Effects of hyperuricaemia, with the superposition of being overweight and hyperlipidaemia, on the incidence of acute kidney injury following cardiac surgery: a retrospective cohort study

Yiqi Su, Haoxuan Li, Yang Li, Xialian Xu, Bo Shen, Wuhua Jiang, Yimei Wang, Yi Fang, Chunsheng Wang, Zhe Luo, Xiaoqiang Ding, Jie Teng, Jiariu Xu

ABSTRACT

Objectives Acute kidney injury (AKI) is a common complication of cardiac surgery. This study aimed to explore the effects of hyperuricaemia, being overweight and hyperlipidaemia as risk factors for AKI in patients following cardiac surgery (cardiac surgery-associated acute kidney injury (CSA-AKI)).

Design Retrospective observational study.

Setting University teaching, grade-A tertiary hospital in Shanghai, China.

Participants Patients who underwent cardiac surgery from July 2015 to December 2015 in Zhongshan Hospital, Fudan University.

Main outcome measures We investigated the effect of hyperuricaemia, in combination with being overweight and hyperlipidaemia, on the risk of CSA-AKI.

Results A total of 1420 patients were enrolled. The AKI incidence in the highest uric acid group was 44.4%, while that in the lowest uric acid group was 28.5% (p<0.001). Patients in the higher uric acid quartiles were more likely to be overweight and hyperlipidaemic at the same time (p<0.001). Multivariate logistic regression analysis showed that hyperuricaemia was an independent risk factor for AKI (OR=1.237, 95%CI 1.095 to 1.385; p=0.009); being overweight or hyperlipidaemia alone was not an independent risk factor, but the combination of being overweight and hyperlipidaemia was (OR=1.544, 95%CI 1.509 to 2.252; p=0.024). In the final model, the OR value increased to 3.126 when hyperuricaemia was combined with being overweight and hyperlipidaemia, and the Hosmer-Lemeshow test showed that all three models fit well (p=0.433, 0.638 and 0.597, respectively).

Conclusions The combination of being overweight and having hyperlipidaemia was an independent risk factor, but being overweight or having hyperlipidaemia alone was not. The combination of hyperuricaemia, being overweight and hyperlipidaemia further increased the risk of CSA-AKI.
hyperuricaemia is an independent risk factor for CSA-AKI. A meta-analysis including 18 cohort studies with 75,200 patients found that patients with hyperuricaemia have a significantly higher risk of AKI compared with the control group (OR 2.24, 95% CI 1.76 to 2.86; p<0.01). The mechanism of AKI caused by hyperuricaemia is related to the crystallisation of uric acid, which may also activate an epithelial–mesenchymal proinflammatory response.

Hyperuricaemia is often associated with metabolic disorders, such as being overweight and hyperlipidaemia. Studies have confirmed that serum uric acid level is positively correlated with serum total cholesterol (TC), triglycerides and low-density lipoprotein (LDL) levels and negatively correlated with high-density lipoprotein (HDL) levels. Other studies have suggested that hyperlipidaemia is a risk factor for AKI after surgery. In addition, the incidence of AKI can increase with increasing BMI. Previous studies also confirmed that preoperative serum creatinine (SCr) and uric acid levels increased with an increase in BMI, which was an independent risk factor for AKI.

With economic development and changes in lifestyle and diet patterns, the risk factors for AKI in the Chinese population have increased rapidly in recent years. An increasing number of people tend to be obese or have hypertension, diabetes, hyperuricaemia and hyperlipidaemia. Considering that many risk factors might have additive effects and to provide a reference for clinicians, this study explored the relationship between hyperuricaemia, being overweight and hyperlipidaemia, and the effect of these factors on the risk of CSA-AKI.

MATERIALS AND METHODS

Patient selection

We retrospectively analysed data from patients who underwent cardiac surgery between July 2015 and December 2015 in our hospital. Patients were excluded if they were <18 years of age, had pre-existing end-stage renal disease, had kidney transplantation, intended to receive heart transplantation or had missing data.

