Body Mass Index as a Predictor of Acute Kidney Injury in Critically Ill Patients: A Retrospective Single-Center Study

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Background: The aim of this study was to examine the influence of body mass index (BMI) on the development of acute kidney injury (AKI) in critically ill patients in intensive care unit (ICU).

Methods: Data of patients admitted to medical ICU from December 2011 to May 2014 were retrospectively analyzed. Patients were classified into three groups according to their BMI: underweight (<18.5 kg/m^2), normal ($18.5–24.9$ kg/m^2), and overweight (≥25 kg/m^2). The incidence of AKI was compared among these groups and factors associated with the development of AKI were analyzed. AKI was defined according to the Risk, Injury, Failure, Loss of kidney function, and End-stage (RIFLE) kidney disease criteria.

Results: A total of 468 patients were analyzed. Their mean BMI was 21.5 ± 3.9 kg/m^2, including 102 (21.8%) underweight, 286 (61.1%) normal-weight, and 80 (17.1%) overweight patients. Overall, AKI occurred in 82 (17.5%) patients. The overweight group had significantly ($p<0.001$) higher incidence of AKI (36.3%) than the underweight (9.8%) or normal group (15.0%). In addition, BMI was significantly higher in patients with AKI than that in those without AKI (23.4 ± 4.2 vs. 21.1 ± 3.7, $p<0.001$). Multivariate analysis showed that BMI was significantly associated with the development of AKI (odds ratio, 1.893; 95% confidence interval, 1.224–2.927).

Conclusion: BMI may be associated with the development of AKI in critically ill patients.

Keywords: Body Mass Index; Acute Kidney Injury; Intensive Care Unit

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Introduction

Body mass index (BMI), calculated from the height and weight of a patient, is a simple and useful index for obesity[1]. BMI has been reported to be an important prognostic factor for many medical conditions. For example, in chronic obstructive pulmonary disease, chronic renal failure, and cancer, mortality is increased in underweight patients[2,3], whereas in many metabolic diseases, including hypertension, diabetes mellitus, and dyslipidemia, mortality is commonly increased in overweight patients[4]. Moreover, the relationship between BMI and all-cause mortality in the general population is known to be 'J'- or 'U'-shaped[5].

Many studies have examined the usefulness of BMI as a prognostic factor in critically ill patients with differing results.

Mortality appears to be increased in morbidly obese patients[6], while no relationship between mortality and obesity was observed in another prospective study[7]. Moreover, recent studies have shown that mortality in the intensive care unit (ICU) is lower in obese patients than in those who are underweight[7-9]. The development of acute kidney injury (AKI) in ICU patients is a frequent complication that can affect the prognosis[10,11]. Therefore, the development of AKI in these patients and the associated risk factors have been extensively studied[11]. However, only a few studies have assessed the relationship between BMI and AKI in critically ill patients[12-15]. Accordingly, the purpose of this study was to assess the influence of BMI on the development of AKI in critically ill patients.

Materials and Methods

1. Study design and settings

All critical-ill patients who were admitted to the medical intensive care unit (MICU) at Gyeongsang National University Hospital (hospital total, 890 beds; MICU, 13 to 15 beds) between December 2011 and May 2014 were retrospectively studied. The admission was decided by attending physician according to general criteria of ICU admission[16]. Before admission, consents were received from patients' family or caregiver. Patients were excluded if they were admitted for acute coronary syndrome, overdose, acute cerebrovascular disease, and chronic renal failure or were <18 years of age.

This study was approved by the institutional review board of Gyeongsang National University Changwon Hospital (GNUCH-2018-05-014). Informed consent was waived due to the retrospective nature of the study.

2. Data collection and definitions

Demographic information, past medical history, and reason for ICU admission were collected for each patient on admission and discharge from the MICU according to the MICU registry at our institution. The Acute Physiology and Chronic Health Evaluation (APACHE) II score and Sequential Organ Failure Assessment (SOFA) score, measures of severity of illness and predictors of mortality[17], were also calculated. Height was recorded based on previous medical records or the ICU admission measurement. Body weight was measured automatically using a calibrated bed scale (VersaCare Bed; Hill-Rom, Batesville, IN, USA) at ICU admission. BMI was calculated as body weight (kg)/height (m^2). The patients were classified into three groups based on the degree of obesity as defined by the World Health Organization and the National Heart, Lung and Blood Institute of the National Institutes of Health as follows: underweight (BMI, <18.5 kg/m^2), normal (BMI, 18.5–24.9 kg/m^2), and overweight (BMI, ≥25.0 kg/m^2)

groups[18].

