

Exercise Training and Testing of an Advanced Heart Failure Patient – From LVAD to Transplant

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PATIENT BACKGROUND

Mr. DA, a 55-year-old black man with a history of non-ischemic cardiomyopathy, reported for what he thought was a routine right heart catheterization at Henry Ford Hospital in Detroit Michigan, on May 13, 2015. He had been living with this condition since 1998 and, for the most part, had been able to avoid hospitalization through adherence to his medications. However, more recently, he noticed that his shortness of breath and ability to perform everyday activities was progressively getting worse. This led to starting milrinone a few months ago, which improved his symptoms temporarily; unfortunately, his conditioned worsened to the point where he could walk only 10 feet without stopping to rest. Therefore, he was not surprised when it was recommended that he receive a left ventricular assist device (LVAD).

DISCUSSION

Epidemiology

Heart failure (HF) is a condition where the heart's ability to maintain cardiac output is compromised, leading to an inability to adequately supply blood flow to meet the metabolic demands of the body, especially with physical activity. There are roughly 6.5 million Americans who have heart failure, with an additional 960,000 new cases per year (1). Factors contributing to the large prevalence of HF include: improved survival from myocardial infarction (MI), increased rates of diabetes, and the growing age of the population with incident rates approximately 20 per 1,000 for individuals >65 years of age (2).

Patients with HF are classified using two complementary systems based on symptoms and progression of disease:

The New York Heart Association (NYHA) functional class, and the ACCF/AHA Stages of HF (Figure 1). Patients refractory to standard HF treatments are considered stage D, which is advanced heart failure. While those with stage D HF represent only a small percentage of all HF cases (i.e. ~1%), the mortality rates for these individuals are very high at ~75% at 1 year (3).

Etiology

HF can progress to stage D incipiently over time, but it can also occur acutely as a result of a myocardial infarction or cardiogenic shock (3). While the leading cause of heart failure is ischemic cardiomyopathy, there are multiple etiologies of non-ischemic HF, including: hypertensive dilated cardiomyopathy, valvular heart disease, viral cardiomyopathy, and cancer-related cardiomyopathy (e.g., chemotherapy and mediastinal radiation cardiotoxicity; 2,3). Risk factors for HF include: diabetes, obesity, metabolic syndrome, smoking, and high sodium intake (1). Having one or more of the above risk factors, in absence of symptoms or structural heart disease, places a person at increased risk for HF and is considered ACCF/AHA stage A. Subsequently, based on these criteria, it is estimated that one-third of the US adult population is classified as stage A (1).

Diagnosis and Clinical Manifestations

While often associated with LV dysfunction and cardiomyopathy, HF is not the equivalent of these but rather a syndrome defined largely by clinical diagnosis (2). The key clinical manifestations of HF are fatigue and dyspnea on exertion (see Table 1 for other HF signs and symptoms). These symptoms are secondary to reduced cardiac output

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A Stepped Approach to Guideline-Based HFrEF Care

