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Effect of a KDIGO-Guideline–Based Preventive Bundle on Acute Kidney Injury After Cardiac Surgery in High-Risk Patients: A Randomized Controlled Trial.

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Abstract

Background: Acute kidney injury (AKI) is a frequent and serious complication after cardiac surgery, associated with increased morbidity, mortality, and longer hospital stays. Despite various preventive strategies, no intervention has consistently reduced cardiac surgery–associated AKI (CSA-AKI). The KDIGO guidelines recommend supportive care bundles for high-risk patients, but their clinical effectiveness remains uncertain. This randomized controlled trial evaluated whether a KDIGO guideline–based supportive care bundle in biomarker-identified high-risk patients undergoing cardiac surgery reduces the incidence and severity of postoperative AKI.

Methodology: In this single-center randomized clinical trial, adult patients undergoing cardiac surgery with cardiopulmonary bypass were screened for AKI risk using urinary biomarkers TIMP-2 and IGFBP7. Patients with urinary [TIMP-2]·[IGFBP7] ≥ 0.3 were classified as high risk and randomized to receive either standard postoperative care or a KDIGO guideline–based preventive bundle, including hemodynamic optimization, avoidance of nephrotoxic drugs, strict glycemic control, and close renal monitoring. The primary outcome was AKI incidence within 72 hours post-surgery based on KDIGO criteria. Secondary outcomes included AKI severity, need for renal replacement therapy, ICU and hospital length of stay, persistent renal dysfunction, and mortality at 30, 60, and 90 days.

Results: A total of 86 patients were randomized equally between intervention and control groups. The incidence of AKI within 72 hours did not differ significantly (15/43 vs 17/43; OR 0.82, 95% CI 0.34–1.97; p = 0.824). The KDIGO bundle improved postoperative hemodynamic parameters, reduced hyperglycemia (p = 0.026), and decreased ACE inhibitor use (p < 0.001), but no significant differences were observed in AKI severity, renal replacement therapy, ICU or hospital stay, or mortality.

Conclusion: Implementation of a KDIGO-guided supportive care bundle did not significantly reduce AKI incidence or severity compared with standard care. Larger multicenter trials are needed to evaluate its impact on long-term renal outcomes and survival.

Keywords

Acute Kidney Injury, Cardiac Surgical Procedures, Cardiopulmonary Bypass, Biomarkers, Randomized Controlled Trial

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Introduction

Acute kidney injury (AKI) is a frequent and serious complication following cardiac surgery and contributes substantially to postoperative morbidity, mortality, and healthcare costs[1]. The incidence of AKI after cardiac surgery varies widely but may occur in up to 30% of patients, depending on patient risk factors and the diagnostic criteria used[2]. Although severe dialysis-dependent AKI occurs less frequently, affecting approximately 1% of cardiac surgery patients, it is associated with extremely poor clinical outcomes and significantly increased mortality[3].

The pathophysiology of cardiac surgery–associated acute kidney injury (CSA-AKI) is complex and multifactorial. Mechanisms such as renal ischemia–reperfusion injury, inflammation, oxidative stress, hemolysis, and exposure to nephrotoxic agents contribute to renal tubular injury during and after surgery[4]. Despite extensive research exploring pharmacological and non-pharmacological strategies to prevent AKI, no single intervention has consistently demonstrated clear clinical benefit[4].

Traditionally, clinical interventions for AKI have been initiated only after changes in renal function markers such as serum creatinine or urine output become evident. However, these markers typically reflect late stages of kidney injury and therefore limit opportunities for early preventive intervention[5,6]. The KDIGO clinical practice guidelines recommend initiating supportive preventive strategies in patients who are identified as being at high risk for AKI. These measures include optimization of intravascular volume and hemodynamics, avoidance of nephrotoxic medications, and maintenance of adequate blood pressure to preserve renal perfusion[7]. Nevertheless, the effectiveness of these strategies in reducing the incidence of AKI has not been conclusively demonstrated[8,9].

Previous studies have explored biomarker-guided strategies for early detection and prevention of AKI[10]. The EARLYARF study was among the first clinical trials to evaluate a biomarker-guided approach for early intervention in AKI; however, the biomarkers used in that study demonstrated limited predictive accuracy and did not significantly improve clinical outcomes[11].

