The Harmless Acute Pancreatitis Score: A Clinical Algorithm for Rapid Initial Stratification of Nonsevere Disease

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This article has an accompanying continuing medical education activity on page 607. Learning Objectives—At the end of this activity the learner should be able to appreciate the potential utility of a simple scoring system for determination of a benign course in acute pancreatitis.

See CME exam on page 607.

Background & Aims: Only severe acute pancreatitis requires treatment, according to the principles of intensive care medicine in an intensive care or intermediate care unit. The aim of the study was to define and evaluate a simple clinical algorithm for rapid initial identification of patients with a first attack of acute pancreatitis who do not require intensive care. Methods: This prospective study included 394 patients who were admitted to the Municipal Clinic of Lüneburg, Germany, between 1987 and 2003. From a number of parameters of disease severity on admission, 3 parameters that showed the strongest prediction of a nonsevere course (no rebound tenderness and/or guarding, normal hematocrit level, and normal serum creatinine level) were combined to form the harmless acute pancreatitis score (HAPS). The score then was validated in a German multicenter study including 452 patients between 2004 and 2006. Results: In both the initial and the validation set, the HAPS correlated with a nonsevere course of the disease (\( P < .0001 \)). The score correctly identified a harmless course in 200 (98%) of 204 patients. Conclusions: The HAPS enables identification, within approximately 30 minutes after admission, of patients with acute pancreatitis whose disease will run a mild course. The high level of accuracy of this test (98%) will allow physicians to identify patients quickly who do not require intensive care, and potentially those who will not require inpatient treatment at all. Thus, the HAPS may save substantial hospital costs.

Severe acute pancreatitis requires intensive treatment according to the principles of intensive care medicine in an intensive or intermediate care unit. On admission, however, it is hard to predict whether the disease will take a mild or a severe course in a given patient.

A lot of scores used to predict severe acute pancreatitis have been developed, but they are insufficiently sensitive, too complicated, too expensive, and not available soon enough or not available at all outside specialized centers.

Therefore, we set out to develop an instrument to identify not the severe, but rather the harmless, cases: the harmless acute pancreatitis score (HAPS).

This article shows the evaluation of this score in an initial and a validation set, both of which were prospective studies; the first was a single-center study, and the second a multicenter investigation.

Patients and Methods

From January 1987 to December 2006 we performed a population-based study on the incidence, etiology, severity, and course of the disease in patients with acute pancreatitis admitted to the Department of General Internal Medicine of the Municipal Clinic of Lüneburg.

Acute pancreatitis was diagnosed on the basis of characteristic signs and symptoms (upper abdominal pain with or without guarding and/or rebound tenderness), increased serum enzyme levels, and abnormal findings on diagnostic imaging (ultrasound and/or contrast-enhanced computed tomography [CT], the latter scored according to Balthazar et al\(^1\)).

The etiology of acute pancreatitis was considered to be biliary if stones were detected in the gallbladder and/or common bile duct and of alcoholic etiology if the patient or his/her relatives reported consumption of more than 60 g pure alcohol/day. Other identified causes were endoscopic procedures (endoscopic retrograde cholangiopancreatography with or without sphincterotomy), hyperlipidemia, trauma, Salmonella infections, and drugs.\(^2\) In the remaining cases the etiology was classified as unknown or idiopathic.

In all patients the following parameters of severity were estimated when indicated:

On admission: time between onset of symptoms and admission; signs of peritonitis (ie, either rebound tenderness [pain after slowly pressing on the abdomen and then suddenly releasing the pressure] or guarding [contraction and tensing of the...

Abbreviations used in this paper: APACHE II, Acute Physiology and Chronic Health Evaluation II; CT, computed tomography; HAPS, harmless acute pancreatitis score; SOFA, Sequential Organ Failure Assessment.

