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Original article

Echocardiographic assessment of right ventricular function in routine practice: Which parameters are useful to predict one-year outcome in advanced heart failure patients with dilated cardiomyopathy?

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ABSTRACT

Background: Right ventricular (RV) function has recently gained attention as a prognostic predictor of outcome even in patients who have left-sided heart failure. Since several conventional echocardiographic parameters of RV systolic function have been proposed, our aim was to determine if any of these parameters (tricuspid annular plane systolic excursion: TAPSE, tissue Doppler derived systolic tricuspid annular motion velocity: S', fractional area change: FAC) are associated with outcome in advanced heart failure patients with dilated cardiomyopathy (DCM).

Methods: We retrospectively enrolled 68 DCM patients, who were New York Heart Association (NYHA) Class III or IV and had a left ventricular (LV) ejection fraction <35%. All patients were undergoing evaluation for heart transplantation or management of heart failure. Primary outcomes were defined as LV assist device implantation or cardiac death within one year.

Results: Thirty-nine events occurred (5 deaths, 32 LV assist devices implanted). Univariate analysis showed that age, systolic blood pressure, heart rate, NYHA functional class IV, plasma brain natriuretic peptide concentration, intravenous inotrope use, left atrial volume index, and FAC were associated with outcome, whereas TAPSE and S' were not. Receiver-operating characteristic curve analysis showed that the optimal FAC cut-off value to identify patients with an event was <26.7% (area under the curve = 0.74). The event-free rate determined by Kaplan–Meier analysis was significantly higher in patients with FAC ≥ 26.7% than in those with FAC < 26.7% (log-lank, $p = 0.0003$). Moreover, the addition of FAC < 26.7% improved the prognostic utility of a model containing clinical variables and conventional echocardiographic indexes.

Conclusions: FAC may provide better prognostic information than TAPSE or S' in advanced heart failure patients with DCM.

Introduction

There is increasing appreciation of the potential impact of right ventricular (RV) function on outcome in patients with left-sided heart failure [1–3]. Since cardiovascular magnetic resonance has allowed noninvasive measurement of RV ejection fraction with high accuracy and reproducibility [4,5], it has become the gold-standard for the assessment of ventricular function, especially RV function. Gulati et al. [6] reported that RV ejection fraction assessed by cardiovascular magnetic resonance was an independent predictor of outcome in patients with dilated cardiomyopathy (DCM). However, cardiovascular magnetic resonance is still not readily available in daily practice. Moreover, it is not useful in patients who are hemodynamically unstable such as those with advanced heart failure, or in patients with some devices such as implantable cardioverter defibrillators. Therefore, echocardiography is an essential noninvasive tool to evaluate cardiac function in those patients.

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Since the availability of new techniques such as 3D echocardiography or 2D speckle tracking imaging for assessing RV systolic function [7–9] is still limited in routine practice, several conventional parameters of RV systolic function, which can be measured in routine practice, have been recommended in the current guideline of the American Society of Echocardiography [10]. However, the usefulness of these parameters in the management of advanced heart failure has not been firmly established. Therefore, our aim was to determine if conventional echocardiographic parameters for assessing RV function are associated with one-year outcome in patients with advanced heart failure due to DCM.

Materials and methods

Patients and protocol

We retrospectively analyzed Stage C/D, New York Heart Association (NYHA) Class III/IV patients with DCM, who were admitted to our institution for evaluation for heart transplantation or management of heart failure between November 2012 and June 2015. The diagnosis of DCM was established as left ventricular (LV) dysfunction in the absence of coronary artery disease documented by coronary angiography, and the absence of specific heart muscle disease or active myocarditis at endomyocardial biopsy. Patients with mechanical circulatory support or on ventilators at admission were excluded. The echocardiography findings after admission were reviewed, and patients with LV ejection fraction $\geq$35%, lack of RV parameters, or inadequate image quality to assess RV parameters were also excluded. The final study population included a total of 68 patients with DCM. All patients were on adequate medical therapy and resynchronization therapy and/or a defibrillator, if appropriate. Vital status, information about medical treatment, plasma brain natriuretic peptide (BNP) concentration at the time of echocardiography, and outcome data were collected from medical records. The date of echocardiography was considered the entry time-point of observation. Primary outcomes were defined as implantation of a LV assist device or cardiac death within the first year. The attending physician determined the timing of device implantation based on whether the patient developed cardiogenic shock, had progressive decline of end-organ function in spite of maximal treatment, or was considered inotrope-dependent despite optimal medical therapy. Our data collection protocol was approved by the institutional review board of the University of Tokyo Hospital.