More recently, novel biomarkers such as tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP7) have shown improved predictive ability for identifying patients at high risk of AKI. These biomarkers reflect early renal tubular cell stress and G1 cell cycle arrest, enabling earlier detection of kidney injury before conventional functional markers become abnormal[12]. Previous studies have demonstrated that the combined measurement of [TIMP-2]·[IGFBP7] is a highly accurate predictor of cardiac surgery–associated AKI[13].

Given this background, the present randomized controlled trial was conducted to evaluate whether implementation of a KDIGO guideline–based supportive care bundle in patients identified as high risk for AKI using urinary biomarkers could reduce the incidence and severity of cardiac surgery–associated acute kidney injury. Specifically, this study aimed to determine whether early application of these preventive strategies could improve postoperative renal outcomes in patients undergoing cardiac surgery with cardiopulmonary bypass.

Methodology

Trial Design

This study was designed as a prospective, single-center randomized controlled trial evaluating the effectiveness of implementing a Kidney Disease Improving Global Outcomes (KDIGO) supportive care bundle in patients at high risk of cardiac surgery–associated acute kidney injury (CSA-AKI). The trial compared outcomes between patients receiving the KDIGO bundle intervention and those receiving standard postoperative care following cardiac surgery with cardiopulmonary bypass. The primary objective was to determine whether early implementation of KDIGO-recommended preventive measures in biomarker-identified high-risk patients could reduce the incidence of acute kidney injury within the first 72 hours after surgery.

Secondary objectives included evaluation of AKI severity, renal replacement therapy requirement, persistent renal dysfunction, mortality, and length of hospital and ICU stay[14].

Participants

Adult patients undergoing cardiac surgery using cardiopulmonary bypass (CPB) were screened for eligibility. Participants were considered at high risk for AKI if urinary biomarkers tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP7) measured four hours after discontinuation of CPB were ≥0.3 ng/ml²/1000 using the NephroCheck test. Eligible patients who met this biomarker threshold and provided informed consent were enrolled in the trial. Patients who did not meet inclusion criteria or declined participation were excluded. A total of 140 cardiac surgery candidates were assessed for eligibility, of whom 86 participants fulfilled the criteria and were randomized equally into intervention and control groups (43 participants in each group).

Interventions

Participants randomized to the intervention group received a structured implementation of KDIGO guideline–based preventive strategies, referred to as the "KDIGO cardiac surgery bundle." The bundle included several measures aimed at minimizing renal injury: optimization of hemodynamic status and intravascular volume, avoidance of nephrotoxic medications, discontinuation of angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs) for the first 48 hours after surgery, tight monitoring of serum creatinine and urine output, strict glycemic control to avoid hyperglycemia for the first 72 hours postoperatively, consideration of alternatives to radiocontrast agents, and close hemodynamic monitoring to maintain renal perfusion.

Participants in the control group received standard postoperative care according to institutional protocols. Standard care included maintaining a mean arterial pressure (MAP) greater than 65 mmHg and central venous pressure (CVP) between 8 and 10 mmHg. ACE inhibitors or ARBs were administered when clinically indicated once hemodynamic stability was achieved and hypertension developed. All surgical procedures and perioperative management, including anesthetic protocols and postoperative monitoring, followed the routine standards of care at the participating center.

Outcomes

The primary outcome of the study was the incidence of acute kidney injury within the first 72 hours after cardiac surgery, defined according to the KDIGO diagnostic criteria based on changes in serum creatinine levels and urine output. Secondary outcomes included the severity of AKI within the first 72 hours, requirement for renal replacement therapy during the index hospitalization and at 30-, 60-, and 90-day follow-up, persistent renal dysfunction (defined as an increase in serum creatinine ≥0.5 mg/dL compared with baseline), and major adverse kidney events (MAKE), defined as the composite of mortality, renal replacement therapy requirement, and persistent renal dysfunction at 30, 60, and 90 days. Additional outcomes included duration of ICU stay, total hospital stay, and postoperative complications.

Sample Size

The required sample size was calculated based on an expected incidence of postoperative AKI of approximately 30% among cardiac surgery patients. Using a confidence level of 95% and statistical power of 80%, the Fleiss method with continuity correction was applied. Based on these assumptions, the estimated sample size required to detect a clinically meaningful difference between groups was 86 participants, with 43 participants allocated to each study arm.

Randomization

Participants were randomized using a 1:1 allocation ratio. The randomization sequence was generated by an independent staff member who was not involved in patient enrollment or outcome assessment. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. After confirming eligibility and

obtaining informed consent, the enrolling investigator opened the next envelope in the sequence to assign the participant to either the intervention group (KDIGO bundle) or the control group (standard care).

