CardioRenal Medicine

Cardiorenal Med 2018;8:9–17

DOI: 10.1159/000477824
Received: January 6, 2017
Accepted: May 17, 2017
Published online: September 16, 2017

Original Paper

Role of Body Mass Index in Acute Kidney Injury Patients after Cardiac Surgery

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Keywords

Acute kidney injury · Body mass index · Cardiac surgery · Hospital mortality · Renal replacement therapy

Abstract

Background/Aims: To explore the association of body mass index (BMI) with the risk of developing acute kidney injury after cardiac surgery (CS-AKI) and for AKI requiring renal replacement therapy (AKI-RRT) after cardiac surgery. ***Methods:*** Clinical data of 8,455 patients undergoing cardiac surgery, including demographic preoperative, intraoperative, and postoperative data were collected. Patients were divided into underweight (BMI <18.5), normal weight (18.5≤ BMI <24), overweight (24≤ BMI <28), and obese (BMI ≥28) groups. The influence of BMI on CS-AKI incidence, duration of hospital, and intensive care unit (ICU) stays as well as AKI-related mortality was analyzed. ***Results:*** The mean age of the patients was 53.2 ± 13.9 years. The overall CS-AKI incidence was 33.8% (n = 2,855) with a hospital mortality of 5.4% (n = 154). The incidence of AKI-RRT was 5.2% (n = 148) with a mortality of 54.1% (n = 80). For underweight, normal weight, overweight, and obese cardiac surgery patients, the AKI incidences were 29.9, 31.0, 36.5, and 46.0%, respectively ($p < 0.001$). The hospital mortality of AKI patients in the 4 groups was 9.5, 6.0, 3.8, and 4.3%, whereas the hospital mortality of AKI-RRT patients in the 4 groups was 69.2, 60.8, 36.4, and 58.8%, both significantly different ($p < 0.05$). Hospital and ICU stay durations were not significantly different in the 4 BMI groups. ***Conclusion:*** The hospital prognosis of AKI and AKI-RRT patients after cardiac surgery was best when their BMI was in the 24–28 range.

Zhouping Zou, Yamin Zhuang, and Lan Liu contributed equally to this study.

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Introduction

Acute kidney injury (AKI) is a common and serious complication of cardiac surgery; AKI has been reported to occur in 5–50% of hospitalized patients undergoing cardiac surgery based on different definitions of AKI [1–3]. AKI after cardiac surgery (CS-AKI) patients have higher mortality rates than those who did not develop AKI [4, 5], and the mortality rate of AKI-renal replacement therapy (AKI-RRT) patients has been reported to be 41.4–65% [6–9]. Current research has found that there are many factors related to the incidence of CS-AKI and its outcome, with body mass index (BMI) being one of these risk factors. Obesity and high BMI have recently been demonstrated to be associated with AKI in intensive care units and post-surgical populations [10–14]. Few studies have focused on the role of BMI in the incidence and prognosis of CS-AKI in China; therefore, the relationship between BMI and AKI in China remains unclear. In addition, BMI classification standards, primary diseases, and complications are differently defined in Caucasian patients, and related foreign research may not be completely applicable to the Chinese.

In the present study, BMI classification was carried out following the standards established for the Chinese population in order to understand the impact of BMI on CS-AKI in Chinese people and provide prevention and control strategies in Asians.

Patients and Methods

Study Population

This was a retrospective study of patients who underwent valve and cardiopulmonary bypass (CPB) cardiac surgery between January 2009 and December 2014 in the Zhongshan Hospital affiliated to Fudan University. The Ethical Committee of Zhongshan Hospital approved the study, and all participating patients gave their informed consent. A total of 8,455 eligible adult patients were included. The exclusion criteria were: patients ≤18 years old; solitary kidney or history of kidney transplants; undergoing cardiac transplantation; preoperative circulatory assist devices; patients who had preoperative RRT; or a lack of clinical data (Fig. 1).

AKI and BMI Definitions

AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) [15, 16] criteria: (1) increase in serum creatinine (SCr) by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 h; (2) increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; (3) urine volume <0.5 mL/kg/h for 6 h and was staged according to the SCr and urine output.

The BMI classification (BMI = weight [kg]/height [m^2]) followed the standards established for the Chinese according to the Department of Disease Control Ministry of Health [17], and the patients were divided into 4 groups: underweight group (BMI <18.5); normal-weight group (18.5≤ BMI <24); overweight group (24≤ BMI <28); and obese group (BMI ≥28).

