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Comprehensive Prognosis Assessment by CMR Imaging After ST-Segment Elevation Myocardial Infarction

Ingo Eitel, MD,*† Suzanne de Waha, MD,*‡ Jochen Wöhrle, MD,§ Georg Fuernau, MD,* Phillipp Lurz, MD,* Matthias Pauschinger, MD,‖ Steffen Desch, MD,*† Gerhard Schuler, MD,* Holger Thiele, MD*†

ABSTRACT

BACKGROUND Although the prognostic value of findings from cardiac magnetic resonance (CMR) imaging has been established in single-center center studies in patients with ST-segment elevation myocardial infarction (STEMI), a large multicenter investigation to evaluate the prognostic significance of myocardial damage and reperfusion injury is lacking.

OBJECTIVES The aim of this study was to assess the prognostic impact of CMR in an adequately powered multicenter study and to evaluate the most potent CMR predictor of hard clinical events in a STEMI population treated by primary percutaneous coronary intervention (PCI).

METHODS We enrolled 738 STEMI patients in this CMR study at 8 centers. The patients were reperfused by primary PCI <12 h after symptom onset. Central core laboratory–masked analyses for quantified left ventricular (LV) function, infarct size (IS), microvascular obstruction (MO), and myocardial salvage were performed. The primary clinical endpoint of the study was the occurrence of major adverse cardiac events.

RESULTS Patients with cardiovascular events had significantly larger infarcts ($p < 0.001$), less myocardial salvage ($p = 0.01$), a larger extent of MO ($p = 0.009$), and more pronounced LV dysfunction ($p < 0.001$). In a multivariate model that included clinical and other established prognostic parameters, MO remained the only significant predictor in addition to the TIMI (Thrombolysis In Myocardial Infarction) risk score. IS and MO provided an incremental prognostic value above clinical risk assessment and LV ejection fraction (c-index increase from 0.761 to 0.801; $p = 0.036$).

CONCLUSIONS In a large, multicenter STEMI population reperfused by primary PCI, CMR markers of myocardial damage (IS and especially MO) provide independent and incremental prognostic information in addition to clinical risk scores and LV ejection fraction. (Abciximab i.v. Versus i.c. in ST-elevation Myocardial Infarction [AIDA STEMI]; NCT00712101) (J Am Coll Cardiol 2014;64:1217–26) © 2014 by the American College of Cardiology Foundation.

Predicting the risk of future cardiovascular events after acute ST-segment elevation myocardial infarction (STEMI) has been a subject of great interest over the past decades. The identification of patients at high risk for adverse clinical events is essential to further improve patient prognosis and guidance of therapy. Patient prognosis after STEMI is influenced by many factors, and as a result, risk stratification often includes clinical risk scores, biomarkers, or a multimodality imaging approach with echocardiography, ventriculography, and/or cardiac magnetic resonance (CMR) imaging (1,2).

CMR can be used to assess almost all relevant prognostic pathophysiological consequences of myocardial ischemia and reperfusion after an acute reperfused STEMI (3,4). Thus, CMR is uniquely positioned

From the *Department of Internal Medicine-Cardiology, University of Leipzig-Heart Center, Leipzig, Germany; †Department of Cardiology, Angiology, Intensive Care Medicine, University of Lübeck, Medical Clinic II, Lübeck, Germany; ‡Department of Cardiology, Heart Center Bad Segeberg, Bad Segeberg, Germany; §Department of Internal Medicine II-Cardiology, University of Ulm, Ulm, Germany; and the ‖Klinikum Nürnberg, Medizinische Klinik/Kardiologie, Nürnberg, Germany. Dr. Thiele has received an unrestricted grant from Lilly Germany. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.
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ABBREVIATIONS AND ACRONYMS

AUC = area under the curve

CMR = cardiac magnetic resonance

IQR = interquartile range

IS = infarct size

LGE = late gadolinium enhancement

LV = left ventricle/ventricular

LVEF = left ventricular ejection fraction

MACE = major adverse cardiac event

MO = microvascular obstruction

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

TIMI = Thrombolysis In Myocardial Infarction

to be used to comprehensively evaluate the morphological, functional, and microvascular sequelae of the post-infarction patient.

