Effect of left ventricular assist device implantation and heart transplantation on habitual physical activity and quality of life

Jakovljevic, DG., McDiarmid, A., Hallsworth, K., Seferovic, PM., Ninkovic, VM., Parry, G., Schueler, S., Trenell, MI. & MacGowan, GA.

Published PDF deposited in Coventry University's Repository

Original citation:
Jakovljevic, DG, McDiarmid, A, Hallsworth, K, Seferovic, PM, Ninkovic, VM, Parry, G, Schueler, S, Trenell, MI & MacGowan, GA 2014, 'Effect of left ventricular assist device implantation and heart transplantation on habitual physical activity and quality of life', American Journal of Cardiology, vol. 114, no. 1, pp. 88-93.
https://dx.doi.org/10.1016/j.amjcard.2014.04.008

DOI 10.1016/j.amjcard.2014.04.008
ISSN 0002-9149
ESSN 1879-1913

Publisher: Elsevier

Open access under a under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC BY-NC-ND).

Copyright © and Moral Rights are retained by the author(s) and/ or other copyright owners. A copy can be downloaded for personal non-commercial research or study, without prior permission or charge. This item cannot be reproduced or quoted extensively from without first obtaining permission in writing from the copyright holder(s). The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the copyright holders.

Effect of Left Ventricular Assist Device Implantation and Heart Transplantation on Habitual Physical Activity and Quality of Life☆

Djordje G. Jakovljevic, PhD[a,*], Adam McDiarmid, MB[b], Kate Hallsworth, PhD[a], Petar M. Seferovic, MD, PhD[c], Vladan M. Ninkovic, MD[d], Gareth Parry, MD[e], Stephan Schueler, MD[e], Michael I. Trenell, PhD[a], and Guy A. MacGowan, MD[b,f]

The present study defined the short- and long-term effects of left ventricular assist device (LVAD) implantation and heart transplantation (HT) on physical activity and quality of life (QoL). Forty patients (LVAD, n = 14; HT, n = 12; and heart failure [HF], n = 14) and 14 matched healthy subjects were assessed for physical activity, energy expenditure, and QoL. The LVAD and HT groups were assessed postoperatively at 4 to 6 weeks (baseline) and 3, 6, and 12 months. At baseline, LVAD, HT, and HF patients demonstrated low physical activity, reaching only 15%, 28%, and 51% of that of healthy subjects (1,603 ± 302 vs 3,036 ± 439 vs 5,490 ± 1,058 vs 10,756 ± 568 steps/day, respectively, p <0.01). This was associated with reduced energy expenditure and increased sedentary time (p <0.01). Baseline QoL was not different among LVAD, HT, and HF groups (p = 0.44). LVAD implantation and HT significantly increased daily physical activity by 60% and 52%, respectively, from baseline to 3 months (p <0.05), but the level of activity remained unchanged at 3, 6, and 12 months. The QoL improved from baseline to 3 months in LVAD implantation and HT groups (p <0.01) but remained unchanged afterward. At any time point, HT demonstrated higher activity level than LVAD implantation (p <0.05), and this was associated with better QoL. In contrast, physical activity and QoL decreased at 12 months in patients with HF (p <0.05). In conclusion, patients in LVAD and HT patients demonstrate improved physical activity and QoL within the first 3 months after surgery, but physical activity and QoL remain unchanged afterward and well below that of healthy subjects. Strategies targeting low levels of physical activity should now be explored to improve recovery of these patients. **© 2014 The Authors. Published by Elsevier Inc. All rights reserved.** **(Am J Cardiol 2014;114:88−93)**

Physical inactivity increases the risk for all-cause and cardiovascular mortality by 30% to 40% in the general population[1] and is considered as an independent risk factor for heart failure (HF).[2] Conversely, habitual physical activity, that is, daily walking performance, as objectively evaluated by an accelerometer, is an important determinant of functional capacity in patients with chronic HF.[3] Furthermore, increased physical activity in the form of a structured exercise intervention improves exercise tolerance and quality of life (QoL) in HF[4] and heart transplantation (HT) patients,[5] but limited number of studies evaluated its impact in patients implanted with a left ventricular assist device (LVAD).[6,7] Before critically evaluating exercise as a potential therapy for patients on LVAD support, it is important to understand the pattern of habitual, daily physical activity and its relation to QoL. Consequently, the aim of this study was to define the short- and long-term effects of LVAD implantation and HT on everyday physical activity, energy expenditure, and QoL.

