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Depression and disease severity as correlates of everyday physical activity in heart transplant candidates

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Summary

It is unclear to what extent patients awaiting heart transplantation (HTx) engage in physical activities. We examined the everyday physical activity and its associations with depressive symptoms and disease severity in 318 patients newly registered for HTx in the multi-site study 'Waiting for a New Heart' (aged 53.5 ± 11.4 years, 18% female patients). Participants completed questionnaires assessing depressive symptomatology and physical activity (number of physical activities, caloric expenditure associated with each activity), and estimated the distance they were able to walk without a break. Medical parameters at the time of listing [e.g. peak oxygen consumption (peakVO_2); the German Transplant Society Score (GTSS)] were provided by Eurotransplant. Almost 50% of patients engaged in activities of daily living (housework, walking), but <10% engaged in regular exercise. All physical activity measures correlated significantly with peakVO_2 (Ps < 0.01). Elevated depression scores were present in 39% of patients. Controlling for confounding variables (e.g. peakVO_2, diastolic blood pressure, GTSS, age), depressive symptomatology accounted for additional variance in all physical activity measures (Ps < 0.05). The association of depressive symptoms with reduced physical activity suggests two important perspectives: attempts to increase physical activity (especially in the area of daily living) might benefit from targeting depression, and increased physical activity might also help to reduce depressive symptoms.

Introduction

Sixty per cent of the European population hold the view that patients with heart failure need rest and should avoid physical activities [1]. Yet exercise training, both supervised and home-based, has proven capable of conferring multiple benefits in stable heart failure [2–4], and regular physical activity has become a standard in heart failure management [5,6]. However, with more severely ill patients usually being excluded from exercise trials, it is unclear if patients with heart failure severe enough to be listed for heart transplantation (HTx), can benefit from increasing their physical activity [7].

Some evidence that physical activity may benefit adult HTx candidates comes from an uncontrolled study of 107 ambulatory patients [8]. Patients were instructed to go for 20- to 30-min walks at least four times per week. After 6 months, 68 patients were able to undergo repeat exercise testing. Of these, 38 had peakVO_2 improvements ≥2 ml/kg/min, with 31 removed from the waiting list.

After 21 months, 28 of these patients were still alive without HTx [8].

We currently know very little about *everyday physical activities* (e.g. walking, exercising at home) in HTx candidates. However, we do know that emotional factors such as depression impede physical activity. For example, depression and lack of motivation and energy affect adherence to exercise prescriptions in patients with heart failure [9,10], impair physical activity in patients after bypass surgery or myocardial infarction [11], as well as in healthy adult populations [12].

The aim of this study was to examine depressive symptoms as correlates of everyday physical activities in newly listed HTx candidates, controlling for disease severity. It is hypothesized that depressive symptoms are related to physical activity, potentially posing as a barrier to adopting a more physically active everyday life.

Materials and methods

Procedures

The Waiting for a New Heart Study is a 2-year prospective multi-site observational study of patients newly registered for HTx with Eurotransplant. This report focuses on baseline data and presents cross-sectional analyses. The study procedure has been described in detail elsewhere [13]. Briefly, patients newly registered with Eurotransplant were enrolled consecutively in 17 German-speaking HTx centres (one in Austria) between April 2005 and December 2006. Questionnaires measuring demographic, behavioural, and psychosocial characteristics [13] were mailed to patients who had furnished informed consent. Medical information was provided by Eurotransplant. Approval for the study by local ethics committees had been obtained before starting recruitment and the study conforms to the principles outlined in the Declaration of Helsinki.

Participants

Newly registered HTx candidates were eligible for inclusion in the study if they were aged 18 years or older, fluent in German, had not received a donor heart before, and did not need a combined heart–lung transplantation. All underlying causes of heart failure were accepted.

There were 479 patients who met these general eligibility criteria. Ninety-nine patients were not approached, primarily because they were 'in poor condition' (i.e. not able to answer the questionnaire or interview) as determined by their physician (71%), or had been referred to another hospital [13]. This resulted in 380 patients who were invited to participate. Of these, 340 provided informed written consent. Questionnaires were returned by 318 patients (response rate = 93.5%). The 161 non-participants (99 not included, 40 decliners, 22 drop-outs) were more likely to be categorized into New York Heart Association (NYHA) class IV (51%) than the 318 participants [24%, $\chi^2(2) = 32.6$, $P < 0.001$]. Both groups were similar regarding age and percentage of women [13].