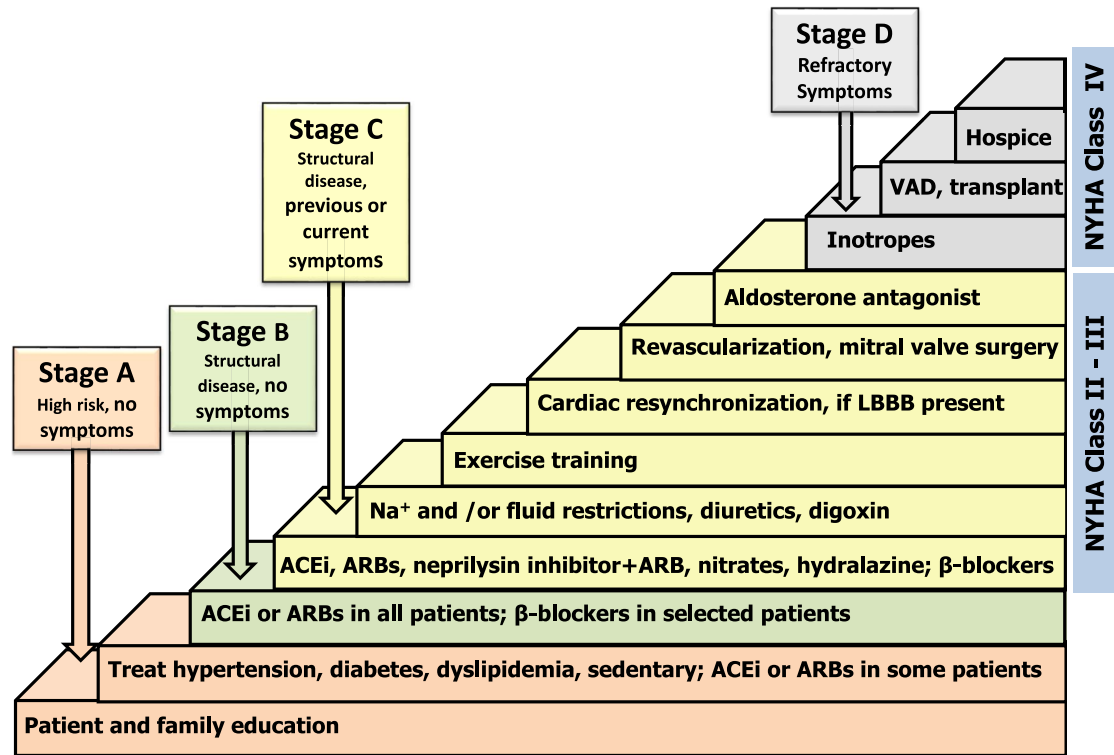


FIGURE 1. ACCF/AHA stages of heart failure. Adapted from Jessup et al., NEJM, 2003. Staging based on ACC/AHA criteria. ACCF = American College of Cardiology Foundation; AHA = American Heart Association; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; β-blocker = beta adrenergic receptor blocker; LBBB = left bundle branch block; VAD = ventricular assist device.

and, often, volume overload. Rapid weight gain (i.e., 3 pounds in a day or 5 pounds a week) and difficulty breathing while lying in the supine position (known as orthopnea) are important signs of possible worsening HF, which can result in rehospitalization.

Since the majority of patients with HF have impaired systolic LV function, a two-dimensional echocardiogram with Doppler is generally used to assess LV function. If LV systolic or diastolic dysfunction is present, patients are classified as either HF with reduced EF (HFrEF) or HF with a preserved EF (HFpEF), respectively (2). An EF <35% is also a criterion for an implantable cardioverter defibrillator since these patients are at high risk for lethal ventricular arrhythmias (2).

Clinical criteria for defining stage D HF is challenging due to the variability of HF progression and typically requires a multitude of clinical indicators (3). These indicators include: worsening of NYHA functional class, escalation of diuretic therapy, recurrent ICD shocks, persistent hyponatremia (sodium <134 mEq • L⁻¹), frequent emergency department visits, progressive renal dysfunction, worsening right-sided heart failure, and severely reduced exercise capacity (3). Cardiopulmonary exercise testing has shown to be a valuable clinical tool in differentiating between individuals who have stable HF versus those who need advanced treatments (4). Those individuals with a peak VO₂ below 10

mL • kg⁻¹ • min⁻¹ and a VE-VCO₂ slope >45 have a particularly poor prognosis (4). Taking into account the above criteria, stage D patients are ultimately defined as being refractory to optimal medical therapies, thereby needing advanced treatments such as mechanical circulatory support (MCS) or transplantation.

TABLE 1. Heart failure signs and symptoms.