Methods

A prospective, observational, repeated-measures design was chosen to characterize changes over time that occur in physical activity and QoL in patients on LVAD support and HT patients. The setting for the study was an inpatient HT assessment. Based on the assessment, patients were listed for HT, if judged to be too unwell to wait for a transplant, or an LVAD was implanted, if they would become better transplant candidates after a period of LVAD support. Those too well for transplant were continued on optimal medical management. These 3 scenarios were the basis of the 3 patients groups: LVAD, HT, and HF. HF patients had not received LVAD or HT during the study. Changes in physical activity and QoL of 12 HT patients were compared with those of 14 LVAD and 14 HF patients. Physical activity−related subgroup comparisons were performed with age-, gender-, and body mass

[a]Institute of Cellular Medicine, Faculty of Medical Sciences, and [f]Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom; [b]Department of Cardiology, Freeman Hospital, Newcastle upon Tyne, United Kingdom; [c]Cardiology Department, Clinical Centre of Serbia, Medical School, University of Belgrade, Belgrade, Serbia; [d]Department of Cardiology, Specialistic Hospital Merkur, Vrnjacka Banja, Serbia; and [e]Departments of Cardiothoracic Surgery and Transplantation, Freeman Hospital, Newcastle upon Tyne, United Kingdom. Manuscript received January 27, 2014; revised manuscript received and accepted April 3, 2014.

☆This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/3.0/).

This study was supported by a research grant from the United Kingdom National Institute for Health Research Newcastle Biomedical Research Center in Ageing and Chronic Diseases in Newcastle.

See page 92 for disclosure information.

*Corresponding author: Tel: (+44) 0191 222 8257; fax: (+44) 0191 222 0723.

E-mail address: d.jakovljevic@ncl.ac.uk (D.G. Jakovljevic).

0002-9149/14/$ - see front matter © 2014 The Authors. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjcard.2014.04.008

Table 1
Subject demographic and clinical characteristics

Patients Characteristics	LVAD (n = 14)	HT (n = 12)	HF (n = 14)	Healthy Subjects (n = 14)	ANOVA p Value
Age (years)	49 14	48 17	46 10	48 14	0.959
Men (%)	100	70	67	71	—
Weight (kg)	85 16	77 11	80 15	84 17	0.617
Height (cm)	177 10	170 8	169 9	174 13	0.081
Body mass index (kg/m^2)	27 6	27 6	29 5	27 4	0.725
Etiology of heart failure					
Idiopathic dilated cardiomyopathy	5	6	11	N/A	—
Ischemic cardiomyopathy	9	2	3	N/A	—
Other	—	4	—	N/A	—
LVEF (%)	13 2	14 6	18 3	64 8	0.004*
NYHA class	3.7 0.2	3.8 0.3	3.3 0.5	—	
Cardiac index (l/min/m^2)	1.7 0.4	1.8 0.3 4	2.1 0.4	3.6 0.7	0.002*
Peak O_2 consumption (ml/kg/min)	9.9 2.1	10.2 2.3	14.6 2.8	34.6 9.2	
INTERMACS score	2.8 0.9	—	—	—	—

Other includes tricuspid atresia (2) and restrictive cardiomyopathy (2).
ANOVA = analysis of variance; HF = heart failure; HT = heart transplantation; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association functional class.
* Healthy versus LVAD, HT, and chronic heart failure (p <0.01).

Table 2
Energy expenditure, physical activity and quality of life at baseline

Variables	LVAD	HT	HF	Healthy Subjects	ANOVA p Value
Total energy expenditure (kcal/day)	2164 112	2240 163	2108 211	2880 153	0.004*
Steps (per day)	1603 302	3036 439	5490 1058	10,756 568	<0.001*†
Average METs (kcal/kg/hour)	1.07 0.06	1.28 0.08	1.23 0.06	1.45 0.04	<0.001*‡
Active energy expenditure (kcal/day)	78 30	330 129	313 95	751 77	<0.001*‡
Physical activity duration (min/day)	18 8	69 22	65 18	128 10	<0.001*‡
Sedentary time (min/day)	1410 10	1303 32	1322 24	1261 17	<0.001‡
Moderate physical activity (min/day)	18 8	66 25	64 18	120 9	<0.001*‡
Vigorous physical activity (min/day)	0 0	3.5 2.3	0.5 0.3	5.9 1.7	0.014§
Very vigorous physical activity (min/day)	0 0	0.1 0.3	0 0	1.6 1.5	0.489
MLHF quality of life	81 5	72 8	74 4	N/A	0.445

