Morbid Obesity in the Medical ICU*

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Study objective: **To describe the clinical course, complications, and prognostic factors of morbidly obese patients admitted to the ICU compared to a control group of nonobese patients.**
Design: **A retrospective study.**
Setting: **Two university-affiliated hospitals.**
Methods: **We reviewed the medical records of 117 morbidly obese patients (body mass index ≥ 40 kg/m^2) admitted to the medical ICU between January 1994 and June 2000. Data collected included demographic information, comorbid condition, APACHE (acute physiology and chronic health evaluation) II score, invasive procedures, organ failure, and in-hospital mortality.**
Results: **Obstructive airway disease, pneumonia, and sepsis were the main reasons for admission to the ICU in the morbidly obese group. Sixty-one percent of the morbidly obese patients and 46% of the nonobese group required mechanical ventilation (p = 0.02). The mean lengths of mechanical ventilation and ICU stay were significantly longer for the morbidly obese group (7.7 ± 9.6 days and 9.3 ± 10.5 days vs 4.6 ± 7.1 days and 5.8 ± 8.2 days, respectively; p < 0.001). APACHE II scores were not significantly different in the two groups (19.1 ± 7.6 and 20.6 ± 12.2; p = 0.6). Overall mortality was 30% for the morbidly obese patients and 17% for the nonobese group (p = 0.019). By multivariate analysis, multiorgan failure (odds ratio [OR], 4.6; 95% confidence interval [CI], 2.1 to 16.6), Pa_{O_2}/fraction of inspired oxygen < 200 for > 48 h (OR, 2.3; 95% CI, 1.2 to 7.8), and depressed left ventricular ejection fraction < 40% (OR, 1.4; 95% CI, 1.03 to 13.8) were independently associated with ICU mortality in the morbidly obese group.**
Conclusion: **We conclude that critically ill morbidly obese patients are at increased risk of morbidity and mortality compared to the nonobese patients.**

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Key words: APACHE II; central venous access; ICU; mortality; obesity; outcome; mortality

Abbreviations: APACHE = acute physiology and chronic health evaluation; BMI = body mass index; CI = confidence interval; F_{IO_2} = fraction of inspired oxygen; LVEF = left ventricular ejection fraction; MOF = multiorgan failure; OR = odds ratio; SIRS = systemic inflammatory response syndrome

Obesity is associated with a host of adverse health outcomes and imposes considerable strains on the US health-care system.[1,2] In 1986, the economic costs of illness associated with being overweight were estimated to be > $39 billion.[3] The prevalence of obesity has been increasing steadily since 1960 when the first National Health and Nutrition Examination Survey was conducted.[4] The most recent survey has indicated that 34.9% of the US adult population is considered to be overweight and 2.9% to be morbidly obese.[5,6] Furthermore, the prevalence of obesity is reported to be three times higher in the United States than France and one and a half times that of England.[6]

Obesity has been linked to increased morbidity and mortality resulting from acute and chronic medical problems, including noninsulin diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, gallstones, cholecystitis, arthritis, and certain forms of cancer.[1] It is speculated that morbid obesity increases the incidence of complications in patients requiring intensive care and that these complications are associated with prolonged[1] hospital stay and poor outcome. However, very few data on critically ill obese patients have been collected, and ICU survival statistics are not available for this particular subset of the population. Two reviews[7,8] acknowledged the lack of studies addressing the impact of obesity on

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ICU outcome. Hence, we conducted a retrospective study to test the hypothesis that morbidly obese critically ill patients are at an increased risk of morbidity and mortality, and to identify discriminant prognostic factors of survival using multivariate analysis.

Materials and Methods

Patients

After obtaining Institutional Review Board approval from the University at Buffalo, we have reviewed the medical records of all hospitalized morbidly obese adults patients admitted to the medical ICUs of two university affiliated hospitals. Both hospitals (Erie County Medical Center and the Buffalo General Hospital) are tertiary-care centers with separate medical and surgical ICUs managed by house-staff and critical-care attending physicians. The degree of obesity was assessed by the body mass index (BMI), which is the ratio of weight (in kilograms) to height (in meters squared). Morbidly obese patients were defined as those with BMI ≥ 40 kg/m^2. Patients were identified by cross-referencing our demographic ICU database from January 1994 to June 2000 with the International Classification of Diseases codes listing all obesity categories. Computer-generated random numbers were used to select the nonobese group sample (BMI < 30 kg/m^2) in proportion to the number of morbidly obese patients over the same time period. Patients who remained in the ICU for < 24 h were not included in the study. The admissions comprised of inpatient transfers and emergency department admissions. For those patients with more than one ICU admission during the study period, only the first ICU admission was included in the analysis to ensure independence of observations.

