Prevalence and Predictive Value of Microvascular Flow Abnormalities after Successful Contemporary Percutaneous Coronary Intervention in Acute ST-Segment Elevation Myocardial Infarction

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Background: Although microvascular flow abnormalities have been observed following epicardial recanalization in acute ST-segment elevation myocardial infarction (STEMI), the prevalence and severity of these abnormalities in the current era of rapid percutaneous coronary intervention (PCI) has not been evaluated. The objective of this study was to assess microvascular perfusion (MVP) following successful primary PCI in patients with STEMI and how it affects clinical outcome.

Methods: In this single-center, retrospective study, 170 patients who successfully underwent emergent PCI for STEMI were assessed using real-time myocardial contrast echocardiography using a continuous infusion of intravenous commercial microbubbles (3% Definity). Three patterns of myocardial contrast replenishment were observed following intermittent high–mechanical index impulses: infarct zone replenishment within 4 sec (normal MVP), delays in contrast replenishment but normal plateau intensity (delayed MVP [dMVP]), and both delays in replenishment and reduced plateau intensity (microvascular obstruction [MVO]). Changes in left ventricular ejection fraction at 6 months and clinical event rate at 12 months (death, recurrent infarction, need for defibrillator placement, or heart failure admission) were compared.

Results: Normal MVP was seen in 62 patients (36%), dMVP in 49 (29%), and MVO in 59 (35%). Left anterior descending coronary artery infarct location was the only parameter independently associated with dMVP or MVO, independent of age, cardiac risk factors, door-to-dilation time, pre-PCI Thrombolysis In Myocardial Infarction flow grade, and thrombus burden. A dMVP pattern had a similar reduction in left ventricular ejection fraction as MVO at hospital discharge but had recovery of left ventricular ejection fraction at 6 months and a greater than fourfold lower event rate than the MVO group ($P < .001$).

Conclusions: MVO and dMVP are frequently seen following contemporary successful PCI for STEMI, especially following left anterior descending coronary artery infarction. Despite a similar area at risk, a dMVP pattern has better functional recovery and clinical outcome than MVO. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Ultrasound, Acute myocardial infarction, Microvascular obstruction

In the contemporary era, emergent primary percutaneous coronary intervention (PCI) is the standard of care for treatment of ST-segment elevation myocardial infarction (STEMI).[1,2] Rapid access to interventional techniques and adjunctive antiplatelet and antithrombotic therapies have now made it possible to achieve Thrombolysis In Myocardial Infarction (TIMI) grade 3 epicardial flow in >90% of patients.[3] In patient populations in which TIMI grade ≤2 flow in the infarct vessel was observed following PCI, microvascular obstruction (MVO) has frequently been detected during follow-up imaging of patients with STEMI.[4-6] This phenomenon has been attributed to the combined effects of inflammation, endothelial injury, edema, atheroembolization, and vasospasm, leading to increased postinfarction complications and reduced survival rate.[2,7,8]

In the previous era of fibrinolysis with either delayed or rescue angioplasty, microvascular perfusion (MVP) imaging with either real-time myocardial contrast echocardiography (RTMCE) or delayed enhancement imaging with cardiac magnetic resonance imaging was found to be abnormal in significant percentages of individuals who achieved TIMI grade 3 flow in the infarct vessel. Furthermore, detection of MVO in these patients was an independent predictor of functional

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Abbreviations

dMVP = Delayed microvascular perfusion

DUS = Diagnostic ultrasound

EFS = Event-free survival

LAD = Left anterior descending coronary artery

LV = Left ventricular

MI = Myocardial infarction

MVO = Microvascular obstruction

MVP = Microvascular perfusion

PCI = Percutaneous coronary intervention

RTMCE = Real-time myocardial contrast echocardiography

RWM = Regional wall motion

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

outcomes.[8-10] Although clinical outcomes are thought to be better in the current era of primary PCI and upstream dual-antiplatelet bolus therapy, there has not been a formal evaluation of the range of microvascular flow abnormalities that exist with these improved strategies. Furthermore, it is not known whether the combination of minimizing door-to-balloon time, upstream use of dual-antiplatelet therapy, and use of drug-eluting stents affects the frequency of MVO. RTMCE permits one to examine both capillary blood flow and volume abnormalities in multiple imaging planes and thus can differentiate in one setting both the extent and severity of microvascular blood flow abnormalities. The objective of this study was to use RTMCE to reassess the frequency of microvascular flow abnormalities following successful restoration of epicardial flow in patients with STEMI in the contemporary era. We also evaluated the impact of persistent microvascular blood flow and volume abnormalities on recovery of left ventricular (LV) systolic function and clinical outcome.