ANOVA = analysis of variance; HF = heart failure; HT = heart transplantation; LVAD = left ventricular assist device; METs = metabolic equivalent units; MLHF = Minnesota Living with Heart Failure Questionnaire; N/A = not applicable.
* Healthy versus LVAD, HT, and HF (p <0.05).
† LVAD versus HF (p <0.05).
‡ LVAD versus HF, HT, and healthy (p <0.05).
§ Healthy and HT versus HF and LVAD (p <0.05).

index−matched 14 HF patients and 14 healthy subjects. In LVAD and HT patients, data on physical activity and QoL were collected at 4 different time points: baseline assessment, that is, 4 to 6 weeks after surgery and after discharge from hospital and then follow-up assessments at 3, 6, and 12 months after surgery. The data on patients with HF were collected at baseline and at 12 months, and on the healthy subjects data were only collected at 1 time point. Both LVAD and HT patients completed in-hospital postsurgery mobility and rehabilitation program guided by a physiotherapist. The study protocol was approved by the County Durham and Tees Valley Research and Ethics Committee. All participants gave written informed consent. All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki.

All patients undergoing LVAD implantation (HeartWare, HeartWare International Inc., Framingham, Massachusetts) or HT who met study inclusion criteria were recruited into the study from September 2010 to June 2013 at the Freeman Hospital, Newcastle upon Tyne, United Kingdom. Their baseline physical activity and QoL data were compared with those of 14 patients with chronic HF who were assessed but not listed for HT and 14 healthy participants. Subjects' demographic and clinical characteristics are presented in Table 1. The study inclusion criteria included age from 18 to 60 years, sufficient English language skills to answer the questionnaires, completion of follow-up visits, and willingness to participate. Study exclusion criteria included physical condition limiting rehabilitation or mobility such as stroke; myopathy; neuropathy; renal, pulmonary, or hepatic dysfunction; or active uncontrolled infection. Written informed consent was received from all subjects enrolled in the study.

Patients on LVAD support were treated with warfarin for a target international normalized ratio of 2.7 and antiplatelets

Table 3
Longitudinal changes in energy expenditure, physical activity, and quality of life

Variables	Patient Group	Baseline		3 Months		6 Months		12 Months	
Weight (kg)	LVAD	86	17	86	16	89	16	83	11
	HT	76	15	78	14	77	15	80	17
	HF	81	17	—		—		82	16
Steps (per day)	LVAD	1603	302	3712	807	4007	1084	3997	956*
	HT	3036	439	6265	443	6563	824	6288	701*
	HF	5490	1058	—		—		3560	885*†
Total energy expenditure (kcal/day)	LVAD	2164	112	2392	105	2398	108	2421	117*
	HT	2240	163	2406	137	2443	148	3572	202*‡
	HF	2108	211	—		—		1989	198†
Average METs (kcal/kg/hour)	LVAD	1.07	0.06	1.18	0.07	1.19	0.08	1.20	0.09
	HT	1.28	0.08‡	1.31	0.05	1.35	0.07‡	1.39	0.06‡
	HF	1.23	0.06	—		—		1.14	0.05†
Sedentary time (min/day)	LVAD	1410	10	1353	26	1293	52	1280	62
	HT	1303	32	1308	21	1329	18	1260	29
	HF	1322	24	—		—		1388	21†
Moderate physical activity (min/day)	LVAD	18	8	48	17	55	16	51	20*
	HT	66	22‡	86	46‡	84	14‡	144	22§‡
	HF	64	18	—		—		41	12*†
Vigorous physical activity (min/day)	LVAD	0	0	1.3	0.7	2.4	1.9	0.5	0.3
	HT	3.5	2.3	2.3	1.3	2.9	1.5	4.3	2.3
	HF	0.5	0.3	—		—		0	0
Very vigorous physical activity (min/day)	LVAD	0	0	0	0	0	0	0	0
	HT	0	0	0	0	0	0	0	0
	HF	0	0	—		—		0	0
MLHF quality of life	LVAD	81	5	57	7	63	7	60	5*
	HT	72	8	39	5‡	30	6‡	29	7*‡
	HF	74	4	—		—		82	6*†‖

