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ORIGINAL RESEARCH

Pre-Load Stress Echocardiography for Predicting the Prognosis in Mild Heart Failure

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ABSTRACT

OBJECTIVES This study sought to introduce and confirm the efficacy of pre-load stress echocardiography with leg-positive pressure (LPP) for improving risk stratification of patients with mild stable heart failure.

BACKGROUND Heart failure patients with mild symptoms and a poor prognosis should be identified and treated aggressively to improve clinical outcome.

METHODS We performed transthoracic echocardiography with LPP in 202 patients with chronic cardiac disease. Twenty-two of these patients also underwent cardiac catheterization, and left ventricular pressure was measured during LPP along with simultaneous Doppler recordings. Patients were classified into 3 groups on the basis of their left ventricular (LV) diastolic dysfunction as assessed by transmitral flow velocity: restrictive or pseudonormal (PN) at rest, impaired relaxation (IR) at rest and during LPP (stable IR), and IR at rest and PN during LPP (unstable IR). Clinical outcome was compared among these groups.

RESULTS The LPP increased LV end-diastolic pressure from 15.8 ± 4.7 mm Hg to 20.5 ± 5.0 mm Hg in the unstable IR group and from 10.5 ± 2.6 mm Hg to 14.7 ± 3.8 mm Hg in the stable IR group (both $p < 0.001$). During an average follow-up of 548 ± 407 days, 5 patients had cardiac death, 37 had acute heart failure, 4 had an acute myocardial infarction, and 7 had a stroke. The all-cause cardiac event rate in unstable IR was higher than in stable IR ($p < 0.001$), and was similar in the PN group ($p = 0.81$). Event-free survival was significantly lower in unstable IR than in stable IR ($p = 0.003$). In a Cox proportional hazards model, unstable IR was an independent predictor of all-cause cardiac events (hazard ratio: 8.0; $p < 0.001$).

CONCLUSIONS The left LV end-diastolic pressure-volume relationship can be estimated by changes in transmitral flow velocity during LPP. Thus, pre-load stress echocardiography using LPP provides additional prognostic information in mild heart failure beyond that provided by conventional Doppler echocardiography at rest. (J Am Coll Cardiol Img 2014;7:641–9) © 2014 by the American College of Cardiology Foundation.

The assessment of left ventricular (LV) diastolic dysfunction using the transmitral flow (TMF) velocity pattern obtained by Doppler echocardiography has been widely used in the management of various cardiac diseases, especially in patients with heart failure (1). Its prognostic value in a variety of cardiac conditions has been demonstrated by several investigators (2–4). Most previous

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ABBREVIATIONS AND ACRONYMS

A = peak atrial systolic transmitral flow velocity

a′ = peak atrial systolic mitral annular velocity

BNP = B-type natriuretic peptide

DT = deceleration time of early diastolic transmitral flow velocity wave

E = peak early diastolic transmitral flow velocity

e′ = peak early diastolic mitral annular velocity

IR = impaired relaxation

IVRT = isovolumic relaxation time

LPP = leg-positive pressure

LV = left ventricular

LVEDP = left ventricular end-diastolic pressure

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

PN = pseudonormal

TMF = transmitral flow

studies found a poor survival prognosis in patients with a restrictive or pseudonormal (PN) filling pattern, and patients with an impaired relaxation (IR) pattern seemed to have a better prognosis.

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It has been shown that the TMF velocity pattern varies dramatically with a change in loading conditions (5). This may limit the prognostic value of a single baseline Doppler evaluation; however, the change in the TMF velocity pattern to an altered load may provide an estimate of cardiovascular reserve and improve risk assessment. Pozzoli et al. (6) demonstrated that the responses to nitroprusside and leg lifting identified subgroups of patients who have markedly different prognoses despite similar baseline TMF velocity patterns. Moreover, Ishizu et al. (7) showed that passive leg lifting was useful to identify patients at high risk of the development of diastolic heart failure. Leg lifting is an easy noninvasive maneuver to increase pre-load, although it is sometimes difficult to perform, especially in obese or elderly patients. In this study, we used leg-positive pressure (LPP) as an alternative technique for noninvasive pre-load augmentation.

Consequently, the first purpose of this study was to evaluate the effect of LPP on LV hemodynamics by performing this maneuver during LV catheterization. Second, we aimed to assess whether changes in TMF in response to LPP could provide additional information on the prognosis of mild heart failure patients with intermediate diastolic dysfunction, in which there was an IR pattern of TMF velocity.

METHODS

PATIENT POPULATION. The study population consisted of 202 consecutive patients with various chronic cardiac diseases (134 men and 68 women) with a mean age of 67 ± 11 years (range 36 to 92 years) undergoing transthoracic echocardiography for the evaluation of their hemodynamic status between January 2006 and December 2007. All patients fulfilled the following inclusion criteria: 1) sinus rhythm; 2) stable clinical condition at the time of echocardiography defined by no signs of peripheral or pulmonary congestion and stable body weight with optimal medical treatment; 3) absence of severe primary diseases of other organs such as malignancy or pulmonary disorders; 4) absence of unstable angina; and 5) technically adequate 2-dimensional and Doppler echocardiograms. There were 175 patients taking an angiotensin receptor blocker or angiotensin-converting enzyme inhibitor, 67 taking a beta-blocker, 52 taking a nitrate, 48 taking a diuretic, and 20 taking digitalis. The patient population consisted of 104 patients with hypertension with left ventricular hypertrophy (52%), 60 with ischemic cardiomyopathy (30%), and 42 with nonischemic cardiomyopathy (21%). Patients with reduced LV ejection fraction (LVEF) (<50%), significant coronary artery stenosis (>50%) in >1 epicardial coronary vessel on angiography, revascularization, and/or a history of myocardial infarction were classified as having ischemic cardiomyopathy. Patients with reduced LVEF were classified as having nonischemic cardiomyopathy if they had none of these ischemic features. This study, which was performed in accordance with the Declaration of Helsinki, was approved by the Institutional Review Board of the University of Tokushima, and each subject gave written informed consent.

ECHOCARDIOGRAPHY. Two-dimensional, M-mode, pulsed Doppler, color Doppler, and tissue Doppler echocardiography were performed using a commercially available ultrasound machine (SSA-770, Toshiba Medical Systems, Tokyo, Japan or EUB-8500, Hitachi Medico, Kashiwa, Japan) with patients in the left lateral decubitus position. Left ventricular end-diastolic volume (LVEDV), LV end-systolic volume, and LVEF were measured and calculated from the apical 2- and 4-chamber view using the modified Simpson rule (8). LV mass was calculated as reported previously (9). Sex-specific values of LV hypertrophy were defined: LV mass index >95 g/m^2 (female) and >115 g/m^2 (male). TMF velocity was recorded from the apical long-axis or 4-chamber view. The peak early diastolic (E) and the peak atrial systolic (A) velocities, isovolumic relaxation time (IVRT), and deceleration time of early diastolic TMF velocity wave (DT) were measured. Similarly, pulmonary venous flow velocity signals were recorded from the apical 4-chamber view and systolic and diastolic pulmonary venous flow peak velocity as well as atrial reversal pulmonary venous flow velocity, and the duration was calculated. Stroke volume was calculated as the product of the cross-sectional area of the LV outflow tract and the time-velocity integral in the LV outflow tract flow velocity wave. The mitral annular motion velocity pattern was recorded from the apical 4-chamber view with a sample volume placed at the lateral side of the mitral annulus using pulsed tissue Doppler echocardiography. Early diastolic (e′) and atrial systolic (a′)