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The Impact of Diabetes on Acute Kidney Injury After Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Background: Acute kidney injury (AKI) is one of the most frequent complications after coronary artery bypass grafting. Previous studies have shown that diabetes is a key pathogenic factor. But how diabetes is related to AKI in off-pump CABG patients still is in debate. Here, we aim to study the relationship between diabetes and AKI after off-pump coronary artery bypass grafting (off-pump CABG).

Methods: Patients who underwent off-pump CABG from April 2017 to December 2020 in The First Affiliated Hospital of USTC were enrolled in this retrospective study. AKI was defined and classified, according to the criteria proposed by the Acute Kidney Injury Network. The incidence risk of acute kidney injury was measured by logistic regression and compared.

Results: A total of 395 patients, who underwent off-pump CABG, were included in this study. The postoperative acute kidney injury rate for a patient with diabetes was significantly higher than for patients without diabetes ($x^2 = 5.09$, $P = 0.024$). Logistic regression analysis showed that patients with diabetes have a much higher risk with acute kidney injury occurring after off-pump coronary artery bypass grafting (OR 1.852, 95% CI 1.161 - 2.954, $P = 0.01$).

Conclusions: Diabetes is an independent risk factor for postoperative AKI for patients undergoing off-pump CABG.

INTRODUCTION

Coronary artery bypass grafting (CABG) is one of the most effective methods for coronary artery disease. After CABG operations, acute kidney injury (AKI), as one of the complications, occurred in up to one-third of patients and approximately 2% require dialysis therapy [Rosner 2006]. Also, the AKI has been suggested as an independent risk factor for increased short-term and long-term death after CABG operations [Yue 2019; Coca 2009; Pickering 2015]. Therefore, the occurrence of AKI after CABG has attracted a lot of attention.

For patients with coronary artery disease, diabetes is a key pathogenic factor and accounted for nearly 50% [Garg 2014; Tolpin 2012; Gallagher 2014]. Meanwhile, diabetes was a known risk factor for developing postoperative AKI [Duran-Salgado 2014; Heyman 2013]. And, previous studies have reported that the occurrence of AKI was correlated with diabetes in patients with the operation of CABG. Compared with normal patients, the incidence rate of AKI for patients with diabetes was much higher after CABG operations [Wang 2020].

Off-pump CABG, a technique of performing CABG on a beating heart, was developed to reduce perioperative complications and to improve short-term and long-term outcomes [Lamy 2017]. Some complications after CABG have been indicated as related to the cardiopulmonary bypass in the on-pump CABG operation, including the AKI. Randomized clinical trials and meta-analyses have indicated the association of lower odds of AKI for off-pump CABG [Garg 2014; Zhu 2019; Gaudino 2018; Seabra 2010; Nigwekar 2009]. But whether diabetes is related to AKI in off-pump CABG patients still is in debate. Research from Hong et al. reported that diabetes was the independent risk factor for AKI [Hong 2010], while other research indicated that diabetes was not correlated with AKI after off-pump CABG [Kim 2011].

Thus, it is necessary to figure out the relationship between diabetes and AKI after off-pump CABG. Here, we retrospectively analyzed 395 patients who underwent off-pump CABG to evaluate the relation between diabetes and postoperative AKI in patients undergoing off-pump CABG operation. Univariate and multivariate logistic regression analyses showed that diabetes is a risk factor for postoperative AKI, the incidence risk of AKI for diabetes patients was much higher than those patients without diabetes.

MATERIALS AND METHODS

Study population: The perioperative data were collected from patients undergoing off-pump CABG who were enrolled in the first affiliated hospital of USTC between April 2017 and December 2020. This study was approved by the

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Ethics Committee of the First Affiliated Hospital of USTC, and patients' identifiers were removed before analysis. The exclusion criteria were as follows: (1) other concomitant surgical procedures, (2) lack of accurate records of the main demographic and clinical characteristics, surgical details, and postoperative outcomes, (3) death within 48 hours post-operation, (4) emergency surgery, and (5) preoperative renal replacement therapy. The patient's information was anonymized and de-identified.

Off-pump CABG operation: The details of off-pump CABG operation previously have been described in detail [Wang 2020]. Specifically, all off-pump CABG surgeries were performed by an experienced cardiovascular surgery team under general anesthesia with standard median sternotomy and achieved complete revascularization. After surgery, the patients were transferred to the cardiovascular intensive care unit. Patients were extubated when they could breathe spontaneously, achieved adequate blood gases, and had stable hemodynamics.

