Impact of Remote Ischemic Post-Conditioning on Lv Remodeling in Patients With Anterior St-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention

Thesis

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Ayman Mohamed Galal Yehia

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List of Contents

List of Tables

List of Figures

List of Abbreviations

Abb.	Full term
ACE	Angiotensin converting enzyme inhibitors
ACS	Acute coronary syndrome
AKI	Acute kidney injury
AHA/ACC	American Heart Association/American College of Cardiology
ATP	Adenosine triphosphate
BAX	Bcl2-assoicated X protein
BAD	Bcl2-assoicated death promoter
BBB	Bundle branch block
BMS	Bare metal stent
BP	Blood pressure
Ca^{2+}	Calcium ion
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CAPTIM	Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction
CCU	Coronary care unit
CK	Creatine kinase
CKD	Chronic kidney disease

List of Abbreviations

Abb.	Full term
CK-MB	Creatine kinase myocardial band
cTn	Cardiac troponin
CVD	Cerebrovascular disease
DANAMI	The Danish Multicenter Randomized Study on Thrombolytic Therapy versus Acute Coronary Angioplasty in Acute Myocardial Infarction
DM	Diabetes mellitus
ECG	Electrocardiography
EF	Ejection fraction
eNOS	Endothelial nitric oxide synthase
EPO	Erythropoietin
ERK1/2	Extracellular signal–regulated kinases
EXPIRA	Thrombectomy with Export Catheter in Infarct- Related Artery During Primary Percutaneous Coronary Intervention
FH	Family history
FTT	Fibrinolytic Therapy Trialists
GIK	Glucose-insulin-potassium
GP	Glycoprotein
GPCR	G protein-coupled receptor
GSK3ß	glycogen synthase kinase-3ß

List of Abbreviations

Abb.	Full term
h	hour
H^+	hydrogen ions
H_2O_2	Hydrogen peroxide
HF	Heart Failure
HTN	Hypertension
ICH	Intracranial Hemorrhage
IHD	Ischemic heart disease
IPC	Ischemic pre conditioning
IPostC	Ischemic post conditioning
IRA	Infarct related artery
IRI	Ischemia/reperfusion injury
IS	Infarct size
IV	Intravenous
KAI-9803	Inhibitor of protein kinase delta
KATP	ATP-sensitive potassium channels
LA	Left atrium
LAD	Left anterior descending
LBBB	left bundle branch block

List of Abbreviations

Abb.	Full term
LV	left ventricular
LVEDD	Left ventricular end diastolic diameter
LVEDV	Left ventricular end diastolic volume
LVESD	Left ventricular end systolic diameter
LVESV	Left ventricular end systolic volume
LVH	Left ventricular hypertrophy
MAC	Membrane attack complex
MACE	Major adverse cardiac events
MBG	Myocardial blush grade
mg	Milligram
MI	Myocardial infarction
mmHg	millimeter of mercury
MR	mitral regurgitation
MRI	Magnetic resonance imaging
mV	Milli-volt
Na- H	sodium–hydrogen exchange
Na–Ca	sodium–calcium exchange
NAD^+	Nicotinamide adenine dinucleotide

List of Abbreviations

Abb.	Full term
NADPH	Nicotinamide adenine dinucleotide phosphate
NO	Nitric oxide
PAR2	protease-activated receptor type 2
PCI	Percutaneous Coronary Intervention
PDH	pyruvate dehydrogenase
pGC	particulate guanylyl cyclase
pH	Log hydrogen ion concentration
PI3-K	phosphatidylinositol-3-kinase
PKG	cGMP-dependent protein kinase
PMNs	Polymorphonuclear leukocytes
POC	Post conditioning
PR	Peripheral resistance
PTCA	Primary percutaneous transluminal coronary angioplasty
PTP	Permeability transition pore
PVD	Peripheral vascular disease
RIC	Remote ischemic conditioning
RIPC	Remote ischemic preconditioning
RIPostC	Remote ischemic postconditioning

