Assessing the predictive value of elevated postoperative syndecan-1 levels for progressive acute kidney injury and kidney replacement therapy necessity in adult cardiac surgery patients

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Abstract

Background The development of acute kidney injury (AKI) post-cardiac surgery significantly increases patient morbidity and healthcare costs. Prior researches have established Syndecan-1 (SDC-1) as a potential biomarker for endothelial injury and subsequent acute kidney injury development. This study assessed whether postoperative SDC-1 levels could further predict AKI requiring kidney replacement therapy (AKI-KRT) and AKI progression.

Methods In this prospective study, 122 adult cardiac surgery patients, who underwent valve or coronary artery bypass grafting (CABG) or a combination thereof and developed AKI within 48 h post-operation from May to September 2021, were monitored for the progression to stage 2–3 AKI or the need for KRT. We analyzed the predictive value of postoperative serum SDC-1 levels in relation to multiple endpoints.

Results In the study population, 110 patients (90.2%) underwent cardiopulmonary bypass, of which thirty received CABG or combined surgery. Fifteen patients (12.3%) required KRT, and thirty-eight (31.1%) developed progressive AKI, underscoring the severe AKI incidence. Multivariate logistic regression indicated that elevated SDC-1 levels were independent risk factors for progressive AKI (OR = 1.006) and AKI-KRT (OR = 1.011). The AUROC for SDC-1 levels in predicting AKI-KRT and AKI progression was 0.892 and 0.73, respectively, outperforming the inflammatory cytokines. Linear regression revealed a positive correlation between SDC-1 levels and both hospital ($\beta = 0.014$, $p = 0.022$) and ICU stays ($\beta = 0.013$, $p < 0.001$).

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Conclusion Elevated postoperative SDC-1 levels significantly predict AKI progression and AKI-KRT in patients following cardiac surgery. The study's findings support incorporating SDC-1 level monitoring into post-surgical care to improve early detection and intervention for severe AKI.

Keywords Cardiac surgery, Acute kidney injury, Risk factors, Syndecan-1, Endothelial injury, Kidney replacement therapy

Introduction

Cardiac surgery-associated acute kidney injury (AKI) represents a significant challenge in modern medicine, leading to dire outcomes where patients face increased risks of morbidity and mortality, extended hospital stays, and an increased likelihood of chronic kidney disease, placing a significant burden on healthcare systems globally [1–3]. The progression of severe AKI, including stages 2–3 AKI or AKI necessitating kidney replacement therapy (AKI-KRT), exacerbates these outcomes further [4, 5]. Therefore, there exists a pressing need to identify patients at risk of progressive AKI early in their postoperative course, enabling the implementation of preventive strategies and improvement of patient outcomes.

Syndecan-1 (SDC-1) has been identified as a potential biomarker for endothelial injury and AKI development. Previous studies have demonstrated SDC-1's predictive role in general populations undergoing cardiac surgery, emphasizing its association with an increased risk of postoperative AKI [6–8]. Our previous research further underscored the significance of SDC-1 in the context of fluid overload and AKI progression following adult cardiac surgery, demonstrating a crucial link between elevated SDC-1 levels and adverse kidney outcomes [9]. Our previous animal experiments also found that the level of SDC-1 in the kidney increased when AKI was induced by ischemia-reperfusion injury in CKD rat models crafted with aristolochic acid [10]. Unlike prior studies, we explored a more targeted patient demographic, providing a refined understanding of SDC-1's predictive capacity.

Given the considerable global burden of cardiac surgeries and the critical role of preventing severe AKI in this patient cohort, our study was predicated on the assumption that elevated postoperative SDC-1 levels are indicative of progressive AKI, particularly stages 2–3 AKI or AKI requiring kidney replacement therapy, following cardiac surgery. This hypothesis extended from the established role of SDC-1 as a marker of endothelial damage. We seek to elucidate the relationship between postoperative SDC-1 levels and the AKI progression, and AKI necessitating KRT, in patients who have developed AKI following cardiac surgery. Consequently, our research objectives were to validate the predictive value of postoperative SDC-1 levels for progressive AKI and AKI-KRT in a specific cohort of adult cardiac surgery patients. By doing so, we aimed to offer valuable insights that could facilitate earlier identification and intervention for those at greatest risk, thereby enhancing postoperative patient care and outcomes.

Methods

Patients and inclusion/exclusion criteria

This investigation enrolled adult subjects who underwent valve or coronary artery bypass grafting (CABG) operations, or a combination thereof, and who developed AKI (defined and graded based on the Kidney Disease Improvement Global Outcomes (KDIGO) 2012 guidelines [11], with both creatinine and urine output criteria) within 48 h post-operation, from May to September 2021 at our center. Exclusion criteria included individuals under 18, those who underwent kidney replacement therapy prior to surgery, those presenting with preoperative AKI according to KDIGO criteria, those lacking comprehensive medical documentation, those deceased within 48 h post-ICU admission, or those subjected to emergency surgical procedures (Fig. 1). Ethical approval was obtained from the Zhongshan Hospital Ethics Committee, and all eligible participants provided written informed consent.

