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# Left ventricular assist device recovery: does duration of mechanical support matter?

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**Abstract**
Heart failure is a widespread condition in the United States that is predicted to significantly increase in prevalence in the next decade. Many heart failure patients are given a left ventricular assist device (LVAD) while they wait for a heart transplant, while those that are not able to undergo a heart transplant may be given an LVAD permanently. However, past studies have observed a small subset of heart failure patients that recovered cardiac function of their native heart after being placed on an LVAD. As a result, some patients have been able to have their LVAD explanted and no longer needed a heart transplant. In this review, we analyzed the data of 15 studies that observed recovery of cardiac function in LVAD patients in order to investigate the effects that duration of LVAD support has on patient outcomes. From our review, we identified that there may be negative consequences of prolonged duration of mechanical support such as myocardial atrophy and abnormal calcium cycling as well as circumstances that may allow for a longer duration of LVAD support such as in patients using a continuous-flow LVAD, non-ischemic cardiomyopathy patients, and the specific pharmacological therapy.

**Keywords** Heart failure · LVAD · Reverse remodeling · Cardiac recovery

## Introduction

Heart failure is a prevalent condition with approximately 6.5 million Americans over the age of 20 with this particular diagnosis [1]. The number of Americans with heart failure is predicted to increase to over 8 million by 2030 [2]. Currently, the best treatment for end-stage heart failure is a heart transplant. However, there is a large shortage of available donor hearts for patients in need of a heart transplant [3].

For many patients that are waiting for a heart transplant or are unable to receive a transplant, a left ventricular assist device (LVAD) may be the best treatment option. The main goal of an LVAD is to improve cardiac output and decrease intracardiac pressure by mechanical unloading of the left ventricle [4].

An LVAD can be used as a bridge to transplant (BTT) for heart failure patients waiting for a heart transplant. Heart failure patients that are ineligible for a heart transplant may be implanted with an LVAD as permanent destination therapy (DT) [5]. An observed phenomenon is the occurrence of myocardial recovery in patients that are supported with an LVAD, also known as bridge to recovery (BTR) [6].

The duration of mechanical support for patients that experienced myocardial recovery has varied widely in previous studies. Two important factors must be considered when determining the optimal duration of mechanical support—the amount of time necessary for maximal improvement and the negative consequences that can arise with prolonged mechanical support.

This review will examine how the duration of mechanical support plays a role in the process of cardiac reverse remodeling. More specifically, factors that may justify longer durations of mechanical support without compromising long-term outcomes will be discussed.

## Methods

PubMed, Google Scholar, and Web of Science databases were searched from origin of database until August 2017, with the exception of one recent study from April 2018. The data was gathered by one reviewer and the validity of the data was determined by two reviewers. Over 500 articles related to LVADs and Cardiac Recovery were screened for relevance. Inclusion criteria consisted of studies that had a sample size greater than 5 patients, evidence of cardiac recovery in LVAD patients and/or observation

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of patients with LVAD explantation, and studies that monitored variables related to cardiac recovery. Exclusion criteria consisted of case reports, studies with a sample size less than or equal to five patient, and studies that did not monitor any variables related to cardiac recovery. After screening all related articles, 15 full-text articles were considered for inclusion in this review.

## Results

### Maximal cardiac recovery

Cardiac recovery can be assessed by the systolic and diastolic functioning of the heart [7]. LVAD patients may experience reverse remodeling of the heart that can lead to cardiac recovery. Some of the common criteria used between studies to assess cardiac recovery include the left ventricular ejection fraction (LVEF), left ventricular end diastolic diameter (LVEDD), left ventricular mass, cardiomyocyte size, and myocardial contractility. Multiple studies have concluded that maximal cardiac recovery as a result of LVAD support tends to occur early on. In a prospective study with 80 patients, the greatest improvement in cardiac function after LVAD implantations was observed within the first 6 months. The improvement in cardiac function was seen by improvement of LVEF, decrease in left ventricular end-diastolic and end-systolic volumes, and decrease in left ventricular mass [7].

In another prospective study, 36 LVAD patients showed a significant improvement in LVEF and a significant decrease in LVEDD compared to pre-implantation measurements within 30 days after LVAD implantation. However, no further cardiac function improvement was observed after the initial 30 days [8].

In a retrospective study of 22 LVAD patients, cardiac recovery that eventually led to LVAD explantation occurred in 50% of patients within 50 days after LVAD implantation and 80% of patients within 90 days of LVAD implantation [9].

These studies point towards maximal cardiac recovery occurring within the first 6 months, if not earlier. Furthermore, it has been shown that shorter durations of mechanical support until patients experienced maximal cardiac recovery have led to lower chances of heart failure recurrence [6, 10]. Given the variability in duration of mechanical support observed before maximal cardiac recovery is attained, it is important to monitor cardiac improvement closely. It has been recommended to wait until there is no further cardiac improvement, rather than to adhere strictly to a set amount of time on mechanical support [10].

### Negative consequences of prolonged mechanical support

Myocardial recovery in LVAD patients may be limited by time. Some studies have shown that prolonged mechanical support may lead to a regression of cardiac function.