The median time interval between date of listing and questionnaire return was 15 days (interquartile range 15.25, $M = 19.7$, SD = 20.1).

Medical baseline variables

Medical variables at the time of wait-listing are presented in Table 1. The German Transplant Society Score (GTSS) was calculated to provide an estimate of disease severity [14]. The GTSS was developed from medical characteristics of all patients newly registered in Germany in 1997, and was validated on all new patients registered in 1998, using death-while-waiting as outcome [14]. The model includes left ventricular function [cardiac index, left ventricular ejection fraction (LVEF)], patient location (home, ward, intensive care unit), use of catecholamines, mechanical circulatory support, and dialysis. A higher score indicates a worse health status [14]. Missing data for medical parameters including comorbidities, current stay, and medications ranged from 0.9% (blood pressure, resting heart rate) to 11.6% (pulmonary capillary wedge pressure). As a result of several patients being too ill to perform the exercise test, 24.8% of the participants did not have peakVO_2. Brain natriuretic peptide (BNP), which is not routinely assessed, was only available for 13% of the sample and is not included in the analyses.

Questionnaire variables

Physical activity

Physical activity was assessed by a modified version of the Community Healthy Activities Model Program for Seniors (CHAMPS), a Physical Activity Questionnaire for Older Adults [15]. The original instrument was developed to meet the needs of older people engaging in less intensive activities. Our adaptation lists 15 activities of light to moderate intensity, i.e. with 'metabolic equivalents of task' values (MET values) ≥2.5 and <6. (1 MET is equivalent to a metabolic rate at rest consuming 3.5 ml of oxygen per kg of body weight per min) [16]. Items include light gardening, walk to do errands (e.g. shopping, taking children to school), ride a bike, walk leisurely, light exercises (e.g. exercises while seated), stretching, or Nordic walking (cf. Fig. 1). To aid recollection of activities, the participants are presented with the list of activities and are first asked to indicate whether or not they were engaged in each activity in a typical week during the past

Table 1. Demographic and medical characteristics of newly registered heart transplant candidates.

	Total sample Original data			Total sample Imputed data (N = 318)			
	n	M/n	SD/%	M	SD/%	Min_M/Min_n	Max_M/Max_n
Demographic characteristics							
Age	318	53.09	11.11				
Women (n, %)	318	58	18.2				
Married (n, %)	318	212	66.7				
Living with others (n, %)	318	264	83.0				
Education 9 years or less (n, %)	318	119	37.4				
BMI (kg/m^2)	318	25.90	3.95				
Medical characteristics							
Diagnosis (n, %)	318						
Ischemic		122	38.4				
Idiopathic dilated cardiomyopathy		160	50.3				
Other		36	11.3				
Time since diagnosis (months)	318	113.86	114.99				
peakVO_2 (ml/min/kg)	239	11.06	3.00	10.88	3.13	10.73	11.04
Cardiac index ($l/min/m^2$)	289	2.05	0.61	2.05	0.61	2.03	2.07
LVEF (%)	312	23.69	10.64	23.68	10.63	23.54	23.85
BP systolic (mmHg)	316	105.09	16.22	105.1	16.21	104.95	105.19
BP diastolic (mmHg)	316	63.87	12.08	63.87	12.09	63.77	63.98
Pulse pressure (mmHg)	316	41.17	14.02	41.22	13.97	41.14	41.24
Heart frequency (beats/min)	316	77.25	16.59	77.56	16.61	77.46	77.63
PCWP (mmHg)	281	20.34	8.93	20.45	9.21	20.19	20.80
BNP	40	836.30	1105.33			Not imputed	
GTSS	262	28.19	50.92	32.18	52.91	31.00	33.3
Current stay (n, %)	285						
Home		179	62.8		59.7	185	192
Ward		96	33.7		36.2	110	116
Intensive care unit		10	3.5		4.1	10	16
NYHA (n, %)	316						
II, II–III, III		125	39.6		39.7	125	127
III–IV		114	36.1		36.1	114	116
IV		77	24.4		24.2	77	78
Comorbidities, devices (n, %)							
Atrial fibrillation	258	48	18.6		20.0	60	67
Mitral valve regurgitation	224	90	40.2		40.3	124	134
Peripheral artery disease	263	11	4.2		4.4	12	16
Apoplexy	274	12	4.4		4.2	12	16
Diabetes mellitus	279	75	26.9		26.4	80	88
Previous heart surgery	290	95	32.8		33.7	102	109
Dialysis/haemofiltration	292	5	1.7		1.6	5	6
ICD	279	173	62.0		60.7	189	197
VAD	314	7	2.2		2.2	7	8
Medication (n, %)							
Catecholamines	309	49	15.9		15.9	49	52
Beta-blockers	313	272	86.9		86.8	275	277
ACE-Inhibitors, AT_1-blocker	312	237	76.0		75.9	240	243
Aldosterone antagonists	312	208	66.7		66.6	210	213
Diuretics	312	279	89.4		89.1	282	285
Digitalis	313	154	49.2		40.0	155	158