AKI was defined by the Risk, Injury, Failure, Loss of kidney function, and End-stage (RIFLE) kidney disease criteria using the creatinine level, glomerular filtration rate, and urine output[19]. The number of days the patient required mechanical ventilation, length of stay (LOS) in the ICU and hospital, and mortality in the ICU and hospital were assessed.

3. Statistical analysis

Continuous variables are reported as the mean±standard deviation. Categorical variables are described as number (%). Differences between groups were compared using analysis of variance, Student's t test, or chi-square test as appropriate. Univariate and multivariate logistic regression analysis was performed to examine the relation between BMI and the factors associated with the development of AKI. Statistical significance was defined as a p-value of <0.05. All data were analyzed using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

1. Patient characteristics

A total of 468 patients were analyzed. The average age was 68.6±13.9 years, with a male-to-female ratio of 2:1. The mean BMI was 21.5±3.9 kg/m^2 (range, 12.2–39.6 kg/m^2). The mean APACHE II and SOFA scores were 18.8±8.8 and 7.9±4.4, respectively. The average LOS was 10.0±18.1 days in the ICU and 25.7±35.8 days in the hospital. The ICU morality rate was 35.8%, with an overall hospital mortality rate of 44.7%. AKI developed in 82 patients (17.1%).

2. Comparison of clinical characteristics according to the BMI groups

The baseline characteristics of the patients according to BMI group are summarized in Table 1. Of the 468 patients, 102 (21.8%) were underweight, 286 (61.1%) were normal-weight, and 80 (17.1%) were overweight. The mean age of the underweight group was 71.3±12.7 years, which was significantly older than that of the overweight patients (64.9±13.8 years, p=0.008). For the underweight, normal-weight, and overweight groups, the mean BMI values were 16.5±1.5, 21.6±1.8, and 27.7±2.5 kg/m^2, respectively. The overweight group had a significantly higher incidence of AKI (36.3%) than the underweight (9.8%) and normal groups (15.0%) (p<0.001 for all). In addition, the overweight group had a higher incidence of hypertension, liver cirrhosis, and chronic kidney disease (p<0.05 for all). The diagnoses on admission included septic shock, acute respiratory distress syndrome (ARDS),