Fatigue
Dyspnea
Orthopnea
Peripheral edema
Weight gain
Tachypnea
Paroxysmal nocturnal dyspnea
Cold, pale, and possibly cyanotic extremities
Hepatomegaly
Jugular venous distension
Crackles (rales)
Tubular breath sounds and consolidation
Presence of a third (S3) or fourth (S4) heart sound
Sinus tachycardia

Treatment

Patients with HF exhibit increased sympathetic nervous system (SNS) and renin-angiotensin-aldosterone system (RAAS) activation in response to reduced systemic blood flow. This can result in adverse structural changes to the heart (e.g., cardiac remodeling, myocardial fibrosis, cardiac valve regurgitation) and the surrounding vascular system (e.g., peripheral vasoconstriction, cachexia, pulmonary vascular remodeling). Thus, medical therapy in appropriate patients includes the use of RAAS inhibitors (e.g., ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonist) and beta-blockers. Diuretics are important for improving symptoms associated with fluid overload, and noncompliance with this medication is often cited as a reason for rehospitalization (5). Another class of medications shown to improve symptoms—but not survival—are inotropes (e.g., milrinone). The inotrope dependent trial reported 6-month and 1-year survival at 22% and 11%, respectively, for stage D patients on inotropic support and optimal medical therapies, respectively (6).

The gold standard treatment for patients in end-stage HF is a heart transplantation, with a mean survival rate of ~10 to 13 years and >90% return of functional capacity (7). However, the number of patients needing a transplant far exceeds the number of potential recipients. While there have been over 26,000 heart transplants in the United States between 1987 and 2012, during that same period, more than 40,000 patients have been placed on the transplant waiting list (1). Additionally, it is estimated that 250,000 to 300,000 US citizens may benefit from MCS for management of end stage HF.

Because many individuals on the transplant waiting list do not survive long enough to receive a heart and still others do not qualify to be on the list, MCS is known to improve survival and quality of life in many patients with end-stage HF (8). For individuals who have both right-and left-sided HF, there are some institutions implanting total artificial hearts (TAH); however, the vast majority of patients on MCS have a left ventricular assist device (LVAD). Clinically indicated as a bridge to heart transplant, destination therapy, or (in rare cases and typically outside of the United States) a bridge to recovery, worldwide there were about 2,400 LVADs implanted in 2017. The advancements in LVADs have greatly improved over the past decade, with current 1-year survival rates on LVAD support at around 80% compared to the 52% 1-year survival reported in the original landmark REMATCH trial (8,9). The three current FDA approved devices—HeartMate II (HMII), HeartMate 3 (HM3), and Heartware Ventricular Assist Device System (HVAD)—are all continuous flow devices, unloading the left ventricle at the apex of the heart (inflow cannula) and sending roughly 4 to 6 liters of blood per minute through the ascending aorta (Figure 2; 8).

Common medical concerns with the device and this population include bleeding, percutaneous drive line infection, device malfunction, and stroke (10). Another unique