Clinical Trial Design and Methods

The clinical data including preoperative as well as intraoperative and postoperative variables of patients were recorded. Preoperative data included baseline characteristics, complications, preoperative renal function (defined as the latest available SCr value prior to cardiac surgery), and perioperative cardiac functions (classification by NYHA [18]). Intraoperative variables included cardiac output data from echocardiography, duration of CPB time in minutes, aortic cross-clamp times, and type of surgery. Postoperative variables included duration of mechanical ventilation, urine output in the first 24 h after cardiac surgery, incidence and stage of AKI as well as hospital mortality of AKI and AKI-RRT patients.

Outcomes

The primary outcome was all-cause hospital mortality. The secondary outcome was length of stay in the ICU and hospital.

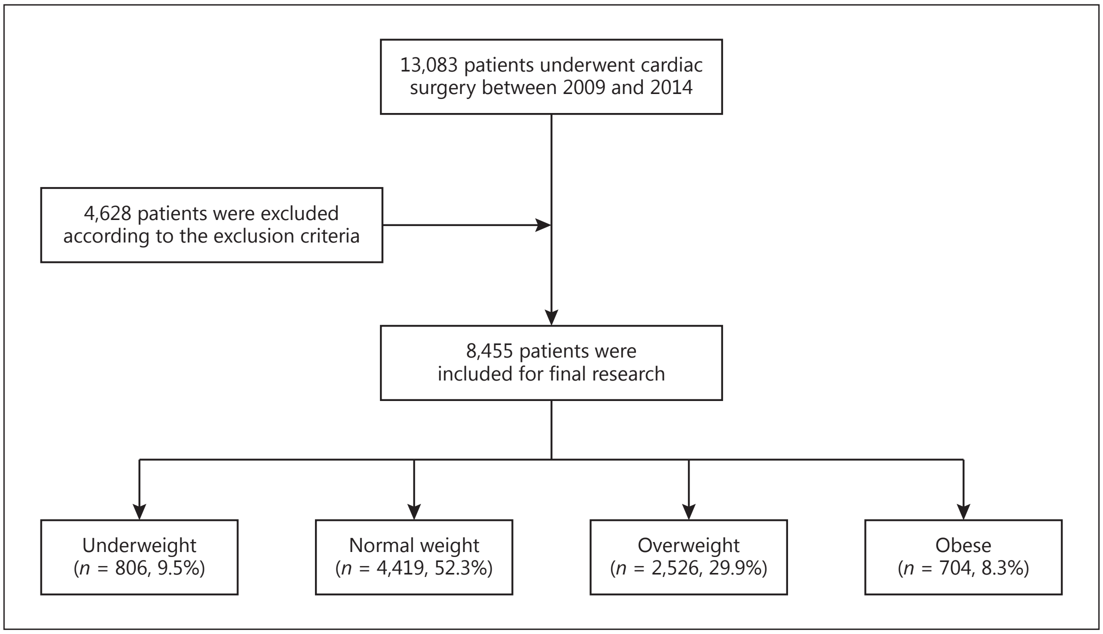

Fig. 1. Flowchart of the present study.

Statistical Analysis

All statistical analyses were performed using SPSS Statistics for Windows, (version 20.0; IBM Corp., Armonk, NY, USA). AKI Incidence was compared among the BMI groups using the Pearson χ^2 test. Demographic, preoperative, intraoperative, and postoperative variables were compared among the BMI groups using a one-way ANOVA test for the continuous variables and the Pearson χ^2 test for the categorical variables. The association of the demographic, preoperative, intraoperative, and postoperative variables with AKI was tested using a two-sample *t* test or a Wilcoxon rank-sum test for the continuous variables and the Pearson χ^2 test for the categorical variables. Values are expressed as the mean ± SD, or median (interquartile range) for continuous variables, and as frequency counts (%) for the categorical variables. Two-tailed p values <0.05 were considered to be statistically significant.

Results

A total of 8,455 patients were enrolled, of which 4,706 (55.7%) were male and 3,749 (44.3%) were female. The mean age was 53.2 ± 13.9 years, and the mean BMI 23.0 ± 3.6. The distribution of patients by BMI group was 806 (9.5%) in the underweight group, 4,419 (52.3%) in the normal weight group, 2,526 (29.9%) in the overweight group, and 704 (8.3%) in the obese group. The mean age, proportion of males, baseline SCr, proportions of hypertension, diabetes, coronary angiography, chronic heart failure (NYHA >II), and baseline uric acid were increased with increasing BMI (Table 1).

