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The outcome of acute respiratory distress syndrome in relation to body mass index and diabetes mellitus

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ABSTRACT

Objective: To determine the 28 day mortality of patients with ARDS in relation to body mass index (BMI) and presence diabetes mellitus (DM).
Design: Retrospective cohort study of patients enrolled in the ARDS Network randomized controlled trials.
Results: 2914 patients were enrolled in these trials. 112 patients were underweight (BMI $<$ 18.5), 948 patients were normal range (18.5 $\leq$ BMI $<$ 25.0), 801 patients were overweight (25.0 $\leq$ BMI $<$ 30.0), 687 patients were obese (30.0 $\leq$ BMI $<$ 40.0), and 175 patients were severely obese (BMI $\geq$ 40.0). 469 patients had DM. There was no significant difference in the 28 day mortality in relation to BMI or presence of DM (underweight adjusted OR, 1.217; 95% CI, 0.749–1.979; overweight adjusted OR, 0.887; 95% CI, 0.696–1.131; obese adjusted OR, 0.812; 95% CI, 0.624–1.056; severely obese adjusted OR, 1.102; 95% CI, 0.716–1.695; and DM adjusted OR, 0.938; 95% CI, 0.728–1.208).
Conclusions: The short term mortality in patients with ARDS is not affected by BMI or the presence of DM.

Introduction

The prevalence of obesity and diabetes mellitus (DM) in the United States is increasing dramatically. Reports indicate that 34.9% of the United States population is obese, and 8.3% have DM.[1,2] These conditions have been implicated in the development of chronic illnesses such as coronary artery disease, cancer, osteoarthritis, and depression. Furthermore, patients with these conditions commonly require intensive care for a variety of critical illnesses.[3]

ARDS is one of the serious complications of critical illness affecting an estimated 150,000 annually in the US and at least 20% of mechanically ventilated patients.[4,5]

Previous studies have shown conflicting results between outcome and BMI and presence or absence of DM in critically ill patients. These studies have suggested that the effect of excessive weight ranged from worse outcome, to protective effect or no association.[6–10] Similar observations were reported for those with underlying DM.[11–13] There are, however, only a few studies that address the effect of these two variables on the outcome of mechanically ventilated patients with ARDS. These reports also show inconsistent findings.[14–19] The purpose of this analysis is study the influence of BMI and history of DM on the outcome of patients with ARDS in a large database.

Methods

The ARDS Network has conducted several randomized controlled trials to evaluate therapeutic interventions for the management of acute lung injury. These trials have been previously published.[20–25] Table 1 summarizes the relevant features of these trials. Briefly, all patients fulfilled diagnostic criteria for acute lung injury and were mechanically ventilated. Similar inclusion and exclusion criteria were used in all of the trials. The National Institute of Health and the local Institutional review boards of each of the sites approved all studies.

We were given authorized access to the original data for each of these studies in order to study the outcome of ARDS patients in relation to BMI and the presence or absence of DM. This manuscript was prepared using Ketoconazole and Respiratory Management in ALI/ARDS (KARMA), Late Steroid Rescue Study (LaSRS), Lisofylline and Respiratory Management in ALI/ARDS (LARMA), Assessment of Low tidal Volume and elevated End expiratory volume to Obviate Lung Injury (ALVEOLI), Fluids And Catheters Treatment Trial (FACTT), and Albuterol for the Treatment of Acute lung injury (ALTA) research materials obtained from the NHLBI Biologic

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Table 1
Summary of the ARDSnet trials including data related to BMI and DM.