Study design

In this prospectively designed study, clinical data were gathered from electronic health records, encompassing a broad array of information, including patient demographics, pre-existing health conditions, EuroScore II, laboratory findings (specifically inflammatory cytokine levels), surgical details, CPB duration, APACHE score by admission of ICU, post-surgical medication, urine output, duration of ICU/hospital stays, and mortality. To estimate glomerular filtration rates, the CKD-EPI formula was employed, based on the most recent pre-surgical serum creatinine measurements. Serum creatinine monitoring was conducted daily in the ICU post-surgery, with additional renal function assessments performed initially every three days following ICU discharge and subsequently every other day until discharge.

The primary outcome was defined as cases requiring KRT and progressive AKI, characterized by the deterioration of an existing AKI from stage 1 to stages 2 or 3, or the progression within stages 2 to 3 during hospitalization. Participants were categorized into two groups based on whether they developed AKI necessitating KRT. KRT was initiated when patients with AKI developed life-threatening conditions such as severe hyperkalemia,
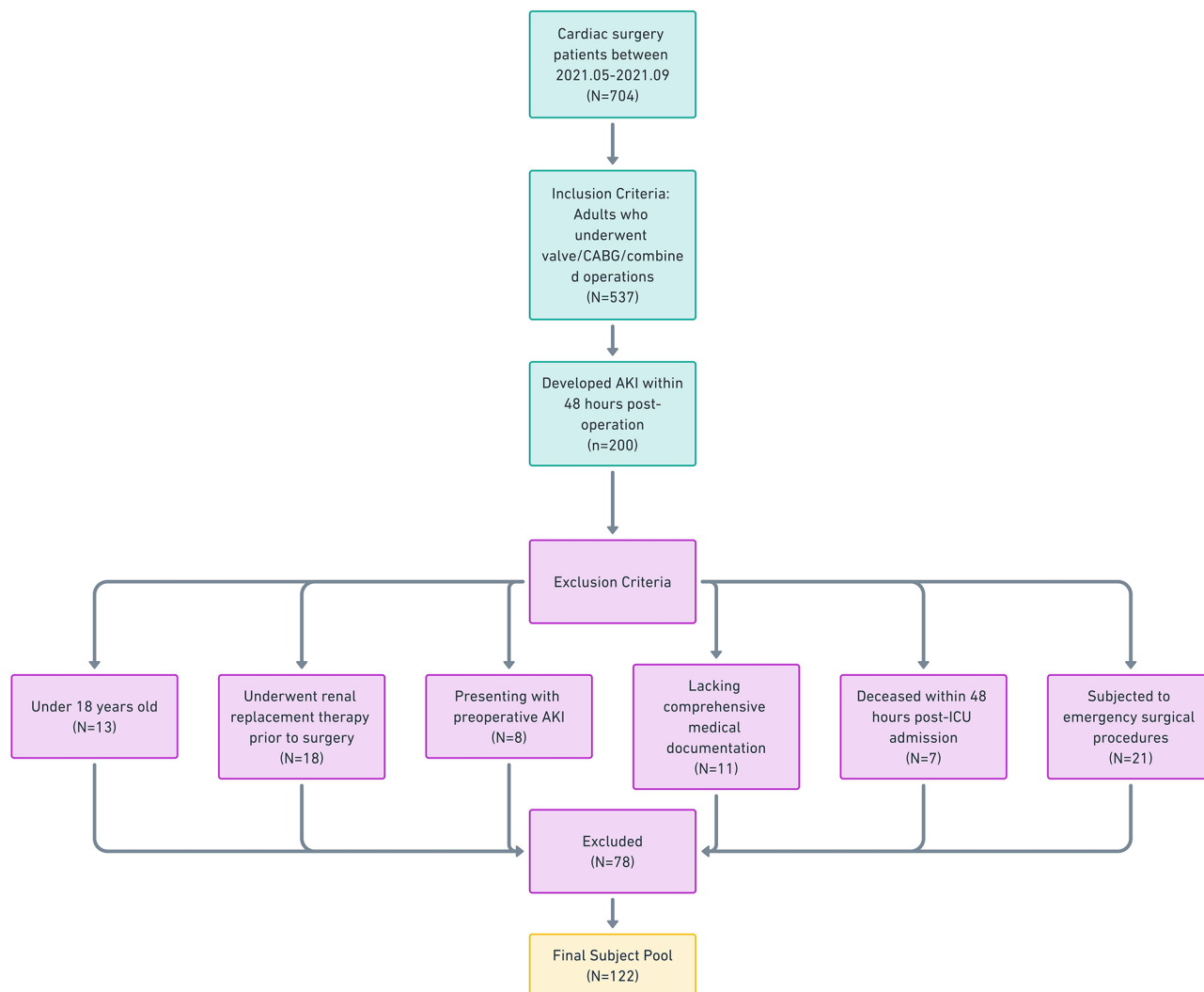
Fig. 1 Study flowchart

metabolic acidosis, or fluid overload impacting other organ functions, or when serum creatine levels elevated drastically, indicating a severe decline in kidney function. The ST150®-polyacrylonitrile filter with the Prismaflex was used to perform KRT. The secondary outcome was the duration of ICU/hospital stay.

Biomarker analysis

For AKI patients, blood samples were collected at the time of AKI diagnosis to analyze SDC-1 levels. Samples were centrifuged at 3,000 rpm for 10 min to separate the plasma, subsequently stored at -80 °C. Measurements of serum SDC-1 were conducted within six months post-surgery using sCD138 ELISA kits (Human Syndecan 1, Abcam), in accordance with the provided guidelines [12]. SDC-1, also known as CD138 or soluble CD138 in circulation, was assessed with a detection range of 8–256 ng/mL, ensuring precision as indicated by a 6.2% coefficient of variation.