Definitions

AKI was defined according to the following Kidney Disease: Improving Global Outcomes (KDIGO) criteria: (1) increase in SCr by ≥26.5 µmol/L within 48 hours; (2) increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; and (3) urine volume of <0.5 mL/kg/hour for 6 hours and staged according to the SCr and urine output. Severe AKI was defined as having KDIGO stage 2 or 3. Hyper-tension was defined as having a systolic blood pressure (BP) of ≥140 mm Hg or a diastolic BP of ≥90 mm Hg or an individual currently using antihypertensive drugs. Hyperuricaemia was defined as having serum uric acid levels of ≥360 µmol/L (women) and ≥420 µmol/L (men and postmenopausal women). Hyperlipidaemia was defined as having levels of triglyceride of ≥1.70 mmol/L and high-density lipoprotein cholesterol (HDL-c) of <1.04 mmol/L (and/or) TC of ≥5.18 mmol/L. Being overweight was defined as having a BMI of ≥24 kg/m². High-risk surgery was defined as either aortic surgery, macrovascular surgery or combined surgery. CKD was defined as having an estimated glomerular filtration rate (eGFR) of <60 mL/(min/1.73 m²).

Data collection and groups

Preoperative information of all patients was collected, including sex, age, preoperative comorbidities (hypertension and diabetes), New York Heart Association (NYHA) cardiac function classification grade, SCr, eGFR, blood glucose and blood lipid levels. Intraoperative data included surgical type, extracorporeal circulation time and aortic clamping time. Postoperative data included length of hospital stay, length of intensive care unit (ICU) stay and mechanical ventilation days. Patients were divided into AKI versus non-AKI groups, and hyperuricaemia versus normal uric acid groups. The uric acid levels were categorised into four groups according to the quartiles of gender-specific distribution: for men: Q1, <311 ± 41 µmol/L; Q2, 311–366 ± 41 µmol/L; Q3, 366–442 ± 41 µmol/L; Q4, >442 ± 41 µmol/L; for women: Q1, <246 ± 31 µmol/L; Q2, 246–304 ± 31 µmol/L; Q3, 304–369 ± 31 µmol/L; Q4, >369 ± 31 µmol/L. Poor short-term outcomes include death during hospitalisation or discharge from the hospital automatically after abandoning treatment.

Patient and public involvement

The patients and the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Statistical analysis

Statistical analysis was performed using SPSS V.20.0. The independent sample t-test or the Mann-Whitney test was used to compare continuous variables, and dichotomous variables were analysed using the χ² test or Fisher’s exact test. Pearson’s correlation was used to analyse the relationship between uric acid, blood lipid and BMI. A logistic regression model was used to analyse the risk factors for AKI. We first performed univariate analysis of all variables, then the backward stepwise selection method was used for multiple regression analysis, with a p value of <0.05 as the inclusion criterion and p value of ≥0.10 or higher as the exclusion criterion. The Hosmer-Lemeshow test was used to verify the goodness of fit of the models. Statistical significance was set at a p value of <0.05.

RESULTS

Baseline characteristics

We identified 1420 patients who underwent cardiac surgery with a mean age of 57.1±12.2 years. The baseline demographic and medical characteristics for all patients, as divided by the uric acid quartiles, are shown in table 1. A history was documented for hypertension in 532
patients (37.5%) and diabetes in 221 patients (15.6%). When analysed by the quartile of the uric acid level, the patients with higher uric acid levels were more likely to be older, with more occurrences of hypertension, higher BMI and levels of blood urea nitrogen, SCr, albumin and triglycerides. There were no significant differences in cholesterol, low-density lipoprotein cholesterol (LDL-c), glycosylated haemoglobin and blood glucose levels among the four groups. Moreover, patients in the higher uric acid quartiles were more likely to be overweight and to have hyperlipidaemia (all p<0.001). In contrast, the patients in the higher uric acid quartiles showed lower levels of eGFR and HDL-c (all p<0.001) (table 1). We also found significant differences between the AKI group and the non-AKI group for male sex, age, diabetes, NYHA grade >II, hyperuricaemia, preoperative SCr and uric acid levels (all p<0.001) (online supplemental table 1). A total of 117 patients (8.2%) were diagnosed with CKD. Compared with the non-AKI group, the AKI group also had a higher proportion of patients with CKD (11.8% vs 6.2%, p<0.001). The AKI group had a higher proportion of being overweight (47.9% vs 39.1%, p=0.006) and higher BMI (24.1±3.5 vs 23.4±3.1, p<0.001). There were no significant differences in levels of cholesterol, triglycerides and LDL-c between the two groups (online supplemental table 1). There was no significant difference in extracorporeal membrane oxygenation support and the use of inotropic agents between the two groups, but the AKI group had a higher proportion of using nephrotoxic drugs (20.3% vs 4%, p<0.001), diuretics (97.1% vs 93.2%, p=0.002) and vasoactive agents (93.2% vs 89.4%, p=0.015). The AKI group also had a higher proportion of 24-hour fluid balance (1.2 vs 0.3, p<0.001) and the incidence of low cardiac output syndrome (LCOS; 19.7% vs 8.4%, p<0.001; online supplemental table 1).

