IJC Heart & Vessels 4 (2014) 203–207

Contents lists available at ScienceDirect

IJC Heart & Vessels

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vessels

Left atrial emptying fraction predicts limited exercise performance in heart failure patients

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ARTICLE INFO

Article history:
Received 26 February 2014
Accepted 13 April 2014
Available online 24 April 2014

Keywords:
Heart failure
Six-minute walk test
Exercise capacity
Left atrial emptying function

ABSTRACT

Aim: We aimed in this study to assess the role of left atrial (LA), in addition to left ventricular (LV) indices, in predicting exercise capacity in patients with heart failure (HF).
Methods: This study included 88 consecutive patients (60 ± 10 years) with stable HF. LV end-diastolic and end-systolic dimensions, ejection fraction (EF), mitral and tricuspid annulus peak systolic excursion (MAPSE and TAPSE), myocardial velocities (s′, e′ and a′), LA dimensions, LA volume and LA emptying fraction were measured. A 6-min walking test (6-MWT) distance was performed on the same day of the echocardiographic examination.
Results: Patients with limited exercise performance (≤300 m) were older ($p = 0.01$), had higher NYHA functional class ($p = 0.004$), higher LV mass index ($p = 0.003$), larger LA ($p = 0.002$), lower LV EF ($p = 0.009$), larger LV end-systolic dimension ($p = 0.007$), higher E/A ratio ($p = 0.03$), reduced septal MAPSE ($p < 0.001$), larger LA end-systolic volume ($p = 0.03$), larger LA end-diastolic volume ($p = 0.005$) and lower LA emptying fraction ($p < 0.001$) compared with good performance patients. In multivariate analysis, only the LA emptying fraction [0.944 (0.898–0.993), $p = 0.025$] independently predicted poor exercise performance. An LA emptying fraction <60% was 68% sensitive and 73% specific (AUC 0.73, $p < 0.001$) in predicting poor exercise performance.
Conclusion: In heart failure patients, the impaired LA emptying function is the best predictor of poor exercise capacity. This finding highlights the need for routine LA size and function monitoring for better optimization of medical therapy in HF.

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1. Introduction

Heart failure (HF) is a clinical syndrome, which is becoming a major problem in public health in recent decades [1,2]. Despite many new achievements in pharmacological and non-pharmacological treatments, the morbidity and mortality associated with HF still remain high [2–6]. Several echo-parameters were tested previously [7–15] for clinical outcome prediction in patients with HF. Different indices were also, proposed as predictors of survival [11–17], quality of life [11–15] and exercise capacity [22–26] in these patients. Six-minute walk test (6-MWT) has been introduced as an accurate tool for assessing exercise capacity in HF patients, being safe, simple to perform and its results can predict clinical outcomes [18–21].

Left ventricular (LV) systolic function indices [22,23] and those of global mechanical dyssynchrony [24–26] have been shown to independently predict exercise capacity in HF patients. However, the left atrial (LA) function indices and their relationship with exercise markers have not been completely tested yet in this setting. Therefore, we aimed to test LA total emptying fraction as a potential predictor of exercise capacity in HF patients in comparison with other clinical and echocardiographic parameters.

2. Methods

2.1. Study population

We studied 88 patients (mean age 60 ± 10 years, 61% female) with clinical diagnosis of HF, and New York Heart Association (NYHA) functional class I–class III. Patients were referred to the Service of Cardiology, Internal Medicine Clinic, University Clinical Centre of Kosovo, between February 2013 and November 2013. At the time of the study, all patients were on conventional medical treatment, optimized at least 2 weeks prior to enrollment, based on patient's symptoms and renal function:

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http://dx.doi.org/10.1016/j.ijchv.2014.04.002
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84.6% were receiving ACE inhibitors or ARB, 70.5% beta-blockers, 55% diuretics, 77% aspirin and 20.5% Ca-blockers. Of the studied cohort, 19% had ischemic etiology, 65.5% hypertension, 7.14% valve disease and 8.3% unknown etiology.

Patients with clinical evidence for cardiac decompensation, limited physical activity due to factors other than cardiac symptoms (e.g. arthritis), chronic renal failure with a stage >2 (glomerular filtration rate ≥ 89 mL/min), chronic obstructive pulmonary disease (COPD) or those with recent acute coronary syndrome, stroke or anemia, were excluded. Patients gave a written informed consent to participate in the study, which was approved by the local Ethics Committee.

2.2. Data collection

Detailed history and clinical assessment were obtained in all patients, in whom routine biochemical tests were also performed including, lipid profile, blood glucose level and kidney function tests. Estimated body mass index (BMI) was calculated from weight and height measurements. Waist and hip measurements were also made and waist/hip ratio calculated.

