Identification of risk factors for postoperative stage 3 acute kidney injury in patients who received surgical repair for acute type A aortic dissection

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Abstract

Background: Acute kidney injury (AKI) is a serious complication that often occurred after acute type A aortic dissection (ATAAD) surgery. Previous studies proved that the Kidney Disease Improving Global Outcomes (KDIGO) defined stage 3 AKI was associated with lower long-term survival rate. However, the risk factors for developing stage 3 AKI had not been identified. The aim of the study was to explore the risk factors for developing KDIGO stage 3 after ATAAD operation.

Methods: This study included 993 patients who received ATAAD operation from 2014 to 2019 at the Nanjing Drum Tower Hospital. Postoperative AKI was diagnosed according to the KDIGO criteria. Multivariate logistic regression analyses were applied to identify risk factors for stage 3 AKI. Kaplan–Meier survival analyses and Cox proportional hazards regression model were conducted to explore the association between different AKI stages and postoperative survival rate.

Results: The mean age of all enrolled patients was 53.0 ± 13.1 years. A total of 236 (23.8%) patients suffered postoperative stage 3 AKI including 165 patients who required renal replacement therapy. Advanced age (odds ratio [OR] 1.031; 95% confidence interval [CI] 1.005–1.057; \( P = 0.018 \)), prolonged cardiopulmonary bypass (CPB) duration (OR 1.010; 95% CI 1.002–1.018; \( P = 0.013 \)), and higher drainage volume 24 h after surgery (OR 1.000; 95% CI 1.000–1.001; \( P = 0.033 \)) were identified as independent risk factors for developing stage 3 AKI. In addition, our result showed that the mortality rate was correlated significantly with the severity of AKI defined by KDIGO criteria and the Cox regression analysis showed that only stage 3 AKI, but not stage 1 and 2, was an independent risk factor for mortality (Hazard ratio 10.365, 95% CI 4.208 to 25.528; \( P < 0.001 \)) after adjusting for important confounding factors.

Conclusions: Our study suggested that stage 3 postoperative AKI was significantly associated with decreased postoperative survival rate after ATAAD surgery. Advanced age, increased CPB duration and drainage volume 24 h after surgery were identified as risk factors for developing stage 3 AKI.

Keywords: Acute kidney injury, Type A aortic dissection, Outcomes

Introduction

It is well accepted in the field that acute kidney injury (AKI) is a common and serious complication after acute type A aortic dissection (ATAAD) surgery. However, the incidence of AKI after aortic arch surgery varied...
widely (20–67%) in previous studies largely due to the lack of consensus in AKI definition until 2012 when the Kidney Disease Improving Global Outcome (KDIGO) criteria was published [1–5].

Inconsistent association between the development of postoperative AKI and long-term adverse outcomes in patients with ATAAD had been suggested in previous studies. Some studies demonstrated that only stage 3 AKI was significantly associated with lower long-term survival [6, 7], whereas others have found all stages postoperative AKI increased the mortality of patients with ATAAD [2, 3, 8]. However, most of these studies were conducted in a relatively small population and designed differently.

The current study not only aimed to decipher the association between different stages of AKI and disease outcomes but also to identify the risk factors for developing stage 3 AKI in patients after receiving ATAAD surgery. We present the following article in accordance with the STROBE reporting checklist.

Materials and methods
Study population
We retrospectively reviewed the medical records of 1052 patients who received ATAAD surgery at Nanjing Drum Tower Hospital between January 2014 and December 2019. Patients who were admitted to our hospital more than 48 h after symptom onset were excluded from the analysis (n = 13). Patients who required renal replacement therapy (RRT) before surgery (n = 27) were also excluded due to difficulty in measuring the progression of renal dysfunction. Patients who died during surgery or within 24 h after surgery (n = 19) were excluded when the death was considered irrelevant with postoperative renal dysfunction. The protocol of this study was approved by the institutional review board and individual consent was waived considering the retrospective nature of the study.

The stage 3 AKI was defined according to the serum creatinine (sCr) component of the KDIGO criteria at day 7 after the surgery (> 3.0 × baseline sCr or increase in sCr to ≥ 4.0 mg/dL or initiation of RRT) (Table 1). This study did not apply the urine output as the criteria in defining stage 3 AKI considering the high risk of inaccuracy in this retrospective study. Preoperative hepatic dysfunction was diagnosed in patients with Model of End-Stage Liver Disease (MELD) score ≥ 12. Routine follow up of patients’ general health status was conducted by telephone contact since 2014 once every year. If patients had died at the time of contact, the date and the cause of deaths was collected. All patients were divided into the stage 3 AKI group and the control group.