The Relationship between BMI and AKI Incidence

The overall incidence of CS-AKI was 33.8% (2,855/8,455). The AKI incidences were 29.9, 31.0, 36.5, and 46.0% in the underweight, normal weight, overweight, and obese groups, respectively ($p < 0.001$). Each increment of 5 in admission BMI was associated with a 5.8% (95% CI, 4.2–7.4%; $p < 0.001$) higher adjusted risk of AKI according to the AKI diagnosis criteria of KDIGO. The incidence of AKI stage 2 and 3 was 33.2, 26.2, 27.7, and 31.2% in the 4

Table 1. Comparison of baseline characteristics among the four BMI groups

	Underweight (*n* = 806)	Normal weight (*n* = 4,419)	Overweight (*n* = 2,526)	Obese (*n* = 704)	*p* value
Male, %	340 (42.2)	2,251 (51.0)	1,644 (65.1)	471 (66.9)	<0.001
Age, years	47.8±16.6	52.6±14.1	55.3±12.2	55.0±11.9	<0.001
Height, cm	163.6±7.3	163.4±7.2	166.4±7.0	166.1±8.0	<0.001
Body weight, kg	46.0±5.2	58.0±6.6	71.2±6.8	83.0±8.2	<0.001
Hypertension, %	97 (12.0)	1,042 (23.6)	922 (36.5)	344 (48.9)	<0.001
Diabetes mellitus, %	38 (4.7)	292 (6.6)	307 (12.2)	111 (15.8)	<0.001
NYHA					
I–II	313 (38.8)	1,890 (42.8)	1,130 (44.7)	300 (42.6)	0.030
III–IV	493 (61.2)	2,529 (57.2)	1,396 (55.3)	404 (57.4)	0.030
Preoperative LVEF, %	62.1±9.2	61.8±9.2	62.1±8.5	61.5±9.3	0.710
CPB time, min	93.9±44.6	93.6±37.8	98.1±38.0	100.4±42.4	<0.001
ACC time, min	54.9±25.7	56.1±26.8	58.2±25.9	57.3±26.5	0.009
Preoperative coronary angiography *n*, %	206 (25.6)	1,524 (34.5)	1,090 (43.2)	304 (43.2)	<0.001
Interval between coronary angiography and cardiac surgery, days	3 (2.5)	3 (2.6)	4 (2.6)	4 (2.6)	0.048
Albumin baseline, g/L	39.8±4.1	40.2±3.6	40.3±3.3	40.4±3.1	0.014
UA baseline, µmol/L	342.0±114.6	354.7±117.4	377.8±141.8	396.0±109.5	<0.001
eGFR baseline, mL/min	98.2±28.6	91.9±25.1	89.3±23.1	87.3±23.1	<0.001
SCr baseline, µmol/L	73.4±25.0	77.4±25.3	80.9±24.0	83.0±24.4	<0.001
BUN baseline, mmol/L	6.6±3.0	6.6±2.9	6.3±2.2	6.3±2.0	0.005

NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass; ACC aortic cross-clamp; UA, uric acid; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; BUN, blood urea nitrogen.

Table 2. Incidence of AKI after cardiac surgery among the four groups

	Underweight	Normal weight	Overweight	Obese	*p* value
AKI, *n* (%)	241 (29.9)	1,368 (31.0)	922 (36.5)	324 (46.0)	<0.001
AKI stage 1, *n* (%)	161 (66.8)	1,010 (73.8)	667 (72.3)	223 (68.8)	0.067
AKI stage 2 *n* (%)	51 (21.2)	205 (15.0)	154 (16.7)	67 (20.7)	0.018
AKI stage 3, *n* (%)	29 (12.0)	153 (11.2)	101 (11.0)	34 (10.5)	0.948
AKI stage 2–3, *n* (%)	80 (33.2)	358 (26.2)	255 (27.7)	101 (31.2)	0.067

AKI, acute kidney injury.

groups, respectively ($p = 0.067$) (Table 2). The adjusted odds ratios of AKI were 1.18 (95% CI, 0.96–1.46), 1.20 (1.04–1.37), and 1.50 (1.20–1.88) when underweight, overweight, and obesity groups were compared with the normal-weight group (Fig. 2).

