Original Article

Relation between uric acid and stroke in aortic dissection

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Background: Stroke is one of the severe complications following surgery in patients with acute type A aortic dissection (ATAAD). This study investigates the relationship between the preoperative serum uric acid to serum creatinine ratio (SUA/Scr) and postoperative stroke in patients undergoing total arch replacement with elephant trunk implantation for aortic dissection.

Methods: We included ATAAD patients who were hospitalized and underwent surgery between June 1, 2015 and June 1, 2023, with complete clinical information. Preoperative SUA and Scr levels were collected to calculate SUA/Scr. The association between SUA/Scr and postoperative stroke was analyzed using univariate and multivariate logistic regression, as well as subgroup analysis. The optimal cut-off value of SUA/Scr was determined by receiver operating characteristic (ROC) curve analysis.

Results: A total of 332 patients were included in the study. Patients who developed postoperative stroke had lower SUA/Scr compared to those who did not (P=0.03). Univariate logistic regression indicated that higher SUA/Scr was associated with a reduced risk of postoperative stroke [odds ratio (OR) =0.80; 95% confidence interval (CI): 0.65–0.98; P=0.03]. This association remained significant after adjusting for confounding factors (OR =0.66; 95% CI: 0.45–0.97; P=0.04). Subgroup analysis revealed that the association between higher SUA/Scr and reduced risk of postoperative stroke was significant only in male patients (OR =0.81; 95% CI: 0.65–1.01; P=0.046) and those younger than 65 years (OR =0.82; 95% CI: 0.66–1.02; P=0.048), and was observed only in patients who underwent non-axillary artery cannulation (OR =0.65; 95% CI: 0.50–0.84; P=0.001), left femoral artery cannulation (OR =0.74; 95% CI: 0.58–0.96; P=0.02), and bilateral cerebral perfusion (OR =0.51; 95% CI: 0.32–0.81; P=0.004). The ROC curve analysis identified 3.36 as the optimal cut-off value for SUA/Scr.

Conclusions: A higher SUA/Scr is associated with a reduced risk of postoperative stroke in patients with aortic dissection undergoing total arch replacement with stented elephant trunk implantation and may serve as a potential predictor of postoperative stroke.

Keywords: Uric acid; serum uric acid to serum creatinine ratio (SUA/Scr); aortic dissection; stroke

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Introduction

Acute type A aortic dissection (ATAAD) is one of the most fatal conditions among aortic diseases, with mortality rates increasing by 1–2% per hour if left untreated. Surgery remains the primary treatment modality for this condition (1). Although emergency surgery can effectively save patients' lives, the process of circulatory arrest and the prolonged duration of cardiopulmonary bypass often leads to postoperative complications, significantly impacting the prognosis. Stroke is one of the most common and serious complications, with an incidence ranging from 13% to 19% (2-4). Therefore, it is crucial to identify high-risk populations for postoperative stroke.

Serum uric acid (SUA), a product of purine metabolism, is believed to be associated with neurological diseases. Some studies have suggested that higher SUA levels are a significant protective factor against ischemic stroke (5,6); however, other studies have found no significant association between SUA levels and the prognosis of ischemic stroke (7,8). This discrepancy may be related to variations in renal function among patients (9). Consequently, some studies have used the serum uric acid to serum creatinine ratio (SUA/Scr) to reflect uric acid levels, minimizing the influence of renal function. SUA/Scr has been associated with early neurological deterioration in patients with ischemic stroke and atherosclerotic diseases (10,11).

Highlight box

Key findings

- A higher serum uric acid to serum creatinine ratio (SUA/Scr) is associated with a reduced risk of postoperative stroke in patients with aortic dissection undergoing total arch replacement with stented elephant trunk implantation.

What is known and what is new?

- The SUA/Scr is generally considered to be associated with neurological disorders such as cerebral infarction.
- A higher SUA/Scr is associated with a reduced risk of postoperative stroke in patients with aortic dissection undergoing total arch replacement with stented elephant trunk implantation and may serve as a potential predictor of postoperative stroke.

What is the implication, and what should change now?

- Patients with a lower preoperative SUA/Scr have a higher risk of postoperative stroke. For these patients, it is necessary to implement more comprehensive intraoperative cerebral protection measures and more rigorous postoperative monitoring.

