Severe Acute Pancreatitis Requiring Drainage Therapy: Findings on Computed Tomography as Predictor of Patient Outcome

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Key Words
Severe acute pancreatitis • Computed tomography • Morphologic features • Prognosis assessment

Abstract

\textbf{Background/Aims:} To evaluate whether morphologic features on computed tomography (CT) correlate with outcome of patients with severe acute pancreatitis (SAP). \textbf{Methods:} 80 patients with SAP requiring percutaneous drainage therapy were retrospectively analyzed. Twelve CT features beyond the CT severity index (CTSI) were studied. Endpoints for patient outcome were patient death, length of hospital and ICU stay. The twelve features and the CTSI score were correlated with mortality using Kaplan-Meier estimator and correlated with length of hospital and ICU stay using the \(\chi^2\) test. A \(p\) value \(\leq 0.05\) was considered statistically significant. \textbf{Results:} Two CT features exhibited a significant correlation with mortality: (1) the number of parts of pancreas (head, corpus, tail) that exhibited areas of necrosis and (2) the presence of distant fluid collections (posterior pararenal space and/or paracolic gutter). Mortality was 42\% (21 of 50 patients) and 20\% (6 of 30 patients) if two/all three parts or none/one part of the pancreas exhibited necrosis, respectively. Mortality was 46\% (18 of 39 patients) and 22\% (9 of 41 patients) if distant fluid collections were present or absent, respectively. All other imaging features including the CTSI showed no significant correlation with patient outcome. \textbf{Conclusion:} We identified two morphologic features on CT that might be helpful to predict prognosis of patients suffering from SAP.

Introduction

The course of acute pancreatitis (AP) ranges from a mild transitory edematous to a severe necrotizing form. Severe acute pancreatitis (SAP) with necrosis of the pancreatic or peripancreatic tissue exhibits two phases [1]: In the first phase, pancreatic inflammation and necrosis are associated with systemic inflammatory response syndrome that may lead to multiple organ failure. The second phase usually beginning in the third week after symptom onset is dominated by infection of the necrotic tissue with possible progression to overt sepsis and septic multiple organ failure [2]. Mortality due to SAP ranges between 5 and 70\% [3–6].

Over the past two decades, advances in intensive care as well as surgical and interventional management have resulted in a significant reduction of morbidity and mortality [2, 7]. The improved outcome is based on early identification of patients at risk and subsequent aggressive pa-
tient monitoring and treatment [1]. Hence, rapid and reliable assessment of prognosis is essential, which includes (1) stratification of patients with AP to identify those with edematous versus those with evidence of or predicted SAP (early risk stratification), and (2) further stratification of patients with SAP into a low- and high-risk group (delayed risk stratification of patients with SAP).

To assess prognosis, various clinical, laboratory- and imaging-based scoring systems have been developed [2, 8, 9]. For example, the imaging-based computed tomography (CT) severity index (CTSI) quantifies the extent of inflammation and necrosis of the pancreas as well as the presence of peripancreatic inflammation and fluid collections. In several studies the CTSI was helpful in predicting the outcome of patients with AP [5, 8, 10–14].

In a recent study at our institution, we analyzed 80 patients with SAP requiring percutaneous drainage therapy. The CTSI did not correlate with mortality in this severely ill patient group [15]. Hence, the purpose of the present study was to evaluate whether there are morphologic features on CT which correlate better with outcome of this subgroup of patients suffering from SAP.

Patients and Methods

Patient Characteristics

This retrospective study was performed at a university hospital that is a regional tertiary referral center for pancreatitis. By searching the radiological, surgical and internal medicine databases, all patients with the diagnosis of AP treated with percutaneous drainage placement between 1992 and 2004 were identified. 80 patients (26 women and 54 men, aged 17–79 years, median 57 years) fulfilled the inclusion criteria and were included in the study. The majority of patients (71 of 80 patients, 89%) were transferred from other hospitals where they had been hospitalized before for a median period of 7 days. The first drainage was placed at a median period of 3.5 days after admission to our hospital. Hence, the median time interval between admission to hospital and performance of index CT was approximately 10.5 days.