	KARMA	LaSRS	LARMA	ALVEOLI	FACTT	ALTA
Years	1996–1998	1997–2003	1998–1999	1999–2002	2000–2005	2007–2008
Number of patients	667	180	235	550	1000	282
Intervention	Low tidal volume ventilation/ ketoconazole use in ARDS	Use of steroids in ARDS	Low tidal volume ventilation/ Lisofylline use early in ALI/ARDS	High PEEP/Low FiO_2 vs low PEEP/ High FiO_2 ventilation strategy	PA catheter vs central venous catheter. Conservative vs liberal fluid strategy in management of patient's with ALI/ARDS	Aerosolized albuterol vs saline placebo in patients with ALI/ARDS
Outcome	No effect of ketoconazole on mortality. Improved mortality with low tidal volume ventilation	No change in mortality	No effect of lisofyllineon mortality. Improved mortality with low tidal volume ventilation	No change in mortality	No change in mortality	No change in mortality
BMI median	25.54	28.63	26.87	26.70	27.34	27.38
Range	13.35–58.78	18.39–61.03	11.39–57.42	14.66–53.28	10.03–60.52	15.09–52.89
Missing	45 (6.75)	8 (4.44)	7 (2.98)	45 (8.18)	84 (8.40)	2 (0.71)
Underweight (<18.50)	34 (5.10)	1 (0.56)	8 (3.40)	20 (3.64)	36 (3.60)	13 (4.61)
Normal range (18.50 to <25)	251 (37.63)	52 (28.89)	80 (34.04)	191 (34.73)	293 (29.30)	81 (28.72)
Overweight (25 to <30)	191 (28.64)	49 (27.22)	67 (28.51)	144 (26.18)	264 (26.40)	86 (30.50)
Obese (30 to <40)	120 (17.99)	54 (30.00)	56 (23.83)	122 (22.22)	249 (24.90)	86 (30.50)
Severely obese (≥40)	26 (3.90)	16 (8.89)	17 (7.23)	28 (5.09)	74 (7.40)	14 (4.96)
Diabetes mellitus	84 (12.59)	26 (14.44)	42 (17.87)	83 (15.09)	173 (17.30)	61 (21.63)
Missing	7 (1.05)	0 (0.00)	0 (0.00)	7(1.27)	33 (3.30)	0 (0.00)

Specimen and Data Repository Information Coordinating Center. The findings of this study do not necessarily reflect the opinions or views of the KARMA, LaSRS, LARMA, ALVEOLI, FACTT, and ALTA investigators or the NHLBI. Of note is that the effect of BMI on outcome of mechanically ventilated patients with acute lung injury in KARMA and LARMA studies was analyzed and published in 2004.[19] We did include the data from these two trials in our analysis and combined them with data from the rest of the studies. As for the analysis specifically related to the effect of DM on the outcome of these patients, to our knowledge the data were never published.

Demographic and clinical data were collected and included age, gender, race, and co-morbid illnesses. Baseline measurements immediately prior to randomization were also collected and included Acute Physiology and Chronic Health Evaluation (APACHE) III score, vasopressor use, hemodynamic, respiratory and ventilator parameters. The BMI was calculated from data on enrollment to the studies by dividing the patient's body weight in kilograms by the square of their height in meters. We classified BMI according to the WHO classification into 5 categories: underweight (BMI $<$ 18.5), normal range (18.5 $\leq$ BMI $<$ 25.0), overweight (25.0 $\leq$ BMI $<$ 30.0), obese (30.0 $\leq$ BMI $<$ 40.0), and severely obese (BMI $\geq$ 40.0).[1]

The primary outcome for our analysis was mortality at 28 days after enrollment in the study in relation to the BMI and presence or absence of history of DM. The secondary outcome was 60 days mortality in relation to these two variables.

Statistical analysis

We assessed the independent prognostic role of BMI in this analysis. The primary clinical endpoint for this analysis is the 28-day mortality. Patients who were discharged home and breathing without mechanical ventilation were assumed to be alive at day 28. The secondary clinical endpoints are 60-day mortality, and overall survival (OS) defined as time from enrollment to death due to any reason. Patient baseline characteristics across six studies were reported descriptively. The association between various patient characteristics and BMI were evaluated with chi-square test for categorical variables and an analysis of variance (ANOVA) for continuous variables. If the large sample assumption or normality does not hold, the Fisher's exact test for categorical and Kruskal–Wallis test for continuous variables were used. Multivariable logistic regression was used as primary analysis to evaluate the potential independent prognostic role of BMI. The model was adjusted for baseline covariates including APACHE III, age, gender, ethnic (white, black, and other), vasopressor use, cause of Lung Injury (Pneumonia, Severe Sepsis, Aspiration, Trauma, and Others), Lung Injury Score, DM, cancer status, and study ID. In our previous study, cancer was identified as an important independent prognostic factor for 28-day mortality after adjusting for the APACHE III score.[26] Hence, cancer status was included as one of the covariates in our multivariable logistic model as well. For the secondary endpoints, the logistic regression for 60-day mortality and the Cox regression model for OS were performed, and adjusted for the same set of covariates as the analysis for primary endpoint. The Kaplan–Meier analysis was used for plot and for estimating median OS. Log-rank test was used for evaluating the difference of OS among the subgroups of BMI.

Because of missing values in our set of covariates, all the multivariable regression analyses were carried out in two parallel sets: one only with subjects that have complete data; the other with imputed missing values. The multiple imputations used the fully conditional specification (FCS) method which assumed the