Data Abstraction and Variable Definition

The data collected were of two categories: demographic and ICU related. Demographic data included age, gender, height, weight, ICU admitting diagnosis, smoking history, recent drug abuse, and comorbid conditions (Table 1).

ICU-related data included date of admission to the ICU, length of ICU stay, date and length of mechanical ventilation, and the most deranged values related to vital signs (temperature, heart rate, respiratory rate, and BP), laboratory data (arterial blood gas, serum sodium, potassium, chloride, bicarbonate, creatinine, bilirubin, lactate dehydrogenase, liver function tests, CBC count, prothrombin and prothromboplastin time), and Glasgow coma scale for each ICU day. The weaning period was assessed from the time a written order was documented in the medical record until the patient was liberated from mechanical ventilation. APACHE (acute physiology and chronic health evaluation) II scores were computed retrospectively for the first day of admission to the ICU. All invasive and noninvasive procedures, and related complications were also recorded. A catheter-related bacteremia was defined as the isolation of the same species of microorganisms on semiquantitative culture of the catheter and from blood cultures obtained by separate venipuncture.

The development of organ failure was identified according to the following manner[9]: liver failure, a serum bilirubin level > 6 mg/dL and a prolongation of the prothrombin time at least 4 s greater than the control; renal failure, a serum creatinine level > 3.4 mg/dL, the need for hemodialysis or peritoneal dialysis; respiratory failure, the need for intubation and mechanical ventilation; hematologic failure, a WBC count $< 2.0/\mu$L and/or platelet count $< 40{,}000/\mu$L; neurologic failure, a Glasgow coma scale score < 8 for > 24 h in the absence of sedatives, analgesics, or neuromuscular blockade; cardiovascular failure, the need for dobutamine or vasopressors (norepinephrine, or epinephrine at any dose, or dopamine at > 8 μg/kg/min); GI failure, documented GI bleed associated with a drop in hematocrit, pancreatitis, or bowel obstruction preventing enteral feeds for at least 48 h. Multiorgan failure (MOF) was defined as the presence of three or more organ failures.

Table 1—*Definition of Comorbidities*

Organ or System	Definitions
Cardiac	Abnormal cardiac catheterization, a positive stress test finding for ischemia, or if a treatment is being provided for coronary artery disease, or congestive heart failure
Pulmonary	Presence of pulmonary hypertension, defined as mean pulmonary artery pressure of ≥ 25 mm Hg documented by echocardiography or right-heart catheterization, or if a treatment is being provided for obstructive lung disease, or interstitial lung disease
Renal	Preexisting renal disease with documented abnormal creatinine level prior to hospitalization
Hepatic	Preexistent chronic viral hepatitis or liver cirrhosis
Endocrine	Documented or receiving treatment for hypercholesteremia, hypertriglyceridemia, or diabetes mellitus
CNS	Presence of symptomatic acute or chronic vascular or nonvascular encephalopathy
Neoplastic	Presence of active malignancy (solid tumor or hematologic malignancy) at the time of presentation
Immune system	Use of steroids at a dose ≥ 20 mg/d for > 2 mo, HIV infection with CD4 count < 200 cells/μL, neutropenia with absolute neutrophil count $< 1{,}000$ cells/μL, or the use of cytotoxic drugs

Systemic inflammatory response syndrome (SIRS), sepsis, and septic shock were defined according to the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference.[10] ARDS was defined according to the American-European Consensus Conference.[11] The causes of respiratory failure were classified into four subtypes. Type 1 is acute hypoxic respiratory failure referred to any alveolar-filling pathology present on chest radiography associated with impaired gas exchange (*eg*, pulmonary edema, ARDS, pneumonia). Type 2 is hypercapnic respiratory failure referred to any process associated with excessive respiratory load, impaired neuromuscular function, or a decreased ventilatory drive (*eg*, obstructive lung disease, obesity hypoventilation, muscle weakness). Type 3 is metabolic respiratory failure referred to any state of severely deranged acid-base disorder leading to the need of mechanical ventilation. Type 4 is airway protection-related respiratory failure. Type 4 respiratory failure was not considered evidence of organ dysfunction. If the cause of respiratory failure was multifactorial, the patient was classified by the primary reason for intubation and mechanical ventilation as discerned from the ICU progress notes. The immediate cause of death and code status with regard to "do not resuscitate" orders were noted.

