Early Severe Acute Pancreatitis: A Subgroup of Critical Acute Pancreatitis

To the Editor:

We read with interest the excellent article, titled "Determinant-Based Classification of Acute Pancreatitis Severity: An International Multidisciplinary Consultation," published in *Annals of Surgery* by Dr Dellinger and his colleagues[1] and the comments, "Atlanta Redux: Revisiting the Severity Stratification System for Acute Pancreatitis," by Edward L. Bradley III.[2] They developed a new classification of severity of acute pancreatitis on the basis of a sound conceptual framework, comprehensive review of published evidence, and worldwide consultation. The new classification of severity is based on the actual local and systemic determinants of severity, rather than description of events that are noncausally associated with severity. The local determinant relates to whether there is peripancreatic necrosis or not and, if present, whether it is sterile or infected. The systemic determinant relates to whether there is organ failure or not and, if present, whether it is transient or persistent.

The major impetus to revision has been the recent significant advances in understanding the pathophysiology of acute pancreatitis and especially the role of systemic complications. Although the original Atlanta classification assessed only the presence or absence of organ failure, it is now recognized that the number of organs that fail, the timing of onset, the change in organ failure in response to initial treatment, and the duration of organ failure all contribute to severity.

It has become apparent that there are 2 phases of acute pancreatitis: an early phase (usually within the first week of onset) and a subsequent phase occurring after the first week of disease onset. During the first phase, which usually lasts a week or so, the severity is related to the organ failure secondary to the host's systemic inflammatory response elicited by the tissue injury and not necessarily to the extent of necrosis. In the second phase, the disease either resolves (edematous pancreatitis without necrosis) or tends to stabilize (but not normalize) or progress and enter into a more protracted course lasting weeks to months related to the necrotic process of necrotizing pancreatitis.[3]

TABLE 1. Proposed Classification of Severity of Acute Pancreatitis

(Peri) pancreatic necrosis	No	Sterile (early phase)			Infected (late phase)		
Organ failure	No	Transient	Persistent SOF	Persistent MODS	No	Transient	Persistent
	Mild AP	Moderate AP	Severe AP	Critical AP	Moderate AP	Severe AP	Critical AP

AP indicates acute pancreatitis; MODS, multiorgan dysfunction syndrome; SOF, single organ failure.

The first phase is characterized more by the presence or absence of organ failure. Approximately one third to half of the deaths from acute pancreatitis occur during the first week as a result of progressive organ failure (multiple organ dysfunction syndrome). Persistent organ failure, whether present at admission or occurring during the first week, was significantly associated with a fatal outcome. The determinant of severity of acute pancreatitis during the early phase is primarily the presence and duration of organ failure. Therefore, the definition of severe or moderately severe acute pancreatitis in the early phase depends on the presence and duration of organ failure.

In 2001, Isenmann et al[4] introduced a subgroup called early severe acute pancreatitis (ESAP). This subgroup comprises a quarter of patients with acute necrotizing pancreatitis and has nearly double the mortality rate of patients with organ failure and no infected peripancreatic necrosis. Another group from China also documented a mortality rate of 43.4% in patients developing organ failure within 72 hours of development of AP.[5] ESAP is characterized by the following features: a high incidence of extended pancreatic necrosis, no infected peripancreatic necrosis, frequent progressive organ failure, and a poor prognosis. In nearly 80% of the ESAP patients, multiple organ failure developed or progressed during hospitalization despite intensive care treatment. The overwhelming majority of patients with ESAP had sterile pancreatic necrosis.[4] Therefore in ESAP, it is not the bacterial infection that poses the main therapeutic problem and impairs patient prognosis but the high incidence of intractable organ failure. These characteristics provide strong justification for the introduction of a new category for severity of acute pancreatitis, with the worst prognosis group being termed "critical acute pancreatitis."[3]

In the clinical setting, there is another group that was not mentioned in the new classification. Some patients experienced the presence of infected peripancreatic necrosis and the absence of organ failure. The development of infected necrosis among patients with no organ failure is associated with a low mortality rate.

Although the 4-tier classification by Dr Delligner and his colleagues seems logical, the classification would represent the disease biology more closely if the subgroups of ESAP (critical acute pancreatitis) and late moderately acute pancreatitis (infected peripancreatic necrosis and the absence of organ failure) are included (Table 1). It also recognizes the dynamic nature of these complications, allowing for the transition from sterile to infected pancreatic and peripancreatic necrosis and transient to persistent organ dysfunction.

It should be noted that none of the existing classifications are based on uniform study designs and outcomes. However, just as stated by Edward L. Bradley III, the article[1] may represent another milestone in our path toward clinical management of acute pancreatitis and its complications. Therefore, further multicenter studies to validate the different classes of acute pancreatitis using consistent and predefined study criteria are urgently needed.

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Disclosure: Supported by the Colleges and Universities in Jiangsu Province Plans to Graduate Research and Innovation (No: CXZZ13_0061). The authors declare no conflicts of interest.

ISSN: 0003-4932/14/00000-0001
DOI: 10.1097/SLA.0000000000000537

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