Original Research

Increased Right Atrial Volume Index Predicts Low Duke Activity Status Index in Patients with Chronic Heart Failure

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Key words: **Right ventricle, right atrial enlargement, volume overload, prognostic factors, functional capacity.**

Introduction: The aim of the present study was to examine the value of the right atrial volume index (RAVI) as predictor of functional capacity in patients with heart failure.

Methods: A total of 51 patients with stable chronic heart failure of ischaemic or non-ischaemic aetiology were prospectively enrolled. The systolic function of the right ventricle was quantified using the tricuspid annular plane systolic excursion (TAPSE). Right atrial volume was measured in the apical 4-chamber view and was indexed to body surface area. The functional capacity was assessed by the Duke Activity Status Index (DASI).

Results: Patients with a low functional capacity (DASI<10) had lower TAPSE (1.4 ± 0.3 cm versus 2.0 ± 0.4 cm, p<0.001), higher RAVI (42 ± 15 ml/m^2 versus 22 ± 9 ml/m^2, p<0.001), higher estimated right ventricular systolic pressure (61 ± 13 mmHg versus 40 ± 16 mmHg, p<0.001), larger right ventricular end-diastolic diameter (4.7 ± 0.8 cm versus 3.6 ± 0.7 cm, p<0.001) and lower left ventricular ejection fraction (26 ± 6% versus 30 ± 7%, p=0.022). Multivariate analysis revealed that TAPSE was the single independent predictor of DASI. In the subgroup of patients with reduced right ventricular systolic function (TAPSE<2 cm), RAVI was the single independent predictor of low DASI. In the overall population RAVI≥30.6 ml/m^2 had 75% sensitivity and 83% specificity in predicting DASI<10. Within the subgroup of patients with TAPSE<2 cm, RAVI≥30.6 ml/m^2 had better sensitivity and specificity (79% and 90% respectively) in predicting DASI<10.

Conclusions: Increased right atrial volume index predicts low functional capacity quantified by the Duke Activity Status Index in patients with stable chronic heart failure.

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Left ventricular ejection fraction (LVEF) has proven to be a powerful predictor of cardiovascular events and it is commonly used to describe the severity of chronic heart failure.[1] However, it is well known that LVEF does not accurately reflect the functional capacity of patients with heart failure.[2] Previous studies have recognised the effect of left ventricular diastolic dysfunction on patients' functional capacity and survival.[3] More recently, the role of the right ventricle in the clinical presentation of the heart failure syndrome has been emphasised.[4-6] A recent study showed that the right atrial volume indexed to body surface area is an independent predictor of prognosis in patients with chronic heart failure.[7] The value of standard echocardiographic indexes of the right heart in the evaluation of the functional capacity of patients with heart failure has not been adequately studied.

The aim of the present study was to explore whether the right atrial volume index and the systolic function of the right ventricle are related to the functional capacity of patients with heart failure, quantified by the Duke Activity Status Index (DASI) questionnaire.

Methods

Patient population

Consecutive patients with stable chronic heart failure, evaluated at a tertiary cardiac centre, were screened for eligibility in a prospective observational study designed to assess newer indices for the assessment of dilated cardiomyopathy. Inclusion criteria were age >18 years, ejection fraction <45%, and a history of known heart failure due to ischaemic or non-ischaemic dilated cardiomyopathy. Non-ischaemic dilated cardiomyopathy was diagnosed after the exclusion of severe coronary artery disease (causing >50% stenosis in one or more coronary arteries) by coronary angiography, or exclusion of ischaemia and scar by nuclear perfusion scan in 2 cases of young patients who refused to undergo coronary angiography. Exclusion criteria were recent (≤30 days) acute coronary syndrome, pulmonary oedema or decompensation of heart failure, permanent pacemakers or cardiac resynchronization devices, malignancy, and severe renal failure requiring haemofiltration. The study protocol was approved by the ethics committee of our institution and all subjects gave written informed consent.

Echocardiographic study

All study subjects underwent a complete echocardiographic study, including two-dimensional (2D), colour-flow and spectral Doppler, as well as tissue Doppler imaging (TDI) using a GE Vingmed Vivid 7 system (GE Vingmed Ultrasound, Horten, Norway). All images were saved for offline analysis by an experienced echocardiographer who was blinded to the study population.