Although SUA/Scr has been linked to neurological diseases, its relationship with postoperative stroke in patients with aortic dissection remains unclear. Therefore, this study aims to investigate the association between preoperative SUA/Scr and postoperative stroke in patients with aortic dissection undergoing total arch replacement combined with stented elephant trunk implantation. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1383/rc).

Methods

Study population and data collection

The study data were obtained from Tianjin Chest Hospital. Baseline information and preoperative laboratory data were collected from the electronic medical record system, while intraoperative data were retrieved from the electronic anesthesia system. A total of 365 patients with ATAAD, who were hospitalized, underwent surgery, and had complete information, between June 1, 2015 and June 1, 2023, were initially included. Among them, 15 patients who were unconscious before surgery or had new-onset stroke, and 18 patients who died within 48 hours postoperatively without being diagnosed with stroke, were excluded. Finally, 332 patients were retained for the study (*Figure 1*). The time from onset to surgery for all patients did not exceed 2 weeks. The variables collected and analyzed included patient demographics, preoperative symptoms, medical history, preoperative laboratory results, and key intraoperative information. The outcome was defined as the occurrence of new neurological deficits during the postoperative hospital stay, with new structural brain changes detected by computed tomography (CT) or magnetic resonance imaging (MRI). In cases where imaging did not reveal structural changes but a neurologist confirmed a diagnosis of stroke, the patient was also considered to have met the outcome. Due to the lack of routine postoperative brain CT or MRI examinations, patients with asymptomatic stroke were not included in this study. All procedures involving participants in this study complied with the Declaration of Helsinki (2013 revision). This study was a single-center, retrospective study and has been approved by the Ethics Committee of Tianjin Chest Hospital (approval No. 2020YS-028-01). As this research is a retrospective study, informed consent from participating patients or their family members was waived.

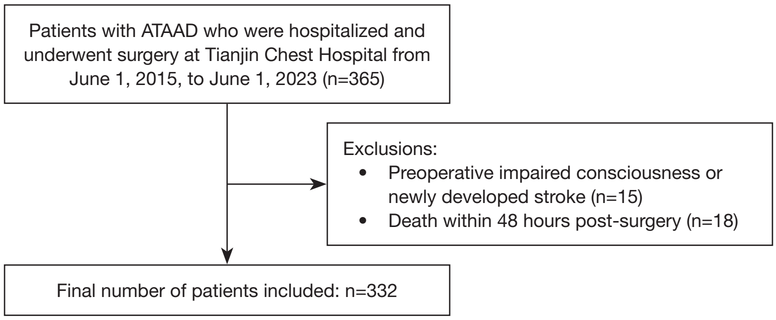

Figure 1 Patient screening process. ATAAD, acute type A aortic dissection.

Statistical analysis

Before conducting further analysis, categorical variables were preprocessed based on their characteristics. For example, patient gender was encoded as 1 and 2 (1= male, 2= female). Clinically relevant binary features such as smoking, alcohol consumption, and medical history were encoded as 0 or 1 (0= absent, 1= present). Continuous variables with a normal distribution were described as mean and standard deviation (SD), while those with a skewed distribution were described as median with interquartile range. Categorical variables were presented as frequencies (percentages). A preliminary analysis was performed to compare variables between patients with and without postoperative stroke. Qualitative data were analyzed using the Chi-squared test, normally distributed quantitative data were analyzed using the independent samples *t*-test, and non-normally distributed quantitative data were analyzed using the Mann-Whitney *U* test. Univariate and multivariate logistic regression analyses were sequentially applied to examine the association between SUA/Scr and outcomes. In the multivariate logistic regression analysis, in addition to including variables significantly associated in the univariate analysis as confounders, previous literature was reviewed to retain gender, age, weight, stroke, circulatory arrest time, nasal temperature, axillary artery cannulation, and cerebral perfusion as confounding factors (12-16). Subgroup analyses were also conducted based on age, gender, type of arterial cannulation, and cerebral perfusion. The association between the SUA/Scr and outcomes was assessed using univariate logistic regression analysis. The optimal cutoff value of SUA/Scr was determined through Youden's index and receiver operating characteristic (ROC) curve analysis, while its diagnostic value was also evaluated, and the odds ratio (OR) was calculated. All analyses were performed using the R statistical software version 4.4.2, with a P value of less than 0.05 considered statistically significant.