Medical records were reviewed by two separate data extractors experienced in critical-care chart abstraction. Information from charts was logged onto a standardized computer data collection form. Interobserver quality control was assessed by having an associate coordinator re-enter 10% random sample of enrolled subjects. The spreadsheet of the original and quality control was evaluated using the κ statistic.[12] All κ values ≥ 0.75 are considered excellent agreement beyond chance; values < 0.4 are considered poor agreement beyond chance; values between 0.4 and 0.75 represent fair-to-good agreement beyond chance. The interobserver agreement for this study was κ = 0.85 (95% confidence interval [CI], 0.64 to 0.97).

Statistical Analysis

Parametric interval data were analyzed using a two-tailed Student's *t* test. These data are reported as mean ± SD. Nonparametric data were examined using a Mann-Whitney *U* test or Kruskal-Wallis test as appropriate. Nominal data were analyzed by χ^2 analysis with Yates continuity correction or Fisher's Exact Test where appropriate. A multiple linear regression was used to evaluate differences in length-of-stay variables (days on the ventilator and in the hospital) after controlling for gender, number of comorbidities, and APACHE II scores in obese and nonobese patients. These covariates were selected because they may act as confounders of the relation between severity of illness and length of stay. Then, we conducted a forward stepwise logistic regression to ascertain which factors contributed independently to mortality, with hospital death as the dependent variable, and the retrospectively identified independent variables including gender, APACHE II score, BMI, and comorbidities. Another analysis was performed on the group of 117 patients using those variables found significant at p < 0.10 in univariate analysis, with in-hospital mortality as the dependent variable. Pairwise correlations between predictor variables and the variance inflation factor were computed to assess for multicollinearities according to the method described by Slinker and Glantz.[13] As for influential observations, no patients with outlier values in any variable were detected. Mortality odds ratios (ORs) were expressed with their 95% CIs. A p value < 0.05 was considered significant. All statistical analyses were performed using software (SPSS, version 10.0; SPSS; Chicago, IL).

Results

Demographic Characteristics

There were 132 critically ill morbidly obese patients admitted to the ICU of 9,727 ICU admissions between January 1994 and June 2000. Three patients remained in the ICU for < 24 h, and 12 patients had more than one hospital admission, leaving 117 patients eligible for analysis. Nine of 117 (8%) patients were transferred from the medical wards of the same hospital, and 108 patients (92%) were admitted from the emergency department. In the nonobese group, 14 patients (11%) were in-hospital transfers, 3 patients (2%) were from outlining hospitals, and 115 patients (87%) came through the emergency department. Table 2 displays the demographic characteristics of the critically ill morbid obese patients in comparison to the nonobese group.

There were 19 morbidly obese and 23 nonobese patients, respectively, in the 21- to 30-year age group, 47 morbidly obese and 44 nonobese patients in the 31- to 40-year age group, 32 morbidly obese and 35 nonobese patients in the 41- to 50-year age group, 19 morbidly obese and 30 nonobese patients in the 51- to 60-year age group, and 1 morbidly obese and 2 nonobese patients in the ≥ 60-year age group. There were no age or gender differences between the two groups; however, patients in the morbidly obese group had significantly higher prevalence of cardiac, pulmonary, and endocrine comorbidities (Table 2). The presence of hypertension and sleep-related disorders were more commonly reported in the morbidly obese group compared to the nonobese group. Seventy-seven patients (66%) in the morbidly obese group were being treated for hypertension, and 18 patients (15%) were prescribed continuous positive airway pressure for documented obstructive sleep apnea. In contrast, 39 of the patients in the nonobese group (29%) had a history of elevated BP, while none had documented sleep-related disorders (p < 0.001). Immunodeficiency was more frequently denoted in the nonobese group: 11 patients (8%) vs 1 patient (1%) [p < 0.014]. This observation is attributed mainly to the presence of eight patients with AIDS in the nonobese cohort.

