Classifying an unpredictable disease: the revised Atlanta classification of acute pancreatitis

Markus M Lerch

Pancreatitis is among the most variable diseases known to us, and is the number 1 benign disorder leading to hospital admission.[1] Its natural history ranges from complete recovery after a single episode, to chronic debilitating disease over decades, to rapid death. In acute pancreatitis, the problem of unpredictability is compounded because 80% of patients with mild pancreatitis require only short hospital admissions and little in terms of resources. The remaining 20% with severe pancreatitis will have to be triaged to either aggressive early treatment, transfer to intensive care, or referral to tertiary specialist centres. When evidence emerged that certain clinical and diagnostic imaging characteristics allow to distinguish mild from severe pancreatitis on hospital admission, severity classifications of pancreatitis were introduced. The earliest such efforts date back half a century,[2] but a better understanding of the natural history and refinements in diagnostic tools required updates roughly every decade. The most widely accepted such systems were the Marseille classification of 1984[3] and the Atlanta classification of 1992.[4] A revision of the Atlanta classification has now been accomplished and appears in this issue of *Gut*.[5]

The genesis of pancreatitis is interesting. Rather than withdrawing to a secluded but sunny location for a meeting of world experts, or using the established instruments of evidence-based medicine with their formalised literature search and consensus-finding tools, the authors have chosen a web-based consensus-building approach. They first considered required revisions to the original Atlanta classification, composed an initial draft, and distributed it through the email lists of 11 international pancreas societies. Their initial call for suggestions and corrections was answered by 40 respondents, the second call by 57 and the third by 58 more. When the draft was put on the internet, while falling short of going viral, it not only led to direct discussion with the authors and within the community, but also prompted several publications referring to preliminary versions of the paper. The authors decided which suggestions to ignore and which to incorporate into each revision, and what you hold in your hands[5] is the final, authorised and official Atlanta revision (and the only one having undergone formal peer review). I think it was worth waiting for.

Banks and coworkers have delivered the most concise system of definitions and classifications for acute pancreatitis in two decades. It is clearly written with clinicians in mind, and will greatly improve the reporting of pancreatitis (if readers bother to download the supplementary files), communication between clinicians, and the design of clinical trials. The authors claim to not having provided a management guideline, but the classification will clearly influence future practise[6] and, possibly, also reimbursement.

The new classification retains the distinction between interstitial-oedematous and necrotising pancreatitis, which was once abandoned, but corresponds well to modern imaging criteria. In terms of severity, it proposes to group patients into mild, moderately severe and severe pancreatitis, a classification that is not uncontroversial. An earlier version of the paper had stayed with the established mild versus severe classification which divided patients depending on whether or not they suffered from organ failure (single or multiple; cardiovascular, renal or respiratory) for more than 48 h. That distinction was easy. The newly introduced moderately severe category is more impractical because it not only includes patients with organ failure, albeit for less than 48 h, but also patients whose pre-existing diseases (eg, chronic airway disease or diabetes) deteriorates, as well as patients with local complications on imaging studies, such as necrosis or fluid collections. This constitutes a rather mixed bag of systemic and local characteristics, but is based on a retrospective analysis in which patients with moderately severe disease differed from other severity groups in morbidity and mortality.[7] It may be worth using the moderately severe descriptor in the future, although this category will comprise at least three diverse patient cohorts. However, one should not attempt to 'upgrade' one's patients from mild to moderately severe by using CT scanning early in the disease course (although that would be simple). The authors stress that during the first week, CT is usually not required because (1) local changes still evolve, and understaging by CT is common and (2) no clinical consequences arise from imaging findings in stable patients in the first week.

The paper also highlights the evolution of the disease into an early phase, an intermediate period and a late phase after 4 weeks from onset. During the first week, SIRS (septic inflammatory response syndrome) is prevalent, parameters indicating organ failure guide therapy, and imaging by CT is usually not required. I am not sure whether this timetable can be so strictly applied since the transition from initial SIRS (with high proinflammatory cytokine levels such as Il6) to subsequent compensatory anti-inflammatory response syndrome in which monocytes become unresponsive to Lipopolysaccharite (LPS) stimulation and show reduced expression of human leukocyte antigen DR (HLA-DR) is highly variable and usually not determined biochemically in patients. The latter phase is, however, responsible for susceptibility to infection, infected necrosis and persistent organ failure.[8] After the fourth week, the authors' late phase, even different definitions for imaging changes of the pancreas should be applied according to the revised Atlanta classification. These represent the greatest change from previous classification systems.

The new classification requests a distinction between intrapancreatic and extrapancreatic changes, specifically necrosis and fluid collections. This is based on the observation that extrapancreatic changes are associated with different outcomes from those within the pancreas,[9] and not distinguishing the two has been a shortcoming of previous classifications. The new morphological categories assigned by the authors to the early disease period include acute peripancreatic fluid collections (APFC), which do not involve the pancreas proper and contain only fluid without solid

Correspondence to Professor Markus M Lerch
Department of Medicine A, University Medicine Greifswald, Ferdinand-Sauerbruch-Strasse, Greifswald 17475, Germany; lerch@uni-greifswald.de

components. Whether the fluid is mere fluid or pus is now immaterial for the designation. The alternative lesion is called an acute necrotic collection (ANC, previously known as necrosis), which may involve the pancreas and/or the extrapancreatic space, and contains solid components like fat, tissue or clotted blood in addition to fluid. Both collections can be sterile or infected. While a distinction between infected and sterile necrosis remains important, the need for fine needle aspiration to demonstrate bacterial infection is much de-emphasised, since most cases of infected necrosis are now treated conservatively, and the decision whether and when to resort to interventional treatment is mostly based on clinical criteria such as organ failure.

