The association between renal impairment and cardiac structure and function in patients with acute myocardial infarction

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Background Renal dysfunction in patients with acute myocardial infarction (MI) is an important predictor of short- and long-term outcome. Cardiac abnormalities dominated by left ventricular (LV) hypertrophy are common in patients with chronic renal dysfunction. However, limited data exists on the association between LV systolic- and diastolic function assessed by comprehensive echocardiography and renal dysfunction in contemporary unselected patients with acute MI.

Methods We prospectively included 1054 patients with acute MI (mean age 63 years, 73% male) and performed echocardiographic assessment of systolic and diastolic function within 48 hours of admission as well as estimated glomerular filtration rate (eGFR).

Results Reduced eGFR was significantly associated with LV mass, LV ejection fraction, LV global strain (GLS) and E/e' ratio. After multivariable adjustment, E/e' ratio (P = .0096) remained the only echocardiographic measure independently associated with decreasing eGFR. During follow-up a total of 113 patients (10.7%) patients experienced the composite endpoint of all-cause mortality or hospitalization for heart failure. An eGFR <60 mL/min per 1.73 m^2 was significantly associated with outcome (HR, 1.71; 95% CI, 1.12-2.62; P = .0131) after adjustment for age, diabetes, hypertension, Killip class >1, multivessel disease and troponin. The prognostic impact of an eGFR <60 mL/min per 1.73 m^2 was only modestly altered by addition of LV mass or E/e' ratio whereas addition of LV ejection fraction or GLS attenuated its importance considerably.

Conclusion Renal dysfunction in patients with acute MI is independently associated with echocardiographic evidence of increased LV filling pressure. However, the prognostic importance of renal dysfunction is attenuated to a greater degree by LV longitudinal systolic function. (Am Heart J 2014;167:506-13.)

Background

Impaired renal function has consistently been associated with adverse clinical outcome after acute myocardial infarction (MI).[1] The risk of mortality, heart failure (HF), malignant arrhythmia and re-infarction increases with only mildly impaired renal function and continues in a curvi-linear fashion with progressive renal impairment.[1] This effect is independent of important clinical risk factors, natriuretic peptides[2] as well as left ventricular (LV) systolic dysfunction and is maintained during long-term follow-up.[2,3]

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Impaired renal function in the acute phase of MI correlates with advanced age and risk markers of adverse clinical outcome including hypertension, diabetes and in-hospital HF.[3,4] An association between renal dysfunction and LV systolic dysfunction complicating acute MI has been suggested by some studies[2,3,5] while others have come to an opposite conclusion.[1,6] Structural alterations in myocardial geometry dominated by LV hypertrophy and concentric remodeling are present in the early stages of renal impairment[7] and become manifest in the majority of patients with end stage renal disease.[8] The tight coupling between cardiac structural alterations and renal dysfunction is demonstrated by the progressive evolution of myocardial fibrosis, myocyte apoptosis and diastolic dysfunction in experimental unilateral nephrectomy[9] and the improvement in myocardial systolic function seen with renal replacement therapy and renal transplantation.[10,11]

Diastolic dysfunction and LV hypertrophy (LVH) have been suggested to be the major factors portending the increased risk in patients with high risk acute MI and renal dysfunction.[6] However, limited data exists on the

association between renal dysfunction and myocardial mechanical function assessed utilizing comprehensive systolic and diastolic evaluation in contemporary patients with acute MI. We therefore sought to assess the associated echocardiographic findings and their relative prognostic impact on metrics of renal dysfunction in patients with acute MI.

Methods

Study design and patient population

We conducted a prospective study of patients referred for invasive coronary angiography due to either ST-elevation MI (STEMI) or non-STEMI at 2 tertiary cardiac centers in the Copenhagen region. All patients provided written informed consent prior to transthoracic echocardiographic examination. Exclusion criteria were age <18 years, non-cardiac disease with a life expectancy <1 year or inability to provide written informed consent. Echocardiograms obtained in patients with atrial fibrillation, paced rhythm or severe aortic stenosis were excluded from the analyses.

Based on hospital records obtained on admission information on diabetes mellitus, hypertension, a history of ischemic heart disease and prior MI was registered. Findings in relation to coronary angiography including culprit lesion, number of diseased vessels and type of revascularization (percutaneous coronary intervention [PCI], coronary artery bypass grafting [CABG], or no intervention) were registered. Objective signs of HF at presentation or during hospitalization were scored according to the Killip classification scheme.[12] Peak troponin I or troponin T was obtained during the hospital stay.

