Incidence and Progression of Cardiac Surgery-associated Acute Kidney Injury and its Relationship with Bypass and Cross Clamp Time

Abstract

Introduction: Cardiac surgery-associated kidney injury (CSA-AKI) is common but relatively less is known about its progression. The present study is aimed at evaluating the incidence and course of CSA-AKI and its relationship with the different durations of cardiopulmonary bypass (CPB) and cross clamp times. Materials and Methods: Occurrences of CSA-AKI are evaluated as per the Akin Kidney Injury Network (AKIN) criteria over the course of 5 postoperative day (POD) in 100 patients. The relationship of different durations of CPB and aortic cross clamp time with CSA-AKI is analyzed by Chi-squared test for trend and other appropriate tests using INSTAT software. Results: One hundred (43 male, 57 female; mean age of 37.01 ± 12.28 years, and baseline mean serum creatinine 0.99 ± 0.20 mg %) patients undergone mostly valve replacement, and congenital heart disease correction was evaluated. Nearly 49% suffered CSA-AKI (81.63% AKIN Class I) with maximum numbers on 2nd POD. Serum creatinine followed a falling trend 3rd POD onward except in 8.16% cases of CSA-AKI. Oliguria was absent even in AKIN Class II. The CPB time >70 min and cross clamp time >60 min increase CSA-AKI risk by an OR of 4.76 and 2.84, respectively (P < 0.05). Conclusion: CSA-AKI is very prevalent; mostly of AKIN Class I and increases with increasing CPB and cross clamp time. Urine output is not a reliable indicator of CSA-AKI. The AKIN Class II on the very 1st POD or increasing trend of serum creatinine beyond 3rd POD should alert for early intervention.

Keywords: Aortic cross clamp, Cardiac surgery-associated kidney injury, Cardio pulmonary bypass

Introduction

Cardiac surgery-associated acute kidney injury (CSA-AKI) is a frequent happening affecting nearly 30% of the cases undergoing cardiac surgery.[1] This is associated with increased hospital length of stay and mortality.[2,3] Despite being known for decades, there is relative lack of effective therapeutic approaches to address this major problem till date. Therefore, risk modification appears to be an important strategy to reduce the incidence of CSA-AKI. The cardiopulmonary bypass (CPB) and aortic cross clamp time are few of the modifiable risk factors.[1-5] However, relatively less is known about the relationship of different durations of CPB and cross clamp time with CSA-AKI and its natural course over the next few postoperative days (PODs). The current study is aimed to evaluate the relations which, in turn, will facilitate our knowledge on the course of CSA-AKI, help in risk stratification, and give a basis for detecting the potential worsening case to initiate early intervention for improved outcome.

Materials and Methods

After the Institutes’ Research Board approval, the present retrospective evaluation of prospectively collected data was conducted on patients who underwent cardiac surgeries on CPB with aortic cross clamp during 2012–2014. The study was planned with an 1-alfa 95, 1-beta 80, unexposed to exposed ratio of 0.5, and expected incidence in unexposed and exposed at 20% and 50%, respectively; which gave a sample of 95 total by Kelsey method, but 100 patients’ data were included (calculated using http://www.openepi.com/SampleSize/SSCohort.htm). Demographic parameters, baseline preoperative serum creatinine, and blood urea were noted. Patients having preoperative serum creatinine >2 mg/dl and known cases of chronic renal failure and/or on hemodialysis (HD) were excluded from

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the present analysis. Estimated glomerular filtration rate (eGFR) has been calculated using the Cockcroft and Gault equation.\[6\] Perioperative care was given by the same team of surgeon, anesthesiologist, intensivist, perfusionist, and nursing team. All cases were done through median sternotomy incision. Hemodynamics was targeted within ±20% of baseline during prebypass period, and a mean arterial pressure (MAP) of 55–65 mmHg was maintained during CPB. During nonpulsatile CPB, a flow of 2.4 L/min/m² body surface area (BSA) was maintained. Vasopressor, vasodilator, and/or ionotropic supports were given as needed while coming out of bypass and postoperatively to maintain minimum of 65–70 mmHg MAP and effective left ventricular contraction. Serum creatinine and blood urea level were obtained and urine output (UO) was recorded daily from POD 1–5. CSA-AKI incidence and severity were determined using the Akin Kidney Injury Network criteria (AKIN)\[7\] and expressed in absolute number and percentage scale. The serum creatinine, blood urea, and UO of different PODs and levels among the CSA-AKI positive and negative cases were also analyzed to know the trend and course of the CSA-AKI. The cohort is further stratified based on the different durations of CPB and cross clamp time (i.e., <70, 71–140, >140 min and <60, 61–120, and >120 min, respectively), and relationship with CSA-AKI is evaluated by Chi-squared test for trend. The INSTAT software (Graphpad software, Inc, La Zolla, CA, USA) was used for analyzing statistical significance, and P < 0.05 was considered significant.