Obese patients had a significantly greater risk of developing AKI than those in the lower BMI groups. The odds ratio of CS-AKI in obese patients relative to the lower BMI groups was 1.39 (95% CI, 1.12–1.72; $p < 0.001$), even after accounting for covariates (i.e., diabetes mellitus, hypertension, age, heart function, preoperative albumin, preoperative SCr, and CPB time). According to the RIFLE standard, in which eGFR elevation or decline greater than or equal to 25% are set as a diagnostic criteria of AKI, the AKI incidences were 36.5% (294/806), 32.9% (1,454/4,419), 35.3% (892/2,526), and 42.5% (299/704) in the 4 groups, respectively ($p <$ 0.001). Compared with KDIGO, when using RIFLE criteria, the AKI incidences from normal BMI to obese patients group all increased, while the AKI incidence rate in the underweight group was enhanced compared to normal-weight patients.

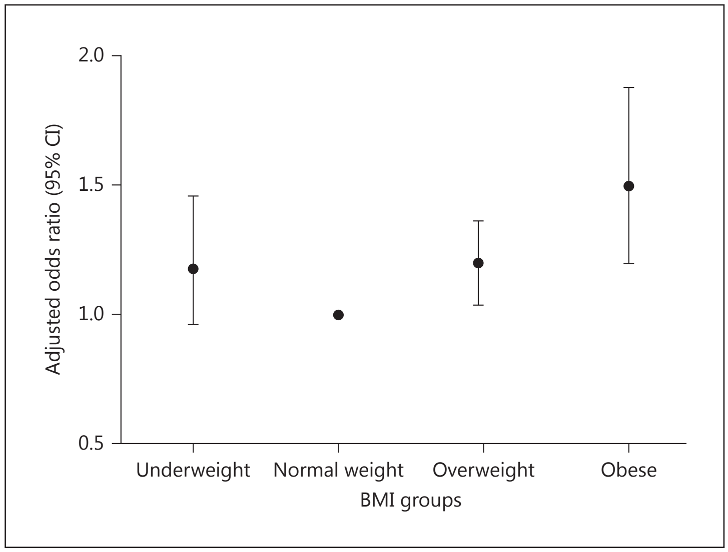

Fig. 2. Adjusted odds ratios for the incidence of AKI in the respective BMI groups.

Table 3. Univariate logistic regression analysis of risk factors for CS-AKI

	OR	95% CI	*p* value
Age, years	1.031	1.027–1.035	<0.001
Gender (male)	1.910	1.740–2.097	<0.001
BMI (additional BMI 5)	1.282	1.210–1.359	<0.001
Hypertension	1.704	1.546–1.879	<0.001
Diabetes mellitus	1.444	1.239–1.683	<0.001
CHF (NYHA >II)	1.475	1.345–1.618	<0.001
Preoperative coronary angiography	1.429	1.303–1.568	<0.001
Albumin baseline	0.955	0.942–0.968	<0.001
BUN baseline	1.174	1.145–1.190	<0.001
SCr baseline	1.014	1.012–1.016	<0.001
eGFR baseline	0.990	0.988–0.992	0.035
UA baseline	1.003	1.003–1.004	<0.001
CPB additional 30 min	1.487	1.425–1.551	<0.001
ACC additional 20 min	1.263	1.215–1.313	<0.001
Valve surgery	0.762	0.686–0.846	<0.001
CPB surgery	1.040	0.929–1.164	0.498
CPB + valve surgery	3.024	2.407–3.801	<0.0001

BMI, body mass index; CHF, chronic heart failure; NYHA, New York Heart Association; BUN, blood urea nitrogen; SCr, serum creatinine; eGFR, estimated glomerular filtration rate; UA, uric acid; CPB, cardiopulmonary bypass; ACC aortic cross-clamp.

Risk Factors for the Development of CS-AKI

Next, we analyzed risk factors for CS-AKI in a univariate logistic regression model, and the results are presented in Table 3. Apart from BMI and combined valve and CPB surgery, in particular gender (male), hypertension, diabetes mellitus, CHF, and CPB and aortic cross-clamp times were risk factors for developing CS-AKI (Table 3).

The odds ratios of CS-AKI for the independent risk factors that were computed from the multivariate logistic regression model are shown in Table 4.

