A Correlation Study between Plasma Neutrophil Gelatinase Associated Lipocalin and Serum Creatinine in Cardiac Surgery Patients

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Abstract

Background & objectives: Neutrophil Gelatinase Associated Lipocalin NGAL predicts Acute Kidney Injury earlier than creatinine in cardiac surgery patients. This study aims at understanding the correlation between the two biomarkers.

Methods: 53 patients who underwent major cardiac surgery were included in the study. Venous blood samples were collected before surgery and at 4 hours after surgery to estimate plasma NGAL and before surgery, at 4 hours, 24 hours, 48 hours and 72 hours after surgery from the patients to estimate serum creatinine. Correlation analysis was done between NGAL and creatinine using Pearson Correlation Coefficient.

Results: The correlation coefficients for plasma NGAL values at 4 hours after surgery with the serum creatinine values were r = 0.87 at 4 hours, r = 0.86 at 24 hours, r = 0.91 at 48 hours and r = 0.87 at 72 hours after surgery.

Interpretation: The correlation coefficient values shows that plasma NGAL values at 4 hours after surgery were highly correlated with the serum creatinine values at 4 hours, 24 hours, 48 hours and 72 hours after surgery.

Conclusion: This study shows that NGAL values are highly correlated with creatinine values.

Keywords: NGAL, Creatinine, Aki, Cardiac Surgery

Introduction

AKI is considered as a syndrome that occurs due to different causative factors and in varied clinical settings. The clinical manifestations may vary from a mild elevation in serum creatinine to anuria[1]. An acute deterioration in renal function is a common complication following cardiac surgery, with an incidence of 7.7% to 42% depending on the criteria used to define AKI[2-6]. AKI may be accompanied by complications such as increased duration of intensive care and stay at hospital, requirement of dialysis and mortality[7]. AKI that requires dialysis occurs in 5% of the patients following cardiac surgery and is considered as the strongest risk factor for death [2-6].

AKI is mostly asymptomatic and arriving at the diagnosis depends on functional biomarkers such as serial serum creatinine measurements[1]. However serum creatinine is not reliable in indicating AKI because of different reasons. Serum creatinine cannot depict kidney function in an accurate manner and also may take many days[8-11]. But, studying the early response of the kidney to acute injury has led to the discovery of different potential biomarkers. Neutrophil Gelatinase Associated Lipocalin (NGAL) is considered one among them[1].

A number of investigators have studied NGAL as an early biomarker for AKI in various clinical settings like heart surgery, intensive care, nephropathy following contrast administration and transplantation of kidney.

NGAL has shown to satisfy characteristics of an ideal AKI biomarker such as non-invasiveness, rapidity of measurements, sensitive to facilitate early detection and amendable to clinical assay platforms[1]. This study highlights the correlation of NGAL with creatinine in patients undergoing cardiac surgery.

Materials and Methods

This prospective study was done at the Department of Cardiothoracic and Vascular Surgery, SRMC & RI. 53 patients in the age group of 18 - 60 years posted for major cardiac procedures such as coronary artery bypass grafting, cardiac valve repair or replacement, repair of congenital heart defects/large septal defects with or without cardiopulmonary bypass were included in the study. The patients of age group less than 18 years and greater than 60 years, pre-existing renal disease, malignancies, neurological and endocrine surgeries, emergency surgeries were not included in the study. The study was conducted for a period of 8 months. Venous samples were collected before surgery (to establish a baseline value) and at 4 hours after surgery to estimate plasma NGAL levels and venous samples were collected before surgery (to establish a baseline value) and at 4 hours, 24 hours, 48 hours and 72 hours after surgery to estimate serum creatinine. The blood samples were collected in EDTA tubes for plasma NGAL and gel tubes for serum creatinine estimation. The blood samples for plasma NGAL were centrifuged immediately and for serum creatinine half an hour after collection. The samples were centrifuged at 3000 rpm for 15 min. The plasma and the serum were separated and preserved in vials at -70^0 C. Serum creatinine was measured by modified Jaffe kinetic method and plasma NGAL by ELISA.