2.3. Echocardiographic examination

A single operator performed all echocardiographic examinations using a Philips Intelligent E-33 system with a multi-frequency transducer and harmonic imaging as appropriate. Images were obtained with the patient in the left lateral decubitus position and during quiet expiration. LV end-systole and end-diastole dimension measurements were made from the left parasternal long axis view with the M-mode cursor positioned by the tips of the mitral valve leaflets. LV volumes and EF were calculated from the apical 2 and 4 chamber views using the modified Simpson's method. MAPSE and TAPSE were studied by placing the M-mode cursor at the lateral and septal angles of the mitral annulus and the lateral angle of the tricuspid annulus.

Total amplitude of long axis motion (MAPSE or TAPSE) was measured as previously described [27] from peak inward to peak outward points. LV and right ventricular (RV) long axis myocardial velocities were also studied using Doppler myocardial imaging technique. From the apical 4-chamber view, longitudinal velocities were recorded with the pulsed wave Doppler sample volume placed at the basal part of LV lateral and septal segments as well as RV free wall. Systolic (s′) and early and late (e′ and a′) diastolic myocardial velocities were measured with the gain optimally adjusted. Mean value of the lateral and septal LV velocities was calculated.

Diastolic function of the LV and RV was assessed from filling velocities using spectral pulsed wave Doppler with the sample volume positioned at the tips of the mitral and tricuspid valve leaflets, respectively, during a brief apnea. Peak LV and RV early (E wave) and late (A wave) diastolic velocities were measured, and E/A ratios were calculated. The E/e′ ratio was calculated as the ratio between transmitral E wave and mean lateral and septal e′ wave velocities. The isovolumic relaxation time was also measured from aortic valve closure to mitral valve opening on the pulsed wave Doppler recording. LV filling pattern was considered "restrictive" when E/A ratio was >2.0, E wave deceleration time <140 ms and the left atrium dilated of more than 40 mm in transverse diameter [28].

Mitral regurgitation severity was assessed by color and continuous wave Doppler and was graded as mild, moderate or severe according to the relative jet area to that of the left atrium as well as the flow velocity profile, in line with the recommendations of the American Society of Echocardiography [29]. Likewise, tricuspid regurgitation was assessed by color Doppler and continuous-wave Doppler. Retrograde transtricuspid pressure drop >35 mmHg was taken as an evidence for pulmonary hypertension [30]. All M-mode and Doppler recordings were made at a fast speed of 100 mm/s with a superimposed ECG (lead II).

2.4. Measurements of left atrial dimensions and function

LA diameter was measured from aortic root recordings with the M-mode cursor positioned at the level of the aortic valve leaflets. LA volumes were measured using area-length method from the apical four and two chamber views, according to the guidelines of the American Society of Echocardiography [31]. Left atrial maximum volume (LA end-systolic volume) was measured at the end of LV systole, just before the opening of the mitral valve, LA minimum volume (LA end-diastolic volume) was measured at end diastole, right after the closure of the mitral valve, and left atrial total emptying fraction (LA emptying function) was calculated automatically [31,32].

2.5. Six-minute walk test

Within 24 h of the echocardiographic examination, a 6-MWT was performed on a level hallway surface for all patients and was administered by a specialized nurse, blinded to the results of the echocardiogram. According to the method of Gyatt et al. [33], patients were informed of the purpose and protocol of the 6-MWT, which was conducted in a standardized fashion while patients on their regular medications [34,35]. A 15-m flat, obstacle-free corridor was used, and patients were instructed to walk as far as they can, turning 180° after reaching the end of the corridor, during the allocated time of 6 min. Patients walked unaccompanied so as not to influence walking speed. At the end of the 6 min, the supervising nurse measured the total distance walked by the patient. Pulse and blood pressure were measured before and at the end of the walking test.

2.6. Statistical analysis

Data are presented as mean ± SD or proportions (% of patients). Continuous data were compared with two-tailed unpaired Student *t* test and discrete data with chi-square test. Correlations were tested with Pearson coefficients. Predictors of 6-MWT distance were identified with univariate analysis, and multivariate logistic regression was performed using the step-wise method. A significant difference was defined as $p < 0.05$ (2-tailed). Patients were divided according to their ability to walk >300 m into good and limited exercise performance groups [36] and were compared using unpaired Student *t* test.

3. Results

Patients' mean age was 60 ± 10 years, and 61% were females (Table 1). The patients group as a whole exercised for a mean of 298 ± 109 m.

Table 1
Baseline patient's data.

Clinical data	
Sex (female, %)	61
Age (years)	60 ± 10
Smoking (%)	21.5
Diabetes (%)	29
Body mass index	29 ± 3.5
Body surface area	1 ± 0.2
Waist/hip ratio	0.95 ± 0.5
NYHA class	1.8 ± 0.8
LBBB	19
Fasting glucose (mmol/L)	7 ± 2.9
Total cholesterol (mmol/L)	4.6 ± 1.2
Triglycerides (mmol/L)	1.7 ± 1
Urea (mmol/L)	8.8 ± 6
Creatinine (mmol/L)	93 ± 29

NYHA: New York Heart Association; LBBB: left bundle branch block.

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