Statistical analysis

Data analysis was conducted using R, version 4.3.0. Statistical methods distinguished between normally and non-normally distributed data, presenting them respectively as mean±standard deviation and medians with interquartile ranges. The Kolmogorov-Smirnov test was utilized to assess data normality and homogeneity. P values were obtained using the one-way Student t test for comparing groups with normally distributed data and the Mann–Whitney nonparametric test for other variables in two-group comparisons. For categorical variables, comparisons were made using Fisher's exact test or the chi-squared test. The correlation between hospital/ICU stay and syndecan-1 was assessed using linear regression. The predictive value of the biomarkers for primary outcomes

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were presented and compared with the area under the receiver operator characteristic curve. The optimal cutoff values for SDC-1 in predicting the primary outcome were determined by maximizing the Youden index. Univariate logistic regression was employed to identify potential risk factors for outcomes, while multivariate stepwise forward selection was used to focus on variables significantly associated with outcomes, maintaining a significance level of $p < 0.05$. Odds ratios (OR) of predictors were calculated with 95% confidence intervals (CI).

Results

In our study, 122 eligible patients were evaluated to investigate predictive markers for progressive AKI and AKI-KRT. Of these, 38 patients (31.1%) developed progressive AKI. 15 patients (12.3%) required kidney replacement therapy, representing a significant incidence of this outcome. The overall in-hospital mortality rate was 9.9%, underscoring the severity of this syndrome. A comparative analysis of patients requiring KRT ($n=15$) and those not requiring KRT ($n=107$) revealed significant differences in various preoperative and postoperative characteristics. The KRT group had significantly higher Euroscore II (6.40±2.75 vs. 3.93±2.14) and APACHE II score (21.43±6.58 vs. 10.47±5.15). Significant differences were observed in surgical procedures, with a higher incidence of combined valve and coronary artery bypass grafting surgeries in the KRT group (60.0% vs. 14.0%) and extended cardiopulmonary bypass (CPB) durations in the KRT group (201.60±99.00 min vs. 123.31±44.58 min). Additionally, the hospital stay was significantly longer for patients requiring KRT, with a median duration of 20 days (IQR 16.50–26.50 days) compared to 13 days (IQR 10.00–16.00 days) for those not requiring KRT. (refer to Table 1)

Postoperative indices demonstrated significant differences, with serum SDC-1 levels significantly elevated in patients undergoing KRT, measured at 277.34 ng/mL (interquartile range [IQR] 252.34–380.37 ng/mL), compared to 70.29 ng/mL (IQR 41.01–137.75 ng/mL) in those not requiring KRT, $p < 0.001$. IL-6 and IL-8 levels were significantly higher in the KRT group, at 275.00 pg/mL (IQR 179.50–319.14 pg/mL) for IL-6 and 55.22 pg/mL (IQR 38.00–116.36 pg/mL) for IL-8, indicating enhanced inflammatory responses, compared to 146.00 pg/mL (IQR 89.35–257.10 pg/mL) for IL-6 and 21.00 pg/mL (IQR 12.91–34.75 pg/mL) for IL-8 in the non-KRT group. Procalcitonin (PCT) levels followed this trend, significantly elevated at 8.25 ng/mL (IQR 3.71–12.98 ng/mL) in the KRT group compared to 1.31 ng/mL (IQR 0.63–3.83 ng/mL) in the non-KRT group. (refer to Table 1)

Data from Table 2 indicated that serum SDC-1 levels significantly predict AKI-KRT, demonstrated by odds ratio (OR) of 1.010 (95% CI: 1.005 ~ 1.014) in univariate

and OR of 1.011 (95% CI: 1.003 ~ 1.020) in multivariate analyses. Similarly, Table 3 demonstrated that serum SDC-1 levels predict progressive AKI, with OR of 1.004 (95% CI: 1.001 to 1.007) in univariate and OR of 1.006 (95% CI: 1.002 ~ 1.010) in multivariate analyses. Furthermore, cytokine Interleukin 6 (IL-6) was identified as a significant predictor for progressive AKI, with ORs of 1.05 (95% CI: 1.001 to 1.010) in both univariate and multivariate analyses.

Figure 2 focused on the prediction of AKI-KRT. Serum SDC-1 significantly excelled with an AUROC of 0.892, indicating excellent predictive accuracy. The optimal cutoff point for SDC-1 was determined to be 187 ng/mL, with a sensitivity of 86.7% and a specificity of 79%. IL-6 and IL-8 also demonstrated good predictive capabilities, with AUROCs of 0.700 and 0.731, respectively. PCT's predictive performance was markedly improved in this context, with an AUROC of 0.724. TNF-α's AUROC, at 0.392, remained low, suggesting limited utility in predicting AKI-KRT.

Figure 3 demonstrated the predictive accuracy for progressive AKI, with serum SDC-1 achieving an AUROC of 0.73, showcasing good predictive ability. SDC-1=67.28ng/mL was the best cut-off point, with a sensitivity of 78.9%, a specificity of 51.2%. IL6 followed closely with an AUROC of 0.711. IL8 and PCT displayed moderate predictive capabilities with AUROCs of 0.609 and 0.649, respectively, while TNF-α had a low AUROC of 0.450, indicating poor predictive performance. These visual analyses highlighted the superior predictive value of serum SDC-1 for both progressive AKI and AKI-KRT, demonstrating varying degrees of effectiveness among the other cytokines.