Table 2—*Demographic Characteristics and Comorbidities of the Critically Ill Morbidly Obese Patients and the Nonobese Group**

Variables	Morbidly Obese (n = 117)	Nonobese (n = 132)	p Value
Male/female gender, No.	51/66	73/59	0.09
Age, yr	44.4 ± 18.2	46.2 ± 21.7	0.8
BMI	51.3 ± 25.9	27.6 ± 3.1	< 0.001
Current smoker	23 (18)	38 (29)	0.127
IVDA	7 (6)	27 (20)	0.002
Comorbid illnesses			
Cardiac			
Coronary artery disease	35 (30)	17 (13)	0.002
Congestive heart failure	6 (5)	2 (2)	0.2
Pulmonary			
Obstructive lung disease	38 (32)	24 (18)	0.01
Pulmonary hypertension	18 of 78 (23)	2 of 65 (3)	0.014
Endocrine			
Diabetes mellitus	61 (52)	11 (8)	< 0.001
Hypertriglyceridemia	28 (24)	6 (5)	0.001
Hepatic			
Cirrhosis	1 (1)	9 (7)	0.038
Neurology	4 (3)	7 (5)	0.68
Immunosuppression	1 (1)	11 (8)	0.014
AIDS	0	8 (6)	0.02

*Data are presented as mean ± SD or No. (%) unless otherwise indicated. IVDA = IV drug abuser.

ICU Course

The reasons for ICU admission, the need for mechanical ventilation, and the associated mortality for the morbidly obese and the nonobese groups are provided in Table 3. Pneumonia and reactive airway disease were the main reasons for ICU admission in both groups. No predominant pathogen was responsible for the cases of infectious pneumonitis, nor was there a characteristic radiographic pattern that would characterize one group from the other. Asthma was the predominant disorder of the reactive airway disease in the morbidly obese group (10 of 14 patients; 71%), whereas COPD was the prevalent disorder in the nonobese group (11 of 13 patients; 84%).

Respiratory failure occurred in 71 of 117 patients (61%) in the morbidly obese group and in 61 of 132 patients (46%) in the nonobese group ($p = 0.02$). Figure 1 displays the causes of respiratory failure in both cohorts by subtypes. Only, type 4 respiratory failure was more commonly observed in the nonobese group compared to the obese patients ($p = 0.1$).

Durations of Mechanical Ventilation, ICU, and Hospital Stay

The hospital length of stay was significantly longer for patients in the morbidly obese group (17.7 ± 19.8 days) compared to patients in the nonobese group (11.3 ± 10.8 days; $p = 0.007$). Similarly, the ICU length of stay and the duration of mechanical ventilation were significantly longer for the morbidly obese patients (9.3 ± 13.5 days and 7.7 ± 10.6 days, respectively) in comparison to the nonobese cohort (5.8 ± 8.2 days and 4.6 ± 7.1 days, respectively) [$p = 0.007$ and $p = 0.0004$, respectively]. Moreover, morbidly obese patients required a longer "weaning" time off mechanical ventilation compared to the control group (3.2 ± 6.5 days and 1.8 ± 3.7 days, $p = 0.009$), and oxygen requirements during hospital stay were significantly higher in the obese group (fraction of inspired oxygen [FIO_2], 38.4 ± 15.6%) than their counterpart (FIO_2, 31.1 ± 12.6) [$p < 0.001$]. After we used multiple linear regression to control for gender, comorbidities, and APACHE II scores, BMI was the only significant independent determinant of the time difference spent on the ventilator between the morbidly obese and the nonobese group ($\beta = 0.337$; 95% CI, 0.183 to 0.657; $p = 0.03$).

In-hospital Mortality

The in-hospital mortality rate was 30% (35 of 117 patients) in the morbidly obese group and 17% (22 of 132 patients) in the nonobese group ($p = 0.02$). The immediate causes of death in the morbidly obese group were bacterial infections in 17 patients; right ventricular failure in 5 patients; acute pancreatitis in 4 patients; pulmonary embolus in 2 patients; congestive heart failure in 3 patients; and intracranial hemorrhage, liver failure, renal failure, Stevens-Johnson syndrome each in 1 patient. A "do not resuscitate" order was written for 9 patients (8%) in the morbidly obese group during the course of their hospitalization, compared to 14 of the nonobese patients (11%). None of the obese patients had prior advance directives before the ICU admission.

The in-hospital mortality rate of morbidly obese patients requiring mechanical ventilation was 49%

Table 3—*Reasons for ICU Admission, Need for Mechanical Ventilation, and Associated Mortality of Critically Ill Morbidly Obese and Nonobese Patients**

