Use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers increases the risk of postoperative acute kidney injury after elective endovascular abdominal aortic aneurysm repair

Yuwei Xiang, Yang Liu, Jichun Zhao, Bin Huang, Zhoupeng Wu, Xiyang Chen

Department of Vascular Surgery, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, China.

Abstract

Background: Endovascular abdominal aortic aneurysm repair (EVAR) is the major treatment for abdominal aortic aneurysm (AAA); however, EVAR still carries a considerable risk of acute kidney injury (AKI). The present study aimed to investigate the risk factors for AKI after elective EVAR procedures.

Methods: This was a retrospective observational study. Eligible patients who underwent EVAR from September 2011 to March 2019 in West China Hospital were included. The primary outcome was the occurrence of AKI within two days after EVAR, which was defined by the Kidney Disease Improving Global Outcomes Clinical Practice Guideline. Demographics, comorbidities, medications, laboratory tests, anatomical parameters of AAA, and relative operative details were collected as variables. Univariable and multivariable logistic regression analyses were applied to identify the risk factors among variables, and covariate interactions were further assessed.

Results: A total of 679 eligible patients were included. The incidence of postoperative AKI was 8.2% (56/679) in the whole cohort, and it was associated with a lower 5-year survival rate (63.5% *vs.* 80.9%; $\chi^2 = 4.10$; $P = 0.043$). The multivariable logistic regression showed that chronic kidney disease (OR, 5.06; 95% CI: 1.43–17.95; $P = 0.012$), angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs) (OR, 2.60; 95% CI: 1.17–5.76; $P = 0.019$), and short neck (OR, 2.85; 95% CI: 1.08–7.52; $P = 0.035$) were independent risk factors for postoperative AKI. In the covariate interaction analysis, the effect of ACEIs/ARBs use on postoperative AKI was similar across all subgroups ($P > 0.05$), thereby suggesting a robust effect of ACEIs/ARBs use in all patients undergoing elective endovascular abdominal aortic aneurysm repair.

Conclusions: Postoperative AKI was associated with lower survival rate, and the use of ACEIs/ARBs was the only adjustable independent risk factor. Clinicians should consider withdrawing ACEIs/ARBs in high-risk patients undergoing elective endovascular abdominal aortic aneurysm repair to prevent postoperative AKI.

Keywords: Acute kidney injury; Endovascular procedures; Abdominal aortic aneurysms; Risk assessment; Angiotensin-converting enzyme inhibitors; Angiotensin receptor blockers

Introduction

Endovascular abdominal aortic aneurysm repair (EVAR) is a major treatment for abdominal aortic aneurysm (AAA) and has lower rates of perioperative morbidity and mortality than open surgical repair (OSR).[1] Although the incidence of postoperative acute kidney injury (AKI) after EVAR is significantly lower than that after OSR, EVAR still carries a considerable risk for AKI.[2,3] Recent data have suggested that approximately 9.4% to 24.0% of patients develop AKI after EVAR,[2,4-7] and the rate is even higher in patients with poor cardiovascular function.[8,9] It has been demonstrated that postoperative AKI, even when only temporary, is related to high mortality after cardiovascular surgery.[10-12] Some studies have reported the risk factors for AKI after EVAR, including chronic kidney disease, peripheral arterial disease, ischemic heart disease, the use of beta-blockers, and the use of angiotensin blockers.[7,13-15]

The samples of previously reports were either small or lack of homogeneity, for example, some included both EVAR and OSR patients, or included patients using different types of stent grafts or with ruptured AAA.[4,6,7] Few studies have reported acute kidney injury after elective EVAR using the same stent graft, especially in the Chinese population. Therefore, the present study aimed to identify the risk factors for AKI and their potential interaction after elective EVAR procedures.

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000002352

Correspondence to: Dr. Bin Huang, Department of Vascular Surgery, West China Hospital, Sichuan University, No. 37 Guo Xue Alley, Chengdu, Sichuan 610041, China
E-Mail: xgwkhb@126.com

Chinese Medical Journal 2022;135(23)

Received: 25-10-2021; **Online:** 02-01-2023 **Edited by:** Peifang Wei and Xiangxiang Pan

Methods

Study design and patients

The present study was approved by the Ethical Committee of West China Hospital, which issued a waiver for informed consent (No. 2018-44). All AAA patients who underwent elective EVAR in our hospital from September 2011 to March 2019 were potential research subjects, and their information was extracted from the hospital information system. The following patients were excluded from this study: (1) patients who were under reintervention for prior EVAR; (2) patients who were diagnosed with ruptured AAA; and (3) patients who had missing data of perioperative serum creatinine or urine output.

Procedures and outcomes

All elective patients underwent laboratory tests and computed tomography (CT) angiography (CTA) before the operation. EVARs were performed in operating room under a standard and unified protocol. Patients were routinely hydrated with at least 500 ml of 0.9% saline over 4 hours before the operation, and 1 L of 0.9% saline in the first 8 hours after the operation, and patients were encouraged to drink. Postoperative laboratory tests were performed within 2 days after the operation. All the patients were asked to visit the outpatient clinics at 1, 3, and 12 months as well as annually thereafter.