Table 1. Baseline characteristics of patients by BMI groups

Characteristic	Total	Underweight (BMI <18.5)	Normal (BMI 18.5–24.9)	Overweight (BMI ≥25.0)	p-value
No. of patients	486	102	286	80	
Sex (male/female)	306/162	62/40	197/89	47/33	0.132
Age, yr	68.6±13.9	71.3±12.7	68.6±14.1	64.9±13.8	0.008
Age >80 yr	106 (22.6)	31 (30.4)	62 (21.7)	13 (16.3)	0.020
BMI, kg/m²	21.5±3.9	16.5±1.5	21.6±1.8	27.7±2.5	<0.001
AKI	82 (17.1)	10 (9.8)	43 (15.0)	29 (36.3)	<0.001
Comorbidities					
DM	155 (33.1)	27 (26.5)	94 (33.0)	34 (42.5)	0.074
HTN	192 (41.0)	34 (33.3)	114 (39.9)	44 (55.0)	0.011
CVD	89 (19.0)	25 (24.5)	47 (16.4)	17 (21.3)	0.174
LC	45 (9.6)	3 (2.9)	29 (10.1)	13 (16.3)	0.009
CKD	69 (14.7)	8 (7.8)	42 (14.7)	19 (23.8)	0.011
Malignancy	59 (12.6)	15 (14.7)	32 (11.2)	12 (15.0)	0.510
Heart failure	23 (4.9)	6 (5.9)	15 (5.2)	2 (2.5)	0.530
Alcoholism	70 (15)	10 (9.8)	46 (16.1)	14 (17.5)	0.510
Reason for admission					
Severe sepsis/Septic shock	162 (34.6)	28 (27.5)	97 (33.9)	37 (46.2)	0.010
Lower respiratory tract infection	84 (17.9)	15 (14.7)	56 (19.6)	13 (16.3)	
Gastrointestinal tract infection	10 (2.1)	0 (0)	5 (1.7)	5 (6.3)	
Urinary tract infection	8 (1.7)	3 (2.9)	4 (1.4)	1 (1.3)	
Hepatobiliary tract infection	5 (1.1)	1 (1.0)	2 (0.7)	2 (2.5)	
Intra-abdominal infection	2 (0.4)	0 (0)	1 (0.3)	1 (1.3)	
Wound infection	2 (0.4)	1 (1.0)	1 (0.3)	0 (0)	
Mediastinal infection	1 (0.2)	0 (0)	0 (0)	1 (1.3)	
Unknown	51 (10.7)	8 (7.8)	28 (9.8)	14 (17.5)	
ARDS	73 (15.6)	12 (11.8)	44 (15.4)	17 (21.3)	0.213
Pulmonary cause	60 (12.8)	8 (7.8)	39 (13.6)	13 (16.3)	
Extrapulmonary cause	13 (2.8)	4 (3.9)	5 (1.7)	4 (5.0)	
APACHE II score	18.8±8.8	16.7±7.5	18.8±8.8	21.4±10.0	0.002
SOFA score	7.9±4.4	6.6±4.2	7.9±4.2	9.4±5.0	<0.001
Extubation failure	115 (24.6)	34 (33.3)	63 (22.0)	18 (22.5)	0.067
Transfusion requirement	179 (38.2)	36 (35.3.7)	104 (36.4)	39 (48.8)	0.103
Renal replacement therapy	113 (24.1)	19 (18.6)	66 (23.1)	28 (35)	0.030
ECMO	8 (1.7)	0 (0)	3 (1)	5 (6.3)	0.011
Use of systemic steroid before ICU admission	87 (18.6)	27 (26.5)	50 (17.5)	10 (12.5)	0.041
MV duration, day	9.6±16.9	10.7±11.8	9.8±19.8	7.4±10.5	0.412
ICU LOS, day	10.0±18.1	11.7±13.4	10.3±21.0	6.9±9.8	0.184
Hospital LOS, day	25.7±35.8	28.3±39.2	26.6±37.5	19.2±22.2	0.186
ICU death	180 (38.5)	41 (40.2)	104 (36.4)	35 (43.8)	0.448
Hospital death	209 (44.7)	48 (47.1)	121 (42.3)	40 (50.0)	0.406

Values are presented as mean±SD or number (%).
AKI: acute kidney injury; BMI: body mass index; DM: diabetes mellitus; HTN: hypertension; CVD: cardiovascular disease; LC: liver cirrhosis; CKD: chronic kidney disease; ARDS: acute respiratory distress syndrome; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; MV: mechanical ventilation; LOS: length of stay.

Table 2. Baseline characteristics according to development of AKI

Characteristic	AKI	No AKI	p-value
No. of patients	82	386	
Sex (male/female)	54/28	252/134	0.105
Age, yr	66.3±13.9	69.1±13.8	0.105
Age >80 yr	14 (17.1)	98 (23.8)	0.185
BMI, kg/m^2	23.4±4.2	21.1±3.7	<0.001
Comorbidity			
DM	36 (43.9)	119 (30.8)	0.028
HTN	38 (46.3)	154 (39.9)	0.323
CVD	7 (8.5)	50 (13.0)	0.352
LC	17 (20.7)	28 (7.3)	0.001
CKD	8 (7.8)	42 (14.7)	0.011
Malignancy	13 (15.9)	46 (11.9)	0.359
Heart failure	6 (7.3)	17 (4.4)	0.264
Alcoholism	21 (25.6)	49 (12.7)	0.006
Reason for admission			
Septic shock	43 (53.8)	119 (31.2)	<0.001
Lower respiratory tract infection	17 (20.7)	67 (17.4)	
Gastrointestinal tract infection	7 (8.5)	3 (3.7)	
Urinary tract infection	3 (3.7)	5 (3.7)	
Hepatobiliary tract infection	2 (2.4)	3 (3.7)	
Intra-abdominal infection	2 (2.4)	0 (0)	
Wound infection	0 (0)	2 (0.5)	
Mediastinal infection	0 (0)	1 (0.3)	
Unknown	12 (14.6)	38 (9.8)	
ARDS	20 (24.4)	53 (13.7)	0.019
Pulmonary cause	15 (18.3)	45 (11.7)	
Extrapulmonary cause	5 (6.1)	8 (2.1)	
RIFLE criteria			
Injury	63 (76.8)		
Failure	19 (23.2)		
APACHE II score	23.5±8.6	17.8±8.6	<0.001
SOFA score	10.5±4.4	7.3±4.2	<0.001
Extubation failure	33 (40.2)	82 (21.2)	0.001
Transfusion requirement	58 (70.7)	121 (31.3)	0.000
Renal replacement therapy	40 (48.8)	73 (18.9)	0.000
ECMO	5 (6.1)	3 (0.8)	0.003
Use of systemic steroid before ICU admission	14 (17.1)	73 (18.9)	0.750
MV duration, day	6.9±7.0	10.2±18.4	0.009
ICU LOS, day	7.7±8.5	10.5±19.5	0.040
Hospital LOS, day	19.5±22.0	27.1±38.0	0.082
ICU death	61 (74.4)	119 (30.8)	0.000
Hospital death	61 (74.4)	148 (38.3)	0.000