The etiology of pancreatitis was alcohol abuse (32 of 80 patients, 40%), biliary (26 of 80 patients, 33%) and others (22 of 80 patients, 27%). Details of patient characteristics are published elsewhere [15]. According to the definitions of the Atlanta Classification of Acute Pancreatitis, all 80 patients suffered from SAP [16, 17]. 73 patients presented with necrosis of the pancreatic parenchyma itself and 7 patients demonstrated extensive peripancreatic fluid collections with presumed necrosis of the peripancreatic fat.

52 patients (65%) had microbiologically proven infection of the necrotic tissue with the need for drainage therapy. In 28 patients (35%) culture was negative. Drainage therapy was performed in this group as well, because the clinical, laboratory and radiological findings strongly suggested infection. In addition to drainage therapy, surgical and percutaneous necrosectomy [18] were performed in 20 and 18 patients, respectively. 65 patients (81%) were referred to the intensive care unit (ICU). All patients received antibiotic therapy.

Computed Tomography

All examinations were performed on helical CT scanners (Somatom Plus S, Somatom Plus 4, or Somatom Sensation 16; Siemens Medical Solutions). For opacification of the digestive tract, 2,000 ml of positive contrast agent was administered orally. 150 ml non-ionic contrast material (300 mg iodine/ml; iopromide (Ultravist®); Bayer Schering Pharma or iomepil (Imeron®); Bracco Altana Pharma) was power injected intravenously at a rate of 3 ml/s in all patients. Portal venous phase scans of the abdomen were acquired in the cranio-caudal direction (reconstructed slice thickness in axial plane, 5 mm).

The CT examination at the time of first drainage placement (index CT) was reviewed by two board-certified radiologists (H.P. and O.W.H. with 7 and 11 years of experience in body imaging, respectively) in a consensus decision unaware of patient outcome. The data of the CTSI and the Balthazar score [19] of the study population have been published elsewhere [15]. In the present study the modified CTSI [10] as well as twelve morphologic alterations on CT beyond the CTSI were chosen to be studied, because either a correlation of these alterations and patient outcome has been described in previous studies or we assumed that these alterations might show a correlation with patient outcome. The following features on contrast-enhanced CT were analyzed:

(1) Extent of pancreatic necrosis was determined according to the CTSI necrosis score [14, 16]. Areas of pancreatic parenchyma that exhibited non-enhancement on contrast-enhanced CT were considered to represent necrosis. The extent of pancreatic necrosis was graded with 0 points (0% necrosis), 2 points (0–30% necrosis of the pancreatic tissue), 4 points (30–50% necrosis) and 6 points (>50% necrosis) [14, 16].

(2) Distribution of pancreatic necrosis was evaluated. Two parallel lines were drawn on CT down both sides of the spine to divide the pancreas into head (to the right of right paraspinal line), body (between the paraspinal lines), and tail (to the left of the left paraspinal line) [20]. The head, the corpus and the tail of the pancreas were separately analyzed for presence of necrosis. The number of parts of pancreas that exhibited areas of necrosis was determined (graduation: 0 part (no pancreatic necrosis) to 3 parts (necrosis in all three parts of the pancreas)).

(3) Presence of necrosis in the head of the pancreas [21].

(4) Inflammation of the peripancreatic fat as evidenced by streaky increased density.

(5) Ten specific localizations were analyzed for the presence of fluid collections: pancreatic parenchyma itself, bursa omentalis, mesenteric root, transverse mesocolon, right and left paracolic gutter, and anterior and posterior pararenal space to the right and left. The number of localizations with fluid collections was determined.

(6) Fluid collections in the paracolic gutter and posterior pararenal space to the right and left were defined as distant fluid collections. The presence of distant fluid collections was evaluated.

(7) Presence or suspicion of solid material/debris within the fluid collections was determined.