Blinding

Due to the nature of the intervention, treating clinicians were aware of the assigned treatment strategy. However, clinicians were initially blinded to urinary biomarker results until completion of group allocation. Laboratory analyses and outcome assessments were performed according to predefined criteria to minimize potential bias.

Ethics

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment in the study. Ethical approval for the trial was obtained from the institutional ethics review committee of the participating center. The trial was registered in a clinical trial registry prior to initiation of patient enrollment.

Statistical Methods

Data were analyzed using SPSS version 25. Continuous variables were evaluated for normality using the Shapiro–Wilk test and visual inspection of histograms and Q–Q plots. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using the independent samples t-test. Non-normally distributed continuous variables were summarized as median with interquartile ranges and compared using the Mann–Whitney U test. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square test or Fisher's exact test when expected cell counts were less than five. Effect sizes were expressed as odds ratios with corresponding 95% confidence intervals. All analyses were performed according to the intention-to-treat principle, and a p-value of less than 0.05 was considered statistically significant.

Results

Recruitment

Participant recruitment was conducted between 27 February 2022 and 24 March 2023 among patients scheduled to undergo cardiac surgery with cardiopulmonary bypass. During the screening phase, 140 patients were assessed for eligibility. Of these, 27 patients did not meet the predefined inclusion criteria and were therefore excluded from the study. An additional 27 eligible patients declined participation after being informed about the trial procedures. The remaining 86 patients consented to participate and were randomly allocated in a 1:1 ratio into two groups: the intervention group receiving the KDIGO bundle and the control group receiving standard postoperative care. Each group included 43 participants. The flow of participants through the study stages, including screening, allocation, and follow-up, is presented in the CONSORT flow diagram (Figure 1).

Baseline Data

Baseline demographic, clinical, and intraoperative characteristics of the participants are summarized in Table 1. The two groups were generally comparable at baseline with respect to age, severity of illness scores, renal function, and comorbid conditions. The mean age of participants in the control group was 62.38 ± 11.32 years, compared with 67.10 ± 13.78 years in the intervention group. Baseline renal function parameters, including serum creatinine levels and estimated glomerular filtration rate (eGFR), were similar between groups. Severity of illness was also comparable, with similar APACHE and SOFA scores at enrollment.

The distribution of sex and major comorbidities, including diabetes mellitus, hypertension, chronic kidney disease, and chronic obstructive pulmonary disease, did not differ substantially between the groups. Surgical characteristics such as cardiopulmonary bypass time, cross-clamp duration, and type of cardiac procedure performed (coronary artery bypass grafting, valve surgery, combined procedures, or other cardiac operations) were also comparable.

