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Exercise blood pressure response during assisted circulatory support: Comparison of the total artifical heart with a left ventricular assist device during rehabilitation

Harajeshwar S. Kohli, JD, MA,[a] Justin Canada, RCEP,[b] Ross Arena, PhD, PT,[b] Daniel G. Tang, MD,[c] Mary Ann Peberdy, MD,[a] Suzanne Harton, RN, MS,[a] Maureen Flattery, NP,[a] Kelly Doolin, BA,[a] Gundars J. Katlaps, MD,[c] Michael L. Hess, MD,[a] Vigneshwar Kasirajan, MD,[c] and Keyur B. Shah, MD[a]

From the [a]Division of Cardiology, [b]Department of Physical Therapy and [c]Division of Cardiothoracic Surgery, Virginia Commonwealth University, Richmond, Virginia.

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BACKGROUND: The total artificial heart (TAH) consists of two implantable pneumatic pumps that replace the heart and operate at a fixed ejection rate and ejection pressure. We evaluated the blood pressure (BP) response to exercise and exercise performance in patients with a TAH compared to those with a with a continuous-flow left ventricular assist device (LVAD).

METHODS: We conducted a single-center, retrospective study of 37 patients who received a TAH and 12 patients implanted with an LVAD. We measured the BP response during exercise, exercise duration and change in tolerated exercise workload over an 8-week period.

RESULTS: In patients with a TAH, baseline BP was 120/69 ± 13/13, exercise BP was 118/72 ± 15/10 and post-exercise BP was 120/72 ± 14/12. Mean arterial BP did not change with exercise in patients with a TAH (88 ± 10 vs 88 ± 11; $p = 0.8$), but increased in those with an LVAD (87 ± 8 vs 95 ± 13; $p < 0.001$). Although the mean arterial BP (MAP) was negatively correlated with metabolic equivalents (METs) achieved during exercise, the association was not statistically significant ($\beta = -0.1$, $p = 0.4$). MAP correlated positively with METs achieved in patients with LVADs (MAP: $\beta = 0.26$, $p = 0.04$). Despite the abnormal response to exercise, patients with a TAH participated in physical therapy (median: 5 days; interquartile range [IQR] 4 to 7 days) and treadmill exercise (19 days; IQR: 13 to 35 days) early after device implantation, with increased exercise intensity and duration over time.

CONCLUSIONS: During circulatory support with a TAH, the BP response to exercise was blunted. However, aerobic exercise training early after device implantation was found to be safe and feasible in a supervised setting.

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Total heart replacement is an effective bridge to transplant for patients with biventricular heart failure and is an alternative to implantation of biventricular assist devices.[1] The total artificial heart (TAH) is a mechanical circulatory support device that orthotopically replaces a recipient's native ventricles and all 4 cardiac valves. In contrast to a left ventricular assist device (LVAD), the native heart is entirely

Reprint requests: Keyur B. Shah, MD, Heart Failure/Transplantation, Division of Cardiology, Virginia Commonwealth University, MCV Campus, P.O. Box 980204, Richmond, VA 23298-0204. Telephone: 804-828-4571. Fax: 804-828-7710.

E-mail address: kshah@mcvh-vcu.edu

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removed and has no impact on device function or total cardiac output.

The clinician programs the TAH pump rate ("heart rate") and ejection pressures ("contractility"), which are fixed and do not dynamically change during pump operation. The pump is calibrated in the resting state to only partially fill so that the ejection volume ("stroke volume") may increase to accommodate a rise in pre-load.

In apparently healthy individuals, systolic blood pressure rises with exercise (≈10 mm Hg/metabolic equivalent).[2,3] Although stroke volume in patients with a TAH can increase during exercise, heart rate and contractility do not change. Hence, these patients could have a blunted or even hypotensive response to exercise due to arterial vasodilation in working skeletal muscle with a significantly muted increase in cardiac output.[4] These concerns are particularly relevant with the development of a portable driver that permits hospital discharge with the device.

To our knowledge, there are no studies reporting on the blood pressure response to exercise or the feasibility of rehabilitation for patients who have a TAH. We hypothesized that patients with total heart replacement have a blunted response to exercise compared to those with LVADs.

