بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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التوثيق الإلكتروني 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

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INTRODUCTION

Myocardial infarction (MI) occurs when the blood supply to a part of the myocardium is interrupted, which commonly occurs due to an occluded infarct related artery (IRA), following rupture of a vulnerable atherosclerotic plaque. The resulting ischemia and hypoxaemia can lead to damage and death of the myocardium, if left untreated for a sufficient time ***(Armstrong et al., 2013).***

The mainstay of treatment in these patients is immediate reperfusion by primary percutaneous coronary intervention (PCI) or fibrinolytic therapy, however, PCI is regarded to be the treatment of choice ***(Steg et al., 2012).***

Lack of reperfusion at the myocardial tissue level, despite patent IRA after revascularization is attributed to the "no-reflow" phenomenon, which contributes to more tissue damage and is associated with poor functional recovery and worse outcome after acute MI ***(Rezkalla et al., 2017).***

Presence of a definite intracoronary thrombus plays a major role in the slow or no-reflow phenomenon in the IRA after primary PCI, and was found to increase the incidence of in-hospital major adverse cardiac events (MACE) ***(Okamura et al., 2008).***

Based on the hypothesis that microvascular fibrin, vessel wall components, circulating blood cells and fibrinogen participate in the increase of microvascular resistance, it had been postulated that low-dose intracoronary fibrinolytic agent (streptokinase) administration immediately after primary PCI is among the pharmacological modalities for reducing the thrombus burden and improving left ventricular function in patients with acute MI having culprit vessels with high thrombus burden ***(Sezer et al., 2007).***

Aim of the Work

To assess the effect of low dose intracoronary streptokinase (ICSK) during primary PCI in patients presenting with acute anterior wall S-T segment elevation myocardial infarction with a definite thrombus in the left anterior descending artery on clinical, angiographic and echocardiographic outcomes.

MYOCARDIAL REPERFUSION AND NO-REFLOW

Definition of acute myocardial infarction:

The terminology acute myocardial infarction (AMI) means an established myocardial injury (high cardiac troponin values with at least one of them above the 99th percentile upper reference limit) with associated necrosis in the setting of myocardial ischaemia **(*Thygesen et al., 2012*).**

AMI is a result of sudden deprivation of an area of heart muscle of its blood supply by occlusion of the main supplying artery or a sufficient number of its branches by a thrombus burden. Although most of S-T segment elevation myocardial infarction (STEMI) patients are classified into a type 1 MI (with evidence of coronary thrombosis), some STEMI cases can even occur in the absence of obstructive coronary artery disease (CAD) on angiography. Such a scenario is called 'myocardial infarction with non-obstructive coronary arteries' (MINOCA) **(*Agewall et al., 2017*).**

Primary PCI is defined as angioplasty and/or stenting without prior fibrinolytic therapy, and is the preferred therapeutic option when it can be performed expeditiously by an experienced team **(*Steg et al., 2012*).**

Primary PCI significantly reduces mortality for patients with STEMI and has a greater benefit in high-risk patients. The mechanism of benefit for primary PCI may be associated with improved the IRA re-canalization and stabilization of the ruptured atherosclerotic plaque making the post procedural TIMI 3 flow rates in primary PCI trials higher than those demonstrated with fibrinolysis **(*Armstrong et al., 2013*).**

Microvascular damage and no-reflow phenomenon:

Restoration of blood flow to a previously ischemic area causes physiological and anatomical changes, including neutrophil infiltration, tissue edema, microvascular damage, with impairment of microcirculatory flow, causing further injury to the myocardium. Therefore, beside restoring flow in the epicardial infarct artery, an ideal reperfusion strategy in patients with STEMI should focus on adjunctive treatments that reduce the amount of microvascular damage**.** Such phenomenon was referred to as slow flow which was defined as coronary blood flow of less than TIMI 3 without the presence of significant stenosis, dissection or an angiographically observed thrombus distal to the part of the IRA where PCI took place **(*Rezkalla et al., 2017*).**

Pathophysiology involved in such phenomenon is either:

- Capillary structure becomes disrupted in the no-reflow or slow flow zone due to oedema of the tissues, endothelial disruption, microthrombi and neutrophils plugging the capillaries, generation of oxygen-free radicals, complement activation and myocytes contracture caused by reperfusion injury ***(Harrison et al., 2013).***

