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RV Longitudinal Deformation Correlates With Myocardial Fibrosis in Patients With End-Stage Heart Failure

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ABSTRACT

OBJECTIVES This study was performed to determine the accuracy of right ventricular (RV) longitudinal strain (LS) in predicting myocardial fibrosis in patients with severe heart failure (HF) undergoing heart transplantation.

BACKGROUND RVLS plays a key role in the evaluation of its systolic performance and clinical outcome in patients with refractory HF.

METHODS We studied 27 patients with severe systolic HF (ejection fraction ≤25% and New York Heart Association functional class III to IV, despite full medical therapy and cardiac resynchronization therapy) using echocardiography before heart transplantation. RV free wall LS, right atrial LS, sphericity index (SI), and tricuspid annular plane systolic excursion (TAPSE) were all measured. Upon removal of the heart, from the myocardial histologic analysis, the ratio of the fibrotic to the total sample area determined the extent of fibrosis (%).

RESULTS RV myocardial fibrosis correlated with RV free wall LS ($r = 0.80$; $p < 0.0001$), SI ($r = 0.42$; $p = 0.01$) and VO_2 max ($r = -0.41$; $p = 0.03$), with a poor correlation with TAPSE ($r = -0.34$; $p = 0.05$) and right atrial LS ($r = -0.37$; $p = 0.03$). Stepwise multivariate analysis showed that RV free wall LS ($\beta = 0.701$, $p < 0.0001$) was independently associated with RV fibrosis (overall model $R^2 = 0.64$, $p < 0.0001$). RV free wall LS was the main determinant of myocardial fibrosis. In the subgroup of patients with severe RV fibrosis, RV free wall LS had the highest diagnostic accuracy for detecting severe myocardial fibrosis (area under the curve = 0.87; 95% confidence interval: 0.80 to 0.94).

CONCLUSIONS In late-stage HF patients, the right ventricle is enlarged, with reduced systolic function due to significant myocardial fibrosis. RV free wall myocardial deformation is the most accurate functional measure that correlates with the extent of RV myocardial fibrosis and functional capacity. (J Am Coll Cardiol Img 2015;8:514–22) © 2015 by the American College of Cardiology Foundation.

Right ventricular (RV) systolic function is an important prognostic factor in heart failure (HF) with longitudinal systolic amplitude of motion and myocardial strain predicting exercise capacity and survival (1–4). Such measurements of RV free wall have proved essential in contributing to 80% of its stroke volume and are able to explain the cavity adaptive mechanisms to volume and pressure overload (5). RV longitudinal and transverse shortening decline also occurs in RV failure in pulmonary arterial hypertension, which in late stages is associated with progressive leftward septal displacement (6,7). The aim of this study was to determine the value of right ventricular longitudinal strain (RVLS) in predicting the extent of RV myocardial fibrosis in patients with end stage HF requiring heart transplantation (HT).

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METHODS

STUDY POPULATION. We enrolled 27 patients with end-stage HF (left ventricular [LV] ejection fraction ≤25%; New York Heart Association [NYHA] functional class III to IV despite full medical therapy and cardiac resynchronization therapy [CRT]), referred to Le Scotte Hospital of Siena for a simultaneous right heart catheterization and echocardiographic evaluation before HT (8,9).

Tissue samples of the RV free wall were obtained from explanted hearts. Patients were excluded if they were not in sinus rhythm, on mechanical ventilation, had severe mitral/tricuspid regurgitation, other valve disease, or suboptimal echocardiographic image quality. Patients' echocardiographic results were compared with those from 25 controls, none of whom had a cardiac condition or history of any systemic disease. Patients and controls gave written informed consent before participating in the study. The project complied with the declaration of Helsinki and had been approved by the local ethics committee.

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STANDARD ECHOCARDIOGRAPHY. All echocardiographic examinations were performed according to the recommendations of the American and European Society of Echocardiography (10,11). Studies were performed using Vivid 7, GE Medical System echocardiograph (Horten, Norway), equipped with an adult 1.5- to 4.3-MHz phased array transducer, and an echocardiogram continuously displayed. LV ejection fraction was calculated from the apical views using the biplane modified Simpson method (10) and LV mass using the Penn formula (12) and was indexed to body surface area (BSA).

LV DIASTOLIC FUNCTION. Pulsed-wave Doppler velocities of LV filling were recorded from the apical 4-chamber view by placing the sample volume by the tips of the mitral leaflets. Early (E) and late (A) diastolic LV filling velocities were registered and E/A ratio was calculated (13) and used as standard index of LV diastolic function (14). The LV filling pattern was considered restrictive when the E/A ratio was >2.0, E-wave deceleration time <140 ms, and the left atrium dilated, and >40 mm in diameter (15). Raised E/e' was also taken as a marker of raised filling pressures (16). The same method was used to obtain RV filling velocities and measurements (17).

RV MEASUREMENTS. RV volume was measured from the 4-chamber view at end-diastole. The mid-cavity diameter was measured in the middle third at the level of the LV papillary muscles (18).

RV LONGITUDINAL FUNCTION. RV longitudinal function was studied using the pulsed tissue Doppler imaging technique with the sample volume at the level of tricuspid lateral annulus from the apical 4-chamber view (19). Peak systolic (s'), early diastolic (e'), and late diastolic (a') tricuspid annular velocities were obtained. s' is considered to be a relatively load-independent index of RV longitudinal systolic function, and e' and e'/a' ratio are considered to be load-independent markers of diastolic relaxation. Tricuspid annular plane systolic excursion (TAPSE) was measured with the cursor placed at the lateral angle of the annulus from the apical 4-chamber view (20).

LV AND RV LONGITUDINAL MYOCARDIAL INTRINSIC FUNCTION. LV and RV myocardial function was studied using speckle tracking echocardiography of the apical long axis, obtained from the apical 4- and 2-chamber views, during a quiet breath hold, with a frame rate of 60 to 80 per s. Three consecutive heart cycles were recorded and averaged. The off-line analysis was performed using a commercially available semiautomated 2-D strain software (EchoPac, GE, Waukesha, Wisconsin).

The peak LV longitudinal strain (LS) was defined as the peak negative value on the strain curve. The LV cavity was traced manually from the innermost endocardial edge at end-systole, and the software automatically defined the LS throughout the cardiac cycle. LS was analyzed first in the apical long axis view where the closure of the aortic valve was defined with respect to the R wave to mark end-systole. Then the same process was used for the 4-chamber and 2-chamber views. The automated algorithm provided the longitudinal peak systolic strain value for each LV segment from a 17-segment model polar plot and an average value for the 3 apical views (LV global LS) (21).

Calculation of RV free wall LS was obtained with the same method delineating a region of interest composed of three segments of the lateral wall: basal, mid-cavity, and apical. After segmental tracking, the RV LS curves were generated by the software and the average value of LS was calculated (22) (RV free wall LS [**Figure 1**]).

RV SYSTOLIC FUNCTION. RV sphericity index (SI), was calculated at end-diastole by dividing the short axis by the long-axis diameters (18,23).

RIGHT ATRIAL STRUCTURE AND FUNCTION. Right atrial (RA) area and volume were measured using the biplane method of disks in the apical 4-chamber view at end-systole (10) and were indexed to BSA. RA

ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy

HF = heart failure

NT-proBNP = N-terminal pro-hormone of brain natriuretic peptide

NYHA = New York Heart Association

ROC = receiver operating characteristic

TAPSE = tricuspid annular plane systolic excursion