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# Acute kidney injury after open heart surgery in seyyed-al-Shohad heart center urmia(Iran)

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## ABSTRACTS

*Cardiac surgery-associated acute kidney injury (CSA-AKI)is a serious, well known medical problem with significant morbidity and marked predisposition to mortality in 9-45% of patients undergoing cardiac surgeries. Clinical studies have identified several risk factors for AKI that can be used to determine effectively the risk for AKI in patients who undergo coronary bypass grafts. These high risk patients then can be targeted for more kidneys protective enterprises before cardiac surgeries. This prospective case-control study enrolled 203 adult (> 18 years of age) patients whom underwent on-pump cardiac surgeries at seyyed-ol-shohada heart center of Urmia From September 1, 2013 to March 1, 2014. CSA-AKI defined as 50% increase in the plasma creatinine concentration during 7 postoperative days compared to the baseline value and by 25% decrease in glomerular filtration rate or a urine output less than 0.5 mL kg -1 per hour for more than 6 h (according to the criteria of the Risk Injury Failure Loss End-Stage Renal Disease(RIFLE).Patients divided into two groups, based on outcome, patients who developed CSA-AKI as cases group and patients who didn't developed CSA-AKI as controls group. Statistical analysis performed using SPSS program (version 18, Chicago, IL, USA). Kaplan Meier, T-test and log linear tests used to compare variables between cases and controls. The incidence of CSA-AKI was 23.2%.Among 47 patients with CSA-AKI, 42 patients detected with CSA-AKI Stage 1, 4 patients with stage 2 and 1 person with stage 3.The mean age of patients was 59.85 ± 10.65 years (minimum age 18, maximum age 81 years). The mean age of the patients with CSA-AKI is equal to 61.45 ± 9.27 years and the mean age of patients who had not CSA-AKI is equal to 59.37 ± 11.01 years. Preoperative and intraoperative variables that were associated with the development of CSA-AKI included:preoperative LVEF<35%(p=0.017),needs to infusion of inotropic drugs(P=0.001),type of surgery(p=0.044),reoperation(p = 0.071)The following factors weren't associated with the development of CSI-AKI: Diabetes Mellitus (p = 0.809),hypertension(p = 0.210),smoking (p = 0.573),intake of diuretic drugs(p = 0.876),mean of Hematocrit during surgery(p = 0.632),gender difference(p = 0.332) ,reeintubation((p = 0.548).*
*There is significant difference between postoperative mortality and incidence of CSA-AKI at 95% (p = 0.010).Our conclusion is the development of CSA-AKI is associated with a high mortality. We have identified perioperative risk factors, which may be useful in reducing of risk for the development of CSA-AKI.*

## INTRODUCTION

Acute kidney injury [AKI] is a serious, well known medical problem with significant morbidity and marked predisposition to mortality in patients with critical illnesses, [1-3], remaining as a major issue through years, it still results in loss of life even with mild renal injury [4].Cardiac surgery-associated acute kidney injury [CSA-AKI] is a

common complication of cardiac surgeries observed in 9-45% of patients undergoing cardiac surgeries [5-9], associated with higher short and long term mortality [10, 11].

Several variables has been associated with CSA-AKI including: Gender, Age, Weight, Diabetes[Type 1 or 2], Hypertension, Chronic Obstructive Pulmonary Disease, Low ejection fraction[<40%], Preoperative intra-aortic balloon pump, preoperative hemoglobin, Redo surgery, Cardiopulmonary Bypass[CPB] duration, Clamp-time, lowest Hematocrit during CPB, Renal insufficiency[12-16], these factors led to development of several predictive models for prognostic classification and risk-adjustment [17, 18]. Looking forward to finding further contributory variables is indispensable regarding high incidence of CSA-AKI, aforementioned investigations has a similar convergence point over preoperative and non-modifiable factors , implying demand for clarify and eliminating modifiable factors as a practical approach to dominate mortality, morbidity and economic burden imposed by CSA-AKI.