Serum SDC-1 (β=0.014, $p=0.022$), IL-6 (β=0.012, $p=0.011$), and cardiopulmonary bypass (CPB) duration (β=0.03, $p=0.048$) were identified as significant factors associated with the duration of hospital stays (refer to Table 4). Conversely, serum SDC-1 (β=0.013, $p < 0.001$), EuroScore II (β=0.59, $p=0.004$), age (β=-0.09, $p=0.028$), and albumin levels (β=-0.25, $p=0.014$) were identified as variables associated with the length of ICU stays (refer to Table 5).

Discussion

Our study revealed that Syndecan-1 levels significantly predict severe acute kidney injury and its prognosis following cardiac surgery. This research underscored the crucial role of endothelial damage in the pathogenesis of post-surgical AKI, demonstrating SDC-1's superior predictive value over traditional inflammatory markers. These insights contributed to a broader understanding of AKI mechanisms and advocate for the integration of SDC-1 monitoring in postoperative care, enhancing early detection and intervention strategies and potentially

Table 1 Perioperative characteristics of the Study Population

Characteristics	Total (*n* = 122)	No-KRT (*n* = 107)	KRT (*n* = 15)	*p*
Demographic data				
Male (%)	95 (77.87)	81 (75.70)	14 (93.33)	0.227
Age (years)	61.48 ± 11.76	61.92 ± 11.38	58.40 ± 14.28	0.280
BMI (kg/m2)	24.26 ± 3.61	24.45 ± 3.54	22.87 ± 3.96	0.111
Preoperative context				
Hypertension (%)	63 (51.64)	53 (49.53)	10 (66.67)	0.214
DM (%)	17 (13.93)	16 (14.95)	1 (6.67)	0.638
LVEF (%)	61.00 (55.25–65.00)	61.00 (55.50–65.00)	61.00 (55.00–67.00)	0.656
EuroScore II	4.23 ± 2.36	3.93 ± 2.14	6.40 ± 2.75	< 0.001
Baseline laboratory indices				
Hemoglobin (g/L)	127.13 ± 24.01	125.58 ± 23.87	138.20 ± 22.80	0.056
Albumin (g/L)	39.68 ± 4.27	39.57 ± 4.19	40.47 ± 4.93	0.449
eGFR (mL/min/1.73m^2)	71.55 ± 20.10	72.22 ± 19.96	66.73 ± 21.09	0.324
Uric acid (μmol/L)	420.30 ± 122.94	424.04 ± 120.66	393.60 ± 139.73	0.371
Surgery				
Sole Valve (%)	82 (67.2)	77 (72.5)	5 (33.3)	0.002
Sole CABG (%)	16 (13.1)	15 (14)	1 (6.7)	0.429
Valve & CABG (%)	24 (19.7)	15 (14)	9 (60.0)	< 0.001
CPB duration (mins)	134.19 ± 61.08	123.31 ± 44.58	201.60 ± 99.00	0.009
Aortic clamping time (mins)	78.46 ± 32.74	74.46 ± 26.76	108.75 ± 54.32	0.053
Postoperative indices				
APACHE II Score	11.75 ± 6.37	10.47 ± 5.15	21.43 ± 6.58	< 0.001
Serum SDC1 (ng/mL)	81.03 (43.34–216.42)	70.29 (41.01–137.75)	277.34 (252.34–380.37)	< 0.001
IL-6 (pg/mL)	152.50 (94.75–274.50)	146.00 (89.35–257.10)	275.00 (179.50–319.14)	0.023
IL-8 (pg/mL)	23.50 (14.00–37.85)	21.00 (12.91–34.75)	55.22 (38.00–116.36)	< 0.001
TNF-α (pg/mL)	10.20 (6.92–14.15)	10.20 (6.70–14.50)	9.70 (7.29–10.70)	0.413
PCT (ng/mL)	1.38 (0.75–5.01)	1.31 (0.63–3.83)	8.25 (3.71–12.98)	< 0.001
Prognosis				
In-hospital mortality (%)	12 (9.9)	10 (9.4)	2 (13.3)	0.644
Length of ICU stay (days)	3.35 (1.83–5.80)	3.10 (1.80–5.30)	4.00 (2.50–17.65)	0.100
Length of hospital stay (days)	13.00 (10.25–17.00)	13.00 (10.00–16.00)	20.00 (16.50–26.50)	< 0.001

AKI: Acute kidney injury; APACHE: Acute Physiology, Age, Chronic Health Evaluation; BMI: Body mass index; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; DM: Diabetes mellitus; eGFR: Estimated glomerular filtration rate, calculated by CKD-EPI formulae; ICU: Intensive care unit; KRT: kidney replacement therapy; LVEF: Left ventricular ejection fraction; PCT: Procalcitonin; TNF: Tumor necrosis factor

The values are expressed as the median (IQR) and mean ± SD or number (%)

P- values are the results of unpaired t-test or Mann–Whitney U test for continuous variables, and χ2 test or Fisher's exact test for categorical variables

improving patient outcomes in the cardiac surgery population.

