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Research Article

ROLE OF SERUM CREATININE IN FORECASTING THE OUTCOME AFTER CARDIAC SURGERY BEYOND ACUTE KIDNEY INJURY- A CROSS-SECTIONAL STUDY

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ABSTRACT

Objectives: Acute kidney damage (Acute kidney injury [AKI]) is defined by elevations in serum creatinine levels that occur after surgery. In cardiac surgery, creatinine is a critical determinant. This study highlights the detection of serum creatinine as an early diagnostic and predictive marker of AKI following coronary artery bypass grafting (CABG) and to estimate the serum creatinine concentrations before and at 24 and 48 h after CABG.

Methods: It is a single center, Cross-sectional study. Patients from Cardiothoracic and Vascular surgery undergoing CABG in Sri Ramachandra Medical College and Research Institute were included in the study. A total of 80 cases were included in the study. The method used for measurement of serum creatinine is by modification of kinetic Jaffe reaction. Data were analyzed using Stata/SE version 16.0 and represented in terms of means, standard deviation at 95% confidence level and t' test was performed as statistical analysis and $p<0.05$ indicates significance. Sigma plot software version 10.0 was used to draw the standard error mean graphs.

Results: The serum creatinine values at 24 h after the surgery was statistically higher than the preoperative values at 5% significance level ($p=0.04$). The serum creatinine values 48 h after the surgery was also statistically higher than the preoperative values at 1% significance level ($p=0.001$). The serum creatinine values 48 h after surgery are highly significant ($p=0.001$) when compared to the serum creatinine values 24 h after surgery.

Conclusion: Before an increase in serum creatinine level is detected, over 50% of renal function must be lost. It was concluded that serum creatinine is an inadequate and delayed marker of AKI.

Keywords: Coronary artery bypass grafting, Serum creatinine, Acute kidney injury, Preoperative, Postoperative.

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INTRODUCTION

Acute kidney injury (AKI) is described as a sudden decrease in glomerular filtration rate (GFR), with clinical symptoms ranging from a little increase in blood creatinine to anuric renal failure [1]. The range of injuries varies from moderate to advance with renal replacement therapy sometimes. AKI affects 7 to 18 percent of hospitalized patients, complicating their courses and leading to morbidity or mortality in 50–60% of those hospitalized to an Intensive Care Unit (ICU). Although many AKIs are reversible within days to weeks of onset, there is evidence of a strong relationship between AKI and chronic kidney disease and end-stage renal disease from many substantial observational and epidemiologic research over the past decade [2-6]. AKI is essentially driven by changes in serum creatinine evels perioperatively. In this increasingly common disorder, AKI is largely asymptomatic and is nowadays based on functional biomarkers such as serum creatinine and blood urea nitrogen [7-9]. Unfortunately, diagnosis of AKI is based on these functional biomarkers which are not very specific or sensitive because they are affected by many renal and non-renal factors [10].

Obviously, the term for risk of renal failure, kidney damage, kidney failure, loss of kidney function and end-stage renal failure (RIFLE), AKI Network (AKIN), and Kidney Disease: Enhancing Global Outcomes (KDIGO) is used to grade the seriousness of AKI with creatinine [11,12]. The primary role of creatinine as a key indicator in risk assessment scoring systems is well understood. Creatinine was also used by newer prediction scores in the first three major risk factors for mortality after cardiac surgery. It has been named AKI-associated cardiac surgery because of the distinctive features and conditions of AKI that arise after cardiac surgery (Cardiac surgery-associated [CSA]-AKI). At present, several studies have been conducted to find answers to key questions about the management and cure of perioperative CSA-AKI and interesting results have been achieved, particularly in prophylactic management [13,14].

For patients undergoing both cardiac surgery and vascular surgery, AKI is a common perioperative complication, progressing in 20–70% of cases, based on the type of surgery and the description of AKI used [5,15]. Coronary Artery Bypass Grafting (CABG) which employs cardiopulmonary bypass (CPB) is the utmost usual cause of AKI in the ICU [16,17].