* $p < 0.05$, 12 months versus baseline.
† $p < 0.05$, HF versus HT.
‡ $p < 0.05$, HT versus LVAD.
§ $p < 0.05$, 12 months versus 3 and 6 months.
‖ $p < 0.05$, HF versus LVAD.

as well as with angiotensin-converting enzyme inhibitors, β blockers, aldosterone antagonists, angiotensin receptor blockers, and diuretics as appropriate. HT patients received triple-drug immunosuppressive maintenance therapy, usually including a calcineurin inhibitor, prednisolone, and azathioprine. Patients with chronic HF were treated with β blockers (n = 14), angiotensin-converting enzyme inhibitors (n = 10), aldosterone antagonists (n = 6), diuretics (n = 12), statins (n = 8), angiotensin receptor blockers (n = 5), anticoagulants (n = 9), antiarrhythmics (n = 5), and digoxin (n = 3).

Habitual physical activity was objectively evaluated using a validated portable multisensor array (SenseWear Pro3, BodyMedia Inc., Pennsylvania).[8] The monitor was worn for 7 days and was only removed for bathing. The multisensor array measures 4 key metrics: skin temperature, galvanic skin response, heat flux, and motion by way of a 3-axis accelerometer. The sensors, combined with algorithms, calculate the average daily energy expenditure relative to baseline metabolism (metabolic equivalent: MET per day [1 MET = resting metabolic rate]), total energy expenditure (calories per day), active energy expenditure (total calories expended over 3 METs per day), physical activity duration (minutes >3 METs per day), average daily number of steps walked, sedentary activity (minutes <3 METs per day), moderate activity (minutes between 3 and 6 METs per day), vigorous activity (minutes between 6 and 9 METs day), and very vigorous activity (minutes >6 METs day).[8,9] HF-related QoL was assessed with the Minnesota Living with Heart Failure (MLHF) Questionnaire.[10]

All statistical analyses were carried out using SPSS, version 19.0 (SPSS Inc., Chicago, Illinois). Before statistical analysis, data were checked for univariate and multivariate outliers using standard z-distribution cutoffs and Mahalanobis distance tests. Normality of distribution was assessed using a Kolmogorov-Smirnov test. Analysis of variance was used to test differences in physical activity and QoL among LVAD, HT, and HF patients and healthy controls as well as to evaluate changes at different time points in LVAD and HT patients. To identify groups that differed significantly from one another, a post hoc Tukey test was performed. The relation between QoL and physical activity in the patients was evaluated using the Pearson coefficient of correlation. Statistical significance was indicated if $p < 0.05$. All data are presented as mean SEM unless otherwise indicated.

Results

The total number of patients screened for the study was 52 (18 LVAD, 14 HT, and 20 HF). Study participants' demographic and clinical characteristics are described in Table 1. The groups were not randomly assigned, and the treatment was based on the outcome of the transplant