In a study of 19 pulsatile-flow LVAD patients, the optimal improvement in LVEF and LVEDD values occurred around 3 months after device implantation. However, a regression in LVEF and LVEDD values was observed by 6 months after implantation [6]. A multicenter study observed reverse remodeling in 67 patients utilizing a pulsatile-flow LVAD. Cardiac function improvement was evident in the early stages of mechanical support, while a deterioration in function was observed with prolonged mechanical support. Peak improvement of cardiac function was observed around 30 days. However, by 120 days on mechanical support, cardiac function had declined to the same functioning level as before the implantation of the LVAD [7].

In another study, 47 chronic cardiomyopathy patients that were explanted from pulsatile and continuous flow devices were evaluated. Of the 47 explanted patients, 33 patients met criteria to be evaluated for long-term cardiac stability and heart failure recurrence. From these 33 patients, it was shown that patients without heart failure recurrence within 5 years of device explantation had an average duration of mechanical support of 3.5 months while those with heart failure recurrence within 5 years of device explantation had an average duration of mechanical support of 6.7 months which was significantly higher. Furthermore, patients that required > 6 months of mechanical support had a positive predictive value of 72.7% for HF recurrence within 5 years after explantation [11].

Experiments have shown that myocardial atrophy may be the reason that prolonged mechanical support leads to a regression of cardiac function [12, 13]. One study showed that the diameter of myocytes and the left ventricle weight decreased to normal values at 2 weeks after implantation of mechanical support. However, after 8 weeks of assistance in unloading, the values for these categories decreased to 67% of normal values which suggests that cardiac atrophy may occur with prolonged mechanical support [12]. Likewise, papillary muscle function of the heart also improved to a maximal function at 4 weeks, with decline occurring by 8 weeks on mechanical support [12].

Another reason for the regression of cardiac function observed during prolonged mechanical support is abnormal calcium cycling [14, 15]. With the use of mechanical support, the calcium handling of the sarcoplasmic reticulum improved within the first 150 days of LVAD support. However, mechanical support greater than 150 days caused a return to calcium cycling dysfunction, leading to deterioration of myocardial contractility and relaxation [14].

These studies suggest that the duration of mechanical support may cause the heart to become even more dependent on an LVAD than prior to implantation, potentially leading to heart failure recurrence after LVAD explantation. There are many predictors of heart failure recurrence in addition to duration of mechanical support, such as duration of heart failure

**Table 1** Duration of mechanical support and long-term outcomes for continuous-flow device patients

| | Average duration of mechanical support | Long-term outcomes |
|---|---|---|
| Birks et al. (2011) [22] | 286 ± 97 days | Survival rate (HF-Free): 3 years = 83.3% |
| Birks et al. (2018) [23] | 351 ± 165 days | Survival rate: 78% at 609 ± 328 days |
| Frazier et al. (2015) [24] | 533 ± 424 days | Death = 7.4% |
| Goldstein et al. (2012) [3] | 324 days | Survival rate: 1 year = 95% and 3.5 years = 85% |
| Tchantchaleishvili et al. (2016) [25] | 870 days | HF-free at 276 days (avg.) = 75% |
| Wever-Pinzon et al. (2016) [26, 27] | 323.3 days | HF-free = 85.7% |

symptoms prior to LVAD implantation, LVEF instability, pre-explant values of LVEF and LVEDD, and age of patient [16–19]. As a result, duration of mechanical support may play a role in the prediction of heart failure recurrence but may not be the direct or only cause of heart failure recurrence.

Heart failure recurrence more commonly occurred in explanted patients that had missed the optimal recovery period as a result of waiting for an even greater improvement of cardiac function that never came [6]. As a result, there has to be a balance between waiting for myocardial recovery to occur and the declining function of innate cardiac functions due to extended mechanical support [14].

## Factors that may justify longer duration of mechanical support

Although prolonged mechanical support may lead to negative consequences in LVAD patients, there may also be circumstances that allow for extended durations of mechanical support without long-term sequelae. From our review, we delineated a few variables that may be important in determining the use of an LVAD for longer periods of time, such as the type of LVAD used, the type of cardiomyopathy, and the pharmacological regimen.

## Type of left ventricular assist device flow: pulsatile flow vs. continuous flow

Currently, the most commonly used ventricular assist device is the continuous-flow LVAD due to its more compact size and greater durability compared to the pulsatile-flow LVAD. As a result, this has led to the decline of pulsatile-flow LVADs [20]. For example, the HeartMate 1, a pulsatile-flow LVAD, is no longer commercially available.

In a prospective study of 80 patients with continuous-flow LVADs, a significant improvement of cardiac function was seen within 30 days of mechanical support and the greatest improvement was seen within 6 months [7]. However, unlike pulsatile-flow LVADs, the cardiac function did not significantly decline after maximal improvement of cardiac function. Though a decrease in left ventricular volume and mass was seen within 30 days, the values stayed within normal range 1 year after LVAD implantation [7]. This may be suggestive of a difference in long-term outcomes of prolonged mechanical support between pulsatile-flow and continuous-flow LVADs.