### AKI incidence and short-term outcomes

When analysed by quartile of the uric acid level, the AKI incidence correlated with higher uric acid levels (p<0.001). The patients in the higher uric acid quartiles displayed longer lengths of hospital stay and ICU stay (all p<0.001) (table 2). However, the incidence of severe AKI, renal replacement therapy (RRT) treatment and poor short-term prognosis showed no statistical differences among the uric acid quartiles (all p>0.05) (table 2).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics of the study population according to uric acid quartiles</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (=1420)</td>
</tr>
<tr>
<td>Gender (male), n (%)</td>
<td>833 (58.7)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.1±12.2</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.6±3.3</td>
</tr>
<tr>
<td>Overweight, n (%)</td>
<td>601 (42.3)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>532 (37.5)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>221 (15.6)</td>
</tr>
<tr>
<td>Blood glucose (mmol/L)</td>
<td>5.2±0.7</td>
</tr>
<tr>
<td>Glycosylated haemoglobin (%)</td>
<td>5.8±0.5</td>
</tr>
<tr>
<td>Blood urea nitrogen (mmol/L)</td>
<td>6.0±2.0</td>
</tr>
<tr>
<td>Serum creatinine (μmol/L)</td>
<td>80.8±22.4</td>
</tr>
<tr>
<td>eGFR (mL/(min/1.73 m²))</td>
<td>86.4±20.6</td>
</tr>
<tr>
<td>eGFR &lt;60mL/(min/1.73 m²), n (%)</td>
<td>117 (8.2)</td>
</tr>
<tr>
<td>Albuminuria, n (%)</td>
<td>109 (7.7)</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>4±0.9</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.3±0.8</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (mmol/L)</td>
<td>2.3±0.8</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (mmol/L)</td>
<td>1.2±0.3</td>
</tr>
<tr>
<td>Hyperlipidaemia, n (%)</td>
<td>292 (20.6)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>40.8±3.9</td>
</tr>
<tr>
<td>Urolithiasis</td>
<td>76 (5.4)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>30 (2.1)</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
<td>141 (9.9)</td>
</tr>
<tr>
<td>Low cardiac output syndrome</td>
<td>178 (12.5)</td>
</tr>
</tbody>
</table>

Results presented as mean±SD or number (percentage).

eGFR, estimated glomerular filtration rate.
When grouped by AKI and non-AKI, the patients with AKI required longer ICU and hospital stays (all p<0.001, online supplemental table 1); the incidence of poor short-term outcomes in the AKI group was significantly higher than that in the non-AKI group (3.3% vs 0.2%, p<0.001; online supplemental table 1).