Results

Patient characteristics

The baseline characteristics of patients with and without postoperative stroke are summarized in *Table 1*. Categorical variables are described using frequencies and percentages, while continuous variables with a normal distribution are presented as mean and SD, and those with a non-normal distribution are described using median and interquartile range. A total of 71 (21.4%) people experienced stroke after the surgery. Patients who developed postoperative stroke had a higher proportion of males (88.7% *vs.* 73.9%, P=0.01) and a higher prevalence of chronic obstructive pulmonary disease (COPD) (4.2% *vs.* 0.4%, P=0.04). They also had higher body weight (84.11 *vs.* 78.55 kg, P=0.01) and body surface area (1.96 *vs.* 1.90 m^2, P=0.04).

There were also some differences in preoperative laboratory indicators between the two groups. Patients with postoperative stroke had higher preoperative white blood cell (WBC) count (12.22×10^9/L *vs.* 10.42×10^9/L, P=0.02), neutrophil count (10.70×10^9/L *vs.* 8.97×10^9/L, P=0.009), creatinine level (104.00 *vs.* 80.00 μmol/L, P<0.001), uric acid level (398.63 *vs.* 340.16 μmol/L, P<0.001), troponin T level (0.03 *vs.* 0.02 ng/mL, P=0.02), and creatine kinase (CK) level (104.00 *vs.* 85.00 U/L, P=0.01). However, the SUA/Scr was lower in patients with stroke (3.63 *vs.* 4.06, P=0.03). Other laboratory indicators are shown in *Table 2*. In contrast, there were no significant differences between the two groups in terms of intraoperative data, including surgery duration, circulatory arrest time, nasopharyngeal temperature, intraoperative blood loss, and cerebral perfusion method. Details of the intraoperative information are provided in *Table 3*.

Table 1 Baseline information of patients

Variables	Non-stroke (n=261)	Stroke (n=71)	P value
Sex, n (%)			
Male	193 (73.9)	63 (88.7)	0.01
Female	68 (26.1)	8 (11.3)	0.01
Age (years), mean (SD)	50.94 (12.29)	52.68 (11.20)	0.28
Height (cm), mean (SD)	171.36 (8.43)	172.01 (6.10)	0.54
Weight (kg), mean (SD)	78.55 (16.07)	84.11 (16.60)	0.01
Body surface area (m^2), mean (SD)	1.90 (0.24)	1.96 (0.24)	0.04
Hypertension, n (%)	171 (65.5)	54 (76.1)	0.12
Duration of hypertension (years), median [IQR]	5.00 [0.00, 10.00]	6.00 [1.00, 10.00]	0.14
Diabetes, n (%)	9 (3.4)	1 (1.4)	0.62
Stroke, n (%)	13 (5.0)	6 (8.5)	0.41
CHD, n (%)	16 (6.1)	7 (9.9)	0.41
COPD, n (%)	1 (0.4)	3 (4.2)	0.04
Smoke, n (%)	126 (48.3)	35 (49.3)	0.99
Alcohol abuse, n (%)	39 (14.9)	14 (19.7)	0.43

SD, standard deviation; IQR, interquartile range; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease.

Table 2 Preoperative laboratory parameters of patients

Variables	Non-stroke (n=261)	Stroke (n=71)	P value
WBC ($\times 10^9$/L), median [IQR]	10.42 [8.92, 13.66]	12.22 [9.81, 14.77]	0.02
Neutrophil ($\times 10^9$/L), median [IQR]	8.97 [7.06, 11.93]	10.70 [8.91, 13.25]	0.009
Lymphocyte ($\times 10^9$/L), median [IQR]	0.90 [0.61, 1.31]	0.83 [0.63, 1.15]	0.59
RBC count ($\times 10^{12}$/L), mean (SD)	4.26 (0.60)	4.29 (0.59)	0.72
Hb level (g/L), median [IQR]	130.00 [117.00, 144.00]	133.00 [123.50, 141.50]	0.52
Plt ($\times 10^9$/L), mean (SD)	179.20 (65.42)	180.24 (61.76)	0.91
SUA/Scr, mean (SD)	4.06 (1.41)	3.63 (1.47)	0.03
Creatinine (μmol/L), median [IQR]	80.00 [66.00, 106.00]	104.00 [84.00, 142.50]	<0.001
Uric acid (μmol/L), mean (SD)	340.16 (114.33)	398.63 (140.18)	<0.001
C-reactive protein (mL/L), median [IQR]	12.30 [3.82, 50.50]	10.20 [3.42, 28.05]	0.11
D-dimer (mg/L), median [IQR]	9.28 [2.71, 20.00]	10.40 [4.60, 20.00]	0.09
Troponin T (μg/mL), median [IQR]	0.02 [0.01, 0.07]	0.03 [0.01, 0.10]	0.02
CK (U/L), median [IQR]	85.00 [52.00, 135.00]	104.00 [68.00, 180.00]	0.01
CK-MB (U/L), median [IQR]	15.00 [11.00, 21.00]	17.00 [12.00, 22.50]	0.24
ALT (U/L), median [IQR]	19.00 [12.30, 30.80]	21.80 [11.30, 39.60]	0.48
AST (U/L), median [IQR]	19.70 [14.50, 31.40]	20.80 [15.15, 38.00]	0.35

