

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

بسم الله الرحمن الرحيم





MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



Ain Shams University Faculty of Medicine

Department of Anesthesia, Intensive Care & Pain Management

Neutrophil Gelatinase-associated Lipocalin as a Biomarker for Predicting Acute Kidney Injury After Coronary Artery Bypass Grafting

Thesis
Submitted for Partial Fulfillment of M.D. Degree in
Anesthesiology

By

Haitham Mohy El Din Mahmoud Othman

M.B.B.Ch, M.Sc., Anesthesiology, Faculty of Medicine, Ain Shams University

Supervised by:

Prof. Dr. Alaa Eid Mohamed Hassan

Professor of Anesthesiology, Intensive Care and pain management Faculty of Medicine - Ain Shams University

Prof. Dr. Mayar Hassan El Sersi

Assistant Professor of Anesthesiology, Intensive Care and pain management

Faculty of Medicine - Ain Shams University

Dr. Ahmed kamal Mohamed Ali Soliman

Lecturer of Anesthesiology, Intensive Care and pain management Faculty of Medicine - Ain Shams University

Dr. Dalia Fahmy Emam

Lecturer of Anesthesiology, Intensive Care and pain management Faculty of Medicine - Ain Shams University

> Faculty of Medicine Ain Shams University 2020



First of all, all gratitude is due to **GOD** almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Prof. Dr. Alaa Eid Mohamed Hassan**, Professor of Anesthesiology, Intensive Care and pain management, Faculty of Medicine - Ain Shams University, for her supervision, continuous help, encouragement throughout this work and tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her guidance and supervision.

I would like also to express my sincere appreciation and gratitude to **Prof. Dr. Mayor Hassan** ., Professor of Anesthesiology, Intensive Care and pain management, Faculty of Medicine - Ain Shams University, for his continuous directions and support throughout the whole work.

I cannot forget the great help of **Dr. Ahmed Kamal & Dr. Dalia Fahmy**, Lecturers of Anesthesiology, Intensive Care and pain management, Faculty of Medicine - Ain Shams University, for their invaluable efforts, tireless guidance and for her patience and support to get this work into light.

Words fail to express my love, respect and appreciation to my wife for her unlimited help and support.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Haitham Mohy Eldin.

List of Contents

	Page	
Acknowledgment		
List of Abbreviations		
List of Figures		
List of Tables		
Introduction		
Aim of The study		
Review of Literature	3	
1. Acute kidney injury after coronary artery		
bypass graft surgery	. 4	
2. Preoperative risk factors of acute kidney inju		
after cardiac surgery	•	
3	21	
4	30	
Patients and Methods	38	
Results	48	
Discussion	70	
Summary	90	
Conclusion	94	
Recommendations	96	
References	98	
Arabic Summary		

List of Abbreviations

ACE: angiotensin converting enzyme

ACx: Aortic cross clamping

ADQI: Acute disease quality initiative

AKI: Acute kidney injury

AKIN: Acute kidney injury network

ARB_S: Angiotensin receptor blocker

ARF: Acute renal failure

ASA: American Society of Anesthesiologist

AUC: Area under the curve

CABG: Coronary artery bypass grafting

CAD: Coronary artery disease

CIN: Contrast induced nephropathy

CKD: Chronic kidney disease

CPB: Cardiopulmonary bypass

CRS: Cardiorenal syndrome

CSA-AKI: Cardiac surgery-associated acute kidney injury

CVP: Central venous pressure

FDA: Food and drugs administration

GDT: goal directed therapy

GFR: Glomerular filtration rate

HR: Heart rate

ICU: intensive care unit

KDIGO: Kidney Disease: Improving Global Outcomes

LVEF: Left ventricular ejection fraction

MAP: Mean arterial pressure

NAC: N-acetylcysteine

NGAL: Neutrophil gelatinase-associated lipocalin

NSAID: Non-steroidal anti-inflammatory

OPCAB: Off pump Coronary artery bypass

PRBCS: Packed red blood cells

RCT: Randomized controlled trial

RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease

RIPC: Remote ischemic preconditioning

ROC: Receiver operating characteristic

ROS: Reactive oxygen species

RRT: Renal replacement therapy

SCr: Serum creatinine

TEA: Thoracic epidural analgesia

UOP: urine output

(Cont.)

