Intensive Care Med (2009) 35:1152–1170
DOI 10.1007/s00134-009-1424-5

REVIEW

Charles W. Hogue Jr
Joshua D. Stearns
Elizabeth Colantuoni
Karen A. Robinson
Tracey Stierer
Nanhi Mitter
Peter J. Pronovost
Dale M. Needham

The impact of obesity on outcomes after critical illness: a meta-analysis

Received: 12 September 2008
Accepted: 16 November 2008
Published online: 3 February 2009

C. W. Hogue Jr · J. D. Stearns · E. Colantuoni · T. Stierer · N. Mitter · P. J. Pronovost
Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Medical Institutions, Baltimore, USA

C. W. Hogue Jr (✉)
Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Hospital, 600 N. Wolfe St, Tower 711, Baltimore, MD 21287, USA
e-mail: chogue2@jhmi.edu
Tel.: +1-410-6141516
Fax: +1-410-9550994

D. M. Needham
Division of Pulmonary and Critical Care Medicine, Department of Medicine, The Johns Hopkins Medical Institutions, Baltimore, USA

D. M. Needham
Department of Physical Medicine and Rehabilitation, The Johns Hopkins Medical Institutions, Baltimore, USA

K. A. Robinson
Department of Medicine, The Johns Hopkins Medical Institutions, Baltimore, USA

Abstract *Purpose:* To assess whether obesity is associated with mortality or other adverse intensive care unit (ICU) and post-ICU outcomes. *Methods:* A meta-analysis of studies from PubMed and EMBASE databases. *Results:* Twenty-two studies ($n = 88{,}051$ patients) were included. Pooled analysis demonstrated no difference in ICU mortality, but lower hospital mortality for obese and morbidly obese subjects (RR 0.76; 95% CI 0.59, 0.92; RR 0.83; 95% CI 0.66, 1.04, respectively) versus normal weight subjects. There was no association between obesity and duration of mechanical ventilation or ICU stay. Morbidly obese versus normal weight patients had longer hospitalizations. No study reported physical function, mental health, or quality of life outcomes after discharge. *Conclusions:* Obesity is not associated with increased risk for ICU mortality, but may be associated with lower hospital mortality. There is a critical lack of research on how obesity may affect complications of critical illness and patient long-term outcomes.

Keywords Intensive care · Critical illness · Mortality · Body weight · Meta-analysis

Introduction

Nearly one-third of intensive care unit (ICU) patients are obese and nearly 7% are morbidly obese, frequencies that are predicted to increase as the prevalence of obesity in the general population rises [1, 2]. Thus, understanding the consequences of obesity on critical illness has great public health importance. In the general population, obesity is associated with increased risk for mortality and excess costs of care [3, 4]. Although frequently studied as a chronic disease, the influence of obesity on acute illnesses is poorly understood. Given the rising prevalence of obese patients in ICUs, this issue is especially important in critical care.

Obesity is associated with multiple co-morbid conditions and physiologic derangements (e.g., pro-inflammatory state, insulin resistance), physical limitations, and pharmacokinetic alterations that may complicate acute illness and impede the implementation and/or efficacy of evidence-based interventions in the ICU [5, 6]. Nonetheless, little is known regarding the impact of obesity on short- and long-term outcomes from critical illness. We identified two systematic reviews that examined the role of obesity on ICU and hospital mortality [1, 2]. Akinnusi et al.

[1] reported that obesity [body mass index (BMI) ≥30 kg/m^2 of body surface area] was not associated with crude ICU mortality. Of note, in that meta-analysis, the reference group for comparisons was non-obese (BMI <30 kg/m^2) patients rather than normal weight patients. Prior studies suggest that the relationship between BMI and patient outcomes is “U” shaped [7–13] with worse outcomes for both underweight (BMI <18.5 kg/m^2) and morbidly obese (>40 kg/m^2) patients. Hence, inclusion of underweight patients in the reference group and morbidly obese patients in the obese group might conceivably bias the results. In their meta-analysis, Oliveros et al. [2] used a reference group of normal weight patients (BMI 18.5–24.9 kg/m^2), however, they combined data for ICU and hospital mortality. These investigators found a lower mortality for obese (BMI 30.0–39.9 kg/m^2), but not morbidly obese (BMI ≥40 kg/m^2) patients. There were inconclusive results from both studies on whether obesity or morbid obesity is associated with prolonged mechanical ventilation or extended ICU length of stay compared with non-obese or normal weight patients. Importantly, although the importance and study of long-term outcomes after critical illness has grown, whether obesity impacts these outcomes were not examined in these prior analysis [14–16].

Our objective was to perform a systematic review of the literature and meta-analysis to evaluate whether obesity impacts the risk for ICU or hospital mortality as well as long-term patient outcomes including physical function and quality of life compared with normal weight patients. We further sought to assess whether obesity affects the duration of mechanical ventilation, ICU and hospital length of stay, and ICU complications.

Methods

Data sources and searches

Relevant English-language publications were identified by searching PubMed and EMBASE databases (as of 10 March 2008) using text words and controlled vocabulary terms, including intensive care, critical care, critical illness, obesity and body weight. No limit by date was used in the search strategy. References from identified citations and relevant review articles were hand searched for additional eligible citations.

Study selection

Criteria for inclusion of publications in this systematic review were: (1) a quantitative comparison of outcomes between obese and non-obese subjects, (2) adult subjects (i.e., <16 years of age), and (3) subjects admitted to an ICU. Publications were excluded if: (1) there were no original data (e.g., review, commentary), (2) a full-length publication was not reported (e.g., abstract only) in a peer-reviewed journal, (3) obese adult ICU patients were not the primary focus, or (4) there were no data on mortality.

Based on these criteria, each title and/or abstract retrieved from the electronic database search was screened for eligibility independently by two of four reviewers (CH, JS, TS, NM). The full text of potentially eligible papers were independently reviewed by two investigators (CH, JS). For eligible publications, relevant data were abstracted. Data abstraction for methodological aspects of studies include: study design, sample size, and study quality (described later). Data on exposures and potential confounders included: definitions of weight categories evaluated (in kg/m^2), and severity of illness and organ dysfunction scoring. When available, data was collected on the following outcomes (including outcomes after hospital discharge when applicable): mortality rate in the ICU and hospital; duration of mechanical ventilation, ICU and hospital length of stay; presence of deep venous thrombosis, pulmonary embolism, systemic inflammatory response syndrome (SIRS), catheter-related blood stream infections, sepsis, and acute respiratory distress syndrome; acute renal failure; multiple organ failure; destination after hospital discharge; physical function and quality of life. The methodological quality of eligible studies was assessed using a modified Newcastle–Ottawa scale, a validated instrument designed to evaluate the quality of observational studies in systematic reviews and meta-analyses [17, 18]. Using this scale, methodology was evaluated in three domains: the selection of study groups, the comparability of groups, and the quality of ascertainment of either the exposures (for case–control studies) or of the outcomes (for cohort studies). In the event of unclear or missing data, attempts were made to contact the authors of the publication. Replies were received from the authors of four reports [8, 19–21].

Data synthesis

Because outcomes may vary for under-weight versus normal weight subjects, quantitative synthesis (i.e., meta-analysis) of the data was limited to those studies using a reference group of normal weight subjects, specifically excluding underweight patients (<18.5 kg/m^2). A Bayesian model was used to pool data across studies within weight categories while allowing for study to study differences in the outcome measures. Specifically, for ICU and hospital mortality, we extracted the total number of subjects and the number of deaths in each study and each weight category. For each study, this data was incorporated into a binomial regression model with a log link in order to model the log relative risk of mortality across the weight categories (normal weight as the reference group). These estimates of the log relative risk with the corresponding variance estimates represent the maximum likelihood estimates (MLEs) of the study specific associations between mortality and the weight categories. These MLEs were then incorporated into a two-stage normal–normal model in which we estimated a pooled log relative risk for each weight category (normal weight as the reference group) with corresponding 95% credible intervals (CI). We define a significant result to be a 95% CI that does not include a relative risk of 1. To evaluate statistical heterogeneity, we utilized the I^2 statistic which represents the proportion of total variation in the log relative risks that is attributable to heterogeneity across studies [22]. An I^2 of 0 indicates no heterogeneity in the true log relative risks across studies with all variation attributable to within-study statistical uncertainty. An I^2 close to 1 indicates large heterogeneity across studies which indicate large differences across the studies which may be due to mortality differences or inherent differences in the study populations, study designs, patient severity, etc. For duration of mechanical ventilation, and ICU and hospital stay, we extracted the mean and standard deviation duration for each study and each weight category. For studies that reported the durations of mechanical ventilation and ICU and hospital stay with only a range, rather than a standard deviation, we estimated the standard deviation by taking the largest difference between the mean and minimum/maximum and dividing by two. To address the potential effect of estimating the standard deviation, we performed a sensitivity analysis of the results excluding those studies which did not report the standard deviation. Thereafter the analysis of these non-mortality outcomes was completed in a similar fashion to analysis of mortality data. We define a significant result to be a 95% credible interval for the difference in mean duration that does not include zero. Statistical analyses were conducted using R (version 2.7.0) and WinBugs (version 1.4.3) software.