Definition of kidney function: AKI was defined and classified, according to the criteria proposed by the Acute Kidney Injury Network (AKIN), as an increase of creatinine as × 1.5 from baseline or an increase of > 0.3 mg/dL within 48 h. Diabetes was defined as the requirement for dietary modification, oral agents, and/or insulin to lower blood glucose concentrations and was accepted as present based on the patient's history corroborated where possible by the medical records.

Statistical analysis: Data are represented as the mean ± SD unless otherwise indicated. Categorical variables are represented as frequency distributions and single percentages. Normally distributed continuous variables were compared using a student t-test, non-normally distributed continuous variables were compared using the Mann-Whitney U test, and categorical variables were compared by the χ^2 test.

All statistical tests were two-sided. A *P*-value of less than 0.05 was considered significant. All statistical analysis was done with IBM SPSS Statistics 20.0 software.

RESULTS

Patient demographics: From April 2017 and December 2020, 457 patients underwent off-pump CABG in our hospital. Sixty-two patients were excluded, according to the

Table 1. Patient demographics in relation to diabetes

Variables	Diabetes (*N* = 104)	Non-Diabetes (*N* = 291)	*P*-value
Age, year	63.5 ± 7.5	64.7 ± 8.4	0.098
Female gender, %	39 (37.5)	82 (28.2)	0.077
BMI, kg/m^2	25.0 ± 2.9	24.6 ± 3.9	0.199
Hypertension, %	83 (79.8)	187 (64.3)	0.003
Hyperlipidemia, %	64 (61.5)	136 (46.7)	0.010
Smoking history, %	16 (15.4)	56 (19.2)	0.382
COPD, %	19 (18.3)	40 (13.7)	0.267
PVD, %	72 (69.2)	209 (71.8)	0.617
CVD, %	24 (23.1)	51 (17.5)	0.215
Hemoglobin, g/L	123.0 ± 16.7	125.3 ± 14.2	0.167
WBC, ×10^9/L	6.5 ± 1.7	6.5 ± 1.9	0.727
PLT, ×10^9/L	204.6 ± 73.1	197.4 ± 59.5	0.323
ALT, IU/L	33.8 ± 30.5	35.6 ± 31.6	0.395
AST, IU/L	28.7 ± 22.4	34.3 ± 26.5	0.0002
PFG, mmol/L	7.5 ± 3.8	5.1 ± 1.2	< 0.0001
Serum albumin, g/L	38.3 ± 3.6	37.7 ± 3.9	0.215
BUN, mmol/L	6.4 ± 2.7	6.2 ± 5.1	0.028
Preoperative creatinine, umol/L	73.8 ± 32.2	70.6 ± 22.1	0.744
Operation time, min	310.0 ± 56.2	308.9 ± 73.3	0.887
AKI, %	54 (41.9)	114 (39.0)	0.024

Continuous data are shown as the means ± SD and categorical data as number (%). COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CVD, cerebrovascular disease; WBC, white blood cell count; PLT, platelet count; ALT, alamine aminotransferase; AST, aspartate aminotransferase; PFG, preoperative fasting glucose; BUN, preoperative blood urea nitrogen

exclusion criteria. A total of 395 patients, who underwent off-pump CABG, were included in this study. The baseline clinical characteristics of the study groups are shown in Table 1. (Table 1) Compared with the non-diabetes group, the diabetes group had a higher incidence of hypertension and hyperlipemia, lower AST, and higher preoperative fasting glucose.

Risk of AKI in relation to diabetes: To ascertain the risk of diabetes for postoperative AKI occurrence, we further divided patients into the AKI group and the Non-AKI group. Table 2 shows the difference between AKI and Non-AKI groups. (Table 2) The AKI group showed significantly greater mean age and longer operation time than the Non-AKI group. Also, the rate of persons with diabetes in AKI (54, 32.1%) was much higher than in the Non-AKI group (50, 22.0%, $x^2 = 5.09$, $P = 0.024$). The factors with a $P < 0.2$ were then chosen as covariates to adjust the multivariate logistic regression analysis.