BMI: body mass index; AKI: acute kidney injury; DM: diabetes mellitus; HTN: hypertension; CVD: cardiovascular disease; LC: liver cirrhosis; CKD: chronic kidney disease; ARDS: acute respiratory distress syndrome; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; MV: mechanical ventilation; LOS: length of stay.

gastrointestinal bleeding, with septic shock and ARDS being the main reasons for admission to the MICU. The established causes of septic shock and ARDS were described in the Table 1. Compared to the underweight (27.5%) and normal (33.9%) groups, the overweight group had a significantly higher incidence of septic shock (46.2%) as the reason for ICU admission (p=0.010). The APACHE II and SOFA scores of the overweight group were also significantly higher than those of the other two groups (p=0.002 and p<0.001, respectively). Regarding the clinical outcomes, the LOS in the ICU and hospital tended to be shorter when the BMI was increased. The highest mortality was found in the overweight group, and the lowest mortality was found in the normal weight group. However, there were no significant differences among the three BMI groups regarding the ICU LOS, hospital LOS, ICU death rate, and in-hospital death rate (p>0.05 for all).

3. Comparison of clinical characteristics according to development of AKI

The BMI was significantly higher in patients with AKI than in those without it (23.4±4.2 kg/m^2 vs. 21.1±3.7 kg/m^2, p<0.05). Patients with AKI had a higher incidence of liver cirrhosis, diabetes, chronic kidney disease, and alcoholism. Moreover, these patients showed a higher incidence of septic shock and ARDS than patients without AKI at the time of admission. Extubation failure, need for transfusion, use of renal replacement therapy, and application of extracorporeal membrane oxygenation were also more common in patients with AKI than in those without it. Regarding the clinical outcomes, the LOS in the ICU and hospital were significantly longer for patients with AKI than for those without AKI (p<0.05). The ICU and hospital mortality rates were also significantly higher in

patients with AKI than in those without it (74.4% vs. 30.8% for ICU mortality; 74.4% vs. 38.3% for hospital mortality; p<0.05 for both) (Table 2).

4. Risk factors for development of AKI

Finally, we assessed the risk factors for AKI in the ICU by logistic regression analyses. In univariate analysis, BMI, diabetes, chronic kidney disease, liver cirrhosis, alcoholism, septic shock, ARDS, SOFA score, and APACHE II score were found to be risk factors for AKI. However, BMI groups were found to be significantly associated with a risk of developing AKI in the multivariate analysis (odds ratio, 1.893; 95% confidence interval, 1.224–2.927; p=0.004) (Table 3).

Discussion

This study revealed that BMI was an independent risk factor for the development of AKI in critically ill patients.

Although BMI has been shown to be a useful prognostic marker in critically ill patients, the relationship between BMI and the development of AKI has not been extensively investigated in the literature[12-15]. However, several reports investigated the association between BMI and the development of AKI in critically ill patients. Soto et al.[13] retrospectively analyzed risk factors for AKI in 751 patients with ARDS. The study showed that the prevalence of AKI increased significantly with increasing weight. In addition, there was a 2-fold increase in the risk of AKI in obese patients compared to those of normal weight. The study also reported that the risk could not be completely explained by the severity of illness. A study of 390 patients with sepsis also showed that BMI was higher

Table 3. Univariate and multivariate logistic regression analysis for factor associated with development of AKI