Results

The initial literature search retrieved 1,524 citations. Review of titles, abstracts, and full-length articles resulted in selection of 23 eligible publications (Fig. 1). The studies included 14 retrospective cohort, 6 prospective cohort, and 3 case control studies and they included a wide variety of critically ill patients and sample sizes (Table 1) [7–13, 19–21, 23–35]. The studies by Marik et al. [7] and Tremblay et al. [20] both obtained data from the Project IMPACT database and included significant overlap in the patients populations; hence, only the former study was included in the quantitative synthesis since it encompassed a larger sample size and reported more outcomes. Consequently, this review included data from 88,051 patients with the studies by Marik et al. [7] and Finkielman et al. [8] contributing 48,176 and 19,669 patients (77% of the total sample), respectively. Our assessment of the methodological quality of the cohort studies is provided in Table 2 and for case-control studies in Table 3. Only three of the cohort studies reported masking of the outcome assessor [7, 23, 34] and only four studies were

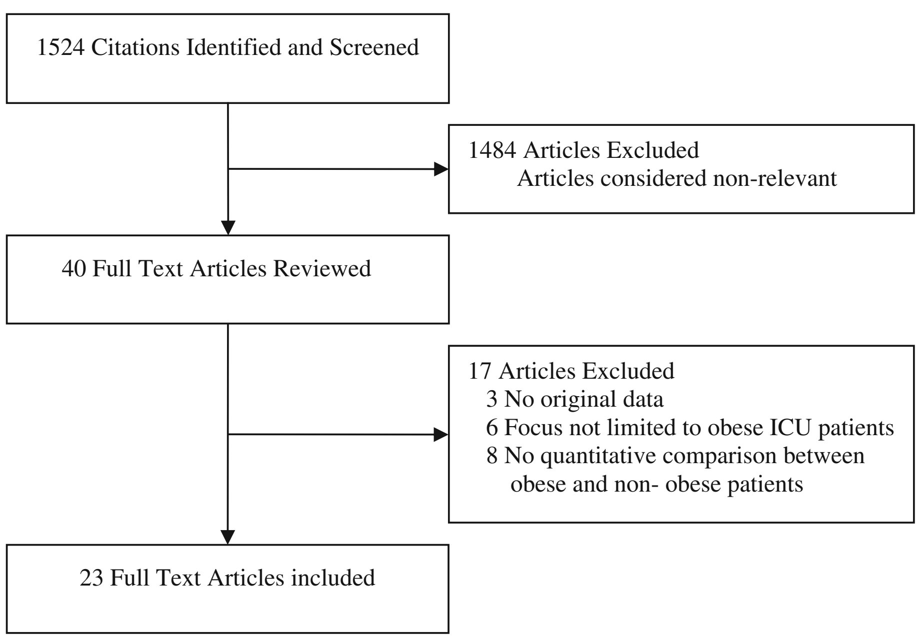

Fig. 1 Flow diagram of study selection process

Table 1 Study characteristics by body mass index category

References	Enrollment criteria	ICU type	Study design (total n)	Patient groups (n)	Age mean ± SD or median	Severity of illness mean ± SD or median
El-Solh [31]	ICU admission >24 h	MICU	Case-control (249)			Apache II
				Non-obese: <30 kg/m^2 (132)	46 ± 22	20.6 ± 12.2
				Morbidly obese: ≥40 kg/m^2 (117)	44 ± 18	19.1 ± 7.6
Marik [7]	Project impact ICU database[a]	Medical and surgical	Retrospective cohort (48,176)			SAPS II
				Underweight: <18.5 kg/m^2 (3,465)	64 ± 19	37.4 ± 18.2
				Normal weight:18.5–24.9 kg/m^2 (18,592)	62 ± 19	34.1 ± 17.9
				Overweight: 25–29.9 kg/m^2 (14,108)	62 ± 17	32.4 ± 17.5
				Obese (class I): 30.0–34.9 kg/m^2 (6,525)	60 ± 15	31.3 ± 17.3
				Obese (class II): 35–39.9 kg/m^2 (2,813)	58 ± 16	30.9 ± 17.4
				Morbidly obese: >40 kg/m^2 (2,673)	54 ± 14	30.2 ± 17.9
Tremblay [20]	Project impact ICU database[a]	Medical and surgical	Retrospective cohort (37,470)	Underweight: <20 kg/m^2 (4,646)	Data not provided	Data not provided
				Normal weight:20–25 kg/m^2 (12,403)		
				Overweight: 25–30 kg/m^2 (11,166)		
				Obese: 30–40 kg/m^2 (7,119)		
				Morbidly obese: >40 kg/m^2 (2,136)		
Bercault [32]	Mechanical ventilation >48 h	Medical and surgical	Case-control (767)			SAPS-II
				Normal weight: 18.5–24.9 kg/m^2 (586)	65 ± 14	43 ± 14
				Obese: >30 kg/m^2 (181)	65 ± 12	43 ± 14
Neville [25]	Blunt trauma	Trauma	Case-control (242)			Glasgow coma scale
				Non-obese: <30 kg/m^2 (63)	45 ± 22	11 ± 5
				Obese: ≥30 kg/m^2 (179)	49 ± 18	11 ± 5
Nasraway [10]	All patients	Surgical	Retrospective cohort (1,373)			SAPS II
				Underweight: <18.5 kg/m^2 (70)	62 ± 15	20 (10–30)
				Normal weight: 18.5–24.9 kg/m^2 (529)	63 ± 19	10 (0–30)
				Overweight: 25.0–29.9 kg/m^2 (408)	63 ± 14	20 (10–40)
				Obese: 30–39.9 kg/m^2 (272)	59 ± 14	10 (10–30)
				Morbidly obese: ≥40 kg/m^2 (94)	54 ± 16	20 (10–30)
Finkielman [8]	Non-cardiac surgery, neurological surgery, or cardiac care unit patients	1 medical, 2 surgical, and 1 multi-disciplinary	Retrospective cohort (19,669)	Underweight: <18.5 kg/m^2 (812)	Postoperative patients: 64.2 ± 15.9	Median (IQR) Apache III operative patients: 39.0 (29.0–51.0)
				Normal weight 18.5–24.9 kg/m^2 (6,406)		
				Overweight: 25.0–29.9 kg/m^2 (6,570)		
				Obese: 30–39.9 kg/m^2 (4,665)	Non-operative patients: 60.9 ± 19.1	Non-operative patients: 48 (32.0–67.0P
				Morbidly obese: ≥40 kg/m^2 (1,216)		
Goulenok [33]	ICU stay >24 h	Medical	Prospective cohort (813)			SAPS II
				Non-obese: <27 kg/m^2 (215)	48 (34–65)	32 (19–48)

Table 1 continued

References	Enrollment criteria	ICU type	Study design (total *n*)	Patient groups (*n*)	Age mean ± SD or median	Severity of illness mean ± SD or median
				Obese: ≥27 kg/m^2 (598)[a]	58 (47–71)	36 (27–56)
O'Brien [23]	ARDS network trials[b]	Medical and surgical	Retrospective cohort (807)			APACHE III
				Normal weight: 18.5–24.9 kg/m^2 (334)	52 ± 18	78.2 ± 27.4
				Overweight: 25.0–29.9 kg/m^2 (254)	53 ± 18	76.8 ± 27.4
				Obese: ≥30.0 kg/m^2 (219)	49 ± 16	73.0 ± 28.2
Garrouste-Orgeas [9]	ICU stay >48 h	2 medical, 2 surgical, and 2 medical–surgical	Prospective cohort (1,698)			SAPS II
				Underweight: <18.5 kg/m^2 (189)	62 (45–73)	41 (29–59)
				Normal weight: 18.5–24.9 kg/m^2 (806)	65 (48–75)	38 (28–51)
				Overweight: 25.0–29.9 kg/m^2 (476)	69 (56–77)	39 (29–53)
				Obese: >30 kg/m^2 (227)	65.5 (57–74)	38 (28–54)
Ray [34]	ICU stay >24 h	Medical	Prospective cohort (2,148)			APACHE II
				Underweight: <20 kg/m^2 (350)	65 ± 19	18.4 ± 8.9
				Normal weight: 20.0–24.0 kg/m^2 (663)	62 ± 20	18.2 ± 8.3
				Overweight: 25.0–29.9 kg/m^2 (585)	65 ± 16	18.3 ± 9.3
				Obese: 30.0–39.9 kg/m^2 (396)	62 ± 17	17.0 ± 8.7
				Morbidly obese: ≥40 kg/m^2 (154)	57 ± 16	18.2 ± 9.0
Brown [26]	Blunt trauma	Trauma	Retrospective cohort (1,153)			ISS
				Non-obese: <30 kg/m^2 (870)	45 ± 20	21 ± 12
				Obese: ≥30 kg/m^2 (283)	46 ± 18	21 ± 13
Byrnes [27]	Trauma with injury severity score ≥15	Trauma	Retrospective cohort (1,079)			ISS
				Non-obese: <35 kg/m^2 (1,057)	44	8.1
				Obese: ≥35 kg/m^2 (122)	46	9.3
Alban [28]	All patients	Trauma	Retrospective cohort (918)			APACHE II
				Underweight: <25 kg/m^2 (516)	41 ± 0.8	19 ± 0.3
				Normal: 26–30 kg/m^2 (296)	40 ± 1.4	18 ± 0.5
				Overweight: 31–35 kg/m^2 (67)		
				Obese: 36–40 kg/m^2 (25)		
				Morbidly obese: >40 kg/m^2 (14)		
Bochicchio [11]	All patients	Trauma	Retrospective cohort (1,167)			ISS
				Non-obese: <30 kg/m^2 (1,105)	42 ± 21	24.2 ± 12.6
				Obese: ≥30 kg/m^2 (62)	45 ± 17	24.8 ± 12.0
Aldawood[12]	All patients except burns or brain death	Medical-surgical	Prospective cohort (1,835)			APACHE II
				Underweight: <18.5 kg/m^2 (140)	48 ± 24	22 ± 9
				Normal weight: 18.5–24.9 kg/m^2 (631)	52 ± 21	21 ± 9
				Overweight: 25.0–29.9 kg/m^2 (524)	53 ± 18	21 ± 9
				Obese (class I): 30–34.9 kg/m^2 (312)	54 ± 18	21 ± 9
				Obese (class II): 35.0–39.9 kg/m^2 (135)	55 ± 15	23 ± 10