M, mean; SD, standard deviation; Min_M, minimum mean obtained from the ten imputed data sets; Max_M, maximum mean obtained from the ten imputed data sets; Min_n, minimum n obtained from the 10 imputed data sets; Max_n, maximum n obtained from the 10 imputed data sets; BMI, body mass index; peakVO_2, peak oxygen consumption; LVEF, left ventricular ejection fraction; BP, blood pressure; PCWP, pulmonary capillary wedge pressure; BNP, brain natriuretic peptide; GTSS, German Transplant Society Score; NYHA, New York Heart Association; ICD, implanted cardioverter defibrillator; VAD, ventricular assist device; ACE Inhibitors, angiotensin converting enzyme inhibitors.

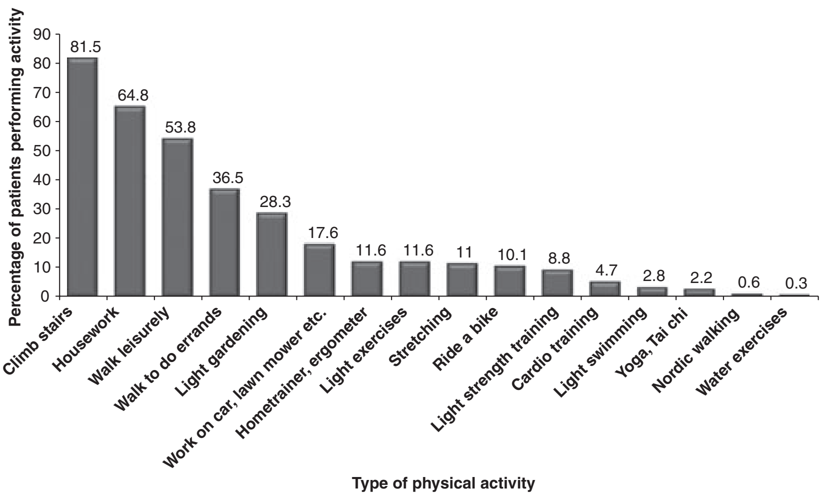

Figure 1 Percentage of newly listed heart transplantation candidates engaging in each of 16 everyday physical activities (N = 318).

4 weeks (yes/no). If the answer is yes, the *frequency* per week is determined. We report the percentage of patients engaging in the indicated activity at least four times per week to arrive at an estimate of regularity. Finally, participants are asked to specify the number of hours per week usually spent in this activity on a six-point scale from '<1 h' to '9 or more hours', providing an estimate of *duration* for each activity. We calculated two physical activity sum scores: (i) Number of activities engaged in, consisting of all 15 physical activities with a MET value ≥2.5. Added was climbing stairs, yielding a score between 0 and 16. (ii) Caloric expenditure per week was based on duration of physical activities according to Stewart *et al.* [15]. The six-point duration scale was recoded to hours per week ranging from 0.5 (<1 h) to 9.75 (>9 h). Each item value was weighted by the MET value of the respective activity and multiplied by 3.5*60*(weight in kg/200). These caloric expenditure values were summed across all 15 activities yielding the total amount of kcal/week spent in these activities [15]. In addition, patients were asked to estimate the distance (metres) they were able to walk without a break yielding a measure of estimated walking ability.