	Univariate analysis				Multivariate analysis			
	β±SE	t	Unadjusted odds ratio (95% CI)	p-value	β±SE	t	Adjusted odds ratio (95% CI)	p-value
Age >80 yr	−0.419±0.317	1.746	0.658 (0.354–1.224)	0.186	−0.086±0.351	0.060	0.917 (0.461–1.825)	0.917
BMI, 3 groups	0.911±0.208	19.097	2.486 (1.652–3.740)	<0.001	0.638±0.222	8.223	1.893 (1.224–2.927)	0.004
DM	0.559±0.248	5.071	1.749 (1.075–2.846)	0.024	0.454±0.275	2.722	1.575 (0.918–2.701)	0.099
LC	1.207±0.336	12.928	3.344 (1.732–6.457)	0.000	0.415±0.416	0.999	1.515 (0.671–3.421)	0.317
CKD	0.752±0.258	8.453	2.210 (1.278–3.519)	0.004	0.223±0.296	0.567	1.250 (0.699–3.421)	0.451
Alcoholism	−0.086±0.296	8.501	0.422 (0.237–0.754)	0.004	−0.040±0.373	1.171	0.668 (0.321–1.387)	0.279
Septic shock	0.470±0.126	13.971	1.600 (1.250–2.047)	0.000	0.202±0.144	1.963	1.224 (0.337–1.431)	0.161
ARDS	0.706±0.297	5.671	2.027 (1.133–3.625)	0.017	0.624±0.325	3.683	1.866 (0.987–3.350)	0.055
SOFA	0.161±0.029	31.672	1.175 (1.111–1.242)	0.000	0.077±0.047	1.634	1.080 (0.985–1.183)	0.201

p-values less than 0.05 were considered as significant.

AKI: acute kidney injury; SE: standard error; CI: confidence interval; BMI: body mass index; DM: diabetes mellitus; LC: liver cirrhosis; CKD: chronic kidney disease; ARDS: acute respiratory distress syndrome; SOFA: Sequential Organ Failure Assessment.

in patients with AKI than in patients without AKI[15]. Another study showed the incidence of AKI in patients requiring renal replacement therapy went up as BMI increased[12]. Further, several studies have reported that AKI develops more frequently in patients with a high BMI after cardiac and abdominal surgery[20,21]. These findings, along with our study, showed that a high BMI was a risk factor for the development of AKI in critically ill patients.

The association between high BMI and risk of AKI development could be explained by several mechanisms. First, obesity causes some hemodynamic changes in the glomerulus such as glomerular hyperperfusion and hyperfiltration due to impaired natriuresis-associated activation of the renin and angiotensin system. Glomerular hyperperfusion and hyperfiltration may be result in glomerular injury. These changes have been demonstrated in an experimental animal model of obesity and in obese patients[22,23]. Second, obesity can increase the hemodynamic and metabolic load on each individual glomerulus, which results in a low number of functional nephrons in obese patients[24]. In turn, a low number of functional nephrons was related to glomerular hypertrophy and glomerulosclerosis due to increased capillary pressure on the remaining functional nephrons[24]. Third, adipocytes may be as a production site for activated inflammatory cytokines and oxidative stress in obese patients[25]. Increased oxidative stress can contribute to detrimental changes in the glomeruli[26]. Taken together, in obese type II diabetes mellitus patients, reduction of body weight has been shown to be associated with significant decreases in proteinuria. This finding support that harmful influence of obesity to kidney injury[27].

Liver cirrhosis and diabetes were more common in patients with AKI than in patients without AKI in our study. In patients with liver cirrhosis, the development of AKI has been shown a relatively frequent problem, especially in critically ill patients, and it has a great impact on prognosis in these patients[28]. Although diabetes and the development of AKI was not studied in critically ill patients, a recent report showed that, in patients with sepsis, underlying diabetes was not associated with the development of AKI[29]. Further study is needed to evaluate diabetes as a risk factor for AKI in critically ill patients.

