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Original article

## Risk factors for and impact of respiratory failure on mortality in the early phase of acute pancreatitis

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## ABSTRACT

**Background:** The incidence of respiratory failure and other respiratory complications in the early phase of acute pancreatitis (AP) is not well investigated.

**Objective:** To evaluate the incidence and risk factors of respiratory failure, and its impact on mortality in the early phase AP.

**Methods:** Retrospective cohort study including 359 patients admitted with acute pancreatitis. Information was gathered from electronic patient records. We defined respiratory failure based on the modified Marshall scoring system in the revised Atlanta criteria. Predictors of respiratory failure were evaluated in univariable and multivariable logistic regression analysis.

**Results:** The cohort included 188 women and 171 men with a mean age of 56.1 years. Respiratory complications including pleural effusion, pneumonia and atelectasis were registered in 80 patients (22%), 100 (29%) needed oxygen therapy, 27 (8%) continuous positive airway pressure, and six (2%) mechanical ventilation. Thirty-two patients (9%) were treated with bronchodilators and 12 (3%) with steroids. Thirty-one patients (9%) fulfilled the diagnostic criteria for respiratory failure. Five of these patients (16%) did not have effusion, atelectasis or pneumonia. Predictors of respiratory failure in multivariable analysis were age (OR 1.04; CI 95% (1.03–1.07)) and smoking (OR 2.67; CI 95% (1.21–5.86)). Thirteen patients died in hospital. The Kaplan-Meier curves and log-rank tests showed that patients with respiratory failure had increased in-hospital mortality as did patients with cardiovascular and renal failure ( $P < 0.01$  for all analyses).

**Conclusions:** Respiratory complications are frequent in the early phase of AP. Respiratory, cardiovascular and renal failure is associated with a poor outcome. The fact that patients without effusion, atelectasis, or pneumonia may develop respiratory failure, suggests that acute lung injury, possibly associated with systemic inflammation, may be important.

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### 1. Introduction

The severity of respiratory complications in acute pancreatitis (AP) ranges from mild hypoxemia to severe respiratory failure. In two previous studies, respiratory failure was the main contributing factor to mortality during the early phase of severe AP [1,2]. The incidence of respiratory failure and other respiratory complications is not well investigated. For more than 20 years, different

terminology and diagnostic criteria of AP and respiratory complications were used leading to various definitions of the parameters. The interpretation of the findings from previous studies can be difficult due to heterogeneous populations, different phases of AP, different treatment modalities, and different definitions of respiratory failure and respiratory complications. In 2012, the revised Atlanta criteria uniformed the terminology and diagnostic criteria for AP [3]. According to these criteria, AP is divided into mild, moderate, and severe disease based on the development of local and systemic complications and development of organ failure. The onset of AP is defined as the time of onset of abdominal pain. The disease comprises an early and a late phase. The early phase is characterized by development of a systemic inflammatory response syndrome usually lasting for one week, but may extend into the

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second week [3]. In the revised Atlanta criteria, respiratory failure is defined corresponding to the modified Marshall scoring system [3].

The aim of this retrospective cohort study was to investigate the incidence and predictors of respiratory failure, the influence of respiratory failure on mortality and the incidence of other respiratory complications in the early phase of AP diagnosed according to the revised Atlanta criteria.

## 2. Methods

The design was a retrospective cohort study including all patients admitted with their first episode of AP to our department from January 2012 to January 2015. The exclusion criteria were previous AP and chronic pancreatitis. We defined AP according to the revised Atlanta criteria [3]. Three investigators (TD, MK and SR) manually reviewed the medical records for each patient in an independent manner and extracted the data based on pre-specified pilot tested data extraction sheets. Disagreements were resolved through discussion before analysis. In case of disagreements that could not be resolved through discussion, a fourth author (SN) acted as ombudsman. The following data were extracted from the electronic medical records: Gender, age, American Society of Anesthesiologists (ASA)-score, body mass index (BMI), smoking, pre-existing chronic obstructive lung disease (COPD), etiology, tracheal and blood culturing results, development of pleural effusion, atelectasis, pneumonia and respiratory failure, cardio-vascular, and renal failure according to the modified Marshall scoring system. Accordingly, respiratory failure was defined as oxygen saturation divided by the fraction of inhaled oxygen of  $\leq 300$  (3). We also registered treatments including pleurocentesis, oxygen therapy, continuous positive airway pressure (CPAP), mechanical ventilation, antibiotics, bronchodilators, and steroids as well as the date of onset of symptoms, admission to hospital, admission to semi-intensive care unit, admission to intensive care unit, death and discharge. Pleural effusion, atelectasis and pneumonia were registered in accordance with the descriptions of chest radiographs and computed tomography scans (CT-scan) compiled by radiologists at the time of hospitalization. If the medical charts contained clinical description of pneumonia and treatment with antibiotics, the patient was registered as having pneumonia even though no radiological imaging were available or radiological imaging showed no pulmonary infiltrations.