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abdominal wall muscles in response to palpation); hematocrit level (abnormal, >43% for men or >39.6% for women); blood glucose level (abnormal, >125 mg/dL); arterial pO2 (abnormal, PO2 ≤ 60 mm Hg); serum creatinine level (abnormal, ≥ 2 mg/dL); and Acute Physiology and Chronic Health Evaluation II (APACHE II) score.3

After 48 hours: Ranson score 6,5 (adjusted for etiology) and Imrie score.6 Within 96 hours: contrast-enhanced CT, scored according to Balthazar et al.1

Outcome parameters: indication for artificial ventilation, dialysis, and/or necrosectomy; severe course: presence of necrosis as assessed by contrast-enhanced CT (Balthazar score, ≥ 5 points), the need for artificial ventilation or dialysis; nonevose (harmless) course: no necrosis (Balthazar score, 0 – 4), no need for artificial ventilation or dialysis at any time of hospital stay or death; and mortality.

**Initial Set**

From January 1987 to December 2003, there were 394 patients with a first attack of acute pancreatitis who were admitted. The severity was stratified according to the selected baseline parameters (Table 1). Of the baseline characteristics recorded for all 394 patients, absence of rebound tenderness/guarding and normal serum creatinine level were the strongest predictors of lack of severity (P < .0001). However, 23 of the 251 patients with no signs of peritonitis and normal serum creatinine level had a severe course. Among these 251 patients, increased hematocrit level (defined as > 43.0% for men and > 39.6% for women) was associated strongly with severity (21 of 152 patients [14%] with an increased hematocrit level had a severe course, compared with 2 of 99 patients [2%] with a normal hematocrit value; P = .001).

Therefore, these 3 parameters (absence of rebound tenderness/guarding, normal serum creatinine level, and normal hematocrit level) were combined to form the HAPS (ie, a harmless course of the disease seemed to be predictable when signs of peritonitis were absent and serum creatinine and hematocrit levels were normal).

### Table 1. Severity of a First Attack of Acute Pancreatitis in 394 Patients Admitted to the Department of General Internal Medicine of the Municipal Clinic Lüneburg, Germany

<table>
<thead>
<tr>
<th>Admission parameters</th>
<th>Patients</th>
<th>Severe course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebound tenderness and/or guarding Serum creatinine level</td>
<td>143</td>
<td>46 (32%)</td>
</tr>
<tr>
<td>≤ 2 mg/dL</td>
<td>132</td>
<td>38 (29%)</td>
</tr>
<tr>
<td>&gt; 2 mg/dL</td>
<td>11</td>
<td>8 (73%)</td>
</tr>
<tr>
<td>Hematocrit level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>47</td>
<td>15 (32%)</td>
</tr>
<tr>
<td>Increased</td>
<td>96</td>
<td>31 (32%)</td>
</tr>
<tr>
<td>No rebound tenderness/no guarding Serum creatinine level</td>
<td>251</td>
<td>23 (9%)</td>
</tr>
<tr>
<td>≤ 2 mg/dL</td>
<td>240</td>
<td>22 (10%)</td>
</tr>
<tr>
<td>&gt; 2 mg/dL</td>
<td>11</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Hematocrit level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>99</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Increased</td>
<td>152</td>
<td>21 (14%)</td>
</tr>
</tbody>
</table>

In accordance with the definition of a severe course, a harmless course was defined as the absence of pancreatic necrosis (Balthazar score, 0–4 points), no need for dialysis or artificial ventilation, and no fatal outcome.

**Validation Set**

After evaluation of the HAPS in the initial set, a validation set was started in the form of a German multicenter study together with members of the Joint Working Group of Senior Hospital Gastroenterologists (Arbeitsgemeinschaft Leitender Gastroenterologischer Krankenhausärzte). This study was performed between January 2004 and December 2006 and comprised 452 patients (including 85 patients from Lüneburg) with a first attack of acute pancreatitis. Contrast-enhanced CT scored according to Balthazar et al 1 was a precondition for inclusion in this study.

**Statistical Analysis**

The chi-square test and the Fisher exact test were used to compare the distribution of patients’ characteristics in the initial and in the validation sets. The diagnostic accuracy of the HAPS scoring system was evaluated by sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy. Data were analyzed using SAS (version 8.2; SAS Institute Inc, Cary, NC); all significance tests were 2-sided.

**Results**

Stratification according to etiology of the patients of the initial and the validation sets showed a statistically significant difference between the 2 groups (Table 2). The difference mainly was owing to a lower proportion of patients with biliary etiology and a higher incidence of idiopathic etiology in the initial set than in the validation set.

