Early detection of acute kidney injury by measuring urinary neutrophil- gelatinase associated Lipocalin after cardiopulmonary bypass in cardiac surgery

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الإكتشاف المبكر للخلل الحاد بوظائف الكلى بقياس معامل الليبوكالين المرتبط بجيلاتينيز النيوتروفيل البولي بعد جراحات القلب المستخدمة لماكينة القلب و الرئة الصناعية

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To my Parents, my lovely wife and my daughters for their enormous support and love; They are always inspiring.

<u>Acknowledgment</u>

"FIRST OF ALL THANK ALLAH"

Abstract

Acute kidney injury (AKI) occurs frequently after cardiopulmonary bypass (CPB) and cardiac surgery (Cardiac Surgery Associated CSA-AKI)occurring in up to 30% of all patients with increased morbidity, mortality,duration of intensive care treatment and more complicated hospital course.

Currently used biomarkers of renal function (as urea, creatinine and estimated creatinine clearance) provide poor estimates of underlying changes in glomerular filtration rate and do not serve as early predictive biomarkers of AKI and the diagnosis is usually confirmed after 36 - 48 hours after occurrence of AKI.

The aim of this work is to study the utility of a novel biomarker urinary Neutrophil Gelatinase–Associated Lipocalin (uNGAL) as early predictorof CSA-AKI.

This study was conducted in two settings at cardiac surgery departments in Ain Shams University Hospital, Cairo, El Minia University Hospital, El Minia in Egypt and in Santa Croce Hospital, Cuneo in Italy and included 100 adult patients undergoing cardiac surgery using CPB.

The results showed that uNGAL within 2 hours after the end of surgery is very useful in early detection of CSA-AKI.So it was concluded that uNGAL can serve as early predictor of CSA-AKI.

Key words:

- Cardiac surgery
- CPB (Cardio-pulmonary Bypass)
- AKI (Acute kidney injury)
- CSA-AKI (Cardiac surgery associated - Acute kidney injury)
- NGAL (Neutrophil Gelatinase Associated Lipocalin)

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List of abbreviations

Abbreviation	Description	Abbreviation	Description
ACEI	Angiotensin Converting Enzyme Inhibitors	K	Potassium
ACT	Activated Clotting Time	kg	Kilogram
ADQI	Acute Dialysis Quality Initiative	L	Liter
AKI	Acute Kidney Injury	L-FABP	liver-type fatty acid-binding protein
AKI-D	Acute Kidney Injury requiring Dialysis	LV	left ventricular
AKIN	Acute Kidney Injury Network	M	Male
ARB	Angiotensin Receptor Blockers	MDRD	Modification of Diet in Renal Disease
ARF	Acute Renal Failure	Mg	Magnesium
ATN	Acute Tubular Necrosis	mg	Milligram
AUC	Area Under the Curve	min	Minute
BMI	Body Mass Index	mL	Milliliter
BP	Blood Pressure	mm	Millimeter
BUN	Blood Urea Nitrogen	μmol	Micro Mole
Ca	Calcium	mmHg	Millimeter Mercury
CABG	Coronary Artery Bypass Graft	Na	Sodium
C&G	Cockcroft-Gault equations	ng	Nanogram
CHD	Congenital Heart Disease	NGAL	Neutrophil Gelatinase Associated Lipocalin
CHF	Congestive Heart Failure	uNGAL	urinary Neutrophil Gelatinase Associated Lipocalin
CI	Confidence Interval	NPO	Nothing by mouth
CL	Chloride	NPV	Negative Predictive Value
CKD	Chronic Kidney Disease	NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
CNS	Central Nervous System	OPCAB	Off Pump Coronary Artery Bypass surgery
COPD	Chronic Obstructive Pulmonary Disease	PLT	Platelets
CPB	Cardio-Pulmonary Bypass	PMNL	Polymorph Nuclear Leucocyte