Table 1 continued

References	Enrollment criteria	ICU type	Study design (total n)	Patient groups (n)	Age mean ± SD or median	Severity of illness mean ± SD or median
				Morbidly obese: >40 kg/m^2 (93)	53 ± 17	22 ± 9
Peake [35]	All patients	Medical-surgical	Prospective cohort (493)			APACHE II
				Underweight: <18.5 kg/m^2 (24)	62 ± 16	20.8 ± 8.0
				Normal weight: 18.5–24.9 kg/m^2 (129)	61 ± 20	19.9 ± 7.9
				Overweight: 25.0–29.9 kg/m^2 (151)	64 ± 16	19.9 ± 7.9
				Obese: 30–34.9 kg/m^2 (75)	63 ± 14	19.9 ± 8.7
				Severely obese: ≥35 kg/m^2 (54)	61 ± 16	19.4 ± 8.0
Brown [29]	Blunt trauma patients with traumatic brain injury	Trauma	Retrospective cohort (690)			ISS
				Non-obese: <30 kg/m^2 (561)	39 ± 22	24 ± 13
				Obese: ≥30 kg/m^2 (129)	46 ± 20	26 ± 13
O'Brien [13]	Patients with acute lung injury in project impact[a]	Medical and surgical	Retrospective cohort (1,488)			SAPS II survival probability
				Underweight: <18.5 kg/m^2 (88)	62.4 ± 16.2	0.53 ± 0.29
				Normal weight: 18.5–24.9 kg/m^2 (544)	61.0 ± 17.8	0.58 ± 0.28
				Overweight: 25.0–29.9 kg/m^2 (399)	59.4 ± 16.7	0.59 ± 0.29
				Obese: 30–39.9 kg/m^2 (326)	58.0 ± 16.3	0.59 ± 0.28
				Morbidly obese: ≥40 kg/m^2 (131)	53.6 ± 14.9	0.68 ± 0.29
Ciesla [30]	Trauma with injury severity score >15 and survival >48 h	Trauma	Prospective cohort (716)	Underweight or normal weight: <25 kg/m^2 (286)	Data not provided	Data not provided
				Overweight: 25.0–29.9 kg/m^2 (278)		
				Obese: ≥30 kg/m^2 (152)		
Morris [24]	Patients with acute lung injury in King County lung injury Project	Medical and surgical	Retrospective cohort (825)			APS
				Underweight: <18.5 kg/m^2 (50)	65 ± 18	82.3 ± 31.5
				Normal weight: 18.5–24.9 kg/m^2 (301)	61 ± 18	74.9 ± 29.2
				Overweight: 25.0–34.9 kg/m^2 (237)	59 ± 17	74.9 ± 30.0
				Obese: 35.0–39.9 kg/m^2 (183)	57 ± 16	70.3 ± 29.8
				Morbidly obese: ≥ 40 kg/m2 (54)	55 ± 14	75.0 ± 35.1
Newell [21]	Blunt trauma patients with injury severity score ≥ 16	Trauma	Retrospective cohort (1,751)			ISS
				Normal weight: 18.5–24.9 kg/m^2 (554)	43 ± 21	24 ± 8
				Overweight: 25.0–29.9 kg/m^2 (529)	46 ± 20	25 ± 10
				Obese: 30–39.9 kg/m^2 (371)	47 ± 17	26 ± 10
				Morbidly obese: ≥40 kg/m^2 (89)	46 ± 17	27 ± 10

Table 1 continued

References	Enrollment criteria	ICU type	Study design (total *n*)	Patient groups (*n*)	Age mean ± SD or median	Severity of illness mean ± SD or median
Smith [19]	Patients with infections excluding uncomplicated acute cholecystitis, non-perforated appendicitis, or non-perforated bowel	Surgical	Retrospective cohort (807)	Underweight: <18.5 kg/m^2 (36) Normal weight: 18.5–24.9 kg/m^2 (258) Overweight: 25.0–29.9 kg/m^2 (240) Obese: 30–39.9 kg/m^2 (191) Morbidly obese: ≥ 40 kg/m^2 (82)	Data not provided	Data not provided

The number of patients in each weight category is listed in parenthesis

[a] Project impact includes 106 ICUs in 84 US hospitals

[b] Patients enrolled in the low versus high tidal volume lung ventilation ($n = 861$) trials, ketoconazole versus placebo ($n = 234$), and lisofylline versus placebo ($n = 194$) trials

assessed as having a representative cohort [13, 21, 34, 35]. Of the three case-control studies, only one provided an adequate case definition [32].Thirteen studies included multiple BMI categories compared to a reference group of normal weight (excluding underweight) patients, seven studies compared obese versus non-obese (including underweight) patients, and three studies compared normal weight versus overweight patients with only a single category of obesity (≥30 kg/m^2).

Mortality

Mortality and other hospital outcomes for the eligible studies are summarized in Table 4. Six studies reported a positive association between obesity or morbid obesity and ICU and/or hospital mortality after risk adjustment [11, 25, 26, 31–33]. In ten studies, obesity was not related [7, 19, 20, 23, 24, 28–31, 34] or in four studies it was protective from risk-adjusted mortality [8, 9, 12, 35]. Two studies did not report risk adjusted mortality outcomes [8–10, 12, 13, 27, 35]. Compared to other BMI categories, underweight patients (<18.5 kg/m^2) had higher hospital mortality in four studies [7–9, 13].

We pooled data from eight and nine studies that provided ICU and hospital mortality results, respectively, by BMI categories (Fig. 2). With ICU mortality, we found no significant difference comparing underweight, overweight, obese, and morbidly obese subjects to the normal weight subjects. With hospital mortality, obese patients had lower mortality versus normal weight patients (RR 0.76; 95% credible interval, 0.59, 0.92). Although not statistically significant, similar trends toward decreased hospital mortality also were observed in the pooled estimates for overweight (RR 0.89, 95% credible interval, 0.74, 1.07) and morbidly obese (RR 0.83; 95% CI, 0.66, 1.04) subjects, while underweight subjects had a trend toward increased hospital mortality (RR 1.11; 95% CI, 0.86, 1.39) versus the normal weight reference group. The I^2 statistic for heterogeneity ranged from 50% (morbidly obese vs. normal) to 80% (underweight vs. normal) for ICU mortality and from 86% (underweight vs. normal) to 93% (obese vs. normal) for hospital mortality indicating the need for caution in interpreting pooled estimates due to important differences across the studies.

Duration of mechanical ventilation

The rate of mechanical lung ventilation in obese versus non-obese patients was reported in seven studies [10, 26, 27, 31, 33–35]. In a non-risk adjusted analysis, obesity was associated with a higher rate of mechanical ventilation in two studies [27, 31] while no relationship between BMI and rates of mechanical ventilation was found in the

Table 2 Quality of included cohort studies based on modified Newcastle-Ottawa Scale [17, 18]

References	Selection				Comparability	Outcome		
	Cohort representative?	Non-exposed cohort adequate?	Ascertainment of exposure clear?	Outcome not present at start of study?	Adjustment for confounding/bias?	Assessment of outcome blinded?	Length of follow-up appropriate?	Adequate of follow-up of cohort?
Marik [7]	No	Yes	No	Yes	Yes	Yes	Yes	Yes
Finkielman [8]	No	Yes	No	Yes	No	No	Yes	Yes
Goulenok [33]	No	No	Yes	Yes	Yes	No	Yes	Yes
O'Brien [23]	No	Yes	No	Yes	Yes	Yes	Yes	Yes
Garrouste-Orgeas [9]	No	Yes	No	No	Yes	No	Yes	Yes
Ray [34]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Brown [26]	No	No	Yes	No	Yes	No	No	Yes
Byrnes [27]	No	No	No	No	No	No	Yes	Yes
Nasraway [10]	No	Yes	Yes	Yes	Yes	No	Yes	Yes
Alban [28]	No	No	No	Yes	Yes	No	Yes	Yes
Bochicchio [11]	No	No	No	Yes	Yes	No	Yes	Yes
Aldawood [12]	No	Yes	Yes	Yes	Yes	No	Yes	Yes
Peake [35]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Brown [29]	No	No	No	No	Yes	No	Yes	Yes
O'Brien [13]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Ciesla [30]	No	No	No	Yes	Yes	No	Yes	Yes
Morris [24]	No	Yes	No	Yes	Yes	No	Yes	Yes
Newell [21]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Smith [19]	No	Yes	No	Yes	Yes	No	Yes	Yes

Table 3 Quality of included case control studies based on modified Newcastle-Ottawa Scale [17, 18]

References	Selection				Comparability	Exposure		
	Adequate case definition?	Representative cases?	Control selection adequate?	Control definition appropriate?	Adjustments for confounding/bias?	Ascertainment of exposure adequate?	Ascertainment of control similar for cases and controls?	Non-response rate for cases and controls similar?
El-Solh [31]	No	No	No	No	Yes	Yes	Yes	Yes
Bercault [32]	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Neville [25]	No	No	No	No	Yes	Yes	Yes	Yes

remaining studies. No study reported a risk-adjusted analysis of duration of mechanical ventilation by weight category. Five studies reported a longer duration of mechanical ventilation for obese versus normal weight patients [24, 26, 29, 31, 35] while three other studies reported no difference (Table 4) [12, 33, 34]. In our pooled analysis, we found no difference in the duration of mechanical ventilation comparing each weight category to normal weight patients (Fig. 3). The sensitivity analysis of our results (i.e., removing those studies without estimates of standard deviation) did not change these findings. The I^2 statistic for heterogeneity in the mean differences comparing the overweight and obese subjects to normal weight subjects is 74 and 58%, respectively, indicating the need for caution in interpreting these pooled estimates. However, for the underweight and morbidly obese comparisons the I^2 statistic was 10% indicating a low level of statistical heterogeneity across studies.