Surgical procedure
The surgical techniques applied in the study was described in detail in a previous study [9]. Briefly, the root procedures included direct repair or replacement of inclusion root, Bentall procedure, or David procedure. The distal arch repair consisted of hemi-arch replacement, island arch replacement, total arch replacement, triple-branched stent, and fenestrated stent depending on patient’s preoperative status, entry tear location, and aortic diameter, as described previously.

Statistical analysis
Continuous variables were expressed as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables were presented as frequencies with percentages. The χ² test or Fisher exact test was used for comparing categorical variables, whereas the t-test or Mann–Whitney U-test was chose for examining continuous variables.

To reduce selection bias, one-to-one propensity score (PS) matching was conducted between two groups. All the pre-operative variables listed in Table 2 and intra-operative variables listed in Table 3 were included in the analysis. The PS for each patient was estimated using the logistic regression model and matched to the nearest neighboring point with a tolerance level on the maximum PS distance (callipers of width 0.2 standard deviations of the logit of the PS).

Multivariate logistic regression analysis was performed (stepwise enter method) using variables identified in the univariable analyses (P-value < 0.20) to identify independent risk factors for developing stage 3 AKI after surgery. We used Kaplan–Meier methods and multivariate Cox proportional hazards regression to assess the impact of AKI for postoperative mortality. For Cox regression analysis, all variables with a P-value < 0.20 identified in univariable analysis were included in the model. A forward stepwise procedure was applied to introduce variables to the final models. A P-value less than 0.05 was considered

| Table 1 | Kidney Disease Improving Global Outcomes (KDIGO) criteria for acute kidney injury |
|---------|----------------------------------------------------------------------------------|
| Stage   | Serum creatinine (sCr) increase                                                  |
| 1       | 1.5–1.9 times baseline or ≥ 0.3 mg/dL increase                                   |
| 2       | 2.0–2.9 times baseline                                                          |
| 3       | > 3.0 times baseline or increase in sCr to ≥ 4.0 mg/dL or initiation of renal replacement therapy |
Table 2  Baseline characteristics of the unmatched and propensity matched groups

