Adverse diastolic remodeling after reperfused ST-elevation myocardial infarction: An important prognostic indicator

Tuan L. Nguyen, MBBS,[a,c] Justin Phan, MBBS,[a,c] Jarred Hogan, BMed,[c] Leia Hee, BMedSci, MClinTRes, PhD,[a] Daniel Moses, BSc, MBBS, MEngSc,[b,c] James Otton, MBBS, PhD,[a,c] Upul Premawardhana, MBBS, MMed,[a,c] Rohan Rajaratnam, MBBS,[a,c] Craig P. Juergens, MBBS, DMedSc,[a,c] Hany Dimitri, MBBS, PhD,[a,c] John K. French, BMedSc, MSc, MBChB, PhD,[a,c] David Richards, BSc (Med), MBBS, MD,[a,c] and Liza Thomas, MBBS, PhD[a,c] *NSW, Australia*

Objectives We sought to determine the relationship of adverse diastolic remodeling (ie, worsening diastolic or persistent restrictive filling) with infarct scar characteristics, and to evaluate its prognostic value after ST-segment elevation myocardial infarction (STEMI).

Background Severe diastolic dysfunction (restrictive filling) has known prognostic value post STEMI. However, ongoing left ventricular (LV) remodeling post STEMI may alter diastolic function even if less severe.

Methods and results There were 218 prospectively recruited STEMI patients with serial echocardiograms (transthoracic echocardiography) and cardiac magnetic resonance imaging (CMR) performed, at a median of 4 days (early) and 55 days (follow-up). LV ejection fraction and infarct characteristics were assessed by CMR, and comprehensive diastolic function assessment including a diastolic grade was evaluated on transthoracic echocardiography. 'Adverse diastolic remodeling' occurred if diastolic function grade either worsened (≥1 grade) between early and follow-up imaging, or remained as persistent restrictive filling at follow-up. Follow-up infarct scar size (IS) predicted adverse diastolic remodeling (area under the curve 0.86) and persistent restrictive filling (area under the curve 0.89). The primary endpoint of major adverse cardiovascular events (MACE) occurred in 48 patients during follow-up (mean, 710 ± 79 days). Kaplan-Meier analysis showed that adverse diastolic remodeling (n = 50) and persistent restrictive filling alone (n = 33) were significant predictors of MACE (both $P < .001$). Multivariate Cox analysis, when adjusted for TIMI risk score and CMR IS, microvascular obstruction, and LV ejection fraction, showed adverse diastolic remodeling (HR 3.79, $P < .001$) was an independent predictor of MACE, as was persistent restrictive filling alone (HR 2.61, $P = .019$).

Conclusions Larger IS is associated with adverse diastolic remodeling. Following STEMI, adverse diastolic remodeling is a powerful prognostic marker, and identifies a larger group of 'at-risk' patients, than does persistent restrictive filling alone. (Am Heart J 2016;180:117-27.)

Left ventricular (LV) infarct scar size (IS), microvascular obstruction (MVO) and reduced LV function on CMR, are established predictors of adverse cardiovascular outcomes and mortality, after acute ST-segment elevation myocardial infarction (STEMI).[1,2] In addition, diastolic dysfunction has demonstrated prognostic value in STEMI patients treated with thrombolytic therapy.[3,4] Diastolic function is altered by myocardial necrosis and microvascular dysfunction consequent to STEMI. In addition, myocardial edema and infarct scar formation can lead to increased LV wall stiffness and altered LV filling.

There are established echocardiographic parameters to determine diastolic function (including transmitral pulse wave Doppler and tissue Doppler assessment). The diastolic function grade incorporates several parameters,

From the [a]Cardiology Department, Liverpool Hospital, Sydney, NSW, Australia, [b]Radiology Department, Liverpool Hospital, Sydney, NSW, Australia, and [c]South Western Sydney Clinical School, The University of NSW, Sydney, NSW, Australia.

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Reprint requests: Liza Thomas, MBBS, PhD, Cardiology Department, Liverpool Hospital, Elizabeth Street, Liverpool, NSW, 2170, Sydney, Australia.

