Early Factors Associated With Fluid Sequestration and Outcomes of Patients With Acute Pancreatitis

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BACKGROUND & AIMS: **Predicting level of fluid sequestration could help identify patients with acute pancreatitis (AP) who need more or less aggressive fluid resuscitation. We investigated factors associated with level of fluid sequestration in the first 48 hours after hospital admission in patients with AP and effects on outcome.**

METHODS: **We analyzed data from consecutive adult patients with AP admitted to the Brigham and Women's Hospital in Boston, Massachusetts, from June 2005 to December 2007 (n = 266) or the Alicante University General Hospital in Spain from September 2010 to December 2012 (n = 137). Level of fluid sequestration in the first 48 hours after hospital admission was calculated by subtracting the total amount of fluid administered and lost in the first 48 hours of hospitalization. Demographic and clinical variables obtained in the emergency department were analyzed to identify factors associated with level of fluid sequestration in the first 48 hours after hospital admission. Outcome assessed included length of hospital stay, acute fluid collection(s), pancreatic necrosis, persistent organ failure, and mortality.**

RESULTS: **The median level of fluid sequestration in the first 48 hours after hospital admission was 3.2 L (1.4–5 L). The simple and multiple linear regression models showed that younger age, alcohol etiology, hematocrit, glucose, and systemic inflammatory response syndrome were significantly associated with increased levels of fluid sequestration in the first 48 hours after hospital admission. Increased level of fluid sequestration in the first 48 hours was significantly associated with longer hospital stays and higher rates of acute fluid collection, pancreatic necrosis, and persistent organ failure. There was a nonsignificant trend toward a higher level of fluid sequestration in the first 48 hours among patients who died.**

CONCLUSION: **Age, alcoholic etiology of AP, hematocrit, glucose, and presence of systemic inflammatory response syndrome in the emergency department were independent predictors of increased levels of fluid sequestration in the first 48 hours after hospital admission. These patients have higher risks of local and systemic complications and longer hospital stays.**

Keywords: Pancreatic Inflammation; Treatment; Morbidity; Intravenous Fluid Therapy; Management.

Acute pancreatitis (AP) is now the most common reason to be hospitalized for a gastrointestinal disease in the United States and cost an estimated 2.6 billion dollars in 2009.[1] The majority of patients with AP experience a mild disease course, with no relevant morbidity and a short length of stay. However, approximately 10%–15% of patients suffer a severe course with high morbidity and significant mortality. Because there are no specific therapies for AP,[2,3] the cornerstone of management has been supportive care, consisting of bowel rest, analgesics, and intravenous fluid therapy.

Abbreviations used in this paper: **AP, acute pancreatitis; APACHE, Acute Physiology and Chronic Health Evaluation; BUN, blood urea nitrogen; FS, fluid sequestration; SIRS, systemic inflammatory response syndrome; VLS, vascular leak syndrome.**

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In recent years, fluid therapy has received increasing attention, with several clinical guidelines and reviews recommending early and aggressive fluid therapy.[4–11] The premise of this approach is to improve pancreatic tissue perfusion and potentially prevent the development of pancreatic necrosis, thus altering the natural history of the disease. The data supporting early and aggressive fluid therapy were based on animal models of AP[12,13] and human studies showing an association between elevated hematocrit[14–16] or blood urea nitrogen (BUN),[17] with worse outcomes. Since 2009, several prospective studies have failed to demonstrate improved outcomes for patients treated with early and aggressive fluid therapy,[18–21] and some of these studies have even suggested that this practice can be detrimental.[18,19,21] Future studies are needed to clarify the role of aggressive fluid resuscitation.[22] It is well known that some patients with AP have an increased need for fluid therapy, but it remains unclear which patients should receive aggressive or nonaggressive fluid therapy as well as at what point in their presentation should fluid therapy commence. Most clinical studies have evaluated the quantity of fluid administered over different time points in AP and have not evaluated the role of fluid sequestration (FS). Because AP can be associated with extensive FS,[23] it is important to delineate what effect FS has on outcomes and whether predictors of FS can be identified on admission. The identification of early predictors of FS might help tailor fluid therapy for each individual patient, with aggressive strategies reserved for those with predicted increased fluid requirements or signs of fluid depletion. There have been few studies of FS in AP, and these have focused only on subgroups of patients, mean FS among patients with mild vs severe AP,[23] mean FS in severe AP,[24] or outcome according to different cutoff points for FS.[25] There are no studies evaluating FS in a large sample of consecutive patients as well as early predictors of FS.

Our primary aim was to investigate which variables at admission are predictors of FS. Our secondary aim was to determine the outcomes associated with FS.

Methods

We retrospectively analyzed 2 cohorts of patients with AP. The first cohort included consecutive patients admitted to the Brigham and Women's Hospital (Boston, MA) between June 2005 and December 2007 (MOSAP database). The second cohort included consecutive patients admitted to the Alicante University General Hospital (Alicante, Spain) between September 2010 and December 2012 (Fluid Therapy database). Data from both cohorts were recorded prospectively. Only adult (≥18 years of age) patients with AP were included in the study. AP was defined in both cohorts as 2 of the following 3 criteria: (1) characteristic abdominal pain, (2) serum amylase and/or lipase greater than 3 times the upper limit of normal, and (3) abdominal imaging demonstrating changes consistent with AP. We excluded patients with chronic pancreatitis, patients with incomplete data regarding fluid administration or loss in the first 48 hours from admission, and patients undergoing hemodialysis (before the episode of AP or within the first 48 hours from admission). Transferred patients from other institutions were included if detailed information about fluid intake and output was available.

Variables

Our main outcome variable was FS in the first 48 hours from admission. FS was calculated by subtracting fluid output from fluid intake in the first 48 hours from presentation. These were collected prospectively in a similar manner at both institutions. Fluid intake included administration of all intravenous crystalloid, colloid preparations, and blood as well as oral fluid intake as reported by the nursing flow sheets. Fluid output included recorded volumes of urine, stool, and vomitus. Fluid output also included insensible losses (calculated as 10 mL per kg body weight per day).[26] Patients with a temperature >37.8°C had an estimated 500 mL extra fluid output per day.[27]

We analyzed the relationship between variables obtained at presentation, in the emergency department (initial history and physical examination as well as laboratories), and FS. We selected the following variables that may be potentially associated with FS or the need for aggressive fluid therapy: age,[21] gender, etiology of AP,[21] body mass index, hematocrit,[28] glucose (because hyperglycemia can increase fluid output as a result of osmotic diuresis), creatinine,[28] sodium, BUN,[28] Acute Physiology and Chronic Health Evaluation (APACHE)-II score,[29] the presence of systemic inflammatory response syndrome (SIRS),[29,30] and time from onset of pain to presentation. Quantitative variables were categorized by using terciles (age, hematocrit, sodium, BUN) or widely used cutoff points (body mass index, glucose, APACHE-II, creatinine, SIRS).

Statistical Analysis

The association of potential predictors obtained at the time of emergency department presentation and FS was determined by simple linear regression. Multiple linear regression was used for adjustment. Secondary outcome variables were pancreatic necrosis and acute fluid collections (both defined in accordance with the revised Atlanta classification[31]), persistent (>48 hours) organ failure (modified Marshall score ≥2 for renal, pulmonary, and/or cardiovascular dysfunction[32,33]), length of hospital stay, and in-hospital mortality. FS did not follow a normal distribution (according to Kolmogorov–Smirnov test). The levels of FS in the categories of these variables were compared by Kruskal–Wallis test or Mann–Whitney *U* test.