The rise in serum creatinine levels has an important effect on surgical outcomes [18]. Also, minor serum creatinine changes that are not large enough to be identified as AKI exacerbate the outcome of patients undergoing cardiac surgery. Serum creatinine has poor sensitivity and has a late response to renal insult. However, due to the simplicity and availability of its calculation, serum creatinine levels still constitute the key test for the assessment of renal function. Similarly, the core of AKI's consensus concepts is serum creatinine [10].

This study highlights the detection of serum creatinine as an early diagnostic and predictive marker of AKI following CABG and to estimate the serum creatinine concentrations before and at 24 and 48 h after CABG.

METHODS

Study design

It is a single centre, cross sectional study.

Study population

Patients undergoing CABG in the department of cardiothoracic and vascular surgery at Sri Ramachandra Medical College and Research Institute. We conducted a cross-sectional study in 80 patients who are in the age group of 30–60 years of both sex and who are undergoing CABG. The study excluded patients less than 30 years and greater than 60 years and with a Pre-existing renal disease, malignancies, and patients who have undergone neurological and endocrine surgeries, emergency surgeries. Patients who use any Nephrotoxic drugs like diuretics, nonsteroidal anti-inflammatory drugs, cyclophosphamide, methotrexate, cyclosporine, lithium, pencillamide, gold salts, large doses of amphotericin B were also excluded. Institutional Ethics Committee clearance approval was obtained before the start of the study (Ref. No: CSP-MED/13/DEC/10/136). Each participant was explained about the details of the study and informed consent was obtained.

Methodology

Blood samples were drawn from the patients preoperatively and postoperatively at 24 h and 48 h for the estimation of serum creatinine. The blood samples were collected using BD vacutainer needles into yellow topped BD gel vacutainers for serum creatinine estimation. The blood samples for serum creatinine were centrifuged at 3000 rpm for 15 min. The serum was separated and stored in storage vials at −70°C until analysis. The method for measurement of serum creatinine is by modification of kinetic Jaffe reaction. There is less interference from the Jaffe-positive compounds. The procedure was based on the principle that strong alkaline medium, picrate reacts with creatinine to form a red-colored chromophore. The rate of increasing absorbance at 510 nm is due to the formation of this chromophore. It is directly proportional to the creatinine concentration in the sample and is measured using a bichromatic (510, 600 nm) rate technique. Bilirubin is oxidized by potassium ferricyanide to prevent interference. This method is linear for Serum Creatinine concentrations up to 20 mg/dl. This method has a measurement range of 0.05–20 mg/dl of Serum Creatinine. The minimum detection limit by this kit is 0.05 mg/dl. The instrument used was Dimension RXL Max. The test conditions involve sample size 20 µL, reagent 1 volume 74 µL, reagent 2 volume 18 µL, diluent volume 258 µL, test temperature 37°C, wavelength 510 and 600 nm and the type of measurement is Bichromatic rate. The reference range of serum creatinine values is 0.9–1.3 mg/dl in males and 0.6–1.1 mg/dl in females.

Statistical analysis

Data were analyzed using Stata/SE version 16.0 and represented in terms of means, standard deviation at 95% confidence level, and t'-test was used to determine the p-value and $p<0.05$ indicates significance. Sigma plot software version 10.0 was used to draw the standard error mean graphs.

RESULTS

The data consists of 80 observations of patients who had undergone CABG. Out of the 80 patients who had undergone CABG, 5 patients had on pump and the rest had off pump surgeries as shown in Table 1. Among the 80 patients who underwent CABG, 10 were classified under AKI category. The criterion used for diagnosis of AKI was the AKIN definition and staging criteria (increase in serum creatinine of ≥50% from baseline developing over 48 h). Since the sample contains only 13 female patients, no analysis was done to determine differences between the two genders.

