Role of no reflow and microvascular obstruction in the prognostic stratification of STEMI patients

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Abstract

Effective reperfusion of ischemic myocardium is the final aim of both pharmacological and mechanical reperfusive strategies in patients with ST-segment elevation myocardial infarction. More effective reperfusion is related to better prognosis. In contrast, ineffective reperfusion (no reflow) has been showed to be related to an increased rate of adverse events in the flow-up. Several techniques can be used to assess the effectiveness of reperfusion, and the evolved over the last decades according to the treatment methods but also to technological advancements. ST-segment resolution represented the only way to assess reperfusion in the era of pharmacological treatment. Later, angiographic assessment became the gold standard to assess reperfusion after primary percutaneous coronary intervention. In the last years, cardiac magnetic resonance showed improved accuracy and prognostic stratification ability compared with angiography. However, in clinical practice, coronary angiographic still remains the more widely used assessment technique for no reflow. *(Anatol J Cardiol 2018; 19: 00-00)*

Keywords: no reflow, MVO, microvascular obstruction, STEMI, PCI

Introduction

Several invasive and noninvasive techniques can be used to evaluate functional and alterations of the coronary microcirculation after myocardial infarction (MI). The characteristics of each assessment method impact its sensitivity, specificity, and prognostic value of each single index (1). Historically, electrocardiographic evaluation was used to assess myocardial reperfusion. This method, despite still being used in the clinical setting, has been replaced by more accurate indices. In recent years, cardiac magnetic resonance (CMR) has been shown to be superior to angiography for the characterization of tissue damage and for the stratification of prognosis. In contrast, coronary angiography might better define the so-called transient no reflow (NR). Moreover, new invasive methods for the measurement of intracoronary pressures and flow have been suggested to provide improved information regarding the status of microcirculation.

ST-segment resolution (STR)

STR is a more available and the simplest clinical evidence of effective myocardial reperfusion. Lack of STR is suggestive of the occurrence of NR (2). STR can be assessed by either continuous monitoring or static ECG recordings. STR <50% or <70% should be considered indicative of NR. However, despite being the immediately used method for NR assessment, STR is not very accurate. In fact, approximately one-third of patients with myocardial blush grade (MBG) 2 to 3 and TIMI flow grade 3 (which has represented the gold standard definition for no reflow for many years) do not exhibit STR (3), and a consistent proportion of patients with angiographic NR exhibit STR.

Despite these limitations, many studies showed that a rapid and significant resolution of ST-segment elevation during the treatment of STEMI is associated with a better prognosis (4, 5).

A continuous ECG recording, with its ability to evaluate dynamic ST-segment changes, has improved accuracy for STR monitoring, and specific time points for specific grades of STR have been suggested for stratifying the risk of major adverse cardiovascular events (MACE). Recurrent ST-elevations during thrombolysis predict subsequent re-occlusion (6) and eventually poor clinical outcomes (7). However, even small fluctuations of the ST-segment during the first four hours of observation have a negative impact on clinical outcomes (8, 9).

Coronary angiography

For a long time, coronary angiography has been considered the gold standard for NR diagnosis after the introduction of pri-

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Accepted Date: 03.01.2018

DOI:10.14744/AnatolJCardiol.2018.62343

mary percutaneous coronary intervention (pPCI), based on the assessment of the TIMI flow grade. A TIMI flow grade 0-2, which is indicative of NR, can be found in 5%-10% of patients undergoing pPCI for STEMI. However, the achieved angiographic patency of the epicardial culprit coronary vessel may not correspond to effective myocardial reperfusion. Moreover, reperfusion injury may cause damage to the microcirculation, thus impairing effective myocardial reperfusion. Therefore, some studies reported discrepancies between outcomes and angiographic evidence of reperfusion (10, 11). A relatively small study showed significant prognostic risk stratification with STR, whereas TIMI flow grades only showed a trend (4). However, a subsequent larger registry, where data of 10455 patients were analyzed, showed a higher incidence of death and MACE at 30 days and at 1 year, with decreasing post-PCI TIMI flow grades (12).

A development in the angiographic evaluation of NR is MBG. A MBG 0 to 1 is suggestive of NR and is observed in as many as 30% of patients with TIMI 3 flow grade (3). MBG has been confirmed to be an independent predictor of long-term mortality and adverse events (13).