Table 4. Multivariate logistic regression analysis of risk factors for CS-AKI

	OR	95% CI	*p* value
Age	1.037	1.031–1.043	<0.001
Gender (male)	1.837	1.615–2.090	<0.001
BMI (additional BMI 5)	1.155	1.058–1.260	0.001
CHF (NYHA >II)	1.216	1.064–1.390	0.004
CPB (additional 30 min)	1.410	1.334–1.491	<0.001
Hypertension	1.156	1.001–1.325	0.048
BUN baseline	1.057	1.027–1.088	<0.001
UA baseline	1.002	1.001–1.002	<0.001
Valve surgery	0.826	0.619–1.102	0.194
CPB surgery	0.652	0.367–0.774	0.070
CPB + valve surgery	1.033	0.975–1.094	0.270
SCr baseline	0.999	0.995–1.002	0.491

BMI, body mass index; CHF, chronic heart failure; NYHA, New York Heart Association; CPB, cardiopulmonary bypass; BUN, blood urea nitrogen; UA, uric acid; SCr, serum creatinine.

Table 5. The short-term prognosis of AKI and AKI-RRT after cardiac surgery among underweight, normal weight, overweight, and obese patients

	Underweight	Normal weight	Overweight	Obese	*p* value
AKI mortality, *n* (%)	23/241 (9.5)	82/1,368 (6.0)	35/922 (3.8)	14/324 (4.3)	0.002
Incidence of AKI-RRT, *n* (%)	13/241 (5.4)	74/1,368 (5.4)	44/922 (4.8)	17/324 (5.2)	0.922
AKI-RRT mortality, *n* (%)	9/13 (69.2)	45/74 (60.8)	16/44 (36.4)	10/17 (58.8)	0.041
Duration of mechanical ventilation, days	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 2)	0.158
LOS in ICU, h	44 (20, 95)	40 (20, 88)	39 (20, 86)	40 (19, 93)	0.398
LOS in hospital, days	14 (10, 18)	13 (10, 18)	14 (11, 18)	14 (11, 18)	0.272

AKI, acute kidney injury; AKI-RRT, acute kidney injury requiring renal replacement; LOS, length of stay; ICU, intensive care unit.

Relationship between BMI and Prognosis of AKI

The overall incidence of AKI-RRT was 5.2% (148/2,855), with the incidence of AKI-RRT being 5.4, 5.4, 4.8, and 5.2% in underweight, normal weight, overweight, and obese patients, respectively ($p = 0.922$). The mortality rate of AKI and AKI-RRT patients was 5.4% (154/2,855) and 54.1% (80/148), respectively. There were significant differences in mortality from AKI in underweight, normal weight, overweight, and obesity patients (9.5, 6.0, 3.8, and 4.3%, respectively; $p = 0.002$), and the adjusted odds ratios of mortality from AKI were 1.89 (95% CI, 1.50–3.41), 0.85 (95% CI, 0.52–1.39), and 0.95 (95% CI, 0.44–2.02) when underweight, overweight, and obese patients were compared with the normal weight group, respectively. There was also a significant difference in the mortality of AKI-RRT patients between the 4 BMI groups (69.2, 60.8, 36.4, and 58.8%, $p = 0.041$). The mortality of the underweight group was greatly increased when SCr levels were elevated to ≥106.4 μmol/L and eGFR declined by more than 60% compared with values before cardiac surgery. Comparisons of the duration of mechanical ventilation, ICU and hospital stay showed no significant differences for AKI or AKI-RRT patients among the 4 BMI groups ($p > 0.05$) (Table 5).