**Results**

Data of 100 patients in the age group of 17–74 years (43 male and 57 female; mean ± standard deviation [SD] age, weight, and height of 37.01 ± 12.28 years, 49.4 ± 6.67 kg and 158.76 ± 6.78 cm, respectively) were evaluated. The mean ± SD preoperative blood urea and serum creatinine were 31.73 ± 17.80, 0.99 ± 0.20 mg%, and eGFR was 67.72 ± 18.89 ml/1.73 m² BSA. Intraoperative UO was well above 1 ml/kg/h with mean ± SD of 6.11 ± 1.22. The mean ± SD duration of CPB was 94.57 ± 43.26 (95% confidence interval [CI]: 85.97–103.17) min while aortic cross clamp duration was 72.80 ± 36.82 (95% CI: 65.48–80.11) min. The predominant surgeries performed were valve replacement (65%), of which 58.46% developed CSA-AKI [Table 1].

Forty nine (49%) patients developed CSA-AKI during the 5 PODs. The mean ± SD serum creatinine level and the point incidence of CSA-AKI were highest on 2nd POD (i.e., 1.22 ± 0.38 mg% and 36 cases, respectively) [Table 2]. The mean serum creatinine level followed a decreasing trend from 3rd POD onward even in the CSA-AKI positive cases [Table 3]. The mean serum creatinine level increased from the baseline by 42.79% on the 1st POD which further increased reaching peak on POD 2 in CSA-AKI positive cases as compared to 3.84% rise on the 1st POD which become equal to baseline on the 2nd POD in CSA-AKI negative cases. The demographic, baseline creatinine, CPB, cross clamp time, etc., of CSA-AKI positive and negative cases are shown in Table 3. The incidence of CSA-AKI increased along with the increase in the CPB and cross clamp time significantly. The CPB time >70 min increased the CSA-AKI risk by an odds ratio (OR) 4.76 as compared to 71–140 min and by an OR 6.30 for >140 min (P < 0.01) while for the aortic cross clamp time >60 min increased the CSA-AKI risk by an OR of 2.84 as compared to 61–120 min and by an OR 3.64 for >120 min (P = 0.01) [Table 4].

**Discussion**

In the present observational cohort study, it was tried to evaluate the incidence of CSA-AKI and its course during the 1st 5 PODs with an intention to get more insight so that more appropriate risk stratification and informed decision-making for timely intervention can be done in perioperative and postoperative period. In the present study, 49% of the patients met the definition of CSA-AKI which is relatively higher as compared to the findings of other studies and reviews.\[1,2\] This is probably and partly because of the criteria used (i.e., AKIN) in the present study which categorizes even 0.3 mg% absolute rise of serum creatinine as Class I acute kidney injury (AKI). The AKIN criteria have shown to diagnose significantly more patients as having AKI as compared to risk, injury, failure, loss of kidney function, and end-stage renal failure.\[3\] The present study finding is showing slightly higher incidence as

| Surgery performed | n=100 | CSA-AKI, n (%) |
|-------------------|-------|---------------|
| Simple congenital heart disease repair (atrial septal defect, ventricular septal defect, patent ductus arteriosus closure, pulmonary atresia) | 27 | 6 (22.22) |
| Valve replacements (aortic, mitral, and double valve replacement-tricuspid annuloplasty-atrial septal defect repair-LA clot removal) | 65 | 38 (58.46) |
| Double outlet right ventricle, rupture aneurysm repair and LA myxoma excision | 5 | 3 (60.0) |
| Coronary artery bypass graft + valve replacement | 1 | 1 (100) |
| Coronary artery bypass graft (triple vessel) | 2 | 1 (50.0) |

