Severity, Treatment, and Outcome of Acute Pancreatitis in Thailand: The First Comprehensive Review Using Revised Atlanta Classification

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Background. Severity and outcome of acute pancreatitis (AP) in Thailand are unknown. Methods. A retrospective study of 250 patients with AP during 2011–2014 was performed. Severity, treatment, and outcome were evaluated. Severity was classified by revised Atlanta classification. Results. The mean age was 58 years and 56% were men. Etiologies were gallstones (45%), alcohol (16%), postendoscopic retrograde cholangiopancreatography (14%), and idiopathic (15%). Overall, 72%, 16%, and 12% of patients had mild, moderately severe, and severe AP, respectively. Two major types of initial intravenous fluid were normal saline (64%) and Ringer’s lactate solution (RLS, 28%). Enteral nutrition was given in 77% of patients with severe AP, median duration 48 hours, and via a nasogastric tube in 67% of patients. Necrotizing pancreatitis (NP) developed in 7% of patients, and 29% of them developed infection (median 17 days). The median length of stay was 6, 9, and 13 days, and the mortality rate was 1%, 3%, and 42% in mild, moderately severe, and severe AP, respectively. The overall mortality rate was 6%. Conclusion. The severity of AP in Thailand was mild, moderately severe, and severe in 72%, 16%, and 12% of patients, respectively. NP was not prevalent. Mortality was high in severe AP. Most treatments complied with standard guidelines except the underuse of RLS.

1. Introduction

Acute pancreatitis (AP) is an acute pancreatic inflammatory process triggered by abnormal activation of pancreatic enzymes and the release of several inflammatory mediators. The disease exhibits variable involvement of other regional tissues and remote organ systems [1]. The overall mortality rate of AP is approximately 5% [2]. There is a wide variation in the disease severity, ranging from mild, self-limiting disease that recovers within 3 to 5 days without mortality to severe, life-threatening disease with a mortality rate of 30% to 40% [3].

The Atlanta classification of 1992 provided a global consensus and universally applicable classification system for AP [1]. Although it is useful and widely accepted, some of the definitions used in this version of the classification remain confusing. A better understanding of the pathophysiology of organ failure (OF) and necrotizing pancreatitis (NP) and their outcomes, as well as improvements in diagnostic imaging techniques, has made it necessary to revise the Atlanta classification. The 2012 revision of the Atlanta classification includes clinical assessment of the severity of AP as mild, moderately severe, or severe and provides more objective terms with
which to describe the local complications of AP. Thus, it
is currently the gold standard for evaluating the severity
of AP [4].

In Thailand, studies on AP are very scarce despite the
importance of the disease [5–8]; this lack of data is partly
due to the uncommonness of AP. Basic information on
the severity and outcomes of AP in Thai patients using
the current classification would represent a milestone in
the development of a Thai guideline for AP; however,
such data are lacking. In the present study, we evaluated
the severity, treatment, and outcomes of patients with AP
in our institution according to the 2012 revision of the
Atlanta classification.

2. Materials and Methods

2.1. Study Design and Population. This retrospective study
involved all adult patients who were admitted to Siriraj
Hospital, Bangkok, Thailand, for the treatment of AP from
December 2011 to December 2014. The study was approved
by the Siriraj Institutional Review Board.

All adult patients aged ≥18 years who were diagnosed
with AP by meeting two of the three diagnostic criteria for
AP [abdominal pain, a serum amylase or lipase activity three
times higher than the upper limit of normal, and pancreatitis
documented by computed tomography (CT)] were enrolled
[1, 4]. Only patients who initially presented to our hospital
within 48 hours were included in the study. Patients with
incomplete medical records, especially in the first 48 hours
of disease, were excluded.

2.2. Clinical Data. Data regarding severity, treatment, and
outcomes of AP were collected using designed case
record forms.

2.3. CT Findings. All CT scans were reviewed by two of the
authors: a gastroenterologist with expertise in pancreatic
diseases (S.P.) and a specialized gastrointestinal radiologist
(P.A.). The terminology used followed the 2012 revision of
the Atlanta classification [4].

2.4. Definitions of Severity of AP and Local Complications.
The severity of AP and terminology regarding systemic and
local complications were classified according to the 2012
revision of the Atlanta classification [4].