The outcome was the occurrence of postoperative AKI, which was defined by the serum creatinine and urine output according to the Acute Kidney Injury Network (AKIN),[16] and Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline.[17]

Variables

Demographics, comorbidities, medications, laboratory tests, anatomical parameters of AAA, and relative operative details were collected as variables. The presence of hypertension or diabetes was defined based on the medical documents or the use of antihypertensive/antidiabetic medications. Coronary artery disease (CAD) was defined based on symptoms, CT examination, angiography, or intervention history. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min per 1.73 m^2, or markers of kidney damage, for at least 3 months.[18] Chronic obstructive pulmonary disease (COPD), and stroke were defined with previous medical documents. The types of medication were also extracted from the admission documents, including antiplatelets, statins, β-receptor blockers, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs). Anatomical parameters of AAA were measured using preoperative CTA, including neck length, α/β angles, neck diameter, and aneurysm size. Short neck (SN) was defined as infrarenal neck length <10 mm down to 4 mm.[19] Severe neck angulation (SNA) was defined as a neck length >15 mm with an infrarenal angle (β) $>75°$ and/or suprarenal angle (α) $>60°$, or neck length >10 mm and ≤ 15 mm with β $>60°$ and/or α $>45°$.[20] Aneurysm size was defined as the maximum transverse diameter of the aneurysm sac. Relative operative details were collected from the operation records, including the proximal diameter of the implanted stent-grafts and the volume of contrast medium (Omnipaque, GE Healthcare, Shanghai, China) used in the procedure. The proximal neck oversize ratio was calculated as follows: proximal neck oversize ratio = (proximal diameter of implanted stent graft–neck diameter)/neck diameter.

Statistical analysis

All assessment variables had less than 5% missing data. Shapiro-Wilk test was used to test the normality of continuous variables. Continuous variables with normal distribution were described as the mean ± standard deviation (SD) and compared with unpaired *t* tests, continuous variables with non-normal distribution were described as medium (Q_1, Q_3) and compared with Mann-Whitney *U* tests. Categorical variables were presented as numbers (%) and analyzed using χ^2 tests or Fisher's exact test, as appropriate. Kaplan–Meier analysis was used to demonstrate the survival rate, and the *P* value was calculated by the log-rank test. Univariable and multivariable logistic regression analysis was applied to analyze the risk factors for AKI, and variables with *P* values < 0.10 in univariable analysis or considered to have clinical value were included in multivariable analysis. The performance of the multivariable analysis was evaluated using the receiver operating characteristic (ROC) curve, the area under the curve (AUC) was used to determine the accuracy of the model (0.50–0.70, low accuracy; 0.71–0.90, moderate accuracy; and 0.91–1.00, high accuracy). The interaction between using ACEIs/ARBs and other variables was assessed separately using logistic regression, and the age variable was converted into a dichotomous variable according to its mean value. All statistical analyses were performed using R statistical software (R Studio, version 1.4, Boston, MA, USA). All *P* values were two-sided, and *P* values less than 0.05 were considered statistically significant.

Results

Patients and demographic characteristics

Data for a total of 821 patients who underwent EVAR were extracted from the hospital information system. The detailed flow diagram is shown in Figure 1. Due to the limited available stent grafts, all the patients in our center were treated with Endurant stent grafts (Medtronic, Minneapolis, MN, USA). At last, 679 patients were included in this cohort, in which 56 patients had postoperative AKI, 50 of whom were graded as AKI stage 1, 5 patients were graded as AKI stage 2 and 1 patient graded as stage 3.

Patients were divided into two groups based on the occurrence of postoperative AKI, and their baseline characteristics are shown in Table 1. All continuous variables conformed to the normal distribution except for creatinine and eGFR. When compared with the AKI group, the non-AKI group had higher baseline hemoglobin (126.53 ± 19.72 g/L *vs.* 116.02 ± 26.25 g/L; $t = 2.84$;

$P = 0.006$) and cholesterol levels (4.51 ± 1.26 mmol/L *vs.* 4.02 ± 1.36 mmol/L; $t = 2.72$; $P = 0.007$), but the serum creatinine and eGFR levels were similar between the two groups. For comorbidities, the AKI group had a higher rate of being complicated by CAD (30.4% *vs.* 16.9%; $\chi^2 = 5.47$; $P = 0.019$) and CKD (17.9% *vs.* 3.7%; $\chi^2 = 19.34$; $P < 0.001$) than the non-AKI group. There were more patients who took ACEIs/ARBs as antihypertensive medicine in the AKI group (26.8% *vs.* 13.7%; $\chi^2 = 5.97$; $P = 0.015$) compared with the non-AKI group. In addition, the AKI group had a higher rate of general anesthesia (41.1% *vs.* 26.0%; $\chi^2 = 5.11$; $P = 0.024$) and short aneurysm neck (16.1% *vs.* 6.3%; $\chi^2 = 7.19$; $P = 0.007$) than the non-AKI group. The aneurysm size (58.32 ± 15.50 mm *vs.* 54.17 ± 14.03 mm; $t = 2.08$; $P = 0.038$) and neck diameter (22.22 ± 3.25 mm *vs.* 21.12 ± 2.76 mm; $t = 2.41$; $P = 0.019$) were significantly larger in the AKI group.