When grouped by hyperuricaemia, the incidence of AKI, severe AKI and RRT treatment in the hyperuricaemia group was significantly higher than that in the normal uric acid group (OR=1.237, 95% CI 1.095 to 1.885; p=0.009) in model 1, after adjusting for the confounding factors of male sex, age, being overweight, diabetes, angiography, NYHA >II, preoperative eGFR <60/min/1.73m², high-risk surgery, extracorporeal CPB time and aortic occlusion time. When the combination of being overweight and hyperlipidaemia was included in model 2, it became a risk factor for AKI (OR=1.544, 95% CI 1.059 to 2.252; p=0.024), while hyperuricaemia became insignificant. In model 3, adjusting for confounding factors, we found that the combination of hyperuricaemia, being overweight and hyperlipidaemia further increased the risk of postoperative AKI (OR=3.126, 95% CI 1.731 to 5.646; p<0.001). The Hosmer-Lemeshow test showed that all models fit well (p=0.433, 0.638 and 0.597, respectively) (table 4).

**Table 2** Comparison of AKI incidence and short-term outcomes according to uric acid quartiles

<table>
<thead>
<tr>
<th>Quartile</th>
<th>AKI, n (%)</th>
<th>Severe AKI, n (%)</th>
<th>Renal replacement therapy, n (%)</th>
<th>Length of hospital stay (days)</th>
<th>Length of intensive care unit stay (hours)</th>
<th>Poor short-term prognosis, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 (n=351)</td>
<td>100 (28.5)</td>
<td>21 (6.0)</td>
<td>6 (1.7)</td>
<td>13.5±15.8</td>
<td>46.6±80.3</td>
<td>6 (1.7)</td>
</tr>
<tr>
<td>Q2 (n=360)</td>
<td>116 (32.2)</td>
<td>26 (7.2)</td>
<td>5 (1.4)</td>
<td>13.2±6.9</td>
<td>46.4±76.4</td>
<td>3 (0.8)</td>
</tr>
<tr>
<td>Q3 (n=353)</td>
<td>144 (40.8)</td>
<td>28 (7.9)</td>
<td>4 (1.1)</td>
<td>13.2±5.1</td>
<td>53.1±74.7</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>Q4 (n=356)</td>
<td>158 (44.4)</td>
<td>33 (9.3)</td>
<td>12 (3.4)</td>
<td>14.2±6.8</td>
<td>64.3±116</td>
<td>8 (2.2)</td>
</tr>
</tbody>
</table>

Results presented as mean±SD or number (percentage). AKI, acute kidney injury.

DISCUSSION

This study found that patients with higher uric acid levels had a higher incidence of AKI, and these patients were more commonly overweight and hyperlipidaemic at the same time. Hyperuricaemia was positively correlated with triglycerides and BMI; it was negatively correlated with HDL-c. Hyperuricaemia was an independent risk factor for CSA-AKI (OR=1.237, 95% CI 1.095 to 1.885; p=0.009); the combination of being overweight and having hyperlipidaemia was an independent risk factor, but being overweight or having hyperlipidaemia alone were not. The combination of hyperuricaemia, being overweight and hyperlipidaemia further increases the risk of AKI.

The incidence of AKI increased according to the uric acid quartile, and patients with higher uric acid levels displayed longer lengths of hospital stay and ICU stay. The level of uric acid is related to blood lipids and BMI, albuminuria (OR=1.394, 95% CI 1.024 to 2.203), hyperuricaemia (OR=1.096, 95% CI 1.275 to 2.022), high-risk surgery (OR=2.065, 95% CI 1.538 to 2.772), extracorporeal cardiopulmonary bypass (CPB) time (OR=1.010, 95% CI 1.007 to 1.014), LCOS (OR=2.241, 95% CI 1.183 to 3.576) and aortic occlusion time (OR=1.015, 95% CI 1.010 to 1.020) (table 3).

The length of ICU stay in the hyperuricaemia group was significantly higher than that in the normal uric acid group (p<0.001) (online supplemental table 2).