Standard 2D and colour-flow Doppler images were obtained using the parasternal long- and short-axis and apical views. Right ventricular global systolic function was assessed as tricuspid annular plane systolic excursion (TAPSE), by two-dimensional difference of end-diastolic and end-systolic lines (in cm) traced between the centre of the ultrasound fan origin and the junction of the right ventricular lateral tricuspid annulus, in apical four-chamber view. Right ventricular end-diastolic diameter was measured at the level of the tricuspid annulus in the apical four-chamber view. Right ventricular systolic pressure was estimated by calculating the maximal velocity of the tricuspid regurgitant jet and then, using the Bernoulli equation, adding to this value an estimated right atrial pressure based on both the size of the inferior *vena cava* and the change in diameter of this vessel during respiration.[15] *Vena cava* diameter was measured in the subxiphoid view. Continuous Doppler echocardiography was used to measure pulmonary artery and aortic velocities, tricuspid regurgitation velocity, and mitral regurgitation velocity. Pulsed Doppler echocardiography for the assessment of the standard diastolic filling velocities of both ventricles was performed using the apical four-chamber view. Thus, the peak early diastolic filling velocity (E-wave) and peak late diastolic filling velocity (A-wave) were recorded. All measurements from three end-expiratory cycles were averaged at a sweep speed of 100 mm/s.

Right and left atrial volumes were calculated from the apical four-chamber view at end systole. The right and left atrial volume indexes were derived by dividing the volumes by body surface area, which was calculated using the Du Bois and Du Bois formula.[8]

Assessment of functional capacity

For the assessment of the patients' functional capacity we used the DASI, which was developed in 1989 by Hlatky et al.[9] DASI is a 12-point scale that evaluates the patient's ability to perform everyday activities (see appendix). The same day that the echo study was performed the patients were asked to fill in the DASI questionnaire. The Greek translation of the questionnaire was used, which was previously validated and presented a high Cronbach reliability coefficient (0.90).[10] A cut-off point of DASI<10 was used to define the subgroup of patients with the lowest functional capacity, because DASI=9.95 is achieved if the subject is able to perform activities below 3 METs, i.e. items 1,2,3 and 6 of the questionnaire.

Statistical analysis

Statistical analysis was performed using SPSS v16 for Windows (Chicago IL, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables as absolute number and percentages. Differences between groups were sought using Student's t-test or the Mann–Whitney U test for the normally or non-normally distributed continuous variables. Correlations between variables were tested with Pearson's r or Spearman's r, as appropriate, and with linear regression analysis. Variables with $p<0.10$ in the univariate analysis were entered into a stepwise multivariate linear regression model. The sensitivity and specificity of RAVI were assessed by the receiver-operator characteristic (ROC) curve. A p-value <0.05 was considered statistically significant.

Results

A total of 51 patients (40 men, 11 women, mean age 62 ± 15 years), with stable chronic heart failure of ischaemic (39%) or non-ischaemic (61%) aetiology and mean LVEF 28 ± 7% were studied. The patients' characteristics are presented in Table 1.

The mean DASI score was 17.9 ± 14.0. Patients were divided into two groups according to functional capacity (Table 2). Twenty patients (39%) had DASI<10 and were older, had a higher prevalence of atrial fibrillation, larger left ventricular end-systolic volume, lower LVEF, larger indexed diameter and volume of left and right atria, larger right ventricular (RV) end-diastolic diameter, lower TAPSE, higher RV systolic pressure (RVSP), and larger inferior *vena cava* (IVC) diameter.

DASI showed a strong correlation with NYHA class (Spearman's r=-0.653, p<0.001) and age (Spearman's r=-0.497, p<0.001). Table 3 shows the univariate and multivariate correlation of clinical and echocardiographic variables with DASI. In the total patient group, age-adjusted DASI was correlated with TAPSE and IVC diameter (Figure 1), RVSP, RAVI, RV end-diastolic diameter and left atrial volume index. Atrial fibrillation was also significant in the prediction of DASI. IVC diameter was not entered into the multivariate model because of the strong correlation with the derived RVSP, which was added instead. TAPSE adjusted for age was the only independent predictor of DASI in the total population (beta=0.633, p<0.001).

Table 1. Patients' characteristics.