Discussion

The overall CS-AKI incidence was 33.8%, which is in accordance with a previously published Chinese frequency of 31.2% [19]. The mortality rates of AKI and AKI-RRT patients were 5.4 and 54.1%, which is also in agreement with previously published rates of 4% for all CS-AKI patients [20] and 50% for CS-AKI-RRT patients [6] in non-Chinese studies. The present research has shown that increasing BMI, especially obesity (BMI ≥28), was associated with an increased incidence of AKI after cardiac surgery, which is in good agreement with previous literature. Billings et al. [14] studied the relationship between BMI and AKI incidence in 445 patients undergoing cardiac surgery, and reported that a higher BMI was associated with independently increased odds of AKI incidence (26.5% increase per 5 kg/m^2; p = 0.02). A single-center retrospective study by Kumar et al. [21] classified the BMI of patients undergoing cardiac surgery after CPB into normal, overweight obesity class I, obesity class II, and obesity class III, based on the NIH definition for overweight and obesity. The results showed that among the BMI groups, the obese cohort (BMI >40) had a significantly higher risk of developing AKI after CPB than those in the lower BMI classes. BMI >40 was significantly associated with development of AKI even after accounting for diabetes mellitus, hypertension, age, the severity of the illness and CPB time (overall p = 0.018). The odds ratio of AKI after CPB in the BMI >40 cohort relative to BMI <25 patients was 2.39 (p = 0.055), with no significant difference in the risk of developing AKI after CPB among the 4 lower BMI classes. Since renal ischemia and reperfusion contribute to the development and progression of AKI [6], the factors related to obesity may cumulatively account for the increased risk of AKI after CPB in obese patients. The possible pathophysiological mechanisms may be that adipose tissue coupled with insulin resistance and hyperinsulinemia in obese patients leads to inappropriate activation of the renin-angiotensin-aldosterone axis and increased oxidative stress in the kidneys by secreted hormones and cytokines [21–25]. In addition, obese patients have elevations in both kidney plasma flow and glomerular filtration rates, thereby promoting glomerular capillary hypertension, underlying occult and declared structural changes in the kidneys of obese patients [24]. However, our results revealed that although the incidence of AKI correlated with BMI, the mortality of AKI and AKI-RRT patients did not, being lowest in overweight patients and in agreement with previous studies, in which a high BMI had a survival benefit for AKI [13], CS-AKI [26], and cardiac surgery [27] patients. A recent Chinese study about the impact of BMI on the prognosis of AKI in geriatric postoperative major surgery patients revealed that elderly AKI patients of normal weight had a lower mortality risk compared to those who were underweight or obese [28]. Other researchers reported associations between mild obesity and hospital mortality after vascular surgery. This phenomenon is referred to as "reverse" or "paradox" epidemiology or "the obesity paradox" [29]. Also for RRT patients, U-shaped mortality rates have been reported [30], which is in accordance with our findings about AKI-RRT mortality and has been previously noted, particularly the mortality rates of Asian American end-stage renal disease patients [31]. However, AKI mortality in our study followed a reversed J shape, indicating that although obese people had an increased mortality risk compared to overweigh patients, their mortality incidence was still lower than for underweight and normal-weight cases, which is similar to the results from a previous report about mortality in nondialyzed advanced chronic kidney disease male patients [32]. The data indicated that in contrast to RRT, obesity was a survival advantage for AKI patients, which supports findings of Sleeman et al. [33], according to which obesity had beneficial effects on kidneys by inducing renal inflammation in a CPB swine model.

A multivariate analysis revealed that age, gender (male), CHF (NYHA >II), CPB, and hypertension were other risk factors besides BMI for developing AKI in cardiovascular surgery patients, which is in agreement with previous studies [19, 34].

It is striking that there were differences in the AKI incidence rates in the BMI groups calculated based on the RIFLE (GFR decline) and KDIGO (creatinine increase) criteria, which is probably related to the muscle mass in these patients, and further studies are warranted to determine unequivocally which method for AKI diagnosis is most suitable for Chinese patients.

One strength of our analysis was that we included a large number of patients undergoing cardiac surgery, and the BMI classification followed the standard established for Chinese patients, thereby considering representative data in Chinese hospitals. However, one limitation of the study is that there are no obesity-specific anthropometric measurement guidelines for Asians, such as abdominal circumference, waist-to-hip ratios, quantification of visceral fat mass and others. BMI as a measure of adiposity might also have inherent limitations, because BMI cannot identify differences in body composition and distribution of body fat, and BMI also does not quantify visceral adipose tissue, which may be the cornerstone in obesity-related pathophysiological processes. In addition, this was a single-center study and the known inherent limitations of this type of analysis apply to the present study.

In summary, the overall CS-AKI incidence was 33.8%, and the mortality rates of AKI and AKI-RRT cases were 5.4 and 54.1%. With increasing BMI, the overall incidence of CS-AKI increased significantly, but the mortality rates were lower in overweight and obese patients than in normal and underweight patients. There were no significant differences in the duration of mechanical ventilation, length of ICU, and hospital stay among the 4 BMI groups. A multivariate analysis revealed that age, gender (male), CHF (NYHA >II), CPB, and hypertension were other risk factors besides BMI for the development of AKI in cardiovascular surgery patients.

Acknowledgements

This study was supported by The Project of Shanghai Municipal Commission of Health and Family Planning (grant 2013SY048); The Project of Shanghai Municipal Commission of Science and Technology (grant 14DZ2260200); The Project of Shanghai Municipal Health Bureau (grant 20134462).

Statement of Ethics

All subjects have given their written informed consent, and the study protocol was approved by the Ethical Committee of Zhongshan Hospital.

Disclosure Statement

The authors declare no conflicts of interest.

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