WBC, white blood cell; IQR, interquartile range; RBC, red blood cell; SD, standard deviation; Hb, hemoglobin; Plt, platelet; SUA/Scr, serum uric acid to serum creatinine ratio; CK, creatine kinase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 3 Intraoperative data of patients

Variables	Non-stroke (n=261)	Stroke (n=71)	P value
Surgical time (min), mean (SD)	373.96 (89.05)	392.81 (76.00)	0.10
CPB time (min), mean (SD)	165.00 [148.90, 184.00]	180.00 [148.50, 198.50]	0.054
Aortic cross-clamping time (min), mean (SD)	102.38 (24.99)	102.05 (27.41)	0.92
Circulatory arrest time (min), median [IQR]	16.00 [10.00, 21.00]	15.00 [9.00, 22.00]	0.79
Intraoperative blood loss (mL), median [IQR]	1,315.00 [1,000.00, 1,600.00]	1,400.00 [1,050.00, 1,800.00]	0.24
Ultrafiltration volume (mL), median [IQR]	2,500.00 [2,000.00, 3,500.00]	2,200.00 [1,550.00, 3,350.00]	0.35
UO during CPB (mL), median [IQR]	600.00 [400.00, 1,100.00]	600.00 [400.00, 1,100.00]	0.83
Axillary artery cannula, n (%)	73 (28.0)	21 (29.6)	0.91
Femoral artery cannula, n (%)			
No	55 (21.1)	21 (29.6)	0.25
Right	11 (4.2)	4 (5.6)	0.25
Left	195 (74.7)	46 (64.8)	0.25
Cerebral perfusion, n (%)			
Unilateral	183 (70.1)	48 (67.6)	0.79
Bilateral	78 (29.9)	23 (32.4)	0.79
Nasal temperature (℃), median [IQR]	27.00 [24.50, 28.00]	25.20 [24.00, 28.00]	0.18
Rectal temperature (℃), median [IQR]	28.40 [26.60, 29.50]	27.70 [26.35, 29.05]	0.10

SD, standard deviation; CPB, cardiopulmonary bypass; IQR, interquartile range; UO, urine output.

Logistic regression analysis and subgroup analysis

In the univariate logistic regression analysis, several factors were significantly associated with the risk of postoperative stroke, including gender [OR =0.36; 95% confidence interval (CI): 0.16–0.79; P=0.01], COPD (OR =11.47; 95% CI: 1.17–112.02; P=0.04), body weight (OR =1.02; 95% CI: 1.00–1.04; P=0.01), body surface area (OR =2.98; 95% CI: 1.04–8.57; P=0.04), preoperative WBC count (OR =1.08; 95% CI: 1.02–1.16; P=0.01), preoperative serum uric acid (SUA) level (OR =1.00; 95% CI: 1.00–1.01; P<0.001), preoperative creatinine level (OR =1.01; 95% CI: 1.00–1.02; P<0.001), and preoperative SUA/Scr (OR =0.80; 95% CI: 0.65–0.98; P=0.03). After adjusting for confounding factors, multivariate analysis indicated that preoperative SUA/Scr (OR =0.66; 95% CI: 0.45–0.97; P=0.04) remained associated with the risk of postoperative stroke (*Table 4*).