- Micro-thromboemboli and particles of plaque gruel are thought to be showered downstream after plaque rupture, leading to microvasculature obstruction ***(Mittal, 2014).***

Clinical implications of the No-Reflow phenomenon:

No-reflow phenomenon causes myocytes in the affected area to die and later recovery of function becomes impossible. A large no-reflow area is associated with reduced left ventricular contractile function, also the presence of no reflow predicts acute complications after AMI. No-reflow phenomenon exhibits further risk and make that group of patients the highest-risk subgroup among those undergoing revascularisation, with high risk of early and sustained heart failure and death ***(Hiroshi, 2014).***

A large region of no reflow might impede the ability of the infarct to heal and prevent delivery of pharmacologic agents into that area. The no-reflow phenomenon has been linked to left ventricular remodeling, ventricular arrhythmias, cardiac rupture and even to increased risk of cardiovascular death ***(Hiroshi, 2014).***

Assessment of Reperfusion

I) Non-invasive assessment of reperfusion:

In the very early reports of the use of intracoronary Streptokinase (SK) in treating AMI, *Ganz and his colleagues* described four criteria which make the clinical picture of recanalized occluded coronary artery responsible for an infarction; chest pain relief, ST elevation resolution, release of biochemical markers from injured myocytes and the development of reperfusion arrhythmias ***(Ganz et al., 1981).***

A) ECG as a Marker of Reperfusion:

A strong correlation was found between patency of an IRA and the degree of S-T segment resolution. Patients with complete (≥ 70%) S-T segment resolution have about 90% probability of having a patent IRA. Unfortunately, S-T segment resolution can hardly differentiate between TIMI 2 from TIMI 3 flow, and the percentage of patients who have patent IRA at the time of coronary angiography despite persistent S-T segment elevation can reach 50% in some cases ***(Zeymer et al., 2001).*** False positive ECG diagnosis of failed epicardial reperfusion in many of those patients often indicates poor microvascular perfusion ***(De Lemos and Braunwald, 2001).*** Accordingly, patients with persistent S-T segment elevation despite patent epicardial artery are deemed to be at high risk ***(De Lemos et al., 2000).***

B) Cardiac biomarkers as a marker of reperfusion

Elevated serum Creatine Kinase (CK) and CK-MB levels usually follow revascularization of an occluded IRA, which was explained by washout of cardiac enzymes from injured cells at the time blood flow is restored ***(Ganz et al., 1981).***

Being the most cardiac specific, troponins I and T have been considered as the gold standard for AMI diagnosis ***(Yang and Zhou, 2006).*** High-sensitivity cardiac troponin assays permit use of lower thresholds for the diagnosis of myocardial infarction. Assessment of troponin 72 hours after primary PCI may be used to determine infarct size ***(Chia et al., 2008).***

C) Transthoracic echocardiography (Conventional 2-D or myocardial contrast)

Global systolic function is a good predictor of outcome after AMI and is linearly related to the extent of myocardial necrosis ***(Mollema et al., 2009).*** Echocardiographic derived wall motion score index (WMSI) is a 16-segment model recommended by the American society of cardiology used for segmentation of the left ventricle. The heart is divided into six segments at both the basal and mid-ventricular levels and four segments at the apex. The septum was defined as the attachment of

the wall of the right ventricle to the left ventricle, which is divided at basal and mid-left ventricular levels into antero-septum and infero-septum. Directing counterclockwise, the remaining segments at both basal and mid-ventricular levels are divided into inferior, inferolateral, anterolateral and anterior. Moreover, the apex was divided into septal, inferior, lateral and anterior segments. Each examined heart segment is scored according to the degree of its motion and wall thickening during systole, with using multiple views for confirming, then the following score is applied: 1 (normal), 2 (hypokinesia), 3 (akinesia) and 4 (dyskinesia). WMSI is calculated by dividing the sum of all scores identified by the number of heart segments. It is reasonable, sometimes to add a 17^{th} segment accounting for the apical cap ***(Lang et al., 2005).***