Variables	Morbidly Obese Patients (n = 117)	Morbidly Obese MV (n = 71)	Morbidly Obese Mortality (n = 35)	Nonobese Patients (n = 132)	Nonobese MV (n = 61)	Nonobese Mortality (n = 22)
Pneumonia	15 (13)	12	5	22 (17)	12	3
ARDS	6 (5)	6	5	5 (4)	5	2
RAD	14 (12)	6	2	13 (10)	9	1
Pulmonary edema	13 (11)	9	2	0	0	0
Cor pulmonale	11 (9)	5	3	0	0	0
Sepsis	13 (11)	11	7	10 (7)	6	3
Acute renal failure	9 (8)	3	1	6 (5)	1	0
Acute pancreatitis	9 (8)	6	4	3 (2)	1	1
Drug overdose	6 (5)	4	0	15 (11)	10	1
Pulmonary embolus	5 (4)	2	2	4 (3)	1	1
Hyperglycemia	5 (4)	1	0	11 (8)	0	0
CVA	3 (3)	2	1	4 (3)	2	1
Liver failure	2 (2)	2	1	11 (8)	6	7
GI bleed	1 (1)	0	0	9 (7)	0	0
Malignancies	0	0	0	5 (4)	2	1
Other	5 (4)	2	2	14 (11)	6	1

*Data are presented as No. (%) or No. MV = mechanical ventilation; CVA = cerebrovascular accident; RAD = reactive airways disease.

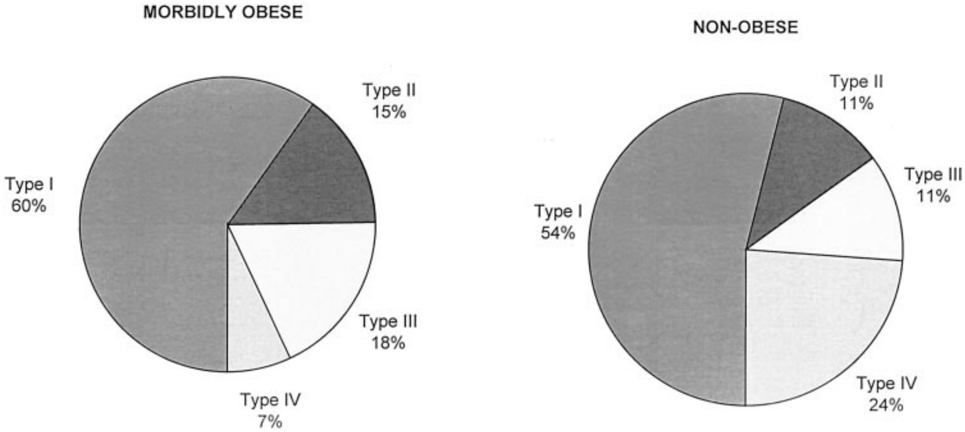

FIGURE 1. Comparison of the causes of respiratory failure by subtypes between the morbidly obese and the nonobese group. Type 1, acute hypoxic respiratory failure; type 2, hypercapnic respiratory failure; type 3, metabolic respiratory failure; type 4, airway protection-related respiratory failure.

(35 of 71 patients). Nineteen of the 40 obese patients (48%) who received mechanical ventilation for pulmonary disorders died, compared to 16 of 31 patients (52%) in the same group who required mechanical ventilation for nonpulmonary disorders ($p = 0.91$). In contrast, the in-hospital mortality for morbidly obese patients with documented depressed left ventricular ejection fraction (LVEF) < 40% was 55% (12 of 22 patients), compared to 26% (17 of 65 patients) for those with LVEF ≥ 40% ($p = 0.03$). In the multiple logistic regression, APACHE II score (OR, 1.11; 95% CI, 1.04 to 1.18), cirrhosis (OR, 3.45; 95% CI, 1.69 to 5.82), and BMI (OR, 1.58; 95% CI, 1.13 to 2.22) were all independent predictors of hospital death.

SIRS developed in 61 of the 117 morbidly obese patients (52%). The most common causes of SIRS were infection, which accounted for 45 of the 61 cases (74%), and acute pancreatitis, which was responsible for 9 of the 61 cases (15%). One or more organ failures occurred in 89 of the 117 hospital admissions (76%). The distribution of organ failures is presented in Table 4. The median number of organ failures in those who survived was one, compared to three organ failures in those who died during hospitalization (Table 5).