This study was performed to assess perioperative variables contribute to developing CSA-AKI in order to determine potential risk factors.

## MATERIALS AND METHODS

This prospective case-control study enrolled 203 adult (> 18 years of age) patients whom underwent on-pump cardiac surgeries at seyed-o-shohada heart center of Urmia From September 1, 2013 to March 1, 2014.Excluded patients with known renal dysfunction requiring renal replacement therapy (n=0) and baseline serum creatinine > 1.5 mg/dl(n=7) . No patient was excluded with incomplete patient data. After research board acceptance, study was approved by Ethics Committee of Urmia University of Medical Sciences. Written informed consent was obtained from all subjects.

CSA-AKI was the primary independent variable. CSA-AKI defined as 50% increase in the plasma creatinine concentration during 7 postoperative days compared to the baseline value and by 25% decrease in glomerular filtration rate or a urine output less than 0.5 mL kg -1 per hour for more than 6 h (according to the criteria of the Risk Injury Failure Loss End-Stage Renal Disease, RIFLE)(19).An alternative criteria presented by Acute kidney injury network defines CSA-AKI based on an absolute increase in plasma creatinine concentration by at least 0.3 mg dL-1 during 2 postoperative days (20, 21). The most updated guideline by Kidney Disease: Improving Global Outcomes(KDIGO) providing combination of these two criteria and suggests a uniform standard for diagnosing AKI(22). According to KDIGO staging classification, in case patients require renal replacement therapy, irrespective of the stage they are considered as stage 3.

| | Serum Creatinine | Urine output |
|---|---|---|
| Stage 1 | ↑sCr x 1.5<br>or<br>↑≥0.3 mg/dl in sCr | <0.5 ml/kg per h x 6h |
| Stage 2 | ↑sCr x 2 | <0.5 ml/kg per h x 12h |
| Stage 3 | ↑sCr x 3<br>or<br>↑≥0.5 mg/dl if baseline sCr>4.0 mg/dl | <0.3 ml/kg per h x 24h<br>or<br>anuria x 12h |

Baseline and preoperative variables included age, gender, BMI, Low Ejection fraction (<35), diabetes mellitus, Hypertension (SBP>140, DBP>90)), Smoking (5 pack*year and more), Use of diuretics, addiction, alcohol usage, preoperative serum creatinine.

Intraoperative variables were ventilation time, pumping time, clamp time, Use of Intra-aortic balloon pump, Intra-venous inotropic drug therapy requirement, minimum hematocrit during pumping, urine output during pumping and type of surgery. Inotropic drug used after wining for pump in case of unstable hemodynamics (SBP<90).

Post-operative criteria measured were tamponade, brain complication, gastrointestinal complication, intubation, dialysis, death.

Patients divided into two groups, based on outcome, patients who developed CSA-AKI as cases group and patients who didn't developed CSA-AKI as controls group. Statistical analysis performed using SPSS program (version 18, Chicago, IL, USA). Kaplan Meier, T-test and log linear tests used to compare variables between cases and controls.

## RESULTS

In this case-control study 203 patients for cardiac surgery were referred with On-Pump method to Cardiology Subspecialty Center of Seyedolshohada Hospital, Urmia during second six months of 2013 were studied. 126 (62.1%) of the patients were male and 77 (37.9%) were women among the 203 patients studied, 47 patients (23.2%) had CSA-AKI.

Among 47 patients with CSA-AKI, 42 patients detected with CSA-AKI Stage 1, 4 patients with stage 2 and 1 person with stage 3.

The mean age of patients was 59.85 ± 10.65 years (minimum age 18, maximum age 81 years). The mean age of the patients with CSA-AKI is equal to 61.45 ± 9.27 years and the mean age of patients who had not CSA-AKI is equal to 59.37 ± 11.01 years. Given the amount of p = 0.242 which is greater than p = 0.05. There was no significant difference between the mean ages of two groups.