Regarding myocardial contrast echocardiography, it is a good measure of ‘‘no reflow’’ effect. Inert, echo-dense micro-bubbles are injected peripherally to assess capillary blood volume, regions of hypoperfusion or obstruction, left ventricular (LV) dimensions and immediate post-infarct contractile function. It also has a good correlation with angiographic myocardial reperfusion ***(Webb and Redwood, 2007).***

D) Magnetic Resonance Imaging (MRI):

Cardiac MRI is a non-invasive gold standard technique with increasing applications in AMI providing the assessment of function, perfusion and tissue characterization ***(Hundley et al., 2010).*** It can identify both location and size of the infarct and show microvascular pathophysiological processes associated with AMI ***(Ganame et al., 2009).*** It was postulated that hypo-enhancement within bright regions of late Gadolinium enhancement (LGE) on delayed post-contrast sequences, so-called 'dark zones', were areas of no-reflow (**Figure 1**) ***(Nijveldt et al.,2008).***

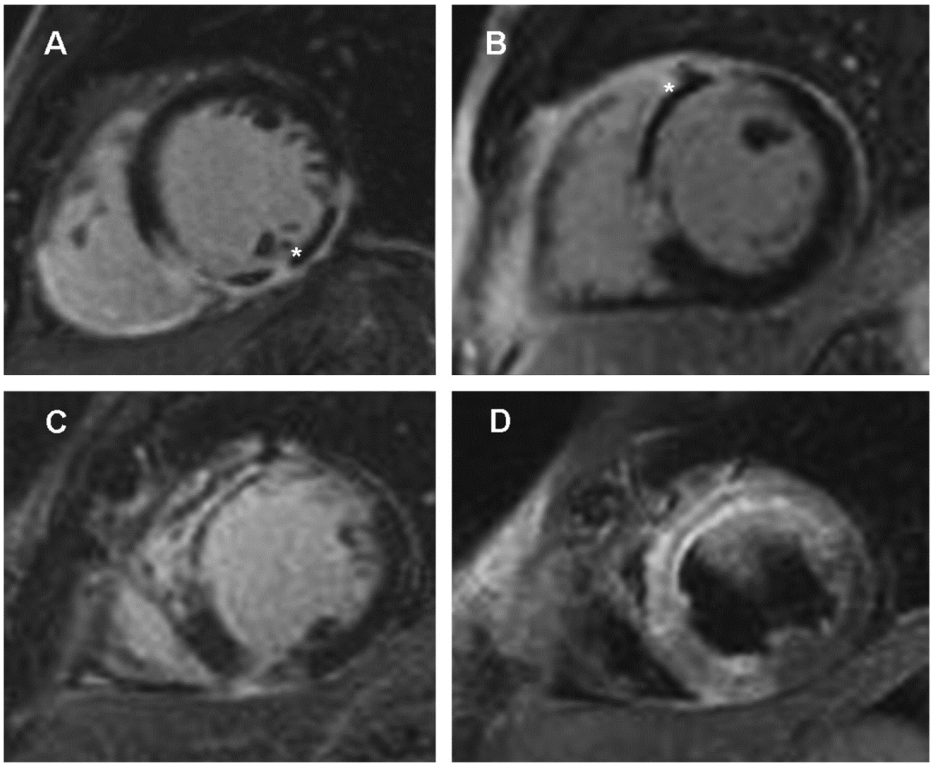

Figure (1): Microvascular damage appears dark (so-called 'dark zones') (white asterisks) in the middle of late gadolinium enhancement, representing the myocardial necrosis on the inferior wall on panel A (note the involvement of right ventricular inferior wall seen as an intense late gadolinium enhancement), and antero-spetal wall on panel B. Panels C and D show the same patient: on C a transmural late gadolinium enhancement on the antero-septal wall with a dark zone is shown, smaller than example B. Panel D represents the T2-weighted sequences of the same patient: inside the oedema (bright signal on anterior and septal wall) can be detected a hypoenhancement core suggesting intramyocardial haemorrhage and corresponding to the dark zone on delayed post-contrast sequence From: MRI in acute myocardial infarction. ***Eur Heart J. Eur Heart J | Published on behalf of the European Society of Cardiology. 2010;32(3):284-293.***