Results

Pearson correlation coefficient was used to estimate the relationship between the two variables, plasma NGAL and serum creatinine. Table 1 shows the mean values of NGAL and creatinine preoperatively and postoperatively. Table 2 shows the correlation matrix between NGAL and creatinine at different time intervals.

Table 1: Mean value of plasma NGAL and serum creatinine preoperative and postoperative

Variable	Mean value	SD	Unit
NGAL preop	115.40	40.21	ng/ml
NGAL postop 4 hrs	181.90	63.88	ng/ml
Creatinine preop	1.04	0.19	mg/dl
Creatinine postop 4 hrs	1.07	0.19	mg/dl
Creatinine postop 24 hrs	1.06	0.30	mg/dl
Creatinine postop 48 hrs	1.13	0.32	mg/dl
Creatinine postop 72 hrs	0.96	0.24	mg/dl

Table 2: Correlation Matrix showing the relationship between NGAL and creatinine.

	NGAL Postop 4	Creatinine Postop 4	Creatinine Postop 24	Creatinine Postop 48	Creatinine Postop 72
NGAL Postop 4	1.00				
Creatinine Postop 4	0.87	1.00			
Creatinine Postop 24	0.86	0.92	1.00		
Creatinine Postop 48	0.91	0.94	0.96	1.00	
Creatinine Postop 72	0.87	0.94	0.98	0.96	1.00

Table: 3 Characterizations of Pearson correlation coefficient

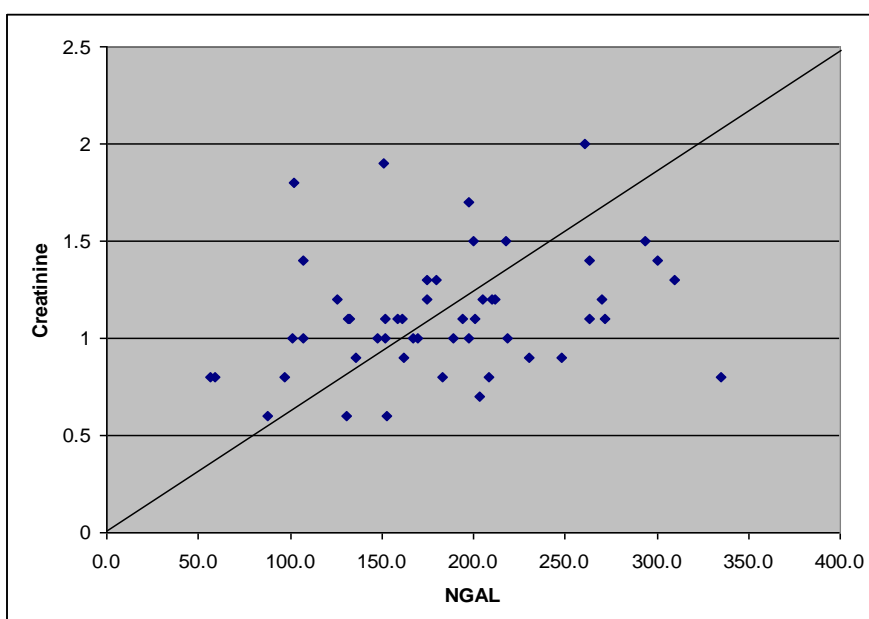| Correlation coefficient r	Correlation level
0.9 to 1	very high correlation
0.7 to 0.9	high correlation
0.5 to 0.7	moderate correlation
0.3 to 0.5	low correlation
0 to 0.3	little if any correlation

Fig. 1: Correlation Plot - NGAL postop (4 hrs)& Creat postop (4 hrs)