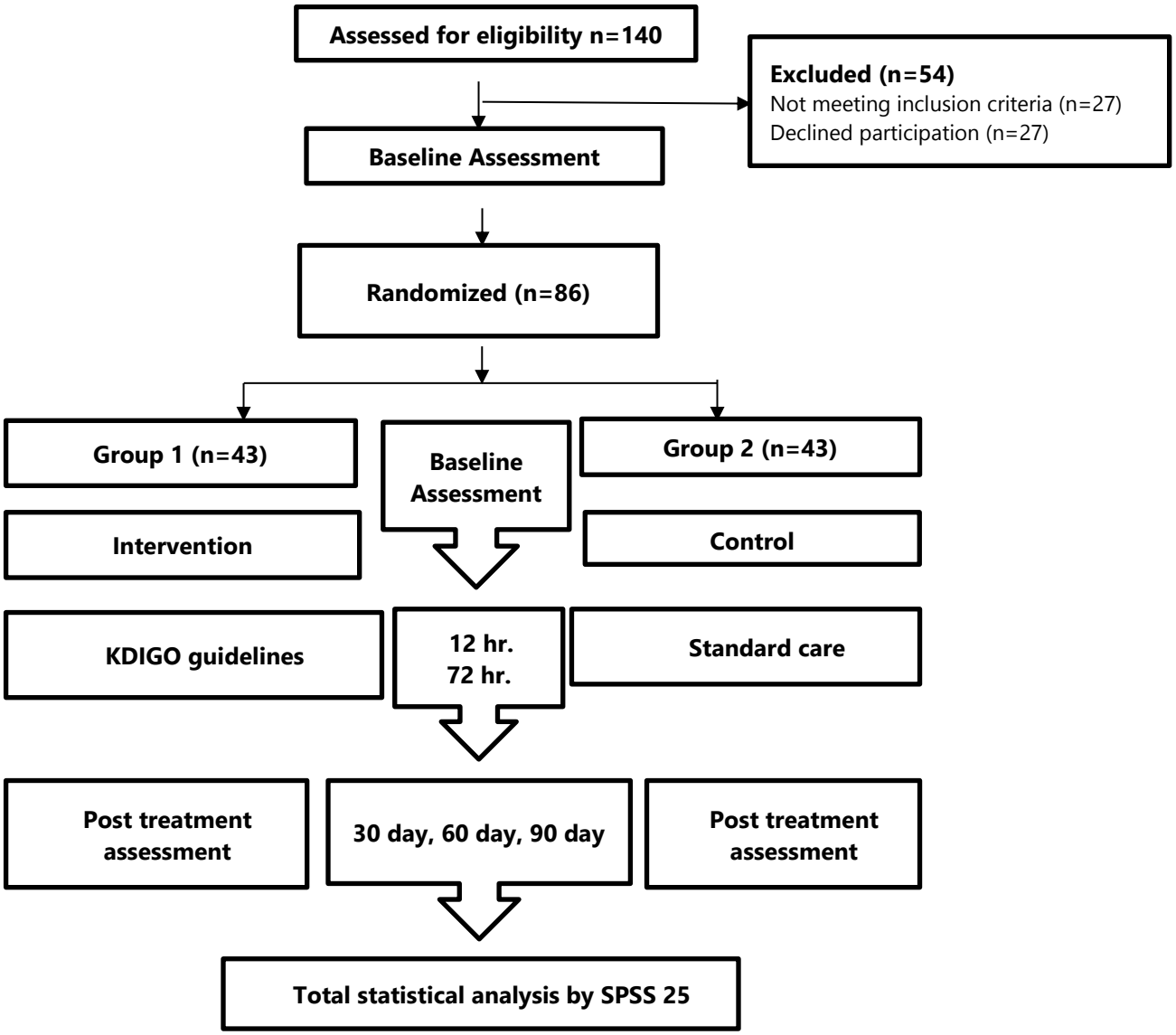

Figure 1: Consort Diagram

Preoperative medications including aspirin, clopidogrel, diuretics, beta-blockers, ACE inhibitors, and statins were used at similar frequencies across the two groups. Baseline urinary biomarker levels of [TIMP-2]·[IGFBP7] were measured in all patients prior to randomization and were slightly higher in the control group compared with the intervention group.

Overall, these findings indicate that the study groups were well balanced with respect to baseline clinical characteristics.

Numbers Analyzed

All randomized participants were included in the final statistical analysis according to the intention-to-treat principle. A total of 86 participants were analyzed, with 43 patients in the intervention group and 43 patients in the control group.

No participants were lost to follow-up during the immediate postoperative period, and outcome assessment was completed for all patients within the primary endpoint period of 72 hours after surgery. Longer-term follow-up outcomes, including persistent renal dysfunction, renal

replacement therapy, and mortality, were evaluated at 30, 60, and 90 days after surgery.

Outcomes and Estimation

The primary outcome of the study was the occurrence of acute kidney injury within the first 72 hours following cardiac surgery according to KDIGO criteria. The overall incidence of AKI among study participants was 37.2%. AKI occurred in 15 of 43 patients (34.9%) in the intervention group and 17 of 43 patients (39.5%) in the control group. The difference between groups was not statistically significant (odds ratio 0.82; 95% confidence interval 0.34–1.97; p = 0.824).

AKI diagnosis was based on serum creatinine criteria in 18 patients and urine output criteria in 16 patients, with two participants meeting both diagnostic criteria. The severity of AKI based on KDIGO staging was also comparable between groups. Stage 1 AKI occurred in 10 patients in the control group and 8 patients in the intervention group, while stage 2 AKI occurred in 9 and 7 patients respectively. Stage 3 AKI was observed in 6 patients in the control group and 4 patients in the intervention group.

Secondary outcomes, including the requirement for renal replacement therapy, length of ICU stay, hospital length of stay, and ventilator support duration, did not differ significantly between the two groups. Renal replacement therapy during the initial hospitalization was required in four patients in each group. Similarly, no significant differences were observed in persistent renal dysfunction or renal replacement therapy requirements during the follow-up period at 30, 60, and 90 days. Mortality rates during follow-up were also comparable between the groups.

