



## Impact of Oral Nicorandil Intake on Incidence of Acute Kidney Injury in Diabetic Patients with Renal dysfunction Undergoing Elective Percutaneous Coronary Intervention

#### A Thesis

Submitted In Partial Fulfillment of the Requirement of Master Degree in Cardiology

By

#### **Mahmoud Mohamed Rabea**

M.B.B.Ch. Cairo University

#### Supervised by

#### Prof. Dr. Walaa Adel Abdel Halim

Professor of Cardiology Faculty of Medicine - Ain Shams University

#### Prof. Dr. Mohamed Abdel Samie

Associate Professor of cardiology Faculty of medicine -Ain Shams University

#### Prof. Dr. Ashraf Salem Ibrahim

Associate Professor of cardiology Military Medical Academy

Faculty of medicine - Ain Shams University 2020



سورة البقرة الآية: ٣٢



First of all, all gratitude is due to Allah 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 **Prof. Dr. Walaa Adel,** Professor of Cardiology 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. Mohamed Abdel Samie**, Associate Professor of cardiology Faculty of medicine-Ain Shams University, for his continuous directions and support throughout the whole work.

I would like also to express my sincere appreciation and gratitude to **Prof. Dr. Ashraf Salem Ibrahim**, Associate Professor of cardiology Military Medical Academy, for his continuous directions and support throughout the whole work.

#### Mahmoud Mohamed Rabea

## **List of Contents**

Title Page N	Vo.
List of Tables	iv
List of Figures	v
Introduction	1
Aim of Work	4
Review of Literature	
• Acute Kidney Injury in Elective Pci	5
• Pevention of Contrast-Induced Acute Ki	dney Inhury19
Diabetic Nephropathy	35
• Nicorandil in Ischemic Heart Disease	54
Subjects and Methods	69
Results	78
Discussion	98
Conclusion	111
Recommendation	112
Summary	113
References	115
Master Sheet	153
Arabic Summary	168

#### List of abbreviations

PCI : Percutaneous coronary angiography : CI-AKI : Contrast-induced acute kidney injury

CHF : Congestive heart failureCKD : Chronic Kidney Disease

**MDRD** : Modification of diet in renal disease

**ROS** : Reactive oxygen species

**CIN** : Contrast-induced nephropathy

**ATP** : Adenosine triphosphate

NO : Nitric oxide

**DM** : Diabetes mellitus

**IABP** : Intra-aortic balloon pumb

**eGFR** : estimated glomerular filtration rate

HOCM : High-osmolar contrast media
LOCM : Low-osmolar contrast media
IOCM : Iso-osmolar contrast media

**AKI** : acute kidney injury

ESC : European society of cardiology
AHA : American heart association
RCT : randomized controlled trial

EBP : extracorporeal blood purificationIDF : International diabetes federationADA : American diabetes association

WHO : world health organizationGDM : gestational diabetes mellitusHIV : Human immunodeficiency virus

**AIDS** :Acquired immune deficiency syndrome

FPG : fasting plasma glucoseESRD : End-stage renal diseaseDKD : Diabetic kidney disease

**Cr** : Creatinine

s. Cr : Serum creatinine

**ACE** : Angiotensin converting enzyme

ischemic heart diseaseglobal burden of disease

voltage sensitive calcium channel
 ROC : Receptor operated calcium channel
 MLCP : Myosin light chain phosphatase