CSA-AKI: Cardiac surgery-associated acute kidney injury, LA: Left atrial
Table 2: Point incidence of cardiac surgery-associated acute kidney injury and comparisons of postoperative day 1-5 serum creatinine, blood urea and urine output using paired t-test

| Time          | Blood urea (mg%) | UO (ml/kg/h) | CSA-AKI (n=100) |
|---------------|------------------|--------------|-----------------|
|               | Mean±SD          | Mean±SD      | Mean±SD         |
| Baseline      | 0.94±0.20        | 31.77±17.80  | 35              |
| POD 1         | 1.20±0.31        | 41.00±14.19  | Data NA         |
| POD 2         | 1.22±0.28        | 43.31±16.63  | Data NA         |
| POD 3         | 1.17±0.43        | 43.36±16.73  | 0.51±0.20       |
| POD 4         | 1.12±0.37        | 40.68±16.35  | 0.4794          |
| POD 5         | 1.05±0.32        | 37.77±15.90  | 0.04±0.01       |
| POD 6         | 1.09±0.12        | 34.36±14.63  | 0.00±0.00       |

The mean serum creatinine level increased up to 51.39% from baseline on the 2nd POD and then started falling from the 3rd POD onward among the cases who suffered from CSA-AKI except in 4 (8.16%) cases. Out of these 4 cases, serum creatinine remained >220% of baseline in 3 patients till the 5th POD. One (2.04%) patient who met the criteria of AKIN Class II on the very 1st POD showed persistent increasing trend beyond 5th POD and progressed from AKI Class II to Class III requiring HD and ultimately succumbed to death on 36th POD. Patients with CSA-AKI progressing to renal failure requiring HD varies from 1% to 3%. A multicenter retrospective study suggests that early renal replacement therapy (RRT) (<3 days after cardiac surgery) is associated with decreased length of hospital stay as well as mortality. The observation of the present study probably give us a basis for identification of the at risk patient for HD and probably can be used to supplement the decision-making on early initiation of RRT on this type of patients.

The mean intraoperative UO was not different in CSA-AKI positive and negative cases. Moreover, it is observed that UO was not low during CPB also. It is probably because mannitol was used in CPB priming solution. This can also be explained by the maintenance of adequate renal blood flow due to relatively low regional vascular resistance during CPB. UO in AKI in postoperative period is usually expected to fall. However, in the present study, the mean postoperative UO was above 1 ml/kg/h even among the patients who developed CSA-AKI in all the 5 PODs evaluated, and the UO was not different (i.e., less) than the non-CSA-AKI cases. Interestingly, the oliguria (i.e., UO <0.5 ml/kg/h) was not present in the patients who suffered from CSA-AKI Class II during the 5 PODs and not even in the patient who later on landed up on HD. This finding suggests that UO is not correlated with the development of CSA-AKI.

CSA-AKI is independently associated with increased mortality, and even minimal increase in serum creatinine postoperatively can have an impact on 30 day’s mortality. The deleterious effect of CPB and cross clamp on renal function is multifactorial and well known and they are regarded as potential modifiable risk factors. Offpump coronary artery bypass graft has shown to be associated with lower need of RRT postoperatively and therefore, emphasis has been given to avoid CPB and aortic cross clamp during cardiac surgeries. However, this is not
always possible, especially in valve replacement surgeries. Therefore, CPB management has also been targeted for research in relation to CSA-AKI. Patients with normal preoperative renal function who developed postoperative acute renal failure have shown to had longer CPB durations, lower CPB perfusion flow, and longer periods on CPB at pressures <60 mmHg. In the present study cohort, BSA-based fixed CPB flow is expected to have an equal impact, if any, on all patients. The finding of significantly increased CSA-AKI numbers (P = 0.0028) with increasing trend of CPB durations suggest that longer CPB duration increases CSA-AKI. The cross clamp time has also shown similar and significant impact on CSA-AKI (P = 0.0159).

The present study has also shown that the CPB duration of 71–140 min and >140 min increases the risk of CSA-AKI by an OR of 4.76 and 6.30, respectively.