Mean BMI of patients were 25.89 ± 4.01 kg/m2. (Lowest BMI was 15.82 and highest BMI was 38.37 kg/m2). The mean BMI of the patients with CSA-AKI are equal to 26.74 ± 3.87kg/m2 and the mean BMI of patients who had not CSA-AKI is equal to 26.54 ± 4.06 kg/m2. Given the amount of p = 0.765 which is greater than p = 0.05. There is no significant difference between the mean BMI of two groups.

Mean of Minimum Hematocrit during surgery was 23.18 ± 4.28% (Lowest Min.HCT was 38% and highest Min.HCT was 15% between patients). Mean Min.HCT of the patients with CSA-AKI is equal to 23.44 ± 4.26% and mean Min.HCT of patients who had not CSA-AKI is equal to 23.09 ± 4.30%. Given the amount of p = 0.632 which is greater than p = 0.05. There is no significant difference between the mean Min.HCT of two groups.

**Table 1- Distribution Profiles of SEX, CABG, Hemo.instable, Tamponade, LowEF, Diabetes Mellitus, HTM, Smoking, Inotropic.Drug, Diuretic.PRN, and Ethanol vs. case and control groups**

| Variable | | Group case | Group control | Total |
|---|---|---|---|---|
| Sex | Female<br>Male | 15 (%13.6)<br>32 (%19.5) | 62 (%86.4)<br>94 (%80.5) | 77 (%37.9)<br>126 (%62.1)<br>P.value = 0.332 |
| CABG** | CABGs<br>Valve Replacement<br>Congenital<br>Aortic dissection<br>Multiple Operations | 38 (%21.7)<br>4 (%36.5)<br>0 (%0)<br>3 (%75)<br>2 (%33.3) | 137 (%78.3)<br>7 (%63.6)<br>7 (%100)<br>1 (%25)<br>4 (%66.7) | 175 (%86.2 )<br>11 (%5.4)<br>7 (%3.4)<br>4 (%2)<br>6 (%3 )<br>P.value = 0.044 |
| Tamponade* | Not have<br>have | 43 (%22.1)<br>4 (%50) | 152 (%77.9)<br>4 (%50) | 195 (%96.1)<br>8 (%3.9)<br>P.value = 0.066 |
| LowEF** | Not have<br>have | 26 (%18.2)<br>19 (%33.9) | 117 (%81.8)<br>37 (%66.1) | 143 (%70.4 )<br>56 (%27.6)<br>P.value = 0.017 |
| Diabetes Mellitus | Not have<br>have | 34 (%23.6)<br>13 (%22) | 110 (%76.4)<br>46 (%23.6) | 144 (%70.9 )<br>59 (%29.1 )<br>P.value = 0.809 |
| HTM | Not have<br>have | 21 (%28)<br>26 (%20.3) | 54 (%72)<br>102 (%79.7) | 75 (%36.9)<br>128 (%63.1)<br>P.value = 0.210 |
| Smoking | Not smoking<br>smoking | 28 (%21.9)<br>19 (%25.3) | 100 (%78.1)<br>56 (%74.7) | 143 (%70.4 )<br>56 (%27.6)<br>P.value = 0.573 |
| Inotropic.Drug** | Not have<br>have | 34 (%19.3)<br>13 (%48.1) | 142 (%80.7)<br>14 (%51.9) | 176 (%86.7 )<br>27 (%13.3 )<br>P.value = 0.001 |
| Diuretic.PRN | Not have<br>have | 3 (%25)<br>44 (%23) | 9 (%75)<br>147 (%77) | 12 (%5.9)<br>191 (%94.1)<br>P.value = 0.876 |
| Ethanol* | Not have<br>have | 45 (%22.5)<br>2 (%66.6) | 155 (%77.5)<br>1 (%33.3) | 200 (%98.5 )<br>3 (%1.5)<br>P.value = 0.072 |

**, ** Respectively indicate the significance level of 5% and 10%*

According to the results in Table 1 of the 203 patients, 47 patients (23.2%) had CSA-AKI. Among males, 32 patients (25.4%) and among females 15 patients (19.5%) had CSA-AKI. According to Chi-Square test, no significant difference was found between gender and the incidence of CSA-AKI (p = 0.332).