(8) Presence of gas bubbles within the fluid collections was determined.
The large peripancreatic veins (superior mesenteric, splenic and portal vein) were analyzed for thrombotic occlusion or stenosis of more than 50% in diameter. Involvement of any of the three veins was considered a positive finding [22, 23].

The superior mesenteric artery was analyzed for occlusion or stenosis [10]. Occlusion or stenosis of more than 50% in diameter was considered a positive finding.

Presence of right-sided pleural effusion was determined [10].

Presence of left-sided pleural effusion was determined [10].

Ranson Score
The pancreatitis-specific clinical Ranson criteria were evaluated on admission [15, 24].

Outcome Parameters
Endpoints for patient outcome were defined as patient death, length of hospital and length of eventual ICU stay. All patients were observed until day 250 or censored at the last day of observation. Survival time was defined as interval between the date AP was diagnosed and patient’s death, censored to day 160. The overall in-hospital mortality was 34% (27 of 80 patients; 24 of 27 patients (89%) died due to septic multiple organ failure, 1 patient each died due to pulmonary embolism, cerebral hemorrhage and complications due to polytrauma). Median length of hospital and ICU stay was 51 days (range 3–241) and 22 days (range 2–104), respectively.

Statistical Analysis
The analyzed morphologic features on contrast-enhanced CT, the modified CTSI and the Ranson score were correlated with mortality using Kaplan-Meier estimator (log-rank test) and correlated with length of hospital and ICU stay using Pearson’s \( \chi^2 \) test. The statistical analysis was made with the SPSS 12.0 statistical software (SPSS Inc., Chicago, Ill., USA). Values are given as total numbers, median with range or as percentages where necessary. A p value \( \leq 0.05 \) was considered statistically significant.

Table 1. Median (range)/frequency of the CTSI, the modified CTSI, the Balthazar score and twelve morphologic CT features as well as their statistical correlation with mortality as well as length of hospital and ICU stay

<table>
<thead>
<tr>
<th>Morphologic feature/score</th>
<th>Median (range)/frequency</th>
<th>p value ( ^a )</th>
<th>hospital stay ( ^b )</th>
<th>ICU stay ( ^b )</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT severity index</td>
<td>median 6; range 4–10 ( ^c )</td>
<td>0.66</td>
<td>0.28</td>
<td>0.49</td>
</tr>
<tr>
<td>Modified CTSI</td>
<td>median 8; range 4–10</td>
<td>0.11</td>
<td>0.25</td>
<td>0.83</td>
</tr>
<tr>
<td>Balthazar score</td>
<td>median 4 ( ^d ); score was 3 and 4 in 3 and 77 patients, respectively</td>
<td>( ^d )</td>
<td>( ^d )</td>
<td>( ^d )</td>
</tr>
<tr>
<td>CTSI necrosis score</td>
<td>median 2; range 0–6</td>
<td>0.51</td>
<td>0.71</td>
<td>0.69</td>
</tr>
<tr>
<td>Number of parts of the pancreas (head, corpus, tail) that exhibited necrosis</td>
<td>median 2; range 0–3</td>
<td>0.05</td>
<td>0.35</td>
<td>0.27</td>
</tr>
<tr>
<td>Necrosis of the pancreatic head</td>
<td>68% (54 of 80 patients)</td>
<td>0.82</td>
<td>0.45</td>
<td>0.56</td>
</tr>
<tr>
<td>Inflammation of peripancreatic fat</td>
<td>99% (79 of 80 patients)</td>
<td>( ^d )</td>
<td>( ^d )</td>
<td>( ^d )</td>
</tr>
<tr>
<td>Number of fluid collections</td>
<td>median 4, range 1–10</td>
<td>0.16</td>
<td>0.66</td>
<td>0.92</td>
</tr>
<tr>
<td>Presence of distant fluid collections</td>
<td>median 49% (39 of 80 patients)</td>
<td>0.01</td>
<td>0.29</td>
<td>0.49</td>
</tr>
<tr>
<td>Paracolic gutter right</td>
<td>33% (26 of 80 patients)</td>
<td>0.17</td>
<td>np</td>
<td>np</td>
</tr>
<tr>
<td>Paracolic gutter left</td>
<td>29% (23 of 80 patients)</td>
<td>0.17</td>
<td>np</td>
<td>np</td>
</tr>
<tr>
<td>Posterior pararenal space right</td>
<td>14% (11 of 80 patients)</td>
<td>0.72</td>
<td>np</td>
<td>np</td>
</tr>
<tr>
<td>Posterior pararenal space left</td>
<td>10% (8 of 80 patients)</td>
<td>0.03</td>
<td>np</td>
<td>np</td>
</tr>
<tr>
<td>Presence or suspicion of debris within fluid collections</td>
<td>13% (10 of 80 patients)</td>
<td>0.80</td>
<td>0.37</td>
<td>( ^d )</td>
</tr>
<tr>
<td>Gas bubbles within fluid collections</td>
<td>15% (12 of 80 patients)</td>
<td>0.79</td>
<td>0.47</td>
<td>0.38</td>
</tr>
<tr>
<td>Patency of veins</td>
<td>50% (40 of 80 patients)</td>
<td>0.16</td>
<td>0.25</td>
<td>0.56</td>
</tr>
<tr>
<td>Patency of superior mesenteric artery</td>
<td>100% (80 of 80 patients)</td>
<td>( ^d )</td>
<td>( ^d )</td>
<td>( ^d )</td>
</tr>
<tr>
<td>Pleural effusion to the right</td>
<td>59% (47 of 80 patients)</td>
<td>0.66</td>
<td>0.40</td>
<td>0.43</td>
</tr>
<tr>
<td>Pleural effusion to the left</td>
<td>69% (55 of 80 patients)</td>
<td>0.90</td>
<td>0.23</td>
<td>0.82</td>
</tr>
</tbody>
</table>