Univariate analysis showed that the risk of AKI for diabetes patients was 1.677-fold (OR 1.677, 95% CI 1.068 - 2.632, $P = 0.025$) than patients without diabetes. After adjusting by

Table 2. Patients' characteristics for the AKI and Non-AKI groups

Variables	AKI (*N* = 168)	Non-AKI (*N* = 227)	*P*-value
Age, year	65.3 ± 7.5	63.6 ± 8.5	0.035
Female gender, %	49 (29.2)	72 (31.7)	0.587
BMI, kg/m^2	25.0 ± 4.1	24.5 ± 3.3	0.245
Hypertension, %	119 (70.8)	151 (66.5)	0.362
Hyperlipemia, %	86 (51.2)	114 (50.2)	0.849
Smoking history, %	37 (22.0)	35 (15.4)	0.093
COPD, %	29 (17.3)	30 (13.2)	0.265
PVD, %	114 (67.9)	167 (73.6)	0.216
CVD, %	39 (23.2)	36 (15.6)	0.065
Hemoglobin, g/L	123.5 ± 15.2	125.6 ± 14.7	0.185
WBC, ×10^9/L	6.5 ± 1.8	6.4 ± 1.8	0.550
PLT, ×10^9/L	198.5 ± 67.0	199.9 ± 60.6	0.830
ALT, IU/L	34.3 ± 29.4	35.7 ± 32.7	0.589
AST, IU/L	32.5 ± 22.0	33.1 ± 28.0	0.913
PFG, mmol/L	6.0 ± 2.9	5.5 ± 2.4	0.077
Serum albumin, g/L	37.6 ± 3.7	38.1 ± 3.9	0.216
BUN, mmol/L	6.5 ± 5.2	6.0 ± 4.1	0.202
Preoperative creatinine, umol/L	71.4 ± 30.6	71.5 ± 20.2	0.407
Operation time, min	322.6 ± 72.6	299.3 ± 64.9	<0.001
Diabetes, %	54 (32.1)	50 (22.0)	0.025

Continuous data are shown as the means ± SD and categorical data as number (%). COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; CVD, cerebrovascular disease; WBC, white blood cell count; PLT, platelet count; ALT, alamine aminotransferase; AST, aspartate aminotransferase; PFG, preoperative fasting glucose; BUN, preoperative blood urea nitrogen

Table 3. AKI risk in diabetes group versus no diabetes group

No. of patients	Risk of AKI (univariate analysis)		Risk of AKI (multivariable adjusted)	
	OR (95% CI)	*P*	OR (95% CI)	*P*
All (*N* = 395)				
No Diabetes (*N* = 291)	1	1		
Diabetes (*N* = 104)	1.677 (1.068 - 2.632)	0.025	1.852 (1.161 - 2.954)	0.01

covariates, logistic regression showed that the risk of AKI for diabetes patients was 1.852-fold (OR 1.852, 95% CI 1.161 - 2.954, $P = 0.01$) than patients without diabetes. (Table 3)

DISCUSSION

In this study, we retrospectively evaluated the relation between diabetes and postoperative AKI in patients undergoing off-pump CABG operation. Univariate and multivariate logistic regression analyses showed that diabetes is a risk factor for postoperative AKI, and the incidence risk of AKI for diabetes patients was much higher than patients without diabetes.

AKI is one of the most frequent postoperative complications for patients undergoing cardiac surgery. Also, AKI has adverse effects on patients' outcomes, including ICU time, long-term kidney impairment even death [Wang 2020; See 2019]. Previous studies have indicated that the incidence of AKI was related to many factors, such as smoking history and hyperchloremia [Wang 2020]. Here, we analyzed the incidence of AKI in patients with and without diabetes after performing the off-pump CABG operation and found that the risk of AKI for patients with diabetes was significantly higher than for patients with no diabetes after off-pump CABG, which means that diabetes is an independent risk factor of AKI for off-pump CABG.

Diabetes previously has proven to be related to kidney disease and even lead to kidney transplantation. With the increasing prevalence of diabetes, the related morbidity and mortality also were more general in this era [Vanhorebeek 2009]. In CABG operation, the inflammation activation has been found [Perros 2020]. Meanwhile, hyperglycemia is also related to inflammatory response, increasing the release of cytokines such as interleukin-6, tumor necrosis factor-α, and transforming growth factor-β [Corrêa-Silva 2018; Esposito 2002; Yu 2003]. Thus, diabetes may enhance the inflammatory response after a CABG operation. Another reason is that hyperglycemia is harmful to the endothelial function [Ren 2017; Siervo 2011], which may increase the AKI risk after CABG.

CONCLUSION

The incidence risk of AKI for diabetes patients is significantly higher than the non-diabetes patients after off-pump patients. It may be a potential risk factor for postoperative AKI for patients undergoing off-pump CABG.

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