Length of hospitalization

No study reported a risk-adjusted analysis of hospital length of stay by weight category. Twelve studies reported that obese patients had a longer ICU and/or hospital stay [7–9, 11, 24–26, 28–31, 33] while four studies found no difference [12, 13, 28, 34, 35] and one study found a shorter duration of ICU and hospital stay in obese versus normal weight controls (Table 4) [10]. In our meta-analysis, there was little difference in duration of ICU and hospital length of stay for overweight and obese patients versus normal weight controls (Fig. 4). For both underweight and morbidly obese subjects versus normal weight

Table 4 Relationship between obesity and hospital outcomes

References	Sample size	ICU mortality	Hospital mortality	Mean ± SD or median (range)			Main findings
				Days of MV	Days in ICU	Days in hospital	
El-Solh [31]		Not reported					Morbid obesity not associated with risk-adjusted hospital mortality
Non-obese	117		16.7%	4.6 ± 7.1	5.8 ± 8.2	11.3 ± 10.8	
Morbidly obese	132		29.9%	7.7 ± 9.6	9.3 ± 10.5	17.7 ± 19.8	
			$P = 0.019$	$P < 0.001$	$P < 0.001$	$P = 0.007$	
Marik [7]							Underweight (but not other BMI categories) independently associated with hospital mortality
Underweight	3,465	14.4%	24.8%	Data not provided	4.4 ± 6.9	13.7 ± 17.3	
Normal weight	18,592	11.4%	18.7%		4.1 ± 6.5	11.2 ± 26.8	
Overweight	14,108	10.2%	15.4%		4.2 ± 7.0	10.5 ± 30.4	
Obese (class I)	6,525	9.9%	14.5%		4.4 ± 7.7	13.0 ± 15.3	
Obese (class II)	2,813	9.1%	13.1%		4.4 ± 7.2	13.1 ± 14.7	
Morbidly obese	2,673	10.4%	15.3%		5.2 ± 8.8	14.5 ± 21.2	
		$P < 0.001$ across groups	$P < 0.001$ across groups		$P < 0.001$ across groups	$P = 0.007$ across groups	
Tremblay [20]	41,011	Data not provided	Data not provided	Data not provided	Data not provided	Data not provided	Only underweight (vs. normal weight) category independently associated with risk-adjusted hospital mortality
Bercault [32]							Obesity was an independent risk factor for ICU mortality (OR, 2.1; 95% CI, 1.2–3.6, $P = 0.007$). Obesity associated with higher rate of ICU acquired complications (OR, 4.0; 95% CI, 1.4–11.8, $P = 0.01$)
Normal weight	586	17%	Data not provided	Data not provided	Data not provided	Data not provided	
Obese	181	32% $P < 0.01$					
Neville [25]							Obesity was an independent predictor of hospital mortality (OR, 5.7; 95% CI 1.9–19.6, $P = 0.003$)
Non-obese	63	Data not provided	9%	Data not provided	11 ± 10	21 ± 17	
Obese	179		32%		10 ± 9	24 ± 23	
			$P = 0.008$		$P = 0.65$	$P = 0.47$	
Finkielman [8]					Postoperative median (95% CI)		Underweight had higher adjusted hospital mortality (postoperative patients, 2.1; 95% CI, 1.4–3.3, $P = 0.0005$; non-operative, OR, 1.5, 95% CI, 1.1–2.0, $P = 0.005$). Obese postoperative patients had lower hospital mortality (OR, 0.7, 95%CI, 0.5–0.9, $P = 0.019$). Underweight ($P = 0.04$) and morbidly obese ($P < 0.0001$) postoperative patients had ICU LOS observed versus predicted ratio significantly higher than patients with normal BMI
Postoperative group							
Underweight	384		9.4%	Data not provided	1.54 (0.85–3.02)	Data not provided	
Normal weight	3,461		3.8%		1.03 (0.81–2.08)		
Overweight	3,878		3.1%		1.04 (0.82–2.17)		
Obese	2,718		2.4%		1.03 (0.81–2.07)		
Morbidly obese	774		2.3%		1.57 (0.84–2.54)		
					Non-operative Group		
Non-operative group							
Underweight	428		21.5%		1.71 (0.87–3.80)		
Normal weight	2,945		16.1%		1.65 (0.87–6.62)		
Overweight	2,692		16.2%		1.63 (0.90–3.58)		
Obese	1,947		16.4%		1.73 (0.91–3.71)		
Morbidly obese	442		14.0%		1.94 (0.92–4.34)		
Goulenok [33]							ICU mortality for obese patients was higher than predicted by SAPS II (32 vs. 18%; $P = 0.0001$)
Non-obese	215	13%	Data not provided	3 (2–8)	3 (2–7)	Data not provided	

Table 4 continued

References	Sample size	ICU mortality	Hospital mortality	Mean ± SD or median (range)			Main findings
				Days of MV	Days in ICU	Days in hospital	
Obese	598	32%		4 (2–9)	4 (2–8)		
O'Brien [23]							No difference in risk-adjusted hospital mortality by BMI category
Normal weight	334	Data not provided	28%	Data not provided	Data not provided	Data not provided	
Overweight	254		13%				
Obese	219		27%				
Garrouste-Orgeas [9]							BMI < 18.5 kg/m^2 was independently associated with hospital mortality (OR 1.6, 95% CI, 1.1–2.4, $P = 0.01$); BMI >30 kg/m^2 was protective of hospital mortality (OR 0.6, 95% CI, 0.4–0.9, $P = 0.01$)
Underweight	189	28.5%	43.9%		6 (4–14)	20 (10–40)	
Normal weight	806	22.4%	31.8%		6 (4–14)		
Overweight	476	19.3%	29.9%		6 (4–11)	20 (10–37)	
Obese	227	18.0%	25.1%		6 (4–13)	20 (11–38)	
					7 (4–19)	25 (14–48)	
					$P = 0.03$	$P = 0.0005$	
Ray [34]							BMI not an independent predictor of ICU or hospital mortality. No relation between BMI and rates of complications
Underweight	350	4.3%	9.1%	5.2 ± 6.7	4.9 ± 6.9	11.9 ± 14.6	
Normal weight	663	11.0%	15.5%	5.0 ± 5.9	4.2 ± 5.8	11.1 ± 11.2	
Overweight	585	12.0%	17.4%	5.3 ± 5.9	4.7 ± 6.8	12.2 ± 13.8	
Obese	396	6.0%	10.1%	5.2 ± 6.6	4.4 ± 5.9	11.0 ± 9.9	
Morbidly obese	154	7.8%	11.0%	5.1 ± 5.3	4.8 ± 7.0	12.8 ± 13.7	
				$P = 0.977$	$P = 0.485$	$P = 0.250$	
Brown [26]		ISS < 16					Obesity was independent risk factor for hospital mortality (OR 1.6; 95% CI, 1.0–2.3, $P = 0.03$)
Non-obese	438	3%	Data not reported	6 ± 9	10 ± 10	19 ± 17	
Obese	(combined)	5%		8 ± 13	13 ± 14	24 ± 21	
		ISS 16–25		($P = 0.07$)	$P = 0.005$	$P = 0.01$	
Non-obese	331	11%					
Obese	(combined)	13%					
		ISS > 25					
Non-obese	384	39%					
Obese	(combined)	49%					
Byrnes [27]		Data not reported					Mortality rates higher for obese than non-obese patients. Nearly 27% obese patients developed complications compared with 17.6% of non-obese patients ($P = 0.02$)
Non-Obese							
Obese	1,057		4.1%	7.2	6.1	4.7	
	122		10.7	9.8	8.7	7.0	
			$P = 0.003$	$P = 0.31$	$P = 0.045$	$P = 0.001$	
Nasraway [10]							ICU and hospital mortality increased in morbidly obese patients versus all other weight groups combined (ICU, 33.3 vs. 12.3%, $P = 0.009$; hospital, 33.3 vs. 16%, $P = 0.045$)
Underweight	70	7.7%	19.2%	Data not provided	3.2 (1.5–6.7)	13.0 (7.0–21.0)	
Normal weight	529	18.9%	23.2%		2.4 (1.1–5.1)	10.0 (6.0–18.0)	
Overweight	408	7.6%	10.2%		2.1 (1.0–4.9)	9.0 (6.0–17.0)	
Obese	272	6.8%	8.1%		2.1 (1.0–4.1)	9.0 (5.0–15.5)	
Morbidly obese	94	33.3%	33.3%		2.0 (1.0–4.5)	6.0 (4.0–15.0)	
					$P = 0.27$	$P = 0.0003$	
Alban [28]					(Means)	(Means)	Obesity not related to hospital mortality based on univariate and multivariate logistic regression analysis
Underweight	516	7.5%	Data not provided	Data not provided	5.0	14.0	
Normal weight	296	8.1%			4.4	12.3	
Overweight	67	7.5%			6.0	14.0	
Obese	25	8.0%			7.0	14.6	
Morbidly obese	14	7.1%			6.8	13.4	
					$P = 0.25$	$P = 0.56$	