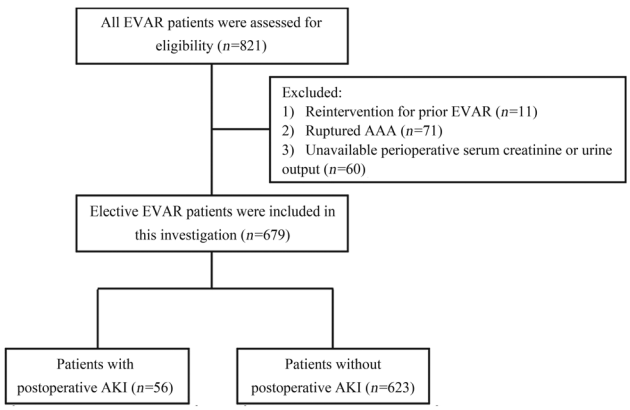

Figure 1: Flow diagram of selecting patients who met inclusion criteria. AAA: Abdominal aortic aneurysm; AKI: Acute kidney injury; EVAR: Endovascular abdominal aortic aneurysm repair.

Postoperative AKI and long-term survival

The included patients were followed up until November 2020, and 23 patients (3.4%) were lost to follow-up. The medium follow-up time was 29.50 months in the AKI group, and 33.00 months in the non-AKI group ($Z = -1.72$, $P = 0.085$). The all-cause mortality during the follow-up period was 16.7% (110/656) in the whole

Table 1: Baseline characteristics of patients undergoing endovascular abdominal aortic aneurysm repair.

Variables	Patients with postoperative AKI ($n = 56$)	Patients without postoperative AKI ($n = 623$)	Statistics	*P* values
Age (years)	72.70 ± 9.13	71.26 ± 9.47	1.09*	0.278
Female	11 (19.6)	107 (17.2)	0.08†	0.777
BMI (kg/m^3)	22.92 ± 3.45	23.23 ± 3.59	0.62*	0.534
Current smoker	37 (66.1)	370 (59.4)	0.70†	0.404
Baseline laboratory test				
Hemoglobin (g/L)	116.02 ± 26.25	126.53 ± 19.72	2.84*	0.006
White blood cell ($\times 10^9$/L)	7.48 ± 2.43	6.84 ± 2.31	1.92*	0.055
Cholesterol (mmol/L)	4.02 ± 1.36	4.51 ± 1.26	2.72*	0.007
Creatinine (μm/L)	82.95 (68.00, 114.00)	78.00 (67.00, 92.95)	-1.71‡	0.088
eGFR (ml/min per 1.73m^2)	76.16 (46.90, 94.95)	84.86 (70.07, 101.80)	-2.36‡	0.068
Comorbidities				
Hypertension	42 (75.0)	415 (66.6)	1.28†	0.257
Diabetes	5 (8.9)	76 (12.2)	0.26†	0.611
CAD	17 (30.4)	105 (16.9)	5.47†	0.019
COPD	16 (28.6)	119 (19.1)	2.33†	0.127
CKD	10 (17.9)	23 (3.7)	19.34†	<0.001
Previous stroke	7 (12.5)	37 (5.9)	2.65†	0.104
Medication§				
Antiplatelet	42 (75.0)	506 (81.6)	1.06†	0.302
Statin	14 (25.0)	114 (18.4)	1.06†	0.302
Beta blockers	15 (26.8)	156 (25.2)	0.01†	0.915
ACEI/ARB	15 (26.8)	85 (13.7)	5.97†	0.015
CCB	29 (51.8)	313 (50.5)	<0.01†	0.962
Anatomy/operative details				
General anesthesia	23 (41.1)	162 (26.0)	5.11†	0.024
Neck diameter (mm)	22.22 ± 3.25	21.12 ± 2.76	2.41*	0.019
Oversize ratio (%)	21.69 ± 6.24	21.59 ± 6.72	0.10*	0.919
Short neck	9 (16.1)	39 (6.3)	7.19†	0.007
Severe neck angulation	16 (28.6)	168 (27.0)	0.01†	0.919
Aneurysm size (mm)	58.32 ± 15.50	54.17 ± 14.03	2.08*	0.038
Contrast volume (ml)	90.27 ± 23.88	84.86 ± 29.89	1.59*	0.116

Data are described as *n* (%), median (Q_1, Q_3), or mean ± stand deviation (SD). * *t* values. † χ^2 values. ‡ *U* values. § The medication information of three patients in the non-AKI group was missing. ACEI: Angiotensin converting enzyme inhibitor; AKI: Acute kidney injury; ARB: Angiotensin receptor blocker; BMI: Body mass index; CAD: Coronary artery disease; CCB: Calcium channel blocker; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; eGFR: Estimated glomerular filtration rate.

cohort. The 1-year, 3-year, and 5-year survival rates were 88.3%, 78.6%, and 63.5% in the AKI group, and 96.2%, 88.4%, and 80.9% in the non-AKI group, respectively. The 5-year survival rate was significantly lower in the AKI group compared with the non-AKI group ($P = 0.043$) [Figure 2].

