Acute pancreatitis reclassified

John A Windsor, Maxim S Petrov

Science is founded on observation and classification. The taxonomist's task to classify is both dependent and limited by what has been observed and is known. Progress in science is made by classifying seeming disorder, highlighting gaps and contradictions in knowledge and addressing them by experimentation. Classifications are stepping-stones, signposting current understanding, promoting hypotheses and enabling comparisons. Such is the iterative nature of science.

Progress has been made in the management of acute pancreatitis, evidenced by a decreasing overall mortality rate. And even though our understanding of the pathophysiology is more complete, specific treatments for acute pancreatitis remain elusive and our classifications have been simplistic. For more than a century we have relied on a binary classification of acute pancreatitis severity.[1] Patients had either mild or severe disease, and this approach was enshrined in the original Atlanta Classification 20 years ago. Classification has not kept pace with our understanding of this disease and has hindered studies of potential treatments.[2] When misclassification error runs to a quarter or a third of those enrolled, it is little wonder that the clinical trials of potential treatments for acute pancreatitis have been described as a 'litany of failure'. And maybe we have discarded certain treatments prematurely.[2] But the point here is that progress towards specific and effective treatments for acute pancreatitis is, at least partially, reliant on accurate classification.

The work of the Acute Pancreatitis Classification Working Group, in updating the original Atlanta classification and as reported in Banks *et al*,[3] is commendable. The group has deliberately avoided producing another guideline to clinical management, but has rather focused on a series of definitions and classifications. Of wider scope than the original Atlanta classification, it seeks to address ambiguous terms and to integrate new knowledge. For instance, the catch-all phrase 'pancreatic abscess' has been removed and the term 'pseudocyst' given a more restricted meaning. Probably the most important contribution of this update is the redefinition of the local complications of acute pancreatitis, based on their content, wall, site and evolution. Using what we can now observe by high resolution CT scanning and drawing on a better understanding of the natural history of these local complications, a series of morphological descriptions have been defined that will ensure more consistent and accurate radiological description of the findings on CT scans. These include the acute peripancreatic fluid collections (APFC), the acute necrotic collections, and the more chronic pseudocyst and walled-off necrosis. Infection can occur with all four types of lesions, although the update only proposes this in the context of acute necrotic collections and walled-off necrosis. Table 1 incorporates infection into the classification, as it can occur with all local complications, including APFCs and pseudocysts. These definitions can only facilitate comparative studies of the many treatment options now available for different lesions in different locations and at different time points.[4]

It has been helpful to re-state the basis for diagnosing acute pancreatitis (ie, two of three features: pain, enzymes and/or radiology) and to define the onset of pancreatitis to symptoms rather than hospital admission. The distinction has been made between interstitial edematous and necrotising pancreatitis, although the former appears to be an unnecessary duplication of terms. The retention of the early/late or two-phase concept to characterise acute pancreatitis is outdated as the sheer complexity of concurrent pro-inflammatory and anti-inflammatory responses belies it and because organ failure, infected necrosis and death can occur early and late in the disease, and at any time in-between.[2 5] A more sophisticated understanding of this dynamic disease will require simulation and modelling, taking into account genotypic susceptibilities and different phenotypic local and systemic complications.[6] A further dimension to be considered is the clinical significance of an individual's response to resuscitation and supportive measures. While inferred in the concept of transient organ failure, there is the need to better understand this responsiveness with regards to threshold organ function, tolerance to intervention and as a guide to the timing, type and extent of intervention.

A late decision was made by the working group to include a 'moderate' category of severity, but the rationale for including all the local complications in that category is not clear. Clinicians know that local complications are not all equivalent with regards to disease severity. The onset of infected pancreatic necrosis most often signifies severe disease, and is quite different in significance to the onset of an acute collection without infection. This is borne out by the Dutch prospective study of more than 700 patients with acute pancreatitis in which patients with confirmed infected pancreatic necrosis had a high mortality of 30%.[7] And other studies demonstrate that what is now proposed to be called APFC often resolves within several days with little clinical impact on the patient.[8] Another issue with the moderate category is that it includes the 'exacerbation of coexisting disease' which is a consequence rather than a cause of acute pancreatitis severity.