Table 4 continued

References	Sample size	ICU mortality	Hospital mortality	Mean ± SD or median (range)			Main findings
				Days of MV	Days in ICU	Days in hospital	
Bochicchio [11]							Obesity (OR, 4.2; 95% CI, 2.5–7.1, $P < 0.01$) and morbid obesity (OR, 8.8, 95% CI, 4.6–11.1, $P < 0.001$) associated with adjusted hospital mortality
Non-obese	1,105	Data not provided	15%	Data not provided	11.6 ± 9	15 ± 12	
Obese	62		21%		19.4 ± 15	25 ± 22	
					$P < 0.001$	$P < 0.001$	
Aldawood [12]							Morbid obesity was an independent predictor of lower mortality after adjusting for confounding factors (OR, 0.51, 95% CI, 0.28–0.92, $P = 0.25$)
Underweight	140	16%	30%	10 ± 15	9 ± 15	41 ± 49	
Normal weight	631	17%	30%	9 ± 12	8 ± 12	42 ± 52	
Overweight	524	17%	30%	8 ± 12	8 ± 11	44 ± 54	
Obese (class I)	312	17%	26%*	8 ± 10	7 ± 9	36 ± 49	
Obese (class II)	135	17%	27%	8 ± 10	7 ± 9	41 ± 47	
Morbidly obese	93	12%	21%**	11 ± 21	10 ± 18	39 ± 46	
			$P = 0.044$ versus normal weight* $P = 0.039$ normal weight**				
Peake [35]			(12-month)	Median hours (IQR)	Median(IQR)	Median (IQR)	Based on accelerated failure time analysis, BMI ≥ 35 kg/m^2 was associated with 30 day (time ratio, 1.85, 95% CI, 1.05–3.26, $P = 0.025$) and 12 month (TR, 1.03, 95% CI, 1.005–1.06, $P = 0.19$) survival
Underweight	24	25.0%	43.5%	36.5 (18.0–109.0)	2.6 (1.3–9.4)	13.9 (10.3–30.7)	
Normal weight	129	15.5%	39.5%	36.0 (15.0–141.0)	2.4 (1.1–6.4)	13.4 (6.3–32.3)	
Overweight	151	13.2%	38.1%	51.9 (20.5–118.0)	3.2 (1.7–5.9)	11.8 (7.9–22.5)	
Obese	75	20.0%	41.9%	42.3 (17.5–120.5)	2.4 (1.0–6.9)	13.9 (7.6–19.6)	
Morbidly obese	54	9.3%	20.8%	67.0 (19.5–170.5)	2.9 (1.4–7.7)	16.7 (8.1–29.9)	
				$P > 0.2$	$P > 0.2$	$P > 0.2$	
Brown [29]							Obesity not an independent predictor of mortality (OR, 1.5 (95% CI, 0.9–2.6, $P = 0.10$)
Non-obese	561	25%	Data not provided	6	11	20	
Obese	129	36%		10	14	27	
				$P = 0.01$	$P = 0.04$	$P = 0.06$	
O'Brien [13]							The odds of hospital mortality were decreased for overweight (OR, 0.72, 95% CI 0.51–1.02, $P = 0.067$) and obese (OR, 0.67, 95% CI, 0.46–0.97, $P = 0.033$) patients. Underweight associated with higher hospital mortality (OR 1.94, 95% CI, 1.05–3.60, $P = 0.035$). No differences in discharge location between BMI classes
Underweight	88	38.6%	54.6%	Data not provided	12.0 ± 10.4	24.6 ± 20.4	
Normal weight	544	31.8%	41.0%		11.6 ± 12.7	24.7 ± 23.6	
Overweight	399	30.6%	35.6%		11.2 ± 11.7	24.7 ± 29.3	
Obese	326	23.0%	30.4%		11.9 ± 11.0	26.9 ± 23.2	
Morbid obesity	131	22.1%	29.0%		14.1 ± 15.6	26.8 ± 27.1	
					$P = 0.180$	$P = 0.095$	
Ciesla [30]							No difference in adjusted hospital mortality between obese and non-obese patients (OR, 0.79, 95% CI, 0.39–1.58, $P = 0.499$). Of survivors, 61% of non-obese and 74% of obese patients transferred to long-term acute care facility ($P = 0.009$)
Non-obese	564	11%	Data not provided	Data not provided	16.1 ± 0.6	20.1 ± 1.6	
Obese	278	7%			21.3 ± 1.4	25.2 ± 1.4	

Table 4 continued

References	Sample size	ICU mortality	Hospital mortality	Mean ± SD or median (range)			Main findings
				Days of MV	Days in ICU	Days in hospital	
					$P < 0.001$	$P = 0.02$	
Morris [24]							No mortality difference between BMI groups. In survivors, morbidly obese had > hospital LOS (14.3 days, 95% CI, 7.1–21.6, $P < 0.001$), ICU LOS (5.6 days, 95% CI, 1.3–9.8, $P = 0.01$) and duration of MV (4.1 days, 95% CI, 0.4–7.7, $P = 0.03$) versus normal weight. Morbidly obese > likely to be discharge to a rehabilitation or skilled nursing facility
Underweight	50	Data not provided	44.0%	9.2 ± 10.9	10.8 ± 11.1	18.2 ± 15.3	
Normal weight	301		40.5%	8.7 ± 10.7	11.8 ± 13.1	19.4 ± 17.2	
Overweight	237		36.7%	10.4 ± 11.5	13.5 ± 13.0	21.8 ± 17.4	
Obese	183		31.7%	8.3 ± 8.4	10.7 ± 9.4	19.0 ± 17.1	
Morbidly obese	54		25.9%	10.8 ± 12.7	15.3 ± 14.7	29.8 ± 41.3	
				$P = 0.13$	$P = 0.23$	$P = 0.28$	
Newell et al. [21]							No difference in adjusted risk of mortality across BMI categories
Normal weight	554	Data not provided	9.2%	4.5	4.8	11.7	
Overweight	529		10.8%	4.3	4.9	12.6	
Obese	371		11.1%	7.4	7.5*	16.6*	
Morbidly obese	89		10.1%	9.2**	10.4**	22.0**	
			$P = 0.962$	$P < 0.\ 0001$ normal versus morbidly obese**	$P < 0.0001$ normal versus obese*	$P < 0.0001$ normal versus obese*	
					$P < 0.0001$ versus morbildy obese**	$P < 0.0001$ morbildy obese**	
Smith [19]							No independent association between increased BMI and mortality
Underweight	36	Data not provided	14%	Data not provided	Data not provided	Data not provided	
Normal weight	258		19%				
Overweight	240		22%				
Obese	191		21%				
Morbidly obese	82		24%				

MV mechanical ventilation

subjects, there was a non-statistically significant trend toward longer mean ICU and hospital length of stays (underweight: 0.40 days, 95% CI, 0.01, 0.78 days and 1.39 days, 95% CI, –0.53, 2.67 days, respectively and morbid obesity: 0.77 days, 95% CI, −0.14, 2.03 days and 1.36 days, 95% CI, −2.08, 5.52 days, respectively). The sensitivity of our results (i.e., removing those studies without estimates of standard deviation) changed the pooled results for only morbidly obese patients such that there was a significant association with increased duration of ICU and hospital stay (1.2 days, 95% CI, 0.5, 2.2 days; and 2.9 days, 95% CI, 1.1, 4.3 days, respectively). For all comparisons, the I^2 statistic for heterogeneity was <40 and <13% for ICU stay and hospital stay, respectively, indicating consistency of results across studies and the utility of pooling the results across studies.

Other complications

The association of obesity with any other complications of critical illness was reported in only 7 of the 23 studies (Table 5). Neville [25] reported that obesity was associated with a higher risk for multi-organ failure while Brown et al. [26] found that the frequency of renal failure, deep venous thrombosis, multi-organ failure, and ARDS was higher in obese versus with non-obese patients. Higher rates of deep venous thrombosis and multi-organ failure, but not ARDS and renal failure, in obese versus non-obese patients were confirmed by these investigators in a subsequent investigation of patients with traumatic brain injury [29]. Ciesla et al. [30] found that obese trauma patients were more likely to develop multi-organ failure than non-obese patients after risk adjustment, but