Our analysis aligns with prior research on SDC-1's predictive value for AKI but extends the understanding to adult cardiac surgery patients, highlighting its specificity and reliability beyond established literature. While previous research has established SDC-1 as a marker of endothelial injury and its potential in AKI prediction [6–8, 13, 14], our findings further delineate its specificity and reliability post-cardiac surgery. Previous studies on SDC-1 and AKI have primarily focused on pediatric cardiac surgery patients [7]. In contrast, our study encompasses adult cardiac surgery patients, covering not only coronary artery bypass but also valve surgeries, particularly those requiring cardiopulmonary bypass. Our methodology, encompassing a comprehensive analysis of SDC-1 levels alongside traditional inflammatory markers, provided a novel comparative perspective previously underexplored. The outcomes of our study, especially the superior predictive value of SDC-1 for progressive AKI and AKI-KRT, underscored the importance of endothelial damage in AKI pathogenesis, suggesting a unique injury pathway in cardiac surgery patients less prevalent in broader AKI research.

Elevated SDC-1 levels' link to severe AKI underscores the pivotal role of endothelial damage in AKI's pathogenesis, reflecting the early and critical events leading to renal complications post-surgery [14]. SDC-1, indicative of endothelial glycocalyx integrity, increases in response to endothelial injury, a critical early event in AKI pathogenesis. This damage facilitates inflammation, enhances vascular permeability, and disrupts renal microcirculation, contributing to kidney injury [15]. The cardiopulmonary bypass process, common in cardiac surgeries,

Table 2 Logistic regression of risk factors for AKI-KRT

	Univariate analysis			Multivariate analysis		
	OR	95%CI	p value	OR	95%CI	p value
Gender	4.49	0.56~35.81	0.156			
Age	0.98	0.94~1.02	0.281			
Hypertension	2.04	0.65~6.36	0.220			
Diabetes Mellitus	0.41	0.05~3.31	0.400			
EUROScore II	1.50	1.19~1.88	<0.001	1.76	1.13~2.73	0.012
Baseline laboratory indices						
Hemoglobin (g/L)	1.03	1.00~1.05	0.059			
eGFR (mL/min/1.73m2)	0.99	0.96~1.01	0.322			
Albumin (g/L)	1.05	0.92~1.20	0.446			
Surgery type						
CABG		1.00 (Reference)				
Valve	0.97	0.11–8.94	0.981			
Valve & CABG	4.49	0.56–35.81	0.996			
CPB duration	1.02	1.01~1.03	<0.001	1.01	0.99~1.02	0.265
Aortic clamping time	1.03	1.01~1.05	0.002	1.02	0.99~1.05	0.125
Postoperative indices						
APACHE II Score	1.33	1.17~1.50	<0.001	1.36	1.07~1.72	0.011
Serum SDC1	1.010	1.005~1.014	<0.001	1.011	1.003~1.020	0.008
IL6	1.00	1.00~1.01	0.125			
IL8	1.01	1.01~1.02	0.006	1.01	0.99~1.03	0.215
TNFa	0.95	0.84~1.07	0.375			
PCT	1.01	0.99~1.03	0.181			

AKI: Acute kidney injury; APACHE: Acute Physiology, Age, Chronic Health Evaluation; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate, calculated by CKD-EPI formulae; KRT: kidney replacement therapy; LVEF: Left ventricular ejection fraction; PCT: Procalcitonin; TNF: Tumor necrosis factor

Table 3 Logistic regression of risk factors for Progressive AKI

	Univariate analysis			Multivariate analysis		
	OR	95%CI	p value	OR	95%CI	p value
Gender	0.88	0.35~2.19	0.781			
Age	1.00	0.96~1.03	0.798			
Hypertension						
Diabetes Mellitus						
EUROScore II	1.32	1.11~1.57	0.002	1.34	1.05~1.70	0.02
Baseline laboratory indices						
Hemoglobin (g/L)	1.00	0.99~1.02	0.557			
eGFR (mL/min/1.73m^2)	0.99	0.97~1.01	0.268			
Albumin (g/L)	1.10	0.99~1.21	0.069	1.14	0.98~1.32	0.10
Surgery type						
CABG		1.00 (Reference)				
Valve	0.97	0.11–8.94	0.981			
Valve & CABG	4.49	0.56–35.81	0.996			
CPB duration	1.010	1.002~1.017	0.011	1.01	1.001~1.020	0.137
Aortic clamping time	1.016	1.002~1.029	0.02	1.015	0.98~1.03	0.282
Postoperative indices						
APACHE II Score	1.15	1.07~1.24	<0.001	1.14	1.02~1.26	0.017
Serum SDC1	1.004	1.001~1.007	0.005	1.006	1.002~1.100	0.045
IL6	1.01	1.01~1.01	0.016	1.005	1.001~1.010	0.008
IL8	1.01	1.01~1.02	0.046			
TNFa	0.98	0.92~1.04	0.415			
PCT	1.00	0.99~1.02	0.630			