Extubation failure was more common in patients with AKI than in patients without AKI in our study. Extubation failure is usually associated with a longer duration of mechanical ventilation and ICU stay[30]. It may increase the risk of several complications in the ICU. As a result, ICU patients with extubation failure may be more vulnerable to developing AKI. Previous reports have showed that the time to extubation may be associated with development of AKI in postcardiac surgery patients[31,32]. These reports suggest that the duration of positive pressure ventilation in critically ill patients is an important risk factor for AKI development. In fact, mechanical ventilation itself has been shown to induce proinflammatory reactions and extrapulmonary end organ injury in animal models of

mechanical ventilation[33,34]. Conversely, AKI may be associated with a higher rate of extubation failure and delayed weaning.

Although there are conflicting results between BMI and mortality in ICU patients. It is generally reported that patients with Low BMI have a higher mortality rate than those with normal BMI. A large-population prospective study conducted in Korea showed that low BMI patients has a higher mortality than in patient with normal and higher BMI[35]. In this study, the mortality rate of patients with low BMI was slightly higher (36% vs. 40%) than the patients with normal BMI although there was no statistically significant in two group.

There are some limitations to this study. First, enrolled patients came from the medical ICU of a single tertiary hospital. The risk factors for AKI in the MICU may differ from those in surgical ICUs. For example, in surgical ICU patients, postoperative AKI due to decreased intravascular volume is a relatively common problem. By contrast, the risk factors for AKI in MICU patients usually include the presence of infection and medications (e.g., antibiotics, vasopressors). Second, the characteristics of the enrolled patients were heterogeneous. Hence, the risk for AKI may be quite different and it depend on the underlying disease and the reason for ICU admission. Therefore, the risk factors for AKI are assessed in a homogenous group of patients such as sepsis or acute lung injury.

In conclusion, compared to low or normal BMI, a high BMI was found to be associated with a higher risk of developing AKI in critically ill patients treated in the MICU in this study. This result suggests that BMI may be associated with the development of AKI in critically ill patients.

Authors' Contributions

Conceptualization: Kim HC. Methodology: Ju S, Kim HC. Formal analysis: Kim HC. Data curation: Ju S, Lee TW. Software: Ju S, Kim HC. Validation: Ju S, Lee TW, Kim HC. Investigation: all authors. Writing - original draft preparation: Ju S. Writing - review and editing: Kim HC. Approval of final manuscript: all authors.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. J Pediatr 1998;132:204-10.

2. Cao C, Wang R, Wang J, Bunjhoo H, Xu Y, Xiong W. Body mass index and mortality in chronic obstructive pulmonary disease: a meta-analysis. PLoS One 2012;7:e43892.

3. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003;348:1625-38.

4. Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, et al. Obesity and the metabolic syndrome in children and adolescents. N Engl J Med 2004;350:2362-74.

5. Jee SH, Sull JW, Park J, Lee SY, Ohrr H, Guallar E, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006;355:779-87.

6. Goulenok C, Monchi M, Chiche JD, Mira JP, Dhainaut JF, Cariou A. Influence of overweight on ICU mortality: a prospective study. Chest 2004;125:1441-5.

7. Frat JP, Gissot V, Ragot S, Desachy A, Runge I, Lebert C, et al. Impact of obesity in mechanically ventilated patients: a prospective study. Intensive Care Med 2008;34:1991-8.

8. Anzueto A, Frutos-Vivar F, Esteban A, Bensalami N, Marks D, Raymondos K, et al. Influence of body mass index on outcome of the mechanically ventilated patients. Thorax 2011;66:66-73.

9. Garrouste-Orgeas M, Troche G, Azoulay E, Caubel A, de Lassence A, Cheval C, et al. Body mass index. An additional prognostic factor in ICU patients. Intensive Care Med 2004;30:437-43.

10. Bagshaw SM, George C, Dinu I, Bellomo R. A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. Nephrol Dial Transplant 2008;23:1203-10.

11. Cartin-Ceba R, Kashiouris M, Plataki M, Kor DJ, Gajic O, Casey ET. Risk factors for development of acute kidney injury in critically ill patients: a systematic review and meta-analysis of observational studies. Crit Care Res Pract 2012;2012:691013.

12. Druml W, Metnitz B, Schaden E, Bauer P, Metnitz PG. Impact of body mass on incidence and prognosis of acute kidney injury requiring renal replacement therapy. Intensive Care Med 2010;36:1221-8.

13. Soto GJ, Frank AJ, Christiani DC, Gong MN. Body mass index and acute kidney injury in the acute respiratory distress syndrome. Crit Care Med 2012;40:2601-8.