Subgroup analyses based on baseline characteristics such as age and gender suggested that the preoperative SUA/Scr was particularly associated with postoperative stroke in males (OR =0.81; 95% CI: 0.65–1.01; P=0.046) and in patients younger than 65 years (OR =0.82; 95% CI: 0.66–1.02; P=0.048). Further subgroup analyses of intraoperative factors indicated that the preoperative SUA/Scr was significantly associated with postoperative stroke in patients without axillary artery cannulation (OR =0.65; 95% CI: 0.50–0.84; P=0.001), with left femoral artery cannulation (OR =0.74; 95% CI: 0.58–0.96; P=0.02), and those who underwent bilateral cerebral perfusion (OR =0.51; 95% CI: 0.32–0.81; P=0.004) (*Figure 2*).

ROC curve analysis

The ROC curve analysis determined that the optimal cutoff value of SUA/Scr for predicting postoperative stroke in aortic dissection patients was 3.36 (*Figure 3*). To evaluate the diagnostic value of SUA/Scr and its optimal cutoff value, three models were fitted, and OR values were calculated. In the crude model of univariate logistic regression, both SUA/Scr and its cutoff value were statistically significant, with the cutoff value yielding a smaller OR (OR =0.47 *vs.* 0.80). Similarly, after calibrating the statistically significant

Table 4 Results of univariate and multivariate analyses

Variables	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Sex	0.36 (0.16–0.79)	0.01	0.53 (0.20–1.40)	0.20
Age	1.01 (0.99–1.03)	0.28	1.02 (0.99–1.05)	0.16
Height	1.01 (0.98–1.04)	0.54	–	–
Weight	1.02 (1.00–1.04)	0.01	1.07 (1.00–1.15)	0.06
Body surface area	2.98 (1.04–8.57)	0.04	0.03 (0.00–3.73)	0.15
Hypertension	1.67 (0.92–3.05)	0.09	–	–
Duration of hypertension	1.02 (0.99–1.05)	0.23	–	–
Diabetes	0.40 (0.05–3.21)	0.39	–	–
Stroke	1.76 (0.64–4.81)	0.27	1.54 (0.47–5.04)	0.48
CHD	1.67 (0.66–4.24)	0.28	–	–
COPD	11.47 (1.17–112.02)	0.04	27.39 (3.42–305.10)	0.004
Smoke	1.04 (0.62–1.76)	0.88	–	–
Alcohol abuse	1.40 (0.71–2.75)	0.33	–	–
WBC	1.08 (1.02–1.16)	0.01	1.06 (0.98–1.15)	0.16
Neutrophil	1.05 (0.99–1.11)	0.09	–	–
Lymphocyte	0.73 (0.45–1.20)	0.22	–	–
RBC count	1.09 (0.70–1.69)	0.72	–	–
Hb level	1.00 (0.99–1.01)	0.72	–	–
Plt	1.00 (1.00–1.00)	0.90	–	–
SUA/Scr	0.80 (0.65–0.98)	0.03	0.66 (0.45–0.97)	0.04
Creatinine	1.01 (1.00–1.02)	<0.001	1.00 (0.99–1.01)	0.98
Uric acid	1.00 (1.00–1.01)	<0.001	1.01 (1.00–1.01)	0.005
C-reactive protein	1.00 (0.99–1.00)	0.33	–	–
D-dimer	1.03 (0.99–1.06)	0.14	–	–
Troponin T	0.99 (0.93–1.06)	0.84	–	–
CK	1.00 (1.00–1.00)	0.16	–	–
CK-MB	1.00 (0.99–1.01)	0.95	–	–
ALT	1.00 (1.00–1.01)	0.42	–	–
AST	1.00 (1.00–1.01)	0.17	–	–
Surgical time	1.00 (1.00–1.01)	0.11	–	–
CPB time	1.01 (1.00–1.01)	0.09	–	–
Aortic cross-clamping time	1.00 (0.99–1.01)	0.92	–	–
Circulatory arrest time	1.00 (0.96–1.03)	0.80	0.96 (0.91–1.01)	0.11
Intraoperative blood loss	1.00 (1.00–1.00)	0.08	–	–