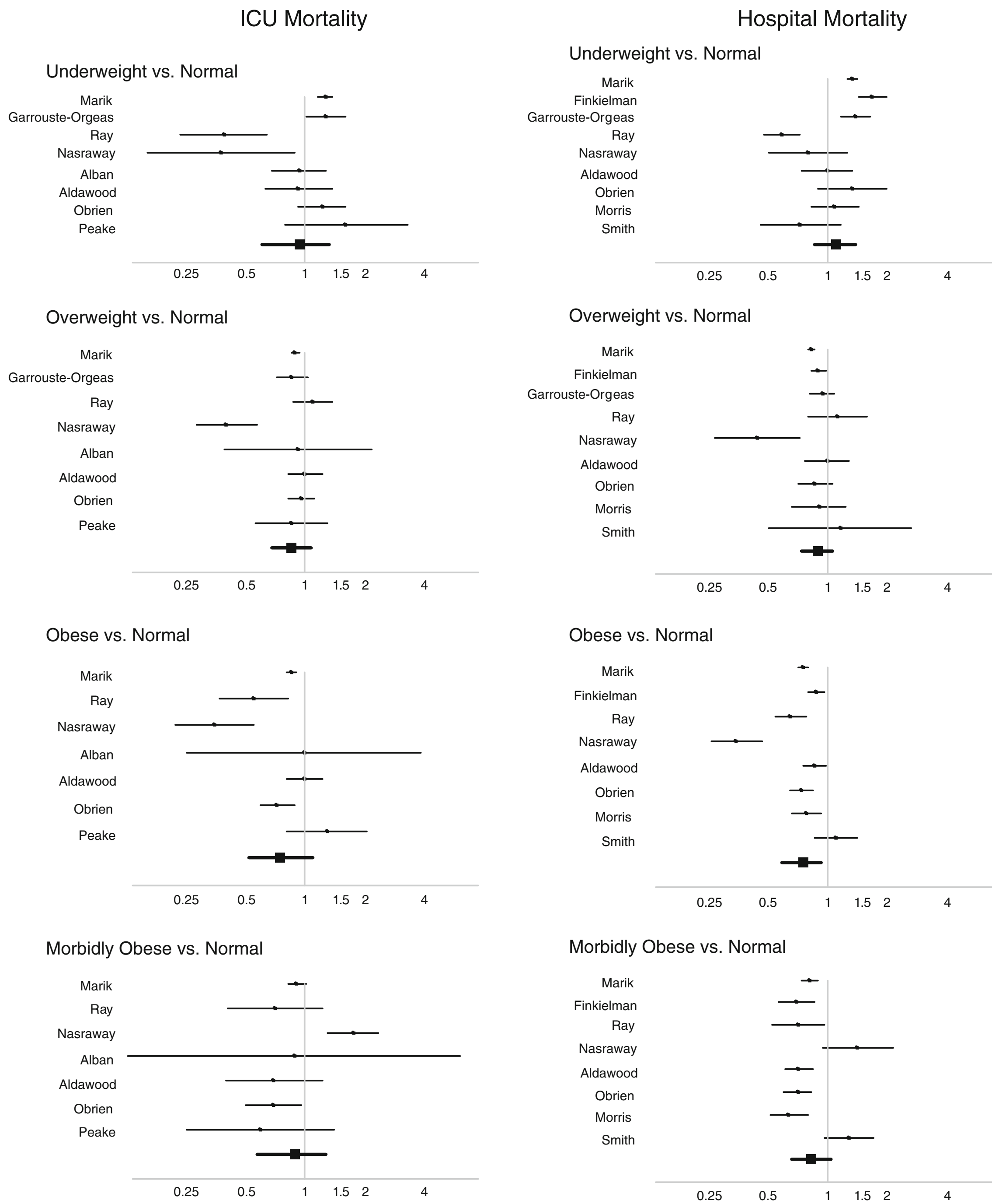

Fig. 2 Forest plots showing the relative risk of ICU and hospital mortality comparing underweight, overweight, obese, and morbidly obese patients to the normal weight patients. For each comparison, we display the Bayesian pooled estimate of relative risk with 95% credible intervals calculated using maximum likelihood estimation

found not difference in the incidence of ARDS or renal failure. These existing studies have important limitations since the sample size was often small, the definition of ICU complications poorly defined, and only a non-obese control group (including underweight patients) was used.

Long term outcomes

Only 1 of 23 studies investigated patient outcomes after hospital discharge, reporting that obesity was associated with improved risk-adjusted survival at 1 year after

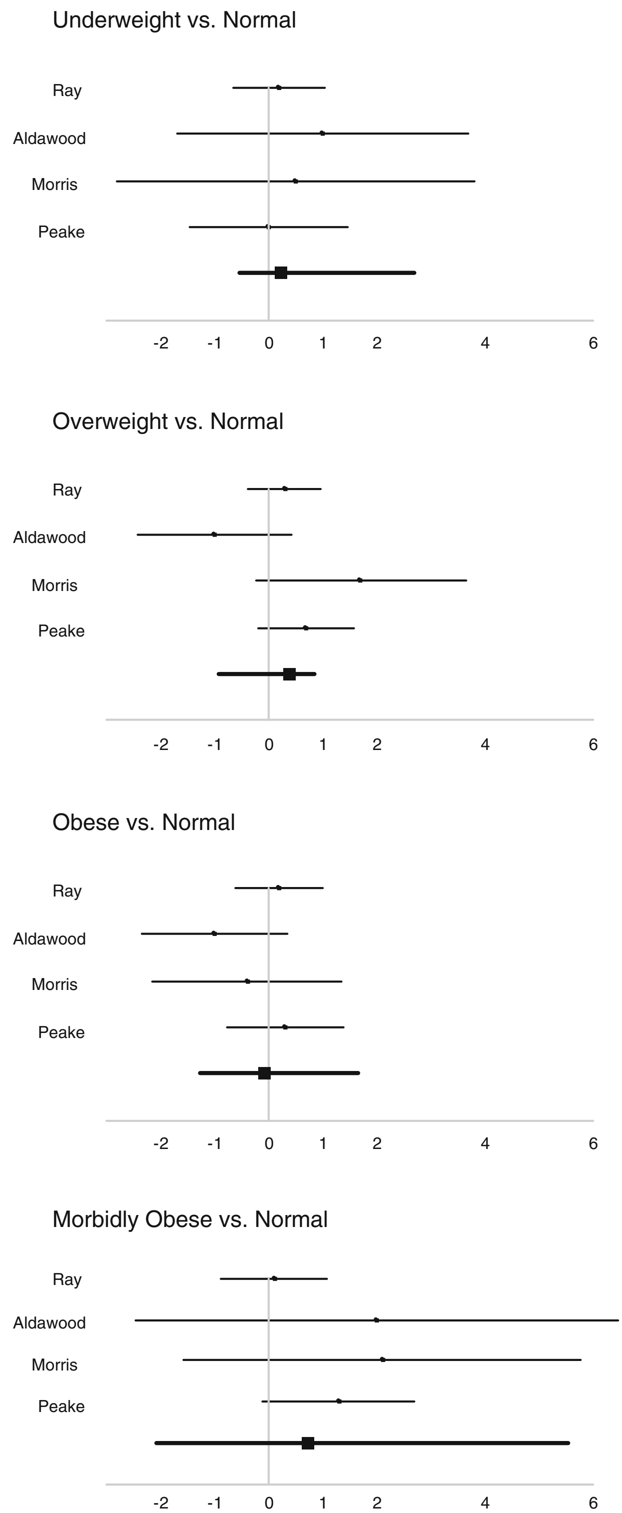

Fig. 3 Forest plots showing the estimated difference in mean days of mechanical ventilation comparing underweight, overweight, obese and morbidly obese patients to normal weight patients. For each comparison, we display the Bayesian pooled estimate of difference in mean days with 95% credible intervals calculated using maximum likelihood estimates

critical illness [35]. The proportion of patients discharge to a secondary care facility was reported in only 3 of 23 studies [13, 24, 30]. Moreover, no data were reported regarding objective measures of ICU survivors' physical function, mental health, or quality of life.

Discussion

In our meta-analysis of the impact of obesity in critical illness, we found that, compared with normal weight patients, obese and morbidly obese patients have no significant difference in ICU mortality, and obese patients may have lower hospital mortality. We found no significant association between obesity or morbid obesity with duration of mechanical ventilation, but morbid obesity may be associated with longer ICU and/or hospital stay. Importantly, we found very little research investigating the impact of obesity on patient outcomes after hospital discharge.

There are several explanations for a potential association between obesity and lower hospital mortality after critical illness including high levels of anti-inflammatory adipokines such as interleukin-10 and leptin that might positively modulate deleterious inflammatory processes [36]. High cholesterol and lipid levels common in obese patients might confer benefits during sepsis by binding endotoxins or by providing necessary precursors for adrenal steroid synthesis during acute illness [36]. Higher body weight has been further suggested to afford a nutritional reserve that becomes important for survival during acute life threatening illness [2]. Moreover, in some institutions, obese patients might be admitted to the ICU regardless of severity of illness given the need for higher nurse staffing not available elsewhere in the hospital. In a risk-adjusted cohort investigation, Bercault et al. [32] studied obese patient requiring mechanical ventilation >48 h. The risk of ICU mortality was double in the obese versus normal weight control group suggesting that, after considering severity of illness, obesity may be associated with mortality. Nonetheless, in studies that performed risk-adjusted analysis (Table 4), there were conflicting findings on whether obesity was independently associated with mortality after critical illness. Due to the marked variation in data reporting, we could not adjust for severity of illness in our meta-analysis.

Our results can be compared with the findings from the two other meta-analyses of obesity and mortality after critical illness. Akinnusi et al. [1] searched the literature up to February 2007 combining data from 14 studies with 62,045 patients. Consistent with our findings, these authors reported that obesity (BMI $\geq$30 kg/m^2) was not associated with crude ICU mortality and that obese patients had lower hospital mortality than non-obese (BMI <30 kg/m^2) patients (RR 0.83, 95% CI, 0.74, 0.92). However, they reported that in obese versus non-obese

Table 5 Other outcomes for obese and non-obese patients

References	Sample size	Renal failure	DVT	PE	Pneumonia	Sepsis	MOF	BSI	ARDS	Other findings
El-Solh [31]										BSI associated with central line occurred in 11 of 103 (11%) lines in morbidly obese and 2 of 60 (3%) lines in non-obese ($P = 0.1$)
Non-obese	117	13%								
Morbidly Obese	132	24%								
Neville [25]										
Non-obese	63	0.2%	1.1%	0.5%	6.7%	5.0%	1.7%		3.3%	
Obese	179	15.9%	4.8%	0%	17.5%	17.5%	20.6%		12.7%	
							$P = 0.02$			
Ray [34]										No difference in total complications between non-obese (13.6%) and obese/morbidly obese (13.3%) ($P = 0.83$)
Underweight	350		10.3%		8.6%			6.9%		
Normal weight	663		6.6%		13.2%			10.5%		
Overweight	585		6.0%		13.1%			8.3%		
Obese	396		6.0%		20.0%			6.0%		
Morbidly obese	154		8.7%		8.7%			0%		
			$P = 0.599$		$P = 0.730$			$P = 0.679$		
Brown [26]										Obese patients had more complications than non-obese (42% vs. 32%, $P = 0.002$)
Non-obese	1,153	4.1%	1.5%	2.2%	15.3%	8.3%	11.1%		5.7%	
Obese	(combined)	8.1%	3.2%	2.5%	18.7%	11.7%	19.0%		11.3%	
		$P = 0.008$	$P = 0.07$	$P = 0.77$	$P = 0.17$	$P = 0.09$	$P = 0.0006$		$P = 0.002$	
Nasraway [10]										
Underweight	70	7.1%								
Normal weight	529	13.8%								
Overweight	408	9.8%								
Obese	272	11.1%								
Morbidly obese	94	9.6%								
		$P = 0.56$								
Brown[29]										Obese patients with traumatic brain injury had trend for more complications than non-obese (34% vs. 28%, $P = 0.17$) but obesity not a significant predictor of complications based on logistic regression analysis
Non-obese	561	4%	1%		15%	8%	10%		5%	
Obese	129	7%	5%		20%	9%	19%		8%	
		$P = 0.13$	$P < 0.01$		$P = 0.15$	$P = 0.68$	$P < 0.01$		$P = 0.29$	
Ciesla [30]										Compared with non-obese patients, ARDS ($P = 0.07$) and renal failure ($P = 0.43$) not different based on multivariable regression analysis. Obese patient more likely to develop MOF than non-obese after risk adjustment (OR, 1.81, 95% CI, 1.20–2.71, $P = 0.004$)
Non-obese	564	9%					22%		29%	
Obese	278	15%					37%		41%	
		$P = 0.042$							$P = 0.006$	