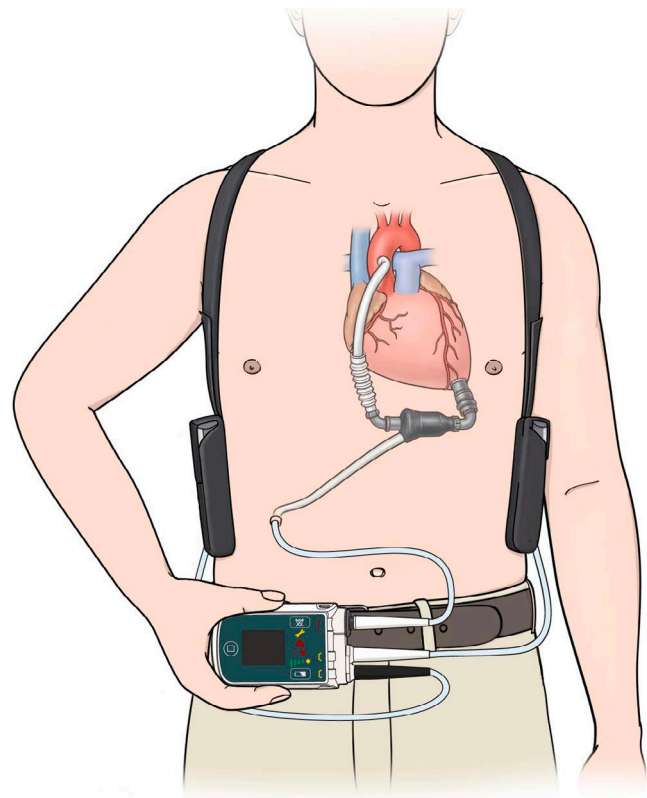


FIGURE 2. Heartmate II Left Ventricular Assist System (LVAS). HeartMate II, and St. Jude Medical are trademarks of St. Jude Medical, LLC or its related companies. Reproduced with permission of St. Jude Medical, 2018. All rights reserved.

challenge is the need for an external power source. This is accomplished through either an AC outlet when the patient is at home or two attached batteries that (depending on the type of LVAD) run for 12 to 16 hours of continuous function.

Exercise Testing

Similar to other heart conditions, a symptom-limited cardiopulmonary (or standard) graded exercise test (GXT) can be used in patients with an LVAD to assess heart rate and hemodynamic responses to exercise, screen for cardiac arrhythmias, and determine an appropriate exercise prescription. Unlike individuals with a heart transplant who have a discordant heart rate response to exercise due to denervated autonomic state, individuals with an LVADs have an intact sympathovagal response to exercise and a strong relationship between VO_2 reserve and heart rate reserve ($r = 0.87$; 11).

What is discordant for the patient with an LVAD is the response of the device itself to exercise. Whereas the first generation LVADs, which were pulsatile devices, increased rate in response to exercise, the current generation of non-pulsatile devices are set at a fixed speed. This means that the operating speed of the rotor (i.e., HMII) or centrifuge (i.e., HVAD or HM3) does not change as an individual goes from sitting to walking. Stimulating cardiac output change in these individuals is a combination of increased preload, decreased afterload, and concomitant native heart

contribution. The latter observation is supported by studies showing the opening of the aortic valve during exercise (12). Interestingly, although the LVAD speed is fixed during exercise, prior studies show that adjustment of the LVAD speed upward can actually improve exercise performance and VO_2 , as was the case with Mr. DA (13). The issue, however, with raising the LVAD speed to a higher setting is that this could cause what is known as “suction events,” where the septal wall is pulled towards the LV, leading to right ventricular heart failure (14).

As with other individuals with advanced HF, the GXT protocol should match the expected functional level; for patients following LVAD surgery, functional level is still limited with achieved peak VO_2 values between 11–14 mL • kg⁻¹ • min⁻¹ (15,16). Therefore, choosing a gradual 1 metabolic equivalent of task (MET) per stage protocol, such as the modified Naughton, is generally recommended (4). This allows an adequate assessment of the physiologic response to exercise as well as an opportunity to measure peak VO_2 . Conversely, an aggressive protocol such as the Bruce has an initial stage (5 METS) that is already above the functional capacity of most patients with an LVAD.

Alternatively, the use of submaximal exercise tests, such as the 6-minute walk (6MW) test has shown to be a good marker to assess functional improvement, as well as a good predictor of survival in this population (17,18). Hasin et al. found that after LVAD surgery, patients had a higher risk of mortality if they were unable to achieve >300 meters during the 6MW (18).

Exercise Training

Training studies have shown improvements in functional capacity and quality of life in patients <1 year following LVAD surgery (16,19–21). While more data is needed to fully support this, in limited studies conducted for this patient population, exercise training appears to be safe with only rare reported untoward events among >1600 patient exercise hours (22).

As mentioned, the functional capacity of this population is limited. With an average peak MET value at or below 4 METS, the starting training levels for these individuals are generally at or below 2.5 METS (i.e., ~60% of peak METS). Due to the linear relationship between heart rate and VO_2 the use of 40%–80% of target heart rate reserve can be used to guide exercise intensity if a recent GXT is available. However, if a recent GXT is not available, the use of the rating of perceived exertion of 11 to 14 on the Borg scale is appropriate. Parenthetically, patients on LVAD support who are paced have a weaker heart rate to VO_2 association; therefore, use of the Borg for this patient population should be considered first (11).