Table 4 *(continued)*

Table 4 *(continued)*

Variables	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Ultrafiltration volume	1.00 (1.00–1.00)	0.44	–	–
UO during CPB	1.00 (1.00–1.00)	0.59	–	–
Axillary artery cannula	1.08 (0.61–1.93)	0.71	0.77 (0.31–1.91)	0.57
Femoral artery cannula	0.62 (0.34–1.12)	0.11	–	–
Cerebral perfusion	1.12 (0.64–1.97)	0.68	1.19 (0.60–2.36)	0.61
Nasal temperature	0.90 (0.80–1.01)	0.08	0.76 (0.64–0.90)	0.002
Rectal temperature	0.90 (0.80–1.02)	0.11	–	–

In the multivariable analysis, gender, age, weight, stroke, circulatory arrest time, nasal temperature, axillary artery cannula, and cerebral perfusion were all retained as mandatory variables. CI, confidence interval; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; Plt, platelet; SUA/Scr, serum uric acid to serum creatinine ratio; CK, creatine kinase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPB, cardiopulmonary bypass; UO, urine output.

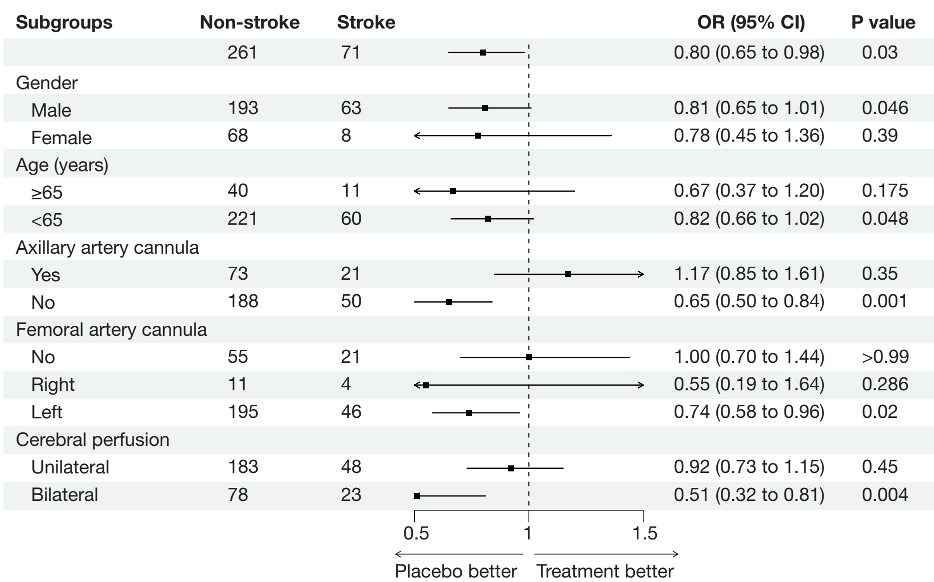

Figure 2 Results of subgroup analysis. OR, odds ratio; CI, confidence interval.

variables retained in the univariate logistic regression analysis, both remained statistically significant, with the cutoff value continuing to show a smaller OR (OR =0.31 *vs.* 0.66). This relationship also persisted after adjusting for all variables (OR =0.30 *vs.* 0.55) (*Table 5*).

Discussion

This retrospective study reveals that a higher SUA/Scr is associated with a reduced risk of postoperative stroke in patients with aortic dissection. Subgroup analysis further indicates that this relationship is specifically observed in male patients, those with hypertension, and patients younger than 65 years. It is also confined to patients who did not undergo axillary artery cannulation, received left femoral artery cannulation, and underwent bilateral cerebral perfusion.

The association between the SUA/Scr and stroke, as well as other cerebral complications, is well-documented in the literature. Zhang *et al.* reported that a lower SUA/Scr is an independent risk factor for recurrent stroke within one year in patients with acute ischemic stroke (AIS) (17). Similarly, Xu *et al.* found that a lower SUA/Scr is linked to poorer outcomes in postoperative AIS patients (18). Liu *et al.* also demonstrated that a higher SUA/Scr is associated with a reduced risk of stroke in patients with branch atheromatous disease (BAD) (11). Although higher SUA/Scr values appear to have a protective effect against stroke and cerebral complications, debate remains regarding the role of SUA when not adjusted for creatinine levels, which reflects renal function. Fernández-Gajardo *et al.* found that elevated SUA levels were associated with smaller infarct volumes in patients with stroke (19) and with a better prognosis in AIS patients (20). In contrast, other studies have identified high SUA as a risk factor for ischemic stroke in patients with essential hypertension (21), while some have found no association between SUA and prognosis in stroke patients (22). Concerning complications, certain studies suggest that elevated SUA increases the risk of stroke in patients with type 2 diabetes (23), while others link higher SUA levels with cardioembolic stroke (CES) (24). Addressing these discrepancies, Zheng *et al.* demonstrated that high SUA correlates with improved prognosis in ischemic stroke patients with normal renal function, whereas this association was absent in patients with renal dysfunction, suggesting that variations in renal function may contribute to the observed inconsistencies (9).