During the intervention period, certain physiological parameters differed between the groups. Patients receiving the KDIGO bundle demonstrated improved hemodynamic stability, reflected by higher mean arterial pressure values at several time points. Additionally, the intervention group showed a significantly lower incidence of postoperative hyperglycemia (p = 0.026) and reduced use of ACE inhibitors during the early postoperative period. Biomarker analysis demonstrated that urinary [TIMP-2]·[IGFBP7] levels at 12 hours after randomization were significantly lower in the intervention group compared with the control group (p = 0.003), suggesting a potential reduction in early renal cellular stress.

Ancillary Analyses

Additional analyses examined perioperative physiological and biochemical variables during the intervention period. The use and dosage of catecholamines, including epinephrine, norepinephrine, and dobutamine, were evaluated. While the proportion of patients receiving catecholamines was similar between groups, some differences were observed in dosing patterns during the treatment period. The intervention group also demonstrated improved hemodynamic parameters and tighter glycemic control during the postoperative period. These ancillary findings suggest that implementation of the KDIGO bundle influenced perioperative management strategies and physiologic stability, although these changes did not translate into a statistically significant reduction in the incidence of AKI.

Harms

No significant differences were observed between the intervention and control groups with regard to adverse events related to the intervention. The incidence of postoperative complications, including infections, arrhythmias such as atrial fibrillation, and renal replacement therapy requirements, was similar between the two groups. Rates of severe AKI and other major postoperative complications were also comparable. Overall, implementation of the KDIGO bundle did not appear to increase the risk of adverse clinical outcomes compared with standard care.

Table 1: Baseline Demographic Characteristics.

Variables		Control Group (n=43)	Intervention Group (n=43)	p-value
Age (years); Mean ± SD		62.38 ± 11.32	67.10 ± 13.78	0.087
APACHE score; Mean ± SD		9.09 ± 2.87	9.14 ± 2.87	0.933
Sofa Score; Mean ± SD		6.80 ± 2.44	5.91 ± 2.48	0.097
Creatinine level before surgery (mg/dl); Mean ± SD		0.87 ± 0.24	0.90 ± 0.28	0.653
eGFR (ml/min/m2); Mean ± SD		90.40 ± 42.37	87.7±31.34	0.205
Gender; n(%)	Male	27 (62.8%)	33 (76.7%)	0.240
	Female	16 (37.2%)	10 (23.3%)	
Weight (kg); Mean ± SD		84.34 ± 14.54	87.28 ± 16.55	0.384
ASA Grade; n(%)	1	7 (16.3%)	8 (18.6%)	0.422
	2	11 (25.6%)	5 (11.6%)	
	3	14 (32.6%)	6 (37.2%)	
	4	11 (25.6%	14 (32.6%)	
NYHA Classification; n(%)	I	10 (23.3%)	9 (20.9%)	0.923
	II	8 (18.6%)	10 (23.2%)	
	III	12(27.9%)	13 (30.2%)	
	IV	13(30.2%)	11(25.5%)	
Comorbidities; n (%)	DM	10 (23.3%)	8 (18.6%)	0.792
	HTN	8 (18.6%)	12 (27.9%)	0.444
	COPD	12 (27.9%)	10 (23.3%)	0.805
	CKD	3 (6.9%)	5 (11.6%)	0.713
	MI	5 (11.6%)	3 (6.9%)	0.713
	AF	5 (11.6%)	5 (11.6%)	1.000
Medicines; n(%)	Aspirin	8 (18.6%)	10 (23.3%)	0.792
	Clopidogrel	12 (27.9%)	8 (18.6%)	0.444
	Diuretics	10 (23.3%)	12 (27.9%)	0.805
	Beta blockers	5 (11.6%)	3 (6.9%)	0.713
	ACE inhibitors	3 (6.9%)	5 (11.6%)	0.713
	Statins	5 (11.6%)	5 (11.6%)	1.000
Time of surgery (min); median Q1, Q3	Bypass	80(59.0, 105.5)	77 (58.0, 103.4)	0.002*
	Cross clamp	116(93.0, 153.5)	120(97.0, 156.5)	0.004*
Procedure; n(%)	CABG	13 (30.2%)	10 (23.3%)	0.850
	Valve	9 (20.9%)	8 (18.6%)	
	Combined	10 (23.2%)	12(27.9%)	
	Other	11(25.5%)	13(30.2%)	
Volume Therapy in surgery (ml); median Q1, Q3	Colloids	0	0	0.003
	Crystalloids	2100(2100,2900)	2400(2100-2900)	
	Erythrocyte conc.	0	0	
	Thrombocytes conc.	0	0	

