Early severity indexes in acute pancreatitis

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Severe acute pancreatitis was defined at the Atlanta symposium (1) as an attack in which a complication occurs, and so severity cannot be determined until the patient has been discharged from hospital and the presence or absence of complications has been documented. However a prediction of severity may be made at the start of the hospital admission, based on a variety of clinical biochemical and radiological features.

Early prediction of severity for individual patients with acute pancreatitis is important for three reasons. First, it is helpful to identify as soon as possible those patients who are most severely ill, who will require aggressive management in the intensive care unit or high dependency area. Second, specific therapy targeted to those patients with severe disease, or predicted severe disease, is becoming a clinical reality. Such therapy should not be offered to patients with mild pancreatitis, who will recover without complications, and who may suffer complications of the treatment offered. There is good evidence to support the use of endoscopic sphincterotomy in patients with gallstones and predicted severe pancreatitis and growing evidence for the use of enteral nutrition in patients with severe disease of any cause (2-8). Selection of these patients for treatment depends on early identification of those at risk of complications. Third, it is helpful when reporting studies of patients with pancreatitis to characterise the group of patients by indicating the numbers who meet criteria of predicted severity at the outset.

Prediction of severity in acute pancreatitis has for many years relied on the pancreatitis specific scores developed in New York by John Ranson (9) and in Glasgow by Clem Imrie (10). These scores allow correct prediction of severity in about 75% of cases, and were designed primarily for the third purpose outlined above, that is they were developed in order to allow comparison of different groups of patients. For an individual patient the classification of 'mild' or 'severe' is not absolute, as 25% of predictions will be incorrect. Furthermore, the complete set of data for these scores is not available until 48hr after admission to hospital, whereas early therapy may be needed before that time.

The clinician must use all available information to detect patients who require general intensive care, and pancreatitis - specific therapies. It is not sufficient to rely on a single measurement or system, as no single test is always accurate.

Clinical assessment is important from the outset, but the initial assessment, although specific, lacks sensitivity. By 48hr after admission, clinical assessment is as accurate as the Glasgow score (11).

APACHE-II score. This was developed as a general intensive care score of severe systemic illness (12), but it performs well as an initial assessment of acute pancreatitis (13). The data collected represent the degree of disturbance of systemic function, so the APACHE-II score in effect is a measure of organ/system failure. For this reason, it correlates well with severity, as all patients with organ failure will have a high score, and by definition have severe pancreatitis. In practice, the APACHE-II score within 24 hr of admission is as good a predictor of severity as the Glasgow score at 48 hr, and so it can be used for early assessment to identify patients who require intervention (13).

An additional feature of the APACHE-II score is the range of values ; this permits variation of the cut-off level for prediction of severity. A low cut-off will allow inclusion of almost all patients with severe disease, a high cut-off is more specific, but less sensitive. For example using a score of > 6 will identify a group of patients with 12% mortality and 62% severe AP (14). The Atlanta criteria recommend a cut-off of > 8 ; our unpublished data suggest that almost all patients who die have a score > 8 and at this cutoff, the APACHE-II score has a sensitivity of 70% and specificity of 78%. In contrast, with a cutoff of > 10, sensitivity falls to 56%, but specificity is 90%.

Patient characteristics. Several studies have shown the increased risk of complications with advancing age (9,10), and in patients who are obese (BMI > 30) (9,15-18). This information is available on admission, and should be used in all severity assessments.

Aetiology of pancreatitis is not a predictive risk factor. Although some authors have reported increased risk in patients with gallstone pancreatitis, and after ERCP, large studies have not confirmed this.

Single tests. The chest radiograph gives useful information about severity : the presence of a pleural effusion is the most reliable sign associated with severe acute

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pancreatitis (19). Plasma C-reactive protein (CRP) indicates an inflammatory response, and is elevated in severe pancreatitis. Values > 150 mg/L are associated with a high risk of complications (4), but these values are rarely achieved less than 48 hr from the onset of symptoms, and peak values occur at about 96 hr. CRP is specific, but not sensitive in the early stages of the disease.