Of the 175 patients who underwent Coronary Artery Bypass Graft Surgery (CABG) 38 patients (21.7%), of the 11 patients who underwent Valve Replacement surgery 4 patients (36.4%), of the 4 patients who underwent Aortic dissection repair 3 patients (75%) and of the 6 patients who underwent combination of the surgeries that were mentioned 2 patients (33.3%) had CSA-AKI. Of the 7 patients undergoing surgical correction of congenital heart defects either was found with CSA-AKI. As a result, there is significant difference between the type of surgery performed and the incidence of CSA-AKI at 95% (p = 0.044). And of 56 (27.6%) patients that had ejection fraction less than 35%, 19 patients (33.9%) had CSA-AKI. There is significant difference in ejection fraction less than 35% and the incidence of CSA-AKI at 95% (p = 0.017). Also, of 8 (3.9%) patients with cardiac tamponade 4 patients (50%) had CSA-AKI. There is a significant difference between the incidence of tamponade and the incidence of CSA-AKI at 90% (p = 0.066).

Of 59 patients (29.1%) who had Diabetes Mellitus 13 patients (22%) had CSA-AKI. According to the Chi-Square test there is no significant difference between Diabetes Mellitus and the incidence of CSA-AKI (p = 0.809). Also, of 128 (63.1%) patients who had hypertension, 26 patients (20.3%) patients had CSA-AKI. As a result, there is no significant difference between blood pressure and the incidence of CSA-AKI (p = 0.210). Of 75 (36.9%) patients who smoke, 19 (25.3%) patients had CSA-AKI. Finally, there is no significant difference between smoking and the incidence of CSA-AKI (p = 0.573). And of 27 (13.3%) patients who had received inotropic drugs before, during and after surgery, 13 (48.1%) patients had CSA-AKI. There is a significant difference between receiving inotrope drugs and the incidence of CSA-AKI at 95% (p = 0.001).

Also, of 191 (94.1%) patients who were receiving diuretic therapy, 44 patients (23%) had CSA-AKI. As a result, there is no significant difference between diuretic drugs and the incidence of CSA-AKI (p = 0.876). Finally, of 3 (1.5%) patients who had regular alcohol intake, 2 patients (66.7%) had CSA-AKI. According to Chi-Square test there is a significant difference between regular alcohol consumption and the incidence of CSA-AKI at 90% (p = 0.072).

**Table 2- Distribution Profiles of Addiction, Death, Dialysis, Redo.Operation, Reintubation vs. case and control groups**

| Variable | | Group case | Group control | Total |
|---|---|---|---|---|
| Addiction | Not have | 42 (%22) | 149 (%78) | 191 (%94.1) |
| | have | 5 (%41.7) | 7 (%58.3) | 12 (%5.9) |
| | | | | P.value = 0.117 |
| Death** | Not have | 43 (%21.8) | 154 (%78.2) | 197 (%97 ) |
| | have | 4 (%66.7) | 2 (%33.3) | 6 (%3) |
| | | | | P.value = 0.010 |
| Dialysis* | Not have | 46 (%22.8) | 156 (%77.2) | 202 (%99.5 ) |
| | have | 1 (%100) | 0 (%0) | 1 (%0.5 ) |
| | | | | P.value = 0.068 |
| Redo.Operation** | Not have | 42 (%21.9) | 150 (%78.1) | 192 (%94.6) |
| | have | 5 (%45.5) | 6 (%54.5) | 11 (%5.4) |
| | | | | P.value = 0.071 |
| Reintubation | Not have | 45 (%22.8) | 152 (%77.2) | 143 (%70.4 ) |
| | have | 2 (%33.3) | 4 (%66.7) | 56 (%27.6) |
| | | | | P.value = 0.548 |

**, ** Respectively indicate the significance level of 5% and 10%*

According to the results shown in Table 2, among the 203 patients, 12 patients (5.9%) had a drug addiction. Among these, 5 patients (41.7%) had CSA-AKI. According to the Chi-Square test there is no significant difference between the ejection fraction less than 35% and the incidence of CSA-AKI (p = 0.117).