One of the motives behind knowing the trend or progression of serum creatinine and CSA-AKI was to early suspect and detect the cases. Recently, different biomarkers have been investigated to do the same. CPB is associated with tubular damage which increases the production of kidney-specific proteins such as neutrophils gelatinase-associated lipocalin (NGAL), cystatin C, and kidney injury molecule 1, which have been noted within 2–6 h of surgery and correlate to the extent and duration of AKI as a biomarker.[18-20] Point of care NGAL has been in use recently for the purpose, and although its early appearance is independent of GFR, it is generally predictive of a subsequent decline in GFR.[20] Urinary NGAL has shown to be effective as an earlier marker of AKI than serum creatinine but lacks high sensitivity and specificity.[21] It also lacks the features of ideal biomarker, and serum creatinine remains still a valuable and only reliable tool for AKI.[22]

The present finding is however limited with the fact that it is a single-center, retrospective study. The sample size is also relatively lower although postanalysis power calculation of the present study taking the minimum difference between two CPB duration-based groups (22.2% in 27 patients and 57.6% in 59 patients) gave a power of 87.69% in normal approximation while with continuity correction it became 81.66% (calculated using http://www.openepi.com/Power/PowerCohort.htm); which appears to be acceptable. Prospective study with larger sample is likely to give more insight. Multivariate analysis to establish independent association is not done as the objective of the study was limited to know the relation (i.e., trend) of CSA-AKI with the different durations of CPB and cross clamp time.

Table 3: Comparisons of the cardiac surgery-associated acute kidney injury positive and negative cases using unpaired t-test

| Parameters                  | CSA-AKI present (n=49) | CSA-AKI absent (n=51) | Two-tailed (P) |
|-----------------------------|------------------------|-----------------------|----------------|
| Mean±SD                     | 95% CI                 | Mean±SD               | 95% CI         |                |
| Age (years)                 | 38.53±13.25            | 34.71-42.34           | 35.54±11.20    | 32.39-38.70    | 0.2268         |
| Weight (kg)                 | 49.59±6.72             | 47.66-51.52           | 49.21±6.69     | 47.33-51.10    | 0.7798         |
| eGFR (ml/1.73 m²)           | 68.97±18.73            | 63.53-74.42           | 66.56±19.15    | 61.22-71.90    | 0.5261         |
| CPB time (min)              | 103.83±37.6            | 93.02-114.65          | 85.66±46.74    | 72.50-98.82    | 0.0351         |
| X-clamp (min)               | 81.44±30.99            | 72.53-90.35           | 64.49±40.24    | 53.16-75.82    | 0.0206         |
| Intraoperative UO (ml/kg/h) | 5.89±1.25              | 5.53-6.25             | 6.32±1.17      | 5.99-6.65      | 0.0775         |
| POD 1 UO                    | 1.12±0.20              | 1.06-1.18             | 1.15±0.23      | 1.09-1.22      | 0.3928         |
| POD 2 UO                    | 1.11±0.21              | 1.06-1.17             | 1.14±0.22      | 1.07-1.20      | 0.5348         |
| POD 3 UO                    | 1.12±0.19              | 1.07-1.18             | 1.17±0.25      | 1.10-1.25      | 0.2728         |
| POD 4 UO                    | 1.16±0.21              | 1.10-1.22             | 1.17±0.27      | 1.09-1.25      | 0.8555         |
| POD 5 UO                    | 1.16±0.22              | 1.10-1.23             | 1.16±0.20      | 1.10-1.22      | 0.9956         |
| Serum creatinine (mg%)      |                        |                       |                |
| Preoperative                | 0.93±0.20              | 0.87-0.99             | 1.04±0.19      | 0.99-1.10      | 0.0044         |
| POD 1                      | 1.32±0.36              | 1.22-1.43             | 1.08±0.19      | 1.02-1.13      | <0.0001        |
| POD 2                      | 1.40±0.44              | 1.28-1.53             | 1.04±0.21      | 0.98-1.10      | <0.0001        |
| POD 3                      | 1.40±0.49              | 1.26-1.54             | 0.96±0.20      | 0.90-1.01      | <0.0001        |
| POD 4                      | 1.31±0.39              | 1.20-1.43             | 0.93±0.24      | 0.86-1.00      | <0.0001        |
| POD 5                      | 1.21±0.38              | 1.10-1.32             | 0.90±0.16      | 0.86-0.95      | <0.0001        |
| Blood urea (mg%)            |                        |                       |                |
| Preoperative baseline       | 31.28±16.47            | 26.54-36.02           | 31.31±19.15    | 25.92-36.70    | 0.9938         |
| POD 1                      | 44.75±13.79            | 40.78-48.72           | 37.39±13.79    | 33.52-41.26    | 0.0088         |
| POD 2                      | 49.59±13.53            | 45.70-53.48           | 37.27±13.13    | 33.57-40.97    | <0.0001        |
| POD 3                      | 51.89±15.38            | 47.47-56.32           | 35.15±13.69    | 31.30-39.01    | <0.0001        |
| POD 4                      | 48.10±17.10            | 43.18-53.02           | 33.54±11.96    | 30.18-36.91    | <0.0001        |
| POD 5                      | 42.75±17.61            | 37.69-47.82           | 32.98±11.40    | 29.77-36.19    | 0.0013         

