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Influence of abdominal obesity on multiorgan dysfunction and mortality in acute respiratory distress syndrome patients treated with prone positioning☆,☆☆,★

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ABSTRACT

Purpose: Obesity is a worldwide pandemic, and obese patients face an increased risk of developing acute respiratory distress syndrome (ARDS). Prone positioning (PP) is a frequently used intervention in the treatment of ARDS. There are no data describing the impact of PP on morbidity and mortality in abdominally obese patients. We report our observations in abdominally obese ARDS patients treated with PP.
Materials and methods: Patients with ARDS (n = 82) were retrospectively divided into 2 groups characterized by presence (n = 41) or absence (n = 41) of abdominal obesity as defined by a sagittal abdominal diameter of 26 cm or more.
Results: There was no difference in cumulative time abdominally obese patients were placed in prone position from admission to day 7 (41.0 hours [interquartile range, 50.5 hours] vs 39.5 hours [interquartile range, 61.5 hours]; $P = .65$) or in overall intensive care unit mortality (34% vs 34%; $P = 1$). However, abdominally obese patients developed renal failure (83% vs 35%; $P < .001$) and hypoxic hepatitis (22% vs 2%; $P = .015$) more frequently. A significant interaction effect between abdominal obesity and prone position with respect to mortality risk (likelihood ratio, $P = .0004$) was seen if abdominally obese patients were treated with prolonged cumulative PP.
Conclusion: A cautious approach to PP should be considered in abdominally obese patients.

1. Introduction

Worldwide, there has been an increase in the prevalence of obesity by a factor of 2 over the last 3 decades according to the World Health Organization [1].

Admission of obese patients to intensive care units (ICUs) is common, and they face an increased morbidity as demonstrated by an increased duration of mechanical ventilation and length of stay (LOS) in ICU, a higher incidence of acute renal failure, abdominal compartment syndrome, and acute respiratory distress syndrome (ARDS) [2-6].

There are mixed results regarding the impact of obesity on ICU mortality. Although one study reported an increased ICU mortality in obese patients with H1N1 influenza (even without Advisory Committee on Immunization Practices-recognized medical conditions), another did not find an increased ICU mortality of obese patients as measured by the body mass index (BMI) [2,7]. Similarly, Paolini et al [8] showed that abdominal obesity constituted a risk factor for death in the ICU. Interestingly, however, the latter was only the case if abdominal obesity was determined by the sagittal abdominal diameter (≥26 cm). Body mass index as a measure of obesity without differentiation of body fat distribution did not show an impact on mortality.

In most studies on the effect of obesity on morbidity and mortality in ICU, BMI was used to classify obesity. Estimated height and weight by the patient's care provider, rather than accurate measurement, is common in research and treatment of critically ill patients [3]. The

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accuracy of estimation is poor, and BMI derived from these estimates might therefore be severely inaccurate [9].

In addition, we have demonstrated a high incidence of hepatic failure associated with prolonged cumulative prone positioning (PP) in a small group of obese patients with H1N1-associated ARDS [10].

Against this background, we investigated whether abdominal obesity measured by the sagittal abdominal diameter (and intraperitoneal fat volume) was also associated with a higher risk of morbidity and/or mortality in patients with ARDS and, hence, could constitute a predictive marker of patient outcome. For this purpose, we retrospectively analyzed the association between the clinical data of 82 patients with ARDS and the computed tomography (CT)-derived measures of abdominal obesity.

2. Materials and methods

Eighty-two patients with severe ARDS were admitted to a mixed surgical/medical ICU between January 2008 and December 2010. Clinical data and laboratory values were extracted from comprehensive clinical documentation. The data were taken on the day of admission, days 1, 2, 3, and 7 after admission and weekly thereafter. End points were death or discharge from ICU and the development of hepatic or renal failure. The latter (renal failure) was defined as an increase of serum creatinine more than 2 mg/dL or the need for renal replacement therapy; the former (liver failure) was defined as an increase of bilirubin 4 mg/dL or more following the criteria of the New Simplified Acute Physiology Score scoring system and the Multiple Organ Dysfunction Score [11]. An increase of aspartate aminotransferase or alanine aminotransferase more than 700 U/L was considered as hypoxic hepatitis [12]. The mechanical ventilation strategy was according to the recommendations of the ARDS network group [13]. Venovenous extracorporal membrane oxygenation (ECMO) was started if there was either persisting hypoxia, excessively high end-inspiratory plateau pressure, or uncompensated hypercapnia with respiratory acidosis.

The clinical decision for deploying the prone position was based on clinical and radiologic findings (arterial oxygen concentration to the fraction of inspired oxygen [Pao_2/Fio_2] and increase of Pao_2/Fio_2 in the prone position, thoracic CT scan at admission followed by daily chest x-rays). There was no upper limit concerning the frequency of pronation maneuvers. A single session lasted 12 hours. For the analysis of an interaction effect between cumulative hours in prone position during the first week and abdominal obesity on mortality, all patients were omitted for whom cumulative hours up to day 7 could not be computed due to early death ($n = 12$) or recovery and release from the ICU within the first week because the interaction of obesity and PP on mortality are considered to be time depending.