Methods

Design

This investigation was a single-center, retrospective study that included patients who received a TAH or continuous-flow LVAD at the Virginia Commonwealth University Health System. The institutional review board at Virginia Commonwealth University School of Medicine reviewed and approved this project.

We identified a cohort of 37 patients with TAHs (January 2006 to May 2010) and 12 patients with LVADs (January 2010 to December 2010) implanted with the intention to bridge to heart transplantation. We abstracted pertinent clinical data from medical records and the patients' information was de-identified. Thirty of the 37 TAH patients for whom physical rehabilitation data were available were included in the study. Of the 7 patients not included, 3 underwent heart transplantation early (1 to 2 days) after device implantation, 3 were too sick to participate in physical therapy and died (3 to 78 days) after device implantation, and data were missing for the seventh patient.

Of the 30 TAH patients who participated in physical therapy, exercise data were available for 22 who proceeded to inpatient cardiac rehabilitation, which consisted of treadmill training. We analyzed data from 110 rehabilitation sessions and 2,005 minutes of treadmill exercise. We abstracted data on blood pressure, duration of exercise and sustainable metabolic equivalents (METs) achieved during their first 8 weeks of treadmill exercise. All 12 LVAD patients received a HeartMate II (Thoratec Corp., Pleasanton, CA) continuous-flow LVAD. The LVAD cohort was a convenience sample of clinically stable patients who survived to participate in physical therapy and/or cardiac rehabilitation. Sixty-three sessions were analyzed for this group and a manual anaeroid blood pressure cuff and vascular Doppler probe were utilized to estimate mean arterial blood pressure at rest and during exercise. METs were estimated from treadmill speed and grade.[5]

The CardioWest TAH

The CardioWest TAH (Syncardia, Tucson, AZ), weighing 160 g, composed of two pneumatically driven pumps, has the ability to deliver a cardiac output of >9 liters/min at its maximal stroke volume of 70 ml. The TAH has an external console (weighing 495 lbs. crated) with controllers permitting regulation of each of the ventricles. In addition to the controllers, the console consists of several components essential to the functioning of the device, including a vacuum pump, an alarm panel and 2 high-pressure air tanks.

The basic parameters of the device console that modulate cardiac output include drive pressure, ejection rate, systolic ejection time and vacuum pressure during pump diastole. The drive pressure regulators control the pressure of the air entering the ventricles and can be set between 0 and 300 mm Hg (with a typical range of 150 to 200 mm Hg for the left ventricle and 55 to 90 mm Hg for the right ventricle). The heart rate can be set between 25 and 199 beats/min (typical range 90 to 130 beats/min). The systolic duration, or the percent of the cardiac cycle spent in systole, can be set at between 15% and 95% (typical range expected at approximately 50%, but can range from 45% to 65%). The TAH features a vacuum that can shorten ventricular filling time by drawing blood into the pumping chamber during pump diastole. This vacuum pressure can be set to between 0 and 60 mm Hg (typical range 5 to 12 mm Hg). The aforementioned parameters are adjusted to maintain full ejection during systole of both the right and left pump, and partial filling during diastole. The settings are optimized to provide clinically appropriate cardiac output and systemic blood pressures.

Patients received a TAH if they had severe right ventricular or biventricular failure and were appropriate candidates for orthotopic heart transplantation as determined by the VCU Heart Transplantation Patient Selection Committee. The presence of right ventricular dysfunction was determined by invasive hemodynamics, echocardiography and clinical assessment by both a cardiologist and cardiothoracic surgeon. Other indications included those with acute or chronic allograft failure, restrictive cardiomyopathy, hypertrophic cardiomyopathy, extensive intracavitary thrombus and cardiomyopathy with aortic root aneurysm.

The HeartMate II LVAD

The HeartMate II is a continuous-flow LVAD. It has a titanium axial-flow pump with an inlet cannula that is placed in the left ventricular apex and an outlet cannula that is placed in the ascending aorta. The LVAD parameters were pre-determined by the heart failure cardiologist utilizing clinical parameters and echocardiography, and were not adjusted during the rehabilitation sessions.