AKI: Acute kidney injury; APACHE: Acute Physiology, Age, Chronic Health Evaluation; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate, calculated by CKD-EPI formulae; LVEF: Left ventricular ejection fraction; PCT: Procalcitonin; TNF: Tumor necrosis factor
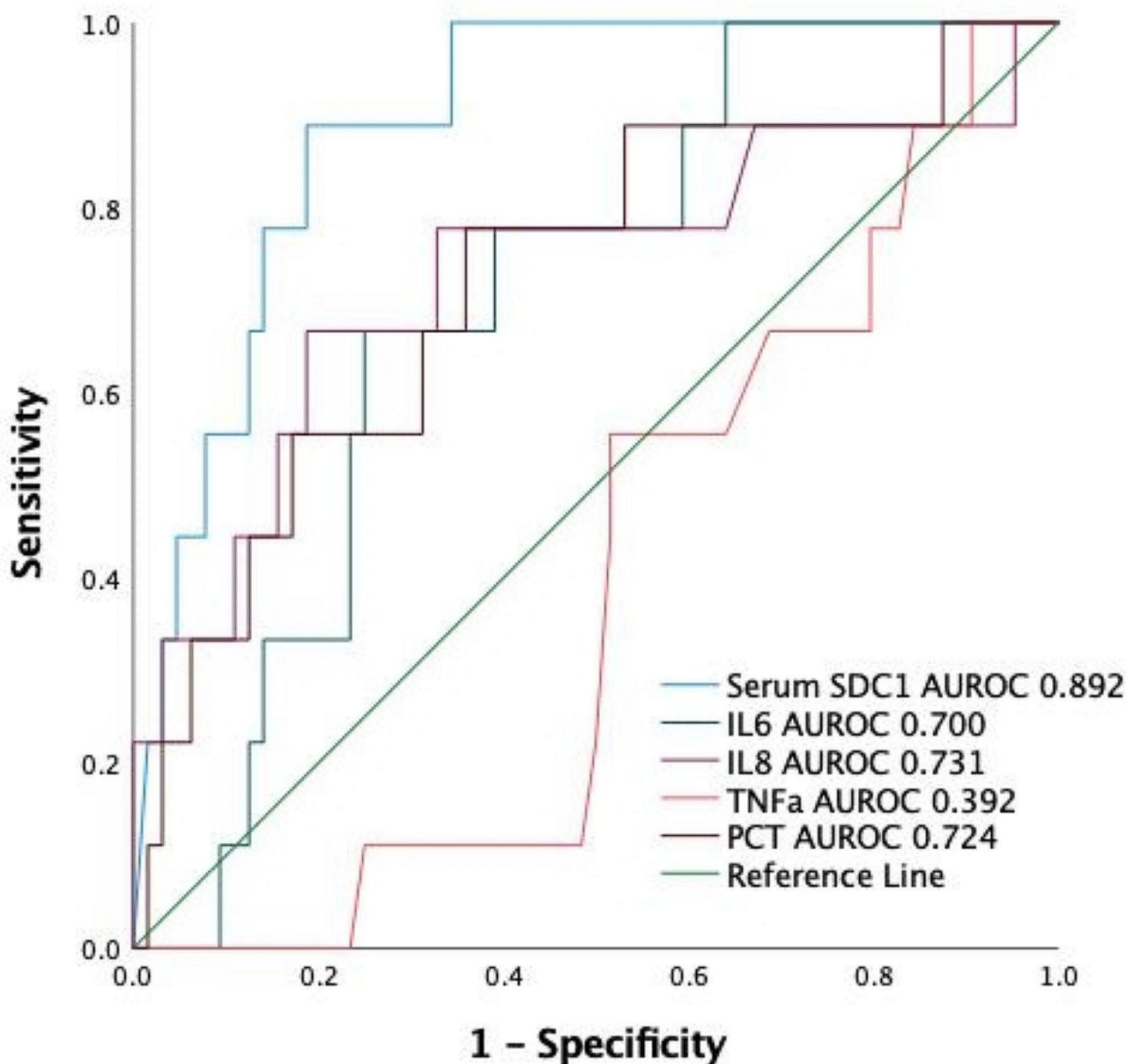
Fig. 2 Receiver operating characteristic curve of biomarkers for predicting acute kidney injury necessitating kidney replacement therapy

contributes to systemic inflammation [16] and endothelial dysfunction [17, 18]. This may result in shedding of endothelial glycocalyx components, such as Syndecan-1, into the bloodstream, indicating vascular damage potentially leading to complications like AKI [15]. Furthermore, SDC-1 may interact with other molecular markers, including inflammatory cytokines and coagulation markers [19, 20], exacerbating endothelial dysfunction and AKI severity. Understanding these interactions is crucial to developing targeted therapies to mitigate AKI progression post-cardiac surgery.

By incorporating inflammatory cytokines, we enhanced the comprehensive understanding of inflammatory processes and endothelial injury mechanisms contributing to AKI post-cardiac surgery. This approach enhanced the predictive framework for AKI, offering deeper insights into patient-specific risk factors and potential therapeutic targets, thus broadening the scope of AKI management strategies in the clinical setting.