\( ^a \) The p value for comparison of patient subgroups was calculated by Kaplan-Meier estimator and log-rank test.

\( ^b \) The p value for comparison of patient subgroups was calculated by Pearson’s \( \chi^2 \) test.

\( ^c \) Published in Bruennler et al. [15].

\( ^d \) Statistical analysis was not performed, because the size of subgroups was \( \leq 6 \) patients (in this setting statistical analysis was considered to be meaningless [25]). np = Statistical analysis was not performed because presence of distant fluid collections in general did not correlate with hospital and ICU stay.
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Results

The study population consisted of 80 patients with SAP that required percutaneous drainage therapy. As reported before, the CTSI did not correlate with mortality in this patient group \cite{15, 19}. Further analysis was performed in the present study revealing no significant correlation between the CTSI and length of hospital and ICU stay (table 1). In addition, the modified CTSI was determined which also did not correlate with patient outcome. To note, extrapancreatic complications (e.g. pleural effusion, vascular complications) which are a major constituent of the modified CTSI were present in the majority of patients (75 of 80 patients, 94%; table 1).

Beyond the CTSI, we analyzed twelve morphologic features on CT and evaluated them as possible predictors of patient outcome. In table 1, the frequency of each feature and the statistic relationship between the alteration and the endpoints of patient outcome are given. Two parameters showed a significant correlation with patient outcome:

First, the number of parts of the pancreas that exhibited areas of necrosis correlated with mortality ($p = 0.05$). Mortality was 42% (21 of 50 patients) and 20% (6 of 30 patients) if two/all three parts or none/one part of the pancreas exhibited necrosis, respectively (table 2). The subgroups of patients that exhibited necrosis of one, two or all three parts of the pancreas were further analyzed. The subgroup of patients without pancreatic necrosis consisted of only 7 patients and was therefore not included in this subgroup analysis. It was found that mortality was significantly higher in patients who exhibited necrosis in two or all three parts of the pancreas compared with patients who exhibited necrosis in only one part. Comparison of mortality between the subgroup of patients that exhibited necrosis of two parts versus those patients with necrosis in all three parts did not show a statistically significant difference (fig. 1–3).