Estimated glomerular filtration rate (eGFR) was measured from the 4-variable MDRD formula[13] incorporating plasma creatinine obtained at the time of echocardiography, age and gender. Since all patient were of Caucasian descent no corrections for race were needed. The study was approved by the Regional Scientific Ethics Committee (reference number H-D-2009-063). Additional results of analyses from the present registry have been published previously.[4,14–17] The present study was supported by an unrestricted research grant from Rigshospitalet, Copenhagen. The authors are solely responsible for the design and conduct of this study, all study analyses and drafting and editing of the paper.

Echocardiography

Echocardiography was performed within 48 hours of admission to the tertiary center. All examinations were performed on a Vivid e9 (General Electric, Horten, Norway). Images were obtained at a frame rate of at least 60 frames per second and digitally transferred to a remote work station for offline analysis (Echopac BT 11.1.0; General Electric). All analyses were performed by a single experienced operator (ME) blinded to follow-up information.

Left atrial volume index (LAVi) was determined from the biplane area length method and LV ejection fraction (LVEF) was determined using the biplane Simpson model. Wall motion scoring was performed by dividing the LV into 16 segments, and each segment was assigned a score based on myocardial thickening (1 = normal or hyperkinesis, 2 = hypokinesis, 3 = akinesis and 4 = dyskinesis). Wall motion score index (WMSI) was calculated from the average score of all segments. LV mass index (LVMi) was calculated from the LV linear dimensions in the parasternal view. Volumetric and dimensional measurements of the LV and left atrium maximum volume (LA max) were indexed to body surface area when appropriate. All volumetric analyses were performed in accordance with current recommendations.[18]

Doppler recordings of mitral inflow were performed by placing a 2.5 mm sample volume at the tip of the mitral valve (MV) leaflets during diastole. Peak velocity of early (E) and atrial (A) diastolic filling and MV deceleration time were measured and E/A-ratio calculated. Pulsed wave (PW) TDI recordings were performed at the lateral and medial mitral annulus using a 2.5 mm sample volume with measurements of myocardial peak early velocity (e′). The mean E/e′ ratio was calculated from an average of lateral and medial values of e′.[19] Categorization of the diastolic performance measures was performed for E/A ratio (<0.75; 0.75-1.5; >1.5), E/e′ ratio (<15; >15) and MV deceleration time (<140 milliseconds; 140-240 milliseconds; >240 milliseconds).[19]

Two-dimensional speckle tracking was performed using a semi-automatic algorithm (Automated Function Imaging [AFI], General Electric). Briefly, manual positioning of 3 points (2 annular and 1 apical) was performed in each of the 3 apical projections. Aortic valve closure was identified on continuous wave Doppler recording through the aortic valve. The AFI algorithm allowed GLS to be calculated for each of the 3 apical projections if at least 5 out of 6 segments were sufficiently tracked. The algorithm then calculated overall GLS as the average value of all 3 projections. If GLS could only be assessed in 2 of 3 apical projections, we calculated overall GLS as the average of these 2. If GLS could not be assessed in at least 2 of the apical projections, the patient examination was classified as having image quality insufficient for strain measurements.

Follow-up and endpoint definition

The primary outcome was a composite of death from any cause and hospitalization for HF, whichever came first. Information on all-cause mortality was obtained from the Danish Civil Registration System. Information on HF hospitalizations were obtained from a systematic review of all hospital admissions after the index MI was defined as admission due to dyspnea with chest radiographic evidence of pulmonary congestion and treatment with intravenous diuretics. The secondary outcome was cardiac mortality. Verification of endpoints was performed by 2 independent reviewers blinded to echocardiographic information relating to the index MI, and in case of disagreement a third reviewer would classify the outcome.

Statistical analysis

All data are reported as mean ± SD or median (first and third quartile, Q1-Q3). Missing values were imputed using multiple imputations 5 times with predictive mean matching for the continuous covariates with the assumption of data being missing at random (R package MICE). Statistical analyses were performed on all of the imputed datasets and results pooled by the method described by Rubin.[20] Baseline clinical and echocardiographic data were analyzed according to 4 categories of eGFR (<45, 45-59.9, 60-74.9 and ≥ 75 mL/min per 1.73 m^2)