OBSERVATIONAL STUDY

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Continuous Renal Replacement Therapy and Mortality in Critically Ill Obese Adults

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IMPORTANCE: The outcomes of critically ill adults with obesity on continuous renal replacement therapy (CRRT) are poorly characterized. The impact of CRRT dose on these outcomes is uncertain.

OBJECTIVES: This study aimed to determine if obesity conferred a survival advantage for critically ill adults with acute kidney injury (AKI) on CRRT. Secondarily, we evaluated whether the dose of CRRT predicted mortality in this population.

DESIGN, SETTING, AND PARTICIPANTS: A retrospective, observational cohort study performed at an academic medical center in Minnesota. The study population included critically ill adults with AKI managed with CRRT.

MAIN OUTCOMES AND MEASURES: The primary outcome of 30-day mortality was compared between obese (body mass index [BMI] $\geq$ 30 kg/m^2) and nonobese (BMI $<$ 30 kg/m^2) patients. Multivariable regression assessed was used to assess CRRT dose as a predictor of outcomes. An analysis included dose indexed according to actual body weight (ABW), adjusted body weight (AdjBW), or ideal body weight (IBW).

RESULTS: Among 1033 included patients, the median (interquartile range) BMI was 26 kg/m^2 (23–28 kg/m^2) in the nonobese group and 36 kg/m^2 (32–41 kg/m^2) in the obese group. Mortality was similar between groups at 30 days (54% vs. 48%; $p = 0.06$) but lower in the obese group at 90 days (62% vs. 55%; $p = 0.02$). CRRT dose predicted an increase in mortality when indexed according to ABW or AdjBW (hazard ratio [HR], 1.2–1.16) but not IBW (HR, 1.04).

CONCLUSIONS AND RELEVANCE: In critically ill adults with AKI requiring CRRT, short-term mortality appeared lower in obese patients compared with nonobese patients. Among weight calculations, IBW appears to be preferred to promote safe CRRT dosing in obese patients.

KEYWORDS: continuous renal replacement therapy; critical illness; kidney; obesity; renal replacement therapy

Acute kidney injury (AKI) is common in critically ill adults and is associated with substantial mortality, morbidity, and cost. The need for renal replacement therapy (RRT) is associated with even higher rates of short- and long-term complications and higher mortality (1, 2). Continuous RRT (CRRT) is often the modality of choice in hemodynamically unstable patients. However, the preferred CRRT dose (calculated as milliliters of replacement fluid adjusted for body weight in an hour) has long been debated. Original studies suggested improved survival with higher CRRT doses. Still, more recent large-scale clinical trials have found no survival advantage with the use of high intensity ($\geq$ 35 mL/kg/hr) compared with lower intensity CRRT ($\leq$ 25 mL/kg/hr) (3–5). Therefore, current guidelines recommend a CRRT dose of 20–25 mL/kg/hr (6).

Although the evidence for appropriate CRRT dosage is compelling, obese patients are poorly represented in contemporary clinical trials. Obesity is

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KEY POINTS

Question: The objective of the study was to determine the impact obesity has on mortality in adult critically ill obese patients with acute kidney injury (AKI) requiring continuous renal replacement therapy (CRRT).

Findings: In this retrospective, single-center cohort study of critically ill adults with AKI and requiring CRRT, obesity was associated with lower mortality at 90 days. The CRRT dose was associated with higher mortality when indexed based on actual body weight and adjusted body weight.

Meaning: Obesity is associated with short-term mortality benefits, and CRRT using ideal body weight may result in better outcomes.

an independent risk factor for developing AKI (7). When reported, the mean weight in landmark CRRT dosing trials was 68–93 kg (± 20 kg), and although obesity based on body mass index (BMI) criteria was not specifically an exclusion in most studies, a weight of greater than 120–128 kg was an exclusion criterion in the majority of studies (5, 8–12). This leads to a general lack of information about CRRT epidemiology in the nearly 30% of critically ill adults in the United States who are obese (7). In general, obesity is associated with comorbidities and worse outcomes (13). Obesity in the critically ill should be associated with worse outcomes. However, the literature suggests otherwise and is termed the obesity paradox (13). There is a scarcity of evidence of CRRT dosing among obese patients. We conducted this retrospective cohort study to evaluate the impact of obesity on the outcomes of CRRT with a focus on CRRT dose. We hypothesized that obesity would be associated with a survival advantage in AKI patients requiring CRRT and that the dose of prescribed CRRT modifies mortality.