Depressive symptomatology

Depressive symptomatology was assessed using the depression subscale of the German version of the Hospital Anxiety and Depression Scale (HADS-D) [17]. This widely used self-report measure comprises seven depression items, excluding somatic symptoms that could be confounded with physical symptoms of heart disease (e.g. 'I look forward with enjoyment to things'; 'I feel cheerful' – both reverse scored; 'I feel as if I am slowed down'). Responses range from 0 to 3 and are added (a high score reflects more depression; maximum sum = 21). A score ≥9 suggests the presence of clinical depression [17]. Both the English and the German version of the scale have been extensively validated and internal consistency of the depression scale is sufficient with Cronbach's $\alpha = 0.81$ in the German norm sample of 6200 (90% cardiology) patients [17] and $\alpha = 0.77$ in our sample [13].

Data analysis

The percentage of patients engaging in each of the physical activities was calculated. The following variables were analysed: number of different activities, sum of caloric expenditure associated with each activity, and estimated walking distance. Associations of the physical activity measures with demographic and medical characteristics, and depression were examined using Pearson correlations. To test if depression was associated with the three continuous physical activity measures, we used multiple linear regression analyses. Three identical hierarchical regression models for each outcome variable were built, entering demographic characteristics (age, gender) in the first step, medical variables (GTSS, peakVO_2) in the second step, and depression as a continuous variable in the third step. In addition, we entered variables that correlated $P < 0.10$ with at least one of the three activity measures as covariates in all models. Results were considered statistically significant if $P < 0.05$.

To address the problem of missing values in the medical variables, multiple imputation technique was employed. If more than 30% of observations in one variable was missing (e.g. BNP), no imputation was performed. For variables with <30% missing values, the semi-parametric multiple imputation procedure of van Buuren and Oudshoorn was used [18,19]. According to this approach, a unique imputation model was specified for each variable with missing values. As predictor variables for the imputation models we selected variables central for planned analyses, variables associated with occurrence of missing data in the target variable, and variables that correlated with the target variables (Pearson correlation ≥ 0.15) [19]. We ran 150 iterations and every 15th estimated data set was retained resulting in ten complete data sets. Multiple imputation was computed using the package MICE 1.16 for R 2.7.2. (R Foundation for Statistical Computing, Vienna, Austria). All analyses were conducted across the 10 imputed data sets and the results pooled using R and the packages MICE, mitools, and Zelig.

To explore the robustness of the obtained results we repeated the regression analyses (i) after exclusion of outliers in physical activity measures and (ii) using only the original (nonimputed) data from the reduced sample with complete medical data ($N = 203$).

Results

Demographic and medical characteristics of the sample are shown in Table 1. Medical characteristics are reported both for original and imputed data. Categorical data are presented with percentages plus minimum and maximum absolute numbers observed in the 10 imputed data sets. Continuous values are presented with means and standard deviations plus minimum and maximum means obtained in the 10 imputed data sets. In general, mean values including imputed parameters were similar to the values based on nonmissing data. One exception was peakVO$_2$, for which the inclusion of imputed values indicated greater disease severity than the values based on nonmissing data. This is not surprising, as peakVO$_2$ is less often determined in more severely ill patients. Indeed, missing values in peakVO$_2$ were more common among inpatients (41.4%) than in ambulatory patients [18.6%, $\chi^2(1) = 17.54$, $P < 0.001$]. Inpatient status is heavily weighted in the GTSS.

Table 2. Behavioural and psychological characteristics of newly registered heart transplant candidates.