eGFR: Estimated glomerular filtration rate, UO: Urine output, CPB: Cardiopulmonary bypass, X-clamp: Aortic cross clamp, SD: Standard deviation, CI: Confidence intervals, POD: Postoperative day, CSA-AKI: Cardiac surgery-associated acute kidney injury.
Table 4: Incidence and relation of cardiac surgery-associated acute kidney injury with different durations of cardiopulmonary bypass and aortic cross clamp time analyzed using ANOVA

| Parameters                        | ≤70 min | 71-140 min | >140 min | P       | ≤60 min | 91-120 min | >120 min | P       |
|-----------------------------------|---------|------------|----------|---------|---------|------------|----------|---------|
| Age (years)                       | 31.66±10.30 | 39.57±12.48 | 36.5±12.30 | 0.0196 | 32.0±11.15 | 40.48±11.91 | 37.45±12.90 | 0.0048 |
| Weight (kg)                       | 49.03±7.23 | 49.18±6.20 | 51.00±7.72 | 0.6282 | 48.13±6.56 | 49.65±6.48 | 52.45±7.43 | 0.1571 |
| Height (cm)                       | 156.88±5.99 | 158.94±6.18 | 161.57±9.62 | 0.1048 | 157.18±5.48 | 158.82±6.82 | 163.72±9.51 | 0.0179 |
| Base serum creatinine (mg%)       | 9.05±0.15 | 1.01±0.21 | 0.97±0.26 | 0.4350 | 0.92±0.16 | 1.03±0.22 | 0.98±0.19 | 0.0468 |
| Baseline eGFR (ml/1.73 m²)        | 72.35±19.09 | 65.08±18.30 | 69.89±20.32 | 0.2299 | 72.98±18.95 | 64.10±18.60 | 67.12±17.48 | 0.0901 |
| Baseline blood urea (mg%)         | 28.33±12.14 | 33.61±20.83 | 27.28±11.08 | 0.2959 | 27.70±12.59 | 34.55±21.22 | 28.00±12.44 | 0.1634 |
| Intraoperative UO (ml/kg/h)       | 7.00±0.62 | 5.97±1.11 | 4.98±1.41 | <0.0001 | 6.75±0.76 | 5.94±1.15 | 4.74±1.47 | <0.0001 |
| CSA-AKI, n (%)                    | 6 (22.22) | 34 (57.62) | 9 (64.28) | 0.0028* | 12 (32.43) | 30 (57.69) | 7 (63.66) | 0.0159* |
| ORa                               | Reference | 4.76      | 6.30      | Reference | 2.84    | 3.64      | 1.17-6.85 | 0.89-14.91 |
| 95% CI of ORa                     | 1.67-13.52 | 1.52-26.09 |

*Chi-squared test of independence and Fisher’s exact test. eGFR: Estimated glomerular filtration rate, UO: Urine output, SD: Standard deviation, CSA-AKI: Cardiac surgery-associated acute kidney injury, OR: Odds ratio, CPB: Cardiopulmonary bypass, X-clamp: Aortic cross clamp, CI: Confidence interval

Conclusion

CSA-AKI is very prevalent; mostly of AKIN Class I and increases with increasing CPB and cross clamp time. UO is not a reliable indicator of CSA-AKI. The AKIN Class II on the very 1st POD or increasing trend of serum creatinine beyond 3rd POD should alert for early intervention.