| Variables                      | Total (n = 993) | Stage 3 (n = 236) | Control (n = 757) | P value* | Stage 3 (n = 119) | Control (n = 119) | P value* |
|-------------------------------|----------------|-------------------|-------------------|----------|-------------------|-------------------|----------|
| Demographic data              |                |                   |                   |          |                   |                   |          |
| Age (year)                    | 53.0 ± 13.1    | 54.0 ± 13.4       | 52.7 ± 13.1       | 0.186    | 53.7 ± 13.3       | 51.2 ± 12.3       | 0.141    |
| Male (%)                      | 73.0 (73.5)    | 179 (75.8)        | 551 (72.8)        | 0.352    | 92 (77.3)         | 93 (78.2)         | 0.876    |
| BMI (kg/m²)                   | 25.6 ± 4.8     | 26.3 ± 4.8        | 25.4 ± 4.8        | 0.036    | 26.5 ± 4.8        | 26.0 ± 4.4        | 0.371    |
| Medical history               |                |                   |                   |          |                   |                   |          |
| Hypertension (%)              | 715 (72.0)     | 186 (78.8)        | 529 (69.9)        | 0.008    | 87 (73.1)         | 91 (76.5)         | 0.550    |
| Diabetes mellitus (%)         | 23 (2.3)       | 4 (1.7)           | 19 (2.5)          | 0.467    | 0 (0)             | 3 (2.5)           | 0.247    |
| Previous cardiac surgery (%)  | 44 (4.4)       | 14 (5.9)          | 30 (4.0)          | 0.199    | 6 (5.0)           | 5 (4.2)           | 0.758    |
| Previous coronary artery disease (%) | 34 (3.4) | 11 (4.7) | 23 (3.0) | 0.231 | 3 (2.5) | 2 (1.7) | 1.000 |
| Cerebrovascular disease (%)   | 36 (3.6)       | 9 (3.8)           | 27 (3.6)          | 0.859    | 6 (5.0)           | 1 (0.8)           | 0.119    |
| LVEF (%)                      | 55.1 ± 6.6     | 54.2 ± 5.9        | 55.3 ± 6.7        | 0.489    | 55.1 ± 5.6        | 54.0 ± 8.7        | 0.728    |
| Time from symptom onset to admission | 10.7 ± 6.0 | 12.3 ± 7.1 | 11.4 ± 6.4 | 0.274 | 12.5 ± 6.8 | 11.7 ± 6.5 | 0.259 |
| Pericardial tamponade (%)     | 166 (16.7)     | 55 (23.3)         | 111 (14.7)        | 0.002    | 21 (17.6)         | 17 (14.3)         | 0.479    |
| DeBakey type I (%)            | 816 (82.2)     | 207 (87.7)        | 609 (80.4)        | 0.011    | 103 (86.6)        | 102 (85.7)        | 0.851    |
| MELD score ≥ 12 (%)           | 268 (27.2)     | 103 (45.2)        | 165 (21.8)        | < 0.001  | 38 (33.0)         | 31 (26.1)         | 0.241    |
| Preoperative laboratory data  |                |                   |                   |          |                   |                   |          |
| WBC (10^3/L)                  | 11.7 ± 11.1    | 12.3 ± 4.7        | 11.5 ± 12.4       | 0.339    | 12.9 ± 5.2        | 11.6 ± 4.2        | 0.171    |
| Hemoglobin (g/L)              | 122.4 ± 29.0   | 121.4 ± 41.2      | 122.8 ± 24.0      | 0.630    | 120.8 ± 48.7      | 117.4 ± 26.6      | 0.381    |
| PLT (10^3/L)                  | 150.9 ± 86.2   | 142.6 ± 62.7      | 153.5 ± 92.3      | 0.091    | 151.8 ± 59.0      | 145.7 ± 62.4      | 0.440    |
| sCr (μmol/L)                  | 81.0 (61.8, 114.2) | 101.2 (68.1, 175.8) | 77.6 (60.0, 104.1) | < 0.001 | 111.1 ± 84.4 | 108.0 ± 88.3 | 0.784 |
| BUN (mmol/L)                  | 8.2 ± 4.0      | 99 ± 5.6          | 77 ± 3.2          | < 0.001  | 83 ± 3.9          | 86 ± 4.1          | 0.658    |
| ALB (g/L)                     | 36.5 ± 5.0     | 35.6 ± 5.9        | 36.8 ± 4.7        | 0.008    | 36.5 ± 5.8        | 36.3 ± 4.9        | 0.758    |
| ALT (U/L)                     | 25.6 (15.7, 46.8) | 30.3 (15.2, 81.1) | 22.3 (143.41)     | < 0.001  | 29.6 (174.749)    | 25.9 (142, 415)   | 0.113    |
| CRP (mg/dL)                   | 23.6 (5.0, 81.6) | 19.2 (48, 664)   | 22.2 (44, 67.5)   | 0.628    | 19.2 (52, 67.2)   | 24.9 (4.5, 106.4) | 0.171    |
| Triglyceride (mmol/L)         | 1.0 (0.7, 1.5) | 1.1 (0.7, 1.6)   | 0.9 (0.7, 1.5)    | 0.166    | 1.1 (0.8, 1.6)    | 1.0 (0.8, 1.4)    | 0.353    |
| Total bilirubin (μmol/L)      | 15.8 (11.3, 23.1) | 14.6 (100, 23.1) | 15.2 (113, 22.2)  | 0.685    | 17.7 ± 15.4       | 18.5 ± 15.4       | 0.674    |
| INR                           | 1.1 (1.0, 1.2) | 1.3 ± 0.8         | 1.2 ± 0.7         | < 0.001  | 1.2 ± 0.5         | 1.1 ± 0.2         | 0.060    |
| D-dimer (ng/mL)               | 4.6 (2.3, 9.3) | 4.9 (2.9, 12.3)   | 3.9 (2, 7.1)      | 0.001    | 4.7 (2.9, 9.5)    | 6.0 (3, 11.5)     | 0.868    |
| Preoperative CTA              |                |                   |                   |          |                   |                   |          |
| Involving the left renal artery (%) | 394 (77.0) | 91 (77.0) | 303 (79.7) | 0.419 | 45 (73.8) | 44 (72.1) | 0.596 |
| Involving the right renal artery (%) | 440 (87.6) | 100 (85.4) | 340 (89.9) | 0.386 | 53 (78.5) | 45 (74.2) | 0.479 |