2.5. Statistical Analysis. Descriptive statistics were used to
summarize the patients’ characteristics. Continuous data
are presented as mean and standard deviation, whereas
categorical data are presented as frequency and percentage. The
chi-square test or Fisher’s exact test was used to compare
categorical variables among the three severity groups. A stan-
ard t-test or the Mann-Whitney U test was used to compare
continuous variables. All statistical analyses were performed
using SPSS software. A two-sided p value of <0.05 was
considered statistically significant.

3. Results

3.1. Patients’ Characteristics. The data of 272 consecutive
patients with AP were reviewed. Twenty-two patients were
excluded due to incomplete data. In total, 250 patients with
AP met the eligibility criteria. One-hundred forty patients
(56%) were male, and 110 patients (44%) were female. The
mean age of the patients was 58 ± 17 years (56 ± 16 years in
male and 62 ± 19 years in female), and 72% had various
comorbidities (Table 1). Almost all patients (99%) presented
with abdominal pain, 64% had referred pain to the back, and
1% presented with altered consciousness. The median dura-
tion of symptoms was 24 hours before admission, of which
was not different between male (median 24 hours, range 6–
48 hours) and female (median 24 hours, range 8–48 hours).
Both the serum amylase and lipase levels had a sensitivity
of 95% for a diagnosis of AP, and the combination of both

| Table 1: Characteristics of the 250 patients with acute pancreatitis. |
|-----------------------------|-------------------|
| Age in years                | 58 ± 17           |
| Male                        | 140 (56)          |
| Comorbidities               | 180 (72)          |
| Hypertension                | 117 (47)          |
| Diabetes                    | 64 (26)           |
| Dyslipidemia                | 35 (14)           |
| Malignancy                  | 29 (12)           |
| Cardiovascular disease      | 28 (11)           |
| Chronic kidney disease      | 16 (6)            |
| Chronic obstructive pulmonar
  y disease                  | 5 (2)             |
| HIV/AIDS                    | 3 (1)             |
| Department of admission     |                   |
| Medicine                    | 173 (69)          |
| Surgery                     | 77 (31)           |
| Signs and symptoms          |                   |
| Abdominal pain              | 247 (99)          |
| Back pain                   | 160 (64)          |
| Altered consciousness       | 2 (1)             |
| Dyspnea                     | 1 (0.4)           |
| Duration of symptoms in hours| 24 (7–48)        |
| Serum pancreatic enzymes    |                   |
| Amylase ≥ 3 times upper limit of normal | 229 (95) |
| Lipase ≥ 3 times upper limit of normal | 212 (95) |
| Amylase and lipase ≥ 3 times upper limits of normal | 196 (91) |
| Performance of CT           | 62 (25)           |
| Number of days after admission| 5 (1–39)        |
| Etiology of AP              |                   |
| Gallstones                  | 113 (45)          |
| Alcohol-related disease     | 41 (16)           |
| Post-ERCP                   | 35 (14)           |
| Miscellaneous               | 24 (10)           |
| Idiopathic                  | 37 (15)           |

Age and BMI are presented as mean ± standard deviation; all other data are
presented as n (%) or median (range). AP: acute pancreatitis; CT: computed
tomography; ERCP: endoscopic retrograde cholangiopancreatography.
enzymes was not superior to the use of either enzyme alone. One-fourth of the patients underwent CT at a median of 5 days after admission.

The etiologies of AP were gallstones (45%), alcohol-related disease (16%), postendoscopic retrograde cholangiopancreatography (ERCP) (14%), idiopathic (15%), and miscellaneous (10%). When comparing the etiology of AP in women to those in men, women had significantly more gallstone pancreatitis (60.9% versus 33.6%), but less alcoholic pancreatitis (4.5% versus 25.7%) (Table 2).

### 3.2. Severity of AP

The severity of AP according to the 2012 revision of the Atlanta classification was mild, moderately severe, and severe in 72%, 16%, and 12% of patients, respectively (Figure 1). Eighty-two percent of patients had no OF, 6% had transient OF, and 12% had persistent OF.

### 3.3. Accuracy of Early Severity Assessment Tools to Predict Severe AP

Using the 2012 revision of the Atlanta classification as the gold standard, the sensitivity, specificity, positive predictive value, and negative predictive value of the two most commonly used severity assessment tools [bedside index for severity in AP (BISAP) score of ≥ 3 and the presence of systemic inflammatory response syndrome (SIRS) upon admission] are shown in Table 3. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was evaluated in very few patients; thus, this score was not analyzed.