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We and others have convincingly demonstrated that CMR markers of myocardial and microvascular damage (myocardial salvage, infarct size [IS], microvascular obstruction [MO], intramyocardial hemorrhage) add incremental prognostic information to clinical, electrocardiographic, biomarker, and angiographic outcome markers (5–14); however, almost all of these studies share important limitations, including retrospective single-center designs, small sample sizes, absence of core laboratory CMR analysis, and limited statistical power (few fatal events). A large, multicenter, multivendor investigation to evaluate the prognostic significance of myocardial damage and reperfusion injury, as determined by CMR, is completely lacking. Moreover, there is no consensus as to which CMR marker is the most potent predictor of outcome in STEMI. The aims of our study were, therefore, to assess the prognostic significance of CMR in an adequately powered multicenter study and to evaluate the most potent CMR predictor of hard clinical events in a STEMI population treated by primary percutaneous coronary intervention (PCI).

METHODS

AIDA STEMI CMR SUBSTUDY DESIGN. This prospective CMR study was a predefined substudy of the AIDA STEMI (Abciximab Intracoronary versus intravenously Drug Application in STEMI) trial, which compared intravenous versus intracoronary abciximab application in STEMI patients and did not show differences between the treatment groups in IS, reperfusion injury, and clinical outcome. The detailed design and main results of the trial were published previously (15–17). Briefly, AIDA STEMI was a randomized, open-label, multicenter trial. Patients were eligible for the study if they were ≥18 years of age and had clinical symptoms of acute myocardial infarction of >30 min and <12 h with specific echocardiographic criteria for STEMI. The echocardiographic criteria for inclusion were ST-segment elevation >1 mm in ≥2 extremity leads and/or ST-segment elevation >2 mm in ≥2 adjacent precordial leads. Patients with new or presumably new left bundle branch block were not included. Patient randomization was performed in a 1:1 ratio by a central Internet-based randomization system to intracoronary versus intravenous abciximab bolus (0.25 mg/kg body weight) during primary PCI with a subsequent 12-h intravenous infusion at 0.125 μg/kg/min (maximum 10 μg/min). Exclusion criteria were pregnancy; known allergy to abciximab, aspirin, or heparin; contraindications to abciximab, such as active gastroduodenal ulcer; history of major surgery within the previous 4 weeks; active internal bleeding; stroke within the previous 2 years; known coagulation defects; severe liver insufficiency; renal insufficiency necessitating dialysis; hypertensive retinopathy; vasculitis; or thrombolysis within the previous 12 h.

Patients were enrolled at 22 sites in Germany, with a final enrolled trial group of 2,065 patients (intracoronary abciximab, n = 1,032; intravenous abciximab, n = 1,033). The study was approved by national regulatory authorities and by the ethics committees of the participating centers. All patients provided written informed consent. This trial is registered with ClinicalTrials.gov, NCT00712101.

Consecutive patients enrolled in the AIDA STEMI trial at 8 sites were included in the CMR substudy (17). The sites were chosen on the basis of proven expertise in performing CMR examinations in patients with acute myocardial infarction. By protocol, CMR was performed on days 1 to 10 after the index event for the assessment of myocardial salvage, IS, presence and extent of MO, left ventricular ejection fraction (LVEF), and end-systolic and end-diastolic volumes. Exclusion criteria for the CMR substudy were: 1) severe claustrophobia; 2) hemodynamic instability; 3) pacemaker or internal cardioverter-defibrillator; 4) metallic cerebral or intracranial implants; 5) known allergy to gadolinium; and 6) severe renal insufficiency (creatinine clearance <30 ml/min).

The detailed scan protocol on a clinical 1.5- or 3.0-T magnetic resonance scanner has been described previously (17). In brief, IS and late MO were assessed in late gadolinium enhancement (LGE) short-axis images covering the whole left ventricle (LV) approximately 15 min after injection of gadolinium chelate. An inversion-recovery turbo gradient-echo sequence was used for image acquisition. For determination of edema/area at risk, we obtained short-axis slices covering the whole LV using a T2-weighted imaging triple-inversion recovery turbo spin-echo sequence before contrast administration. Assessment of LV function and volumes was performed by a standard steady-state free precession technique, with short-axis slices acquired from base to apex. LVEF was calculated from the short-axis functional views. CMR images were sent on storable media to the CMR