	Fresh plasma	0	0	
	Blood	0	0	
Baseline Urine (TIMP-2).(IGFBP7) (ng/ml2/1000); Median Q1, Q3		0.75 (0.59, 1.00)	0.61 (0.47, 0.75)	0.007*

*p<0.05 is considered statistically significant.

Table 2: During Treatment measures.

Variables		**Control Group (n=43)**	**Intervention Group (n=43)**	**p-value**
Patients receiving catecholamine during treatment; n (%)	Epinephrine	12 (27.9%)	10 (23.2%)	0.805
	Nor epinephrine	23 (53.5%)	24 (55.7%)	1.000
	Dobutamine	8 (18.6%)	9 (20.9%)	1.000
Catecholamine dose during treatment (µg/kg); median (Q1, Q3)	Epinephrine	33.6 (8.3, 48.0)	17.2 (7.5, 33.8)	0.150
	Nor epinephrine	23.7 (9.3, 48.0)	15.5 (7.2, 37.9)	
	Dobutamine	1207.8 (506.6, 1487.6)	1407.9 (507.6, 1487.6)	
Volume Therapy in intervention (ml); median Q1, Q3	Volume total	2855 (1878, 4615)	2475 (1765, 2519)	0.181
	Colloids	2120 (1418, 2210)	2220 (1630, 4250)	
	Crystalloids	0	0	
	Blood	0	0	
	H2O	230 (0, 513)	210 (0, 210)	
MAP (mmHg); mean ±SD	Baseline	73±11	76±13	0.994
	3h	71±11	76±10	
	6h	71±11	74±9	
	9h	70±10	75±8	
	12h	70±11	74±7	
CVP (mmHg); mean ±SD	Baseline	10±6	10±5	0.047
	3h	10±5	11±6	
	6h	10±4	12±6	
	9h	10±4	11±5	
	12h	11±5	11±3	
SvO2 (%); mean ±SD	Baseline	68±8	68±8	0.399
	3h	67±6	70±6	
	6h	66±4	70±9	
	9h	66±7	69±6	
	12h	65±5	69±5	
Relative change Urine (TIMP-2).(IGFBP7) at 12 h/baseline (ng/ml2/1000); median Q1, Q3		1.24 (0.42, 2.43)	1.06 (0.21, 1.88)	0.221
At 12 h Urine (TIMP-2).(IGFBP7) (ng/ml2/1000); median Q1, Q3		0.83 (0.35, 1.57)	0.58 (0.26, 1.20)	0.003*
Artial fibrillation 12h; n (%)		12 (27.9%)	10 (23.2%)	0.805
Infections; n (%)		23 (53.5%)	13 (30.2%)	0.049
Hyperglycemia 72 hr after surgery; n (%)		10 (23.2%)	2 (4.6%)	0.026*
Nephrotoxic agents within 72 hr; n (%)		16 (37.2%)	9 (20.9%)	0.153

*p<0.05 is considered statistically significant.