Other markers of the inflammatory response become elevated before CRP. IL8 and IL6 reliably correlate with severity, and neutrophil elastase is the earliest marker, which several authors have found to be accurate. None of these tests is currently available for clinical practice.

Activation peptides of pancreatic enzymes (trypsinogen activation peptide, TAP ; carboxypeptidase activation peptide, CAPAP) are not normally present in the plasma, but are released in amounts that correspond to the extent of the pancreatic injury. Accordingly, both TAP and CAPAP are markers of severity, with the advantage that they are released from the pancreas at a very early stage in the disease. Because they are small molecules, they are filtered by the kidney, and best results for severity prediction are obtained from measurement of urine concentrations (20,21). However, at present there is not a rapid assay for either of these peptides that could be used in clinical practice.

Computed tomography (CT). Dynamic CT within with first 4 days in hospital is reported to identify patients with pancreatic necrosis, or extensive fluid collections (22). Those patients have in effect severe disease, as the CT is showing the presence of a local complication, but they are also at high risk of systemic complications.

Concerns about the use of CT include the difficulty of transport to, and supervision of ill patients in, the radiology department during the examination, and the possible harmful effects of large doses of contrast agent, particularly if renal function is impaired.

Many centres in the UK delay CT until the end of the first week, when the detection of peripancreatic necrosis will prompt intervention such as fine needle aspiration to detect infection, or, when indicated, surgical debridement.

Integrated risk assessment. How can the clinician combine the findings of all these scores and tests to produce a reliable indicator of the risk that a complication will occur in an individual patient ? If only one score or test is used, useful information will be lost. If a large number are used, and any one positive result is accepted as a positive prediction, sensitivity will be high, but specificity will be poor, and many patients will be wrongly classified as severe. If the threshold is set for all or many tests to be positive before a prediction of severe disease is accepted, the predictions will be specific, but many patients with severe disease will not be included because they fail to reach the stringent threshold. The solution is to incorporate several parameters into a logistic calculation which takes account of the various strengths of prediction, and calculates the probability of a severe attack for each patient, based on the findings in that individual.

We have derived a logistic equation from a group of 186 patients with acute pancreatitis. This uses the acute physiology score from APACHE-II, age and obesity to calculate the probability index (PI), or risk of complications, for that individual. The score can be calculated in a few seconds using a hand-held scientific calculator. When applied to a second group of 100 patients, the score predicted individual risks that matched the observed outcome at most levels of risk. The advantage of the PI is that it makes clear the inherent uncertainty of prediction, which may be overlooked when predictions are into categories ('predicted mild' or 'predicted severe'). Further refinement of the PI will include the incorporation of other variables available during the first 24 hr in hospital, such as activation peptides, and the presence of pleural effusion.

Persistent organ failure. The Atlanta criteria (1) defined useful cut-offs for definition of organ failure, but recently these simple yes/no categories have been re-examined, with the appreciation that patients with acute pancreatitis follow a dynamic course, in which outcome depends not only on the presence of organ failure, but also on its timing, severity and duration. These will be affected by the patient's genetic makeup, the duration of symptoms before admission to hospital, and the effectiveness of early treatment. Approximately half the patients with organ failure recover rapidly, within 48 hr. Other complications are rare in these patients (23,24). Patients with persistent organ failure have a high mortality rate (30-50%) (1,23,24). The importance of these observations lies in the possibility that patients with transient organ failure could be excluded from the definition of severe acute pancreatitis, as they will almost certainly have an uncomplicated recovery.

In conclusion, prediction of severity in acute pancreatitis depends on the best use of a range of clinical and biochemical information. It is not sufficient to use one score alone. Clinical information such as age, BMI, and chest X-ray should be taken into account, and best predictions will be made using all these combined with a number of biochemical markers in a logistic equation.

The boundary between prediction and detection of severity is blurred, and perhaps should be removed altogether : patients with persistent organ failure, or CT evidence of local complications can be identified within 3 or 4 days in hospital, and clearly constitute a group that requires aggressive treatment.

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