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ORIGINAL ARTICLE

Diastolic dysfunction is associated with sedentary leisure time physical activity and smoking in females only

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Abstract

Objectives. Left ventricular diastolic dysfunction with preserved systolic function (DD-PSF) is associated with an increased risk of morbidity and mortality. Population-based surveys studying the associations between DD-PSF and lifestyle-associated risk factors, such as leisure time physical activity (LTPA) and smoking, are scarce. Thus, the aims were to explore the associations between DD-PSF and LTPA and smoking, employing optimal echocardiographic techniques. *Design.* Cross-sectional study conducted from 2001 to 2003. *Setting.* The study was conducted in a random sample of a rural Swedish population. *Subjects*. Men and women of 30–75 years of age were consecutively invited for conventional echocardiography and tissue velocity imaging (n = 1149). Structured questionnaires and physical examinations were conducted using standardized methods. *Main outcome measures*. DD-PSF was defined according to the European Society of Cardiology criteria excluding subjects with ejection fraction < 45%, or a self-reported history of heart failure. *Results*. Complete information was available in 500 men and 538 women. In a multivariate model, DD-PSF was independently associated with sedentary LTPA and smoking in females; sedentary LTPA odds ratio (OR) 2.91, 95% confidence interval (CI) 1.02 to 8.27, and smoking OR 3.42, 95% CI 1.35 to 8.64. The probability of identifying DD-PSF in females with a sedentary LTPA was 37% and increased to 80% if they also had hypertension and were obese. *Conclusions*. Sedentary LTPA and smoking are independently associated with DD-PSF in females. Identification of a sedentary lifestyle in females increases the probability of diagnosing DD-PSF.

Key Words: *Echocardiography, gender, family practice, leisure time physical activity, smoking*

The clinical presentation of diastolic dysfunction is diverse and ranges from asymptomatic diastolic dysfunction (i.e. left ventricular diastolic dysfunction with preserved systolic function, DD-PSF) to symptomatic diastolic heart failure that manifests as congestive heart failure (CHF). Even though DD-PSF is a common condition that occurs without impaired physical performance or other symptoms, it significantly predicts future events of cardiac heart failure, cardiac death, and all-cause mortality [1,2].

Diastolic dysfunction is, according to the European Society of Cardiology, considered when evidence of abnormal left ventricular diastolic relaxation, filling, or diastolic distensibility and stiffness is found in the presence of normal or only mildly reduced left ventricular systolic dysfunction (left ventricular ejection fraction, LVEF > 45%) [3]. Hypertension, obesity, and diabetes are identified as independent risk factors for DD-PSF [2,4]. Sedentary lifestyle and smoking are associated with unfavourable health effects, increasing the risk for several chronic diseases including cardiovascular disease (CVD) [5–7] but, to the best of our knowledge, no community-based studies on the associations between lifestyle associated risk factors and diastolic dysfunction have been published. Thus in this population-based survey we focused on studying the associations between echocardiography (UCG) confirmed DD-PSF and lifestyle-associated risk factors.

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Hypertension, diabetes, and obesity are independent risk factors for diastolic dysfunction with preserved systolic function (DD-PSF).

- This population-based study shows that sedentary leisure time physical activity (LTPA) and smoking are also independently associated with DD-PSF in females but not in males. The probability of diagnosing DD-PSF was 80% in females with hypertension, obesity, and a sedentary lifestyle.
- DD-PSF is reversed by physical activity, which further increases the implications in primary health care (PHC) of diagnosing this condition and in motivating females with a sedentary lifestyle to become more active in their leisure time.

Material and methods

Within the framework of the Skaraborg Project, this study includes data from a surveillance of the population in Vara, a small community in a rural area of south-western Sweden, between 2001 and 2003 [8]. The sampling, inclusion of participants, and UCG examination were carried out as previously described [9].

Demographic and lifestyle data

Information on demographic and socioeconomic data was gathered by questionnaires developed at the Department of Clinical Sciences, University Hospital of Malmö and Lund University [9]. The nurses used structured forms to interview the participants on smoking and drinking habits, level of leisure time physical activity (LTPA), level of work time physical activity (WTPA) and education, and also on previous diagnoses of diabetes, hypertension, hyperlipidaemia, angina pectoris, and atrial flutter and fibrillation. Information was gathered on previous hospitalisation for heart failure, acute stroke, acute myocardial infarction, or invasive procedures for treating coronary artery stenosis.

Standardized physical examinations were carried out and blood samples were drawn including oral glucose tolerance tests as previously described [9].