Another consideration for exercise training in this population is the need for a handheld Doppler and proper training in obtaining a blood pressure via Doppler. Since these patients are often nonpulsatile, using a stethoscope to measure pressure is not reliable and, in fact, the sound heard when taking a Doppler blood pressure is a close

approximation to that of the mean arterial pressure (MAP). Blood pressure control is very important in this population, as the margin between under perfusion of vital organs and risk of stroke is relatively narrow. The mean arterial pressure target for patients with an LVAD is between 70 to 80 mm Hg. Exercise should not be initiated in patients with a pressure <64 mm Hg, and one should first consult with the LVAD team if a patient has a resting MAP >90 mm Hg. While exercise pressures can be obtained and should increase with exercise, care should be taken. This is particularly true during treadmill walking, since the extra weight of the equipment can potentially place the patient at greater risk for falls.

Importantly, the patient's driveline and power cords should be kept close to the patient and away from moving parts of any exercise equipment. Pulling of the driveline increases the risk of infection or a potential line fracture. Resistance training can be implemented, consistent with current postthoracotomy recommendations (i.e., ~12 weeks post). Again, the patient should avoid exercises that could result in a driveline or battery line pull, as well as exercises that involve excessive trunk flexion (i.e., sit-ups).

An observational study of Medicare beneficiaries found that patients with an LVAD who participate in cardiac rehabilitation had a reduced risk of hospitalization and 1-year mortality (23). Although more studies are needed to support the clinical outcomes of cardiac rehabilitation in this population, these individuals have severely reduced EFs (i.e., < 35%), already qualify through Medicare to participate in CR and should be encouraged to do so.

PATIENT CLINICAL COURSE

Mr. DA received his LVAD (HeartWare) on May 18, 2015. Shortly after, he immediately felt better and was scheduled for hospital discharge earlier than expected. Unfortunately, he suffered a setback when it was found that his hemoglobin was low, secondary to a gastrointestinal (GI) bleed. After three separate procedures, his hemoglobin stabilized, and he was discharged 17 days after he was admitted.

A month after recovering at home and receiving home physical therapy, Mr. DA enrolled into cardiac rehabilitation (CR) in Detroit. He presented to CR tachycardic (pulse = 114 b • min⁻¹) and was able to perform only 2 METS on the treadmill (i.e., 1.3 mph), complaining of dyspnea on exertion and extreme fatigue. His LVAD controller estimated his device flow rate to be ~5.0 L • min⁻¹. After 2 weeks in CR, his symptoms persisted, and his exercise capacity remained attenuated. On July 13, 2015, Mr. DA saw his cardiologist, who increased the speed on his LVAD from 2660 to 2720 rpm. Immediately, Mr. DA's symptoms improved as well as his exercise capacity. His workload on the TM increased by nearly 1 MET within the first week, and his estimated LVAD flow was up to ~6 • min⁻¹.

Over the next 3 months, Mr. DA continued to participate in CR and progressed appropriately, increasing his estimated training METS on the TM from 2.0 on his first day to 6.6 at graduation. To help guide his exercise, he completed a CPX on September 14, 2015. Interestingly, his peak VO_2 , which

was 17.5 mL • kg⁻¹ • min⁻¹, was similar to the last recorded peak VO₂ measured 5 years prior to his LVAD surgery. Based on his CPX result, his exercise intensity while on the TM and upright cycle was set at 135 to 145 b • min⁻¹ (i.e., 60%–80% HRR). In addition to performing 40 to 50 minutes of aerobic exercise in CR, he also began resistance training using the following machines: seated chest press, hip abductor, hip adductor, bicep curl, leg curl, leg extension, seated back row, and supine leg press. He would perform 1 to 2 sets of 15 to 20 reps at a moderate intensity.