Echocardiography

Our echocardiography laboratory is maintained under the guidelines of the Japanese Society of Echocardiography [11]. In all subjects, cardiac chamber quantification by 2D echocardiography was performed according to guidelines [10]. LV diameters were measured using 2D echocardiography according to the recommended criteria. The thickness of the interventricular septum and the LV posterior wall were measured at end-diastole. LV mass was calculated using diastolic measurements of LV diameter and wall thickness on 2D echocardiography according to the cube formula [10]. LV end-diastolic and end-systolic volumes were determined from the apical views using the biplane disk summation method. LV ejection fraction was calculated by the following equation: $100 \times$ (end-diastolic volume − end-systolic volume)/end-diastolic volume. Left atrial (LA) volume was measured using the biplane method of disks. Each parameter was indexed for body surface area, when appropriate. For assessing conventional diastolic parameters, mitral inflow velocities were determined by pulsed Doppler imaging [12]. The peak early (E) and late (A) diastolic velocity, the E-wave deceleration time from the peak of the early diastolic wave to baseline and the E/A ratio were assessed from the mitral inflow velocity pattern. The mitral annular motion velocity was recorded at both the lateral and medial mitral annulus in the apical 4-chamber view by pulsed tissue Doppler. Peak early diastolic velocity (e') of the annulus was measured and the ratio of peak early diastolic transmitral flow velocity to annular velocity (E/e') was calculated. Because quantitative assessment of mitral regurgitation was not performed in all patients, qualitative assessment (mild, moderate, or severe) by 1 expert sonographer and the physician were used. Grading of tricuspid regurgitation severity was performed according to the guideline [13].

Study of RV function

Based on the guideline [10], tricuspid annular plane systolic excursion (TAPSE), tissue Doppler-derived systolic tricuspid annulus motion velocity (S'), and RV fractional area change (FAC) were used to assess RV systolic function in the present study. An example of data acquisition is displayed in Fig. 1. TAPSE was measured on the M-mode tracing obtained from the RV-focused apical 4-chamber view, with the M-mode cursor aligned through the lateral site of the tricuspid annulus. Pulsed Doppler tissue imaging at the lateral site of the tricuspid annulus was acquired from the RV-focused apical 4-chamber view to measure peak systolic, early diastolic and late diastolic annular velocities at the end of expiration to minimize translational motion. Angle-dependent parameters, including TAPSE and S' were obtained using the optimal angle of incidence available. FAC was calculated from the RV-focused apical 4-chamber view using the following formula: $100 \times$ (RV end-diastolic area − RV end-systolic area)/RV end-diastolic area. To determine the reproducibility of RV systolic function parameters, a total of 10 randomly selected examinations were analyzed twice by a first investigator at a 1-week interval, as well as by a second investigator. Intra- and inter-observer variability was expressed as the absolute difference between the repetitive measurements divided by their mean value.

Right atrial area was also measured from the apical 4-chamber view at end-systole based on the guideline. Moreover, we measured the tissue Doppler myocardial performance index from pulsed Doppler tissue imaging at the lateral site of the tricuspid annulus (Fig. 1). In cases of atrial fibrillation, RV measurements were averaged over five cardiac cycles based on the guideline [10].

Statistical analysis

All data were expressed as the mean ± standard deviation (SD) or the number (%) of patients. A Student's t-test was used to assess differences between the mean values of continuous variables. Categorical variables were compared with a Fisher's exact test. The relationships among all possible pairs of RV systolic parameters were assessed using Pearson's correlation coefficient. The association of selected variables with one-year outcome was evaluated using a univariate Cox proportional hazards model. The cumulative event-free rates were obtained using the Kaplan–Meier method, and the difference between survival curves was tested by the log-rank test. Moreover, Cox proportional hazards models were compared to find the increase in prognostic benefit of RV parameters in comparison with clinical and routine echocardiographic variables. A statistically significant increase in the global log-likelihood chi-square of the model was interpreted as indicating incremental prognostic value. A probability value of $p < 0.05$ was considered significant. All data were statistically analyzed using JMP version10.0.0 (SAS Institute, Cary, NC, USA) and SPSS version 17.0 (SPSS Inc., Chicago, IL, USA).

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