Data presented as mean (%), median (IQR), or mean ± standard deviation

BMI: body mass index; LVEF: left ventricular ejection fraction; MELD: model of end-stage liver disease; WBC: white blood cell; PLT: platelet; sCr: serum creatinine; BUN: blood urea nitrogen; ALB: albumin; ALT: alanine transaminase; CRP: c-reactive protein; INR: international normalized ratio; CTA: computed tomography angiography; PSM: propensity score matching

*p-values indicate differences between stage 3 AKI and control group patients. P < 0.05 was considered statistically significant

statistically significant. All analyses were conducted with SPSS software (version 25, SPSS Inc, Chicago, IL).

Results

A total of 993 patients were eventually enrolled in this study. The patients were predominantly male (73.5%), with a mean age of 53 ± 13 years (range 19–87). Postoperative AKI was identified in 528 patients (53.6%) including 161 (16.2%) stage 1, 131 (13.2%) stage 2, and 236 (23.8%) stage 3. A total of 238 patients (119 pairs) selected by this PS-based matching procedure with similar baseline characteristics were eventually enrolled in the analysis.

Patient baseline demographic information was presented in Table 2. For the unmatched patients, compared to the control group, patients with increased body weight and hypertension diagnosis were more commonly occurred in the stage 3 AKI group. Unsurprisingly, the baseline serum creatinine (sCr) level was significantly
increased among patients in the stage 3 AKI group compared to the control group ($P<0.001$). However, no significant difference of time from symptom onset to admission and renal artery involvement was observed between two groups. In the PSM model, the baseline characteristics of the PSM matched groups did not reveal any significant differences.

Patient surgical parameters were shown in Table 3. Before PSM matching, our data indicated that the cardiopulmonary bypass (CPB) time ($P<0.001$), aortic cross-clamp time ($P<0.001$), and deep hypothermic circulatory arrest time ($P<0.001$) were all significantly prolonged in patients who developed stage 3 AKI. After PSM matching, the intro-operative variables showed no significant differences between the two groups.

The postoperative outcomes are summarized in Table 4. Before matching, a total of 165 patients (16.6%) required temporary RRT after surgery and 86 (52.1%) of them developed dialysis-dependent end-stage renal disease. Furthermore, mechanical ventilation duration, intensive care unit (ICU), and hospital stay were prolonged in patients who developed stage 3 AKI compared to controls. Furthermore, the 30-Day mortality was 30.5% in the stage 3 group and 7.5% in the control group with a significant difference. In the PSM matched analysis, ICU stay time and the 30-Day mortality consistently showed significant difference between two groups.

Next, multivariate logistic analyses were conducted which suggested that advanced age (odds ratio [OR] 1.031; 95% confidence interval [CI] 1.005–1.057; $P=0.018$), prolonged CPB duration (OR 1.010; 95% CI 1.002–1.018; $P=0.013$), and higher drainage volume within 24 h after surgery (OR 1.000; 95% CI 1.000–1.001; $P=0.033$)

### Table 3 Operative variables of the unmatched and propensity matched groups

| Variables          | Total (n = 993) | Overall cohort | Stage 3 (n = 236) | Control (n = 757) | P value* | PSM Cohort |
|--------------------|----------------|----------------|-------------------|-------------------|----------|------------|
|                    |                | Stage 3 (n = 119) | Control (n = 119) |                  |          |
| TAR (%)            | 478 (48.1)     | 131 (55.5)      | 347 (45.8)        | 0.009             | 71 (59.7) | 75 (63.0)  |
| CABG (%)           | 59 (5.9)       | 22 (9.3)        | 37 (4.9)          | 0.012             | 12 (10.1) | 10 (8.4)   |
| CPB time (min)     | 233.8 ± 80.0   | 258.6 ± 74.6    | 226.1 ± 63.9      | < 0.001           | 258.3 ± 66.2 | 261.8 ± 73.3 | 0.701 |
| Aortic cross-clamp time (min) | 164.2 ± 55.6 | 176.7 ± 61.6 | 160.3 ± 53.1 | < 0.001 | 180.8 ± 62.2 | 182.9 ± 61.7 | 0.801 |
| DHCA time (min)    | 29.3 ± 12.9    | 32.1 ± 13.5     | 28.5 ± 12.6       | < 0.001           | 32.0 ± 14.5 | 29.8 ± 11.8 | 0.216 |

Data presented as n (%), median (IQR), or mean ± standard deviation.