List of Figures

Fig.	Title	Page
1	The RIFLE classification separates criteria for	9
	serum creatinine and urine output (UO)	
2	AKIN classifications for acute kidney injury	10
3	Pathophysiology of cardiac surgery-associated acute	13
	kidney injury.	
4	Receiver operator characteristic curves	44
5	The site of NGAL production in the nephron	52
6	mean age in acute kidney injury and no acute	65
	kidney injury patients	
7	Mean value of serum creatinine in acute	68
	kidney injury and no acute kidney injury	
	patients	
8	Mean value of plasma neutrophil gelatinase-	69
	associated lipocalin in acute kidney injury and	
	no acute kidney injury patients	
9	Receiver-operating curve (ROC) curve	70
	of NGAL levels (cutoff value = 145	
	ng/mL) on 6 hrs postbypass for diagnosis of	
	kidney injury according to the KDIGO	
	criteria.	

List of Tables

Table	Title	Page
1	KDIGO criteria for AKI diagnosis	11
2	Preoperative risk factors associated with	15
	development of acute kidney injury	
3	Intraoperative risk factors associated with	19
	development of acute kidney injury.	
4	postoperative factors contributing to the	27
	development of acute kidney injury	
5	Vasoactive agent and cytoprotective therapy	30
	used for protection from acute kidney injury	
6	Basic demographics and clinical data of	64
	patients	
7	Comparison of aortic and cross clamping	
	time in acute kidney injury and no acute	
	kidney injury patients	

Introduction

Acute kidney injury is a frequent complication after cardiac surgery. According to the literature and the various definitions of acute kidney injury, cardiac surgery associated kidney injury may concern 1% to 30% of the patients. Mortality raises from 1% up to 50% for patients who undergo renal replacement therapy following cardiac surgery (Thiele et al., 2015).

Early detection of renal dysfunction is often presented as a "holy grail" because it could allow interventions (both diagnostic and therapeutic) to prevent evolution to renal failure (Bataille et al., 2017).

Serum creatinine reflects the balance between the synthesis of creatinine and its excretion by the kidney. Creatinine production in the body varies with muscle mass, physical activity, protein intake, and catabolism while creatinine excretion is dependent on the glomerular filtration rate (GFR). The serum creatinine and GFR are inversely and exponentially related. Halving of GFR implies that there will be doubling of creatinine concentration. There are several limitations for creatinine as a marker of kidney injury in acute perioperative situations. However, it has a poor,

predictive accuracy for kidney injury, particularly in the early stages of AKI (Mcilroy & Sladen, 2015).

Neutrophil gelatinase-associated lipocalin (NGAL) is an iron-transporting glycoprotein which accumulates in the kidney tubules and urine after nephrotoxic and ischemic insults. This glycoprotein increases 3–4-fold within 2–3 h and up to 10,000-fold by 24 h of renal insult. NGAL has been proposed as an early, sensitive, noninvasive biomarker for AKI. NGAL measured in the immediate postoperative period is an excellent predictor of AKI following adult cardiac surgery (Jain et al., 2016).

In this study we measured both NGAL and serum creatinine to predict renal adverse outcomes in patients undergoing elective CABG.

Aim of the study

The aim of this study is to determine serum neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker in predicting AKI in patients undergoing coronary artery bypass grafting(CABG).

Chapter one:

Acute Kidney Injury after Coronary artery bypass graft surgery

Complicated cardiac surgery and major non-cardiac surgery are associated with significant morbidity and mortality and strong correlation exists between the development of in-hospital complications and survival. One of these is acute kidney injury (AKI) which is independently associated with morbidity and mortality in a wide range of surgical settings (*O'Connor et al.*, 2016).

Acute kidney injury (AKI) is a condition that is characterized by a sudden deterioration of kidney function as indicated by a reduced glomerular filtration rate (GFR). cardiac surgery is considered the second most common cause of AKI in the intensive care unit (ICU) (*Mao et al.*, 2013).

Moreover, postoperative AKI is associated with long-term adverse events including chronic kidney disease and late mortality. Furthermore, even in cases of apparent recovery of renal function at hospital discharge, persistent decrease of glomerular filtration rate (GFR) with respect to