Although a definite therapy for NR is still lacking, a study by Rezkalla et al. (14) suggested that patients whose NR improved after pharmacologic therapies had better clinical outcomes than those who did not receive therapy, which in turn significantly increased the incidence of congestive heart failure and cardiogenic shock.

Invasive assessment

International guidelines discourage the fractional flow reserve (FFR) assessment of the culprit lesion in STEMI patients during pPCI. In fact, the pathogenesis of STEMI is mainly related to plaque erosion/rupture and thrombosis. However, the microvascular dysfunction and/or damage that are often observed in STEMI patients might interfere with the accurate assessment of the true hemodynamic significance of the culprit lesion, with a high rate of false negative FFR. Recovery of the microcirculatory function after STEMI may take up to weeks (15, 16).

Another validated technique for evaluating the microcirculatory function, which can be calculated during any PCI procedure, is the index of microcirculatory resistance (IMR), which allows the measurement of microvascular resistance.

STEMI patients with an elevated IMR (that can be related to microvascular dysfunction and/or damage) in the infarct-related artery may show falsely high FFR values (15, 16). In contrast, patients with preserved microvascular function have maintained hyperemic responses and lower FFR values, despite less severe culprit lesion stenoses at angiography, and show improved prognosis (17).

IMR at the end of primary PCI has been demonstrated to correlate with the presence of microvascular obstruction (MVO) at CMR two days after STEMI (18). IMR measured after primary PCI correlates with infarct size and predicts recovery of left ventricular function at follow-up. In fact, an elevated IMR predicts bigger myocardial damage with higher cardiac enzyme peak and larger area of necrosis at noninvasive assessment with CMR imaging or positron emission tomography (19-21).

IMR has also been suggested to be the only invasive method of assessment of microvascular function that is an independent predictor of survival and MACEs (22).

CMR

CMR is an accurate method to evaluate the structural damages to both the myocardium and microvasculature after STEMI. This enables stratification of patients according to the STEMI-related damages and thus better prediction of prognosis. In fact, a recent study showed that CMR performed during index hospitalization with MVO assessment provides better prognostic stratification of STEMI patients who underwent pPCI than coronary angiography assessment trough TIMI flow and MBG (23).

Overall in literature, the occurrence of NR is much higher with CMR assessment than that with angiographic assessment.

CMR performed during index hospitalization allows the assessment of several damages related to MI. CMR enables measurement of the proportion of myocardium salvaged with primary PCI by comparing the size of the area at risk (edematous myocardium) and late gadolinium enhancement (necrotic myocardium). Moreover, CMR is the best method, to date, to assess an MVO. In contrast, angiographic assessment could show an apparent NR, whereas microvascular bed is not irreversibly damaged. This is due to the fact that NR can be either persistent or transient, probably due to the type of changes (structural and functional) at the level of microcirculation (24).

MVO is the main CMR criterion of NR and can be divided into both early and late MVO inside necrotic areas (25). Impaired microvascular reperfusion after STEMI, despite the patency of the culprit epicardial vessel, is associated with a reduced recovery of wall motion and eventually with a poor prognosis (26).

Infarct size determined by CMR is also directly related to a long-term prognosis. Despite this observation, MVO remains an independent strong prognostic indicator, even after adjustment for infarct size (27).

Several trials consistently showed that MVO has the best predictive value above all CMR parameters. Its predictive value resulted to be additive to clinical scores, left ventricular ejection fraction, and infarct size (28, 29). Moreover, the extent of MVO areas has been demonstrated to better stratify prognosis than the sole assessment of its presence (28, 30).

The prognostic role of MVO is wide. A recent study showed a high rate of clinically driven target lesion revascularization (TLR) in patients with MVO compared with no TLR in patients without MVO (23). Microvascular dysfunction might be the basis for stent restenosis (related to impaired flow characteristics) and for the higher rate of adverse events in patients with MVO.

Conclusion

Prognostic stratification is very important in STEMI patients to set the follow-up. Although clinical assessment with STR is

still used due to the ease of access, with the advent of mechanical reperfusive strategies, angiographic scores represent the frequently used technique for the evaluation of myocardial reperfusion and thus to evaluate the result of pPCI. However, CMR has been shown to be the best tool to assess the damages at myocardial and microvascular levels, and to stratify patients' prognosis.

Conflict of interest: None declared.

Peer-review: Internally peer-reviewed.

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