EDITORIAL

Early Prognostic Evaluation of Acute Pancreatitis: An On-Going Challenge

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Acute pancreatitis remains a serious disease. In 2009, acute pancreatitis accounted for more than 274,000 hospital discharges, (ranking first among all gastro-intestinal discharge diagnoses), with an aggregate cost of more than $2,500,000 (the costliest of all gastro-intestinal disorders). It also ranked 14th among causes of death from gastrointestinal and liver diseases [1]. Mortality from acute pancreatitis is approximately 3% for interstitial pancreatitis [2], and 15% for necrotizing pancreatitis [3]. For several years, considerable effort has been targeted to the early evaluation of patients with acute pancreatitis, with the goal of identifying those who will develop severe acute pancreatitis.

The potential benefits of this effort are multi-fold. First, it would facilitate the triage of patients with predicted severe disease for intensive monitoring and nursing care. Second, it would hasten the transfer of such patients from community hospitals to pancreatitis centers capable of more advanced care. Third, it would facilitate comparison of clinical outcomes among institutions. And fourth, accurate early prognostic evaluation would facilitate the evaluation of new therapies as they become available.

Two key components to early prognostic evaluation are risk factors of severity and prognostic indicators of severity. Risk factors of severity are patient-related factors or clinical features present at baseline that contribute to a poor outcome. Older age (55 or more years) [3, 4, 5, 6], alcohol [7], obesity (body mass index: BMI greater than 30 kg/m^2) [8, 9], first or second episode of disease [9, 10, 11] and presence of co-morbid conditions [2, 12] have all been established as risk factors of severity.

Prognostic indicators are markers of severity that can be measured at admission and at various stages thereafter in order to assess response to therapy. Prognostic indicators available at admission include blood urea nitrogen (BUN) and hematocrit. In an international study, BUN levels at admission equal to, or greater than, 20 mg/dL correlated with increased mortality [13]. Studies examining admission hematocrit have reached varying conclusions [9, 14, 15, 16, 17], with two recent studies concluding that hemoconcentration predicts pancreatic necrosis [18] and mortality [19] only among transferred patients, but not among directly-admitted patients. In this issue of JOP. Journal of the Pancreas, we have demonstrated that directly-admitted patients with hemoconcentration in the setting of a shorter duration of abdominal pain prior to admission had an increased prevalence of pancreatic necrosis [20].

Prognostic indicators that have been measured at stages to assess response to therapy include BUN and creatinine. Serial measurements of BUN have been shown to reliably predict mortality, with increases during the initial 24 hours of hospitalization associated with a corresponding increased risk of mortality [13, 21]. In addition, a peak serum creatinine greater than 1.8 mg/dL within the first 24 hours has been shown to predict the development of pancreatic necrosis [17].

Among prognostic indicators of severity obtained during the first 24 hours of hospitalization, four scoring systems that have received considerable research attention are the bedside index for severity of acute pancreatitis (BISAP), the systemic inflammatory response syndrome (SIRS) score, the APACHE II score and contrast-enhanced-computed-tomography (CT)-based scoring systems. Incremental increases in the BISAP score (3 or more) have been shown to correlate with an increased risk of persistent organ failure [22, 23], pancreatic necrosis [22, 23] and mortality [6, 22, 23]. The presence of SIRS and in particular, of 3 or 4 SIRS criteria within the first 24

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Abbreviations BISAP: bedside index for severity of acute pancreatitis; BUN: blood urea nitrogen

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hours, have been shown to correlate with an increased risk of persistent organ failure, pancreatic necrosis, need for intensive care and mortality [24]. The APACHE II score has been shown to have an accuracy similar to various scoring systems and individual markers, but is more difficult to calculate [6, 22, 23]. CT-based scoring systems for severity have not been shown to be superior to clinical scoring systems [25].

There is concern that the prognostic indicators of severity currently in use may have reached their maximal benefit, and that newer markers (proteomic patterns, genetic polymorphisms, cytokine profiles, etc.) and analytic methods (computational learning theory, artificial neural networks (ANNs), systems biology, etc.) will be needed to improve the accuracy of early prognostic evaluation [26, 27]. Artificial neural networks have received particular attention [28], and in one report out-performed the APACHE II score [29].

Ultimately, the accuracy of prognostic indicators is related to the measures that are used during the hospitalization to classify the severity of acute pancreatitis. A drawback of many studies thus far has been the use of a variety of measures of severity, and in particular, reliance on the outdated initial Atlanta classification [30, 31]. In this regard, the 2012 revision of the Atlanta classification stratifies severity into three levels. Mild acute pancreatitis is characterized by the absence of organ failure and absence of local or systemic complications. Moderately severe acute pancreatitis is characterized by the presence of transient organ failure, local complications, or systemic complications. Transient organ failure is defined as organ failure that persists for 48, or less, hours. Local complications include pancreatic necrosis; systemic complications are exacerbations of pre-existing comorbidity. Finally, severe acute pancreatitis is characterized by the presence of persistent organ failure, defined as organ failure that persists for more than 48 hours. Persistent organ failure may be single or multiple. Mortality rates in mild pancreatitis are negligible, in moderately severe pancreatitis somewhat higher, and in severe acute pancreatitis in the range of 36-50% [31].

The revised classification also provides more precise definitions of radiologic findings, including peripancreatic necrosis, walled-off-necrosis and pseudocyst [26, 30, 31]. Furthermore, the revised classification points out that pancreatic necrosis can rarely be identified accurately during the first several days of hospitalization, and that a follow up CT scan 5-7 days after admission is usually required for this purpose [30, 31, 32]. The revision also suggests that for the purposes of clinical research, data on patients who are admitted directly to a hospital should be analyzed separately from data on patients who are transferred from outside hospitals in order to allow separate evaluation of the outcomes of these two groups of patients. Finally, the revised classification suggests that time to admission be recorded for each patient [31].

It is important that future studies focusing on early prognostic evaluation utilize the definitions of severity in the 2012 revision of the Atlanta classification, including pancreatic necrosis (indicating moderately severe acute pancreatitis) and persistent organ failure (indicating severe acute pancreatitis). Death should not be considered as a marker of severity, but as an end result of severity. Length of hospital stay, need for intensive care unit and other variables should also be considered as consequences of severity [33].

Even with improvements in accuracy of prognostic indicators of pancreatic necrosis and persistent organ failure, it remains uncertain whether this information would reduce severity during hospitalization. For example, at the present time the only widely available preventative therapy is early vigorous fluid resuscitation [3, 21]. The optimal rate has not yet been determined [34, 35, 36], and its efficacy has not been proven [21, 26].

Early prognostic evaluation of acute pancreatitis remains an on-going challenge.

Conflicts of interest None

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