14. Suneja M, Kumar AB. Obesity and perioperative acute kidney injury: a focused review. J Crit Care 2014;29:694.e1-6.

15. Plataki M, Kashani K, Cabello-Garza J, Maldonado F, Kashyap R, Kor DJ, et al. Predictors of acute kidney injury in septic shock patients: an observational cohort study. Clin J Am Soc Nephrol 2011;6:1744-51.

16. Smith G, Nielsen M. ABC of intensive care: criteria for admission. BMJ 1999;318:1544-7.

17. Moreno R, Morais P. Outcome prediction in intensive care: results of a prospective, multicentre, Portuguese study. Intensive Care Med 1997;23:177-86.

18. Choo V. WHO reassesses appropriate body-mass index for Asian populations. Lancet 2002;360:235.

19. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: a systematic review. Kidney Int 2008;73:538-46.

20. Billings FT 4th, Pretorius M, Schildcrout JS, Mercaldo ND, Byrne JG, Ikizler TA, et al. Obesity and oxidative stress predict AKI after cardiac surgery. J Am Soc Nephrol 2012;23:1221-8.

21. Thakar CV, Kharat V, Blanck S, Leonard AC. Acute kidney injury after gastric bypass surgery. Clin J Am Soc Nephrol 2007;2:426-30.

22. Henegar JR, Bigler SA, Henegar LK, Tyagi SC, Hall JE. Functional and structural changes in the kidney in the early stages of obesity. J Am Soc Nephrol 2001;12:1211-7.

23. Chagnac A, Weinstein T, Korzets A, Ramadan E, Hirsch J, Gafter U. Glomerular hemodynamics in severe obesity. Am J Physiol Renal Physiol 2000;278:F817-22.

24. Hostetter TH, Olson JL, Rennke HG, Venkatachalam MA, Brenner BM. Hyperfiltration in remnant nephrons: a potentially adverse response to renal ablation. J Am Soc Nephrol 2001;12:1315-25.

25. Pausova Z. From big fat cells to high blood pressure: a pathway to obesity-associated hypertension. Curr Opin Nephrol Hypertens 2006;15:173-8.

26. Chander PN, Gealekman O, Brodsky SV, Elitok S, Tojo A, Crabtree M, et al. Nephropathy in Zucker diabetic fat rat is associated with oxidative and nitrosative stress: prevention by chronic therapy with a peroxynitrite scavenger ebselen. J Am Soc Nephrol 2004;15:2391-403.

27. Morales E, Valero MA, Leon M, Hernandez E, Praga M. Beneficial effects of weight loss in overweight patients with chronic proteinuric nephropathies. Am J Kidney Dis 2003;41:319-27.

28. Garcia-Tsao G, Parikh CR, Viola A. Acute kidney injury in cirrhosis. Hepatology 2008;48:2064-77.

29. Venot M, Weis L, Clec'h C, Darmon M, Allaouchiche B, Goldgran-Toledano D, et al. Acute kidney injury in severe sepsis and septic shock in patients with and without diabetes mellitus: a multicenter study. PLoS One 2015;10:e0127411.

30. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112:186-92.

31. Doddakula K, Al-Sarraf N, Gately K, Hughes A, Tolan M, Young V, et al. Predictors of acute renal failure requiring renal replacement therapy post cardiac surgery in patients with preoperatively normal renal function. Interact Cardiovasc Thorac Surg 2007;6:314-8.

32. Heringlake M, Nowak Y, Schon J, Trautmann J, Berggreen AE, Charitos EI, et al. Postoperative intubation time is associated with acute kidney injury in cardiac surgical patients. Crit Care 2014;18:547.

33. Imai Y, Parodo J, Kajikawa O, de Perrot M, Fischer S, Edwards V, et al. Injurious mechanical ventilation and end-organ epithelial cell apoptosis and organ dysfunction in an experimental model of acute respiratory distress syndrome. JAMA

2003;289:2104-12.

34. O'Mahony DS, Liles WC, Altemeier WA, Dhanireddy S, Frevert CW, Liggitt D, et al. Mechanical ventilation interacts with endotoxemia to induce extrapulmonary organ dysfunction. Crit Care 2006;10:R136.

35. Lim SY, Choi WI, Jeon K, Guallar E, Koh Y, Lim CM, et al. Body mass index and mortality in Korean intensive care units: a prospective multicenter cohort study. PLoS One 2014;9:e90039.