The serum creatinine values for all the patients were measured thrice, once before surgery and twice after surgery (one 24 h and other 48 h after surgery). The mean creatinine value pre-operatively for the patients without AKI is 0.944 mg/dl. The mean creatinine value pre-operatively for the patients with AKI is 1.09 mg/dl. The mean serum creatinine value 24 h post-operatively for the patients with out AKI is 0.962 mg/dl. The mean creatinine value 24 h postoperatively for the patients with AKI is 1.67 mg/dl. The mean creatinine value 48 h post-operatively for patients without AKI is 0.902 mg/dl. The mean creatinine value 48 h post-operatively for patients with AKI is 3.04 mg/dl. as shown in Table 2.

Figs. 1-2 showing the mean of creatinine preop and postop (24, 48 h) values for patients with AKI or without AKI. Fig. 3 shows the comparison graph for the mean of creatinine versus standard error means preoperative and postoperative (24, 48 h) values for patients with AKI.

The serum creatinine values at 24 h after the surgery was statistically higher than the preoperative values at 5% significance level ($p=0.04$). The serum creatinine values 48 h after the surgery was also statistically higher than the preopeartive values at 1% significance level ($p=0.001$). The serum creatinine values 48 h after surgery is highly significant ($p=0.001$) when compared to the serum creatinine values 24 h after surgery as shown in Table 3.

DISCUSSION

AKI is a disease that, as indicated by a decreased GFR, and characterized by a sudden impairment of kidney function. CSA-AKI results from cardiac surgery and percutaneous coronary procedures with extended intensive care stays, resulting in either renal injury and/or postoperatively [19,20]. AKI after CABG is responsible for high mortality rates; with an incidence between 8% and 53% and nearly 1–7% of individuals require dialysis. As CABG is a generally accepted and safe treatment for CAD, the incidence of AKI in patients who undergo CABG has increased. It is also affected by comorbidities due to advancing age [21]. CSA-AKI is associated with an increased risk for postoperative complications like infections, complicated hospital course, increased short-term and long-term mortality [14,22]. Serum creatinine retains the AKI diagnostic standard in clinical practice. As per the KDIGO definition, if serum creatinine rises within 48 h by 0.3 mg/dl (26.5 µmol/l) or the serum creatinine values greater than the baseline in the first 7 days, or if the production of urine for 6 h is below 0.5 ml/kg/h, the patient is considered to have AKI [23].

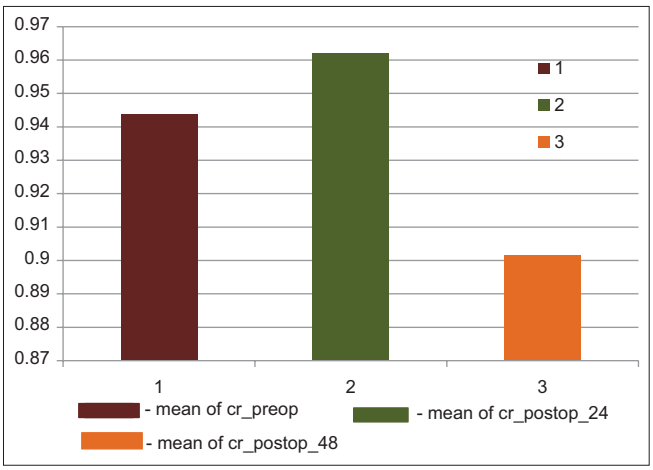

Fig. 1: Bar diagram showing the mean of creatinine preop and postop (24, 48 hours) values for patients without acute kidney injury

Table 1: Demographic data

Demographic parameters	Total number (percentage) of patients
Gender	
Male	67 (83%)
Female	13 (17%)
Surgery	
CABG	80 (100%)
On/off-pump technique	
On pump	5 (94%)
Off pump	75 (6%)
Comorbidities	
Diabetes	32 (40%)
Hypertension	28 (35%)
Nil	20 (25%)