	Total sample (*N* = 318)			
	M	SD	Min	Max
Physical activity				
Number of physical activities	3.46	2.36	0	16
Caloric expenditure (kcal/week)	1694.92	1716.64	0	8124
Estimated walking distance (metres)	608.99	976.40	0	6000
Psychosocial characteristics				
Depression (HADS, 0–21)	7.67	3.91	0	20
HADS depression scores ≥9 (*n*, %)	123	38.70		
Psychological counselling (*n*, %)	113	35.50		
In depressed patients (*n* = 123)	43	35.00		
In not depressed patients (*n* = 195)	70	35.90		

M, mean; SD, standard deviation; HADS, Hospital Anxiety and Depression Scale.

Table 3. Associations of physical activity scores with demographic, medical, and psychosocial baseline characteristics.

	Number of physical activities	Caloric expenditure	Estimated walking distance
Demographic characteristics			
Age	0.03	0.04	−0.01
Gender (0 = men, 1 = women)	−0.12*	−0.15**	−0.15**
Married	0.05	−0.03	0.05
Living with others	−0.02	−0.11*	0.01
Education > 9 years	0.04	0.01	0.08
BMI (kg/m^2)	0.02	0.19***	0.09†
Medical characteristics			
Time since diagnosis (months)	−0.05	−0.09†	−0.10†
Current stay[a] (1 = home, 2 = ward, 3 = ICU)	−0.24***	−0.14*	−0.10†
NYHA	−0.27***	−0.16**	−0.32***
peakVO$_2$ (ml/min/kg)	0.24***	0.19**	0.21**
Cardiac index (l/min/m^2)[a]	0.06	0.03	0.05
LVEF (%)[a]	0.01	0.04	0.01
PCWP (mmHg)	−0.06	−0.03	−0.06
BP systolic (mmHg)	0.06	−0.01	0.15**
BP diastolic (mmHg)	0.18**	−0.02	0.24***
Pulse pressure	−0.08	0.00	−0.04
Heart rate (bpm)	−0.05	−0.06	0.18**
GTSS	−0.23***	−0.15**	−0.10†
BNP (*n* = 40)	−0.28†	−0.37*	−0.17
Comorbidities, devices			
Atrial fibrillation	0.05	0.02	0.01
Mitral valve regurgitation	−0.06	−0.07	−0.05
Peripheral artery disease	0.05	0.02	−0.01
Apoplexy	0.03	0.01	0.03
Diabetes mellitus	0.01	0.01	0.04
Previous heart surgery	−0.07	−0.04	−0.14*
Dialysis[a]	−0.08	−0.07	−0.05
ICD	−0.00	0.00	0.09
VAD[a]	0.04	0.06	0.01
Medications			
Catecholamines[a]	−0.17**	−0.09	−0.10†
Beta-blocker	0.07	0.11†	−0.01
ACE-inhibitors, AT$_1$-blocker	−0.06	−0.01	−0.06
Aldosterone antagonists	0.04	0.12*	−0.05
Diuretics	0.06	0.08	−0.05
Digitalis	0.09	0.09	−0.07
Psychosocial variables			
Depression	−0.12*	−0.10†	−0.13*
Psychological counselling	0.02	0.01	0.11*

For abbreviations see Table 1. All dichotomous variables are coded 0 = no, 1 = yes.
†$P < 0.10$, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
[a]Included in the GTSS.

Elevated depression scores suggesting the presence of clinical depression were prevalent in 38.7% of the patients (Table 2). Psychosocial counselling was reported by 35% of patients, and this proportion did no differ by depression status [$\chi^2(1) = 0.029$, NS, Table 2]. Antidepressant medication was assessed in only three hospitals ($n = 190$), representing 60% of our sample. Of these, 7.4% (nine men, five women) received antidepressant medication.

Nearly half of the patients still engaged in physical *activities of daily living* like climbing stairs, household chores, walking leisurely, and walking to do errands (36.5–81.5%, Fig. 1). With regard to physical *exercises*, however, the percentage of active patients was considerably lower (between 2% engaging in yoga/tai chi and 11.6% using the ergometer or doing light exercises, Fig. 1). Accordingly, *regular* physical activity (at least four times a week) was more often reported with regard to *activities of daily living* like housework (41.2%), walking leisurely (26.1%), or walk to do errands (12.3%), than with regard to *exercising* (varying between 6% for stretching 4% for bicycle ergometer, and 1% for cardio training, yoga/tai chi). Thirty-three participants (10.4%) engaged in none of the 16 specified physical activities with 28 of these patients being inpatients at the time of questionnaire completion (data not shown). The wide range of physical activities reported in this sample is also reflected in the three measures of physical activity (Table 2).