Invasive Procedures and Complications

Central venous access was present in 103 of 117 morbidly obese patients (88%) and in 60 of 132 nonobese patients (45%; Table 6). The subclavian approach was more likely to be attempted in the morbidly obese group: 48 of 103 patients (47%) compared to 9 of 60 patients (15%) in the nonobese group ($p < 0.001$). Cannulation of the femoral veins was the most common site of access to the central circulation in the nonobese group (23 of 60 patients; 38%) and the third-most-common accessed route in the morbidly obese group (19 of 103 patients; 18%). A pulmonary artery catheter was inserted in 21 of 117 morbidly obese patients (18%), compared to 11 nonobese patients (8%). The indication for insertion in the obese group was homeostatic failure including shock in 13 patients, ARDS in 5 patients, and oliguria unresponsive to fluid challenge in 3 patients. There was no significant difference in the rate of complications between the two groups regarding

Table 4—*Distribution of Organ Failure in the Study Population**

Organ Failure	Morbidly Obese	Nonobese
Pulmonary	71 (61)	61 (46)
Cardiovascular	43 (37)	29 (22)
Renal	28 (24)	17 (13)
GI	14 (12)	21 (16)
Liver	6 (5)	12 (9)
Hematologic	3 (3)	6 (5)
CNS	2 (2)	4 (3)

*Data are presented as No. (%).

Table 5—*Organ Failures and Associated Mortality in the Study Population**

Organ Failures	Morbidly Obese		Nonobese	
	Patients	Mortality	Patients	Mortality
0	19	1 (5)	13	0
1	35	2 (6)	26	1 (4)
2	32	11 (34)	54	6 (11)
3	23	15 (65)	25	5 (20)
4	7	6 (86)	11	7 (64)
5	1	1 (100)	3	3 (100)

*Data are presented as No. or No. (%).

Table 6—*Catheter-Related Procedures and Complications**

Variables	No.	Pneumothorax, No.	Catheter-Related Bacteremia, No.	Duration of Catheterization, days
Morbidly obese (n = 117)				
Swan-Ganz	21	0	2 (9)	8.3 ± 6.5
Central line	82	2	9 (11)	13.6 ± 14.8
Arterial line	13	0	0	7.4 ± 5.4
Nonobese (n = 132)				
Swan-Ganz	11	0	0 (0)	5.1 ± 2.5
Central line	49	0	2 (4)	6.3 ± 8.4
Arterial line	4	0	0	3.6 ± 1.8

*Data are presented as No. (%) or mean ± SD unless otherwise indicated.

pulmonary artery cannulation. Similarly, the incidence of pneumothorax was comparable between the two groups in cannulation of the central venous circulation.

The duration of arterial and venous catheterization was significantly longer for the morbidly obese group in contrast to the nonobese group (Table 6). The most cited reasons for the prolonged central venous catheterization were lack of IV access and the administration of IV antibiotics. Eleven of 103 morbidly obese patients 10% had a catheter-related bacteremia, compared to 2 of 60 nonobese patients (3%; $p = 0.1$). *Staphylococcus epidermidis* and *Staphylococcus aureus* accounted for 9 of the 13 catheter-related infections. *Candida albicans* was responsible for two cases, and *Escherichia coli* and Enterobacter species were responsible for one case each. Two patients in the morbidly obese group had catheter-related septicemia with fever > 38°C, hypotension, and oliguria necessitating inotropic support.

Fourteen of 117 morbidly obese patients (12%) underwent tracheostomy during the ICU stay, while only 5 of the nonobese patients (4%) had the same procedure ($p = 0.03$). Three of the 14 patients with morbid obesity had history of obstructive sleep apnea, and 2 patients showed evidence of hypercarbia prior to their ICU admission.

Table 7—*Relationship Between Observed and APACHE II-Predicted Mortality in the Morbidly Obese Group*

Predicted Mortality, %	Patients, No.	Observed Mortality, No. (%)
0–10	21	4 (19)
11–20	29	8 (28)
21–30	27	8 (30)
31–40	15	3 (20)
41–50	11	5 (45)
51–60	5	2 (40)
61–70	6	2 (33)
71–80	2	2 (100)
81–90	0	0 (0)
91–100	1	1 (100)

Table 8—*Predictors of Mortality by Logistic Regression Analysis*

Independent Variables	p Value	OR (95% CI)
MOF	0.003	4.6 (2.1–16.6)
$PaO_2/FIO_2 < 200$ for > 48 h	0.02	2.3 (1.2–7.8)
LVEF < 40%	0.04	1.7 (1.1–13.4)
SIRS	0.09	
APACHE II score	0.17	
Bilirubin	0.33	

Determinants of Outcome

There was no significant difference in the APACHE II scores of critically ill morbidly obese patients (19.1 ± 7.6) compared to the nonobese group (20.6 ± 12.2) [$p = 0.6$]. The APACHE II scores of survivors for the morbidly obese and the nonobese group were 16.3 ± 4.7 and 14.9 ± 8.2, respectively, while the APACHE II scores for nonsurvivors were 31.2 ± 10.5 and 44.1 ± 9.8 ($p < 0.001$ and $p < 0.001$, respectively). However, the predicted mortality of survivors in the morbidly obese group was not significantly different from nonsurvivors (27% and 41%; $p = 0.09$) in contrast to the nonobese group, in which the predicted mortality of survivors was significantly lower compared to nonsurvivors (22% and 68%; $p < 0.0001$). The relationship between the observed mortality and the APACHE II predicted mortality is listed in Table 7.