E-mail: nguyenletuan@hotmail.com

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Table I. Diastolic function grade assessment

	Normal (Grade 0)	Impaired relaxation (Grade 1)	Pseudonormal (Grade 2)	Restrictive filling (Grade 3)
Mitral inflow PW Doppler	E/A = 0.8–1.5 DT = 160-200 ms	E/A < 0.8 DT >200 ms	E/A = 0.8–1.5 DT = 160-200 ms	E/A > 1.5 DT <160 ms
Tissue Doppler*	E/e′ ≤ 8	E/e′ ≤ 8	E/e′ = 9–12	E/e′ ≥ 13
Pulmonary inflow PW Doppler	S = D	S > D	S < D	S > > D

*Mean of septal and lateral tissue Doppler measurements. Adapted from Moller et al[5] and Nagueh et al[8] DT, Deceleration time; PW, pulse wave.

to define severity of diastolic dysfunction (Table I).[5] Severe diastolic dysfunction, or restrictive filling, is a powerful prognostic marker that identifies high-risk patients post STEMI; however it may only identify a limited proportion of at-risk patients. Diastolic function is dynamic, and diastolic grade can be altered by LV remodeling, IS and myocardial viability, all of which are important factors post STEMI.[6] However, there is a paucity of literature on diastolic function 'remodeling' and in particular, its prognostic value post STEMI. Furthermore, evaluation of the relationship between diastolic function and IS has not been well described.

Our study aims were to determine the relationship of adverse diastolic remodeling with CMR infarct scar characteristics, and its prognostic significance after acute STEMI treated by primary percutaneous coronary intervention (PCI) or thrombolytic reperfusion.

Methods

Study population

We prospectively evaluated patients presenting with acute STEMI (defined as clinical symptoms with ST-segment elevation in 2 or more contiguous leads), treated by primary PCI, reperfusion by thrombolysis with nonemergent PCI, or rescue PCI after unsuccessful thrombolysis, who had presented to our tertiary care facility. The study population included both patients with first presentation STEMI, which have been previously described,[7] and patients with a prior history of myocardial infarction. Electrocardiograms and/or coronary angiography reports were used to confirm a prior history of myocardial infarction. The exclusion criteria included: severe chronic kidney disease (eGFR <30 mL/min per 1.73 m^2, or renal replacement therapy), prior valvular/coronary bypass surgery or congenital heart disease, known cardiomyopathy, previous history of atrial fibrillation, coexistent conditions with survival of <1 year or significant psychiatric illness, CMR exclusions (including claustrophobia, gadolinium allergy and ferrous metallic implants), and age <18 years or >85 years. PCI was considered successful if there was TIMI III flow and <20% residual stenosis of the culprit vessel was achieved, with resolution of their presenting symptoms as determined by the interventionalist. Detailed patient demographics, discharge medications, and cardiac risk factors were recorded after obtaining patient consent. Patients underwent 'early' (median 4 days, interquartile range 3-7 days) and 'follow-up' (median 55 days, interquartile range 46-64 days) transthoracic echocardiogram (TTE) and CMR, after STEMI presentation. Patients were followed up to determine adverse clinical events for up to 2 years (730 days) post STEMI.

Diastolic function assessment

Comprehensive TTEs were performed on commercially available Vivid E9 machines (GE Healthcare, Norway). All measurements and analysis were performed offline, using an EchoPAC Clinical Workstation (GE Healthcare, Version 12). Pulsed Doppler mitral inflow measurements were obtained from the apical four-chamber view, with the sample volume placed at the tips of the mitral valve leaflets. Early mitral inflow velocity (E) late mitral inflow velocity (A), E/A ratio, and mitral E wave deceleration time were measured. Pulmonary venous inflow measurements were acquired by placing the sample volume 1–2 cm into the superior pulmonary vein. Tissue Doppler early diastolic mitral annular velocity (e′) was an average of septal and lateral e′. The E/e′ ratio was calculated using the average e′ velocity. Three measurements were made on consecutive cardiac cycles, and their average recorded.

All individual diastolic parameters mentioned above were evaluated using established criteria[5,8] to categorize patients to a diastolic function grade (0 = normal, 1 = impaired relaxation, 2 = pseudonormal, 3 = restrictive pattern filling) with consensus between two blinded independent observers (Table I). 'Adverse diastolic remodeling' included patients whose diastolic function grade increased (≥1 grade) from the 'early' to 'follow-up' scans, as well as those with persistent restrictive filling (grade 3) at 'follow-up'.

CMR acquisition protocol

A detailed protocol with specific CMR parameters used, has been previously described.[7] In brief, patients underwent early and follow-up CMR, using a commercially available MRI 1.5 T scanner (Siemens Symphony, Germany), and a standard CMR multisequence protocol with image sequences performed during breath-hold.[9] A 6-channel body array coil and a spine coil were used. Cardiac synchronization was obtained by retrospective vector electrocardiographic gating. Cine images, using a steady state free precession pulse sequence, were acquired in three long-axis views, and contiguous short-axis images from LV base to apex.