Of 6 (3%) patients who had expired after surgery, 4 patients (66.7%) had CSA-AKI. There is significant difference between postoperative mortality and incidence of CSA-AKI at 95% (p = 0.010).

And only 1 patient (0.5%) under dialysis had CSA-AKI. There is a significant difference between patients who require dialysis and the incidence of CSA-AKI at 90% (p = 0.068).

Also, of 11 (5.4%) patients who had undergone reoperation, 5 patients (45.5%) had CSA-AKI. As a result, according to the Chi-Square test there is a significant difference between reoperation and the incidence of CSA-AKI at 90% (p = 0.071).

Finally, of the 6 patients (3%) who had undergone re-intubation, 2 patients (33.3%) had CSA-AKI. There is no significant difference between re-intubation and the incidence of CSA-AKI (p = 0.548).

In the survey of Ventilation time variable that is equal to the time of intubation and connection to ventilator, variable is considered as an event that has marked beginning and end, and in the case of death during this event or entire event or failure to complete this event, the findings has been removed from the review.

According to the results of Kaplan-Meier test and Figure 1, the mean survival time in the group which had not CSA-AKI was equal to 5.620±0.196 hours and the mean survival time in the group which had CSA-AKI was equal to 8.207±0.984 hours and given that p = 0.001, which is less than p = 0.05 there is a significant difference between the mean survival times of ventilation time of the two groups.

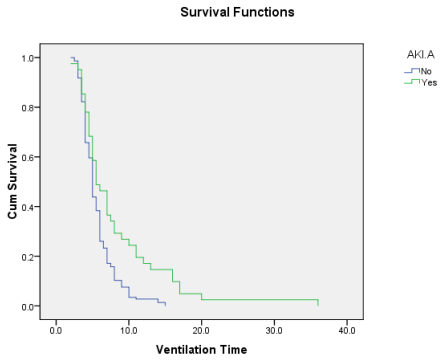


**Figure 1- Survival Curve of Ventilation time vs. AK1.A**

In the survey of Pumping time variable that is equal to the time of connecting to pump, variable is considered as an event that has marked beginning and end, and in the case of death during this event or entire event or failure to complete this event, the findings has been removed from the review.

According to the results of Kaplan-Meier test and Figure 2, the mean survival time in the group which had not CSA-AKI was equal to 119.129±0.005minutes and the mean survival time in the group which had CSA-AKI was equal to 153.277±7.115minutes and given that p = 0.000, which is less than p = 0.05 there is a significant difference between the means of survival times of pumping time of the two groups.

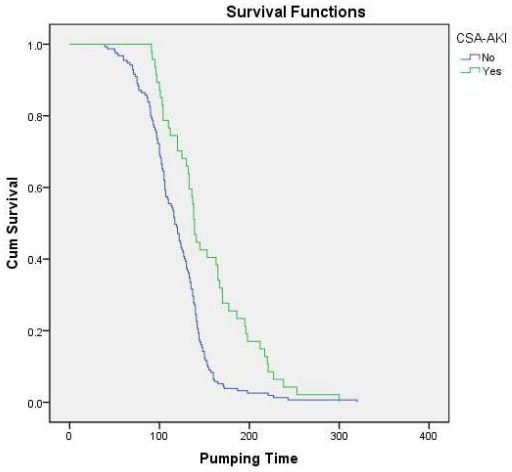


**Figure 2- Survival Curve of Pumping time vs. AK1.A**

In the survey of Clamp time variable that is equal to the time of connecting clamp, variable is considered as an event that has marked beginning and end, and in the case of death during this event or entire event or failure to complete this event, the findings has been removed from the review.