CABG: Coronary artery bypass grafting

Table 2: Descriptive statistics showing the creatinine values

Variable creatinine	Mean mg/dl	Std. Dev.	Std. Err.	(95% confidence interval)	
Patients without AKI pre-operative (n=66)	0.944	0.188	0.023	0.9	0.99
Patient with AKI pre-operative (n=10)	1.09	0.128	0.041	1.01	1.17
Patients without AKI 24 h post-operatrive (n=66)	0.962	0.165	0.118	0.92	1
Patient with AKI 24 h postopeartive (n=10)	1.67	0.189	0.060	1.55	1.79
Patients without AKI 48 h postopeartive (n=66)	0.902	0.214	0.026	0.85	0.95
Patient with AKI 48 h post-opeartive (n=10)	3.04	0.306	0.097	2.85	3.23

AKI: Acute kidney injury

Table 3: Results of creatinine pre-op and post-op comparison

Variable 1	Variable 2	p-value
Creatinine pre-opeartive	Creatinine post-operative 24 h	0.04*
Creatinine pre-opeartive	Creatinine post-operative 48 h	0.001**

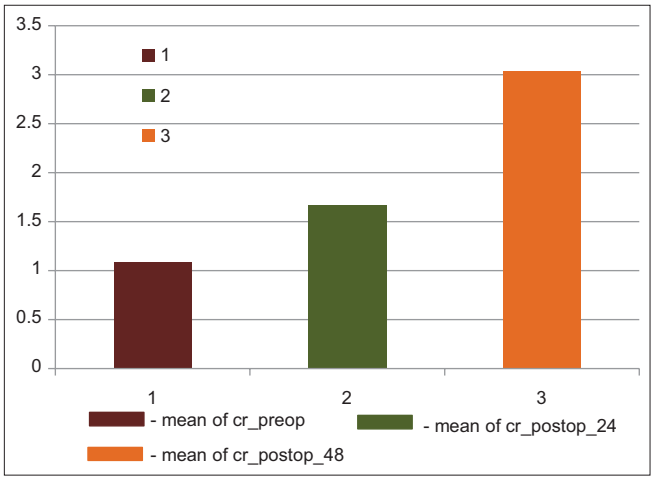

Fig. 2: Bar diagram showing the mean of creatinine preop and postop (24, 48 hours) values for patients with acute kidney injury

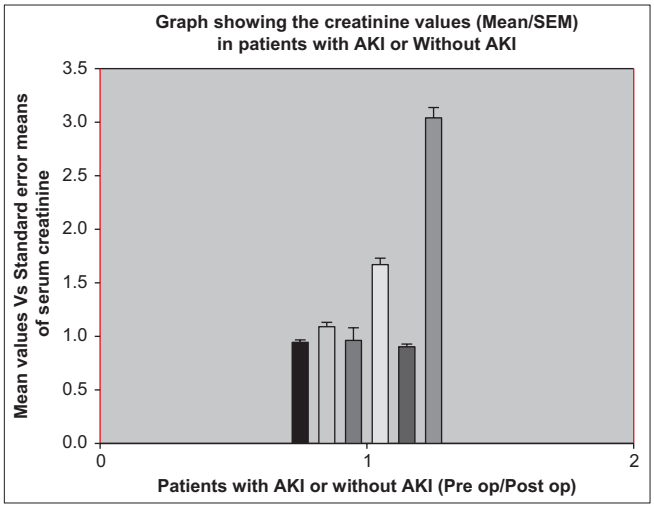

Fig. 3: Graph showing the comparative mean and standard error mean creatinine values in patients with acute kidney injury (AKI) or Without AKI

Even very small increases in serum creatinine have been demonstrated to be associated with adverse effects in hospitalized patients over the past decade. There is also a substantial decrease in survival due to minimal changes in serum creatinine in the postoperative stage [26]. Diagnosis of AKI is based generally on either RIFLE or the AKIN criteria by monitoring the changes in serum creatinine levels and on the urine output [1].