List of abbreviations

Cr	Creatinine	pO2	Partial pressure of Oxygen
CSA-AKI	Cardiac Surgery Associated Acute kidney injury	PPV	Positive Predictive Value
CVP	Central venous pressure	PT	Prothrombin Time
dL	Deciliter	PVD	Peripheral Vascular Diseases
DM	Diabetes Mellitus	RIFLE	Risk, Injury, Failure, Loss, End Stage Kidney Disease
eCrCL	estimated Creatinine Clearance	ROC	Receiver Operator Characteristic
ECG	Electro Cardio Graphy	RRT	Renal Replacement Therapy
EF	Ejection Fraction	S.Cr	Serum Creatinine
eGFR	Estimated Glomerular Filtration Rate	SD	Standard Deviation
ELISA	Enzyme Linked Immuno-Sorbent Assay	SIRS	Systemic Inflammatory Response Syndrome
ESKD	End-stage Kidney Disease	SPSS	Statistical Package for Social Science
F	Female	Std	Standard
GFR	Glomerular Filtration Rate	TNF-α	Tumor Necrosis Factor alpha
Hct	Hematocrite level	VO2	Minute oxygen consumption
HTN	Hypertension	UO	Urine Output
IABP	Intra Aortic Balloon Pump	WHO	World Health Organisation
IL	Inter Lukin		
IU	International Unit		
IV	Intra Venous		

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Introduction

Acute renal failure (ARF) or acute kidney injury (AKI), as it is now referred to in the literature, occurs frequently after cardiopulmonary bypass (CPB) and cardiac surgery and isassociated with increased morbidity, mortality, and duration of intensive care treatment.[1–4]

Often AKI manifests as a transient rise in serum creatinine and is managed conservatively; however, a group of patients, often with significant co-morbidity, require temporary renal replacement therapy.[5]

The 30-day mortality of patients requiring dialysis after cardiac surgery is 60%–80%.[6,7]

AKI after cardiac surgery is more common in individuals with pre-existing renal impairment and co-morbidity. Clinical prediction tools have been developed to estimate the chance of AKI after cardiac surgery.These have identified female gender, impaired left ventricular function, insulin-requiring diabetes, emergency surgery, and abnormal baseline renal function as independent predictors of requirement for dialysis.Currently used biomarkers of renal function such as urea, creatinine, estimated creatinine clearance, and urine output provide poor estimates of underlying changes in glomerular filtration rate and do not accurately predict the likelihood of postoperative AKI or serve as early marker of impending acute renal dysfunction.[8–11]

Although serum creatinine is routinely used as a marker of renal function, it performs poorly in the immediate postoperative period. This is mainly due to hemodilution resulting from CPB.This often results in a fall in serum creatinine even in the presence of significant renal injury. More importantly, serum creatinine usually rises only after 24–36 hours after renal tubular damage and therefore does not fulfill the criteria for an early predictive biomarker of AKI.[12]

Introduction

Thus, there is a need for rapidly available, sensitive, and specific biomarkers for AKI that would allow early prediction at a time when intensive care optimization can be performed.Early intervention is likely to be of benefit because experimental studies of AKI have demonstrated that novel therapies designed to reduced ischemic renal injury are most effective when administered early in the time course of injury.

Thus, the ability to detect renal dysfunction at the earliest possible stage is important in the development of such treatments.

Recently, a proteomic approach in a murine model of renal injury demonstrated that neutrophil gelatinase–associated lipocalin (NGAL)-1 is consistently upregulated in the kidney and appears in the urine within a few hours of injury. [13–15]

Aim of the Work

The aim of this work is to study the utility of a novel biomarker urinary Neutrophil Gelatinase–Associated Lipocalin (uNGAL) as early predictor (within 2 hours after the end of surgery) of acute kidney injury (AKI) in adult patients undergoing cardio-pulmonary bypass (CPB) for cardiac surgery.