*P values indicate differences between stage 3 AKI and control group patients. $P<0.05$ was considered statistically significant.

### Table 4 Postoperative variables of the unmatched and propensity matched groups

| Variables                  | Total (n = 993) | Overall cohort | Stage 3 (n = 236) | Control (n = 757) | P value* | PSM cohort |
|----------------------------|----------------|----------------|-------------------|-------------------|----------|------------|
|                            |                | Stage 3 (n = 119) | Control (n = 119) |                  |          |
| Drainage volume 24 h surgery (mL) | 720.5 ± 650.0 | 950.0 ± 839.1 | 652.3 ± 565.2 | < 0.001           | 975.0 ± 926.4 | 790.4 ± 729.1 | 0.099 |
| Re-exploration for bleeding (%) | 36 (3.6) | 15 (6.4) | 21 (2.8) | 0.010             | 8 (6.7)   | 2 (1.7)    | 0.053 |
| Dialysis (%)               | 165 (16.6)    | 165 (69.9)     | 0 (0)             | < 0.001           | 80 (67.2) | 0 (0)       | < 0.001 |
| Ventilation time (hour)    | 170 (110.0, 43.0) | 26.0 (15.0, 90.0) | 15.0 (11.0, 28.8) | < 0.001           | 34.0 (16.2, 106.8) | 24.0 (14.2, 62.0) | 0.067 |
| Stroke (%)                 | 85 (8.6)      | 24 (10.2)      | 61 (8.1)          | 0.311             | 15 (12.6) | 12 (10.1)  | 0.540 |
| Paraplegia (%)             | 32 (3.2)      | 20 (8.5)       | 12 (1.6)          | < 0.001           | 8 (6.7)   | 3 (2.5)    | 0.123 |
| Tracheostomy (%)           | 45 (4.5)      | 23 (9.7)       | 22 (2.9)          | < 0.001           | 9 (7.6)   | 7 (5.9)    | 0.605 |
| Deep sternal wound infection (%) | 14 (1.4) | 7 (3.0) | 7 (0.9) | 0.029             | 5 (4.2)   | 1 (0.8)    | 0.213 |
| 30-day mortality (%)       | 115 (11.6)    | 72 (30.5)      | 43 (5.7)          | < 0.001           | 39 (32.8) | 22 (18.5)  | 0.012 |
| ICU Stay time (day)        | 5.0 (3.0, 8.0) | 6.0 (3.5, 11.5) | 4.0 (3.0, 5.0) | < 0.001           | 9.4 ± 8.3 | 5.8 ± 5.1  | < 0.001 |
| Hospital stay time (day)   | 21.4 ± 12.3   | 24.3 ± 16.3    | 20.5 ± 10.7       | < 0.001           | 24.0 ± 16.7 | 22.1 ± 14.8 | 0.351 |

Data presented as n (%), median (IQR), or mean ± standard deviation.

*ICU intensive care unit; PSM propensity score matching.

*P values indicate differences between stage 3 AKI and control group patients. $P<0.05$ was considered statistically significant.
Table 5 Multivariable analysis of risk factors for stage 3 acute kidney injury with KDIGO

| Variable                  | OR   | 95% CI          | P value |
|---------------------------|------|-----------------|---------|
| Age (year)                | 1.031| 1.005–1.057     | 0.018   |
| BMI (kg/m²)               | 1.063| 0.993–1.138     | 0.079   |
| Hypertension              | 1.033| 0.939–1.982     | 0.921   |
| Previous cardiac surgery  | 1.110| 0.309–3.986     | 0.837   |
| Pericardial tamponade     | 1.268| 0.451–3.567     | 0.653   |
| MELD score ≥ 12           | 1.883| 0.758–4.679     | 0.173   |
| PLT (10⁹/L)               | 1.002| 0.998–1.007     | 0.338   |
| sCr (μmol/L)              | 1.005| 1.000–1.010     | 0.053   |
| Bun (mmol/L)              | 0.958| 0.863–1.063     | 0.417   |
| ALB (g/L)                 | 0.946| 0.885–1.012     | 0.104   |
| Triglyceride (mmol/L)     | 1.238| 0.985–1.557     | 0.067   |
| INR                       | 1.689| 0.698–4.084     | 0.245   |
| Total bilirubin (μmol/L)  | 0.993| 0.972–1.015     | 0.518   |
| D-dimer (ng/mL)           | 1.009| 0.993–1.024     | 0.266   |
| TAR                       | 1.695| 0.868–2.038     | 0.012   |
| CABG                      | 1.850| 0.540–6.336     | 0.327   |
| CPB time (min)            | 1.010| 1.002–1.018     | 0.013   |
| Aortic cross-clamp time (min) | 0.996 | 0.988–1.005 | 0.419 |
| DHCA time (min)           | 1.019| 0.992–1.046     | 0.163   |
| Drainage volume 24 h after surgery (mL) | 1.000 | 1.000–1.001 | 0.033 |
| Paraplegia                | 2.578| 0.583–11.390    | 0.212   |