Table 3: Outcomes after intervention

Variables	Control Group (n=43)	Intervention Group (n=43)	p-value	OR(95% CI)
AKI in 72 hr diagnosis	17 (39.5%)	15 (34.9%)		
On basis of Creatinine	11	7	0.824	0.82 (0.34–1.97)
On basis of urine output	7	9		
Both	1	1		
AKI stage 1 Diagnosis	10(23%)	8(18%)		
On basis of Creatinine	6	3	0.727	-
On basis of urine output	2	2		
Both	2	3		
AKI stage 2 Diagnosis	9(20%)	7(16%)		
On basis of Creatinine	3	4	0.727	-
On basis of urine output	4	2		
Both	2	1		
AKI stage 3 Diagnosis	6(13%)	4(9.3%)		
On basis of Creatinine	3	2	0.727	-
On basis of urine output	5	1		
Both	1	1		
RRT requirement	4 (9.3%)	4 (9.3%)		
In 72 hr	4 (9.3%)	4 (9.3%)	1	1.00 (0.23–4.29)
hospital stay	4 (9.3%)	4 (9.3%)	1	1.00 (0.23–4.29)
PRD				
30th day	3(6.9%)	5(11.6%)	0.713	1.75 (0.39–7.85)
60th day	5(11.6%)	2(4.6%)	0.433	0.37 (0.07–2.03)
90th day	2(4.6%)	3(6.9%)	1.000	1.54 (0.24–9.70)
RRT requirement				
30th day	5(11.6%)	3(6.9%)	0.152	0.57 (0.13–2.55)
60th day	2(4.6%)	5(11.6%)	0.89	2.70 (0.49–14.74)
90th day	3(6.9%)	2(4.6%)	0.789	0.65 (0.10–4.10)
Mortality				
30th day	2(4.6%)	3(6.9%)	0.801	1.54 (0.24–9.70)
60th day	3(6.9%)	2(4.6%)	0.566	0.65 (0.10–4.10)
90th day	3(6.9%)	3(6.9%)	0.119	1.00 (0.19–5.26)
ICU stay days (median Q1, Q3)	3(2,4)	4(3,5)	0.332	-
Hospital stay days (median Q1, Q3)	10(9,18)	10(9,17)	0.556	-
Ventilator support in hr (Q1, Q3)	6(1,10)	7(3,13)	0.661	-
Severe AKI	8 (18.6%)	5 (11.6%)	0.549	0.58 (0.17–1.93)

*p<0.05 is considered statistically significant.

Discussion

In this randomized controlled trial, we evaluated the effectiveness of implementing a Kidney Disease: Improving Global Outcomes (KDIGO) guideline–based supportive care bundle in cardiac surgery patients identified as being at high risk for acute kidney injury (AKI) using urinary biomarkers. The results of this study demonstrate that the

application of the KDIGO bundle did not significantly reduce the incidence of AKI within 72 hours after cardiac surgery compared with standard postoperative care. Although the intervention group showed improvements in several perioperative management parameters, including better hemodynamic control and reduced postoperative hyperglycemia, these improvements did not translate into a statistically significant reduction in the primary clinical outcome.

Early identification of patients at risk for AKI remains a major challenge in perioperative and critical care medicine. Traditionally, AKI diagnosis relies on functional markers such as serum creatinine and urine output; however, these parameters often increase only after significant renal injury has already occurred. As a result, these markers may fail to detect early stages of kidney injury when preventive interventions may still be effective. The concept of "acute kidney stress" has therefore been introduced to emphasize the detection of early cellular responses to renal injury before functional deterioration becomes apparent[15]. This shift toward earlier detection has led to growing interest in biomarker-based approaches for identifying patients at risk of AKI. Biomarker-guided treatment strategies have already been successfully applied in other medical fields, including oncology and cardiology, where early molecular detection allows targeted therapeutic interventions and improved patient outcomes[16–18].

Experts in critical care nephrology have suggested that early identification of high-risk patients may allow clinicians to implement targeted preventive strategies before overt kidney injury develops[19,20]. In this context, urinary biomarkers such as tissue inhibitor of metalloproteinases-2 (TIMP-2) and insulin-like growth factor binding protein-7 (IGFBP7) have emerged as promising tools for the early detection of renal tubular stress. These biomarkers reflect G1 cell-cycle arrest in renal tubular epithelial cells and have been shown to predict the development of AKI in patients undergoing cardiac surgery[21,22]. Their ability to detect early cellular stress provides an opportunity to implement preventive interventions before clinical AKI becomes evident.

Cardiac surgery–associated AKI is a complex and multifactorial condition that involves several pathophysiological mechanisms. These include renal ischemia–reperfusion injury during cardiopulmonary bypass, systemic inflammatory responses triggered by surgical trauma, oxidative stress, hemolysis, microembolization, and exposure to nephrotoxic medications[23,24]. Because multiple mechanisms contribute to renal injury in this setting, it is unlikely that a single pharmacological intervention will be sufficient to prevent AKI in all patients. Consequently, multifactorial preventive strategies such as the KDIGO supportive care bundle have been proposed.

The KDIGO guidelines recommend several supportive measures aimed at minimizing renal injury in patients at increased risk of AKI. These include optimization of intravascular volume status and hemodynamics, maintenance of adequate blood pressure to ensure renal perfusion, avoidance of nephrotoxic agents, and careful monitoring of renal function during the perioperative period[25,26]. In the present study, implementation of these recommendations resulted in improvements in several perioperative management variables. Patients in the intervention group demonstrated improved hemodynamic parameters at multiple postoperative time points, suggesting better cardiovascular stability and potentially improved renal perfusion.