Our comparison between SDC-1 and cytokines elucidates different aspects of AKI risk, suggesting SDC-1's superior predictive value could lead to more effective early interventions in post-surgical AKI. While SDC-1 directly reflected
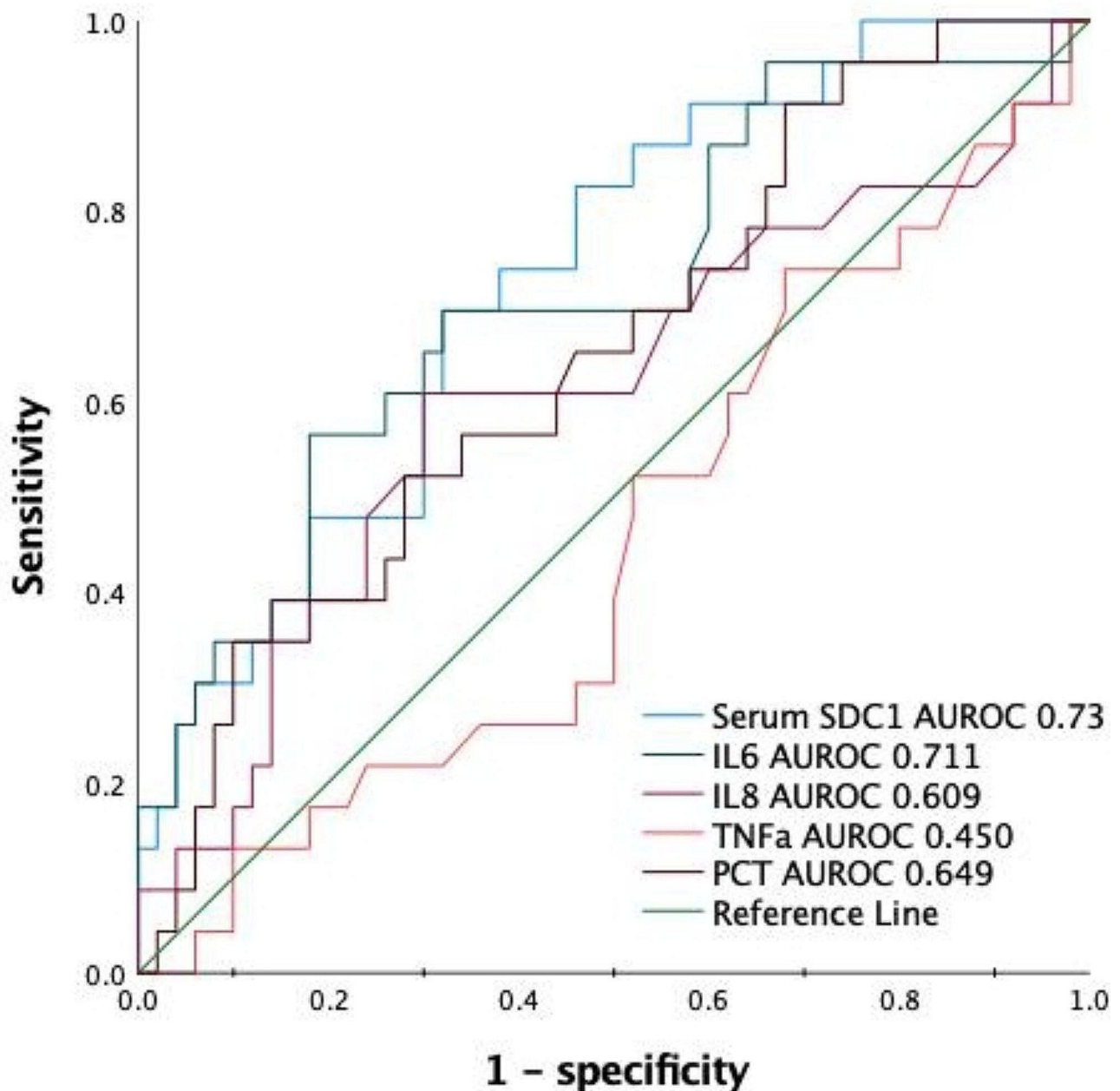
Fig. 3 Receiver operating characteristic curve of biomarkers for predicting progressive acute kidney injury

endothelial injury, cytokines indicate generalized inflammation. This comparison could delineate specific versus systemic responses to surgical stress, thus enhancing AKI prediction accuracy. The merit lied in the potential to identify a more reliable biomarker for early intervention, thereby improving patient outcomes by more effectively targeting the underlying mechanisms of AKI. SDC-1 may offer superior predictive value over traditional inflammatory markers due to its direct involvement in endothelial injury [21], a critical early event in AKI pathogenesis. Unlike inflammatory markers that indicates a general response to injury or

infection, SDC-1 specifically reflects the endothelial glycocalyx condition, providing a more direct assessment of endothelial health and AKI potential. Studies comparing AKI biomarkers have highlighted endothelial damage's role in AKI development, suggesting that markers like SDC-1, closely related to endothelial integrity, might provide earlier and more specific predictive capabilities for AKI after cardiac surgery [6–9, 13].

Our findings indicated that elevated SDC-1 levels are associated not only with the incidence and severity of AKI but also with prolonged ICU and hospital stays. This

Table 4 Linear regression of risk factors for length of hospitalization

	Univariate analysis			Multivariate analysis		
	β	95%CI	p value	β	95%CI	p value
Gender	-1.93	-5.14~1.29	0.243			
Age	-0.07	-0.18~0.05	0.247			
Hypertension	-0.84	-3.52~1.84	0.541			
Diabetes Mellitus	-1.28	-5.15~2.59	0.518			
EUROScore II	0.51	-0.06~1.07	0.081			
Baseline laboratory indices						
Hemoglobin (g/L)	0.03	-0.02~0.09	0.260			
eGFR (mL/min/1.73m2)	0.03	-0.04~0.10	0.402			
Albumin (g/L)	0.04	-0.27~0.36	0.790			
Surgery type						
CABG		0.00 (Reference)				
Valve	-1.84	-5.85~2.18	0.372			
Valve & CABG	1.02	-3.72~5.76	0.674			
CPB duration	0.04	0.02~0.06	0.001	0.03	0.01~0.06	0.048
Postoperative indices						
APACHE II Score	0.16	-0.05~0.37	0.137			
Serum SDC1	0.02	0.01~0.03	<0.001	0.014	0.010~0.027	0.022
IL6	0.01	0.01~0.02	0.022	0.012	0.012~0.029	0.011
TNFa	0.00	-0.06~0.07	0.896			
PCT	0.07	0.01~0.14	0.045	0.04	-0.03~0.11	0.290