Age (years)	62 ± 15
Sex (male/female), n (%)	40 (78)/11 (22)
Heart failure aetiology, n (%):	
Ischaemic	19 (39)
Non-ischaemic	32 (61)
NYHA Class	2.8 ± 0.6
Left ventricular ejection fraction (%)	28 ± 7
Hypertension, n (%)	23 (46)
Diabetes mellitus, n (%)	18 (36)
Dyslipidaemia, n (%)	17 (36)
Family history of CAD, n (%)	10 (20)
Smoking, n (%)	9 (18)
Rhythm, n (%):	
Sinus rhythm	41 (80)
Atrial fibrillation	10 (20)
QRS morphology, n (%):	
Normal	21 (41)
Left bundle branch block	27 (53)
Right bundle branch block	3 (6)
QRS duration (ms)	124 ± 42
Medication, n (%):	
β-Blockers	43 (90)
ACE inhibitors or ARBs	42 (88)
Spironolactone antagonists	35 (73)
Diuretics	47 (98)
Digitalis	13 (27)
Statins	22 (47)
Aspirin	22 (47)
Clopidogrel	15 (32)

NYHA – New York Heart Association; CAD – coronary artery disease; ACE – angiotensin converting enzyme; ARBs – angiotensin receptor blockers.

Subgroup analysis

In the subgroup of 32 patients with impaired RV systolic function (TAPSE<2 cm) DASI was correlated with RAVI (Figure 2), RV end-diastolic diameter, TAPSE, left atrial volume index, RVSP, and atrial fibrillation (Table 4). Multivariate analysis revealed that only RAVI was an independent predictor of DASI in patients with reduced RV systolic function (beta=-0.513, p=0.009).

Relation between RAVI and other variables

RAVI showed a strong correlation with IVC diameter (r=-0.544, p=0.002), RV end-systolic diameter (r=0.475, p=0.002), TAPSE (r=-0.466, p=0.001), left atrial volume index (r= 0.459, p=0.001), and a weaker correlation with LVEF (r=-0.360, p=0.012) and LV end-systolic volume (r=0.358, p=0.013).

Sensitivity and specificity of RAVI in predicting low functional capacity

The sensitivity and specificity of RAVI in predicting low functional capacity (DASI<10) was calculated using ROC curves (Figure 3). A cut-off value of RAVI ≥30.6 ml/m^2 had 75% sensitivity and 83% specificity (AUC=0.874, p<0.001) in predicting DASI<10. In the subgroup of patients with impaired RV systolic function (TAPSE<2 cm) a cut-off value of RAVI ≥30.6 ml/m^2 had 79% sensitivity and 90% specificity in predicting DASI<10 (AUC=0.937, p<0.001).

Table 2. Demographic and echocardiographic parameters in the subgroups according to the patients' Duke Activity Status Index score.

	DASI<10 n=20	DASI≥10 n=31	p
Age (years)	68 ± 11	58 ± 16	0.012
Sex (male/female)	15/5	25/6	0.897
HF aetiology (ischaemic/non-ischaemic)	10/10	9/22	0.224
Heart rate	77 ± 15	72 ± 12	0.200
Sinus rhythm/ atrial fibrillation	11/9	30/1	0.001
NYHA class	3.2 ± 0.3	2.6 ± 0.6	<0.001
Interventricular septum thickness (cm)	1.07 ± 0.19	0.88 ± 0.26	0.008
LV posterior wall thickness (cm)	1.11 ± 0.22	1.01 ± 0.24	0.163
LV end-diastolic diameter (cm)	6.65 ± 0.98	6.48 ± 0.63	0.435
LV end-systolic diameter (cm)	5.88 ± 1.44	5.60 ± 0.77	0.380
LV end-diastolic volume (ml)	213 ± 84	178 ± 54	0.082
LV end-systolic volume (ml)	161 ± 70	124 ± 39	0.043
LV ejection fraction (%)	26 ± 6	30 ± 7	0.022
Left atrial diameter (cm)	5.2 ± 0.6	4.7 ± 0.6	0.010
Left atrial volume index (ml/m^2)	62 ± 27	43 ± 16	0.002
Right atrial diameter (cm)	4.7 ± 0.8	3.8 ± 0.6	<0.001
Right atrial volume index (ml/m^2)	42 ± 15	22 ± 9	<0.001
RV end-diastolic diameter (cm)	4.7 ± 0.8	3.6 ± 0.7	<0.001
TAPSE (cm)	1.42 ± 0.32	2.03 ± 0.41	<0.001
Pulmonary flow maximum velocity (m/s)	0.8 ± 0.2	0.9 ± 0.2	0.042
Tricuspid regurgitation maximum velocity (m/s)	3.3 ± 0.5	2.7 ± 0.7	0.002
Tricuspid regurgitation peak gradient (mmHg)	45 ± 14	30 ± 15	0.001
Aortic flow maximum velocity (m/s)	1.29 ± 0.48	1.24 ± 0.37	0.943
Mitral regurgitation maximum velocity (m/s)	4.2 ± 0.9	3.8 ± 1.3	0.199
Transmitral Doppler flow velocities (m/s):			
E	0.95 ± 0.24	0.81 ± 0.27	0.065
A	0.41 ± 0.18	0.64 ± 0.30	0.017
Transtricuspid Doppler flow velocities (m/s):			
E	0.54 ± 0.18	0.46 ± 0.14	0.235
A	0.40 ± 0.20	0.41 ± 0.12	0.882
Inferior *vena cava* diameter (cm)	2.34 ± 0.47	1.62 ± 0.39	<0.001
Estimated RV systolic pressure (mmHg)	61 ± 13	40 ± 16	<0.001
DASI	5.66 ± 2.63	25.8 ± 12.47	<0.001