The incidences of pancreatic necrosis, of indication for dialysis, of a severe course (and thus of a nonevose course) of the disease, and of fatal outcome were about the same in both sets (Table 3). The proportion of patients needing artificial ventila-
tion was higher in the validation set. In the initial and in the validation sets the HAPS predicted a harmless course in 94 and 106 patients, respectively (Table 4). Taking both sets together, a severe course of the disease was observed in only 4 of 204 (2%) patients whose pancreatitis was classified as harmless. In 2 patients from the initial set and in 1 patient from the validation set, the clinical condition deteriorated and for a short time contrast-enhanced CT showed small but definite areas of necrosis (Balthazar score, 6 points).

In the fourth patient, from the validation set, the acute pancreatitis healed without complications, but the patient died of methicillin-resistant *Staphylococcus aureus* pneumonia contracted during his hospital stay. Although the cause of death was unconnected with the pancreas, he was assigned to the not-harmless group because the fatal infection was acquired during his hospital stay for pancreatitis treatment.

Sensitivity, specificity, positive predictive value, and negative predictive value were about the same for both parts of the study. In both sets of patients the HAPS showed the same high specificity (97%) and positive predictive value (98%) (Table 5).

**Discussion**

Dozens of articles have reported over the past 3 decades on a wide variety of clinical parameters, single biochemical markers, scoring systems, and imaging procedures for predicting severe acute pancreatitis. Most of these parameters have found no place in clinical routine because of either low reliability or high complexity. The etiology of the disease has no influence on its course and outcome. Advanced age is associated with a higher mortality rate. However, in an earlier study that also analyzed a previous investigation on this topic, we showed that an increase in mortality with age was found only for patients with biliary pancreatitis. Because we were interested in establishing a score for pancreatitis of all etiologies, we therefore dispensed with age as a factor.

Of the signs on physical examination, fever, a palpable abdominal mass, a paralytic ileus, and skin signs have all been related to severe pancreatitis.

A chest radiograph may show pleural effusion and pulmonary infiltrates, both being strong signs of severe disease. However, none of the earlier-mentioned parameters per se is accurate enough to predict severe pancreatitis.

Contrast-enhanced CT is the most useful of the imaging modalities. It is an excellent procedure to determine the extent of organ destruction. However, that says nothing about the overall course of the illness. Organ failure and organ destruction do not run parallel in acute pancreatitis.

Among single biochemical parameters, the most widely used is C-reactive protein as an indicator for necrosis. However, the problem with this parameter is that directly after admission to the hospital patients with the interstitial and necrotizing forms of pancreatitis show a distinct overlap; the highest values are only attained 96 hours after the onset of symptoms. Useful evaluation of the C-reactive protein value thus requires knowledge of when the symptoms began, which in patients with alcohol-induced pancreatitis often is hard to establish.

Other single biochemical markers, such as methemalbumin; markers of protease activation (eg, urinary trypsinogen activation peptide, procarboxypeptidase activation peptide, and phospholipase A2 activation peptide); and markers of inflammatory response, such as granulocytes (polymorphonuclear leukocyte), elastase, tumor necrosis factor, and interleukin-1, interleukin-6, and interleukin-8, have displayed a high prognostic value for the course of acute pancreatitis in isolated studies. Their determination is so complicated, however, that they have not assumed a role in routine clinical practice.

The Atlanta criteria for clinical classification of acute pancreatitis are used worldwide. However, these criteria do not differentiate between transient and persistent organ failure. The former has a good prognosis, the latter has a poor prognosis. The Atlanta criteria thus could not be used for our analysis. For this reason, we chose to define a severe course purely by the presence of persistent organ failure necessitating artificial ventilation and/or dialysis.

The multiple-factor scoring systems developed specifically for predicting the course of acute pancreatitis by Ranson et al and Imrie have proved their worth in numerous studies. These systems yield a score only after 48 hours, however, and a lot can happen in this time.

The APACHE II score, and more recently the Marshall score and the Sequential Organ Failure Assessment (SOFA) score have been used to evaluate the severity of diseases treated in intensive care units. However, these scores are also too complicated and have not been evaluated fully in acute pancreatitis, so that again they have not found wide acceptance.

