



Prognostic evaluation of severity of acute pancreatitis: not as black as it is painted

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Acute pancreatitis (AP) is a systemic disease involving acute inflammation of the pancreatic gland due to premature activation of pancreatic proenzymes and different degree of damage to the adjacent tissues and sometimes more distant organs. An increasing trend is observed with the incidence of AP approximately 72 cases/100,000 inhabitants per year (1).

The specific analysis of causes of death from gastrointestinal and liver diseases shows that AP was ranked 14th (2). The complication is associated with mortality rates of 2–10% but in fulminant case is estimated at about 30% (3).

According to revised Atlanta classification the final assessment of the severity of AP is made on the basis of organ failure and local or systemic complications (4). The most important part of early severity prognosis consists of selecting patients at high risk of severe AP (5), which facilitates implementation of early intensive monitoring or better nursing care, and it would facilitate eventual transfer of the patients to pancreatic reference centers and appropriate medical interventions such as nutritional treatment, possibly antibiotic therapy or endoscopic retrograde cholangiopancreatography (ERCP) in some cases, thus improving the treatment results.

Early prognosis of the course of AP has been the subject of numerous clinical trials for several years.

Multifactorial clinical assessment scales, such as bedside index for severity of acute pancreatitis (BISAP), Ranson scale, the systemic inflammatory response syndrome (SIRS) score, APACHE, Glasgow scale and other scales of varied sensitivity and specificity are broadly used (4-6). Among

them, four systems that have received considerable research attention are BISAP, the APACHE II score, contrast-enhanced-computer-tomography (CT)-based scoring systems and SIRS score. Application of those scoring systems in clinical practice has been shown to correlate with an increased risk of severity of AP (4,5).

Two key components of early evaluation are prognostic indicators of severity, those indicating activation of the inflammatory process [e.g., C-reactive protein (CRP), procalcitonin, D-dimer, IL-2, IL-6, IL-8] and those indicating complications in other organs: estimated glomerular filtration rate (eGFR), neutrophil gelatinase-associated lipocalin (NGAL), creatinine, soluble urokinase-type plasminogen activator receptor (suPAR), hematocrit (Ht).

CRP concentrations increase 6 hours after the onset of AP to reach the maximum serum level between 48 and 72 hours of the disorder (2,3). However, it should be highlighted that the time in which the CRP reaches its peak concentration and thus is of the highest prognostic value corresponds to the final stage of the “therapeutic window” in which the AP patient should undergo the most extensive therapeutic procedures (such as fluid resuscitation, fluid balance monitoring, possibly ERCP). This is one of the reasons why subsequent studies are aimed at determination of novel individual prognostic factor. Among other parameters, concentrations of procalcitonin, and D-dimer are useful in predicting the severity of AP in subsequent days.

Prognostic markers available at admission include also blood urea nitrogen (BUN) and Ht. Studies examining admission

They have reached varying conclusions (7), nevertheless some authors showed that hemoconcentration can predict pancreatic necrosis and mortality (8). Knowledge about distortions in water balance of the body in AP and resulting deviations in laboratory research are potentially useful for clinical needs, both diagnostic and therapeutic ones.

Dynamics of changes in serum creatinine and an eGFR level in AP depends on the disease severity and reveals their relation to CRP levels as well as possible usefulness of studied parameters in early prognosis of the AP severity (9).

The level of NGAL measured in urine sample collected upon admission as well as NGAL level measured in a 24-hour urine collection sample was shown to be a sensitive and specific parameter for prognostication of AP course as early as on the first day of the disease. The availability of simple and low-cost parameters, such as the ones generated by many modern haematological analysers, should be considered an important perspective (10).

suPAR measured during the first hours after admission is an excellent parameter for the prediction of the course of AP (11). In the study, the sensitivity and specificity of suPAR in prognosticating the AP treatment outcomes was higher than the BISAP scale, when used in the same study group. The accuracy of suPAR-based prognostication may be explained by the fact that suPAR is not just an inflammatory marker. Increased suPAR levels are also observed in various hypoxic or ischemic conditions, organ injuries and necrosis; this may be decisive for the superiority of this parameter as compared to other prognostic markers.

Immature granulocytes in peripheral blood (IGs)—simple parameter available during the early hours of hospitalization, deserves special attention due to its diagnostic accuracy and easy availability in evaluation of severity in the course of AP (12). Until now only a few studies have used IGs when trying to characterize patients with sepsis and/or SIRS. According to earlier data from our group, the IGs%, a routinely obtained parameter is a simple, independent and a better method to identify patients at risk of SAP than SIRS.

In an observational study entitled “*Serological diagnosis and prognosis of severe acute pancreatitis by analysis of serum glycoprotein 2*”, Roggenbuck *et al.* assessed the usefulness of glycoprotein 2 (GP2) in evaluation of severity in the course of AP (13). The author pointed, that AP onset is characterized by acinar cell injury, resulting in an impaired polarity of proenzyme secretion and basolateral release of zymogen granules (ZGs) contents (13,14). Although the pathophysiology of AP is still not fully understood,

the concept, that premature intra-pancreatic activation of proenzymes, in particular trypsinogen stored in ZGs, plays a pivotal role, is already known from several years. Diagnostic usefulness of enzymes released from ZG as potential serological AP-specific markers, seems to be also clear. Significantly higher levels of GP2 could be detected in serum of AP patients compared to controls (15). However, the data concerning prognostic usefulness of pancreatic ZG enzymes in early stage of AP are still controversial. According to meta-analysis by Huang *et al.*, urinary trypsinogen activation peptide (uTAP) has the potential to act as a stratification marker on admission for differentiating disease severity of AP (16).

The findings of Roggenbuck *et al.*, that GP2 seems to be a superior marker for AP diagnosis, deserves some attention, however in daily clinical praxis, AP is diagnosed as a association of clinical symptoms, medical imaging and laboratory tests such as serum pancreatic amylase and lipase activity. The most interesting tool from the study is that being a sensitive diagnostic parameter, GP2a could also improve early prognosis of the disease.

GP2a as a specific marker for AP can also help in the differentiation with chronic pancreatitis and pancreatic neoplasms. Diagnosis of AP and, in particular, differentiation with other diseases with similar symptoms is still difficult and constitutes a challenge for clinicians (17). Of note is also the fact that one of the most important aims of the analysis was to assess the possibility of using GP2 as a new marker in differential diagnosis acute upper abdominal pain. The results of this study allow for a more reliable review of a complex area of pancreatic disorders. Another interesting finding from the study is also, that GP2a can be useful to predict fatal AP. All those observations should be a topic of additional studies.

Early prognosis in AP, despite several new directions and interesting results of some research, continues to be difficult and extremely challenging for clinicians, especially in the early stage of the disease. Other large, prospective, multicenter studies are still needed to address these questions by identifying AP risk factors and serum biomarkers of severe disease.

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