The level of uric acid is related to blood lipids and BMI, and patients with higher uric acid levels had the highest AKI incidence, and these patients were more commonly overweight and hyperlipidaemic at the same time. Hyperuricaemia was positively correlated with triglycerides and BMI; it was negatively correlated with HDL-c. Hyperuricaemia was an independent risk factor for CSA-AKI (OR=1.237, 95% CI 1.095 to 1.885; p=0.009) in model 1, after adjusting for the confounding factors of male sex, age, being overweight, diabetes, angiography, NYHA >II, preoperative eGFR <60/min/1.73m², high-risk surgery, extracorporeal CPB time and aortic occlusion time. When the combination of being overweight and hyperlipidaemia was included in model 2, it became a risk factor for AKI (OR=1.544, 95% CI 1.059 to 2.252; p=0.024), while hyperuricaemia became insignificant. In model 3, adjusting for confounding factors, we found that the combination of hyperuricaemia, being overweight and hyperlipidaemia further increased the risk of postoperative AKI (OR=3.126, 95% CI 1.731 to 5.646; p<0.001). The Hosmer-Lemeshow test showed that all models fit well (p=0.433, 0.638 and 0.597, respectively) (table 4).
**Figure 1** Correlation of uric acid with blood lipid, body mass index and blood glucose.

- **A** and **B**: Correlation between preoperative uric acid and cholesterol and triglycerides.
  - $r = 0.014$
  - $P = 0.603$
  - $r = -0.221$
  - $P < 0.001$

- **C** and **D**: Correlation between preoperative uric acid and high-density lipoprotein and low-density lipoprotein.
  - $r = 0.044$
  - $P = 0.095$
  - $r = -0.190$
  - $P < 0.001$

- **E** and **F**: Correlation between preoperative uric acid and body mass index and blood glucose.
  - $r = 0.157$
  - $P < 0.001$
  - $r = -0.016$
  - $P = 0.549$
respectively. The mechanism of hyperuricaemia caused by AKI is related to the crystallisation of uric acid. Urate crystals have a proinflammatory effect, which can cause renal tubular damage. Moreover, elevated serum uric acid may lead to endothelial dysfunction, oxidative stress and elevated C reactive protein.11 18–22 Multiple studies have confirmed that hyperuricaemia is an independent risk factor for AKI. A retrospective study of 18 444 hospitalised patients divided into four groups according to uric acid levels showed that blood uric acid of >6.7 mg/dL (men) or >5.4 mg/dL (women) correlated with a higher risk of AKI compared with blood uric acid of <4.5 mg/dL (men) and <3.6 mg/dL (women) with ORs of 3.2 (95% CI 2.55 to 4.10) in men (p<0.001) and 3.1 (95% CI 2.40 to 4.19) in women (p<0.001).8 Another retrospective study including 1536 patients with rheumatic heart disease showed that uric acid was independently associated with in-hospital (OR=1.21, 95% CI 1.06,1.37; p=0.004) and 1-year (HR=1.17, 95% CI 1.05,1.29; p=0.003) mortality after valve replacement surgery.10 A prospective study by Gaipov et al showed that uric acid seemed to predict the progression of AKI and RRT requirement in patients who underwent cardiac surgery better than neutrophil gelatinase-associated lipocalin.8 A meta-analysis including 18 cohort studies with 75 200 patients found that the hyperuricaemia group had a significantly higher risk of AKI compared with the controls (OR 2.24, 95% CI 1.76 to 2.86; p<0.01). The risk rate after percutaneous coronary intervention (PCI) was much higher in the hyperuricaemia group than in the control group (16.0% vs 5.3%, OR 3.24, 95% CI 1.93 to 5.45; p<0.01).4 Similar findings on AKI and in-hospital mortality have been reported in Asian populations.23

Previous studies have confirmed that hyperuricaemia is closely related to lipid metabolism.24 Ali et al found that serum uric acid level was positively correlated with serum levels of TC, triglycerides and LDL.25 A study involving 536 patients undergoing radical gastrectomy concluded that age, BMI, hypertension, hyperlipidaemia and preoperative cystatin C level were independent risk factors for AKI.12 The results of our study showed that the incidence of hyperlipidaemia in the AKI group was higher than that in the non-AKI group (36.5% vs 34%, p=0.351). In addition, there was a positive correlation between uric

Figure 2 Comparison of acute kidney injury incidence among different subgroups.
Previous studies have shown that the incidence of postoperative AKI in obese patients (BMI ≥28) increased significantly, and that BMI was an independent risk factor for AKI. Another analysis involving 445 patients after cardiac surgery found that BMI was associated with an increased risk of AKI within 30 days, with the risk of AKI increasing by 26.5% for every 5 kg/m² increase in BMI.

