Treatment Strategies of NSTEMI-ACS with Multivessel Disease

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Introduction

The pathophysiology of acute myocardial infarction: STEMI vs NSTEMI

Acute coronary syndrome (ACS) is caused when myocardial blood supply is acutely compromised, which results in prolonged chest pain. The common underlying mechanisms of ACS include erosion or sudden rupture of an atherosclerotic plaque within the wall of a coronary artery. The disrupted plaque consequently stimulates both thrombosis and coagulation through different mechanisms, which end with thrombus formation. The thrombus itself further obstructs the blood flow within the affected coronary artery, with its effect on the myocardium e.g. irreversible necrosis if reperfusion is not re-established.[1]

STEMI-ACS

Acute complete and persistent occlusion of the coronary artery causes ST-segment elevation myocardial infarction (STEMI) and significant myocardial damage which begins at the moment of the blood supply interruption and correlates with the duration of occlusion. The injury spreads from the innermost layer of the myocardium (the sub-endocardium) to the outermost layer (the sub-epicardium) thus involving the full thickness. In patients who survive STEMI, the infarcted muscle is gradually replaced by scar tissue, causing left ventricular (LV) remodeling and deterioration of its pump function which may clinically progress into heart failure.[2]

NSTEMI-ACS

When the coronary artery is incompletely or transiently occluded by a thrombus, the non-ST-segment elevation myocardial infarction (NSTEMI) occurs. These patients may present with no abnormality but only subtle changes on the surface ECGs. The pathophysiology of NSTEMI and the mechanism of thrombus formation is the same as that with STEMI: disruption of plaque fibrous cup and exposing the lipid core to the arterial lumen which stimulates platelet aggregation at the endothelial surface. Fibrinogen bridges the activated platelets by binding the two glycoprotein IIa/IIIb receptors, resulting in the formation of a platelet-fibrin hemostatic plug, which progresses into thrombus formation.[3] Despite incomplete or transiently complete occlusion of the artery in NSTEMI patients, the elevation of cardiac troponin levels reflects myocardial cellular]

damage, which may result from distal embolization of platelet-rich thrombi from the site of a ruptured or eroded plaque. Accordingly, troponin may be seen as a surrogate marker of active thrombus formation.[4]

Prevalence of multivessel disease in NSTE-ACS

Despite the fact that ACS is caused by single (culprit) artery disease and the main treatment goal in primary percutanous coronary intervention (PPCI) is to treat the culprit vessel and to improve myocardial reperfusion, it is well recognized that the prevalence of multi-vessel significant (>50%) disease in STEMI patients could be as high as 80%.[5] Similar prevalence has also been reported in NSTEMI-ACS[1,6,7] and approximately half of patients undergoing PCI have been shown to have multivessel significant coronary stenosis[8], they even dominate ACS in Western European countries.[9,10]

Treatment of multivessel disease in ACS: STEMI vs NSTEMI

STEMI-ACS

Compared with pharmacological reperfusion with thrombolysis for STEMI, PPCI has been shown to be associated with better clinical outcome. Current European and American guidelines recommend PPCI to culprit lesion in stable patients irrespective of the presence of multivessel coronary disease. The remaining non-culprit arteries are recommended for staged PCI treatment or optimal medical therapy.[11-13] The staged treatment is based on the basis of limited spontaneous ischemia or evidence

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for high risk on predischarge noninvasive testing. However, the findings of four Randomized Controlled Trials[14-17] have suggested that a strategy of multivessel PCI, either at the time of PPCI or as a planned, staged procedure, may be beneficial and safe in selected patients with STEMI. These findings, recently forced ACC and AHA to update their guidelines and upgrade the previous Class III (Harm) recommendation in hemodinamically stable patients to a Class IIb recommendation. It now states that PCI of a non-infarct artery may be considered in selected patients with STEMI and multivessel disease who are hemodynamically stable, either at the time of PPCI or as a planned staged procedure.[18]

NSTEMI-ACS

Invasive coronary angiography should be performed in the majority of patients in well-established health care systems for the following objectives:
a) to confirm diagnosis of ACS related obstructive CAD;
b) to identify the culprit artery;
c) to establish the indication for revascularization and to assess the suitability of coronary anatomy for PCI or CABG procedure; and
d) to stratify the patient's short- and long-term risk
(Ref: NSTEMI new guideline). While 20% of NSTEMI-ACS patients have no significant stenosis most of those with obstructive coronary lesions (40-80%) have multivessel CAD.[5,9,10,19]

In contrast to STEMI, determining the culprit artery in NSTEMI is not always feasible in all patients. A coronary lesion should be considered culprit if it fulfills at least two of the following criteria: intraluminal filing defect, plaque ulceration, plaque irregularity, dissection or impaired flow.[20, 21, 22] It has been shown that approximately 40% of patients with NSTEMI-ACS and multiple CAD, have more than one plaque that fulfill the angiographic criteria of a culprit artery[23, 24] and one-quarter of them have one artery completely occluded, which in most is collateralized.[20, 25] Attempts to determine the culprit lesion over and above angiography have been tried.[26], including ST depression on ECG in certain leads, segmental hypokinesia on echocardiography or ventriculography, a provocative test with acetylcholine or ergonovin, and the newer intracoronary imaging, such as optical coherence tomography.[27,28, 29]

A meta-analysis of available observational studies showed that routine full revascularization strategy was associated with a lower risk of death (p=0.001), and lower rate of hospitalization (p<0.001) compared to selective invasive strategy in NSTEMI patients.[30] This is reflected in the ESC guidelines which recommend very high risk NSTEMI-ACS patients for immediate (<2 hours from hospital admission, analogous with STEMI management) complete revascularization, intermediate risk patients for PPCI within 72 hours of admission and low risk patients for non-invasive stress testing.[26]

Despite the discrepancy between the results of the observation studies with the majority[31-36] supportive of complete revascularization compared to the minority that showed no additional effect for full revascularization[37, 38], there are no RCT that has compared the complete vs. incomplete, neither simultaneous vs. staged revascularization, in patients with NSTEMI-ACS. Recently two meta-analyses showed that in patients with NSTEMI and multivessel disease, complete PCI reduced MACE more than in single-vessel PPCI[39, 40]. In view of these observational retrospective studies, current guidelines,[26] have been non-decisive with regards to the ideal treatment strategy of these patients. While a complete revascularization of significant lesions is proposed, it is left in the hand of the operator to decide based on the clinical presentation, comorbidities, complexity of coronary anatomy and lesions, ventricular function, revascularization modality, etc, hence the lack of standardized management strategies.

Declarations of Interest

The authors declare no conflicts of interest.

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