Second, mortality was significantly higher if distant fluid collections were present ($p = 0.01$). Mortality was 46% (18 of 39 patients) and 22% (9 of 41 patients) if distant fluid collections were present or absent, respectively (fig. 4–6). It was thought to be of interest whether there was a location of distant fluid collections that was on its own associated with increased mortality. Therefore, the statistic relationship between the presence of fluid collections in the four distant sites each and mortality was calculated. It was found that presence of fluid collections in the posterior pararenal space to the left was significantly associated with mortality ($p = 0.03$). Mortality was 63% (5 of 8 patients) and 31% (22 of 72 patients) if a fluid collection at the posterior pararenal space to the left was present or absent, respectively (fig. 7). All other analyzed morphologic features on CT showed no significant correlation with patient outcome (table 1).

Taking these findings into account, we introduced a new CT score which was evaluated. Presence of necrosis in two or three parts of the pancreas and presence of dis-

\begin{table}[h]
\centering
\caption{Frequency of patients that exhibited areas of necrosis of none, 1, 2 or all 3 parts of the pancreas (head, corpus, tail) as well as mortality of each subgroup}
\begin{tabular}{|l|l|l|}
\hline
Parts of the pancreas that exhibited areas of necrosis, n & Frequency & Mortality \\
\hline
0 part & 9% (7 of 80 patients) & 43% (3 of 7 patients) \\
1 part & 29% (23 of 80 patients) & 13% (3 of 23 patients) \\
2 parts & 23% (18 of 80 patients) & 50% (9 of 18 patients) \\
All 3 parts & 40% (32 of 80 patients) & 38% (12 of 32 patients) \\
\hline
\end{tabular}
\end{table}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Kaplan-Meier plot of survival times of patients who exhibited necrosis of 1, 2 or all 3 parts of the pancreas. The $p$ value for comparison of patient subgroups that exhibited necrosis of 1 and 2 parts, 1 and 3 parts, and 2 and 3 parts of the pancreas was 0.01, 0.05 and 0.21, respectively (log-rank test). The subgroup of patients that exhibited no necrosis of the pancreas consisted of only 7 patients and was therefore not included in the statistic analysis of subgroups and not included in this figure for the sake of clarity.}
\end{figure}
tant fluid collections was assigned 1 point each. The score was calculated by adding the value (0 or 1 point) of both variables ($\chi^2$ test of both variables revealed a $p$ value of 0.69, indicating that variables were independent). The score showed a significant correlation with mortality ($p = 0.004$). Compared with patients with score 0, mortality was two- and fourfold higher in patients with score 1 and 2, respectively (fig. 8).

The Ranson score (median score 2; range 0–4) showed a significant correlation with mortality ($p = 0.04$) and duration of hospital stay ($p = 0.007$) but not with duration of ICU stay ($p = 0.08$).

**Discussion**

In previous studies the CTSI was determined (1) in patient populations that covered the entire range of disease severity from mild over moderate to severe pancreatitis [5, 8, 10–14], and (2) in the early phase of AP [10, 14]. In these patient populations the CTSI proved to be helpful to predict patient outcome.
**Fig. 5.** A 38-year-old man with AP. Transverse contrast-enhanced CT image demonstrates fluid collections within the anterior (A) and posterior (P) pararenal space as well as paracolic gutter (G) to the left (the descending colon is marked with C). Perihepatic ascites is noted (arrows).

**Fig. 6.** A 54-year-old man with AP. Transverse contrast-enhanced CT image depicts a fluid collection (F) at the paracolic gutter to the right (the ascending colon is marked with C).

**Fig. 7.** Kaplan-Meier plot of survival times of patients with or without fluid collections in the posterior pararenal space to the left (8 and 72 patients, respectively). Mortality was 63% (5 of 8 patients) and 31% (22 of 72 patients) if a fluid collection at the posterior pararenal space to the left was present or absent, respectively. The p value for comparison of both subgroups was 0.03 (log-rank test).