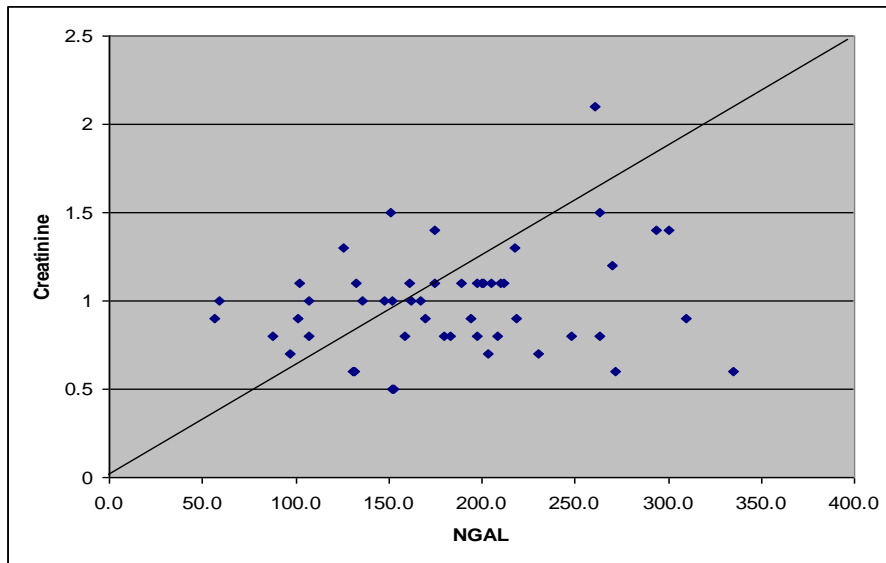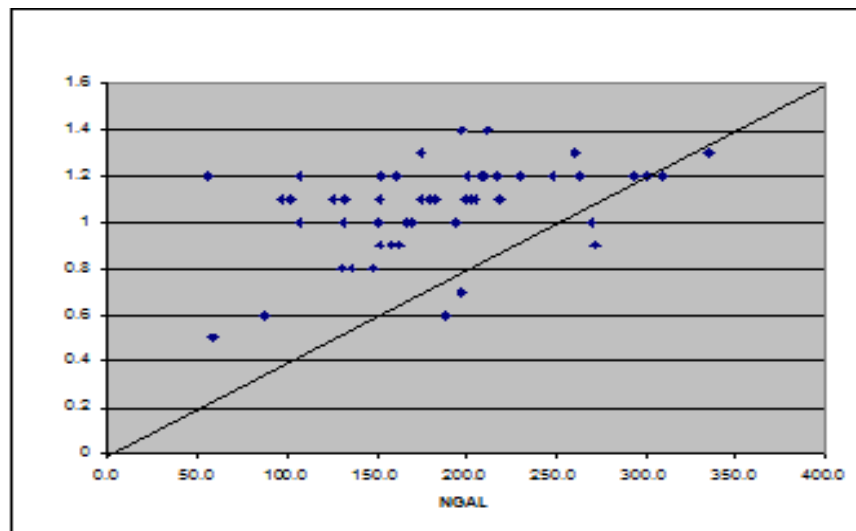**Fig. 2: Correlation Plot - NGAL postop (4 hrs) & Creat postop (24 hrs)**

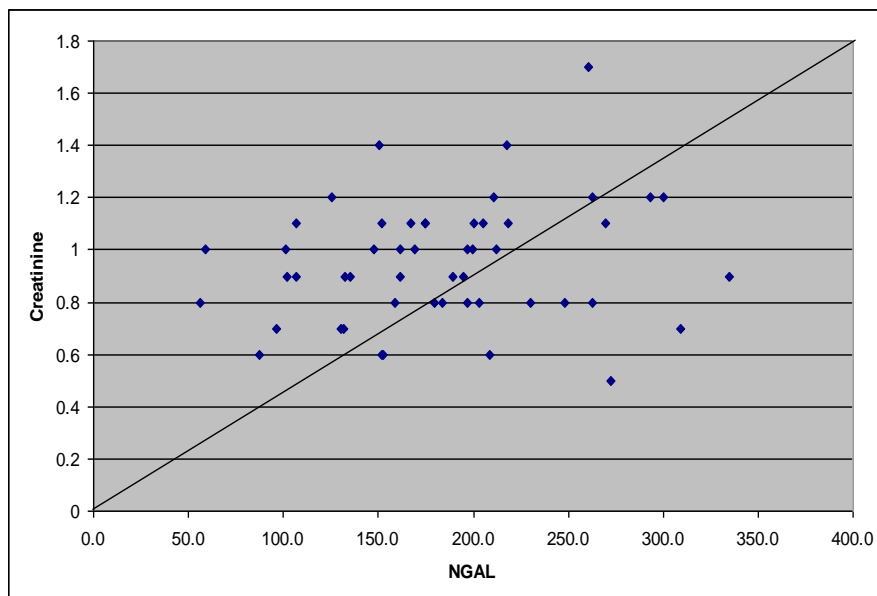**Fig. 3: Correlation Plot - NGAL postop (4 hrs) & Creat postop (48 hrs)**