After he completed CR, he transitioned to the Henry Ford Hospital CR maintenance program, where he resumed his exercise routine. There, he continued to exercise without issues through December 2015. In 2016, Mr. DA had three separate hospital admissions for ongoing GI bleeds. However, despite persistently low hemoglobin levels, he was able to continue to exercise, until finally in January 2017, he received a call that a donor heart was available.

One month following his discharge from Henry Ford Hospital, Mr. DA again enrolled in cardiac rehabilitation.

His initial workload of just under 4 METS was lower than what he completed (6.6 METS) during his first course of CR. However, it did not take him long to return to his previous exercise capacity, and he eventually completed CR, for a second time, without any complications.

CONCLUSION

Advances in LVAD technology have extended longevity and quality of life in many patients with advanced HF. However, due to a combination of prolonged bedrest and extended periods of poor perfusion (prior to LVAD), patients with an LVAD typically have limited functional capacity. Cardiac rehabilitation has been shown to help restore function and improve patient reported outcomes in this population. Additionally, because these patients can have undetected arrhythmias or other complications, the surveillance provided by cardiac rehabilitation makes it an important supportive clinical service in this growing and unique patient population.

REFERENCES

1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C, Isasi CR, Jimenez MC, Jordan LC, Judd SE, Lackland D, Lichtman JH, Lisabeth L, Liu S, Longenecker CT, Mackey RH, Matsushita K, Mozaffarian D, Mussolino ME, Nasir K, Neumar RW, Palaniappan L, Pandey DK, Thiagarajan RR, Reeves MJ, Ritchey M, Rodriguez CJ, Roth GA, Rosamond WD, Sasson C, Towfighi A, Tsao CW, Turner MB, Virani SS, Voeks JH, Willey JZ, Wilkins JT, Wu JH, Alger HM, Wong SS, Muntner P. Heart disease and stroke statistics – 2017 update: a report from the American Heart Association. *Circulation*. 2017;135:e146–e603.
2. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL. 2013 ACCF/AHA guideline for the management of heart failure: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:1810–52.
3. Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M, Dickinson MG, Levy P, Stough WG, Sweitzer NK, Teerlink JR, Whellan DJ, Albert NM, Krishnamani R, Rich MW, Walsh MN, Bonnell MR, Carson PE, Chan MC, Dries DL, Hernandez AF, Hershberger RE, Katz SD, Moore S, Rodgers JE, Rogers JG, Vest AR, Givertz MM; Heart Failure Society of America Guidelines Committee. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. *J Card Fail*. 2015;21:519–34.
4. Guazzi M, Arena R, Halle M, Piepoli MF, Myers J, Lavie CJ. 2016 focused update: clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation*. 2016;133:e694–711.
5. Sueta CA, Rodgers JE, Chang PP, Zhou L, Thudium EM, Kucharska-Newton AM, Stearns SC. Medication adherence based on Part D claims for patients with heart failure after hospitalization (from the Atherosclerosis Risk in Communities Study). *Am J Cardiol*. 2015;116:413–9.
6. Rogers JG, Butler J, Lansman SL, Gass A, Portner PM, Pasque MK, Pierson RN III. Chronic mechanical circulatory support for inotrope-dependent heart failure patients who are not transplant candidates: results of the INTrEPID Trial. *J Am Coll Cardiol*. 2007;50:741–7.
7. Yusef RD, Christie JD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, Dobbels F, Kirk R, Lund LH, Rahmel AO, Stehlik J. The Registry of the International Society for Heart and Lung Transplantation: thirtieth adult lung and heart-lung transplant report – 2013; focus theme: age. *J Heart Lung Transplant*. 2013;32:965–78.
8. DeVore AD, Patel PA, Patel CB. Medical management of patients with a left ventricular assist device for the non-left ventricular assist device specialist. *JACC Heart Fail*. 2017;5:621–31.
9. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL; Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med*. 2001;345:1435–43.
10. Drazner MH. A new left ventricular assist device – better, but still not ideal. *N Engl J Med*. 2018;378:1442–3.
11. Kerrigan DJ, Williams CT, Brawner CA, Ehrman JK, Saval MA, Peterson EL, Lanfear DE, Tita C, Velez M, Selektor Y, Keteyian SJ. Heart rate and VO₂ concordance in continuous-flow left ventricular assist devices. *Med Sci Sports Exerc*. 2016;48:363–7.
12. Brassard P, Jensen AS, Nordsborg N, Gustafsson F, Moller JE, Hassager C, Boesgaard S, Hansen PB, Olsen PS, Sander K, Secher NH, Madsen PL. Central and peripheral blood flow during exercise with a continuous-flow left ventricular assist