Unfortunately, the serum creatinine levels do not change until 50% of the kidney function has been lost and it does not depict kidney function until a steady state has been reached. Furthermore, serum creatinine levels start to increase 2–4 days after CABG. Due to above-mentioned reasons, serum creatinine is considered to be a delayed marker of AKI [24]. The identification of reliable biomarkers that allow earlier diagnosis of AKI in the postoperative period may increase the success of therapeutic interventions [25].

In the present study, the mean serum creatinine values 24 h post-operatively in patients who developed AKI was higher than that of patients who did not develop AKI. As per the results of hypothetical testing in the current study, the postoperative serum creatinine values at 24 h after the surgery was statistically higher than the preoperative values at 5% significance level (p=0.04). The serum creatinine values 48 h after the surgery was statistically higher than the pre-operative values at 1% significance level (p=0.001). As noticed, the serum creatinine values 48 h after surgery is highly significant (p=0.001) when compared to the serum creatinine values 24 h after surgery. Serum creatinine is an inadequate and delayed marker of AKI. More than 50% of the renal function must be lost before a rise in serum creatinine level is detected. Unfortunately, the diagnostic and staging criteria (RIFLE and AKIN criteria) of AKI are based on levels of serum creatinine. By the time renal dysfunction is diagnosed by the increase in serum creatinine levels, satisfactory clinical intervention is not possible. Even a small rise in creatinine level of about 0.2–0.3 mg/dl is associated with increase in morbidity and mortality after cardiac surgery. And also, serum creatinine is affected by dilutional effect of total body water in the early postoperative period.

Wagener *et al.* [26] found that the serum creatinine levels were significantly elevated 48 h after cardiac surgery in adult patients with AKI. Serum creatinine is increased by 50% 2–3 days after cardiac surgery in children with AKI. Mishra *et al.* [27] showed that serum creatinine was elevated 1–2 days after CABG in children. Bennet *et al.* [28] showed that serum creatinine was significantly elevated 48, 72, and 96 h in children who developed AKI after cardiac surgery. Prabhu *et al.* [29] showed increase in creatinine by 50% from baseline occurred at 24 h and 48 h after CABG in adult patients. All the above mentioned studies showed that serum creatinine increased only 1–3 days after cardiac surgery. In this present study also the serum creatinine levels were significantly elevated at 48 h (p=0.001) after surgery. Among the 80 patients who have undergone CABG, 5 surgeries were done using on-pump technique (cardiopulmonary-CPB) and the rest of them were off-pump technique. Out of 5 patients who had on-pump CABG, 4 of them have developed AKI. CPB is considered to be one of the most important causes of AKI in patients undergoing CABG. Increased duration of CPB and aortic clamping increase the severity of renal injury. Patients with the bypass time greater than 90 min showed more pronounced kidney injury than those with bypass time less than 70 min. Several studies have shown that off-pump technique is associated with lesser incidence of AKI. In this present study, out of 75 patients who underwent off-pump CABG, only 6 patients have developed AKI.

CONCLUSION

The serum creatinine values 48 h after surgery is highly significant when compared to the serum creatinine values 24 h after surgery. Serum creatinine is an inadequate and delayed marker of AKI. More than 50% of the renal function must be lost before a rise in serum creatinine level is detected. Even a small rise in creatinine level of about 0.2–0.3 mg/dl is associated with increase in morbidity and mortality after cardiac surgery. And also, serum creatinine is affected by dilutional effect of total body water in the early postoperative period. CPB is considered to be one of the most important causes of AKI in patients undergoing CABG. Increased duration of CPB and aortic clamping increase the severity of renal injury. Patients with the bypass time greater than 90 min showed more pronounced kidney injury than those with bypass time less than 70 min.

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AUTHOR'S CONTRIBUTION

Author BDD performed the work, drafted the manuscript, compiled information from the literature, performed the statistical analysis and designed the figures and tables.

CONFLICT OF INTEREST

The authors declared "No conflict of interest."

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript and/or the Supplementary Files.

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