All patients were treated conservatively with early enteral nutrition, analgesics, intravenous fluids and supportive treatment.

## 3. Statistics

We used STATA, version 14 (Stata Corp, USA) for the statistical analyses. We summarized continuous variables as means with standard deviations (SD) or percent. We performed univariable and multivariable binary logistic regression analysis with results presented as odds ratios (OR) with 95% confidence intervals (CI). In the multivariable regression analysis, we used stepwise backward elimination and set the level of significance to  $P < 0.05$ . We compared in-hospital mortality in groups of patients with or without respiratory failure, cardiovascular failure and renal failure using Kaplan Meier Plots and log-rank tests.

## 4. Results

We initially identified 606 potentially eligible cases and excluded 247 with previous AP, chronic pancreatitis, or misdiagnosed. In total, 359 patients fulfilled the inclusion criteria and none of the exclusion criteria (Table 1). Our cohort included 188 women (52%) and 171 men with a mean age of 56.1 years (range

**Table 1**  
Baseline characteristics of the 359 included patients.

Variable	N (%)
<b>Gender</b>	
Female	188 (52)
Male	171 (48)
<b>ASA-score</b>	
1	49 (14)
2	190 (53)
3	109 (30)
4	11 (3)
<b>Smoking</b>	
No	208 (58)
Yes	140 (39)
Unknown	11 (3)
<b>COPD</b>	
No	320 (89)
Yes	37 (10)
Unknown	2 (1)
<b>BMI (kg/m<sup>2</sup>)</b>	
$\leq 18.5$	9 (3)
18.6–24.9	89 (25)
$\geq 25$	203 (56)
Unknown	58 (16)
<b>Etiology</b>	
Gallstone	204 (57)
Alcohol	59 (16)
Unknown	76 (21)
Post-ERCP	10 (3)
Drugs, hyperlipidemia, hypercalcemia	10 (3)
<b>Onset of symptoms</b>	
On day of admission	113 (31)
One or two days before admission	152 (43)
>Two days before admission	94 (26)
<b>Intensive care</b>	
Semi-intensive care unit	16 (4)
Intensive care unit	10 (3)
None	333 (93)

ASA-score, American Society of Anesthesiologists score.  
BMI, body mass index.

18.2–97.5). The mean duration of hospitalization was eight days. Ten percent required hospitalization beyond 14 days. One patient remained in hospital for 208 days whereas the remaining patients were discharged or died within 39 days. In total, 74% of the patients were admitted within two days of the onset of symptoms and 95% within seven days. Twenty-six patients (7%) were transferred to semi-intensive care unit or intensive care unit. Fourteen patients (4%) developed cardio-vascular failure and 25 (7%) patients developed renal failure.

### 4.1. Respiratory complications

In total, 128 patients (36%) developed respiratory complications. Eighty patients (22%) developed one or more of following: pleural effusion, atelectasis or pneumonia, of which 27 (33%) were treated with CPAP. Twenty (16%) of 129 patients who had blood cultures performed were positive. In 14 patients, culturing from respiratory tract secretions was performed of which three (21%) were positive.

### 4.2. Respiratory failure

In total, 31 patients (9%) developed respiratory failure. Five of these patients (16%) did not have effusion, atelectasis or pneumonia (Table 2). Conversely, a number of patients with effusion, atelectasis or pneumonia did not fulfil the diagnostic criteria for respiratory failure.

The mean age of patients who developed respiratory failure was 67.5 years (61.0–74.0). Nine (29%) of these patients had chronic lung disease and 17 (55%) were smokers. Sixteen (52%) patients

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