Diagnosis of hypertension and diabetes: Blood pressure was measured in a supine position after five minutes with the arm at heart level. Diagnosis of hypertension was based on ongoing blood pressure lowering medication for hypertension, or three consecutively repeated blood pressure readings one minute apart, ≥ 140/90 mm Hg (one or both). Diagnosis of diabetes was confirmed if there was a known history of physician diagnosis, and in new cases when the fasting plasma glucose value was ≥ 7.0 mmol/L (twice) and/or when the two-hour plasma glucose value in the OGTT was ≥ 11.1 mmol/L. Measurement and diagnosis of hypertension and diabetes conformed to international guidelines [10,11].

Previous cardiovascular disease (CVD) was considered in individuals with a history of angina pectoris, acute myocardial infarction, atrial flutter/fibrillation, coronary surgery or stroke.

Level of LTPA was based on four answer alternatives to the question "How much physical effort do you put yourself through in your leisure time?" *Inactive*, mostly physically inactive, and less strenuous LTPA (walking, cycling, gardening etc.) less than four hours a week (h/w); *Moderate*, less strenuous LTPA > 4 h/w; *Strenuous*, strenuous physical activity (jogging, swimming, tennis etc.) > 2 h/w and *Highly strenuous*, including those who participate in competitions on a weekly basis.

Residents with *Strenuous* or *Highly strenuous* LTPA were considered as *Active* in leisure time while the others were considered *Sedentary*.

Level of WTPA was based on five answer alternatives to the question "Is your daily work physically light or heavy?" ranging from *Light sitting* to *Very heavy* intensity. The two most sedentary WTPA levels, *Light sitting* and *Light standing*, were then categorized into *Sedentary WTPA* and the three other levels into *Active WTPA*.

Smoking habits: Participants were categorized as *Never smokers*, *Previous smokers*, and *Active smokers*. *Never smokers* and *Previous smokers* were considered as *Non-smokers*.

Echocardiographic methods

All participants were examined by UCG, using methods described previously [9]. Diastolic dysfunction was categorized into three levels as: *impaired relaxation*, i.e. early diastolic dysfunction; *pseudonormal*, i.e. 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.

Statistical analysis

Statistical analysis used SPSS 14.0 for Windows XP. Standard methods were used for descriptive statistics of the basic characteristics of the study population (see Table I). Differences in means between groups were adjusted for age difference using general linear models (GLM). The associations between DD-PSF and common cardiovascular and lifestyle risk factors were evaluated using logistic regression models. Associations were expressed as odds ratios (OR) with 95% confidence intervals (CI) (see Tables II and III).

All tests were two-sided and a p-value < 0.05 was considered statistically significant. The two-way interaction was used to explore the interaction between LTPA (tested as linear trend) and hypertension, LTPA and diabetes, as well as LTPA and obesity, on DD-PSF.

Results

DD-PSF occurred more frequently in men than women (16.5% vs. 12.9%, p = 0.037) and also occurred earlier in men than women; from 42 years

Table I. Characteristics of male (♂) and female (♀) participants related to diastolic dysfunction with preserved systolic function (DD-PSF).