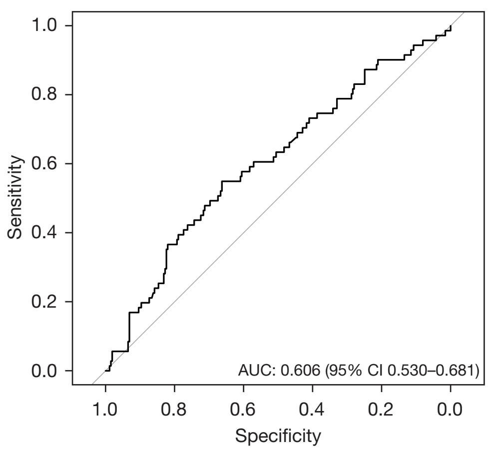

Figure 3 ROC curve for SUA/Scr and postoperative stroke. AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; SUA/Scr, serum uric acid to serum creatinine ratio.

While the SUA/Scr has been associated with stroke and cerebral complications, few studies have examined its relationship with postoperative stroke in patients with ATAAD; our study addresses this gap. In both univariate and multivariate logistic regression analyses, a higher SUA/Scr was found to be a protective factor against postoperative stroke in ATAAD patients. Existing studies have linked SUA to the incidence of aortic dissection (25,26), identified it as a risk factor for increased mortality in aortic diseases such as aortic aneurysms (27), and associated it with increased 30-day and in-hospital mortality rates in ATAAD patients (28,29). The mechanisms underlying these associations may involve macrophage-driven inflammatory responses (30) and the antioxidant effects of uric acid (27), which may similarly explain the relationship between SUA and postoperative stroke in ATAAD patients. During total arch replacement and stented elephant trunk implantation in ATAAD patients, circulatory arrest is often required to maintain a clear surgical field. Despite cerebral perfusion, ischemia cannot be completely avoided due to variations in perfusion methods and anatomical differences among patients (31). Upon resumption of circulation, cerebral blood flow restoration may lead to ischemia-reperfusion

Table 5 Logistic regression analysis evaluating the association between SUA/Scr and the risk of postoperative stroke

Variables	Model 1		Model 2		Model 3	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
SUA/Scr	0.80 (0.65–0.98)	0.03	0.66 (0.45–0.97)	0.04	0.55 (0.34–0.89)	0.02
SUA/Scr >3.36	0.47 (0.28–0.80)	0.005	0.31 (0.14–0.68)	0.004	0.30 (0.12–0.76)	0.01

Model 1: crude model, only univariate logistic regression analysis performed. Model 2: adjusted for variables with statistical significance in the univariate logistic regression analysis and those retained by forced entry, including gender, age, weight, body surface area, COPD, stroke, WBC, creatinine, uric acid, circulatory arrest time, nasal temperature, axillary artery cannulation and cerebral perfusion. Model 3: adjusted for all collected variables. SUA/Scr, serum uric acid to serum creatinine ratio; OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; WBC, white blood cell.

injury, generating reactive oxygen species and causing some degree of cerebral damage (32). SUA, a compound with strong antioxidant properties, may play a significant role in neuroprotection (33). Moreover, Maloberti *et al.* found that while SUA generally exhibits a chronic pro-oxidative effect, it can act as an antioxidant and scavenge reactive oxygen species under acute stress conditions (34), potentially explaining the neuroprotective effects of SUA. Although SUA/Scr was significantly associated with postoperative stroke in both univariate and multivariate analyses, the AUC value for this relationship was relatively low. This may indicate a non-linear association between SUA/Scr and postoperative stroke or suggest other major factors influencing postoperative stroke. Therefore, our study employed the optimal cutoff value and included additional confounding factors in the analysis, which notably reduced the OR for SUA/Scr.