In the current study, multivariate logistic regression analysis found that hyperlipidaemia alone was not an independent risk factor for AKI, but the coexistence of hyperlipidaemia and being overweight was identified as a new risk factor. In the final model, the combination of hyperuricaemia, hyperlipidaemia and being overweight further increased the risk. The results show that hyperlipidaemia alone does not increase the risk of AKI, but in combination with other risk factors, such as being overweight or hyperuricaemia, it greatly increases the AKI risk. This means that controlling a single risk factor might not be effective, but controlling for multiple risk factors simultaneously may be sufficient to prevent AKI.

This study had several limitations. First, this was a single-centre retrospective analysis based on prospectively collected data. Second, the degree of hyperuricaemia was not graded, and the effect of uric acid-lowering treatment on the occurrence of CSA-AKI was not clear. Third, prospective studies should be conducted in the future to confirm the effects of urate-lowering therapy, fat reduction and weight loss therapy on the risk of AKI.

**CONCLUSIONS**

The incidence of AKI increased according to the uric acid quartiles, and patients with higher uric acid levels had higher proportions of hypertension, being overweight and hyperlipidaemia. The level of uric acid is related to blood lipids and BMI, respectively. Hyperuricaemia was associated with increased risk of more severe AKI.

### Table 3 Univariate logistic analysis of risk factors for cardiac surgery-associated acute kidney injury

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>1.524 (1.219 to 1.905)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (1 year added)</td>
<td>1.022 (1.013 to 1.032)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overweight</td>
<td>1.403 (1.100 to 1.790)</td>
<td>0.006</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.197 (0.959 to 1.495)</td>
<td>0.113</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.353 (1.011 to 1.811)</td>
<td>0.042</td>
</tr>
<tr>
<td>Glycosylated haemoglobin</td>
<td>1.208 (0.779 to 1.983)</td>
<td>0.365</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>1.29 (1.039 to 1.602)</td>
<td>0.021</td>
</tr>
<tr>
<td>New York Heart Association grade &gt;II</td>
<td>1.375 (1.043 to 1.812)</td>
<td>0.024</td>
</tr>
<tr>
<td>Preoperative estimated glomerular filtration rate (&lt;60 mL/(min/1.73m²))</td>
<td>2.016 (1.379 to 2.949)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albuminuria</td>
<td>1.394 (1.024 to 2.203)</td>
<td>0.020</td>
</tr>
<tr>
<td>Hyperuricaemia</td>
<td>1.696 (1.275 to 2.022)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>1.257 (0.896 to 1.636)</td>
<td>0.098</td>
</tr>
<tr>
<td>High-risk surgery</td>
<td>2.065 (1.538 to 2.772)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (1 min added)</td>
<td>1.01 (1.007 to 1.014)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic occlusion time (1 min added)</td>
<td>1.015 (1.010 to 1.020)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
<td>1.368 (0.889 to 1.958)</td>
<td>0.064</td>
</tr>
<tr>
<td>Low cardiac output syndrome</td>
<td>2.241 (1.183 to 3.576)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
an independent risk factor for CSA-AKI; the combination of being overweight and having hyperlipidaemia was an independent risk factor, but being overweight or having hyperlipidaemia alone was not. The combination of hyperuricaemia, being overweight and hyperlipidaemia further increases the risk of AKI. Therefore, reducing combinations of risk factors might reduce the risk of AKI. Continued studies are needed to focus on the early detection of, and intervention for, these and other risk factors.

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### Contributors

JX, YS and HL designed the study; YS, YL, BS, WJ, CW, ZL, XD, JT and YW participated in the acquisition of data; YS, JX, YF and HL researched and evaluated the literature; YS, XX and JX undertook the statistical analysis; HL wrote the first draft of the manuscript; YS, HL, JX, JT and YW made substantial contributions to the interpretation of data. JX is responsible for the overall content as guarantor. All authors approved the final manuscript for publication.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the ethical committee of Zhongshan Hospital, Fudan University (number B2017-039). The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request via email to the corresponding author (Su.jiarui@zs-hospital.sh.cn).

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