MATERIAL AND METHODS

Study Setting/Population/Intervention

This retrospective cohort study was conducted in multiple ICUs on the Rochester Campus (including Saint Mary's and Methodist Hospitals) within Mayo Clinic, Rochester, MN. The local institutional review board (IRB) reviewed and approved the study protocol with a waiver of informed consent due to the minimal risk nature of the study. All procedures and protocols were following ethical standards on human experimentation and with the Helsinki Declaration of 1975. Patients were identified utilizing an internal CRRT database originally created for IRB 10-000657, Complications of continuous renal replacement therapy in the ICU, approved on February 12, 2010.

The Mayo Clinic Hospital in Rochester, Minnesota, has 215 ICU beds. A consulting ICU Nephrology team manages all patients with a dialysis indication and determines the appropriate modality (intermittent, continuous, and peritoneal) for the clinical situation. The ICU Nephrology team consists of a senior staff Nephrologist, a complement of Nephrology and Critical Care Fellows, and second-year medical residents. Continuous venovenous hemofiltration is the default method of CRRT used on the Rochester Campus. As general guidance, the Nephrology Department prescribes CRRT at 30 mL/kg/hr at the discretion of the staff Nephrologist. The higher-than-guideline-recommended dosing intends for the patient to be delivered 20–25 mL/kg/hr after considering the differences between the prescribed and delivered dose (about 15% reduced delivered dose) and reduced clearance related to using 50% of the replacement fluid as predialyzer fluid. For this study, we used the average prescribed dose for the duration of the CRRT episode in case of minor variabilities during the treatment.

We included consecutive adult (≥ 18 yr) patients admitted to the ICUs who underwent CRRT to manage AKI for at least 48 hours from December 9, 2006, to December 31, 2014. Patients without research authorization, known pregnancy, moribund who died within 48 hours of CRRT start, had prior end-stage renal disease on dialysis, and prisoners were excluded. In multiple CRRT episodes where orders were discontinued and reordered, only the first CRRT treatment of each unique patient was included in the analysis. Patients were categorized based on obesity status using weight and height measured on ICU admission. Weight was ascertained using bed or standing scales in the ICU. Obesity was defined as a BMI greater than or equal to 30 kg/m^2 according to the World Health Organizations (WHOs) definition of obesity (14). Data was obtained electronically, and manual verification was performed on the missing data.

Study Outcomes

The study had two primary outcomes. The first was to evaluate the association between obesity and 30- and 90-day mortality rates in critically ill adult patients with AKI requiring CRRT. The second aim was to determine whether the CRRT dose (L/hr) was an effect modifier of the relationship between obesity and mortality in adult critically ill patients with AKI on CRRT. Secondary outcomes included ICU and hospital length of stay (LOS) and major adverse kidney events in 30 days ($MAKE_{30}$, including death, need for RRT, and persistent kidney dysfunction in 30 d) (15).