### 3.4. Intravenous Fluid

The two essential treatments of severe AP that are able to reduce OF and/or mortality are early fluid resuscitation and enteral feeding [9]. The mean total intravenous fluid resuscitation volume during the first 24 hours in the studied patients was 2720, 3150, and 4660 mL in patients with mild, moderately severe, and severe AP, respectively. The type of intravenous fluid was normal saline solution in approximately 60% of patients and Ringer’s solution in approximately 30% (Figure 2).

### 3.5. Enteral Nutrition

All patients with mild and moderately severe AP and 77% of those with severe AP received enteral nutrition. The median time until the start of enteral feeding was 16, 24, and 48 hours in patients with mild, moderately severe, and severe AP, respectively. Among patients with mild AP, 97% received enteral nutrition orally and 3% required nasogastric feeding. Among patients with moderately severe AP, 80% received enteral nutrition orally, 18% received it via a nasogastric tube, and only 2% received it via a nasojejunal tube. In contrast, 52% of patients with severe AP required nasogastric feeding, 23% could take it orally, and 3% required nasojejunal feeding (Figure 3).

### 3.6. Necrotizing Pancreatitis and Local Complications

NP occurred in 17 patients (7%). Almost 70% of cases of NP involved parenchymal necrosis with or without peripancreatic necrosis, while only 30% involved solely peripancreatic necrosis. Regarding the local complications, 27 patients (11%) had acute peripancreatic fluid collections (APFC) and 13 patients (5%) developed acute necrotic collections (ANC). Pancreatic pseudocysts were detected in 2 out of 4 patients with APFC, who had follow-up CT. Walled-off necrosis (WON) occurred in 9 out of 12 patients with necrotizing pancreatitis or ANC, who had follow-up CT (Table 4).

### 3.7. Pancreatic Infection

Overall, 5 out of 17 patients (29%) with NP had infected necrosis. The diagnostic methods of infected necrosis were the presence of gas on CT (66.6%) and Gram staining or culture of specimens obtained from fine-needle aspiration or percutaneous drainage (50.0%). The median time until the diagnosis of pancreatic infection was 17 days (range, 7–25 days) after admission. All patients with pancreatic infections were treated by either percutaneous drainage (4 patients, 80%) or open necrosectomy (1 patient, 20%) (Table 5).

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**Table 2: Etiology of acute pancreatitis according to the gender.**

<table>
<thead>
<tr>
<th>Etiology, n (%)</th>
<th>Male (n = 140)</th>
<th>Female (n = 110)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallstone</td>
<td>47 (33.6)</td>
<td>67 (60.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol</td>
<td>36 (25.7)</td>
<td>5 (4.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-ERCP</td>
<td>19 (13.6)</td>
<td>16 (14.5)</td>
<td>0.823</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>23 (16.4)</td>
<td>14 (12.7)</td>
<td>0.413</td>
</tr>
</tbody>
</table>

All data are presented as n (%). ERCP: endoscopic retrograde cholangiopancreatography.

**Table 3: Accuracy of the two most common methods to predict severe acute pancreatitis.**

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIRS upon admission</td>
<td>87</td>
<td>69</td>
<td>29</td>
<td>97</td>
</tr>
<tr>
<td>BISAP score ≥3</td>
<td>61</td>
<td>90</td>
<td>46</td>
<td>94</td>
</tr>
</tbody>
</table>

SIRS: systemic inflammatory response syndrome; BISAP: bedside index for severity in acute pancreatitis; PPV: positive predictive value; NPV: negative predictive value.
3.8. Outcomes. The median length of hospital stay was 6, 9, and 13 days in the mild, moderately severe, and severe AP groups, respectively, with significant differences ($p < 0.001$). Surgery was performed in two patients with severe AP. One patient underwent pancreatic necrosectomy, and another underwent exploratory laparotomy due to a diagnosis of generalized peritonitis and was found to have AP. No surgery was performed in the mild and moderately severe groups. The AP-related mortality rates were 1%, 3%, and 42% in the mild, moderately severe, and severe AP groups, respectively, with significant differences ($p < 0.001$) (Table 6). In the comparison of 13 patients with severe AP who died and 18 patients with severe AP who survived, there was no difference regarding the patients’ age, gender, etiology of AP, timing of admission, the ICU care, type of intravenous fluid resuscitation, presence of local complications, and surgery (data not shown). The median ICU stays were 7 days and 8 days. The two deaths in the mild AP group had nonpancreatic causes (acute cholangitis with septicemia and upper gastrointestinal bleeding, resp.).