Physical rehabilitation protocols

Physical therapy (PT) was initiated by the intensive care team with a PT order for evaluation and treatment in the acute recovery period, typically once patients were off intravenous vasopressors, extubated from mechanical ventilation and of appropriate mental status. Activity orders were "as tolerated" and all patients were placed on sternal precautions. Weight-bearing status was identified as weight-bearing as tolerated while observing sternal precautions. Physical therapy care of the TAH patient required the assistance of two people: 1 for direct patient care and 1 for management of the TAH console. All clinicians who managed the TAH console had completed a training course for

Figure 1 Patient with a total artificial heart ambulating on a treadmill while attached to the pneumatic driver. (Photograph taken by Joe Kuttenkuler, VCU Communications and Public Relations.)

the operation and competencies of device management. The PT plan of care was based on a frequency of 5 days/week. Progression of gait training was based on a functional goal of less than minimal assistance with transfers/ambulation without an assistive device or with baseline/expected discharge assistive device. Ambulation distance was progressed toward an arbitrary goal of ≥600 feet or 10 minutes continuously without adverse signs or symptoms, or a rest break. The ambulation duration goal was based on a minimum duration target to meet American College of Sports Medicine (ACSM)/American Heart Association (AHA) aerobic exercise recommendations for older adults and/or those with significant chronic conditions/functional limitations.[6]

Inpatient cardiac rehabilitation was initiated once patients were sufficiently ambulatory and had reached their acute-care PT goals for functional mobility and gait. Cardiac rehabilitation was utilized to further activity progression in a medically supervised environment. Cardiac rehabilitation is staffed by clinical exercise physiologists and/or PTs. Endurance exercise modalities were performed primarily on a motorized treadmill or upper/lower extremity recumbent stepper. Progression of the cardiac rehabilitation exercise prescription was based on the *ACSM's Guidelines for Exercise Testing and Prescription*, intended for patients with cardiac disease in the inpatient setting.[7] Frequency was set at 3 to 5 days per week. Exercise duration was initially set at targets of 5 to 10 minutes with gradual progression, 1 to 5 minutes per session, toward a goal of ≥30 minutes of continuous aerobic activity. Interval bouts of exercise and rest were utilized if the patient was unable to meet the initial duration target. Patient effort was based on tolerance if asymptomatic and a rating of perceived exertion (RPE) of ≤13/20 on a Borg category scale of 6 to 20.[8] Exercise intensity was quantified by treadmill speed and grade and converted to METs based on the ACSM metabolic equations wherein 1 MET = 3.5 ml O_2 kg^{-1} min^{-1}. Intensity was progressed once the patient tolerated a continuous exercise duration of >10 minutes without adverse signs or symptoms and an RPE of <13/20. Exercise training sessions were modified or discontinued if the patient developed signs or symptoms of exercise intolerance, including marked dyspnea (≥5/10 on modified 10-grade dyspnea scale) or fatigue (>13/20 on RPE scale), orthostasis or ataxia. The PT pathway, target functional goals and cardiac rehabilitation exercise prescription was similar between both TAH and LVAD groups.

Pre-exercise evaluation consisted of confirming appropriate TAH settings, filling and ejection waveforms, identification of interval setting adjustments, and measurement of blood pressure (BP) and pulse oximetry. During exercise, the supervising exercise physiologist monitored BP, pulse oximetry, pump flows and filling pattern waveforms (Figure 1). All BP measurements were obtained manually with a stethoscope and anaeroid sphygmomanometer. On select patients who demonstrated TAH filling pattern waveforms indicative of full-fill and who showed signs or symptoms of exercise intolerance, the normally fixed beat rate was titrated 5 to 10 beats prior to exercise. The decision to manipulate beat rate settings was based on consultation with the attending cardiologist or cardiothoracic surgeon.