HF – Heart failure; LV – left ventricular; NYHA – New York Heart Association; RV – right ventricular; TAPSE – tricuspid annular plane systolic excursion; DASI – Duke Activity Status Index.

Table 3. Univariate and multivariate linear regression between Duke Activity Status Index and clinical and echocardiographic parameters adjusted for age, in all 51 patients.

	Univariate analysis		Multivariate analysis	
	beta	p	beta	p
Female sex	-0.057	0.692	–	
Diabetes mellitus	0.032	0.221	–	
Creatinine	-0.126	0.493	–	
Heart rate	-0.107	0.466	–	
Atrial fibrillation	-0.430	0.002	-0.197	0.165
TAPSE	0.633	<0.001	0.633	<0.001
Estimated RV end-systolic pressure	-0.532	<0.001	-0.259	0.092
Inferior *vena cava* diameter (cm)	-0.608	<0.001	–	
Right atrial volume index	-0.501	<0.001	-0.268	0.060
RV end-diastolic diameter	-0.493	<0.001	-0.252	0.080
Left atrial volume index	-0.352	0.015	-0.159	0.245
Left ventricular ejection fraction	0.216	0.128	–	
Left ventricular end-systolic volume	-0.185	0.198	–	

TAPSE – tricuspid annular plane systolic excursion; RV-right ventricular.

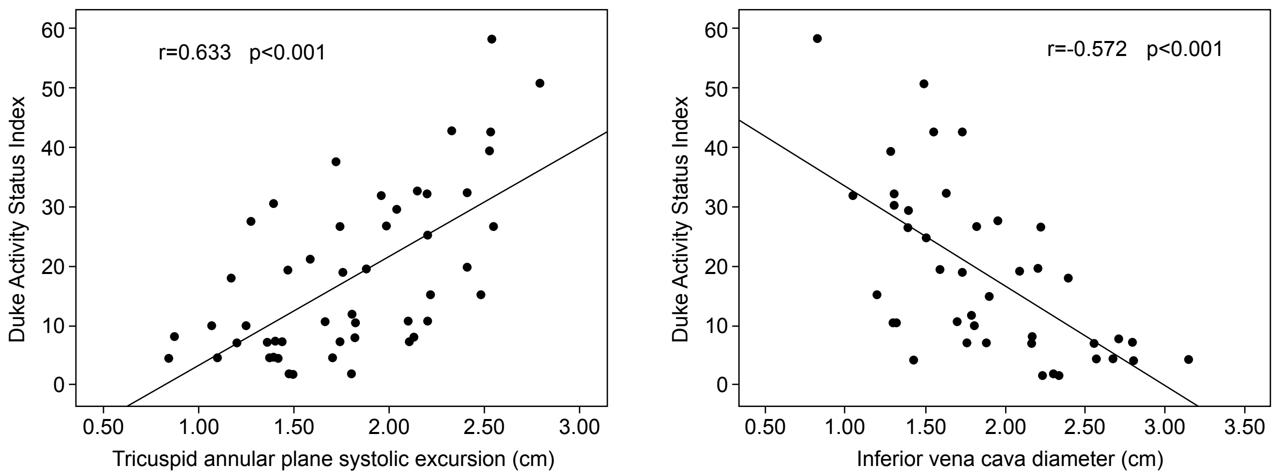

Figure 1. A. Correlation between Duke Activity Status Index and tricuspid annular plane systolic excursion. B. Correlation between Duke Activity Status Index and inferior *vena cava* diameter.