Another important finding of this study was the significant reduction in postoperative hyperglycemia among patients receiving the KDIGO bundle. Hyperglycemia is a common complication after cardiac surgery and has been reported to occur in 33.7–74% of non-diabetic patients undergoing cardiac procedures[27]. Elevated blood glucose levels may exacerbate oxidative stress and inflammatory responses, which can contribute to renal injury. Previous studies have suggested that improved glycemic control may provide renal protective effects in critically ill

patients by reducing inflammatory and metabolic stress responses[28].

Despite these improvements in perioperative management, the overall incidence of AKI remained similar between the intervention and control groups. This observation is consistent with previous studies evaluating preventive strategies for AKI in cardiac surgery patients. Several investigations examining supportive care bundles or goal-directed therapeutic strategies have reported mixed results depending on the patient population, baseline risk factors, and adherence to intervention protocols[29–31]. These findings suggest that although supportive care strategies may improve perioperative management, their impact on clinically defined AKI may be limited.

Cardiac surgery–associated AKI is strongly associated with increased morbidity and mortality as well as long-term renal dysfunction. Observational studies have shown that patients who develop AKI following cardiac surgery have a higher risk of developing chronic kidney disease and other adverse long-term outcomes[32]. However, interpretation of these associations can be challenging because patients who develop AKI often have a greater burden of comorbidities and more severe underlying illness compared with patients who do not develop AKI[33]. These baseline differences may partially explain the relationship between AKI and long-term outcomes.

Several limitations of the present study should be considered. First, this was a single-center study with a relatively small sample size, which may have limited the statistical power to detect modest differences between groups. Although the sample size calculation was based on expected AKI incidence, the relatively low frequency of severe complications may have reduced the ability to identify statistically significant differences in clinical outcomes. Second, most cases of AKI in this study were diagnosed using urine output criteria rather than serum creatinine changes. Although oliguria is included in the KDIGO diagnostic criteria, its clinical relevance in postoperative cardiac surgery patients remains uncertain. Previous studies have suggested that oliguria may sometimes reflect transient hemodynamic changes rather than true structural kidney injury[34,35].

Another important consideration is that several elements of the KDIGO bundle such as optimization of hemodynamics, glycemic control, and avoidance of nephrotoxic medications may already be incorporated into routine postoperative care in many cardiac surgery centers. As a result, the incremental benefit of implementing a formal care bundle may be smaller in settings where high standards of perioperative management already exist. Similar challenges have been observed in other areas of critical care medicine, including sepsis management, where guideline-based care bundles have demonstrated variable effectiveness depending on institutional compliance and baseline clinical practices[36,37].

Despite these limitations, the present study contributes to the growing body of literature evaluating biomarker-guided preventive strategies for AKI in cardiac surgery patients. The findings demonstrate that early identification of high-risk patients using urinary biomarkers is feasible in the perioperative setting and that implementation of guideline-based preventive strategies can influence clinical management. However, larger multicenter trials with greater statistical power will be required to determine whether biomarker-guided preventive approaches can significantly reduce the incidence of AKI and improve long-term renal outcomes in this high-risk patient population.

Conclusion

In this randomized controlled trial, the implementation of a KDIGO guideline–based supportive care bundle in cardiac surgery patients identified as being at high risk for acute kidney injury using urinary biomarkers did not significantly reduce the incidence or severity of AKI within the first 72 hours following surgery when compared with standard postoperative care. Although the intervention was associated with improvements in certain perioperative management parameters, including better hemodynamic stability and reduced postoperative hyperglycemia, these

changes did not translate into significant differences in clinical renal outcomes. Given the multifactorial pathophysiology of cardiac surgery associated AKI, preventive strategies targeting multiple mechanisms may still hold potential for improving outcomes in high-risk patients. However, the findings of this study suggest that implementation of a KDIGO-based care bundle alone may not be sufficient to significantly reduce AKI incidence in this population. Future research involving larger multicenter randomized trials with longer follow-up periods is required to further evaluate the role of biomarker-guided preventive strategies and to determine whether early targeted interventions can improve renal outcomes and long-term prognosis in patients undergoing cardiac surgery.

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