Variables (units) (n ♂/n ♀)		Regular diastolic function (421/480)	DD-PSF (79/58)	p
Age (years)	♂	48.7 (11.0)	63.1 (11.0)	< 0.001
	♀	48.4 (10.6)	65.3 (10.6)	< 0.001
BMI (kg m^2)	♂	26.8 (3.4)	28.2 (3.7)	0.005
	♀	26.8 (5.1)	28.2 (5.6)	0.002
SBP (mm Hg)	♂	125.9 (14.2)	133.5 (15.3)	< 0.001
	♀	121.6 (13.4)	130.4 (14.6)	< 0.001
DBP (mm Hg)	♂	72.5 (9.6)	77.6 (10.4)	< 0.001
	♀	69.4 (9.5)	71.5 (10.4)	0.147
Heart rate (beats/minute)	♂	62.4 (8.6)	65.4 (9.2)	0.009
	♀	64.2 (8.5)	66.5 (9.2)	0.070
Total cholesterol (mmol/L)	♂	4.6 (0.9)	4.4 (1.0)	0.093
	♀	4.5 (0.9)	4.3 (1.0)	0.023
HDL (mmol/L)	♂	1.2 (0.3)	1.1 (0.3)	0.239
	♀	1.3 (0.3)	1.2 (0.4)	0.002
LDL (mmol/L)	♂	3.5 (0.9)	3.3 (1.0)	0.165
	♀	3.2 (0.8)	3.1 (0.9)	0.249
TG (g/L)	♂	1.4 (0.9)	1.6 (0.9)	0.044
	♀	1.2 (0.6)	1.5 (0.6)	0.001
Hypertension (%)	♂	58 (13.8)	38 (48.1)	0.002
	♀	59 (12.3)	38 (65.5)	< 0.001
Diabetes (%)	♂	20 (4.8)	18 (22.8)	0.025
	♀	23 (4.8)	15 (25.9)	0.006
Obesity (%)	♂	74 (17.6)	22 (27.8)	< 0.001
	♀	101 (21.0)	26 (45.6)	< 0.001
History of CVD (%)	♂	19 (4.5)	10 (12.7)	0.473
	♀	16 (3.4)	8 (13.8)	0.339
Sedentary LTPA (%)	♂	254 (60.9)	53 (67.9)	0.287
	♀	330 (69.0)	51 (87.9)	0.018
Sedentary WTPA (%)	♂	237 (67.1)	27 (67.5)	0.688
	♀	282 (75.2)	16 (69.6)	0.697
Smokers (%)	♂	70 (16.7)	15 (19.0)	0.514
	♀	94 (19.7)	11 (19.0)	0.093
Education < HS (%)	♂	154 (37.4)	57 (73.1)	0.615
	♀	130 (27.4)	33 (61.1)	0.964
LVH (%)	♂	27 (7.3)	42 (39.4)	< 0.001
	♀	30 (8.4)	31 (34.5)	< 0.001
EF	♂	73.7 (8.5)	72.4 (9.1)	0.241
	♀	74.2 (7.3)	73.6 (8.5)	0.671
E/A ratio	♂	1.3 (0.3)	0.9 (0.3)	< 0.001
	♀	1.4 (0.3)	1.0 (0.3)	< 0.001
IVRT (ms)	♂	90.6 (14.6)	121.3 (15.7)	< 0.001
	♀	88.5 (14.3)	121.4 (15.6)	< 0.001

Notes: Means were adjusted for age difference using general linear models (GLM). Data are presented in means (SD) or numbers (%). Abbreviations: DD-PSF = diastolic dysfunction with preserved systolic function; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides; CVD = cardiovascular disease; Sedentary LTPA = i.e. leisure time physical activity where strenuous activity did not regularly occur; Sedentary WTPA = daily work with little muscle activity; education < HS i.e. not more than high school exam; LVH = left ventricular hypertrophy; EF = ejection fraction; E/A–ratio = early filling to atrial filling ratio; IVRT = isovolumetric relaxation time.

of age in males and from 46 years of age in females, increasing in prevalence with age. From the age of 70, every second participant was diagnosed with DD-PSF (Figure 1).

Characteristics of male and female participants in relation to DD-PSF are presented in Table I. Men and women with DD-PSF had hypertension, obesity, and diabetes to a significantly higher extent, as well as higher triglyceride levels. Women with DD-PSF also had significantly lower HDL levels. Sedentary LTPA was common but occurred more frequently in females than males, 70.8% vs. 61.4%; p = 0.001. Females diagnosed with diastolic dysfunction significantly more frequently had a sedentary leisure time than males with DD-PSF.

Sedentary LTPA and active smoking were independently associated with DD-PSF in females (Tables II and III). Although the results were different for men and women, the interaction between LTPA and gender, and smoking and gender respectively, were non-significant upon formal testing (p = 0.192 and p = 0.604 respectively). The positive predictive values (PPV) for diagnosing DD-PSF in various conditions are presented in Table IV. The presence of sedentary LTPA in females increased the probability of diagnosing DD-PSF in both the absence and presence of other chronic conditions; the probability of diagnosing DD-PSF in females with sedentary LTPA was almost 40% and the probability of diagnosing DD-PSF increased to almost 80% if females with a sedentary LTPA also were obese and were diagnosed with hypertension. A history of active smoking contributed little to the PPV in both genders. However, if active smoking was identified in females with hypertension, the probability of identifying DD-PSF increased to 50%. In males, information on LTPA and smoking had a marginal effect on the PPV.

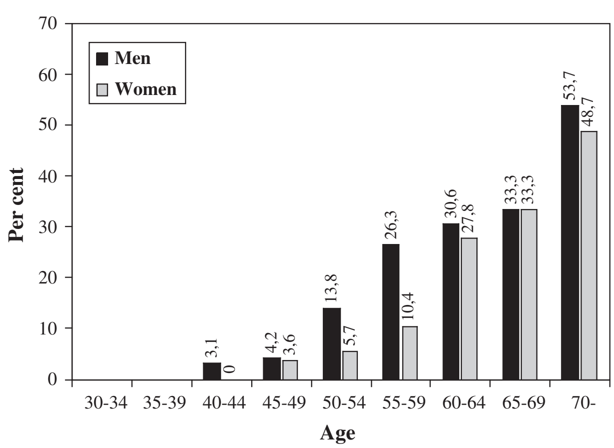

Figure 1. Prevalence of left ventricular diastolic dysfunction with preserved systolic function related to age and sex.

