

# Clinical characteristics of asymptomatic left ventricular diastolic dysfunction and its association with self-rated health and N-terminal B-type natriuretic peptide: a cross-sectional study

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## Abstract

**Aims** Left ventricular hypertrophy, obesity, hypertension, and N-terminal B-type natriuretic peptide (Nt-proBNP) predict left ventricular diastolic dysfunction with preserved systolic function (DD-PSF). Self-rated health (SRH) is shown to be associated with chronic diseases, but the association of SRH with DD-PSF is unclear. In light of the clinical implications of DD-PSF, the following goals are of considerable importance: (1) to determine the role of SRH in patients with DD-PSF in the general population and (2) to study the association between Nt-proBNP and DD-PSF.

**Methods and results** The current study is a cross-sectional study conducted on a random sampling of a rural population. Individuals 30–75 years of age were consecutively subjected to conventional echocardiography and tissue velocity imaging. Data were collected on 500 (48%) men and 538 (52%) women ( $n = 1038$ ). DD-PSF was the main outcome, and SRH and Nt-proBNP were the primary indicators. Diabetes mellitus, hypertension, and obesity were accounted for as major confounders of the association with SRH. DD-PSF was identified in 137 individuals, namely, 79 men (15.8%) and 58 women (10.8%). In a multivariate regression model, SRH (OR 2.95; 95% CI 1.02–8.57) and Nt-proBNP (quartile 4 vs. quartile 1 OR 4.23; 95% CI 1.74–10.26) were both independently associated with DD-PSF.

**Conclusions** SRH, evaluated based on a descriptive question on general health, should be included in the diagnostic process of DD-PSF. In agreement with previous studies, our study confirms that Nt-proBNP is a major indicator of DD-PSF.

**Keywords** DD-PSF; Nt-proBNP; SRH; Cross-sectional; Diabetes mellitus; Population-based

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## Introduction

Developed countries have been facing steady increases in their ageing populations over the past few decades, raising issues regarding the diagnosis and treatment of several chronic diseases.<sup>1</sup> One major challenge has been the prevalence of chronic heart failure among the elderly, which is greater than 10% and is increasing.<sup>2</sup> In addition to clinical signs such as effort intolerance and dyspnoea, echocardiography and

elevated levels of N-terminal B-type natriuretic peptide (Nt-proBNP) have been used as diagnostic landmarks of heart failure (HF).<sup>3</sup> At least one-third of all patients with HF have left ventricular diastolic dysfunction with preserved systolic function (DD-PSF).<sup>4</sup> These patients have similar prognoses to those with HF with reduced systolic function.<sup>5</sup> Patients with asymptomatic ventricular dysfunction classified by echocardiographic abnormalities showed a fivefold increase in mortality when they developed clinical HF.<sup>6</sup> The importance

of identifying these patients in the early stages of cardiac dysfunction is evident. Identifying risk factors underlying DD-PSF is important for the detection of HF in early stages. One approach to risk factor identification is the use of different health metric methods.

Self-rated health (SRH) is a legitimate and recognized survey measure of health that has been used in medical research since the early 1970s when Maddox and Ware began their pioneering work studying measures of general health perception.<sup>7,8</sup> As a single-item question, SRH is known to be a multifaceted and powerful tool that can indicate a decline in physical functionality<sup>9</sup> and predict mortality and morbidity in subjects with chronic disease<sup>10</sup> and the elderly.<sup>11</sup> SRH also has disease-specific predictive capabilities and has been reported to be an excellent predictor of recurrent ischaemic events after myocardial infarction<sup>12</sup> and of the exacerbation of chronic obstructive pulmonary disease.<sup>13</sup> Recently, in a large, nationally representative sample of US adults in late midlife,<sup>14</sup> SRH was found to be a significant independent predictor of global morbidity onset for six major chronic diseases (arthritis, cancer, coronary heart disease, diabetes, lung disease, and stroke). These findings are thought to be explained by patients' functional limitations prior to the onset of disease.

In previous studies, obesity, hypertension, left ventricular hypertrophy, and Nt-proBNP have been shown to predict DD-PSF.<sup>15,16</sup> However, little is known regarding the relationship between SRH and DD-PSF. In light of the clinical implications of DD-PSF, it is of considerable importance to analyse the relationship between DD-PSF and SRH. Therefore, the aims of this study were<sup>1</sup> to determine the role of SRH in patients with DD-PSF in the general population and<sup>2</sup> to study the association between Nt-proBNP and DD-PSF.