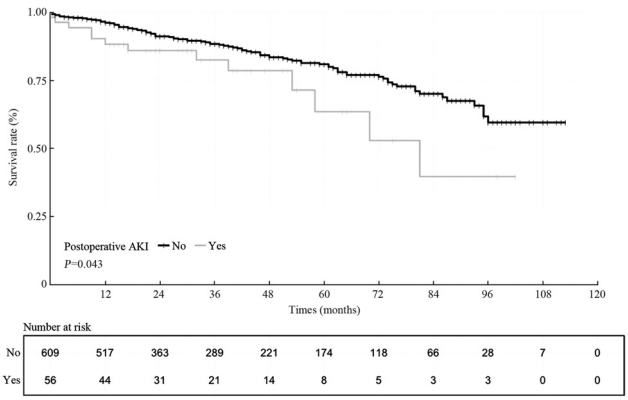

Figure 2: Kaplan-Meier estimates of overall survival rate for patients with or without acute kidney injury (AKI) after elective endovascular abdominal aortic aneurysm repair.

Risk factors for postoperative acute kidney injury

The association between risk factors and postoperative AKI was investigated by logistic univariable analysis. As shown in Table 2, several variables were significantly associated with the occurrence of AKI in univariable analysis, including baseline hemoglobin (OR, 0.98; 95% confidence interval [CI]: 0.96–0.99; $P < 0.001$), cholesterol (OR, 0.69; 95% CI: 0.39–0.85; $P = 0.006$), serum creatinine (OR, 1.08; 95% CI: 1.04–1.23; $P = 0.006$), CAD (OR, 2.15; 95% CI: 1.17–3.95; $P = 0.013$), CKD (OR, 5.67; 95% CI: 2.55–12.63; $P < 0.001$), ACEIs/ARBs use (OR, 2.30; 95% CI: 1.22–4.34; $P = 0.010$), general anesthesia (OR, 1.98; 95% CI: 1.13–3.47; $P = 0.017$), neck diameter (OR, 1.13; 95% CI: 1.04–1.24; $P = 0.006$), SN (OR, 3.13; 95% CI: 1.42–6.90; $P = 0.005$), and aneurysm size (OR, 1.02; 95% CI: 1.00–1.04; $P = 0.039$). Adjusted multivariable logistic regression analysis indicated that CKD (OR, 5.06; 95% CI: 1.43–17.95;

Table 2: Univariable and multivariable analyses of potential risk factors associated with postoperative acute kidney injury.

	Univariable analysis			Multivariable analysis		
Variables	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age	1.02	0.85–1.79	0.277	1.01	0.70–1.90	0.583
Female	1.18	0.59–2.35	0.641	1.22	0.46–3.24	0.687
BMI	0.98	0.62–1.28	0.534	–	–	–
Current smoker	1.33	0.75–2.37	0.330	–	–	–
Baseline laboratory test						
Hemoglobin	0.98	0.96–0.99	<0.001	0.99	0.53–1.42	0.565
White blood cell	1.11	0.99–1.82	0.057	1.10	0.92–1.84	0.134
Cholesterol	0.69	0.39–0.85	0.006	0.84	0.49–1.20	0.238
Creatinine	1.08	1.04–1.23	0.006	1.00	0.94–1.27	0.249
eGFR	0.99	0.53–1.00	0.050	1.01	0.84–1.93	0.260
Comorbidities						
Hypertension	1.50	0.80–2.82	0.203	–	–	–
Diabetes	0.71	0.27–1.82	0.472	–	–	–
CAD	2.15	1.17–3.95	0.013	1.93	0.93–4.09	0.080
COPD	1.69	0.92–3.13	0.092	1.27	0.59–2.75	0.542
CKD	5.67	2.55–12.63	<0.001	5.06	1.43–17.95	0.012
Stroke	2.26	0.96–5.34	0.062	1.33	0.46–3.86	0.596
Medications						
Antiplatelet	0.68	0.36–1.28	0.229	–	–	–
Statin	1.48	0.78–2.80	0.229	–	–	–
β-receptor blocker	1.09	0.58–2.02	0.789	–	–	–
ACEI/ARB	2.30	1.22–4.34	0.010	2.60	1.17–5.76	0.019
CCB	1.05	0.61–1.82	0.852	–	–	–
Anatomy/operative details						
General anesthesia	1.98	1.13–3.47	0.017	1.28	0.63–2.63	0.499
Neck diameter	1.13	1.04–1.24	0.006	1.05	0.76–1.96	0.403
Oversize ratio	1.00	0.71–1.46	0.919	0.99	0.55–1.51	0.729
Short neck	3.13	1.42–6.90	0.005	2.85	1.08–7.52	0.035
Severe neck angulation	1.08	0.59–1.99	0.796	0.75	0.35–1.64	0.471
Aneurysm size	1.02	1.00–1.04	0.039	1.01	0.76–1.93	0.423
Contrast volume	1.01	0.88–1.87	0.188	1.01	0.83–2.02	0.259

ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; BMI: Body mass index; CAD: Coronary artery disease; CCB: Calcium channel blocker; CI: Confidence interval; CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; eGFR: Estimated glomerular filtration rate; OR: Odds ratio.