- device: constant versus increasing pump speed: a pilot study. *Circ Heart Fail*. 2011;4:554–60.
13. 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;96:1390–5.
 14. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatroles AJ, Delgado RM, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009;361:2241–51.
 15. Dunlay SM, Allison TG, Pereira NL. Changes in cardiopulmonary exercise testing parameters following continuous flow left ventricular assist device implantation and heart transplantation. *J Card Fail*. 2014;20:548–54.
 16. Kerrigan DJ, Williams CT, Ehrman JK, Saval MA, Bronsteen K, Schairer JR, Swaffer M, Brawner CA, Lanfear DE, Selektor Y, Velez M, Tita C, Keteyian SJ. Cardiac rehabilitation improves functional capacity and patient-reported health status in patients with continuous-flow left ventricular assist devices: the Rehab-VAD randomized controlled trial. *JACC Heart Fail*. 2014;2:653–9.
 17. Rogers JG, Aaronson KD, Boyle AJ, Russell SD, Milano CA, Pagani FD, Edwards BS, Park S, John R, Conte JV, Farrar DJ, Slaughter MS; HeartMate II Investigators. Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. *J Am Coll Cardiol*. 2010;55:1826–34.
 18. Hasin T, Topilsky Y, Kremers WK, Boilson BA, Schirger JA, Edwards BS, Clavell AL, Rodeheffer RJ, Frantz RP, Joyce L, Daly R, Stulak JM, Kushwaha SS, Park SJ, Pereira NL. Usefulness of the six-minute walk test after continuous axial flow left ventricular device implantation to predict survival. *Am J Cardiol*. 2012;110:1322–8.
 19. Hayes K, Leet AS, Bradley SJ, Holland AE. Effects of exercise training on exercise capacity and quality of life in patients with a left ventricular assist device: a preliminary randomized controlled trial. *J Heart Lung Transplant*. 2012;31:729–34.
 20. Laoutaris ID, Vasiliadis IK, Dritsas A, Mavrogeni S, Kallistratos MS, Manginas A, Chaidaroglou A, Degiannis D, Panagiotakos DB, Cokkinos DV. High plasma adiponectin is related to low functional capacity in patients with chronic heart failure. *Int J Cardiol*. 2010;144:230–1.
 21. Grosman-Rimon L, Billia F, Kobulnik J, Bar-Ziv SP, Cherney DZ, Rao V. The physiological rationale for incorporating pulsatility in continuous-flow left ventricular assist devices. *Cardiol Rev*. 2018.
 22. Marko C, Danzinger G, Kaferback M, Lackner T, Muller R, Zimpfer D, Schima H, Moscato F. Safety and efficacy of cardiac rehabilitation for patients with continuous flow left ventricular assist devices. *Eur J Prev Cardiol*. 2015;22:1378–84.
 23. Bachmann JM, Duncan MS, Shah AS, Greevy RA Jr, Lindenfeld J, Keteyian SJ, Thomas RJ, Whooley MA, Wang TJ, Freiberg MS. Association of cardiac rehabilitation with decreased hospitalizations and mortality after ventricular assist device implantation. *JACC Heart Fail*. 2018;6:130–9.