Bivariate associations of the three physical activity scores with demographic and medical variables, and depressive symptoms are summarized in Table 3. Body mass index (BMI) correlated only with caloric expenditure ($r = 0.19$, $P < 0.01$), which was to be expected as weight is included in the scores' computation, such that persons with higher weight have higher caloric expenditure than leaner persons if engaging in the same activity for the same duration. peakVO_2 was positively correlated with all self-reported physical activity measures (Table 3). Depression was negatively related to subjective walking distance and number of activities, but the association with caloric expenditure attributable to these activities did not reach conventional level of statistical significance.

Results of the hierarchical regression models are displayed in Table 4. After controlling for demographics

Table 4. Multiple regression of physical activity on medical and demographic characteristics and depression.

	Number of activities				Caloric expenditure				Subjective walking distance			
Predictor	*b*	SE (*b*)	*P*	ΔR^2	*b*	SE (*b*)	*P*	ΔR^2	*b*	SE (*b*)	*P*	ΔR^2
Step 1				0.016				0.073***				0.040*
Age	0.02	0.01	0.149		13.57	8.95	0.129		7.52	4.93	0.127	
Gender (0 = men, 1 = women)	−0.62	0.34	0.067		−522.93	244.76	0.033		−321.62	134.69	0.017	
Living with others (0 = no, 1 = yes)	−0.09	0.35	0.795		−542.84	253.78	0.032		31.08	139.25	0.823	
Psychol. counselling (0 = no, 1 = yes)	0.03	0.27	0.909		−37.15	195.48	0.849		210.20	108.17	0.052	
BMI	−0.01	0.03	0.810		81.87	23.79	<0.001		15.76	13.11	0.229	
Step 2				0.133				0.066***				0.137***
Time since diagnosis	−0.00	0.00	0.589		−1.08	0.83	0.194		−0.50	0.46	0.274	
GTSS	−0.01	0.00	0.010		−2.74	1.94	0.159		−0.79	1.11	0.475	
peakVO_2	0.13	0.05	0.007		93.72	37.21	0.013		52.59	19.74	0.008	
Diastolic BP	0.03	0.01	0.008		−9.26	7.97	0.246		14.34	4.38	0.001	
Heart frequency	−0.01	0.01	0.408		−3.18	5.60	0.570		10.31	3.12	<0.001	
Previous heart surgery (0 = no, 1 = yes)	−0.38	0.29	0.184		−127.05	205.25	0.536		−281.50	113.90	0.014	
Aldosterone antagonists (0 = no, 1 = yes)	−0.02	0.29	0.941		253.26	212.37	0.233		−204.35	117.33	0.082	
Beta-blockers (0 = no, 1 = yes)	0.41	0.42	0.325		−152.48	299.72	0.611		59.16	168.10	0.725	
Step 3				0.014*				0.011*				0.023*
Depression	−0.07	0.03	0.028		−47.12	23.76	0.047		−38.71	13.11	0.003	
Intercept	0.70	1.56	0.652		−455.08	1143.97	0.691		−1967.99	628.80	0.002	
		$R^2 = 0.147$				$R^2 = 0.150$				$R^2 = 0.200$		

$N = 318$. Displayed are unstandardized regression coefficients (*b*) and standard errors (*b*) of the final step. BMI, body mass index; GTSS, German Transplant Society Score; peakVO_2, peak oxygen uptake; BP, blood pressure.
*$P < 0.05$, ***$P < 0.001$.

(age, gender, living with others, BMI), psychological counselling, and medical covariates (time since diagnosis, GTSS, peakVO_2, diastolic blood pressure, heart frequency, previous heart surgery, aldosterone antagonists, beta-blockers), depressive symptomatology significantly accounted for variance in all of the three physical activity measures. A one-unit increase in depression was associated with a 47.12 kcal/week decrease in caloric expenditure. Similarly, higher depressive symptomatology was significantly related to a reduced number of different physical activities after adjusting for covariates. The same pattern emerged for subjective walking ability, with one unit increase in depression being associated with a 39 m shorter estimated walking distance.