Statistical Analysis

Continuous variables were expressed as mean ± SD or median with the interquartile range depending on the normality of data distribution. Counts and percentages were used to describe categorical variables. The primary independent variable of interest was obesity, and the primary dependent variable was 30- and 90-day mortality. First, we dichotomized obesity consistent with WHO definitions into two groups, less than 30 or greater than or equal to 30 kg/m^2, and performed a chi-square test for the binary mortality outcome. We then performed a multivariable logistic regression with expected predictors of mortality in critically ill patients, such as age, sex, severity of illness, vasopressor requirements, and the need for mechanical ventilation. Obesity was evaluated as a dichotomous predictor and a continuous variable in these models. As the relationship between obesity and outcomes in critically ill patients with AKI requiring RRT exhibits a U-shaped pattern, we used restricted cubic splines to model BMI in the case of nonlinearity (7). The reported dose was reported as the average dose for the duration of the CRRT episode. We then included CRRT dose in L/hr as a predictor variable and performed a formal test of interaction to determine whether CRRT dose modified the effect of obesity on mortality. Finally, we tested the dosing schemes calculated based on actual body weight (ABW), adjusted body weight (AdjBW), and ideal body weight (IBW) to assess which one of these schemes is associated with minimal effect modification. IBW was calculated as (males–50 kg + [2.3 kg × each inch over 60 inches] and females–45.5 kg + [2.3 kg × each inch over 60 inches]). AdjBW was calculated as ([actual body weight–ideal body weight] × 0.4) + ideal body weight (16).

RESULTS

We screened 1135 patients between December 9, 2006, and December 31, 2014. One thousand thirty-three patients met the eligibility criteria and were analyzed.

Baseline age, sex, and race were balanced between the groups (**Table 1**) (17, 18). As expected, actual and adjusted ICU admission and CRRT initiation weights differed between the groups, while the calculated IBW was not statistically different.

Patients with BMI less than 30 kg/m^2 had a higher Acute Physiology and Chronic Health Evaluation (APACHE) III score 24 hours after ICU admission and a higher Sequential Organ Failure Assessment (SOFA) score on day 1 of ICU admission when compared with obese patients. Additionally, the nonobese group had a higher Vasoactive-Inotropic Score (VIS) within the 24 hours before CRRT initiation than the obese group (**Supplemental Table 1**, http://links.lww.com/CCX/B265). The preadmission estimated glomerular filtration rate as calculated via Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) serum creatinine formula was lower in the nonobese group than in the obese group (17). As the CKD-EPI formula does not include weight, it was not influenced by the baseline weight differences between the groups. We did not find any differences in the duration of CRRT between the two groups. However, the CRRT dosages, calculated based on the ABW, were statistically higher in the nonobese patients (30 ± 9 in nonobese vs. 27 ± 7 mL/kg/hr in obese patients; $p < 0.001$). When the dose was calculated based on IBW (37 ± 10 in nonobese vs. 48 ± 14 mL/kg/hr in obese patients; $p < 0.001$) and AdjBW (33 ± 9 in nonobese vs. 36 ± 9 mL/kg/hr in obese patients; $p < 0.001$), the obese group received significantly higher doses.

Outcomes

The 30-day mortality was 54% in the nonobese group vs. 48% in the obese group ($p = 0.06$). At 90 days, mortality was 62% in the nonobese group vs. 55% in the obese group ($p = 0.02$) (**Table 2**). When BMI was approached as a continuous variable, there was a survival advantage at both 30- and 90-day mortality when BMI increased, that is, for each 5 kg/m^2 increase in BMI, there was a 7–8% decrease in mortality ($p = 0.008$ at 30 d and 0.001 at 90 d, respectively).