METHODS

This was a retrospective single-center cohort study involving 361 patients who presented with the initial diagnoses of STEMI and underwent emergent primary PCI between January 2011 and December 2016 (Figure 1). STEMI was defined according to the 2013 American College of Cardiology/American Heart Association guidelines as prolonged chest pain unrelieved by sublingual nitroglycerin and associated with new ST-segment elevation at the J point in at least two contiguous leads.[2] When electrocardiographic criteria were identified, there was emergent transfer of the patient to the cardiac catheterization laboratory. Patients were also treated with aspirin combined with clopidogrel 300 to 600 mg or ticagrelor 180 mg, followed by emergent placement of a drug-eluting stent. At 24 to 48 hours after PCI, two-dimensional echocardiography with a continuous contrast infusion was performed. Patients who received thrombolytics before PCI, did not achieve recanalization and adequate runoff of contrast in the infarct vessel after PCI, or did not receive contrast perfusion performed with their post–myocardial infarction (MI) echocardiographic examination were excluded from the study (Figure 1).

Echocardiographic Parameters

In-hospital echocardiography was performed with tissue harmonic imaging, and the American Society of Echocardiography 17-segment LV model was used for analysis of regional wall motion (RWM). RTMCE was performed in the three standard apical (four-, two-, and three-chamber) views. The contrast agent used was the commercially available lipid-encapsulated microbubble Definity (Lantheus Medical Imaging, North Billerica, MA). Contrast agents were administered as a continuous 3% intravenous infusion during real-time imaging (Power Modulation, Philips iE33; Philips Medical Imaging, Andover, MA) at a very low mechanical index (0.15–0.19). Frame rates were set at 25 Hz. Time gain compensation and two-dimensional gain settings were adjusted as recommended to suppress any signals from tissue before contrast injection and remained unchanged throughout the study. During contrast infusion, brief high–mechanical index impulses (>1.0) were administered in each apical window, and the rate of myocardial contrast replenishment and plateau intensity were analyzed as described below. RWM analysis was done during the myocardial replenishment period. The number of myocardial segments exhibiting RWM abnormalities (either hypokinesis or akinesis) were used to define potential infarct size.

Analysis of both MVP and RWM was performed in every case by an independent experienced reviewer (F.X.) who had no knowledge of clinical history or angiographic outcome. MVP was defined as normal if there was complete replenishment of contrast in myocardium in all segments supplied by the infarct-related artery within 4 sec following a high–mechanical index impulse (Figure 2). Delayed MVP (dMVP) was defined if perfusion defects were still observed within at least two segments of the infarct zone at >4 sec following a high–mechanical index impulse but complete replenishment was still seen within 10 sec (Figure 3). MVO was defined if there remained a persistent defect in two or more segments of the infarct zone once a plateau intensity had been reached (Figure 4). The transmural extent of any microvascular defect was also assessed at the 4- and 10-sec time periods following a high–mechanical index impulse, with a transmural defect being defined as involving >50% of the entire wall thickness at end-systole. On the basis of this blinded analysis, patients were then divided into three groups: group 1, with normal MVP; group 2, with dMVP; and group 3, with MVO.

Although all segments could be analyzed for RWM, segments were excluded from MVP analysis when there was attenuation from contrast or lung interference or when the endocardial and epicardial borders of a segment could not be visualized and thus were not distinguishable from surrounding tissues. LV ejection fraction was calculated using the biplane Simpson method as recommended in American Society of Echocardiography guidelines on the index echocardiogram and follow-up echocardiograms when available.[11]

Angiographic Parameters

Pre-PCI TIMI flow rates were analyzed and defined as following: TIMI grade 0, no antegrade flow beyond point of occlusion; grade 1, faint antegrade flow beyond occlusion with incomplete filling of distal coronary bed; grade 2, sluggish antegrade flow runoff but complete filling of distal vessel beyond the culprit lesion; and grade 3, normal flow runoff of the distal vessel beyond the culprit lesion.[12] TIMI thrombus burden was defined as grade 0 (no thrombus by angiographic criteria) to 5 (total thrombotic occlusion) on the basis of established criteria.[13] Multivessel coronary artery disease was defined as presence of significant stenosis in the one or more nonculprit vessels with >70% luminal narrowing in a major epicardial vessel and/or >50% narrowing in the left main coronary artery as assessed by the operator. All angiographic evaluations were determined by an expert reviewer (G.P.), who was blinded to clinical and echocardiographic results.