To further illustrate this finding, we solved the equation for a hypothetical 'average' woman (mean age: 53.1; mean time since diagnosis: 113.9 months; mean BMI: 25.90 kg/m^2; mean GTSS: 32.2; mean peakVO_2: 10.88 ml/min/kg; mean diastolic blood pressure = 64 mmHg; mean heart rate: 78 bpm), receiving aldosterone antagonists and beta-blockers at two levels of depression (depression = 0; depression = 20). The presence of depressive symptoms in the clinically relevant range yields a reduction in the number of physical activities from 3.4 to 2.0, a reduction in caloric expenditure from 1391.3 to 448.8, and a reduction in estimated ability to walk without a break of 774.2 m less than a nondepressed woman.

Because of the main effect of gender, similar reductions in physical activity measures are expected in a male patient with scores in the clinically depressed range, but at higher levels.

Outliers in physical activity scores (absolute z-transformed scores > 2.58) constituted 3.5% of scores in estimated walking distance, 1.6% in number of physical activities and 1.6% in caloric expenditure. Excluding outliers from the analyses yielded depression results comparable to the ones reported above for estimated walking distance and number of activities ($P < 0.0001$, $P < 0.05$). The contribution of depression to caloric expenditure was slightly reduced ($P < 0.10$).

Restricting the regression analyses to participants with complete medical data ($N = 203$, i.e. excluding patients with imputed data) a similar pattern of findings emerged: the results regarding disease severity (peakVO_2, GTSS) were comparable to those reported above. Regression coefficients for depression regarding numbers of activities and caloric expenditure were slightly higher than that with imputed data ($b = -0.08$, SE = 0.05 and $b = -57.84$, SE = 32.91), but failed to reach the conventional level of significance because of reduced sample size and increased standard errors ($P < 0.073$ and $P < 0.081$). For estimated walking distance, the depression result was no longer statistically significant ($P = 0.223$).

Discussion

This is the first study describing everyday physical activities in a multi-centre sample of patients newly registered for cardiac transplantation. Considering the severity of disease in this sample, the range of everyday physical activities reported was surprisingly wide. Some patients still engaged in regular exercises, but everyday physical activities like household chores and walking were most prominent. Thus, assessing everyday physical activities including activities of daily living rather than measuring regular physical exercise alone may yield a more accurate picture of severely ill patients' actual physical activity.

Statistically significant correlations of demographic and medical characteristics with the physical activity measures were rather small and should be interpreted with caution. However, it is noteworthy that the results were as expected. Gender contributed significantly to the variance in all physical activity measures. After adjusting for covariates, women's caloric expenditure and estimated walking distance still were significantly lower than men's. This finding is in line with the consistently reported higher physical inactivity in women compared with men [12]. Also, patients with greater disease severity (lower peakVO_2, worse NYHA class, and lower GTSS) consistently reported fewer physical activities. No relationships emerged between the physical activity variables and haemodynamic parameters such as LVEF, cardiac index, or pulmonary capillary wedge pressure, findings in line with the notion that haemodynamic characteristics are unrelated to exercise capacity [20].

The importance of engaging in physical activity for patients with severe heart failure in order to prevent progression of deconditioning has been receiving increasing recognition. For example, a recent AHA Statement [21] recommends that heart failure patients registered for cardiac transplantation start an exercise programme shortly after listing, even in the intensive care setting. Yet, our results clearly show that lack of participating in such programmes does not necessarily indicate physically inactivity. To the contrary, nearly half of the patients (47%) in our study engaged in everyday physical activities, mainly household activities, associated with varying caloric expenditure, a result also reported for post-Tx women [22]. Thus, it appears reasonable to implement individualized physical activity regimens that build upon the patient's everyday activities rather than following standardized exercise protocols 'for all'.