TABLE 1.
Baseline Demographics

Demographics	BMI < 30 kg/m²[a] (*n* = 509)	BMI ≥ 30 kg/m²[a] (*n* = 524)	*p*
Age (yr)	61.4 (16.1)	61.3 (14.4)	0.59
Male sex	305 (60%)	304 (58%)	0.53
Race			0.13
White	429 (84.3%)	463 (88.4%)	
Black or African American	17 (3.3%)	11 (2%)	
Asian	14 (2.8%)	5 (1.0%)	
Other	20 (3.9%)	21 (4.0%)	
Unknown/choose not to disclose	29 (5.7%)	24 (4.6%)	
Weight (kg)			
ICU admission	73.8 (13.5)	108.9 (24.0)	< 0.001
CRRT initiation	78.8 (15.8)	112.4 (24.4)	< 0.001
IBW	64.7 (11.3)	64.0 (11.5)	0.44
AdjBW	70.3 (11.9)	83.4 (13.8)	< 0.001
Difference of hospital admission weight vs. ICU admission weight	−0.3 (8.5)	−1.1 (7.2)	0.34
Body mass index (kg/m²)[a], median (IQR)	26 (23–28)	36 (32–41)	
Charlson Comorbidity Index	5.1 (3.1)	5.1 (3.0)	0.75
Operative admission[b]	280 (55%)	257 (49%)	0.06
Apache III score at 24 hr after ICU admission	107 (31.1)	103 (31.0)	0.03
Sequential Organ Failure Assessment on day 1 of ICU admission	12 (3.9)	11.5 (4.1)	0.04
Vasoactive-Inotropic Score[c], median (IQR)			
At ICU admission	19.1 (11.2–44.4)	18.2 (8.4–44.1)	0.09
In the 24 hr before CRRT initiation	18.9 (10.6–42.4)	15.7 (8.2–36.6)	0.007
In the 24 hr before CRRT discontinuation	15.0 (5.9–36.9)	11.7 (4.5–38.4)	0.12
In the 24 hr after CRRT discontinuation	17.1 (7.0–48.6)	17.4 (5.4–57.5)	0.54
Kidney function parameters, median (IQR)			
Preadmission serum creatinine (mg/dL)[d]	0.9 (0.8–1.1)	0.9 (0.8–1.1)	0.76
Preadmission estimated glomerular filtration rate (mL/min)[e]	87 (59–109)	95 (69–126)	< 0.001
Highest serum creatinine during ICU admission (mg/dL)	3.2 (2.4–4.3)	3.5 (2.6–4.7)	< 0.001
Highest blood urea nitrogen during ICU admission (mg/dL)	75 (52–100)	73.5 (51–96)	0.37
Highest creatinine in the 24 hr before CRRT initiation (mg/dL)	2.8 (2.2–3.7)	3.1 (2.3–4.2)	0.002
Highest cystatin C in the 24 hr before CRRT initiation (mg/L)[f]	2.5 (1.8–3.7)	2.5 (1.7–3.3)	0.64
Highest blood urea nitrogen in the 24 hr before CRRT initiation (mg/dL)	52.5 (35–84)	56 (37–81)	0.44

(*Continued*)

TABLE 1. (*Continued*)
Baseline Demographics

Demographics	BMI < 30 kg/m²[a] (*n* = 509)	BMI ≥ 30 kg/m²[a] (*n* = 524)	*p*
CRRT parameters			
Duration of CRRT (d), median (IQR)	3.7 (1.6–7.0)	3.3 (1.5–7.0)	0.59
Dose (mL/kg/hr)			
Based on actual body weight	30 (9)	27 (7)	< 0.001
Based on IBW	37 (10)	48 (14)	< 0.001
Based on AdjBW	33 (9)	36 (9)	< 0.001

AdjBW = adjusted body weight, BMI = body mass index, CRRT = continuous renal replacement therapy, IBW = ideal body weight, IQR = interquartile range.
[a]BMI based on ICU admission weight.
[b]Operative admission includes operative and interventional procedures, otherwise considered a medical admission.
[c]Vasoactive-Inotropic Score–(mean dobutamine μg/kg/min per timeframe) + (mean dopamine μg/kg/min per timeframe) + ([mean epinephrine μg/kg/min per timeframe] × 100) + ([mean norepinephrine μg/kg/min per timeframe] × 100) + ([mean phenylephrine μg/kg/min per timeframe] × 100) + ([mean vasopressin U/kg/min per timeframe) × 1000) (16).
[d]Mean of all preadmission creatinine results from 365 to 7 d before admission.
[e]Chronic Kidney Disease Epidemiology Collaboration (15).
[f]Only available in 32 (14 nonobese, 18 obese).
Values expressed as mean (SD) or frequency (%) unless otherwise specified.