Statistical analysis

Statistical software, PASW Statistics, version 17 (Chicago, Illinois), was used for all analyses. Continuous data are expressed as mean and standard deviation, and categorical variables are expressed as percentage. A 2-tailed Student's *t*-test was used to compare continuous variables. A repeated measures analysis of variance (ANOVA) was used to compare changes in METs achieved and duration of exercise between weeks and BP between different states of activity. For between-week comparisons (Week 1 vs 4, Week 1 vs 8 and Week 4 vs 8), post hoc testing was performed with a paired *t*-test analysis with Bonferroni's correction for 3 comparisons, and thus only $p < 0.017$ was considered significant. Chi-square analysis was used to compare discrete variables. Associations between BPs and METs achieved were evaluated using Pearson's correlation coefficients. $p < 0.05$ was considered significant.

Results

Clinical characteristics are displayed in Table 1. Patients in both cohorts were of similar age and race. There were no female patients in the TAH group. Utilization of anti-hypertensive medications, including beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, spironolactone and sildenafil, was higher in the LVAD group.

BP response to exercise

For patients with a TAH, the mean pre-exercise BP measured was 120/69 ± 13/13, mean exercise BP was 118/72 ±

Table 1 Clinical Characteristics

Variable	TAH (N = 30)	LVAD (N = 12)	p-value
Age (years)	47.4 ± 13.2	51.2 ± 13.6	0.4
Body mass index	28.2 ± 5.1	30.8 ± 10.8	0.3
Serum creatinine (mg/dl)	1.6 ± 1.2	1.2 ± 0.4	0.3
Male	100%	83%	0.02
African American	40%	55%	0.6
Survival to heart transplant or ongoing device support	89%	92%	0.6
Medical history			
Diabetic	27%	50%	0.1
Hypertension	52%	50%	0.9
History of stroke	10%	0%	0.2
Previous cardiac surgery	20%	8%	0.4
Acute medical interventions prior to device			
Mechanical ventilation	10%	0%	0.4
Intravenous vasopressors	33.3%	25%	0.6
Inotropic agents	63.3%	50%	0.4
Medications at initiation of treadmill therapy	(n = 22)		
Nesiritide	27%	8%	0.2
Beta-blocker	0%	25%	0.01
ACE inhibitor or angiotensin receptor blocker	0%	58%	<0.001
Spironolactone	0%	42%	0.001
Calcium channel blocker	13%	17%	0.8
Loop diuretic	77%	100%	0.05
Sildenafil	0%	25%	0.01

Data expressed as mean ± SD or percentage (N = 30). ACE, angiotensin-converting enzyme; LVAD, left ventricular assist device; TAH, total artificial heart.

15/10 and the mean post-exercise BP was 120/72 ± 14/12. The differences in systolic and diastolic BPs before, during and after exercise were not statistically significant (systolic: $p = 0.3$; diastolic: $p = 0.1$) (Figure 2).

We observed no change in the mean arterial blood pressure (MAP) of patients supported with a TAH with initiation of exercise (88 ± 10 vs 88 ± 11; $p = 0.8$), whereas patients with a continuous-flow LVAD had a significant increase in their estimated MAP with treadmill exercise (87 ± 8 vs 95 ± 13; $p < 0.001$) (Figure 3).

Although BP was negatively correlated with METs achieved during exercise in TAH patients, the association was not statistically significantly (systolic: $\beta = -0.09$, $p = 0.3$; diastolic: $\beta = -0.14$, $p = 0.2$; MAP: $\beta = -0.1$, $p = 0.4$). Conversely, MAP correlated positively with METs achieved in patients with LVADs (MAP: $\beta = 0.26$, $p = 0.04$) (Figure 4).

Of the 110 analyzed TAH treadmill sessions, 6 patients (27%) were receiving a continuous infusion of nesiritide during 18 (17%) sessions. When selecting for patients receiving nesiritide, there was a trend toward decreasing systolic BP with exercise (116/66 ± 18/12 vs 109/67 ± 24/11, $p = 0.1$) and there was a statistically significant interaction measured between nesiritide and systolic BP ($p = 0.03$).

One patient with a TAH never participated in treadmill exercise because of symptomatic hypotension with ambulation.