Most noteworthy is our finding that depressive symptoms accounted for additional variance in all three everyday physical activity measures, independently from demographic factors, disease severity as measured by the GTSS (including inpatient status and use of mechanical circulatory support or dialysis), exercise capacity (peakVO_2), blood pressure, heart frequency, and medications. Considering the importance of physical activity in this patient group [3, 4], our finding regarding the independent association of depressive symptoms with reduced physical activity takes on added significance. Because of the cross-sectional nature of this study, this association can be interpreted in two ways: First, depressive symptoms could be an independent barrier for engaging in physical activity. In general, depression is associated with reduced drive and motivation [23] thereby affecting both intentions and actual behaviours. Thus, depressed patients might exert less effort than nondepressed patients [24] and be less compliant with exercise regimens [10,25–27]. In addition, depressed patients, who are likely to hold negative beliefs about oneself, the world, and the future [28] may not see the same value in physical exercise than nondepressed patients. Second, engagement in physical activities might reduce depressive symptoms [29]. This interpretation is also consistent with findings reported by others. For example, Milani and Lavie [27] report that regular exercise reduced depressive symptoms in patients with coronary heart disease. Similar results have been found in patients with heart failure [30], and in patients diagnosed with major depressive disorder [31]. Furthermore, both depressive symptoms and physical inactivity have been linked to endothelial dysfunction [32,33], an important mechanism for adverse outcomes in heart failure [34,35].

Regardless of its directionality, the association of depressive symptoms to reduced physical activity is important, considering that depressive symptoms are highly prevalent in patients waiting for a donor heart [36]. In our sample, 39% had elevated depressive symptomatology, but only one third of these patients received psychological counselling. In order to promote a physically active lifestyle in patients with heart failure, depressive symptoms should be regarded as a potential barrier and should be targeted accordingly. Also, given the controversy surrounding the appropriateness of antidepressive medication use in this patient group [37] increased use of behavioural approaches, such as physical activity regimens, to reduce depressive symptoms, may be indicated.

Several limitations of our study should be noted. First, both physical activity and depressive symptoms were assessed via self-reports. In regard to physical activity, several studies are available that support the CHAMPS' validity. For example, higher caloric expenditure was significantly associated with higher activity counts per hour as measured by accelerometry in older adults at risk for mobility disability [38]. CHAMPS duration variables regarding walking and total physical activity also correlated significantly with weekly pedometer step counts in adults >65 years of age [39]. In our study, all activity measures correlated positively with peakVO_2, supporting the self-reports' validity. Nevertheless, objective assessment of everyday physical activity via accelerometers would have been desirable. Similarly, our study relied on self-reports for depressive symptomatology. Additional psychological (e.g. health cognitions regarding the potential benefits of regular activity, and fear of experiencing physical symptoms [12]) that were not measured in this study, may have added to the variance in physical activity. In addition, other limiting factors, such as physical ones (e.g. structural changes in peripheral muscles [20] as a result of the disease), and environmental ones (e.g. weather or neighbourhood characteristics [12,40,41]) were not assessed in this study.

Furthermore, the reported analyses were cross-sectional, precluding the establishment of causality. It is conceivable that depression prevents patients from engaging in physical activity, but it is also possible that being physically active alleviates negative emotions. Future prospective studies examining both the role of negative emotions and physical activity in health outcomes in this patient group will shed more light on this question. Initial evidence that depression contributes to outcomes in this study has just been reported [42]. Finally, our findings may not be generalizable to all patients registered for HTx with Eurotransplant. Although our participants were comparable to other adult HTx patients registered with Eurotransplant with respect to age and gender, patients that were excluded from our study were more likely to have more severe heart-failure as documented by NYHA class.

In summary, our finding that depressive symptoms in the clinically relevant range contributed to all measures of physical activity employed in this study independent of disease severity has important implications for preventing deconditioning in HTx candidates. Regardless of the directionality of the physical activity – depression relationship, both decreasing depression and increasing physical activity will be of benefit for patients with chronic heart failure. Attempts to increase physical activity in these patients might benefit from building upon their everyday activities, as well as paying attention to the patients' emotional state.

Authorship

HS and GW: designed the study and wrote the manuscript. DZ and HS: analysed the data. SSS, TS, LR, JMAS, and TM: participated in data collection, and together with HWK: contributed to the writing of the manuscript.

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