TABLE 2.
Outcomes

Outcomes	BMI < 30 (*n* = 509)	BMI ≥ 30 (*n* = 524)	*p*
30-d mortality, *n* (%)	276 (54)	253 (48)	0.06
90-d mortality, *n* (%)	315 (62)	286 (55)	0.02
ICU length of stay, median (IQR)	8.4 (3.9–17.1)	8.3 (4.1–14.4)	0.47
Hospital length of stay, median (IQR)	17.0 (7.5–32.1)	15.9 (7.7–30.5)	0.29
Mechanical ventilation days, median (IQR)	5.5 (1.9–12.1)	4.3 (1.4–10.1)	0.02
Major adverse kidney events in 30 d score, *n* (%)	354 (70)	343 (66)	0.16
	Hazard Ratio (95% CI)		***p***
30-d mortality (per 5 kg/m² increase)	0.93 (0.89–0.98)		0.008
90-d mortality (per 5 kg/m² increase)	0.92 (0.88–0.97)		0.001

BMI = body mass index, IQR = interquartile range.

There were no differences between the groups in ICU LOS, hospital LOS, and $MAKE_{30}$. However, a significant difference was noted in mechanical ventilation days (4.3 vs. 5.5 d; $p = 0.02$) with one less day of mechanical ventilation in the obese group.

A multivariable model was constructed to explore the obesity and mortality relationship further (**Table 3**). Surgical admission was associated with decreased 30-day mortality, whereas APACHE III and age were associated with worse 30-day mortality. Findings were similar at 90 days. After accounting for sex and SOFA, there were no significant differences in 30- and 90-day mortality rates between the two groups. Finally, the year of admission was associated with both a 30- and 90-day mortality improvement as the years progressed to the present.

Effect Modification

We sought to determine if the dose of CRRT modified the relationship between obesity and mortality. The median dose for the entire population was 2.5 L/

TABLE 3.
Multivariable Models

Variable	30-d Mortality		90-d Mortality	
	Hazard Ratio (95% CI)	*p*	Hazard Ratio (95% CI)	*p*
Obese	0.89 (0.75–1.06)	0.20	0.87 (0.74–1.02)	0.10
Age (per decade)	1.07 (1.00–1.14)	0.04	1.08 (1.02–1.14)	0.012
Male sex	1.04 (0.87–1.23)	0.68	0.99 (0.84–1.17)	0.92
Operative admission	0.81 (0.68–0.96)	0.02	0.84 (0.71–0.98)	0.03
Acute Physiology and Chronic Health Evaluation III (per 10 points)	1.11 (1.06–1.15)	< 0.001	1.09 (1.05–1.14)	< 0.001
Sequential Organ Failure Assessment (per 1 point)	1.00 (0.97–1.04)	0.80	1.00 (0.97–1.03)	0.97
Year of admission (per year)	0.96 (0.93–0.98)	0.002	0.95 (0.92–0.97)	< 0.001

hr (IQR, 2–3 L/hr). There was no significant association between dose in L/hr and 30- or 90-day mortality (**Table 4**). When ABW or AdjBW was used to calculate CRRT dose, patients receiving higher CRRT doses had higher mortality rates, despite the finding that higher ABW or AdjBW was associated with improved survival. However, when IBW was used, higher CRRT dose and patient weight were not associated with a higher mortality rate.

We also sought to determine if the dose of CRRT would influence mortality when stratified by obesity status (**Supplemental Table 2**, http://links.lww.com/CCX/B265). In nonobese patients, dosing CRRT based on different weights (i.e., ABW, AdjBW, or IBW) did not influence mortality. In obese patients, as the dose of CRRT based on ABW and AdjBW increased, so did 30-day mortality. Thirty- and 90-day mortality rates were not different between obese and nonobese groups after accounting for CRRT dosage based on IBW.

DISCUSSION

Comparing a nonobese vs. an obese critically ill population experiencing AKI and requiring CRRT, we found significantly lower mortality in obese patients 90 days after CRRT initiation. We also noted when ABW and AdjBW were used to calculate the dose of CRRT, there were significantly higher hospital and 30-day mortality rates only in obese patients when higher CRRT dosages were used. This relationship was not noted when IBW was used to calculate the CRRT dose.

In our critically ill population, those who experienced AKI and required CRRT had 30- and 90-day mortality rates of 51% and 58%, respectively. This underscores the clinical impact of severe AKI on outcomes. This finding is consistent with previously published literature. The reported 30-day mortality rates range from 36% to 56%, and 60- and 90-day death rates are greater than 50% (5, 11, 12). These studies also indicated the average CRRT duration as 6–10 days.