By univariate analysis, seven variables were significantly associated with mortality ($p < 0.1$). After adjusting for multicollinearity, six variables were entered into the logistic regression analysis: LVEF < 40%, $PaO_2/FIO_2 < 200$ for > 48 h, SIRS, APACHE II score, MOF, and serum bilirubin. The use of vasopressors was removed due to interdependence with the other variables. Table 8 summarizes the results of the logistic regression. When used in place of serum bilirubin, neither the duration of mechanical ventilation ($p = 0.22$) nor the ICU length of stay ($p = 0.57$) was significantly related to in-hospital mortality.

Discussion

This study, one of the largest unicenter studies, including 117 consecutive hospitalized patients, provides a comprehensive insight about the morbidity and mortality of the critically ill morbidly obese patients in the ICU. The main findings were as follows: (1) critically ill morbidly obese patients have higher ICU mortality compared to nonobese patients, (2) morbidly obesity is associated with prolonged mechanical ventilation and extended "weaning" period, (3) MOF remains the best predictor of ICU mortality in critically ill morbidly obese patients, and (4) assessment of severity of illness by general scoring system is insufficient in predicting hospital outcome.

The first objective of this study was to examine the mortality of critically ill morbidly obese patients admitted to the medical ICU compared to a group of nonobese patients. The results of our series of 249 patients indicated a significant increase in mortality for those patients with BMI $\geq$ 40 kg/m^2 compared to those with BMI $<$ 30 kg/m^2. This was not surprising given the higher number of comorbidities in the morbidly obese group known to be associated with poor prognosis. Numerous epidemiologic studies have pointed to the association between mortality and increasing BMI in all age groups and for all categories of death.[14–16] The adverse effect of weight on longevity was clearly demonstrated in the Framingham study,[14] in which the mortality rate for overweight nonsmoking men was 3.9 times higher than those for nonsmoking who were at desirable weight. Yet, outcome data from critically ill morbidly obese patients are not widely available. There have been only a limited number of studies addressing ICU mortality of critically ill obese patients; the majority reflects the surgical experience. Smith-Choban and colleagues[17] reviewed the records of 184 patients with blunt trauma. The observed mortality for those with BMI $>$ 31 kg/m^2 was 42.1% compared to 5% and 8% for the average (BMI, $<$ 27 kg/m^2) and the overweight (BMI, 27 to 31 kg/m^2), although the groups did not differ in age, injury severity score, or time of mechanical ventilation. Respiratory failure attributed to ARDS was the primary factor responsible for the increased mortality in that group. A similar conclusion was also reported in patients undergoing liver transplantation, for whom morbid obesity was associated with increased incidence of wound infection and early death from multisystem organ failure.[18]

In this context, one of the significant findings of this study relates to the impact of morbid obesity on the respiratory system. The prolonged time of mechanical ventilation and the higher oxygen requirement reflect the myriad of physiologic alterations in pulmonary function described in obese subjects. Studies[19,20] of conventional respiratory function tests have uniformly showed a reduction in functional residual capacity due to the effect of abdominal contents on the diaphragm. This leads to a reduced expiratory volume in the face of a fixed residual volume. In consequence, ventilation at the lung bases is diminished causing a pronounced ventilation perfusion abnormality, and arterial hypoxemia, particularly in the supine position.[21,22] Vaughan and coworkers[23] have noted that obese patients have a significant preoperative reduction in PaO_2 that tends to worsen during and in the postoperative phase.

Liberation from mechanical ventilation is also delayed in morbidly obese patients due to increased work of breathing resulting from increased airway resistance, abnormal chest elasticity, and inefficiency of the respiratory muscles. Sharp and associates[24] have shown that the mechanical work needed to passively ventilate subjects weighing $\geq$ 114 kg is two to four times that required for lighter individuals. The extra work in moving the chest is attributed to a decrease in chest wall compliance associated with the obese subject's accumulation of fat in and around the ribs, the diaphragm, and the abdomen.[25] Burns and colleagues[26] have suggested that the reverse Trendelenburg position at 45° can facilitate the weaning process by allowing a larger tidal volume and lower respiratory rate.