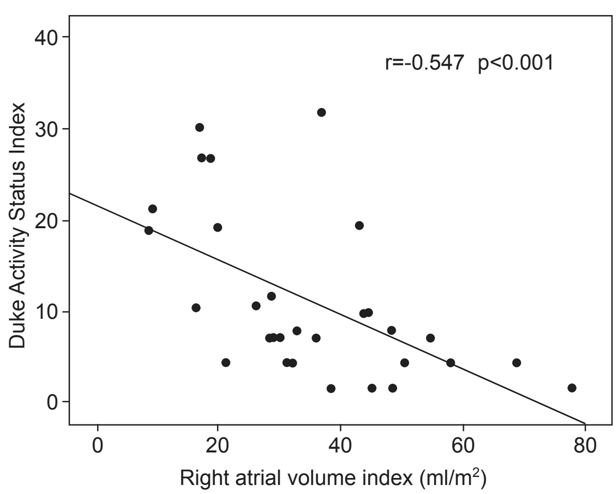

Figure 2. Correlation between Duke Activity Status Index and right atrial volume index in patients with impaired right ventricular systolic function (tricuspid annular plane systolic excursion <2 cm).

Discussion

The present study showed that TAPSE and RAVI are independent predictors of functional capacity in patients with chronic heart failure and reduced LVEF. Although the presence of atrial fibrillation was related to a lower DASI, the present study showed that RAVI was a stronger and independent predictor of DASI.

The relation between RV systolic function and the functional capacity of patients with heart failure has been shown previously. Troisi et al showed that TAPSE is related to BNP levels and peak VO_2 during a cardiopulmonary exercise test in patients with chronic heart failure.[6] In a recent study, Nunes et al indicated that longitudinal RV free wall systolic velocity assessed by tissue Doppler could predict peak VO_2 in patients with dilated cardiomyopathy due to Chagas disease.[5] In line with the previous studies we found that TAPSE was an independent predictor of DASI score.

The DASI score was developed by Hlatky in 1989 as a tool for the assessment of functional capacity that was shown to correlate well (Spearman's correlation coefficient 0.80) with peak oxygen uptake.[9] It has also been used to accurately predict functional capacity in patients with chronic obstructive pulmonary disease.[11] DASI has been validated in cardiovascular disease[13,14] and can predict the long-term survival post cardiac surgery.[12] A recent study by Parissis et al showed that DASI score in combination with NT-proBNP levels had prognostic value in patients with chronic heart failure.[10]

In the present study we additionally showed that increased IVC diameter correlates with low functional capacity in patients with heart failure. IVC dilatation is related to increased central venous pressure and is observed when volume overload of the right ventricle is present.[15,16] IVC diameter showed a strong correlation with RAVI. Sallach et al[7] demonstrated that RAVI increases in parallel with the worsening of RV systolic function (Spearman's $r=0.61$, $p<0.001$), and it also correlates with the diastolic function of the RV (Spearman's $r=0.51$, $p<0.001$), whereas RAVI is only weakly correlated with LVEF (Spearman's $r=0.26$, $p<0.001$). Similarly, in our pop-

Table 4. Univariate and multivariate linear regression between Duke Activity Status Index and clinical and echocardiographic parameters adjusted for age in the subgroup of 32 patients with impaired right ventricular systolic function (TAPSE<2 cm).

	Univariate analysis		Multivariate analysis	
	beta	p	beta	p
Atrial fibrillation	-0.412	0.015	-0.290	0.126
TAPSE	0.383	0.028	0.257	0.173
Estimated RV end-systolic pressure	-0.353	0.071	-0.244	0.191
Right atrial volume index	-0.513	0.003	-0.513	0.009
RV end-diastolic diameter	-0.431	0.014	-0.156	0.529
Left atrial volume index	-0.340	0.066	-0.215	0.256

TAPSE – tricuspid annular plane systolic excursion; RV – right ventricular.

ulation, RAVI had a strong correlation with RV systolic function and no correlation with LVEF. Sallach et al[7] also showed that RAVI is an independent predictor of cardiovascular events in patients with chronic stable heart failure. D'Andrea et al demonstrated that a right atrial area >16 cm^2 had 87.1% sensitivity and 95.4% specificity in predicting a negative response to cardiac resynchronization therapy in patients with dilated cardiomyopathy.[17]