## Materials and methods

Within the framework of the Skaraborg Project,<sup>17</sup> this study includes data from a population survey conducted in 2002–2003 in Vara, a small municipality with 16 000 inhabitants in a rural area of south-western Sweden.<sup>18</sup> A random sample of 1811 individuals was selected from the Vara population (81% participation rate). A consecutive subset of these subjects ( $n=1149$ ) was also invited to participate in an echocardiographic examination (echo-Doppler) during a separate visit. In total, 515 men and 543 women (92%) were successfully examined; however, 20 participants could not fully participate because of at least one of the following reasons: left ventricular systolic dysfunction (ejection fraction <45%) ( $n=2$ ), missing information on self-reported history of heart failure ( $n=6$ ), arrhythmia, pacemaker ( $n=2$ ), rapid atrial fibrillation ( $n=5$ ), heart rate <40 beats per minute ( $n=1$ ), aortic insufficiency ( $n=2$ ), or physical characteristics hindering echo recording ( $n=2$ ). Thus, the presence

or absence of diastolic dysfunction was determined in 500 men and 538 women (90% of those invited for echo-Doppler investigation).

All participants were also examined by a standard oral glucose tolerance test, and by a 12-lead standard electrocardiogram.<sup>19</sup> The diagnoses of diabetes mellitus type 2, hypertension, obesity, and left ventricular hypertrophy were made in accordance with contemporary guidelines' as described for this cohort previously.<sup>20</sup> A history of myocardial infarction was collected by questionnaire.<sup>19</sup> Concentrations of Nt-proBNP were analysed using standard methods.

## Self-rated health

General SRH was defined based on five answer alternatives (very good=1, good=2, fair=3, poor=4, very poor=5) to the question 'How would you rate your current health status in general?' The questionnaire was completed at the clinic with nurses providing assistance when needed.

## Echocardiographic measurements used to diagnosis diastolic dysfunction with preserved systolic function

All participants were examined by echo-Doppler performed by the same senior cardiologist using a Vivid S5 GE VingMed Ultrasound USA operating with a 3.5 MHz probe. The data were stored in the Echo Pac System for playback, analysis, and measurement.

Measurements used for left ventricular calculations were obtained based on the Guidelines of the European Society of Echocardiography.<sup>21</sup> The E-wave-peak (early filling), A-wave-peak (atrial filling), and the ratio between the two were then determined. The isovolumetric relaxation time, from the closure of the atrioventricular valve to the opening of the mitral valve, was also measured. To indirectly measure distensibility of the left ventricle, the deceleration time, that is, the time from the peak E to the baseline slope, was measured. Tissue velocity imaging was used in both the septum and in the more stable lateral wall to detect pseudo-normalization.

Diastolic dysfunction was categorized into three levels as follows: impaired relaxation, that is, early diastolic dysfunction; pseudonormal, that is, a more severe condition indicating increasing left ventricular filling pressures; or restrictive filling pattern. Diastolic dysfunction was further dichotomized as being normal or not with impaired relaxation, pseudonormal, or restrictive filling patterns categorized as DD-PSF.<sup>22</sup>

## Statistical analysis

Statistical analysis was performed using SPSS 21.0 for MAC. Descriptive statistics (frequency distribution percentage, mean, and standard deviation) were calculated to describe clinical

data. All tests were two-sided, and statistical significance was assumed when  $P < 0.05$ . The differences in risk factors and co-morbidities (categorical variables) for men and women are reported using the  $\chi^2$  test (Table 1). Binary logistic regression analysis was used to analyse associations between DD-PSF and categorical variables, and the results are expressed as odds ratios (ORs) with 95% confidence intervals (CIs) (Tables 1 and 2). Differences in means between groups were analysed by general linear models, and means were age-adjusted accordingly (Table 3). Nt-proBNP was used as a continuous variable in Table 2 and further categorized into quartiles to account for a nonlinear distribution in Table 4.

Multivariate logistic regression analyses were performed to assess ORs (95% CIs) associated with SRH accounting for confounding variables. Variables mutually entered into the model were age, gender, SRH, Nt-proBNP, diabetes mellitus type 2, obesity, hypertension, heart rate, and left ventricular hypertrophy (Table 4).