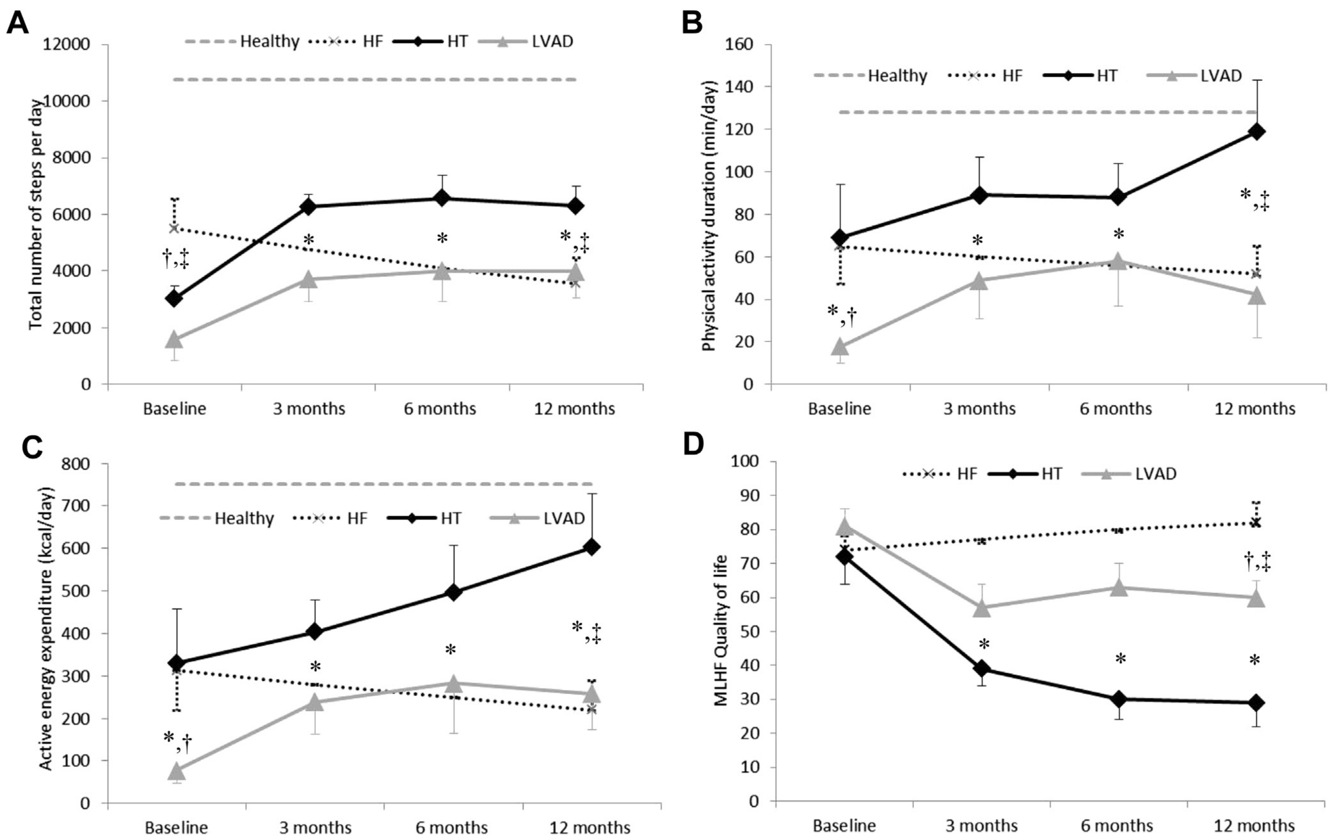

Figure 1. Longitudinal changes in the daily number of steps *(A)*, physical activity duration *(B)*, active energy expenditure *(C)*, and QoL *(D)*. Healthy data is a single reference data point and not a longitudinal series of data. *p <0.05, HT versus LVAD; †p <0.05, HF versus LVAD; ‡p <0.05, HF versus HT.

assessment. No significant differences were found in age and body mass index among LVAD, HT, HF, and healthy subjects. During the follow-up study, 2 patients in the LVAD group died and 2 refused to complete the study. There were 8 hospitalizations in 7 patients in the LVAD group for infections, 2 hospitalizations for arrhythmias, 1 with HF, 1 anemia, 1 with a transient ischemic attack, 1 with a possible deep vein thrombosis, and 1 with light-headedness. Of the heart transplant patients, 3 patients had admissions for infections and 1 patient had 3 admissions for rejection. Of the 20 patients with HF who were initially screened, 4 refused to take part in the study, 2 received HT, and 10 of remaining 14 patients completed investigation at 12 months after the baseline assessment.

Baseline physical activity measures demonstrated that patients in the LVAD and HT groups expended 25% (716 kcal) and 22% (640 kcal) less energy per day, respectively, in comparison with healthy subjects ($p < 0.05$). Similarly, patients with HF expended 27% (772 kcal) less energy per day than healthy subjects (Table 2). Daily physical activity (i.e., number of steps) was significantly reduced in the 3 patient groups with LVAD and HT patients at baseline performing only 15% and 28% and HF 51% of that of healthy subjects (Table 2). At baseline, duration of physical activity (i.e., >3 METs) was significantly reduced in LVAD patients compared with both HT and HF patients (Table 2). LVAD and HT patients showed active energy expenditure that was significantly lower than that of healthy subjects (Table 2). Moderate physical activity, that is, 3 to 6 METs, was a major contributor to active energy expenditure in all 4 groups. Vigorous physical activity was identified in healthy and HT participants but not in LVAD and HF patients (Table 2). The MLHF QoL score was not significantly different among the 3 groups of patients at baseline (Table 2).

