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Relationship Between Infarct Size and Outcomes Following Primary PCI

Patient-Level Analysis From 10 Randomized Trials

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ABSTRACT

BACKGROUND Prompt reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) reduces infarct size and improves survival. However, the intuitive link between infarct size and prognosis has not been convincingly demonstrated in the contemporary era.

OBJECTIVES This study sought to determine the strength of the relationship between infarct size assessed early after primary percutaneous coronary intervention (PCI) in STEMI and subsequent all-cause mortality, reinfarction, and hospitalization for heart failure.

METHODS We performed a pooled patient-level analysis from 10 randomized primary PCI trials (total 2,632 patients) in which infarct size was assessed within 1 month after randomization by either cardiac magnetic resonance (CMR) imaging or technetium-99m sestamibi single-photon emission computed tomography (SPECT), with clinical follow-up for ≥6 months.

RESULTS Infarct size was assessed by CMR in 1,889 patients (71.8%) and by SPECT in 743 patients (28.2%). Median (25th, 75th percentile) time to infarct size measurement was 4 days (3, 10 days) after STEMI. Median infarct size (% left ventricular myocardial mass) was 17.9% (8.0%, 29.8%), and median duration of clinical follow-up was 352 days (185, 371 days). The Kaplan-Meier estimated 1-year rates of all-cause mortality, reinfarction, and HF hospitalization were 2.2%, 2.5%, and 2.6%, respectively. A strong graded response was present between infarct size (per 5% increase) and subsequent mortality (Cox-adjusted hazard ratio: 1.19 [95% confidence interval: 1.18 to 1.20]; $p < 0.0001$) and hospitalization for heart failure (adjusted hazard ratio: 1.20 [95% confidence interval: 1.19 to 1.21]; $p < 0.0001$), independent of age, sex, diabetes, hypertension, hyperlipidemia, current smoking, left anterior descending versus non–left anterior descending infarct vessel, symptom-to-first device time, and baseline TIMI (Thrombolysis In Myocardial Infarction) flow 0/1 versus 2/3. Infarct size was not significantly related to subsequent reinfarction.

CONCLUSIONS Infarct size, measured by CMR or technetium-99m sestamibi SPECT within 1 month after primary PCI, is strongly associated with all-cause mortality and hospitalization for HF within 1 year. Infarct size may, therefore, be useful as an endpoint in clinical trials and as an important prognostic measure when caring for patients with STEMI. (J Am Coll Cardiol 2016;67:1674–83) © 2016 by the American College of Cardiology Foundation.

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Cardiovascular mortality has progressively declined over the last 4 decades, in part due to the prompt delivery of reperfusion therapy to patients with ST-segment elevation myocardial infarction (STEMI) (1). By rapidly restoring coronary artery patency in STEMI, fibrinolytic therapy reduces infarct size (IS) and mortality. In this regard, the greater reduction in IS with tissue plasminogen activator compared with streptokinase has been associated with improved survival (2). Compared with fibrinolytic therapy, primary percutaneous coronary intervention (PCI) further reduces IS and improves survival (3,4), contributing to improved population-level outcomes (1,5). However, the benefits of primary PCI are multifactorial, and include restoring epicardial artery patency, which may have salutatory effects in reducing susceptibility to lethal ventricular arrhythmias, preventing expansive left ventricular remodeling, and preserving collateral flow independent of myocardial salvage (the open artery hypothesis) (6). Early data suggested a modest correlation between IS and survival after medical therapy in STEMI (7). The extent to which IS is correlated with outcomes in STEMI has been incompletely characterized in the contemporary primary PCI era. Moreover, whether IS correlates with hospitalization for heart failure (HF) (as would be expected) or reinfarction (which is less intuitive) has not been studied. Given the generally favorable prognosis following primary PCI, most individual studies in which IS has been assessed have been inadequately powered to explore these relationships.

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We therefore performed a patient-level pooled analysis from 10 randomized trials of primary PCI in STEMI to examine the relationship between IS assessed within 1 month after reperfusion and subsequent mortality, reinfarction, and hospitalization for HF within 1-year follow-up.

METHODS

The present study represents a collaborative effort between the principal investigators of randomized trials that enrolled patients with STEMI undergoing primary PCI in whom IS was assessed by either cardiac magnetic resonance (CMR) imaging or technetium (tc)-99m sestamibi single-photon emission computed tomography (SPECT) within 1 month after reperfusion at a core laboratory, and in whom clinical follow-up was performed for ≥6 months (unless death occurred earlier), with adverse events adjudicated by a clinical events committee. Ten such studies were available, and the data from each were pooled into a common database at the Cardiovascular Research Foundation. The objectives were to examine the relationship between IS assessed within 1 month after primary PCI and the occurrence of the prespecified endpoints of all-cause mortality, reinfarction, hospitalization for HF, and combinations thereof. Specifically, our hypothesis was that after adjustment for differences in baseline clinical and angiographic variables, IS would be independently correlated with all-cause mortality and with HF hospitalization, but not necessarily with reinfarction. This was an independent academic project, and the sponsors of the individual studies were not involved.

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

HF = heart failure

IDI = integrated discriminatory index

IS = infarct size

LAD = left anterior descending

NRI = net reclassification improvement

PCI = percutaneous coronary intervention

SPECT = single-photon emission computed tomography

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

STUDIES AND DEFINITIONS. The 10 primary PCI trials included in the pooled analysis were (in approximate chronological order of patient enrollment): the EMERALD (Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberated Debris) trial, in which patients undergoing primary PCI were randomized to a distal embolic protection filter versus control group (8); the AMIHOT-II (Acute Myocardial Infarction with HyperOxemic Reperfusion II) trial, in which patients undergoing primary PCI were randomized to post-procedural supersaturated oxygen versus control (9); the IS substudy of the IMMEDIATE (Immediate Myocardial Metabolic Enhancement During Initial Assessment and Treatment in Emergency care) trial, in which patients with non-STEMI and STEMI were randomized to receive a pre-hospital intravenous glucose-insulin-potassium infusion versus placebo prior to primary PCI (10); the IS substudy of the APEX-AMI (Pexelizumab in Conjunction With Angioplasty in Acute Myocardial Infarction) trial, in which patients undergoing primary PCI were randomized to intravenous pexelizumab versus placebo (11); the LIPSIA-ABCIXIMAB (Randomized Leipzig Immediate Percutaneous Coronary Intervention Abciximab IV

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