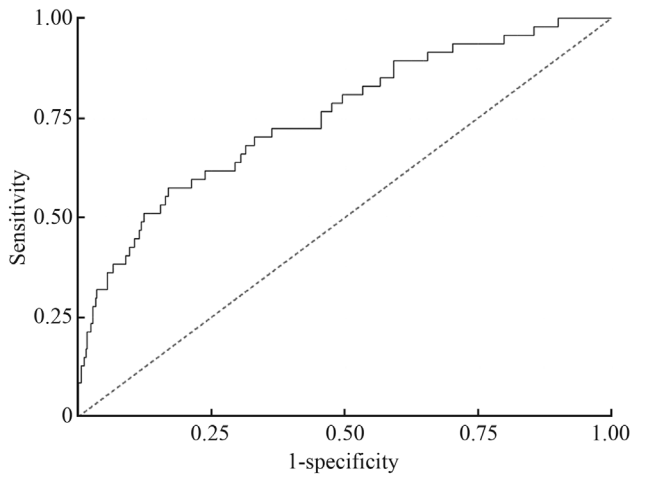

Figure 3: Receiver operating characteristic curve for the adjusted multivariate regression model. Area under the curve was 0.76 (95% CI: 0.68–0.83).

$P = 0.012$), ACEIs/ARBs use (OR, 2.60; 95% CI: 1.17–5.76; $P = 0.019$), and SN (OR, 2.85; 95% CI: 1.08–7.52; $P = 0.035$) were independent risk factors for postoperative AKI. The performance of the adjusted multivariable logistic regression was evaluated by ROC analysis, and the AUC was 0.76 (95% CI: 0.68–0.83) [Figure 3].

In subgroup analyses, the interaction between ACEIs/ARBs use and other variables was investigated. The results demonstrated that the effect of ACEIs/ARBs use was similar in each predefined subgroup. Age, comorbidities, and other medicines did not significantly interact with ACEIs/ARBs use [Figure 4].

Discussion

This was a large single-center observational study that included 679 patients. The incidence of postoperative AKI was 8.2% in the whole cohort, and the majority of AKI was graded as stage 1. Recently, studies reported varied incidences of postoperative AKI defined by the AKIN or KDIGO criteria from 9.4% to 24.0% in patients who underwent EVAR.[2,4-7] The reasons for different AKI incidences are mainly due to the different types of stent grafts used between studies, and the heterogeneity of the population. Some studies had included AAA patients who underwent open repair or emergent operative or fenestrated/branched EVAR procedures. In this study, all included patients had infrarenal AAA and underwent elective EVAR using the same stent graft.

Postoperative AKI was strongly related to worse long-term survival regardless of which stent grafts were used or which type of surgery was performed. Saratzis *et al*[2] reported that AKI patients after elective EVAR using Anaconda (Vascutek, UK) stent grafts have a lower survival rate, and the present study found a similar result using Endurant stent grafts. Saratzis *et al*[4] also reported that AKI patients after both EVAR and OSR are more likely to develop cardiovascular events. Another study involved 10,518 patients who underwent major surgery suggested that long-term survival rate is worse among patients with AKI, even though renal function is completely recovered.[21]

In the present study, multivariable analysis, which was adjusted by several factors that may be associated with AKI, showed that CKD, ACEIs/ARBs use, and SN were independent risk factors for postoperative AKI following elective EVAR using Endurant stent grafts. This result was in accordance with previous studies, which reported that CKD was an independent risk factor for AKI after EVAR.[13,22] However, in previous studies, serum creatinine was not associated with postoperative AKI, and it was not clear whether baseline eGFR was related to postoperative AKI. Some studies have suggested that there is a significant association between baseline eGFR and postoperative AKI,[22,23] while others have suggested that there is no significant association[24,25].

The present study showed that SN was significantly associated with postoperative AKI. In a previous study,[26] no significant difference in postoperative AKI incidence was found between the SN and non-SN groups. The proportions of SN patients were similar between the previous study and the current study; however, the sample in our study was approximately 3 times larger than the previous study, which might lead to different results. An *in vitro* study has also shown that compared to an adequate proximal sealing zone (15 mm), stent grafts anchoring at a shorter zone (10 mm) would obtain dislodgement with a lower force.[27] This dislodgment of bare stent struts may cause direct damage to the renal artery ostium, and lead to postoperative AKI.