During the follow-up period there were no significant changes in body mass during 12 months after LVAD implantation or HT. The body mass was also not changed in patients with HF. Total daily energy expenditure increased significantly from baseline to 3 months in LVAD patients ($p < 0.05$) but remained unchanged from 3 to 12 months after the surgery. In contrast, HT patients demonstrated significantly higher total energy expenditure at 12 months (Table 3). Daily number of steps significantly increased by 60% and 52% from baseline to 3 months in LVAD and HT patients, respectively. It remained, however, unchanged from 3 to 12 months and significantly lower than that of healthy subjects (Figure 1). This was further associated with significant increase in physical activity duration and active energy expenditure (Figure 1). MLHF scores decreased over time from baseline in both LVAD and HT patients indicating an improvement in QoL (Table 3, Figure 1). In contrast with LVAD and HT patients, those with HF had decreased daily number of steps, activity duration, and active energy expenditure at 12 months from baseline and increased MLHF scores (Figure 1).

At any time point during the 12-month follow-up, LVAD patients demonstrated significantly lower number of steps, physical activity duration, and active energy expenditure in comparison with HT patients (Figure 1). HT patients at

12 months after surgery demonstrated average daily physical activity duration that was only 7% below healthy controls (119 vs 128 min/day) and reached 80% active energy of controls (602 vs 751 kcal/day). The QoL score was significantly lower in HT than in LVAD patients at 3, 6, and 12 months after surgery (Figure 1).

Discussion

To our knowledge, this is the first study to report physical activity in patients after LVAD implantation and HT. There are 3 major findings. First, within the first 4 to 6 weeks after surgery, LVAD and HT patients demonstrated low physical activity levels accompanied with low energy expenditure and increased sedentary time. Second, from baseline to 3 months there was a significant increase in physical activity−associated measures and improvement in QoL in both LVAD and HT, but the number of steps remained unchanged from 3 to 12 months after surgery. Finally, HT patients demonstrate higher activity level and better QoL than LVAD patients during the 12-month follow-up. In contrast with HT and LVAD patients, those with HF demonstrated a decrease in physical activity−associated measures at 12 months compared with baseline.

The HT and particularly LVAD patients showed low activity levels on hospital discharge. Although both LVAD and HT patients completed in-hospital postsurgery mobility and rehabilitation program, they remained inactive. Strong association between daily walking performance and functional capacity in HF has been reported.[3] It is therefore not surprising that LVAD and HT patients a few weeks after surgery demonstrate only ∼40% and ∼50% of maximal predicted functional capacity, respectively.[11,12] Inactivity, low energy expenditure, and diminished functional performance early after the surgery are likely to be due to a high incidence of psychological distress and deconditioning found in LVAD and HT patients early after the surgery.[11,13]

In comparison with baseline, there was a significant improvement in physical activity−associated measures and QoL at 3 months after surgery in both LVAD and HT patients. That QoL and functional capacity improve on hospital discharge during longitudinal follow-up of LVAD and HT patients has been previously reported.[12,14,15] It is, however, noticeable that increased daily activity level at 3 months in LVAD and HT patients, found in the present study, is markedly below healthy controls and in case of HT patients similar to that of HF patients. It should further be noted that QoL improved from baseline to 3 months by 24 and 33 points for LVAD and HT patients, respectively. This is important, as a 5-point change in the MLHF score has been previously determined to be clinically meaningful.[10] Further comparison between the different patient groups reveals that 3 months after surgery, LVAD and HT patients show better QoL than patients with HF. QoL was not changed from 3 to 12 months in LVAD patients, likely because of frequent hospitalization. Our findings further suggest that patients' body mass remained unchanged over time. This is particularly interesting for LVAD patients and contrasts findings from a recent large retrospective study that suggests a significant increase in body mass after a continuous LVAD implantation.[16] The limited number of patients recruited in the present study may limit generalization of our findings.