P < 0.05 was considered statistically significant

BMI, body mass index; MELD, model of end-stage liver disease; PLT, platelet; sCr, serum creatinine; ALB, albumin; INR, international normalized ratio; TAR, total arch replacement; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; OR, odds ratio; CI, confidence interval

were independent risk factors for developing postoperative stage 3 AKI (Table 5).

The follow-up of long-term mortality started on the day of surgery. 76 patients in the stage 3 AKI group and 45 patients in the control group died during the hospitalization period. As a result, a total of 872 patients survived the early postoperative period. The median follow-up time of this cohort was 20 months during which time a total of 11 patients (1.3%) who did not develop postoperative AKI, 8 (0.9%) with stage 1 AKI, 5 (0.6%) with stage 2 AKI, and 29 (3.3%) with stage 3 AKI passed away. 53 patients (6.1%) who were lost to follow-up and 1 patient who committed suicide after hospital discharge were identified as censored data in the following outcome analysis. Our data indicated that the mortality correlated significantly with the severity of AKI defined by KDIGO criteria before and after matching (P < 0.001, P = 0.003; by log-rank test respectively), which were shown in Figs. 1 and 2. Multivariate Cox analysis for mortality (Table 6) revealed that the only stage 3 AKI (Hazard ratio 10.365; 95% CI 4.208–25.528; P < 0.001), but not stage 1 and 2, was a significant and independent risk factor after adjusting for other major clinical factors that might increase postoperative AKI rate.

Discussion

In this study, we explored the consequences and risk factors for developing stage 3 AKI after ATAAD surgery. Compared with previous studies, our cohort was much larger and we applied the most updated and well accepted KDIGO criteria to define AKI. We found that advanced age, prolonged CPB duration, and higher drainage volume 24 h after surgery were independent predictors for developing postoperative stage 3 AKI. In addition, consistent with previous studies [6, 7], our study confirmed that only stage 3 AKI, but not stage 1 or 2, was associated with a higher postoperative mortality.

This correlation between AKI severity and long-term survival was also observed in other cardiothoracic operations [5]. A previous meta-analysis discovered that patients who suffered postoperative AKI were more likely to develop chronic kidney disease and end-stage renal disease, and the risk increased with the severity of AKI [10]. Therefore, above results underline the importance of identifying AKI in its early stages and offering appropriate treatment promptly before disease progression.

The incidence of postoperative AKI varied widely among different studies, partially due to the use of different AKI diagnostic criteria. A recent study reported that 24.0% of all patients developed stage 3 AKI after total arch replacement surgery with deep hypothermic circulatory arrest, including 15.4% patients who were treated with RRT [11], which were consistent with our results. However, Ko et al. reported that the incidence of developing stage 3 AKI after aortic arch surgery was 14% and only 9% required RRT [7]. The lower rates might partially due to that patients who received emergency surgery were excluded from that study [12].

Consistent with previous studies, we identified that increased age was an independent risk factor for developing postoperative stage 3 AKI [2, 3, 13]. It has been well accepted in the field that advanced age is associated with structural and functional changes in the kidney including parenchymal mass loss, progressive glomerulosclerosis, tubulopathy, interstitial fibrosis, and afferent-effferent arteriolar shunts, which could all result in reduced renal function [14]. The reduced renal function rendered these patients more vulnerable to the hemodynamic changes during the surgery and it was not surprising that patients with advanced age were more likely to develop postoperative AKI after ATAAD surgery.