**BK Channel:** Big potassium channel

**PKG** : cGMP dependent protein kinase

**IP3** : inositol triphosphate

**mPTP** : mitochondrial permeability transition pore

**ATP** : adenosine triphosphate

**PKC**: protein kinase C

**ROC** : Receptor operated calcium channel

# List of Tables

Tab. No.	Title	Page No.
<b>Table (1):</b> M	Mehran Risk SCORE	121
<b>Table (2):</b> V	VBH Risk SCORE	123
<b>Table (3):</b> Id	odinated contrast media in clinical practice	18
<b>Table (4):</b> P	otential pharmacological Prophylactic Agents	30
<b>Table (5):</b> E	SSC 2018 guidelines on prevention of CI-AKI	34
<b>Table (6):</b> S	taging of diabetic nephropathy	47
<b>Table (7):</b>	level of evidence explanation	53
<b>Table (8):</b> C	Comparison between nicorandil group and con	trol55
<b>Table (9):</b> C	Comparison between nicorandil group and con	trol79
<b>Table (10):</b>	Comparison between nicorandil group and co	ntrol82
<b>Table (11):</b>	Comparison between nicorandil group and co	ntrol60
<b>Table (12):</b>	Comparison between nicorandil group and co	ntrol61
<b>Table (13):</b>	Comparison between nicorandil group and co	ntrol63
<b>Table (14):</b>	Comparison between nicorandil group and co	ntrol64
<b>Table (15):</b>	Comparison between pre-procedural data	65
<b>Table (16):</b>	Comparison after 10 days and after 72 hours.	68

# List of Figures

Fig.	No.	Title	Page No.
Figu	re (1):	The mechanisms by which radiographic contrast	t15
Figu	re (2):	Different pathways and networks involved	45
Figu	re (3):	Normal and diabetic nephron with altered renal	46
Figu	re (4):	N- (2-hydroxyethyl) nicotinamide nitrate (ester)	)56
Figu	re (5):	Possible function of ATP-sensitive potassium	59
Figu	re (6):	Possible functions of nitric oxide (NO) in arteri	al60
Figu	re (7):	Nicorandil-induced signaling pathway in ischae	mic65
Figu	re (8):	Adverse reactions considered to be related	68
Figu	re (9):	Gender regarding nicorandil group and control.	79
Figu	re (10)	): Risk factors regarding nicorandil group and co	ontrol81
Figu	re (11)	: LVDV, LVSV and EF regarding nicorandil gr	oup83
Figu	re (12)	): No. stented vessels regarding nicorandil group	86
Figu	re (13)	): Worst lesion type regarding nicorandil group	87
Figu	re (14)	): Serum cretanin regarding nicorandil group	89
Figu	re (15)	eGFR and BUN regarding nicorandil group	91
Figu	re (16)	: Creatinine pre and after 72 hours	93
Figu	re (1 <b>7</b> )	): BUN pre and after 72 hours	93
Figu	re (18)	: K pre and after 72 hours	94
Figu	re (19)	eGFR pre and after 72 hours	94
Figu	re (20)	: Creatinine after 72 hours and after 10 days	96
Figu	re (21)	BUN after 72 hours and after 10 days	96
Figu	re (22)	: K after 72 hours and after 10 days	97
Figu	re (23)	eGFR after 72 hours and after 10 days	97

## Introduction



### **INTRODUCTION**

Contrast-induced acute kidney injury (CI-AKI) is a serious and prevalent side effect of the administration of iodine contrast medium after Coronary angiography or Percutaneous Coronary Intervention procedures.

The European Society of Urogenital Radiology defines contrast-induced acute kidney injury as any of the following (**Kellum J. et al., 2012**):

- Increase in Serum creatinine by more than or equal 0.3 mg/dl within 48 hours.
- Increase in serum creatinine to more than or equal to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days
- Urine volume less than 0.5 ml/kg/h for 6 hours

CI-AKI incidence ranges from 2-5% in the general population to 50% in high-risk patients (**Cheungpasitporn et al., 2014**).

The risk factors for CI-AKI include diabetes mellitus (which is associated with increased risk even in patients with preserved renal function), congestive heart failure (CHF), age > 75, hypertension, hypotension, decreased renal perfusion, female gender, high-osmolar contrast, contrast volume, urgent versus planned PCI and most importantly, chronic kidney disease (CKD) (Mehran R et al., 2004).