Table II. Associations between sedentary leisure time physical activity (LTPA) and left ventricular diastolic dysfunction with preserved systolic function (DD-PSF), adjusted for lifestyle and cardiovascular risk factors in males and females.

	LTPA			
	Active Reference	OR	Sedentary (95% CI)	p
Covariates				
Males	n = 188	n = 307		
Age	1.0	1.37	(0.77–2.45)	0.287
Age, active smoker	1.0	1.37	(0.77–2.46)	0.284
Age, BMI	1.0	1.16	(0.64–2.11)	0.616
Age, BMI, HT	1.0	1.07	(0.58–1.96)	0.826
Age, BMI, HT, DM, CVD, heart rate, active smoker	1.0	1.04	(0.56–1.94)	0.907
Females	n = 155	n = 381		
Age	1.0	3.04	(1.21–7.63)	0.018
Age, active smoker	1.0	3.15	(1.25–7.94)	0.015
Age, BMI	1.0	3.19	(1.18–8.64)	0.022
Age, BMI, HT	1.0	3.05	(1.09–8.55)	0.034
Age, BMI, HT, DM, CVD heart rate, active smoker	1.0	2.91	(1.02–8.27)	0.046

Note: Data presented as odds ratio (OR) and 95% confidence interval (CI) with DD-PSF as dependent variable.
Abbreviations: BMI = body mass index; HT = hypertension; DM = diabetes; CVD = cardiovascular disease.

Discussion

Principal findings

In this large population-based Swedish study, DD-PSF was independently associated with sedentary LTPA and smoking in females. These associations were not observed in men. The probability of diagnosing DD-PSF in females with obesity, hypertension, and a sedentary leisure time was 80%.

Strengths and limitations

This study had a large study sample and high participation rates (81% in the original survey and 91% of those invited for UCG). DD-PSF occurred in females over 46 years of age, and in males over 42. Although excluding males and females younger than these ages, the results were consistent.

We have relied on self-reported lifestyle data. However, the LTPA question has been validated before [12] and individuals with sedentary LTPA to a greater extent had risk factors established as indicators for sedentary LTPA such as elevated triglyceride levels [13], confirming a high external validity of the LTPA question.

Table III. Associations between smoking and left ventricular diastolic dysfunction with preserved systolic function (DD-PSF), adjusted for lifestyle and cardiovascular risk factors in males and females.

	Smoking status			
	Non-/previous smoker Reference	OR	Active smoker (95% CI)	p
Covariates				
Males	n = 414	n = 85		
Age	1.0	1.26	(0.62–2.55)	0.514
Age, sedentary LTPA	1.0	1.21	(0.59–2.48)	0.604
Age, BMI	1.0	1.33	(0.65–2.72)	0.430
Age, BMI, HT	1.0	1.39	(0.65–2.74)	0.427
Age, BMI, HT, DM, CVD heart rate, sedentary LTPA	1.0	1.18	(0.56–2.52)	0.662
Females	n = 431	n = 105		
Age	1.0	2.03	(0.89–4.65)	0.093
Age, sedentary LTPA	1.0	2.14	(0.93–4.97)	0.075
Age, BMI	1.0	2.93	(1.23–6.99)	0.015
Age, BMI, HT	1.0	3.35	(1.36–8.27)	0.009
Age, BMI, HT, DM, CVD heart rate, sedentary LTPA	1.0	3.42	(1,35–8.64)	0.009

Note: Data presented as odds ratio (OR) and 95% confidence interval (CI) with DD-PSF as dependent variable.
Abbreviations: BMI = body mass index; HT = hypertension; DM = diabetes; CVD = cardiovascular disease; LTPA = leisure time physical activity.

Table IV. The probability of diastolic dysfunction with preserved systolic function in males (♂) and females (♀).