4. Discussion

The 2012 revision of the Atlanta classification is a recently proposed gold standard for the classification of AP [4]. The present study is among one of the few that have used the revised Atlanta classification to evaluate the severity, treatments, and outcomes of AP [10]. The results of this study are of importance and represent a milestone in the development of a guideline for AP in Thai patients. Our results highlight some important points regarding AP in Thai patients.

The age and sex of the patients with AP in this study were very similar to those of patients in recent studies from the West [11] and Japan [12]; however, the mean age was slightly higher than that in a study from China [13, 14]. The typical clinical presentation was abdominal pain in almost all patients. Referred pain to the back was present in two-thirds of the patients of the present study and in close to one-half of patients in another study [15].

The etiology of AP in this study was comparable with that in other studies from Asia [12, 13], with the leading causes of AP being gallstones and alcohol-related disease. However, gallstones were more prevalent in female, while alcohol was
so in male, of which were well known. The incidence of gall-
stone pancreatitis was not different from that in our previous
study in 2007 [7]; however, the incidence of alcohol-related
AP was significantly lower with a paradoxical increase in
post-ERCP pancreatitis, which was the fourth most common
etiology in the present study. This can be explained by the
increasing numbers of ERCP procedures performed during
the last decade in our institution, which is a tertiary hospital.
Idiopathic AP was the third most common etiology in the
present study; it fell within the acceptable range (≤20%) sug-
gested by most guidelines [9, 16–19].

The present study demonstrated that the severity of AP in
our institution according to the 2012 revision of the Atlanta
classification was mild, moderately severe, and severe in
72%, 16%, and 12% of patients, respectively. These data are
consistent with recent data from Western studies, which
reported mild AP in 70% to 85% of patients, moderately
severe AP in 10% to 15% of patients, and severe AP in 5% to
15% of patients [20, 21]. Very few data are available from
Asia because most studies were published before the endorse-
ment of the 2012 revision of the Atlanta classification [12].
However, a recent study from China [22] that utilized the
2012 revision of the Atlanta classification reported mild,
moderate, and severe AP in 30%, 53%, and 17% of patients,
respectively. The major difference between that study and
ours occurred among the patients with moderately severe
AP; the incidence of both OF and local complications dif-
ered considerably between these two studies. The reason
for the very high prevalence of moderately severe AP in this
Chinese study is unclear, but we feel that it is too high when
compared with those in the other studies from Western
countries [20, 21]. It is possible that the Chinese study did
not exclude transferred patients, and therefore, the rates of
mild and severe AP were higher. Our study had a
strength that we excluded transferred patients and, therefore,
would represent the more accurate picture of the severity of
AP. Another possible reason for the lower prevalence of
moderately severe AP in our study might be the lack of CT
examination in all patients. Our CT examinations were
mainly performed in patients suspected to have severe AP,
as reflected by the 25% frequency of CT in our study. Some
patients with mild AP might have actually had local compli-
cations and would have been classified as having moderately
severe AP if CT had been performed. However, our practice
of performing CT complied well with all standard guidelines
of AP [9, 19, 23], which recommend CT mainly for patients
with clinically severe AP.

The use of early severity assessment tools for AP is
another interesting topic. A recent meta-analysis [24] and a
comprehensive review by the present authors [25] concluded
that the four best tools with which to predict the severity of
AP within the first 24 hours were the presence of SIRS and
the APACHE II, BISAP, and Japanese severity scale scores
upon admission. All of these parameters have an advantage of
a very high negative predictive value with which to rule
out severe AP [24, 25]. In our institute, the presence of SIRS
and the BISAP score are frequently used, whereas the
APACHE II score and the Japanese severity scale score are
rarely used. The present study confirmed that the presence
of SIRS and the BISAP score on admission did very well in
ruling out severe AP due to their high NPV (94%–97%).
The presence of SIRS on admission was slightly more effect-
ive than the BISAP score in excluding severe AP.