**Fig. 8.** Kaplan-Meier plot of survival times of patients who exhibited score 0, 1 or 2. The score showed a significant correlation with mortality (p = 0.004; log-rank test). The p value for comparison of patient subgroups who exhibited score 0 and 1, 0 and 2, and 1 and 2 was 0.29, 0.006 and 0.009, respectively (log-rank test).
In the present survey the characteristics of the study population were different: (1) Patients exclusively with SAP requiring drainage therapy were analyzed. (2) The index CT was performed at a later stage of disease (second phase of SAP), because (a) the median time interval between admission to hospital and performance of CT was approximately 10.5 days and (b) infection of necrotic tissue was proven or suspected in all patients. This study population represents the characteristics a tertial referral center has to deal with. In this severely ill patient group the CTSI as well as the modified CTSI showed no statistically significant relationship with the endpoints for patient outcome (table 1) [10, 15]. In addition, Mortele et al. [10] reported that the CTSI determined in the early phase of AP showed no significant correlation with the length of hospital stay when comparing patients with moderate pancreatitis with those with severe pancreatitis. According to the results of Mortele et al. [10] and our results, the CTSI does not seem to be helpful in predicting the outcome in the subgroup of patients with SAP.

Hence, the purpose of the present study was to evaluate whether there are morphologic features on CT that better correlate with outcome of our study population. We analyzed twelve different imaging features and identified two that correlated with outcome (table 1).

First, the number of parts of the pancreas that exhibited necrosis correlated with mortality. Mortality was significantly higher in patients who exhibited necrosis in two or all three parts of the pancreas compared with patients who exhibited necrosis in one part of the pancreas (fig. 1). In other words, in our study population, mortality was related to the distribution but not the percentage of pancreatic parenchymal necrosis (the latter is part of the CTSI necrosis score; table 1). The reason for this relationship can only be suspected. We hypothesize that if more parts of the pancreas exhibit areas of necrosis, there is a larger interface between vital pancreatic juice producing parenchyma and areas of necrosis which might result in an increased release of pancreatic juice to the adjacent tissue and consecutive pronounced inflammatory response.

To note, the second highest mortality occurred in patients without pancreatic necrosis but presumed necrosis of the peripancreatic fat, indicating that these patients are at increased risk; however, this subgroup comprehended only 7 patients and therefore no definite conclusions can be drawn.

Second, the presence of distant fluid collections and, in particular, the presence of fluid collections in the posterior pararenal space to the left was correlated with higher mortality (fig. 4, 7). Presumably, the presence of distant fluid collections indicates a more severe form of pancreatitis which is per se associated with increased mortality.

The remaining ten morphologic features analyzed on CT showed no significant correlation with patient outcome (table 1). In contrast to findings of other surveys, in our study population there was no significant correlation between necrosis of the pancreatic head [21] or presence of pleural effusions [10] and patient outcome.

Beyond morphologic features on CT, clinical and laboratory-based multiple factor scoring systems were determined in our study population. As reported before, the general ICU scores APACHE II and SAPS II correlated well with patient outcome [15]. In addition, the pancreatitis-specific clinical Ranson score showed a significant correlation with mortality and length of hospital stay. Hence, clinical and laboratory-based scoring systems were helpful in our study population and correlated significantly with outcome; however, their complexity limits routine use in daily clinical practice [9, 21].

In summary, in our retrospective study analyzing exclusively patients with SAP requiring percutaneous drainage therapy, two morphologic features on contrast-enhanced CT (number of parts of pancreas that exhibited necrosis as well as presence of distant fluid collections) exhibited a significant correlation with mortality. These two CT features might be helpful to easily and quickly identify patients at risk. Based on these two features, we propose a new simple score to stratify patient risk. However, since our study with a medium-sized number of subjects was of retrospective nature, no definite conclusion can be made. The presented results need to be validated by further prospective studies.

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References

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