CPB duration was another well accepted independent risk factor for postoperative AKI in emergent thoracic aortic surgery. Englberger et al. discovered that longer
CPB time (per 10 min) was associated with increasing postoperative AKI occurrence after studying 851 patients who received elective thoracic aortic operation [15]. Similarly, Roh et al. found that longer CPB duration was an independent risk factor for postoperative AKI among patients who received graft replacement of the thoracic aorta [3]. Furthermore, this correlation has been confirmed in some other studies [16, 17] and might be explained at least partially by the non-pulsatile blood flow and activation of inflammatory factors during the bypass [18]. However, more mechanism studies are needed to better understand this association before modification of the surgery process can be made.

Drainage volume 24 h after surgery was identified as another independent risk factor for postoperative stage 3 AKI by the logistic regression model in this study, which had been already recognized as a risk factor for AKI in previous studies [19]. Increases drainage volume can disrupt the homeostasis and induce pro-inflammatory states as well as increase oxidative stress which both can contribute to the pathogenesis of AKI [20]. Increasing evidences suggested that major perioperative transfusions of large amounts of packed red blood cells units and platelet units were associated with an increased incidence of AKI [7, 21, 22]. In line with this study, a recently published study showed that preoperative dual antiplatelet therapy increased the risk of major bleeding and transfusions, which ultimately increased the risk of AKI [23]. Therefore, decreasing 24 h drainage volume is important and may reduce the incidence of postoperative AKI.

**Limitations**

This study has some limitations. Firstly, although the sample size was large, the cohort was not homogeneous and might include some confounding factors in the baseline that were not recognized in the study. Secondly, our surgical technique evolved over the long study period, and surgeons with different surgical skills and experiences might also influence our results. Thirdly, the urine output was not examined in this study therefore the number of postoperative AKI patients might be underestimated. Therefore, further prospective multicenter studies are needed to better understand the association between postoperative AKI and disease prognosis before more effective strategies can be recommended.

**Conclusions**

This large cohort study underscores the high incidence of postoperative stage 3 AKI following ATAAD repair surgery and its association with worse outcome. Advanced
age, prolonged CPB time and increasing drainage volume 24 h after surgery were independent risk factors for developing postoperative stage 3 AKI.

Abbreviations
AKI: Acute kidney injury; ATAAD: Acute type A aortic dissection; KDIGO: Kidney Disease Improving Global Outcomes; OR: Odds ratio; CI: Confidence interval; CPB: Cardiopulmonary bypass; SCr: Serum creatinine.

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Authors’ contributions
DJW and ZGW conceived or designed the study. DJW, ZGW, MG, ZYW, and CC acquired, analyzed, or interpreted the data. ZGW, MG, ZYW, and CC drafted the manuscript. DJW, ZGW, and MG critically revised the manuscript for important intellectual content. LCL and LFZ performed the statistical analysis. All authors read and approved the final manuscript.

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Availability of data and materials
Data sharing in the current study are available from the corresponding author on reasonable request.

Table 6 Multivariate Cox analysis for mortality

| Hazard ratio | 95% CI   | P value |
|--------------|---------|---------|
| Age (year)   | 1.021   | 0.997–1.046 | 0.085 |
| Hypertension | 1.592   | 0.728–3.484 | 0.244 |
| Preoperative hemoglobin (g/L) | 0.993 | 0.982–1.005 | 0.240 |
| Preoperative CRP (mg/dL) | 0.998 | 0.992–1.004 | 0.454 |
| Preoperative sCr (μmol/L) | 0.998 | 0.995–1.001 | 0.254 |
| Preoperative D-dimer (ng/mL) | 0.990 | 0.967–1.014 | 0.419 |
| Pericardial tamponade | 2.280 | 0.749–6.944 | 0.147 |
| CPB time (min) | 1.003 | 0.998–1.008 | 0.241 |
| KDIGO stage 1 | 2.260 | 0.710–7.196 | 0.167 |
| KDIGO stage 2 | 2.409 | 0.747–7.765 | 0.141 |
| KDIGO stage 3 | 10.365 | 4.208–25.528 | <0.001 |
| Ventilation time (hour) | 1.002 | 0.998–1.007 | 0.307 |

P < 0.05 was considered statistically significant
CRP: c-reactive protein; sCr: serum creatinine; CPB: cardiopulmonary bypass; KDIGO: Kidney Disease Improving Global Outcomes; CI: confidence interval

Declarations
Ethics approval and consent to participate
Ethical approval was obtained from Nanjing Drum Tower Hospital ethics committee. This retrospective study was conducted without informed consent for some objective reasons and was approved by the ethics committee. All procedures performed in studies were in accordance with the Declaration of Helsinki.