## Ethical approval

The research ethical committee at the University of Gothenburg approved this study. Participants provided written informed consent to participate in the study. The study was conducted in accordance with the Declaration of Helsinki.

## Results

### Study population

The study population included 1038 participants. Women constituted 538 (51.8%) of the study group. The mean age of the men was 51.0 (standard deviation 12.2) years, and that of the women was 50.2 (SD 11.8) years. DD-PSF was identified in 137 participants (13.2%); of these, 79 were men (15.8%) and 58 were women (10.8%) (Table 1).

### Relationship of diastolic dysfunction with preserved systolic function with self-rated health and N-terminal B-type natriuretic peptide

In total, 39 individuals with DD-PSF reported their SRH as poor or very poor, representing 23% of the individuals with the disease. The age-adjusted OR of having DD-PSF was approximately threefold higher among participants with poor or very poor SRH, that is, OR 2.86 (95% CI 1.2–7.2) (Table 1), and approximately the same among those with high levels of Nt-proBNP, that is, OR 1.40 (95% CI 1.1–1.7) (Table 2). In both cases, the ORs were higher for men than for women.

**Table 1** Differences in risk factors between patients with left ventricular diastolic dysfunction and those with regular diastolic function

Variables	All N (%)	Regular LV diastolic function N (%)	LVDD-PSF N (%)	Age-adjusted odds ratio OR (95% CI)	P
Participants	1038	901 (86.8)	137 (13.2)		
Men	500 (48.2)	421 (84.2)	79 (15.8)	1.55 (1.03–2.4)	0.037
Women	538 (51.8)	480 (89.2)	58 (10.8)	0.64 (0.04–0.9)	0.037
P-value	0.326				
Low SRH				2.86 (1.2–7.2)	0.025
Men	18 (3.6)	13 (3.1)	5 (6.6)	3.49 (1.0–11.9)	0.046
Women	21 (3.9)	17 (3.6)	4 (6.9)	2.26 (0.5–9.11)	0.251
P-value	0.321				
LV hypertrophy				8.24 (5.1–13.3)	0.001
Men	69 (13.8)	27 (6.4)	42 (53.2)	9.46 (4.9–17.9)	0.001
Women	61 (11.3)	30 (6.3)	31 (53.4)	6.70 (3.3–13.7)	0.001
P-value	0.231				
MI				1.33 (0.5–3.9)	0.458
Men	12 (2.4)	7 (1.7)	5 (6.3)	1.06 (0.3–3.7)	0.921
Women	4 (0.7)	2 (0.4)	2 (3.5)	3.69 (0.4–30.9)	0.230
P-value	0.057				
Hypertension				3.27 (2.1–5.1)	0.001
Men	96 (19.2)	58 (13.8)	38 (48.1)	2.48 (1.4–4.4)	0.002
Women	97 (18.0)	59 (12.3)	38 (65.5)	4.58 (2.3–9.0)	0.001
P-value	0.963				
DM T2				2.74 (1.5–4.8)	0.001
Men	38 (7.6)	20 (4.8)	18 (22.8)	2.40 (1.1–5.2)	0.025
Women	38 (7.1)	23 (4.8)	15 (25.9)	3.26 (1.4–7.5)	0.006
P-value	0.978				
Obesity				2.20 (1.4–3.4)	0.002
Men	96 (19.2)	74 (17.6)	22 (27.8)	1.90 (1.0–3.6)	0.047
Women	127 (23.6)	101 (21.0)	26 (45.6)	2.53 (1.3–4.9)	0.006
P-value	0.062				

All results are expressed as numbers (N) and percentages (%) for both men and women. Associations between various risk factors and left ventricular diastolic dysfunction with preserved systolic function (LVDD-PSF) were estimated using binary logistic regression and expressed as odds ratios (OR) with 95% confidence intervals (CI) accounting for differences in age. DM T2, diabetes mellitus type 2; LVH, left ventricular hypertrophy; MI, myocardial infarction.