Fluid resuscitation during the first 24 hours and enteral
nutrition are currently the two most critical and essential
treatments of AP because they can reduce both OF and mor-
tality [26]. In the present study, the intravenous fluid volume
administered to patients with severe AP complied well with
the guidelines, which recommend administration of 3 to 5 L
of fluid during the first 24 hours [9, 19, 23]. However, we
found that instead of using Ringer’s solution, which is pre-
ferred by most guidelines [9, 19, 23], most of our patients
received normal saline solution. The reason for this differ-
ence is unknown, but we hypothesized that it might be
related to a lack of knowledge among physicians or a more
familiarity with normal saline solution than Ringer’s solu-
tion. This problem is critical and must be urgently solved sys-
tematically by providing education to the physicians or
making a clinical institute policy. Conversely, enteral nutri-
tion, which is the most effective treatment for AP and is
dorsed by all guidelines [9, 19, 23], was prescribed to
almost all patients in the present study.

Regarding necrotizing pancreatitis and local compli-
cations of AP, an interesting finding was that NP was not prev-
alent. The 7% frequency of NP in the present study was much
lower than the 10% to 20% frequency in most studies. The
exact reason for this difference is unknown. However, we
hypothesize that it might be due to the undiagnosed pancre-
atic necrosis, particularly in patients with clinically mild AP,
because CT usually was not done in such patients. Further
study to determine the presence of moderately severe AP
(from local complications) in patients with clinically mild
AP in our country is required. Another possible reason
could be the misclassification of some ANC as APFC,
particularly during the first week of the disease because
majority of the CT in the present study were performed
within the first week. It is also the possible reason for
the very low incidence of late local complications of AP,
pseudocyst, and WON in the present study because we
did not have a systematic follow-up CT for patients who
had APFC and ANC. Therefore, we might underdiagnose
many pseudocyst and WON.

<table>
<thead>
<tr>
<th>Table 6: Treatment outcomes.</th>
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<td>-----------------------------</td>
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<tr>
<td>Length of stay in days</td>
</tr>
<tr>
<td>Surgery</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
</tbody>
</table>

Data are presented as median (range) or n (%).
The major outcomes of AP in the present study were similar to those in most guidelines [2]. The median hospital stay in our study was 6 days (6, 9, and 13 days for mild, moderate, and severe AP, respectively), which is similar to that reported in other studies [22]. Surgery was rare and was only performed in 2 of 250 patients. The mortality of AP in the present study was within the range reported in standard guidelines [2] and another recent study [22]. However, the 42% mortality rate of severe AP in this study was slightly higher than it should be (20–30%) [2]. We could not find any reasonable explanation for this high mortality, including the timing of admission, patients’ age, ICU admission, type of intravenous fluid, enteral feeding, presence of local complications, or surgery. Finally, we could not deny that it might be due to the quality of our intensive care. Thus, this is another opportunity for improvement. Normally, mild AP should have a mortality rate near 0%. In the present study, however, two patients (1%) with mild AP died. The causes of death were cholangitis with severe *Pseudomonas aeruginosa* sepsicaemia and upper gastrointestinal bleeding, respectively, neither of which was directly caused by AP.

The strength of the present study is that it is the first comprehensive study on AP in Thai patients. The "gold standard" 2012 revision of the Atlanta classification was used. All CT scans were reviewed by experts in pancreatic disease according to the 2012 revision of the Atlanta classification, and all treatments aligned with all recent guidelines with no limitations of the facilities. However, the weaknesses of this study are the retrospective and observational nature of the study and the study was conducted in a university hospital setting; therefore, the results might not accurately represent the clinical picture of AP in Thailand. Additionally, the etiology of AP was post-ERCP in 14% of the patients in this study, which would not be found in the community setting. Nevertheless, when we calculated the severity of AP after excluding the 35 patients with post-ERCP pancreatitis, the results were unchanged (data not shown).

### 5. Conclusions

The severity of AP in our study was mild, moderately severe, and severe in 72%, 16%, and 12% of patients, respectively. NP was not prevalent, and infected necrosis occurred in one-third of NP. Mortality was high in severe AP. Most treatments of AP, particularly the amount of intravenous fluid administration and enteral feeding, complied well with the standard guidelines except the use of normal saline solution rather than Ringer’s solution. Further strategies to improve the intensive care quality of severe AP and to endorse the use of Ringer’s solution are urgently needed. Prospective multicenter data collection is also advocated.

### Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

### References


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