is irrelevant. BMV with oxygen delivered at 15 L/minute and 10 breaths per minute with 5-10 cm H_2O PEEP during induction is associated with higher SpO_2, prevents severe hypoxia (number needed to treat = 9 to prevent one episode of severe hypoxemia), and is not associated with a higher risk of aspiration. In carefully selected patients, BMV prevents critical desaturation. Desaturation by 5% from time of induction to laryngoscopy may be expected if no BMV is provided. ■

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ABSTRACT & COMMENTARY

Physicians Cannot Agree on Who Benefits From ICU Care

By Betty Tran, MD, MSc, Editor

Assistant Professor of Medicine, Pulmonary and Critical Care Medicine, Rush University Medical Center, Chicago

Dr. Tran reports no financial relationships relevant to this field of study.

SYNOPSIS: The authors of a study randomizing U.S. critical care physicians to analyze hypothetical patient vignettes found that estimates of whether a patient would benefit from ICU care were widely dissimilar among those surveyed and influenced by factors unrelated to severity of illness.

SOURCE: Valley TS, Admon AJ, Zahuranec DB, et al. Estimating ICU benefit: A randomized study of physicians. *Crit Care Med* 2019;47:62-68.

Appropriate allocation of ICU resources is vital for most settings where the demand for ICU beds exceeds the supply. But it is also important to avoid deleterious effects associated with ICU overuse, including higher costs, more iatrogenic complications, and overaggressive care at the end of life.[1] Current Society of Critical Care Medicine (SCCM) guidelines recommend that patients be admitted strictly on their potential to benefit from ICU care. However, identifying the benefit of critical care for different patient populations remains elusive.[2]

Valley et al recruited volunteer members of SCCM to participate in a study which they were randomized to eight online vignettes of hypothetical patients with pneumonia. Each vignette included a randomized single patient factor related to severity of illness (blood pressure, mental status, oxygen requirement, respiratory rate) or hospital factor (patient age, patient race/ethnicity, presence of patient's family at bedside, number of available ICU beds). Vignettes were designed so that clear indications for ICU admission (e.g., on mechanical ventilation or vasopressors) were avoided.

The primary outcome was an estimate of ICU benefit in the form of the question, "Would this patient receive the most benefit from admission to the general ward or the ICU?" A secondary outcome was the difficulty in assessing ICU benefit in the form of the question, "How difficult was this decision for you?" Responses used a 4-point Likert-type scale (e.g., "definitely general ward" to "definitely ICU").

There was a 14% recruitment rate, and 913 physicians ultimately completed all eight vignettes (75% completion rate). The average age of participants was 42 years. Most were male (65%), most were white (61%), and most worked in an academic clinical setting (73.1%) or academic hospital (66.7%).

Among physicians reviewing the exact same vignette, there was poor consensus (mean intraclass correlation coefficient, 0.06; standard deviation, 0.08; range, 0-0.18). Greater estimated benefit of ICU care was seen for increasing respiratory rate or oxygen requirement, decreasing blood pressure, and patient confusion.

Physicians believed ICU care was more beneficial if they were told one ICU bed was available (compared to ICU bed availability not mentioned). Still, Valley et al observed no difference in estimated ICU benefit if physicians knew that five ICU beds were available.

Physicians believed ICU care was less beneficial if family was present than if family presence was not mentioned and if the patient was younger. Race/ethnicity had no significant effect. Physicians reported it was easier to estimate ICU benefit when the patient was hypotensive, but more difficult when the patient was confused or when the patient's wife was crying at bedside.

■ COMMENTARY

In general, for industrialized countries, for every increase of 100 hospital beds per 100,000 population, there are an extra 3.5 ICU beds.[3] However, the United States is an outlier, spending more resources (and more money on healthcare overall) on ICU beds per capita than its counterparts with similar outcomes.[3,4] These observations shine a light on ICU overuse and call for ideas to both reduce ICU demand while improving the quality of ICU care.

Although current societal guidelines acknowledge the need to triage ICU admissions based on a number of criteria, including specific patient needs, condition, prognosis, and bed availability, there are no benchmarks to delineate the "potential for the patient to benefit from interventions."[2] Valley et al demonstrated that even among a community of critical care colleagues, there is little consensus that defines which types of patients benefit from ICU admission.

Surprisingly, the investigators found that their results conflicted with other studies in that ICU bed availability did not affect ICU admission decisions and that older age did not negatively affect ICU admission. Although the study design was randomized and has been shown to simulate clinical behavior, limitations included a low recruitment rate and sampling biases, as the study participants were more likely to be younger, male, and white compared to the SCCM population as a whole. In addition, one-third of the participants had been in practice for four years or less and one-fifth practiced in surgery or anesthesia, suggesting they may be less experienced treating the patient population presented in the vignettes.

Regardless, this study, especially when considered with prior work, demonstrates that clinicians allocate ICU resources inconsistently based on individual patient presentations. Generating a group of explicit "criteria" to allow or deny ICU admission may be impractical, not to mention fraught with ethical and legal concerns over the concept of explicit "rationing" of ICU care. Furthermore, a single set of decision rules would unlikely function well across hospitals in different communities and of varying capabilities.

[It will take thoughtful approaches to slow an unsustainable rate of healthcare consumption in the United States while improving quality of care for patients, regardless of whether they receive it in the ICU.]

How can healthcare workers reduce ICU overuse? In an opinion piece, Kahn and Rubenfeld argued for implicit "rationing" through efforts to reduce the relative number of ICU beds. They called for introducing certificate of need laws at the state level to slow growth and incentivizing safe and effective triage by physicians, all with close monitoring to ensure no worsening effects on quality, adverse events, or health disparities.[5]

Ultimately, it will take thoughtful approaches to slow an unsustainable rate of healthcare consumption in the United States while improving quality of care for patients, regardless of whether they receive it in the ICU. ■

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CME/CE QUESTIONS

1. Which is recommended as first-line treatment in acute pancreatitis?
a. Prophylactic antibiotics
b. Total parenteral feeding
c. Conservative IV fluid management
d. Early initiation of nutritional support

2. Depending on severity of illness, the mortality range of acute pancreatitis is:
a. 25-35%.
b. 40-50%.
c. 0-2%.
d. 2-17%.

3. In the study by Casey et al, which was a benefit of bag-mask ventilation (BMV) with positive end-expiratory pressure (PEEP) during induction:
a. Improved survival
b. Higher SpO_2 from induction to laryngoscopy
c. Lower incidence of cardiac arrest
d. Lower incidence of aspiration

4. In the study by Valley et al, which statement is true?
a. There was a high recruitment rate (> 50%) of U.S. critical care physicians.
b. Participants predominately worked in community settings.
c. There was poor consensus among physicians regarding which patients would benefit from ICU admission.
d. Race significantly affected the decision to admit to the ICU.

5. In the study by Valley et al, among physicians surveyed, which vignette factor was associated with a greater estimate for ICU benefit?
a. Older patient age
b. Family presence
c. Lower respiratory rate of patient
d. Higher number of ICU beds available

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.