In the general population, obesity is linked to increased comorbidity burden and worse outcomes. In the critically ill, however, there is evidence of an inverse relationship between obesity and mortality, referred to as the "obesity paradox" (13, 19–25). The exact mechanism for this observed association is unclear. It may be linked to increased energy reserves from fat depots mobilized in acute illness, larger skeletal muscle mass, and chronic preconditioning associated with obesity-induced oxidative stress. The obesity paradox has been observed in select studies of patients with AKI undergoing CRRT, but the findings are inconsistent (5, 26–28). In these studies, sample size, BMI distribution, and differences in predictor variables likely influenced these discrepancies. CRRT prescription has been infrequently reported as a covariate in these studies (29). Our findings add more evidence to the "obesity paradox" in the CRRT population. The mortality rate for the total population was 51%. While the 30-day mortality was lower in the obese population, the effect did not reach statistical significance. In a longer-term follow-up, that

TABLE 4.
Continuous Renal Replacement Therapy Dose and Mortality for Total Population

Continuous Renal Replacement Therapy Dose and Weight	In-Hospital Mortality		30-d Mortality		90-d Mortality	
	Hazard Ratio (95% CI)	*p*	Hazard Ratio (95% CI)	*p*	Hazard Ratio (95% CI)	*p*
Total population						
Dose (per 1 L/hr increase)	1.04 (0.93–1.16)	0.54	1.03 (0.93–1.16)	0.55	0.99 (0.89–1.1)	0.79
Actual body weight						
Dose (per 1 L/hr increase)	1.20 (1.05–1.38)	0.008	1.20 (1.05–1.38)	0.008	1.13 (1.00–1.29)	0.06
Per 5 kg increase	0.96 (0.94–0.98)	< 0.001	0.96 (0.94–0.98)	< 0.001	0.97 (0.95–0.98)	< 0.001
Adjusted body weight						
Dose (per 1 L/hr increase)	1.17 (1.02–1.33)	0.02	1.16 (1.01–1.32)	0.03	1.09 (0.96–1.24)	0.17
Per 5 kg increase	0.94 (0.91–0.98)	0.002	0.95 (0.91–0.98)	0.003	0.95 (0.92–0.99)	0.005
Ideal body weight						
Dose (per 1 L/hr increase)	1.05 (0.94–1.18)	0.4	1.04 (0.93–1.17)	0.47	0.99 (0.89–1.11)	0.91
Per 5 kg increase	0.98 (0.94–1.02)	0.34	0.99 (0.95–1.03)	0.58	0.99 (0.96–1.03)	0.62

is, 90 days, we noted obesity associated with lower death rates. When BMI was applied as a continuous variable, we demonstrated a survival advantage for each 5 kg/m^2 increase in BMI at 30- and 90-day follow-ups. In multivariable models, age, and severity of illness scores within the first 24 hours of ICU admission significantly influenced mortality rates in the obese population.

We assessed the relationship of the CRRT dosage with mortality in the obese population. When we used ABW or AdjBW for replacement fluid dose calculation, increasing doses were associated with higher in-hospital and 30-day mortality, despite the previously noted relationship that increasing weight confers a survival advantage in obesity. When IBW was used to calculate CRRT dose, neither dose nor increasing weight was associated with significantly higher mortality. We noted when the CRRT dosages for obese patients were calculated by IBW instead of ABW and AdjBW, the obese patients appeared to have overtly overdosed. This may play a role in increased mortality among those with higher CRRT dosage according to their ABW and AdjBW.

Indeed, the effect modification impact of CRRT dosage on mortality disappeared when IBW was used to calculate the CRRT dosage among obese patients. Therefore, using IBW instead of ABW and AdjBW for calculating CRRT dosage among obese patients may be considered a modifiable risk mitigation strategy among these patients. However, further research is warranted to evaluate the strength and consistency of our finding that CRRT dose calculation based on IBW could mitigate risks among this very high-risk group.