Because of the altered drug pharmacokinetics associated with obesity, the observed differences in ventilatory period and weaning time could be explained potentially by the type or the extended effect of sedatives used during the course of the ICU stay. In particular, benzodiazepines are widely distributed throughout body tissues because of their high lipophilicity. Elimination half-lives and their active metabolites are usually prolonged, and dosing recommendations for these drugs in this subset of population are often nonexistent. In the current study, sedation was maintained primarily with lorazepam, making unlikely that the observed differences in duration of mechanical ventilation and weaning trials were related to the use of different type of sedatives. Nevertheless, further prospective investigations are needed to define the optimal usage and appropriate monitoring of sedation of the critically ill morbidly obese patient.

Our multivariate analysis has indicated that the PaO_2/FIO_2 ratio of $<$ 200 for $>$ 48 h is an independent risk factor for mortality. Several investigators have emphasized that statistical comparisons of the PaO_2/FIO_2 ratio of ARDS survivors and nonsurvivors were not significant on the first day,[27,28] and these reports are consistent with our univariate analysis where the mean PaO_2/FIO_2 in the first 24 h of survivors was 181 $\pm$ 67 and 159 $\pm$ 52 in the obese nonsurvivors, respectively ($p = 0.4$). Bone and colleagues[29] found, however, that the PaO_2/FIO_2 ratio became significantly higher in survivors only after > 24 h of conventional mechanical ventilation.

Complications from indwelling vascular catheters in the morbidly obese group have been considered to occur more frequently than the nonobese group. The loss of anatomic landmarks, and the increase in the depth of insertion to access venipuncture have been cited as potential reasons for catheter malposition, and local puncture complications. Yet, there has been no well-designed comparative study, to our knowledge, to address the rate of complication from central venous catheters in this particular group. In the current study, we found no significant difference in complications attributed to the cannulation of the central venous circulation between the two groups although the subclavian and the internal jugular vein catheterization were more commonly attempted in the morbidly obese group (82% vs 62% in the nonobese group). The use of a small-bore "locator" needle[30,31] and the application of Doppler ultrasound-guided technique are likely to have contributed to the low complication rates. Similarly, the rate of infectious complications was not significantly different between the two groups even though there was a trend toward a higher rate of infection in the morbidly obese group. It is thought that to the greater number of skin punctures during catheter insertion and particularly, the extended duration of catheterization in the obese group are plausible explanation for this observation.

Objective and accurate estimation of outcome is needed more than ever, particularly in a high-risk and high-cost environments such as the ICU. The APACHE III,[32] the simplified acute physiologic score II,[33] and the mortality probability model II[34] represent the most current and updated scoring systems available to predict mortality for adult ICU patients. All these scores were developed using large patient databases. Yet, morbid obesity was not considered in the list of comorbid variables in the development of these scoring systems. Thus, their prediction may be effective only in patients from cohorts similar to those in the original database. The lack of difference between the predicted mortality of survivors and nonsurvivors in the morbidly obese group albeit a significant variance in the APACHE scores emphasizes the concept that differences in patient demographics may influence the behavior of these predictive models,[35,36] and underscores the need for a multicenter study to assess the accuracy of these models in predicting outcome of critically ill morbidly obese patients.

We acknowledge that the study has several limitations that warrant further discussion. First, the control subjects were not selected necessarily in close temporal proximity to the morbidly obese patients; however, they were evenly distributed across the time span of the study period, which might balance seasonal variations or changes in ICU treatments. Second, this was a retrospective study, with all the inherent methodologic problems associated with this type of evaluation of clinical data. Yet, the κ value indicated that interobserver variability was unlikely to have contributed to the significant differences between the two cohorts. Third, individual differences in ICU practices and variation in interhospital policies could not be excluded as potential confounding factors for the observed differences in ICU related data. These individual differences are usually related to varying thresholds applied by physicians in their approach to mechanical ventilation, weaning trials, and their use of invasive procedures. Fourth, the size of the study population was relatively small to assess a dose-response correlation between BMI and mortality, but this is the largest study, to our knowledge, to address the impact of morbid obesity on ICU outcome. Finally, an inescapable limitation of any outcome study is the dynamic nature of the system that makes the observed outcome vulnerable to change in response to new treatment modalities.

In conclusion, we have presented the first report of ICU outcome in critically ill morbidly obese patients compared to a group of nonobese patients. We have observed a substantially higher mortality in these patients and have identified several variables independently associated with mortality. With the rising prevalence of obesity in the US population, future research should focus on implementing strategies designed to reduce organ dysfunction and long-term complications during ICU stay.

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