All in all, there is no genuinely satisfactory parameter by which the attending physician can recognize that a patient admitted with acute pancreatitis will experience a severe disease course. However, only 10% to 15% of cases turn out to be severe (ie, the vast majority of patients will have a mild course). In this unsatisfactory situation, it seemed to us more important to identify the mild cases of acute pancreatitis.

**Table 4. Evaluation of the HAPS in Predicting a Nonsevere Course of Acute Pancreatitis**

<table>
<thead>
<tr>
<th>Study</th>
<th>Predicted course</th>
<th>Nonsevere course</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial set (N = 394)</td>
<td>Harmless</td>
<td>Yes</td>
<td>94</td>
<td>231</td>
<td>98% (92%–100%)</td>
<td>22% (18%–28%)</td>
</tr>
<tr>
<td></td>
<td>Not harmless</td>
<td>No</td>
<td>278</td>
<td>67</td>
<td>98% (92%–100%)</td>
<td>22% (18%–28%)</td>
</tr>
<tr>
<td>Validation set (N = 452)</td>
<td>Harmless</td>
<td>Yes</td>
<td>106</td>
<td>2</td>
<td>98% (92%–100%)</td>
<td>22% (18%–28%)</td>
</tr>
<tr>
<td></td>
<td>Not harmless</td>
<td>No</td>
<td>278</td>
<td>63</td>
<td>98% (92%–100%)</td>
<td>22% (18%–28%)</td>
</tr>
</tbody>
</table>

**Table 5. Evaluation of the HAPS Predicting a Nonsevere Course of Acute Pancreatitis**

<table>
<thead>
<tr>
<th></th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial set (N = 394)</td>
<td>97% (89%–99%)</td>
<td>29% (24%–34%)</td>
<td>98% (92%–100%)</td>
<td>22% (18%–28%)</td>
</tr>
<tr>
<td>Validation set (N = 452)</td>
<td>97% (88%–99%)</td>
<td>28% (23%–32%)</td>
<td>98% (93%–100%)</td>
<td>18% (15%–23%)</td>
</tr>
</tbody>
</table>
Experienced physicians claim they can identify a mild case of acute pancreatitis on the basis of clinical experience, but this does not apply during the first 24 hours. Furthermore, severe cases of acute pancreatitis present themselves at night, during the weekend, and on public holidays, when junior doctors are more likely on duty. They have to make an instant decision and want to be sure they are not unnecessarily giving away what may well be the last intensive care unit bed, but hesitate to disturb their senior attending physicians at an inconvenient time.

The HAPS, a scoring system for nonsevere acute pancreatitis that we have developed, is easy to perform. A physical examination of a patient with acute pancreatitis takes only minutes to find out whether he or she has rebound tenderness and/or guarding. Hematocrit and serum creatinine levels are laboratory investigations that are available in every hospital at all times of day and night and the findings are reported in approximately 30 minutes. Altogether, then, the HAPS yields a result in about half an hour.

In our initial set we showed prospectively that with the help of this score the attending physician of our hospital, regardless of his experience and duration of clinical training, confidently could identify the patients whose acute pancreatitis would run a mild course.

Single-center studies have the disadvantage that they usually are conducted by a highly motivated researcher. Thus, the findings may be more positive than they would be in reality. For this reason we validated the test in a prospective multicenter study in Germany, where the same findings were made by attending physicians of similar experience and training.

On the basis of these prospectively performed single and multicenter studies (initial and validation sets) we can state that the HAPS decides with great accuracy which patients’ acute pancreatitis will run a mild course or who will have only interstitial pancreatitis, with no need for artificial ventilation and dialysis (ie, those who are not in danger of dying of the disease). Moreover, the score helps to decide which patients do not require intensive management and therapy and expensive imaging procedures, such as contrast-enhanced CT.

In times when many medical decisions are legally contested by patients and their relatives, the HAPS offers the responsible physician a secure basis for the decision of whether to transfer a given patient to a general ward rather than the intensive care unit or intermediate unit.

The HAPS thus not only lends confidence in clinical decision making, but also saves substantial hospital costs.

In the near future, given good cooperation between the family doctor and the hospital, the HAPS may be able to detect those patients who do not require inpatient treatment at all, with potentially enormous cost savings.

References

Reprint requests
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Conflicts of interest
The authors disclose no conflicts.