**Table 2** Clinical and laboratory characteristics of the study population and of patients with left ventricular diastolic dysfunction compared with those with regular diastolic function

Variables (Units)	All participants Mean (SD)	Regular LV diastolic dysfunction Mean (SD)	LVDD-PSF Mean (SD)	Age-adjusted odds ratio OR (95% CI)	P
Age (year)				1.14 (1.1–1.2)	0.001
Men	51.0 (12.2)	48.6 (11.5)	63.1 (8.1)	1.12 (1.1–1.2)	0.001
Women	50.2 (11.8)	48.4 (10.9)	65.3 (7.2)	1.16 (1.1–1.2)	0.001
P-value	0.326				
Waist circumference (cm)				1.04 (1.0–1.1)	0.001
Men	95.1 (10.0)	94.2 (9.8)	100.0 (9.6)	1.05 (1.0–1.1)	0.001
Women	85.9 (13.3)	84.8 (13.0)	94.0 (13.9)	1.04 (1.0–1.1)	0.002
P-value	<0.001				
BMI (kg/m <sup>2</sup> )				1.11 (1.1–1.2)	0.001
Men	27.0 (3.4)	26.7 (3.4)	28.4 (3.3)	1.14 (1.1–1.2)	0.001
Women	27.1 (5.2)	26.7 (4.9)	30.4 (5.9)	1.09 (1.0–1.2)	0.001
P-value	0.962				
fP-Glucose (mmol/L)				1.30 (1.2–1.5)	0.001
Men	5.6 (1.5)	5.5 (0.8)	6.2 (1.7)	1.54 (1.3–1.9)	0.009
Women	5.4 (1.1)	5.2 (1.2)	6.6 (2.7)	1.45 (1.2–1.7)	0.001
P-value	0.014				
fP-Cholesterol (nmol/L)				0.93 (0.8–1.2)	0.390
Men	5.4 (1.0)	5.4 (1.0)	5.5 (1.0)	0.93 (0.8–1.2)	0.843
Women	5.3 (1.0)	5.2 (1.0)	5.7 (1.0)	0.98 (0.7–1.3)	0.211
P-value	0.016				
P-Nt-proBNP (pg/mL) <sup>a</sup>				1.40 (1.1–1.7)	0.002
Men	414 (203–769)	414 (203–710)	524 (245–879)	1.48 (1.1–2.0)	0.007
Women	406 (414–736)	397 (414–701)	473 (304–955)	1.30 (0.9–1.7)	0.090
P-value	0.398				
SBP (mmHg)				1.03 (1.0–1.1)	0.001
Men	130 (17)	128 (15)	142 (20)	1.03 (1.0–1.1)	0.001
Women	125 (19)	122 (17)	147 (20)	1.03 (1.0–1.1)	0.001
P-value	0.001				

All results are expressed as means and standard deviations (SD) for both men and women. The associations between independent variables and left ventricular diastolic dysfunction with preserved systolic function (LVDD-PSF) were estimated using binary logistic regression and expressed as odds ratios (OR) and 95% confidence intervals (CI) accounting for differences in age.

BMI, body mass index; DM T2, diabetes mellitus type 2; Nt-proBNP, N-terminal pro-brain natriuretic peptide; SBP, Systolic Blood Pressure.

<sup>a</sup>Values for Nt-proBNP are expressed as median and quartiles.

[Correction added after online publication on 18 May 2016: Confidence interval added for Age-adjusted odds ratio for Age, and Age-adjusted odds ratio added for fP-Cholesterol row].

**Table 3** Echocardiographic characteristics in men and women, respectively, comparing subjects with left ventricular diastolic dysfunction with preserved systolic function with those with regular diastolic function