Another potential argument for IBW-based CRRT dosing in obese patients is resource utilization. The total amount of replacement fluid used would decrease, which may decrease the cost of CRRT treatment. For example, utilizing average CRRT initiation weight and CRRT dose based on ABW in our study, the obese population required an average of six additional bags of replacement fluids per day in comparison with dose calculation based on IBW.

Interpretation of presented data needs to be taken with caution, considering the potential limitations of our study. First, the two groups were not completely balanced at baseline. The nonobese group appeared to have a higher severity of illness at baseline, as evidenced by higher APACHE III, SOFA, and VIS scores before CRRT initiation. Neither APACHE III nor SOFA scores account for weight in the scoring parameters. However, the VIS score is based on a dose normalized to μg/kg/min (U/kg/min for vasopressin) (29–31). Similar to the CRRT dose calculation, there is no standard weight or weight adjustment for vasopressors when accounting for obesity. Vasopressors are not reliably adjusted for obesity. Using μg/min vs.

μg/kg/min could misinterpret the degree of vasoactive support described by Radosevich et al (32) and Vadiei et al (33). Despite this limitation of the VIS score, it still provides context for vasoactive support, as higher scores have been associated with worse outcomes (18). Decreased VIS could be interpreted as reducing vasoactive agent exposure and, thus, fewer adverse events related to the vasopressors. Second, the presented data are retrospective and only evaluates overall mortality but does not consider the reason for starting RRT, solute clearance, and volume control. We did not present data describing the prescribed dialysis's adequacy for solute clearance or volume control. This retrospective cohort study may have been associated with biases inherently related to this study's design. For instance, while we could adjudicate surgical vs. medical admissions in our cohort, the details related to the type of surgeries were unavailable. This will limit the generalizability of our results and does not establish any causal relationships. The data set is drawn from 2006 to 2014. While the guideline recommended CRRT dose has not changed since this time frame, other practice changes may have occurred in the last ten years which affect the generalizability of these findings to today. Nevertheless, the focus of the article is on the relationship between obesity and outcomes, reflective of biology which is unlikely to have changed. It is reported that fluid resuscitation could be associated with weight changes; therefore, if patients received fluid before CRRT initiation, it could have impacted their BMI and, thus, their study groups. Due to the variability of weight measurement methods, the amount of fluid received before CRRT initiation, and differences in sources of admission (e.g., hospital floor or emergency department), we opted to use the weight closest to the CRRT initiation time to classify patients, acknowledging the potential biases that could be induced. Finally, during the time frame of this database, multiple nephrologists calculated the CRRT dosages. Although they all used a similar protocol for the CRRT dosages, there was no formal protocol for adjusting CRRT dose based on obesity. While ABW was used to calculate CRRT dosage during the study in most cases, we cannot determine what percentage of patients had their CRRT dosage calculated based on AdjBW or IBW.

Despite the limitations of our study, our investigation had several strengths as well. We used a relatively large cohort of greater than 1000 patients, of which over 500 were classified as obese and likely excluded from clinical trials. Prior studies involving CRRT range from less than 100 patients to greater than 1200 patients (4, 5, 8, 9, 11). In future studies, investigators should define obesity and the CRRT dose calculation based on different weights (ABW, AdjBW, or IBW) to normalize the effect of CRRT dose on obese patient outcomes.

CONCLUSIONS

This retrospective cohort study in multiple ICUs comparing a nonobese vs. an obese critically ill population experiencing AKI and requiring CRRT found a lower 90-day mortality and duration of mechanical ventilation in the obese population compared with the nonobese population. Therefore, we found further evidence of the "obesity paradox," with a survival advantage associated with a higher BMI. Furthermore, when comparing CRRT doses in the obese population using different weights, there was no difference in mortality based on CRRT dosage when the CRRT dose was calculated using IBW. However, escalating doses utilizing ABW and AdjBW were associated with higher in-hospital and 30-day mortality. This evidence indicates using IBW to calculate the CRRT dosage might provide a safer dosing scheme for obese patients. However, our results need to be validated in future prospective studies.

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