Recent evidence has shown that the use of ACEIs/ARBs is associated with an increased risk of postoperative AKI after surgical valve replacement and colorectal cancer surgery.[28,29] A previous study on EVAR with a cohort of 149 patients has reported that ARBs use is a risk factor for AKI after EVAR, while ACEIs use does not increase the risk.[15] However, in the present study, ACEIs or ARBs were combined as one variable because the usage rates of ACEIs and ARBs are relatively low, and both ACEIs and ARBs are targeted at the renin-angiotensin system (RAS). The interaction between ACEIs/ARBs use and other predefined variables was further analyzed, which suggested that there was no significant interaction and indicated a robust effect of ACEIs/ARBs use in all patients. A large meta-analysis including 1663 patients has suggested that withdrawal of ACEIs/ARBs before coronary angiography and cardiac surgery may reduce the incidence of postoperative AKI.[30] The potential association between ACEIs/ARBs and AKI is that the RAS blockade lowers the angiotensin II levels or antagonizes receptor binding, thus blunting the effect of vasoconstriction of peritubular blood flow. These events result in a lower filtration fraction and lower glomerular filtration rate of the kidney, resulting in high serum creatinine.[31] These findings indicated that ACEIs/ARBs use increases the risk of AKI after EVAR. Because ACEI/ARB use is the only adjustable risk factor, withdrawing or switching ACEIs/ARBs to another antihypertensive drug before EVAR might be beneficial to the patients, but further assessment is required.

Contrast administration is the main mechanism for AKI,[18] however, the occurrence of postoperative AKI was not associated with contrast load in the present study.

Characteristics	With ACEI/ARB Events/total (*n*/*N*)	Without ACEI/ARB Events/total (*n*/*N*)	Odds ratio for acute kidney injury (95% CI)	*P* for interaction
Overall	15/100	41/576	2.30 (1.22–4.34)	
Age				**0.385**
<72 years	5/46	19/272	1.62 (0.57–4.59)	
⩾72 years	10/54	22/304	2.91 (1.29–6.56)	
CAD				**0.343**
Yes	7/25	10/96	3.34 (1.12–9.96)	
No	8/75	31/480	1.73 (0.76–3.92)	
CKD				**0.433**
Yes	2/6	8/26	1.12 (0.17–7.45)	
No	13/94	33/550	2.51 (1.27–4.98)	
Short neck				**0.463**
Yes	2/4	7/44	6.39 (0.83–49.36)	
No	13/96	34/532	2.77 (1.15–6.68)	
Antiplatelet				**0.348**
Yes	13/84	29/464	2.75 (1.36–5.53)	
No	2/16	12/112	1.19 (0.24–5.88)	
Statin				**0.305**
Yes	4/31	10/97	1.29 (0.37–4.44)	
No	11/69	31/479	2.74 (1.31–5.75)	
Beta-blocker				**0.178**
Yes	10/58	5/113	4.50 (1.46–13.88)	
No	5/42	36/463	1.60 (0.59–4.33)	
CCB				**0.445**
Yes	11/82	18/260	2.08 (0.94–4.61)	
No	4/18	23/316	3.64 (1.11–11.96)	

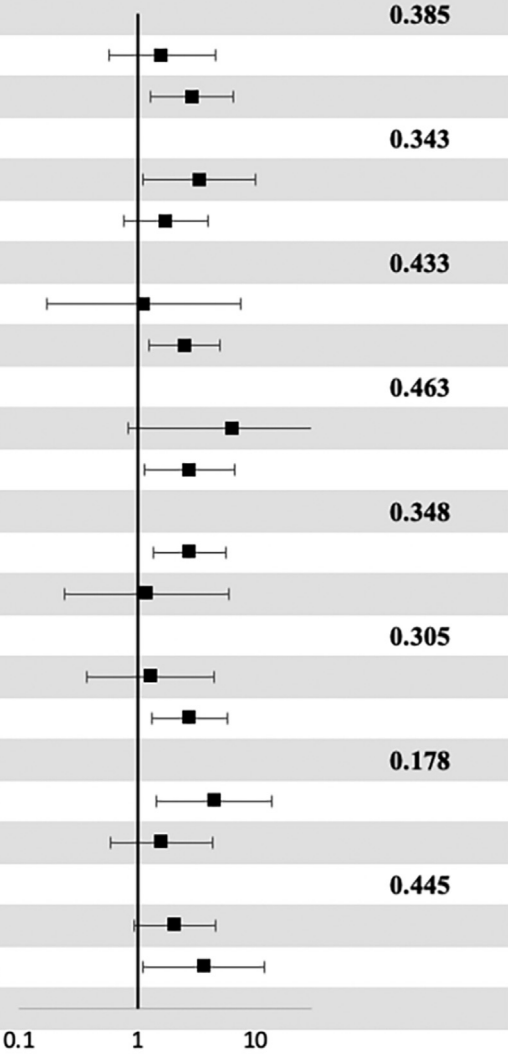

Figure 4: Forest plot about the results of the interaction between ACEIs/ARBs use and other variables by logistic models. ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin receptor blocker; CAD: Coronary artery disease; CCB: Calcium channel blocker; CI: Confidence interval; CKD: Chronic kidney disease.

Most previous studies have reported similar results, showing that contrast load is not an independent risk factor for postoperative AKI.[22-25] Thus, the effect of contrast administration is still unclear.