Variables (units)	All	Regular diastolic function	LVDD-PSF	P <sup>a</sup>
Men	n = 500	n = 421	n = 79	
Septal wall (mm)	9.8 (1.8)	9.6 (1.6)	11.1 (2.0)	<0.001
Posterior wall (mm)	10.1 (3.1)	9.9 (1.8)	11.2 (2.0)	<0.001
LVEDD (mm)	49.9 (4.7)	49.9 (4.9)	49.8 (5.2)	0.908
LVESD (mm)	31.6 (4.2)	31.5 (4.5)	32.0 (4.8)	0.444
Left atrial diameter (mm)	34.6 (4.2)	34.3 (4.3)	36.4 (4.7)	<0.001
Ejection fraction (%)	73.6 (8.0)	73.7 (8.5)	72.4 (9.1)	0.241
E/A ratio	1.3 (0.3)	1.3 (0.3)	0.9 (0.3)	<0.001
E'/A' ratio (TVI)	0.25 (0.3)	0.1 (0.3)	0.8 (0.3)	<0.001
IVRT (ms)	95.1 (17.2)	90.6 (14.6)	121.3 (15.7)	<0.001
Women	n = 538	n = 480	n = 58	
Septal wall (mm)	8.86 (1.8)	8.6 (1.7)	10.5 (1.8)	<0.001
Posterior wall (mm)	9.4 (3.2)	9.2 (4.2)	10.8 (4.5)	0.014
LVEDD (mm)	46.0 (4.6)	46.0 (4.6)	45.6 (5.0)	0.534
LVESD (mm)	28.5 (4.2)	28.6 (4.2)	28.2 (4.5)	0.543
Left atrial diameter (mm)	31.1 (4.4)	30.8 (4.4)	33.0 (4.7)	0.001
Ejection fraction (%)	74.0 (8.0)	74.2 (7.3)	73.6 (8.5)	0.671
E/A ratio	1.4 (0.3)	1.4 (0.3)	1.0 (0.3)	<0.001
E'/A' ratio (TVI)	0.2 (0.4)	0.10 (0.2)	0.9 (0.3)	<0.001
IVRT	92.4 (17.2)	88.5 (14.3)	121.4 (15.6)	<0.001

Data expressed in means (SD). Differences in means were adjusted for age using general linear models.

E/A-ratio, the E-wave-peak (early filling)-to-A-wave-peak (atrial filling) ratio; IVRT, isovolumetric relaxation time; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; TVI, tissue velocity imaging.

<sup>a</sup>Left ventricular diastolic dysfunction with preserved systolic function (LVDD-PSF) vs. regular diastolic function.

**Table 4** Multivariate logistic regression analysis of factors associated with left ventricular diastolic dysfunction with preserved systolic function

Covariates	Odds ratio	95% CI	P-value
Age	1.12	1.09–1.15	0.001
Covariates <sup>a</sup> in model			
Gender	1.64	0.87–2.72	0.056
SRH	2.95	1.02–8.57	0.047
Nt-proBNP (pg/mL) <sup>b</sup>			
Quartile 1 ≤203	1	—	—
Quartile 2 204–406	2.82	1.13–7.05	0.026
Quartile 3 407–727	3.59	1.46–8.84	0.006
Quartile 4 ≥728	4.23	1.74–10.26	0.001
DM T2	1.44	0.70–2.97	0.322
Obesity	1.17	0.65–2.09	0.586
Hypertension	1.77	1.03–3.05	0.040
Heart rate	1.04	1.01–1.07	0.005
LVH	5.76	3.28–10.13	0.001

Associations were estimated using binary logistic multivariate regression and expressed as odds ratios (OR) with 95% confidence intervals (CI).

LVDD-PSF, left ventricular diastolic dysfunction with preserved systolic function.

<sup>a</sup>Covariates in the model were gender, self-rated health (SRH), Nt-proBNP (N-terminal pro-brain natriuretic peptide), diabetes mellitus type 2 (DM T2), obesity, hypertension, heart rate, and left ventricular hypertrophy (LVH).

<sup>b</sup>Values for Nt-proBNP are expressed as median and quartiles (q1–q4)

### Risk factors for diastolic dysfunction with preserved systolic function

The echo-Doppler characteristics (LVEF%, E/A, IVRT, E/E') for those with regular cardiac function and left ventricular diastolic dysfunction, respectively, are shown in *Table 3*. Major chronic diseases, that is, type 2 diabetes mellitus and hypertension, were more common among those with DD-PSF, especially among elderly male participants (*Table 1*).

Significantly more male ( $n=79$ ) than female ( $n=58$ ) ( $P<0.001$ ) participants were diagnosed with DD-PSF, and in both genders, individuals with DD-PSF were older than those with regular diastolic function ( $P<0.001$ ) (*Table 2*). In the multivariate binary regression analysis, the following covariates were mutually entered into the same model: age, gender, SRH, Nt-proBNP, diabetes mellitus, obesity, hypertension, left ventricular hypertrophy, and heart rate. We found both low SRH (OR 2.95; 95% CI 1.02–8.57) and Nt-proBNP (quartile 4 vs. quartile 1 OR 4.23; 95% CI 1.74–10.26) to be significantly associated with DD-PSF (*Table 4*).