In addition to logistic regression analysis, we conducted a subgroup analysis. The results showed that SUA/Scr was associated with outcomes only in the male population. Previous studies have suggested that the relationship between serum uric acid and outcomes may be influenced by gender, though the findings are inconsistent. Yuan *et al.* found that SUA was associated with cardiovascular outcomes after coronary stent implantation only in male (35), whereas Fang *et al.* reported that the impact of SUA levels on cardiovascular disease-related mortality was independent of gender (36). In this study, gender appears to influence the effect of SUA. Before menopause, female typically have lower uric acid levels than male due to the uricosuric effect of estrogens, but postmenopausal estrogen decline leads to a gradual increase in uric acid levels, which may provide a plausible explanation for the gender-related differences observed (37). This also offers some insight into why SUA/Scr was not associated with postoperative stroke in older adults (≥65 years). Although the association between SUA/Scr and postoperative stroke appeared more significant among males and the elderly ($P<0.05$), the 95% CIs of their OR crossed 1, which is typically interpreted as an indication of non-significance. Borenstein *et al.* emphasized that subdividing data into multiple subgroups can lead to reduced sample sizes, thereby decreasing the power to detect statistical significance, including differences in effect sizes (38). In this study, the upper bounds of the 95% CI for OR values only slightly exceeded 1 (1.01, 1.02). Given the reduced sample sizes, the influence of gender and age on the outcomes might still hold, though additional data would be required to substantiate these findings.

Besides gender and age, the type of cannulation used also influenced the relationship between SUA/Scr and postoperative stroke. SUA/Scr was only associated with stroke in patients who did not undergo axillary artery cannulation but instead received left femoral artery cannulation. Compared to femoral artery cannulation, axillary artery cannulation provides antegrade arterial flow, reducing the risk of retrograde perfusion-induced expansion of the false lumen and organ malperfusion (39). Moreover, axillary artery cannulation has been shown to reduce postoperative mortality and the incidence of stroke (40). Improved organ perfusion may mitigate cerebral ischemia and hypoxia, which could explain the limited role of SUA/Scr in patients who underwent axillary artery cannulation. In our study, all patients who did not receive femoral artery cannulation underwent axillary artery cannulation, while the number of patients who received only right femoral artery cannulation was small, potentially introducing bias. This could explain why SUA/Scr was only associated with postoperative stroke in patients with left femoral artery cannulation. Notably, SUA/Scr was significant only in patients who underwent bilateral cerebral perfusion. Although several studies suggest that unilateral and bilateral cerebral perfusion provide similar protection to the brain (41,42), the increased procedural complexity and duration of bilateral cerebral perfusion, along with the elevated risk of embolization from air or tissue debris, may exacerbate cerebral ischemia and hypoxia (43).

There are several limitations in this study. First, as a retrospective study, the data collected may be subject to bias, and the relatively small sample size and single-center design could introduce potential bias in the results. Second, although factors such as circulatory arrest time and cerebral perfusion methods were considered, the extent of dissection and anatomical factors are also important contributors to the occurrence of postoperative stroke. The lack of preoperative imaging data prevented us from accounting for these factors. Additionally, this study focused solely on patients with aortic dissection who required circulatory arrest and cerebral perfusion during surgery, so it remains unclear whether the findings are applicable to other aortic dissection patients. Furthermore, over the 8-year span of the study, surgical techniques have evolved, and the surgeries were performed by multiple surgeons. We did not collect patient-level data on these variables, and thus, their potential impact could not be included in our analysis.

Conclusions

A higher SUA/Scr is associated with a reduced risk of postoperative stroke in patients with ATAAD, indicating its potential as a novel predictive marker. The optimal cutoff values derived from the Youden index and ROC curve significantly enhance this relationship. In subgroup analyses, this association is observed only in male patients, those with hypertension, patients younger than 65 years, and patients who did not undergo axillary artery cannulation, received left femoral artery cannulation, or underwent bilateral cerebral perfusion.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was a single-center, retrospective study and was approved by the Ethics Committee of Tianjin Chest Hospital (approval No. 2020YS-028-01), with a waiver of written informed consent from the participating patients or their family members due to the retrospective nature of this study.

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