DVT deep venous thrombosis, *PE* pulmonary embolism, *MOF* multiorgan failure, *BSI* blood stream infection. *P*-values noted after the frequency of complication are those derived from univariate analysis

Excludes Peake et al. [35] from the analysis for days on MV, excludes Peake et al. [35], Garrouste-Orgeas et al. [9] and Nasraway et al. [10] from the analyses for days in ICU and hospital

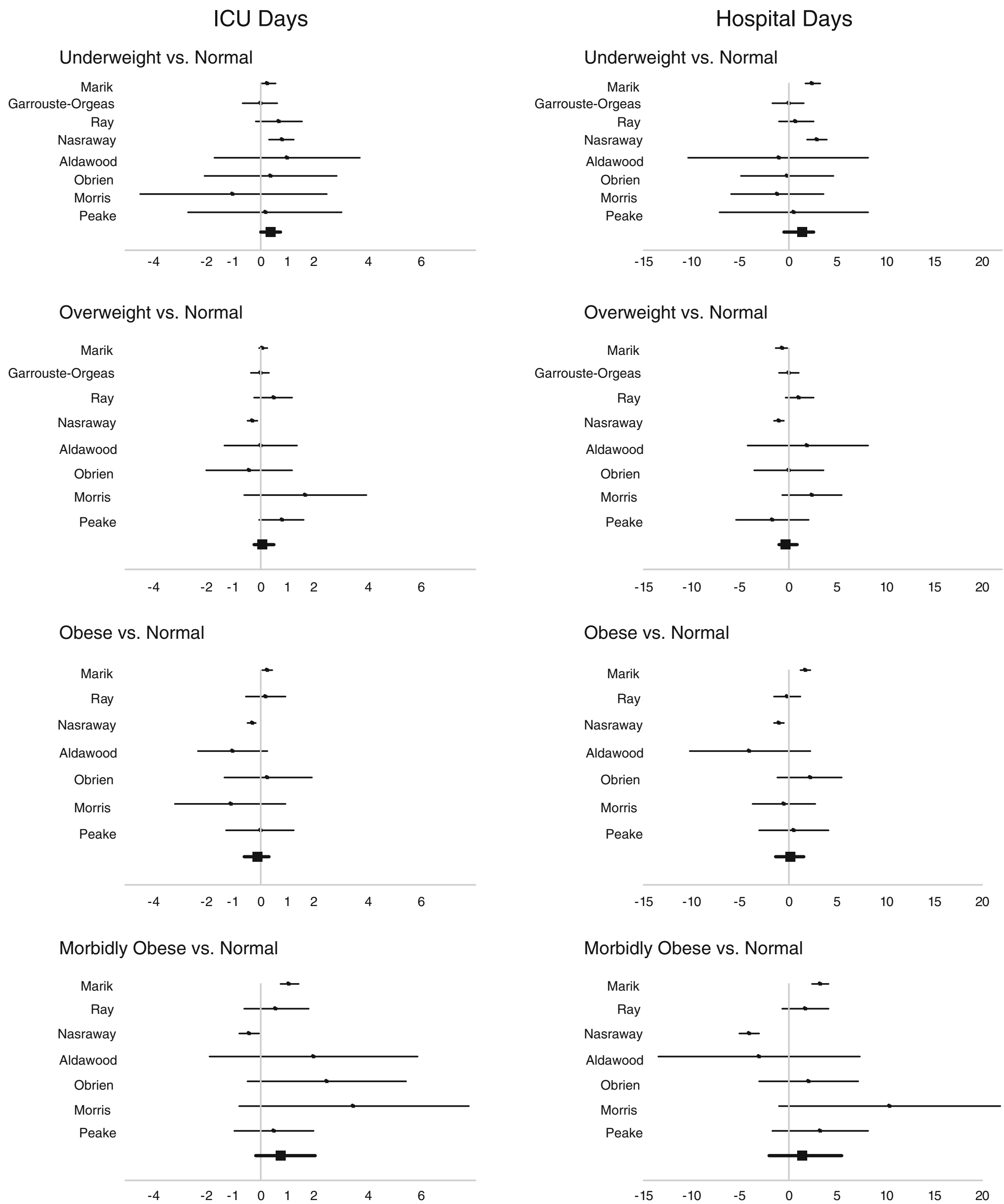

Fig. 4 Forest plots showing the difference in mean days in the ICU and hospital comparing the underweight, overweight, obese and morbidly obese patients to the normal weight patients. For each comparison, we display the Bayesian pooled estimate with 95% credible intervals calculated maximum likelihood estimates

patients, there was a longer duration of mechanical ventilation (1.48 days, 95% CI, 0.07, 2.89,) and ICU length of stay (1.08 days, 95% CI, 0.27, 1.88). Oliveros et al. [2] pooled data from 12 of 23 studies that they identified in a literature search up to June 2007. Similar to our study, these authors compared mortality using a normal weight reference group (BMI 18.5–24.9 kg/m^2). However, they did a combined analysis of ICU and hospital mortality and found a lower mortality for overweight (odds ratio 0.91, 95% CI, 0.84, 0.98) and obese (odds ratio 0.82, 95% CI, 0.68, 0.98), but not morbidly obese (OR 0.94, 0.82, 1.07) patients. Moreover, ICU length of stay was longer for underweight, overweight, and morbidly obese patients. In addition to separately examining ICU and hospital mortality, our study is distinguished from that of Oliveros et al. [2] by including the recently published 807 patient study by Smith et al. [19], and by combining operative and non-operative patients in the study by Finkielman et al. [8]. Furthermore, we excluded the studies by De Waele et al. [37] and Duane et al. [38] because we believed these studies were not limited to ICU outcomes. Finally, unlike this prior study, we excluded the 37,470 patient studied by Tremblay et al. [20] to prevent duplicate inclusion of the overlapping patient population with the 48,176 patient study by Marik et al. [7].

We were surprised that we did not find a relationship between obese patients and increased duration of mechanical ventilation. Obese patients are prone to atelectasis, aspiration, and pneumonia that may increase the duration of mechanical ventilation [5, 6]. Furthermore, obese patients have reduced lung and chest wall compliance leading to high airway resistance interfering with implementation of low airway pressure lung protective ventilation schemes for patients with acute lung injury (especially when ventilator settings are not based on ideal body weight) [23, 39]. Given the marked heterogeneity of the data and the lack of risk adjustment for potential differences in severity of illness between obese and normal-weight patients, the interpretation of the impact of obesity on duration of mechanical lung ventilation remains unresolved.

The improving mortality from critical illness is placing increasing emphasis on understanding the long-term outcomes of ICU survivors particularly since such patients might have physical and mental impairment and reduced quality of life after hospital discharge [15, 40–42]. Outside the context of critical illness, obesity is associated with high rates of disability, and functional impairment [4, 43–45]. Furthermore, obese individuals are reported to have higher levels of anxiety, depression, and lower scores for self-perceived health than non-obese subjects [46, 47]. With the exception of Peake et al. [35] who reported 1 year mortality, this review revealed the lack of data regarding the impact of obesity on outcomes after hospital discharge. Few studies evaluated whether obesity was related to need for nursing home placement or in-patient rehabilitation after critical illness [13, 24, 48]. Only one study evaluated whether obesity impacted functional outcome after hospital discharge, but the assessments were limited to whether a patient was independent, dependent, or deceased [20].

Although our analysis included over 80,000 patients, the varying definitions of obesity and heterogeneity among the included studies created limitations with conducting and interpretation the meta-analysis. We found substantial statistical heterogeneity within our analysis suggesting that a large degree of the differences in outcomes of obesity in the eligible studies might be explained by patient characteristics (other than BMI) across the studies. Most studies did not present risk-adjusted analyses of the association of BMI and duration of mechanical ventilation and ICU and hospital stay. Moreover, the meta-analysis could not consider any risk adjustment for differences in patient populations between the studies due to variation in the severity of illness scoring systems used and the lack of reporting of severity of illness data by BMI category. Moreover, we could not adjust for patient age in our analysis, an important limitation since obese patients tend to be younger than non-obese patients. Other limitations to the existing studies include high (>30% in some studies) or unknown rates of missing data, imprecise measurement of BMI (often estimated or based on patient-reported data), failure to account for the effects of fluid balance on body weight leading to “pseudo-obesity” in some subjects, varying definitions of outcomes, and incompletely defined control groups.