The present study had several limitations. First, this was a nonrandomized, retrospective, observational study, indicating that selective bias could not be avoided. Some patients were lost to follow-up, and the perioperative renal function data of some patients were missing. Second, due to the imperfect follow-up plan, the renal function of patients was not monitored after discharge, and only AKI which occurred within two days after EVAR was considered in the present study. Further attention should be focused on the long-term change in renal function, and the follow-up protocol should be improved. Overall, the present study involved a large number of patients without heterogeneity, and it provided strong evidence that ACEIs/ARBs use independently increases the risk of AKI.

In conclusion, postoperative AKI after elective EVAR was associated with lower survival, and ACEIs/ARBs use is the only adjustable independent risk factor for it. Clinicians should consider withdrawing ACEIs/ARBs in high-risk EVAR patients to prevent postoperative AKI.

Acknowledgments

This study was supported by nurses, surgeons, and graduate students in the Department of Vascular Surgery, West China Hospital.

Funding

This study was supported by the 1·3·5 project for disciplines of excellence, West China Hospital, Sichuan University (No. ZYJC21078), Post-Doctor Research Project, West China Hospital, Sichuan University (No. 2020HXBH103), Sichuan Foundation of Science and Technology Project (No. 2020YFS0247), and Sichuan International Science and Technology Innovation Cooperation Project (No. 2021YFH0149).

Conflicts of interest

None.

