Original Article

Mortality Prediction in Renal Replacement Dependent Acute Kidney Injury Patients After Cardiac Surgery

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ABSTRACT

Objective: This study aims to identify the risk factors and clinical prognostic scores that have a significant predictive value in RRT-dependent AKI patients who developed the disease following cardiac surgery.

Study Design: A cross-sectional, analytical study

Place and Duration of Study: This study was conducted at the Intensive Care Unit in Bakhtawar Amin Trust Teaching Hospital Multan from 1ST September 2020 to 1ST February 2021.

Materials and Methods: A cross-sectional analysis of 35 cardiac surgery patients older than 18 years receiving RRT for treatment of cardiac surgery-related AKI. The Severity scores were recorded and potential risk factors associated with mortality in AKI were evaluated at the start of RRT. Our study defined these severity scores; "Acute Physiology and Chronic Health Evaluation (APACHE) II" as a general score, "Sequential Organ Failure Assessment (SOFA)" as an organ failure score, and "Liano score" as a renal disease severity score. Multivariable logistic regression analysis was also performed to assess the mortality-associated risk factors.

Results: 5 patients (14.2%) died during the hospitalization time. 28.5% continued dialysis even after hospital discharge. The area under curve score was 0.669 for Liano, 0.722 for SOFA and 0.672 for APACHE II. The logistic regression model showed 4 variables associated with patient mortality out of the 16 selected for model selection, "Glasgow coma score < 14 points (OR=3.206,95% Cl;1.020-9.776, P=0.0027) , MAP < 63.5 mmHg (OR = 3.763, 95% CI; 1.11-13.715, P = 0.032), preoperative serum creatinine >108.5 µmol/L (OR = 0.355, 95% CI; 0.234-0.873, P = 0.040), and postoperative platelet count < 115 × 109/L (OR = 3.829, 95% CI; 1.362-11.056, P = 0.020)" significantly affected the mortality of the patients.

Conclusion: Our study observed no relationship between mortality and other factors (demographic, surgical, preoperative, and postoperative variables). The SOFA score is the most reliable to predict the poor outcome at the start of RRT in both groups after 1 month following the cardiac surgery. Glasgow coma score less than 14 points, MAP less than 63.5 mmHg, preoperative serum creatinine greater than 108.5 mmol/L, and postoperative platelet count less than 115 × 109/L affected the mortality rate and were independent risk factors for lethal patient outcome.

Key Words: Acute Kidney Injury, Cardiac Surgery, Renal Replacement Therapy, Cardiac Surgery Outcome, Disease Related Mortality.

Citation of article: Muzammil M. Mortality Prediction in Renal Replacement Dependent Acute Kidney Injury Patients After Cardiac Surgery. Med Forum 2021;32(9):122-126.

INTRODUCTION

Around 2 million people undergo cardiac surgeries annually across the world[1]. Most of these patients face serious complications such as acute kidney injury (AKI) postoperatively[2]. The predisposing factors such as perioperative hemodynamic alterations, pre-existing renal injury, and pharmacological toxins related to cardiovascular surgery are considered as the common causes of AKI[3]. The incidence rate of AKI following a cardiac surgery ranges from 5% to 45% depending upon the cardiac surgery type and the diagnostic criteria for AKI[4]. However, AKI patients requiring dialysis are comparatively low, ranging between 1-6% whereas the overall mortality rate among the cardiac surgery-associated AKI cases could be as high as 19.0%[5]. The mortality is found to be significantly high in more than 50% of dialysis-dependent AKI than other infected patients[6]. Since AKI is associated with raised mortality rate, extended hospital stay, and high post-hospital death rate[7-8] most of the researches has been focusing on the detection of AKI at an early stage and the prediction of the disease[9]. Ineffective renal function in cardiac surgery patients is usually related to multiple organ failure. Therefore, the choice of renal replacement therapy (RRT) is generally made depending upon the progression of the disease and

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Received: May, 2021
Accepted: July, 2021
Printed: September, 2021

associated organ failure. Thus, the treatment for AKI is decided on subjective criteria. Various prognostic tools are available to evaluate the disease progression and risk of the lethal outcome but not one of them is specific for predicting the risk factors among patients who have undergone cardiac surgery, its type and duration as the "General illness severity scores" and "kidney-specific disease severity scores" do not account for these risk factors[10].

This study aims to identify the risk factors and clinical prognostic scores that have a significant predictive value in RRT-dependent AKI patients who developed the disease following cardiac surgery.