In the late phase beyond the fourth week, the authors propose to distinguish between walled-off necrosis (WON) and pancreatic pseudocyst, of which both are encapsulated by a wall of inflammatory or fibrous tissue,[10] but the latter has no solid components and, according to the authors, neither often arises from acute pancreatitis, nor does it develop from ANC. I beg to differ.

I accept that there may be grounds to suggest that the treatment of pseudocysts with non-fluid material (now WON) may differ from that with fluid-only content, say, when the latter can be stent-drained via the papilla in the presence of a disrupted duct, whereas this procedure may be inadequate in the former containing solid material.[11] However, their pathogenesis may still be identical and involve damage of pancreatic tissue, leakage from major or minor pancreatic ducts in the damaged area, and formation of a fibrous or inflammatory cell capsule around the collection. Another problem is the poor performance of CT, the workhorse of imaging in acute pancreatitis, to properly detect the solid components within the fluid of either ANC or WON. The paper's excellent sample images (the ones you should download for review with your radiologist) provide impressive examples for how much more sensitively MRI detects solid content within fluid collections. In the same patient population, there will be many more WONs and ANCs if the classification is based on magnetic resonance imaging (MRI), endoscopic ultrasound (EUS) or even transabdominal ultrasound, and many more APFC and pseudocysts when assessed by CT unless specific specialist training is undertaken. Future studies will have to clarify to what extent the distinction eventually affects clinical decision making, and how robust interobserver and interimaging-technique agreement really is.

These caveats should not detract from the merits of the new classification, which, by the way, does not address pathogenesis.[12] It integrates recent developments in imaging technology and understanding of disease progression into a new system of classifying severity, defining morphological changes, and reporting patient characteristics. Its recommendations are based on solid clinical studies as much as on expert opinion of the international pancreatitis community. Beyond having a direct effect on patient care, the new classification will contribute to the design of clinical studies in which patients need to be categorised for specific interventions. The revised Atlanta classification will, however, need to undergo validation in prospective trials to determine whether its parameters are applicable and practical, whether they are relevant to meaningful predictions of outcome, and whether they can be used to choose between treatment options. I am confident it will soon be widely used.

Funding The author's work is supported by the Alfried-Krupp-von-Bohlen-und-Hahlbach-Foundation (Graduate Schools Tumor Biology and Free Radical Biology), the Deutsche Krebshilfe/Dr. Mildred-Scheel-Stiftung (109102), the Deutsche Forschungsgemeinschaft (DFG GRK840-E3/E4), the Federal Ministry of Education and Research (BMBF GANI-MED 03152061A, BMBF 0314107) and the European Union (EU-FP-7: EPC-TM and EU-FP-7-REGPOT-2010-1).

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.

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

Gut 2013;**62**:2–3. doi:10.1136/gutjnl-2012-303724

REFERENCES

1. **Peery AF,** Dellon ES, Lund J, *et al*. Burden of gastrointestinal disease in the United States: 2012 update. *Gastroenterology* 2012;**143**:1179–87.
2. **Gülzow M.** On the classification of pancreatitis. *Dtsch Z Verdau Stoffwechselkr* 1966;**26**:3–11.
3. **Singer MV,** Gyr K, Sarles H. Revised classification of pancreatitis. Report of the Second International Symposium on the Classification of Pancreatitis in Marseille, France, March 28–30, 1984. *Gastroenterology* 1985;**89**:683–5.
4. **Bradley EL III**. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. *Arch Surg* 1993;**128**:586–90.
5. **Banks P,** Bollen T, Dervenis C, *et al*. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;**62**:102–11.
6. **Mayerle J,** Simon P, Lerch MM. Medical treatment of acute pancreatitis. *Gastroenterol Clin North Am* 2004;**33**:855–69.
7. **Vege SS,** Gardner TB, Chari ST, *et al*. Low mortality and high morbidity in severe acute pancreatitis without organ failure: a case for revising the Atlanta classification to include "moderately severe acute pancreatitis". *Am J Gastroenterol* 2009;**104**:710–15.
8. **Mayerle J.** A novel role for leucocytes in determining the severity of acute pancreatitis. *Gut* 2009;**58**:1440–1.
9. **Bakker OJ,** van Santvoort H, Besselink MG, *et al*. Extrapancreatic necrosis without pancreatic parenchymal necrosis: a separate entity in necrotising pancreatitis? *Gut* Published Online First: 7 July 2012. doi:10.1136/gutjnl-2012-302870
10. **Gress TM,** Müller-Pillasch F, Lerch MM, *et al*. Balance of expression of genes coding for extracellular matrix proteins and extracellular matrix degrading proteases in chronic pancreatitis. *Z Gastroenterol* 1994;**32**:221–5.
11. **Lerch MM,** Stier A, Wahnschaffe U, *et al*. Pancreatic pseudocysts: observation, endoscopic drainage, or resection? *Dtsch Arztebl Int.* 2009;**106**:614–21.
12. **Lerch MM,** Hernández CA, Adler G. Acute pancreatitis. *N Engl J Med* 1994;**331**:948–9.