Our data further suggest that daily number of steps and QoL remained unchanged at 3, 6, and 12 months after surgery for LVAD, but the QoL was further improved at 6 months in HT patients. This is surprising, as a significant improvement in functional capacity has been reported several months after HT and LVAD implantation allowing patients to independently perform activities of daily living.[12,17,18] In agreement with our findings, previous studies also showed that health-related QoL improved from baseline to 3 months after surgery and remained unchanged during 1-year follow-up.[14,19]

Finally, our results suggest that, not only at baseline but also at 3, 6, and 12 months after surgery, HT patients demonstrate higher levels of physical activity and better QoL than LVAD patients. These findings are in line with previous studies suggesting greater functional capacity of HT compared with LVAD patients.[7,11,12,20] In contrast with LVAD patients who showed a plateauing during the follow-up, HT patients at 12 months demonstrated physical activity duration and active energy expenditure that were 93% and 80% of healthy controls, respectively. This is an interesting finding considering that the number of steps remained unchanged from 3 to 12 months. A plausible explanation for such finding is that from 3 to 6 months the intensity of the activity was mostly <3 METs (characterized as sedentary activity), whereas at 12 months moderate activity (3 to 6 METs) was predominantly detected, resulting in a significant increase in activity duration and active energy expenditure. It has further been suggested that vigorous intensity appears to convey greater cardiovascular and functional benefits than exercise of a moderate intensity.[21] Considering that HT and LVAD are different treatment methods, the optimal physical activity and exercise interventions to improve outcomes in these patients remain to be determined in large clinical trials. Therefore, general recommendations for exercise therapy in HT and LVAD patients need to be considered with caution and are likely to differentiate in volume and intensity from those of general cardiology patients.

The present study is not without limitations. First, the lack of presurgical activity monitoring prevents our understanding of individual variation in daily activity level between HT and LVAD implantation candidates. Second, small sample size limits the generalizability of our findings. Finally, the study may be biased by the fact that predominantly male patients were available for this analysis, particularly in LVAD group.

Acknowledgment: The authors thank the participants for contributing to this study. In addition, we acknowledge the significant contribution from Judith Coulson, BSc, the research nurse, for helping with study recruitment, data collection, and follow-up of patients.

Disclosures

Dr Jakovljevic is supported by the UKRC Centre for Ageing and Activity, Newcastle, United Kingdom. Prof Trenell is supported by the NIHR Senior Research Fellowship, London, United Kingdom. Dr MacGowan is supported by the British Heart Foundation Clinical Leave

Research Fellowship number FS/11/89/29162. The other authors have no conflicts of interest to disclose.