MATERIALS AND METHODS

A cross-sectional analysis of 35 cardiac surgery patients, 15 female, and 20 male, aged more than 18 years was conducted from 1ST September 2020 to 1ST February 2021 at Intensive Care Unit in Bakhtawar Amin Trust Teaching Hospital Multan.

All the patients receiving RRT for treatment of cardiac surgery-related AKI were included in the study. Whereas, the patients with preoperative need for RRT, both with renal and non-renal associated requirements for RRT, were excluded from the study. Following clinical indicators directed the need to start dialysis in severe AKI cases: clinical manifestations of uremia, metabolic acidosis, hyperkalemia, hypervolemia, elevated levels of serum urea and creatinine i.e. greater than 30 mmol/L and 600 µmol/L, respectively. The need for slow continuous RRT was predicted through arterial hypotension, hyper-hydration, or/and hyper-catabolism.

We analyzed 16 variables that were divided in four groups of potential risk factors responsible for lethal prognosis: (i) demographics (gender, age); (ii) pre-surgical (serum creatinine and eGFR levels; (iii) surgical data, including cardiopulmonary bypass (CBP) time and cardiac surgery types; and (iv) post-surgical variables, including vasopressors administration, temperature, sepsis, mechanical lung ventilation, mean arterial pressure (MAP), platelet count, oliguria, white blood cell (WBC), Glasgow coma score, serum creatinine level prior to starting the RRT procedures, at the day of initiating RRT.

The Severity scores were recorded at the start of RRT. We utilized the predictive ability of 3 widely used severity scores: “Acute Physiology and Chronic Health Evaluation (APACHE) II" as a general score, "Sequential Organ Failure Assessment (SOFA)" as an organ failure score, and "Liano score” as a renal disease severity score.

The patients with cardiac surgery were diagnosed with AKI if their serum creatinine level was equal to or greater than 26.5 µmol/L after two days or 1.5 fold more than the baseline, in the last week following the surgery. Patients with AKI requiring RRT were diagnosed with AKIN stage 3[11]. Patient survival was characterized as the survival time of one month after heart surgery. In addition, the hospital mortality rate was also assessed for the study participants. Microbiologically induced sepsis was noted when the positive blood culture coupled any 2 of the 4 body conditions: “(1) core body temperature greater than 38.3 °C or less than 36 °C; (2) heart rate more than 90 beats/min; (3) respiratory rate greater than 20 breaths/min; and (4) WBC count greater than 12,000/mm3 or less than 4000/mm3 or a normally ranged WBC count with more than 10% of immature forms”[12].

Statistical analysis: SPSS 20.0 software was used for the evaluation of recorded data. The mean for every suitable variable was calculated along with standard deviation (SD). To establish the significance of the difference between quantitative variables of both independent groups, Mann–Whitney-Wilcoxon test was utilized whereas the Pearson chi-square criterion was opted to compare qualitative data. If $P< 0.05$, it was considered statistically significant. Receiver operating characteristic (ROC) curves for 30-days mortality were built to assess the discrimination of each severity score (Liano, SOFA, and APACHE II). Area of 1.0 under the ROC curve indicates perfect discrimination while the area <0.5 suggests a less predictive value.

RESULTS

During the study, 35 patients underwent 280 RRT procedures. The average number of procedures for every patients was 5.44± 1.00 whereas the average duration of procedure for every patient was 9.25 ± 1.11 days. 12 patients (34.2%) were treated with intermittent hemodialysis (IHD) (total IHD procedures:168),12 (34.2%) received continuous venovenous hemofiltration (CVVH) or continuous venovenous hemodiafiltration (CVVHDF) (total number of procedures was 28 and 15 respectively), 11 (31.4%), received of these both treatments (total number of procedures was 70). 5 patients (14.2%) died during the hospitalization time. 20 patients (57.1%) showed improvement in kidney function and 10 patients (28.5%) continued dialysis even after hospital discharge.

Table I represents the information about the study patients and the data collected before and after the cardiac surgery in both survived and non-survived patients groups. There was a significant different between poor outcome scores and hospital stay duration in the two groups. The mean APACHE II, SOFA, and Liano scores of non-survivors was higher than that in survivors i.e (26.64±0.68, 16.42±0.53, 0.660±0.197) and (23.20±1.15, 12.52±0.992, 0.564±0.352) respectively. The average number of days spent by a survivors in hospital was longer (66.72±8.02 days) than in non-survivors (27.34± 3.02). But the difference

between age and gender, preoperative factors, surgical factors and postoperative factors was not significant when scores of both groups were compared. In addition the average number of RRT in survived patients was also not so different than in non-survived patients (9.92±2.94 and 6.64±1.23) respectively. The time of RRT procedures in survivors was 15.24±5.5 and 8.75±1.8 days in non-survivors.