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Conflicts of interest

There are no conflicts of interest.

References

1. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol 2006;1:19-32.
2. Karkouti K, Wijeysundera DN, Yao TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery: Focus on modifiable risk factors. Circulation 2009;119:495-502.
3. Machado MN, Nakazone MA, Maia LN. Prognostic value of acute kidney injury after cardiac surgery according to kidney disease: Improving global outcomes definition and staging (KDIGO) criteria. PLoS One 2014;9:e89028.
4. Mangos GJ, Brown MA, Chan WY, Horton D, Trew P, Whitworth JA. Acute renal failure following cardiac surgery: Incidence, outcomes and risk factors. Aust N Z J Med 1995;25:284-9.
5. Zanardo G, Michielon P, Paccagnella A, Rosi P, Caló M, Salandin V, et al. Acute renal failure in the patient undergoing cardiac operation. Prevalence, mortality rate, and main risk factors. J Thorac Cardiovasc Surg 1994;107:1489-95.
6. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41.
7. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: Report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
8. Engberg L, Suri RM, Li Z, Casey ET, Daly RC, Dearani JA, et al. Clinical accuracy of RIFLE and Acute Kidney Injury Network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery. Crit Care 2011;15:R16.
9. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl 2012;2:1-138.
10. Grayson AD, Khatber M, Jackson M, Fox MA. Valvular heart operation is an independent risk factor for acute renal failure. Ann Thorac Surg 2003;75:1829-35.
11. Vives M, Wijeysundera D, Marczin N, Monedero P, Rao V. Cardiac surgery-associated acute kidney injury. Interact Cardiovasc Thorac Surg 2014;18:637-45.
12. García-Fernández N, Pérez-Valdivieso JR, Bes-Rastrollo M, Vives M, Lavilla J, Herreros J, et al. Timing of renal replacement therapy after cardiac surgery: A retrospective multicenter Spanish cohort study. Blood Purif 2011;32:104-11.
13. Aronson S, Blumenthal R. Perioperative renal dysfunction and cardiovascular anesthesia: Concerns and controversies. J Cardiothorac Vasc Anesth 1998;12:567-86.
14. Lassnigg A, Schimidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: A prospective cohort study. J Am Soc Nephrol 2004;15:1597-605.
15. de Mendonça-Filho HT, Pereira KC, Fontes M, Vieira DA, de Mendonça ML, Campos LA, et al. Circulating inflammatory mediators and organ dysfunction after cardiovascular surgery.
with cardiopulmonary bypass: A prospective observational study. Crit Care 2006;10:R46.

16. Bucerus J, Gummert JF, Walther T, Schmitt DV, Doll N, Falk V, et al. On-pump versus off-pump coronary artery bypass grafting: Impact on postoperative renal failure requiring renal replacement therapy. Ann Thorac Surg 2004;77:1250-6.

17. Fischer UM, Weissenberger WK, Warters RD, Geissler HJ, Allen SJ, Mehlhorn U. Impact of cardiopulmonary bypass management on postcardiac surgery renal function. Perfusion 2002;17:401-6.

18. Boldt J, Wolf M. Identification of renal injury in cardiac surgery: The role of kidney-specific proteins. J Cardiothorac Vasc Anesth 2008;22:122-32.

19. Bennett M, Dent CL, Ma Q, Dastrala S, Grenier F, Workman R, et al. Urine NGAL predicts severity of acute kidney injury after cardiac surgery: A prospective study. Clin J Am Soc Nephrol 2008;3:665-73.

20. Wyckoff T, Augoustides JG. Advances in acute kidney injury associated with cardiac surgery: The unfolding revolution in early detection. J Cardiothorac Vasc Anesth 2012;26:340-5.

21. Sargentini V, Mariani P, D’Alessandro M, Piolesi V, Lauretta MP, Pacini F, et al. Assessment of NGAL as an early biomarker of acute kidney injury in adult cardiac surgery patients. J Biol Regul Homeost Agents 2012;26:485-93.

22. Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, Fulquet-Carreras E. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth 2016;19:687-98.