The population was divided into 2 groups according to Paolini et al [8]: (i) abdominally obese patients with a sagittal abdominal diameter of 26 cm or more ($n = 41$) (XL) and (ii) a control group of patients with a sagittal abdominal diameter of less than 26 cm ($n = 41$) (ML).

An abdominal CT (in addition to cerebral and thoracic scanning) was acquired as part of the standard operating procedure on admission of patients with severe ARDS. Abdominal contrast-enhanced (Imeron 350; Bracco SpA, Milan, Italy) multi-detector computed tomography (MDCT) scanning (64-MDCT SOMATOM Sensation, 128-MDCT SOMATOM Definition AS; Siemens, Erlangen, Germany) (64-MDCT Brilliance; Philips, Eindhoven, The Netherlands) was made at the time of admission (5 mm slice thickness, 20 or 70 seconds after intravenous administration of nonionic iodine contrast media corresponding to the arterial or portal venous phase, 1.5 mL/kg body weight, followed by 100 mL of saline, 3 mL/min flow). All images were reviewed in the soft tissue and bone window. The sagittal diameter of the abdomen (SAD) at the level of L4/5 and the volumes of the abdominal fatty tissues (subcutaneous, intraperitoneal, and retroperitoneal fat) were measured semiautomatically as described by Weig et al [10] in 2012. To prevent bias introduced by a falsely high SAD caused by free fluid in the abdominal cave (blood, ascites, and hematoma) in the XL group, we compared the abdominal fat volume of patients with pulmonary and extrapulmonary origin of ARDS.

Body mass index was calculated using the formula: BMI = body weight (kg)/height^2 (m^2).

2.1. Statistical analysis

Univariate analyses for differences between ML and XL patients were conducted using Fisher exact test for a categorical variable and Wilcoxon rank sum test for a metric variable. We used an implementation of the Wilcoxon rank sum test that computes exact *P* values (by conditioning on the data), whereas allowing for ties in the data [14].

Linear models and logistic models were fit to test for an interaction effect between abdominal obesity and prone position on the following outcomes: mortality, hepatic failure, renal failure, LOS on ICU, and time on mechanical ventilation. Prone position was measured in terms of cumulative hours a patient spent in prone position during the first 7 days from admission to ICU. The admission day was counted as day 0 and was included in the cumulation if the patient was placed in prone position. For these interaction analyses, the covariates included in the model were abdominal obesity, hours in prone position and the interaction effect between abdominal obesity, and hours in prone position. The interaction effect was tested using the likelihood ratio test, whereas main effects were tested using Wald test. Because of the small sample size, 95% bootstrap percentile intervals were additionally applied and contrasted to the results from asymptotic maximum likelihood theory.

Available case analyses were performed because missing values can be regarded as missing completely at random. An association was considered as statistically significant if the *P* value (not adjusted for multiple testing) was less than 5%. All analyses were performed using the statistical software R (Vienna, Austria) [15].

3. Results

Detailed patient characteristics on admission, clinical course, diagnosis, and underlying medical condition are shown in Tables 1 and 2.

Overall ICU survival was 65.9%. Mortality rates were exactly equal in XL and ML patients.

The median LOS on ICU for all survivors was 26 days (interquartile range [IQR], 28 days). Nonsurvivors died with a median of 10 days (IQR, 31 days) after ICU admission.

Forty-one patients fulfilled the criteria for abdominal obesity (XL) compared with 41 patients without obesity (ML). Both groups were similar regarding age, sex, and severity of disease on admission to the ICU. In our study population, XL patients with extrapulmorary origin of ARDS were comparable with patients with pulmonary origin of ARDS with respect to mean abdominal fat volume (21732 ± 10003 cm^3 vs 22272 ± 14741 cm^3). Therefore, we conclude that SAD was not influenced by hematoma, ascites, intraperitoneal sepsis, or bleeding. The XL patients required more invasive ventilator settings to sustain adequate oxygenation and ventilation.

Survivors among the XL patients had a median LOS of 26 days (IQR, 30 days), nonsurvivors 16 days (IQR, 41 days). Within the ML group of patients, survivors had a median LOS of 26 days (IQR, 19 days), whereas nonsurvivors had a LOS of 8.0 days (IQR, 24 days).

There was a significantly higher rate of renal failure for XL patients ($P < .0001$). A tendency for a higher rate of hepatic failure was observed in XL patients; however, the association was not significant (46% vs 24%, $P = .064$). Hypoxic hepatitis occurred significantly more often in XL patients (22% vs 2%, $P = .015$).

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