Table No.I: Baseline Clinical History of Studied Population (N=30)

Factors	All (n=35)	Survivors (n=30)	Non-survivors (n=5)	P-value
Demographic and preoperative				
Age, years	69.22 ± 1.09	69.67 ± 2.69	69.06 ± 1.18	0.829
Female/Male, n (%)	15(42.8)/20(57.1)	12(40.0)/18(60.0)	3(60.0)/2(40.0)	0.142
Myocardial infarction, n (%)	15(42.8)	12(40.0)	3(60.0)	0.922
Chronic renal failure, n (%)	8(22.8)	5(16.6)	3(60.0)	0.073
Serum creatinine μmol/L	145.58 ± 8.87	143.10 ± 81.09	145.62 ± 88.89	0.896
eGFR using MDRD, mL/min/1.73 m^2	61.25 ± 3.92	67.78 ± 7.42	59.32 ± 3.10	0.300
Surgery				
Urgent surgery, n (%)	20 (57.1)	16(43.3)	4(13.3)	0.512
Cardiac surgery type				
Valve, n (%)	7(20.0)	7(23.3)	-	0.232
CABG, n (%)	18(51.4)	14(46.6)	4(80.0)	
CABG and valve, n (%)	10(28.5)	9(30.0)	1(20.0)	
Reconstruction of aorta, n (%)	-	-	-	
Others, n (%)	-	-	-	
SOFA score	15.64±0.52	12.52±0.992	16.42±0.53	0.0002
Liano score	0.632±0.18	0.564±0.352	0.660±0.197	0.03
Postoperative				
Hospitalization duration in ICU (days)	7.82 ± 1.16	8.62±1.99	7.42±1.32	0.650
Hospitalization duration in ICU before RRT initiation (days	6.72±0.92	5.62±1.02	7.02±0.92	0.427
Risk factors of AKI				
0, n (%)	7(20.0)	6(20.0)	1(20.0)	0.645
1–3, n (%)	22(62.8)	19(30.0)	3(60.0)	
>3, n (%)	6(17.1)	5(16.6)	1(20.0)	
Serum creatinine before RRT, mmol/L	401.44±15.34	450.55 ± 32.99	387.45 ± 16.25	0.045
Blood urea before RRT, mmol/L	28.88 ± 1.42	27.56 ± 2.54	29.33 ± 1.67	0.654
Serum potassium before RRT, mmol/L	5.43 ± 0.10	5.19 ± 0.17	5.49 ± 0.12	0.411
RRT modality, n (%)				
IHD	12 (34.2)	11(36.6)	1(20.0)	0.241
CVVH or CVVHDF	12(34.2)	9(30.0)	3(60.0)	0.604
IHD + CVVH or CVVHDF	11 (31.4)	10(33.3)	1(20.0)	0.167
Other outcomes				
Length of hospital stay, days	36.4 ± 3.33	66.72±8.02	27.34± 3.02	0.0002

Univariate analysis included some variables that were significantly different in both the patient groups. The logistic regression model showed 4 variables associated with patient mortality out of the 16 selected for model selection (Table II). According to the results, mortality and other factors (demographic, surgical, preoperative and postoperative variables) did not have any significant relation. According to the scores recorded, Glasgow coma score less than 14 points (OR=3.206,95% Cl;1.020-9.776, P=0.0027) , MAP less than 63.5 mmHg (OR = 3.763, 95% CI; 1.11-13.715, P = 0.032), preoperative serum creatinine greater than 108.5 μmol/L (OR = 0.355, 95% CI; 0.234-0.873, P = 0.040), and postoperative platelet count less than 115 × 109/L (OR = 3.829, 95% CI; 1.362-11.056, P = 0.020) significantly affected the mortality of the patients.

After the cardiac surgery, 30 patients survived within 1 month following the surgery. In our study, we also

aimed to demonstrate the clinical prognostic scores that have a significant predictive value in RRT dependent AKI patients who developed the disease following a cardiac surgery. The area under curve score was 0.669 for Liano and 0.672 for APACHE II. These scores indicate that severity scores do not have significant predictive values. On the other hand, area under curve score for SOFA was 0.722, which indicates that it has high predictive value (Table III). Consequently, at the start of RRT procedure, SOFA score proved most reliable to predict the poor outcome in both groups after 1 month following the cardiac surgery.