Fig. 4: Correlation Plot- NGAL postop (4 hrs) & Creat postop (72 hrs)

Discussion

NGAL is being recently studied to predict AKI earlier, whereas the conventional biomarker creatinine is a delayed marker. It is imperative that we understand the correlation between these two biomarkers. Table 3 shows the characteristics of Pearson correlation coefficient. Correlation coefficients estimate the strength and direction of relationship between two variables. A positive coefficient indicates the values of one variable vary in the same direction as the other variable. A negative coefficient indicates the values of the variables vary in opposite directions.

The plasma NGAL values at postoperative 4 hours highly correlated with the postoperative 4 hours serum creatinine with correlation coefficient of r = 0.87.Similarly the plasma NGAL values at postoperative 4 hours highly correlated with the postoperative 24 hours serum creatinine with a correlation coefficient of r = 0.86. The correlation coefficient for the plasma NGAL values at postoperative 4 hours and postoperative 72 hours serum creatinine was r = 0.87, which was highly correlated. However the postoperative 4 hours plasma NGAL correlated very highly with the postoperative 48 hours serum creatinine with a correlation coefficient of r = 0.91. This implies that the information what we get from serum creatinine measured at 48 hours after surgery is obtained from plasma NGAL as early as 4 hours.

A prospective study was done by Mishra et al in 71 children who underwent elective cardiac surgery, in which NGAL was estimated in both urine and plasma samples collected at frequent intervals for 5 days after cardiac surgery. This study showed high correlation between NGAL and creatinine[12].

Wagener et al in 2006 found that urinary NGAL levels were elevated within 1 hour and remained significantly higher at 3, 18 and 24 hours in adult patients who developed acute renal dysfunction postoperatively following cardiac surgery and NGAL values correlated highly with creatinine[13]. Dent et al in 2007 did a cross sectional pilot study to find out whether NGAL is a predictor of AKI in children who underwent cardiac surgery and the correlation between the NGAL values measured by ELISA and a point of care device, TRIAGE NGAL device. Further a study was conducted in a larger sample using the TRIAGE NGAL device alone to measure plasma NGAL. The values were raised at 2 hours and were significantly raised till 24 hours postoperatively. The plasma NGAL at 2 hours after the surgery was found to be an independent predictor of AKI and strongly correlated with the duration of AKI and the length of hospital stay[14].

In 2009, Tuladhar et al emphasized the utility of both plasma and urinary NGAL in predicting AKI in adult patients after cardiac surgery. They showed that there was a significant increase in both plasma and urinary NGAL levels at 2 hours after surgery and there was high correlation between NGAL and creatinine [15].

NGAL is a powerful early biomarker of AKI that precedes the increase in serum creatinine by several hours to days. Several studies have demonstrated that both urine and serum NGAL correlated with serum creatinine [14]. The findings in the present study show that there is high correlation between plasma NGAL levels and serum creatinine concentration in the patients who developed AKI which is represented by change in serum creatinine concentration.

Abbreviations

NGAL Neutrophil Gelatinase Associated Lipocalin
AKI Acute Kidney Injury

Conflict of Interest: None
Source of Support: Nil

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