In conclusion, our meta-analysis of studies evaluating the effect of obesity in critical illness suggests that obesity and morbid obesity does not adversely impact ICU mortality. Obesity may be associated with lower hospital mortality compared with normal body weight. Obesity was not associated with the duration of mechanical ventilation or ICU or hospital length of stay. However, morbid obesity may be associated with longer ICU and hospital length of stay. There is a critical deficiency of data on the influence of obesity on complications of critical illness and patient outcomes after hospital discharge. Given that obesity is common, costly, and associated with substantial morbidity and mortality in the general population, efforts to understand the impact of obesity on ICU care, complications and long-term outcomes after critical illness should be a research priority.

References

1. Akinnusi M, Pineda L, El Solh A (2008) Effect of obesity on intensive care morbidity and mortality: a meta-analysis. Crit Care Med 36:151–158
2. Oliveros H, Villamor E (2008) Obesity and mortality in critically ill adults: a systematic review and meta-analysis. Obesity 16:515–521
3. Thompson D, Eldesberg J, Colditz G, Bird A, Oster G (1999) Lifetime health and economic consequences of obesity. Arch Intern Med 159:2177–2183

4. Flegal K, Graubard B, Williamson D, Gail M (2005) Excess deaths associated with underweight, overweight, and obesity. J Am Med Assoc 293:1861–1867
5. Pieracci F, Barie P, Pomp A (2006) Critical care of the bariatric patient. Crit Care Med 34:1796–1804
6. Ebert T, Shankar H, Haake R (2006) Perioperative considerations for patients with morbid obesity. Anesth Clin North Am 24:621–636
7. Marik P, Doyle H, Varon J (2003) Is obesity protective during critical illness? An analysis of a National ICU database. Crit Care Shock 6:156–162
8. Finkielman J, Gajic O, Afessa B (2004) Underweight is independently associated with mortality in post-operative and non-operative patients admitted to the intensive care unit: a retrospective study. BMC Emerg Med 4:1–7
9. Garrouste-Orgeas M, Troché G, Azoulay E, Caubel A, de Lassence A, Cheval C, Montesino L, Thuong M, Vincent F, Cohen Y, Timsit J (2004) Body mass index. An additional prognostic factor in ICU patients. Intensive Care Med 30:437–443
10. Nasraway S Jr, Albert M, Donnelly A, Ruthazer R, Shikora S, Saltzman E (2006) Morbid obesity is an independent determinant of death among surgical critical ill patients. Crit Care Med 34:964–970
11. Bochicchio G, Joshi M, Bochicchio K, Nehman S, Tracy J, Scalea T (2006) Impact of obesity in the critically ill trauma patient: a prospective study. J Am Coll Surg 203
12. Aldawood A, Arabi Y, Dabbagh O (2006) Association of obesity with increased mortality in the critically ill patient. Anaesth Intensive Care 34:629–633
13. O'Brien J Jr, Phillips G, Ali N, Lucarelli M, Marsh C, Lemeshow S (2006) Body mass index is not independently associated with hospital mortality in mechanically ventilated adults with acute lung injury. Crit Care Med 34:738–744
14. Milberg J, Davis D, Steinberg K, Hudson L (1995) Improved survival of patients with acute respiratory distress syndrome (ARDS): 1983–1993. J Am Med Assoc 273:306–309
15. Cheung A, Tansey C, Tomlinson G, Diaz-Granados N, Matté A, Barr A, Mehta S, Mazer C, Guest C, Stewart T, Al-Saidi F, Cooper A, Cook D, Slutsky A, MS H (2006) Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. Am J Respir Crit Care Med 174:538–544
16. Hopkins R, Weaver L, Collingridge D, Parkinson R, Chan K, Orme J Jr (2005) Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med 171:340–347
17. Wells G, O'Connell D, Peterson J, Welch V, Tugwell P (2000) The Newcastle-Ottawa scale for re-assessing the quality of nonrandomised studies in meta-analysis. http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm
18. Stevens R, Dowdy D, Michaels R, Mendez-Tellez P, Pronovost P, Needham D (2007) Neuromuscular dysfunction acquired in critical illness: a systematic review. Int Care Med 33:1876–1891
19. Smith R, Chong T, Hedrick T, Hughes M, Evans H, McElearney S, Pruett T, Sawyer R (2007) Does body mass index affect infection-related outcomes in the intensive care unit? Surg Infect 8:581–588
20. Tremblay A, Bandi V (2003) Impact of body mass index on outcomes following critical care. Chest 123:1202–1207
21. Newell M, Bard M, Goettler C, Toschlog E, Schenarts P, Sagraves S, Holbert D, Pories W, Rotondo M (2007) Body mass index and outcomes in critically injured blunt trauma patients: weighing the impact. J Am Coll Surg 204:1056–1064
22. Higgins J, Thompson S (2002) Quantifying heterogeneity in a meta-analysis. Stat Med 21:1539–1558
23. O'Brien J Jr, Welsh C, Fish R, Ancukiewicz M, Kramer A, National Heart L, and Blood Institute Acute Respiratory Distress Syndrome Network (2004) Excess body weight is not independently associated with outcome in mechanically ventilated patients with acute lung injury. Ann Intern Med 140:338–345
24. Morris A, Stapleton R, Rubenfeld G, Hudson L, Caldwell E, Steinberg K (2007) The association between body mass index and clinical outcomes in acute lung injury. Chest 131:342–348
25. Neville A, Brown C, Weng J, Demetriades D, Velmahos G (2004) Obesity is an independent risk factor of mortality in severely injured blunt trauma patients. Arch Surg 139:983–987
26. Brown C, Neville A, Rhee P, Salim A, Velmahos G, Demetriades D (2005) The impact of obesity on the outcomes of 1,153 critically injured blunt trauma patients. J Trauma 59:1048–1051
27. Byrnes M, McDaniel M, Moore M, Helmer S, Smith R (2005) The effect of obesity on outcomes among injured patients. J Trauma 58:232–237
28. Alban R, Lyass S, Margulies D, Shabot M (2006) Obesity does not affect mortality after trauma. Am Surg 10:966–969
29. Brown C, Rhee P, Neville A, Sangthong B, Salim A, Demetriades D (2006) Obesity and traumatic brain injury. J Trauma 61:572–576
30. Ciesla D, Moore E, Johnson J, Burch J, Cothren C, Sauaia A (2006) Obesity increases risk for organ failure after severe trauma. J Am Coll Surg 203:539–545
31. El-Solh A, Sikka P, Bozkanat E, Jaafar W, Davies J (2001) Morbid obesity in the medical ICU. Chest 120:1989–1997
32. Bercault N, Boulain T, Kuteifan K, Wolf M, Runge I, Fleury J (2004) Obesity-related excess mortality rate in an adult intensive care unit: a risk-adjusted matched cohort study. Crit Care Med 32:998–1003
33. Goulenok C, Monchi M, Chiche J, Mira J, Dhainaut J, Cariou A (2004) Influence of overweight on ICU mortality. Chest 125:1441–1445
34. Ray D, Matchett S, Baker K, Wasser T, Young M (2005) The effect of body mass index on patient outcomes in a medical ICU. Chest 127:2125–2131
35. Peake S, Moran J, Ghelani D, Lloyd A, Walker M (2006) The effect of obesity on 12-month survival following admission to intensive care: a prospective study. Crit Care Med 34:2929–2939
36. Rice T (2007) Obesity in acute lung injury: the "weight" is over. Chest 131:333–334
37. De Waele B, Vanmierlo B, Van Nieuwenhove Y, Delvaux G (2006) Impact of body overweight and class I, II, and III obesity on the outcome of acute biliary pancreatitis. Pancreas 32:343–345
38. Duane T, Dechert T, Aboutanos M, Malhotra A, Ivatury R (2006) Obesity and outcomes after blunt trauma. J Trauma 61:1218–1221
39. Fan E, Needham D, Stewart T (2005) Ventilatory management of acute lung injury and acute respiratory distress syndrome. J Am Med Assoc 294:2889–2896
40. Bernard G (2005) Acute respiratory distress syndrome: a historical perspective. Am J Respir Crit Care Med 172:798–806
41. Hopkins R, Weaver L, Chan K, Orme JJ (2004) Quality of life, emotional, and cognitive function following acute respiratory distress syndrome. J Int Neuropsychol Soc 10:1005–1017

42. Heyland D, Groll D, Caeser M (2005) Survivors of acute respiratory distress syndrome: relationship between pulmonary dysfunction and long-term health-related quality of life. Crit Care Med 33:1549–1556
43. Gregg E, Cheng Y, Cadwell B, Imperatore G, Williams D, Flegal K, Narayan K, Willisamson D (2005) Secular trends in cardiovascular disease risk factors according to body mass index in US adults. J Am Med Assoc 293:1868–1874
44. Allley D, Chang V (2007) The changing relationship of obesity and disability, 1988–2004. J Am Med Assoc 298:2020–2027
45. Mokdad A, Ford E, Bowman B, Dietz W, Vinicor F, Bales V, Marks J (2003) Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. J Am Med Assoc 289:76–79
46. Sullivan M, Karlsson J, Sjöström L, Backman L, Bengtsson C, Bouchard C, Dahlgren S, Jonsson E, Larsson B, Lindstedt S (1993) Swedish obese subjects (SOS)—an intervention study of obesity. Baseline evaluation of health and psychosocial functioning in the first 1743 subjects examined. Int J Obes Relat Metab Disord 17:503–512
47. Doll H, Petersen S, Stewart-Brown S (2000) Obesity and physical and emotional well-being: associations between body mass index, chronic illness, and the physical and mental components of the SF-36 questionnaire. Obes Res 8:160–170
48. Yaegashi M, Raymonde J, Zuriqat M, Noack S, Homel P (2005) Outcome of morbid obesity in the intensive care unit. J Int Care Med 20:147–154