According to the results of Kaplan-Meier test and Figure 2, the mean survival time in the group which had not CSA-AKI was equal to 75.917±2.364 minutes and the mean survival time in the group which had CSA-AKI was equal to 101.064±5.896minutes and given that p = 0.000, which is less than p = 0.05 there is a significant difference between the means of survival times of clamp time of the two groups.

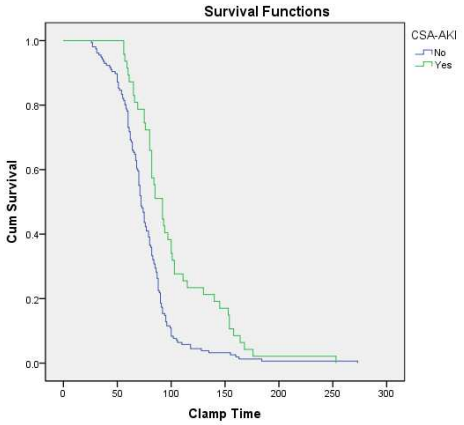


**Figure 2- Survival Curve of Clamp time vs. AK1.A**

Mean Creatinine of patients before surgery was 1.01 ± 0.18 mg / dl (minimum Creatinine was 0.5 and maximum Creatinine was 1.5 kg/m2). Primary mean Creatinine of patients with CSA-AKI patients was equal to 1.07 ± 0.21 mg / dl and primary mean Creatinine of patients who had not CSA-AKI was equal to 0.992 ± 0.17 mg / dl. Given the amount of p = 0.020 which is less than p = 0.05. There is a significant difference between the primary mean Creatinine of two groups at 95%.

Mean Urine output rate of patient during connecting to pump was 3.67 ± 0.18 ml / kg / h (lowest Urine output was 0.19 ml / kg / h and maximum Urine output was 10.75 ml / kg / h). Mean Urine output of patients with CSA-AKI is equal to 3.13 ± 2.00 ml / kg / h and mean Urine output of patients who had not CSA-AKI is equal to 3.86 ± 2.17 ml / kg / h is. Given the amount of p = 0.049 which is less than p = 0.05. There is a significant difference between mean Urine outputs of the two groups at 95%.

## DISCUSSION

Impaired renal function observed up to 45% in surgeries involved extracorporeal circulation(23). AKI has a major impact in survival rates of critically ill patients as it caused development of several predictive models for prognostic classification and risk-adjustment (17, 18). All these efforts aimed to decrease CSA-AKI unwelcome effects, evolving approach to this issue from early recognition to decrease modifiable risk factors.

Definitions of CSA-AKI improved as well as coping with it, broadening the CSA-AKI definition with the intention of covering more vulnerable patients resulting in higher reported percentage of CSA-AKI eventually causing early detection and informing of clinicians about an important phenomenon jeopardizing their medical practice outcomes. As in this study using most updated criteria up to this date, reported CSA-AKI percentage about half of similar studies(23) implying awareness over this issue with presenting descending attitude.

Our study indicated tamponade, Low EF, Use of Inotropic drug, Alcohol consumption, and redo-operation along with higher base creatinine, lower urine output, longer ventilation time, longer pumping time and longer clamp time as a significant risk factor for developing CSA-AKI.

Similar studies confirmed Redo-operation, low ef and longer clamp time as risk factors, but also presented other risk factors that were not significant in this study(12-16). Though we excluded high creatinine values as renal insufficiency but we still see significant difference in Base creatinine even within normal ranges

Though the known morbidity and mortality of CSA-AKI, through this study only one patient (2.1%) developed CSA-AKI severe enough to renal replacement therapy presenting lower severe outcomes with CSA-AKI as well as similar studies in large series (1-1.7%)(24, 25).

Present study had limitations of cases and controls quantity and including patients from a single center hence demanding multi center studies to test analogous models.

Revealed intra-operative risk factors through this study make it necessary to do more studies to focus on intra-operative risk factors.

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