In truth, the number of categories of severity is less important than the basis for classification. A determinant-based classification of severity[5] was published during the 7-year period in which the revised Atlanta evolved. This classification was developed on the epidemiological concept of causal inference,[2] based on actual determinants of severity,[9] honed by international consultation[1 8] and is now prospectively validated.[10] This body of work suggests that accurate severity classification should be based on determinants rather than descriptors or associations of severity. It is no surprise that different approaches have yielded different results. These differences are inevitable and help define the agenda for further studies, for science progresses this way. Clinicians and researchers will need to decide which classification of severity is best founded and meets their needs. Beyond severity classification, the revised Atlanta document takes the field forward.

Contributors Both authors have made a substantial contribution to this commentary, as evidenced by the reference list. Both have been involved in drafting the article and revising it critically for important intellectual content and both have given final approval of the version to be published.

Competing interest None.

Department of Surgery, The University of Auckland, Auckland, New Zealand

Correspondence to Professor John A Windsor, Department of Surgery, The University of Auckland, Private Bag 92019, Auckland 1142, New Zealand; j.windsor@auckland.ac.nz

Table 1 Modified radiological definitions of local complications

	Acute (<4 weeks, with no defined wall)		Chronic (≥4 weeks, with defined wall)	
Content	**No infection**	**Infection**	**No infection**	**Infection**
Fluid only	Acute peripancreatic fluid collection (APFC)	Infected APFC*	Pseudocyst	Infected pseudocyst*
Solid±fluid	Acute necrotic collection (ANC)	Infected ANC	Walled off necrosis (WON)	Infected WON

*Not covered in the revised Atlanta document.

Provenance and peer review Commissioned; internally peer reviewed.

Published Online First 7 November 2012

► http://dx.doi.org/10.1136/gutjnl-2012-302779

Gut 2013;**62**:4–5. doi:10.1136/gutjnl-2012-303725

REFERENCES

1. **Dellinger EP,** Forsmark CE, Layer P, *et al*. Determinant-based classification of acute pancreatitis severity: an international multidisciplinary consultation. *Ann Surg* doi: 10.1097/SLA.0b013e318256f778
2. **Petrov MS,** Windsor JA. Conceptual framework for classifying the severity of acute pancreatitis. *Clin Res Hepatol Gastroenterol* 2012;**36**:341–4.
3. **Banks PA,** Bollen TL, Dervenis C, *et al*. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102–11.
4. **Loveday BP,** Petrov MS, Connor S, *et al*. A comprehensive classification of invasive procedures for treating the local complications of acute pancreatitis based on visualization, route, and purpose. *Pancreatology* 2011;**11**:406–13.
5. **Petrov MS,** Windsor JA. Classification of the severity of acute pancreatitis: how many categories make sense? *Am J Gastroenterol* 2010;**105**:74–6.
6. **Whitcomb DC.** What is personalized medicine and what should it replace? *Nat Rev Gastroenterol Hepatol* 2012;**9**:418–24.
7. **Besselink MG,** van Santvoort HC, Boermeester MA, *et al*. Timing and impact of infections in acute pancreatitis. *Br J Surg* 2009;**96**:267–73.
8. **Petrov MS,** Vege SS, Windsor JA. Global survey of controversies in classifying the severity of acute pancreatitis. *Eur J Gastroenterol Hepatol* 2012;**24**:715–21.
9. **Petrov MS,** Shanbhag S, Chakraborty M, *et al*. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology* 2010;**139**:813–20.
10. **Thandassery RB,** Dutta U, Yadav TD, *et al*. Prospective validation of a four category classification of acute pancreatitis severity. *Pancreas* 2012; (in press).