## Discussion

This was an observational, cross-sectional study on the association between clinical variables and SRH based on echocardiographic findings of diastolic dysfunction (DD-PSF) in a population-based cohort. The aim of the study was to investigate the association between SRH and DD-PSF and to study

the association between Nt-proBNP and DD-PSF compared with their associations with SRH. Our results suggest that health metrics such as SRH are associated with diastolic dysfunction, suggesting the importance of SRH as an associative factor in similar settings. The question of whether SRH is a surrogate marker of cardiovascular disorders deserves more attention in clinical settings. Diabetes mellitus type 2 and hypertension were more common among elderly male participants with DD-PSF compared with the general population. Risk factors such as hypertension and left ventricular hypertrophy add more stress to the left ventricle than other risk factors.

However, the majority of the participants in our study rated their health status as good or very good, despite the high prevalence of co-morbidities among these individuals. The association between SRH and the incidence of cardiovascular disease has been discussed in previous studies.<sup>23</sup> Benyamini *et al.* showed that somatic sensations are possible manifestations of disease and powerful reminders of prior health risks, as well as potential indications of current and future health risks.<sup>24</sup> The Cardiovascular Health Study, which included 8 years of follow-up (mean age of participants 73 years), showed that SRH declined 2 years prior to mortality compared with the 'no event' group. In addition, a worsening of SRH among 625 participants with HF predicted the onset of the disease.<sup>25</sup> In another study, breathlessness or shortness of breath was shown to be associated with poorer SRH.<sup>26</sup> As breathlessness is a major symptom of HF, these findings suggest the importance of examining SRH together with other predictors. Nt-proBNP is known to be elevated in patients with DD-PSF,<sup>27</sup> but the association between natriuretic peptides and diastolic dysfunction has not been shown to be strong.<sup>28</sup> Therefore, other reliable non-invasive indicators are necessary.<sup>15</sup>

The strengths of the current study were the large number of participants who had undergone both echocardiography and the required blood sampling, as well as the frequency of completed questionnaires. Other strengths were the population-based design and the high participation rate in the study, which reduce the possibility of selection bias. However, the cross-sectional design of the study does not allow for the determination of causality, which limits the interpretability of the results. Therefore, the findings of this study should be confirmed in a subsequent prospective study. Including left ventricular hypertrophy, hypertension, and ischaemic heart disease in a multiple regression analysis is not appropriate because of the direct influence they have on DD-PSF (*Table 1*). We believe that the assessment of lifestyle factors should be part of a future analysis. To our knowledge, this is the first attempt to study SRH as an associative factor of DD-PSF related to other risk factors.

Our study, despite the limited size of the study sample, contributes to the body of knowledge on SRH and confirms that known risk factors, such as hypertension and obesity,

are associated with DD-PSF. The latter association (i.e. the association between obesity and DD-PSF) is already known from numerous previous studies. Despite our adjustments for age and gender, the intrinsic dynamic of ageing and the attendant possibility of drug therapy, complex social factors, and co-morbidities could all affect SRH. Whether SRH is a surrogate marker of cardiovascular disorders deserves more attention in clinical settings. Therefore, we feel the results of our study are important to report. However, these findings need to be replicated in other populations and with a cohort design for SRH to be considered a complementary tool in the investigational toolbox of early stages of HF. Furthermore, the association found here between poor SRH and DD-PSF, which remained significant even after adjustments for age, gender, diabetes mellitus, and obesity, raises the question of whether left ventricular dysfunction is as 'asymptomatic' as has been previously claimed. We must keep in mind that obesity and diabetes mellitus have potential interaction risks despite the adjustments performed in our regression analysis. However, they are also potential causes of diastolic dysfunctions and are very common in the elderly, which is the target population of our study.

The results of the present study clearly indicate that patients with DD-PSF have an awareness of their illness. The cross-sectional design of our study requires that findings in the study be confirmed in a subsequent prospective study.

The assessment of HF in the general population requires new approaches. In this respect, having more investigational instruments available is an advantage. SRH has been shown to be a powerful instrument in assessing chronic disease. Taking patient histories and maintaining good communication with patients have always been cornerstones in the detection of cardiovascular diseases. We believe that finding an association between SRH and DD-PSF adds a new instrument to our clinical arsenal and provides a new opportunity to begin

communication by asking 'Sir, how do you feel in general?' In individuals who show this 'sense' of HF, directly targeted investigational strategies can be implemented.

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## Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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