List of Abbreviations

Abb.	Full term
RISK	Reperfusion injury salvage kinase
ROS	Reactive oxygen species
RR	Relative Risk
SC	Subcutaneous
SD	Standard deviation
siRNA	Small interfering RNA
STEMI	ST Segment Elevation Myocardial Infarction
STR	ST-segment resolution
ST–T	ST-segment–T wave
TAPAS	Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study
TDI	Tissue dopple image
TIMI	Thrombolysis in Myocardial Infarction
TLC	Total leukocytic count
TMP	TIMI myocardial perfusion
TNF	Tumor necrosis factors
TNK	Tenecteplase.
tPA	Alteplase
URL	Upper Reference Limit
°C	Degree Celsius

Abstract

Infarct size, reflected by peak CKMB, was non significantly lower in RIPostC group compared to control group (271.93 ± 185.87 vs. 287.67 ± 253.88, respectively; P=0.785).

These results must be weighed in context of the limitations of this study, mainly: The need for a larger sample size for higher power, using more accurate techniques to evaluate LV remodeling and infarct size, as well as following patients for longer periods.

Our study suggests that RIPostC can improve myocardial perfusion and attenuate ischemia reperfusion injury as evidenced by better rates of achieving full STR, and the trend towards less rates of LV remodeling, less peak CKMB, and better MBG results.

Keyword: TIMI myocardial perfusion- Tumor necrosis factors- Tenecteplase.- Alteplase Alteplase- Upper Reference Limit- Degree Celsius.

INTRODUCTION

Ischemic heart disease (IHD) maintains its unrelenting grip as the leading cause of death and disability worldwide. ST segment elevation myocardial infarction is the most serious presentation of atherosclerotic coronary artery disease carrying the most hazardous consequences ***(Bolooki et al., 2010)***. Although primary angioplasty has reduced the risk of mortality as compared with fibrinolysis in ST elevation myocardial infarction, left ventricular (LV) dysfunction still occurs in many patients ***(Keeley et al., 2003).***

The degree of LV dysfunction, the strongest determinant of mortality after STEMI, ***(Halkin et al., 2005)*** has been related to the duration of ischemia, the number of diseased vessels, the completeness of epicardial coronary artery patency and the restoration of microcirculatory flow ***(Ito et al., 1996).*** Nevertheless, abrupt restoration of blood flow causes a lethal injury of myocardial cells that may limit the benefit of such intervention. In pre-clinical studies, the impact of myocardial reperfusion injury accounts for a considerable amount of the final infarct size ***(Yellon et al., 2007)***. Therefore, novel therapeutic strategies were required to protect the heart against acute ischemia/reperfusion injury (IRI) to attenuate cardiomyocyte death, preserve cardiac function, prevent the onset of heart failure, and improve clinical outcomes in patients with IHD.

Murry and colleagues described ischemic pre-conditioning (IPC) extensively ***(Murry et al., 1986)***. The essence of this adaptive interventional method is to induce short periods of local ischemia and reperfusion before target organ ischemia. There is a vast literature on the strong protective effect of IPC, which has been proven by numerous experimental and clinical studies. However, the technique is limited to elective situations in which the onset of ischemia can be predicted. Local preconditioning cannot be used in acute clinical settings such as acute myocardial infarction. It therefore became necessary to develop new techniques suitable for providing protection against unpredictable ischemic events. One option was a modification of the reperfusion period by means of brief coronary artery occlusions and reperfusions applied at the onset of myocardial reperfusion, a phenomenon called ischemic post conditioning (IPostC). The first easily reproducible experimental results on this topic were published in 2003 ***(Zhao et al., 2003b).*** A shortcoming of both preconditioning and postconditioning is the prolongation in operative time, possibly even for a duration of 15–20 min. A further negative aspect is that in the presence of atherosclerosis, these invasive techniques can lead to serious, life-threatening complications, such as plaque rupture.

Przyklenk and colleagues made the intriguing experimental observation that 'brief ischemia in one vascular bed also protects remote, virgin myocardium from subsequent