References

1. Suckow BD, Goodney PP, Columbo JA, Kang R, Stone DH, Sedrakyan A, *et al*. National trends in open surgical, endovascular, and branched-fenestrated endovascular aortic aneurysm repair in Medicare patients. J Vasc Surg 2018;67:1690–1697.e1. doi: 10.1016/j.jvs.2017.09.046.
2. Saratzis A, Melas N, Mahmood A, Sarafidis P. Incidence of acute kidney injury (AKI) after endovascular abdominal aortic aneurysm repair (EVAR) and impact on outcome. Eur J Vasc Endovasc Surg 2015;49:534–540. doi: 10.1016/j.ejvs.2015.01.002.
3. Wijnen MHWA, Cuypers P, Buth J, Vader HL, Roumen RMH. Differences in renal response between endovascular and open repair of abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2001;21:171–174. doi: 10.1053/ejvs.2000.1296.
4. Saratzis A, Harrison S, Barratt J, Sayers RD, Sarafidis PA, Bown MJ. Intervention associated acute kidney injury and long-term cardiovascular outcomes. Am J Nephrol 2015;42:285–294. doi: 10.1159/000440986.
5. Duceppe E, Studzińska D, Devereaux PJ, Polok K, Gajdosz A, Lewandowski K, *et al*. Incidence and predictors of myocardial and kidney injury following endovascular aortic repair: a retrospective cohort study. Can J Anesth 2019;66:1338–1346. doi: 10.1007/s12630-019-01438-0.
6. Minami K, Sugiyama Y, Iida H. A retrospective observational cohort study investigating the association between acute kidney injury and all-cause mortality among patients undergoing endovascular repair of abdominal aortic aneurysms. J Anesth 2017;31:686–691. doi: 10.1007/s00540-017-2380-9.
7. Saratzis A, Joshi S, Benson RA, Bosanquet D, Dattani N, Batchelder A, *et al*. Editor's choice - acute kidney injury (AKI) in aortic intervention: findings from the midlands aortic renal injury (MARI) cohort study. Eur J Vasc Endovasc Surg 2020;59:899–909. doi: 10.1016/j.ejvs.2019.09.508.
8. Boyle JR. Poor cardiac function is associated with renal injury following EVAR. Eur J Vasc Endovasc Surg 2017;53:725. doi: 10.1016/j.ejvs.2017.02.007.
9. Saratzis A, Shakespeare J, Jones O, Bown MJ, Mahmood A, Imray CHE. Pre-operative functional cardiovascular reserve is associated with acute kidney injury after intervention. Eur J Vasc Endovasc Surg 2017;53:717–724. doi: 10.1016/j.ejvs.2017.01.014.
10. Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ, *et al*. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation 2009;119:2444–2453. doi: 10.1161/CIRCULATIONAHA.108.800011.
11. Welten GMJM, Schouten O, Chonchol M, Hoeks SE, Feringa HHH, Bax JJ, *et al*. Temporary worsening of renal function after aortic surgery is associated with higher long-term mortality. Am J Kidney Dis 2007;50:219–228. doi: 10.1053/j.ajkd.2007.04.002.
12. Ellenberger C, Schweizer A, Diaper J, Kalangos A, Murith N, Katchatourian G, *et al*. Incidence, risk factors and prognosis of changes in serum creatinine early after aortic abdominal surgery. Intensive Care Med 2006;32:1808–1816. doi: 10.1007/s00134-006-0308-1.
13. Dang T, Dakour-Aridi H, Rizwan M, Nejim B, Malas MB. Predictors of acute kidney injury after infrarenal abdominal aortic aneurysm repair in octogenarians. J Vasc Surg 2019;69:752–762.e1. doi: 10.1016/j.jvs.2018.05.227.
14. Tang Y, Chen J, Huang K, Luo D, Liang P, Feng M, *et al*. The incidence, risk factors and in-hospital mortality of acute kidney injury in patients after abdominal aortic aneurysm repair surgery. BMC Nephrol 2017;18:184. doi: 10.1186/s12882-017-0594-6.
15. Statius van Eps RG, Nemeth B, Mairuhu RTA, Wever JJ, Veger HTC, van Overhagen H, *et al*. Determinants of acute kidney injury and renal function decline after endovascular abdominal aortic aneurysm repair. Eur J Vasc Endovasc Surg 2017;54:712–720. doi: 10.1016/j.ejvs.2017.09.011.
16. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, *et al*. Acute kidney injury network: Report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31. doi: 10.1186/cc5713.
17. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120:c179–184. doi: 10.1159/000339789.
18. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. Lancet Lond Engl 2017;389:1238–1352. doi: 10.1016/S0140-6736(16)32064-5.
19. Arko FR, Stanley GA, Pearce BJ, Henretta JP, Fugate MW, Mehta M, *et al*. Endosuture aneurysm repair in patients treated with Endurant II/IIs in conjunction with Heli-FX EndoAnchor implants for short-neck abdominal aortic aneurysm. J Vasc Surg 2019;70:732–740. doi: 10.1016/j.jvs.2018.11.033.
20. Oliveira NFG, Bastos Gonçalves FM, de Vries JPPM, Ultee KHJ, Werson DAB, Hoeks SE, *et al*. Mid-term results of EVAR in severe proximal aneurysm neck angulation. Eur J Vasc Endovasc Surg 2015;49:19–27. doi: 10.1016/j.ejvs.2014.10.001.
21. Bihorac A, Yavas S, Subbiah S, Hobson CE, Schold JD, Gabrielli A, *et al*. Long-term risk of mortality and acute kidney injury during hospitalization after major surgery. Ann Surg 2009;249:851–858. doi: 10.1097/SLA.0b013e3181a40a0b.
22. Saratzis A, Nduwayo S, Sarafidis P, Sayers RD, Bown MJ. Renal function is the main predictor of acute kidney injury after endovascular abdominal aortic aneurysm repair. Ann Vasc Surg 2016;31:52–59. doi: 10.1016/j.avsg.2015.10.010.
23. Mun JH, Kwon SK, Park JH, Chu W, Kim DH, Jung HJ, *et al*. Renal function-adjusted contrast medium volume is a major risk factor in the occurrence of acute kidney injury after endovascular aneurysm repair. Medicine (Baltimore) 2021;100:e25381. doi: 10.1097/MD.0000000000025381.
24. Sailer AM, Nelemans PJ, van Berlo C, Yazar O, de Haan MW, Fleischmann D, *et al*. Endovascular treatment of complex aortic aneurysms: prevalence of acute kidney injury and effect on long-term renal function. Eur Radiol 2016;26:1613–1619. doi: 10.1007/s00330-015-3993-8.
25. Pisimisis GT, Bechara CF, Barshes NR, Lin PH, Lai WS, Kougias P. Risk factors and impact of proximal fixation on acute and chronic renal dysfunction after endovascular aortic aneurysm repair using glomerular filtration rate criteria. Ann Vasc Surg 2013;27:16–22. doi: 10.1016/j.avsg.2012.05.006.
26. AbuRahma AF, Campbell J, Stone PA, Nanjundappa A, Jain A, Dean LS, *et al*. The correlation of aortic neck length to early and late outcomes in endovascular aneurysm repair patients. J Vasc Surg 2009;50:738–748. doi: 10.1016/j.jvs.2009.04.061.
27. Bosman WM, Steenhoven TJ, Suárez DR, Hinnen JW, Valstar ER, Hamming JF. The proximal fixation strength of modern EVAR grafts in a short aneurysm neck. An in vitro study. Eur J Vasc Endovasc Surg 2010;39:187–192. doi: 10.1016/j.ejvs.2009.10.019.
28. Ibrahim KS, Kheirallah KA, Mayyas FA, Alwaqfi NA. Predictors of acute kidney injury following surgical valve replacement. Thorac Cardiovasc Surg 2021;69:396–404. doi: 10.1055/s-0040-1710318.
29. Slagelse C, Gammelager H, Iversen LH, Liu KD, Sørensen HTT, Christiansen CF. Renin-angiotensin system blocker use and the risk of acute kidney injury after colorectal cancer surgery: a population-based cohort study. BMJ Open 2019;9:e032964. doi: 10.1136/bmjopen-2019-032964.
30. Whiting P, Morden A, Tomlinson LA, Caskey F, Blakeman T, Tomson C, *et al*. What are the risks and benefits of temporarily discontinuing medications to prevent acute kidney injury? A systematic review and meta-Analysis. BMJ Open 2017;7:e012674. doi: 10.1136/bmjopen-2016-012674.
31. Perazella MA, Coca SG. Three feasible strategies to minimize kidney injury in "incipient AKI". Nat Rev Nephrol 2013;9:484–490. doi: 10.1038/nrneph.2013.80.

How to cite this article: Xiang Y, Liu Y, Zhao J, Huang B, Wu Z, Chen X. Use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers increases the risk of postoperative acute kidney injury after elective endovascular abdominal aortic aneurysm repair. Chin Med J 2022;135:2836–2842. doi: 10.1097/CM9.0000000000002352