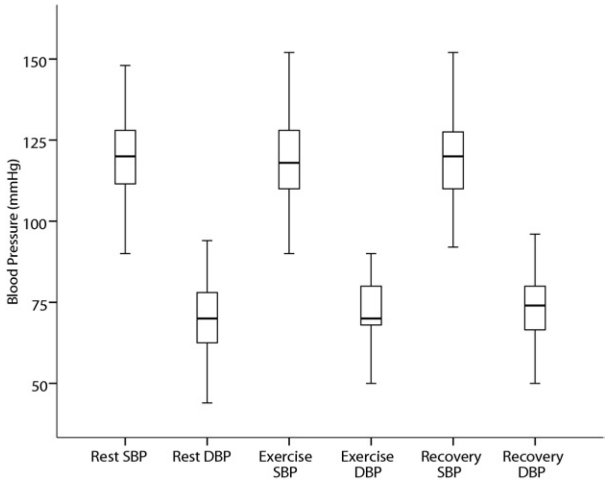

Figure 2 Box-and-whisker plot for systolic and diastolic blood pressure. There was no significant change in blood pressure from baseline compared with during and after exercise. Bold horizontal lines: median; boxed areas: interquartile range; whiskers: range.

Feasibility of rehabilitation with the TAH

Patients initiated physical rehabilitation at a median of 5 days (interquartile range [IQR]: 4 to 7 days) and treadmill exercise at a median of 19 days (IQR: 13 to 35 days) after device implantation (Figure 5A). Patients exercising on the treadmill exhibited an increase in duration of exercise ($p < 0.001$) and METs achieved ($p < 0.001$) (Table 2). The mean

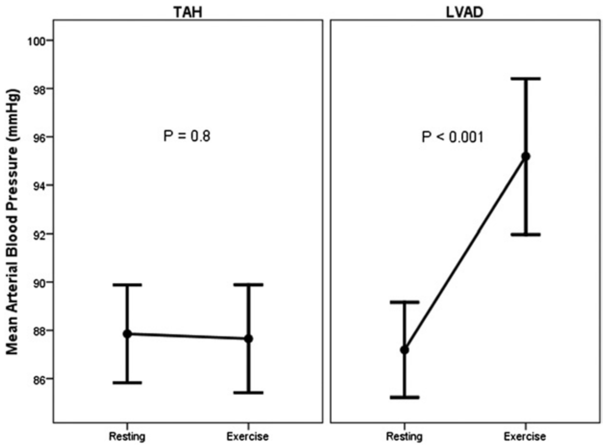

Figure 3 Line-and-whisker plot comparing change in mean arterial blood pressure from resting state to peak exercise in patients on the TAH and LVAD. Filled circles: mean; whiskers: 95% confidence interval.

duration of exercise (Week 1 vs Week 4: 8.35 ± 3.29 vs 18.62 ± 9.07 minutes, $p < 0.001$; Week 1 vs Week 8: 8.70 ± 3.80 vs 25.95 ± 15.06 minutes, $p = 0.006$) increased significantly over the course of rehabilitation. The difference in mean duration of exercise of Week 4 vs Week 8 (21.95 ± 9.27 vs 25.95 ± 15.06 minutes, $p = 0.3$) was not statistically significant. The mean METs achieved (Week 1 vs Week 4: 1.53 ± 0.13 vs 1.85 ± 0.24 METs, $p < 0.001$; Week 4 vs Week 8: 1.88 ± 0.22 vs 2.30 ± 0.52 METs, $p = 0.006$; and Week 1 vs Week 8: 1.53 ± 0.13 vs 2.30 ± 0.52 METs, $p = 0.001$) increased significantly over the course of rehabilitation (Figure 5B).

For the study population, 4 patients were receiving ongoing support with the TAH at the time of analysis and 88% (23 of 26) of the remaining patients underwent transplantation at a median of 65 days (IQR: 40 to 95 days). Patients who participated in PT early had a trend toward shorter waiting periods until heart transplantation (60 days [IQR: 37 to 91 days] vs 89 days [IQR: 59 to 115 days], $p = 0.17$) and significantly higher survival rates to transplantation (100% vs 70%, $p = 0.02$).