Risk factor/condition		n1	PPV	n2	NPV
Sedentary LTPA	♂	39	17.9	456	84.4
	♀	27	37.0	509	90.6
Active smoker	♂	85	17.6	414	84.5
	♀	105	10.5	431	89.1
Hypertension	♂	96	39.6	404	89.9
	♀	97	39.2	441	95.5
Obesity	♂	96	22.9	404	85.9
	♀	127	20.5	410	92.4
Diabetes	♂	38	47.4	462	86.8
	♀	38	39.5	500	91.4
Sedentary LTPA & hypertension	♂	5	40.0	490	84.5
	♀	14	64.3	522	90.6
Sedentary LTPA & hypertension	♂	4	50.0	496	89.2
& Obesity	♀	9	77.8	529	90.4
Active smoker & hypertension	♂	16	37.5	483	84.9
	♀	12	50.0	524	90.1

Abbreviations: PPV = positive predictive value; NPV = negative predictive value; n1 = number of cases identified with the studied risk factor/condition; n2 = number of cases where the risk factor/condition is absent; sedentary LTPA; leisure time physical activity (walking = cycling = gardening etc.) less than two hours a week.

The interactions between LTPA and gender, and tobacco consumption and gender were non-significant upon formal testing, lending further strength to our findings that sedentary LTPA and tobacco consumption act as independent risk factors for DD-PSF. However, in previous smokers, information on the duration of smoking cessation is missing, which is a limitation.

Information on food intake is also missing whereby participants with an active LTPA might be more inclined to eat healthier food, resulting in a more favourable cardiovascular risk profile [14].

It is probable that sedentary LTPA and/or smoking increases the risk of DD-PSF. However, due to the cross-sectional study design, a direct effect of sedentary LTPA and smoking on the risk of DD-PSF cannot be concluded.

Clinical implications and possible mechanisms

To the best of our knowledge, this is the first population-based study of associations between LTPA, smoking, and DD-PSF. Our findings indicate that UCG examinations in a primary health care (PHC) setting may be considered not only in patients diagnosed with the previously identified risk factors for DD-PSF – hypertension, obesity, and/or diabetes – but also in females with a sedentary LTPA, where our results indicate that DD-PSF can be diagnosed with a rather high probability. Thus, in a PHC setting, individual lifestyle information is in females an inexpensive and valuable instrument in the decision-making process on whether or not to proceed with a UCG investigation. DD-PSF is not a permanent condition and it has also been demonstrated that it is reversed by physical activity [15], which further increases the implications of diagnosing this condition and in motivating females with a sedentary lifestyle to become more active in their leisure time. Information from PHC staff on the benefits of an active LTPA has an impact on improving physical activity in patients with a sedentary lifestyle [16].

A smaller study has demonstrated that DD-PSF is more common in individuals with a sedentary lifestyle compared with those who exercise regularly [17]. It has also been demonstrated that physical activity reduces the risk of heart failure [5]. Additionally, in heart failure patients, exercise training is demonstrated to normalise the diastolic relaxation and function as well as improving the prognosis and symptoms related to chronic heart failure [7].

The associations between smoking and DD-PSF in females remained consistent in the full model after adjusting for BMI (see Table III). Further, upon formal testing, there were no significant interactions between BMI and smoking, illustrating that smoking per se is a risk factor for diastolic dysfunction. Our results are in accordance with other studies demonstrating that smoking has acute effects on the diastolic function in healthy individuals, causing impaired endothelial relaxation resulting in diastolic dysfunction [18,19]. Tobacco users, especially women, frequently perceive that smoking helps to control their body weight [20], which might be a reason why smoking is more prevalent amongst females than males [21]. However, PHC personnel play a central part in motivating smokers to stop smoking and supporting non-smokers who have recently stopped to remain non-smokers [22].

DD-PSF was more prevalent amongst males than females and occurred at a younger age in males, which is in accordance with previous studies [2,4]. The risk factors for DD-PSF alter between genders; men, to a greater extent, had increased diastolic blood pressure and heart rate, while women more often had a sedentary leisure time (see Table I), consequently affecting the risk of DD-PSF in men and women differently. Another plausible explanation for the observed gender differences might be the influence of genetic traits associated with DD-PSF acting in a gender-specific manner [9].

To the best of our knowledge there are no figures on how many patients in a Swedish PHC setting that are annually examined with UCG. However, it is probable that the number of undiagnosed cases of DD-PSF is high, since UCG is not a regularly recommended investigation in the national guidelines for diabetes, obesity, or hypertension.

Future research

Since all participants had normal systolic function and were asymptomatic it is likely that sedentary LTPA and smoking increases the risk of DD-PSF, rather than the other way round. However, prospective lifestyle intervention studies are needed to further study the causality.

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Ethical approval

The investigation conforms to the principles outlined in the Declaration of Helsinki. The research ethics committee at the University of Gothenburg approved the study. The participants provided written informed consent for their participation in the health survey, and further written informed consent was obtained before undergoing an ultrasound-Doppler examination of the heart.

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Conflict of interests

The authors declare that they have no conflict of interests.

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