Table No.2: Relation between the mortality of patients with AKI after cardiac surgery and variable in model of multivariable logistic regression analysis (N=30)

Variable	Coefficient estimate	Odds ratio (95% Cl)	P-Value
Glasgow coma points	0.550	3.206 (1.020-9.776)	0.0027
Mean arterial blood pressure	0.652	3.763 (1.11-13.715)	0.032
Postoperative platelet count	0.563	3.829 (1.362-11.056)	0.020
Preoperative serum creatinine	0.540	0.355 (0.234-0.873)	0.040

Table No.3: Area under curve scores for SOFA, APACHE II and Liano (N=30)

	SOFA	APACHE II	Liano
Area under curve (AUC)	0.722	0.672	0.669
Standard error	0.065	0.062	0.067
95% CI	0.610-0.852	0.560-0.790	0.540-0.782

DISCUSSION

Following cardiac surgery, AKI is among the most common and critical complications. It poses a great risk of mortality after the surgery, more complications, longer hospital stays, and high medical costs. Several efforts have been made to lessen the incidence of AKI but none of them have been significantly effective. Increased mortality rate (2.4-19%) has been observed in cardiac surgery-associated AKI patients than in patients who were not diagnosed with AKI (1-8%)[13]. This indicated that mortality is increased 4 times when patients develop AKI after undergoing cardiac surgery.

However, the severity of AKI greatly affects mortality. Unlike many studies, we have studied the patients who developed AKI which required Renal replacement therapy. According to research, the death rate in acute renal injury patients treated with RRT is more than 40-50%[14]. In our study, the mortality rate was low (14.2%). The exceptional low mortality rate can be attributed the short study period and smaller sample size. In a study conducted by Brazilian investigators analyzing AKI following heart surgery[15], the mortality rate in AKI patients as compare to non-AKI patients was 55% and 7.1% respectively.

We evaluated 16 variables to estimate their relation to poor outcomes in AKI patients who required RRT after cardiac surgery. There are not many studies conducted to assess the factors who directly contribute to increasing the rate of mortality in acute kidney injury patients that required RRT after cardiac surgery. Mukhoedova et al.[16] demonstrated 18 variables in patients who underwent cardiac surgery and developed AKI and it was revealed that APACHE II severity score (25 ± 1 scores), severe concomitant hepatic failure, the number of organ dysfunctions, artificial ventilation, high doses of inotropic, oliguria, moderate-to-severe concomitant post hypoxic encephalopathy are the predictive factors of lethal outcome in AKI patients.

We also recorded the clinical prognostic score and determined the one with the highest predictive value. As the results indicated, SOFA has a high mortality rate predictive ability, and Liano and APACHE II have low predictive scores. In RRT dependent acute kidney injury after heart surgery. In Malov et al.[17] the analysis showed that the area under curve value of APACHE II, SOFA, and Liano was recorded as 0.821, 0.855, 0.842 respectively that indicated their good predictive ability. These results were different as compared to those obtained in our study.

Our study did have some limitations which are important to mention. Our study was single-centered and had a short duration, had age limitation, and was only of patients with AKI requiring RRT after cardiac surgery, we may have missed some parameters like cardiac failure, serum lactate level and LVEF (left ventricular ejection fraction) while recording results. We estimated the post-surgery severity scores and risk factors only at the start of RRT procedures. Some mortality associated factors were not evaluated in the multivariate analysis due to these limitations in our study.

CONCLUSION

Our study observed no relationship between mortality and other factors (demographic, surgical, preoperative, and postoperative variables). The SOFA score is the most reliable for prediction of mortality at the start of RRT in both groups after 1 month following the cardiac surgery. Glasgow coma score less than 14 points, MAP less than 63.5 mmHg, preoperative serum creatinine greater than 108.5 mmol/L, and postoperative platelet count less than 115 × 109/L affected the mortality rate

and were independent risk factors for lethal patient outcome.

Author's Contribution:

Concept & Design of Study:	Muhammad Muzammil
Drafting:	Muhammad Muzammil
Data Analysis:	Muhammad Muzammil
Revisiting Critically:	Muhammad Muzammil
Final Approval of version:	Muhammad Muzammil

Conflict of Interest: The study has no conflict of interest to declare by any author.

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