1. Shiroma EJ, Lee IM. Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. *Circulation* 2010;122:743−752.
2. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Arch Intern Med* 2001;161:996−1002.
3. Jehn M, Schmidt-Trucksäss A, Schuster T, Weis M, Hanssen H, Halle M, Koehler F. Daily walking performance as an independent predictor of advanced heart failure: prediction of exercise capacity in chronic heart failure. *Am Heart J* 2009;157:292−298.
4. Piña IL, Apstein CS, Balady GJ, Belardinelli R, Chaitman BR, Duscha BD, Fletcher BJ, Fleg JL, Myers JN, Sullivan MJ. Exercise and heart failure: a statement from the American Heart Association Committee on exercise, rehabilitation, and prevention. *Circulation* 2003;107:1210−1225.
5. Kobashigawa JA, Leaf DA, Lee N, Gleeson MP, Liu H, Hamilton MA, Moriguchi JD, Kawata N, Einhorn K, Herlihy E, Laks H. A controlled trial of exercise rehabilitation after heart transplantation. *N Engl J Med* 1999;340:272−277.
6. Corrà U, Pistono M, Mezzani A, Gnemmi M, Tarro Genta F, Caruso R, Giannuzzi P. Cardiovascular prevention and rehabilitation for patients with ventricular assist device from exercise therapy to long-term therapy. Part I: exercise therapy. *Monaldi Arch Chest Dis* 2011;76:27−32.
7. de Jonge N, Kirkels H, Lahpor JR, Klöpping C, Hulzebos EJ, de la Riviere AB, Robles de Medina EO. Exercise performance in patients with end-stage heart failure after implantation of a left ventricular assist device and after heart transplantation: an outlook for permanent assisting? *J Am Coll Cardiol* 2001;37:1794−1799.
8. St-Onge M, Mignault D, Allison DB, Rabasa-Lhoret R. Evaluation of a portable device to measure daily energy expenditure in free-living adults. *Am J Clin Nutr* 2007;85:742−749.
9. Jakicic JM, Marcus M, Gallagher KI, Randall C, Thomas E, Goss FL, Robertson RJ. Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. *Med Sci Sports Exerc* 2004;36:897−904.
10. Rector TS, Kubo SH, Cohn JN. Validity of the Minnesota Living with Heart Failure questionnaire as a measure of therapeutic response to enalapril or placebo. *Am J Cardiol* 1993;71:1106−1107.
11. Jaski BE, Lingle RJ, Kim J, Branch KR, Goldsmith R, Johnson MR, Lahpor JR, Icenogle TB, Piña I, Adamson R, Favrot LK, Dembitsky WP. Comparison of functional capacity in patients with end-stage heart failure following implantation of a left ventricular assist device versus heart transplantation: results of the experience with left ventricular assist device with exercise trial. *J Heart Lung Transpl* 1999;18:1031−1140.
12. Kugler C, Malehsa D, Tegtbur U, Guetzlaff E, Meyer AL, Bara C, Haverich A, Strueber M. Health-related quality of life and exercise tolerance in recipients of heart transplants and left ventricular assist devices: a prospective, comparative study. *J Heart Lung Transpl* 2011;30:204−210.
13. Heilmann C, Kuijpers N, Beyersdorf F, Berchtold-Herz M, Trummer G, Stroh AL, Schlensak C, Fritzsche K. Supportive psychotherapy for patients with heart transplantation or ventricular assist devices. *Eur J Cardiothorac Surg* 2011;39:e44−e50.
14. Rogers JG, Aaronson KD, Boyle AJ, Russell SD, Milano CA, Pagani FD, Edwards BS, Park S, John R, Conte JV, Farrar DJ, Slaughter MS. Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. *J Am Coll Cardiol* 2010;55:1826−1834.
15. Grady KL, Meyer PM, Dressler D, Mattea A, Chillcott S, Loo A, White-Williams C, Todd B, Ormaza S, Kaan A, Costanzo MR, Piccione W. Longitudinal change in quality of life and impact on survival after left ventricular assist device implantation. *Ann Thorac Surg* 2004;77:1321−1327.
16. Emani S, Brewer RJ, John R, Slaughter MS, Lanfear DE, Ravi Y, Sundareswaran KS, Farrar DJ, Sai-Sudhakar CB. Patients with low compared with high body mass index gain more weight after implantation of a continuous-flow left ventricular assist device. *J Heart Lung Transpl* 2013;32:31−35.
17. McDiarmid A, Gordon B, Wrightson N, Robinson-Smith N, Pillay T, Parry G, Schueler S, MacGowan GA. Hemodynamic, echocardiographic, and exercise-related effects of the HeartWare left ventricular assist device in advanced heart failure. *Congest Heart Fail* 2013;19:11−15.
18. Jakovljevic DG, George RS, Nunan D, Donovan G, Bougard RS, Yacoub MH, Birks EJ, Brodie DA. The impact of acute reduction of continuous-flow left ventricular assist device support on cardiac and exercise performance. *Heart* 2010;96:1390−1395.
19. Hall JL, Fermin DR, Birks EJ, Barton PJ, Slaughter M, Eckman P, Baba HA, Wohlschlaeger J, Miller LW. Clinical, molecular, and genomic changes in response to a left ventricular assist device. *J Am Coll Cardiol* 2011;57:641−652.
20. Pruijsten RV, de Jonge N, Kirkels JH, Klöpping C, Doevendans PA, Oosterom A, Kemperman H, Lahpor JR. Left ventricular assist device: a functional comparison with heart transplantation. *Neth Heart J* 2008;16:41−46.
21. Swain DP, Franklin BA. Comparison of cardioprotective benefits of vigorous versus moderate intensity aerobic exercise. *Am J Cardiol* 2006;97:141−147.