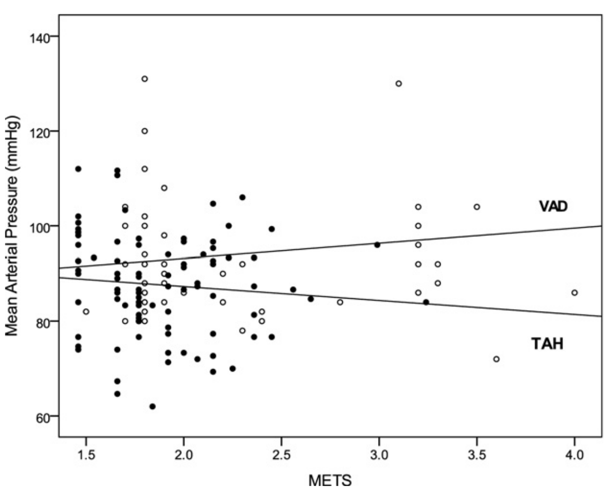

Figure 4 Scatterplots for mean arterial blood pressure vs metabolic equivalents (METS) achieved. Filled black circles: TAH; open circles: LVAD.

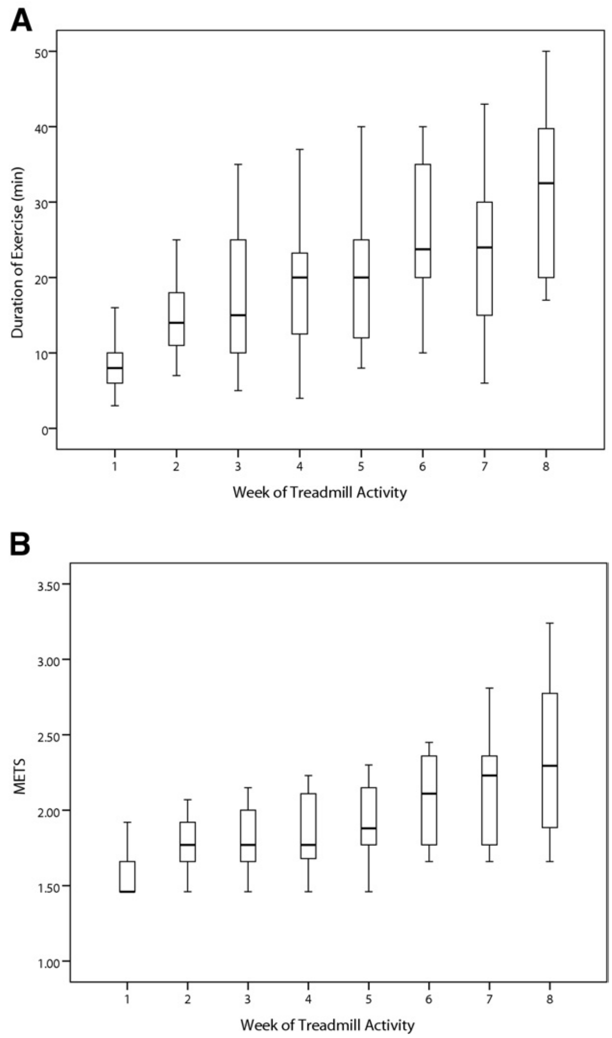

Figure 5 Box-and-whisker plot for (A) metabolic equivalents achieved by week of exercise and (B) duration of exercise by week of exercise. Horizontal lines: median; box: interquartile range; whiskers: range.

Discussion

Compared to patients with LVADs, TAH patients have a blunted BP response to exercise. Furthermore, we showed patients with a TAH can safely participate in a physical rehabilitation program early after device implantation and exhibit improvement in exercise performance over the course of a rehabilitation program. These are the first data to describe the safety, implementation and efficacy of a regimented physical rehabilitation program for patients supported with an artificial heart.