AKI: Acute kidney injury; APACHE: Acute Physiology, Age, Chronic Health Evaluation; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate, calculated by CKD-EPI formulae; PCT: Procalcitonin; TNF: Tumor necrosis factor

Table 5 Linear regression of risk factors for length of ICU

	Univariate analysis			Multivariate analysis		
	β	95%CI	p value	β	95%CI	p value
Gender	1.07	-1.31~3.46	0.380			
Age	-0.07	-0.18~0.05	0.094	-0.09	-0.16~-0.01	0.028
Hypertension	0.20	-1.78~2.19	0.841			
Diabetes Mellitus	0.72	-2.15~3.59	0.623			
EUROScore II	0.73	0.33~1.14	<0.001	0.59	0.20~0.98	0.004
Baseline laboratory indices						
Hemoglobin (g/L)	0.0	-0.04~0.04	0.882			
eGFR (mL/min/1.73m2)	-0.01	-0.06~0.04	0.693			
Albumin (g/L)	-0.31	-0.53~-0.08	0.009	-0.25	-0.45~-0.06	0.014
Surgery type						
CABG		0.00 (Reference)				
Valve	-3.76	-6.66~-0.87	0.012	-4.03	-8.53~0.48	0.083
Valve & CABG	-0.79	-4.20~2.63	0.653	-2.68	-7.60~2.25	0.289
CPB duration	0.02	0.01~0.04	0.023	0.01	-0.01~0.02	0.525
Postoperative indices						
APACHE II Score	0.22	0.07~0.37	0.006	0.18	-0.02~0.26	0.427
Serum SDC1	0.02	0.01~0.03	<0.001	0.013	0.007~0.019	<0.001
IL6	0.00	-0.01~0.01	0.689			
TNFa	0.01	-0.03~0.05	0.652			
PCT	0.04	-0.01~0.09	0.146			

AKI: Acute kidney injury; APACHE: Acute Physiology, Age, Chronic Health Evaluation; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate, calculated by CKD-EPI formulae; PCT: Procalcitonin; TNF: Tumor necrosis factor

association underscored the broader impact of endothelial injury, as indicated by SDC-1 levels, on patient recovery and healthcare resource utilization, highlighting the need for early detection and intervention strategies to mitigate adverse outcomes associated with cardiac surgery-associated AKI.

The study evaluated 122 eligible patients. To ascertain the adequacy of this sample size, a power analysis was

conducted prior to the study. Assuming an expected effect size derived from preliminary studies or literature, we aimed for an 80% power to detect significant differences with a two-sided alpha of 0.05. Based on these parameters, our power analysis indicated that a sample size of 122 patients is sufficient to detect the expected effect size regarding the primary outcome of severe AKI incidence post-cardiac surgery. This ensures that our study had the necessary statistical power to test our primary hypothesis effectively.

While our study provides valuable insights, its single-center nature and limited sample size call for further validation across different populations and clinical settings to ensure broader applicability. These limitations implied that our results may not fully represent the broader population undergoing cardiac surgery. Future research should concentrate on multi-center studies to validate our findings across diverse patient demographics and clinical practices. Longitudinal analyses of SDC-1 levels over time would provide insights into their dynamics relative to AKI progression. It is worth noting that our study did not include common AKI biomarkers because our aim was to ascertain the association between SDC-1 and severe AKI, thereby laying the groundwork for future exploration of the mechanisms of AKI onset and progression from the perspective of endothelial damage. Furthermore, investigating interventions for patients identified as high-risk based on SDC-1 levels could inform targeted strategies to mitigate severe AKI outcomes.

Conclusions

Our study underscored the significance of SDC-1 as a biomarker for early intervention in post-cardiac surgery AKI, highlighting its potential to enhance clinical outcomes through timely and targeted strategies. By demonstrating SDC-1's superior predictive value for AKI severity, our findings pave the way for research focused on integrating SDC-1 monitoring into clinical practice and exploring interventions for high-risk patients. This approach could significantly improve postoperative care and patient prognosis, marking a promising direction for clinical practice and research in managing AKI following cardiac surgery.

Abbreviations

AKI	Acute Kidney Injury
AKI	KRT-Acute Kidney Injury requiring kidney replacement therapy
AUROC	Area Under the Receiver Operator Characteristic curve
CABG	Coronary Artery Bypass Grafting
CKD	Chronic Kidney Disease
CPB	Cardiopulmonary Bypass
ICU	Intensive Care Unit
IL	6-Interleukin 6
IL	8-Interleukin 8
IQR	Interquartile Range
KDIGO	Kidney Disease Improving Global Outcomes
OR	Odds Ratio
PCT	Procalcitonin
KRT	Kidney replacement therapy
SDC	1-Syndecan-1
TNF	α-Tumor Necrosis Factor alpha

Declarations

Ethics approval and consent to participate
This study was approved by the ethical board from Zhongshan Hospital, Fudan University (Approval Number B2021–873R). All eligible participants provided written informed consent. The study was conducted in accordance with the Helsinki Declaration (WMA Declaration of Helsinki, 2013).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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