RAVI was a stronger predictor of functional capacity, with high sensitivity and specificity, in the subgroup of patients with impaired RV systolic function. RV impairment secondary to LV failure usually initiates due to pressure overload, which is translated to increased tricuspid regurgitation maximum velocity and increased estimated RVSP, and evolves to right ventricular and right atrial dilatation.[18] The pathophysiological substrate of the transition from pressure overload to right heart dilatation is not adequately understood, but several neurohumoral factors are likely to play an important role.[19] Right atrial dilatation is probably observed at an advanced stage of pressure and volume overload and consequently it may reflect a more severe clinical presentation and course in patients with heart failure and reduced LVEF.

Limitations of the study

The population studied was relatively small. The functional capacity of the patients was assessed using only the Duke Activity Status index. Our results could have been more robust if we had included a functional test such as cardiopulmonary exercise, but this would have increased the cost of the present study.

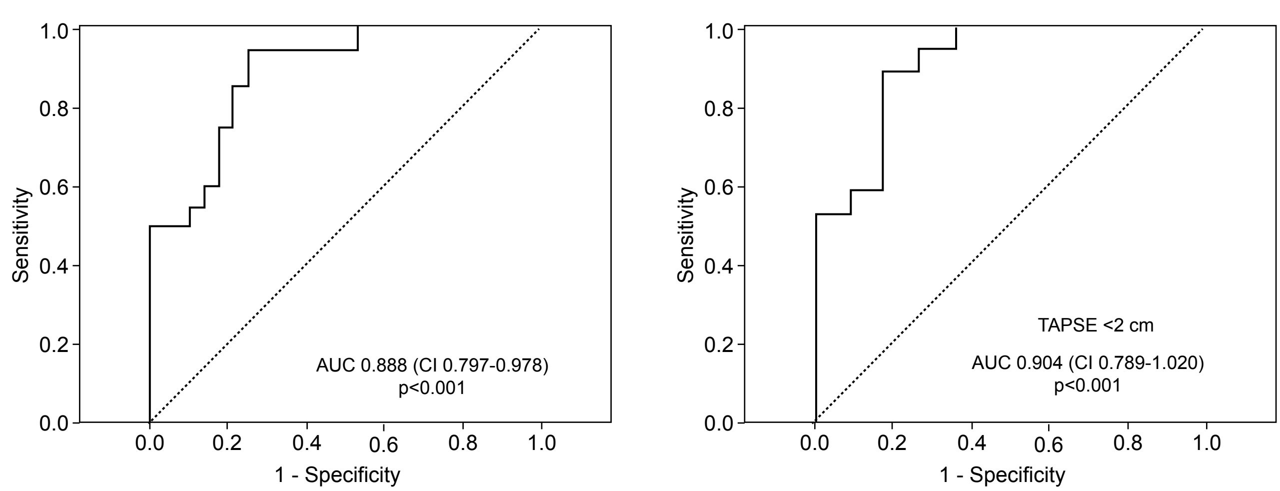

Figure 3. Sensitivity and specificity of right atrial volume index in predicting a Duke Activity Status Index below 10 in the overall population (A) and in patients with impaired right ventricular systolic function (tricuspid annular plane systolic excursion, TAPSE <2 cm) (B).

Finally there are inherent limitations in the echocardiographic measurements of right atrial volume which we addressed by designating the same experienced echocardiographer to perform all the measurements in this study.

Conclusions

Right atrial volume index may accurately predict functional capacity assessed by the Duke Activity Status Index in patients with stable chronic heart failure, and is an independent predictor of low functional capacity in the subgroup of patients with impaired right ventricular systolic function.

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Appendix: Duke activity status index (DASI) questionnaire.

Item	METs
Can you take care of yourself, that is, eat, dress, bathe, or use the toilet?	2.75
Can you walk indoors, such as around your house?	1.75
Can you walk a block or two on level ground?	2.75
Can you climb a flight of stairs or walk up a hill?	5.50
Can you run a short distance?	8.00
Can you do light work around the house like dusting or washing dishes?	2.70
Can you do moderate work around the house like vacuuming, sweeping floors, or carrying groceries?	3.50
Can you do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?	8.00
Can you do yard work like raking leaves, weeding, or pushing a power mower?	4.50
Can you have sexual relations?	5.25
Can you participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	6.00
Can you participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?	7.50