BP response to exercise

Our study shows that, unlike the normal response to exercise, there was no difference in pre-exercise, exercise and post-exercise BPs in patients with a TAH. Conversely, patients with a continuous-flow LVAD had augmentation of their BP during exercise, highlighting the importance of innate chronotropic and inotropic response to the demands

Table 2 Weekly Mean Performance on Treadmill for Patients with the TAH

	Week 1 ($N = 21$)	Week 2 ($N = 17$)	Week 3 ($N = 16$)	Week 4 ($N = 16$)	Week 5 ($N = 10$)	Week 6 ($N = 10$)	Week 7 ($N = 9$)	Week 8 ($N = 8$)
Duration (minutes)	8.24 ± 3.34	15.19 ± 7.17	16.94 ± 9.27	18.84 ± 9.31	21.90 ± 11.09	25.75 ± 10.74	24.10 ± 12.24	31.44 ± 11.89
(METs)	1.56 ± 0.19	1.74 ± 0.19	1.79 ± 0.23	1.85 ± 0.25	1.90 ± 0.27	2.08 ± 0.29	2.18 ± 0.42	2.35 ± 0.56

METs, metabolic equivalents; TAH, total artificial heart.

of exercise. In healthy individuals, the muscle chemoreflex and baroreflex augmentation at the onset of exercise serve to increase heart rate and BP to meet the heightened metabolic demands of the body.[3] Such a physiologic response is impossible once the heart is excised from the body and entirely replaced with a mechanical assist device, raising concern that physical activity may lead to hypotension in patients supported with the TAH.

These data, however, establish the safety of exercise in patients with a TAH. Patients maintained stable hemodynamics during participation in a progressive exercise protocol. The maintenance of systemic BP with activity was possibly related to increased venous return (pre-load) and increased systemic arterial tone. Venous return during exercise is facilitated by skeletal muscle contraction, neurally mediated venocontraction and respiratory pumps.[4,9,10] Both right and left pumps on the TAH were calibrated to fully eject and partially fill when at rest to accommodate increased pre-load and provide increased cardiac output during activity. In addition, concomitant regional vasoconstriction in the splanchnic and renal beds helps maintain and augment systemic BP during exercise.[11]

The hypotensive response to exercise in patients receiving arterial vasodilators suggests an important role for vascular tone for maintaining BP in patients with a TAH. We and others have observed that infusing synthetic brain natriuretic peptide (BNP) provides a renal protective effect after TAH implantation by replacing the abrupt loss of endogenous BNP.[12] In the 6 patients who received this intravenous vasodilator during treadmill exercise, we observed a clinically, but not statistically, significant decrease in systolic BP during exercise. There was, however, a statistically significant interaction observed between nesiritide administration and BP. This observation suggests that arterial tone, due to the absence of a compensatory tachycardia and increase in contractility, is essential for maintaining adequate systemic perfusion, and pharmacologic interruption of the arterial tone may result in adverse decreases in BP during activity.

Although the intensity of exercise was limited to no more than a moderate level, only 1 patient in our entire experience developed symptomatic hypotension with ambulation. These data do not provide information about the BP response at higher levels of exertion, but we advocate that exercise prescriptions be individualized based on observed performance in a supervised environment.

Although the MET levels achieved in this study are not as high as those in previously reported exercise data with ventricular assist devices, the workload measured during the study was during only sub-maximal exercise protocols and does not reflect the peak capacity of the individuals.[13–15] The intensity of activity achieved was comparable to performing activities of daily living or moderate housework.[16]

Patients with a TAH participate in physical rehabilitation early and exhibit steady, gradual improvement in exercise capacity. By replacing the entire heart, the device eliminates potential complications, including right ventricular failure and arrhythmias, which limit cardiac function in late-stage heart failure even with other devices in place, such as biventricular assist devices.[17,18] The only other report of rehabilitation or exercise with a TAH was a single-patient case report, which supports our data.[19] Although other studies have shown increases in exercise capacity for patients with ventricular assist devices, these are the first findings to demonstrate that physical exercise and measurable rehabilitation are feasible with a TAH.[13,14]

Limitations

There are limitations that may influence the findings of this study. Patients only reached moderate levels of exertion, thus we cannot comment on the safety of higher levels of aerobic activity. Often patients were transplanted soon after device implantation and never reached a “plateau” during rehabilitation. We also cannot draw conclusions regarding the safety and effect of isometric activity on TAH function. This was a single-center, retrospective chart review with a relatively small number of patients, which limits the statistical power of the study. However, considering the only other similar report is a single-patient case report, this study advances our understanding of the TAH. In our study we examined the duration of exercise and METs achieved, but did not analyze potential exercise metrics, such as ventilatory efficiency (i.e., the VE/VCO_2 slope) and peak oxygen consumption, which have been recognized as key diagnostic markers in the management of heart failure patients.[20] In addition, further study focusing on the arterial vasoreactivity and endothelial function may shed further light on the role of vascular tone in patients with an artificial heart.

Clinical implications

These data support early initiation of supervised physical rehabilitation for patients after TAH implantation. Prior to exercise, we recommend that the pump parameters be set to ensure that both right and left pumps are partially filling, thus allowing the device to accommodate for increased venous return during exercise. Based on our observations in patients treated with nesiritide, we recommend interruption of intravenous vasodilators for rehabilitation sessions and cautious use of oral vasodilators. These data are insufficient to establish the safety of high levels of exertion.

In conclusion, patients who are supported with a TAH have a blunted BP response to exercise compared to individuals with LVADs. The results of this study are pertinent as patient rehabilitation and mobility will be of increasing concern as TAH patients will be free to return home in the near future. Future studies measuring multiple exercise metrics with more intense exercise in a prospective manner will provide further guidance on rehabilitation for patients with the device.

Disclosure statement

Drs Michael L. Hess and Vigneshwar Kasirajan are consultants for Syncardia Corporation. None of the other authors has any conflicts of interest to disclose.

References

1. Copeland JG, Smith RG, Arabia FA, et al. Cardiac replacement with a total artificial heart as a bridge to transplantation. N Engl J Med 2004;351:859-67.
2. Pickering TG, Harshfield GA, Kleinert HD, et al. Blood pressure during normal daily activities, sleep, and exercise. Comparison of values in normal and hypertensive subjects. JAMA 1982;247:992-6.
3. Rowell LB. Blood pressure regulation during exercise. Ann Med 1991;23:329-33.
4. Anrep GV, von Saalfeld E. The blood flow through the skeletal muscle in relation to its contraction. J Physiol 1935;85:375-99.
5. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. Circulation 2001;104:1694-740.
6. Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Circulation 2007;116:1094-105.
7. Whaley M. ACSM's guidelines for exercise testing and prescription, 7th ed. Philadelphia: Lippincott Williams and Wilkins; 2006.
8. Myers J, Arena R, Franklin B, et al. Recommendations for clinical exercise laboratories: a scientific statement from the American Heart Association. Circulation 2009;119:3144-61.
9. Shoukas AA, Sagawa K. Control of total systemic vascular capacity by the carotid sinus baroreceptor reflex. Circ Res 1973;33:22-33.
10. Shoukas AA, Bohlen HG. Rat venular pressure–diameter relationships are regulated by sympathetic activity. Am J Physiol 1990;259:H674-80.
11. Rowell LB. Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev 1974;54:75-159.
12. Delgado R, Wadia Y, Kar B, et al. Role of B-type natriuretic peptide and effect of nesiritide after total cardiac replacement with the AbioCor total artificial heart. J Heart Lung Transplant 2005;24:1166-70.
13. Simon MA, Kormos RL, Gorcsan J, et al. Differential exercise performance on ventricular assist device support. J Heart Lung Transplant 2005;24:1506-12.
14. de Jonge N, Kirkels H, Lahpor JR, et al. 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;37:1794-9.
15. Haft J, Armstrong W, Dyke DB, et al. Hemodynamic and exercise performance with pulsatile and continuous-flow left ventricular assist devices. Circulation 2007;116:I-8-15.
16. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32(suppl):S498-504.
17. Kormos RL, Teuteberg JJ, Pagani FD, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. J Thorac Cardiovasc Surg 2010;139:1316-24.
18. Andersen M, Videbaek R, Boesgaard S, et al. Incidence of ventricular arrhythmias in patients on long-term support with a continuous-flow assist device (HeartMate II). J Heart Lung Transplant 2009;28:733-5.
19. Nicholson C, Paz JC. Total artificial heart and physical therapy management. Cardiopulm Phys Ther J 2010;21:13-21.
20. Arena R, Myers J, Guazzi M. The clinical and research applications of aerobic capacity and ventilatory efficiency in heart failure: an evidence-based review. Heart Fail Rev 2008;13:245-69.