In another study of continuous-flow devices, it was noted that cardiomyocytes decreased in size as a result of mechanical support. However, the decrease in size was still greater than the size of cardiomyocytes of non-failing hearts, even after 1 year of mechanical support [21]. This finding is contrary to previous studies

**Table 2** Duration of mechanical support and long-term outcomes for pulsatile- or predominantly pulsatile-flow device patients

| | Average duration of mechanical support | Long-term outcomes |
|---|---|---|
| Birks et al. (2006) [28] | 320 ± 186 days | Survival rate: 1 year = 90.9%, 4 years = 81.8% |
| Boehmer et al. (2012) [16] | 106 + −44 days | Transplant-free: 1 year = 78%, 2 years = 68%, 3 years = 68% |
| Dandel et al. (2005) [18] | 4.6 ± 4.4 months | Survival rate: 5 years = 78.3%, HF-free at 3 years = 69.4%, and 5 years = 58.2%, HF-recurrence at 3 years = 31.3% |
| Dandel et al. (2008) [19] (88.6% of devices were pulsatile) | 4.3 months | Survival rate: 5 years = 76.2% and 10 years = 70.7%, HF-free at 5 years = 61.3%, HF recurrence = 37.1% |
| Dandel et al. (2012) [10] (64% of devices were pulsatile) | 3.5 years | HF-free at 5 years = 61.1% |
| Farrar et al. (2002) [9] | 57 days (80% of patients supported for less than 90 days) | Survival rate: 1 year = 86% and 5 years = 77%, heart transplant required = 14%/death = 9% |
| Hetzer et al. (1999) [6] | 187 days | HF recurrence: 26%, death = 11% |

**Table 3** Duration of mechanical support and long-term outcomes for non-ischemic cardiomyopathy patients

| | Average duration of mechanical support | Long-term outcomes |
|---|---|---|
| Birks et al. (2006) [28] | 320 ± 186 days | Survival rate: 1 year = 90.9%/4 years = 81.8% |
| Birks et al. (2011) [22] | 286 ± 97 days | Survival rate (without HF recurrence): 83.3% at 1 and 3 years |
| Birks et al. (2018) [23] | 351 ± 165 days | Survival rate: 78% at 609 ± 328 days |
| Dandel et al. (2005) [18] | 4.6 ± 4.4 months | Survival rate: 5 years = 78.3%/HF-free at 3 years = 69.4% and 5 years = 58.2%/HF-recurrence at 3 years = 31.3% |
| Dandel et al. (2008) [19] | 4.3 months | Survival rate: 5 years = 76.2% and 10 years = 70.7%/HF-free at 5 years = 61.3%/HF recurrence = 37.1 |
| Dandel et al. (2012) [10] | 3.5 years | HF-free at 5 years = 61.1% |
| Frazier et al. (2015) [24] | 533 ± 424 days | Death = 7.4% |
| Goldstein et al. (2012) [3] | 324 days | Survival rate: 1 year = 95% and 3.5 years = 85% |
| Hetzer et al. (1999) [6] | 187 days | HF recurrence: 26%/death = 11% |
| Wever-Pinzon et al. (2016) [26, 27] | 323.3 days | HF-free = 85.7% |

that observed myocardial atrophy from extended length of mechanical support that fell below the normal cardiomyocyte size.

In our review, the duration of mechanical support tended to be greater in the studies that used continuous-flow devices compared to pulsatile-flow devices (Tables 1 and 2). Although patients on continuous-flow devices had extended mechanical support, the heart failure recurrence rate and survival rate were still comparable to, if not better than, patients that had pulsatile-flow devices (Tables 1 and 2). Of note, differences in weaning protocols between pulsatile and continuous-flow devices may play a role in the differences in duration of mechanical support. More demanding updated criteria with the introduction of continuous-flow devices (i.e., LVEDD < 55 mm, off-pump LVEF 45%) may increase duration of mechanical support until criteria are met. Furthermore, the difference in criteria between the types of flow device may also affect the heart failure recurrence rate and survival rate [11].

The absence of significant regression in cardiac function due to prolonged mechanical support on continuous-flow devices may allow for more time to wait for cardiac recovery compared to pulsatile-flow devices. Furthermore, the rate of heart failure recurrence has been observed to be lower in continuous-flow devices compared to pulsatile-flow devices [29]. If the absence of significant myocardial atrophy plays a role in the lower rate of heart failure recurrence in continuous-flow LVADs, this may justify longer durations of mechanical support in continuous-flow LVADs.

## Type of cardiomyopathy

The duration of mechanical support can also differ depending on the type of cardiomyopathy. Unfortunately, we were not able to find studies that met our inclusion criteria which solely observed ischemic cardiomyopathy patients. As a result, we compared the studies of non-ischemic cardiomyopathy patients against studies that had a combination of non-ischemic and ischemic cardiomyopathy patients.

Previous studies have shown that non-ischemic cardiomyopathy patients have the highest success rate of reverse remodeling that resulted in being bridged to recovery [3]. From our review, most studies of only non-ischemic cardiomyopathy patients recorded longer durations of mechanical support and better long-term outcomes compared to studies of non-ischemic/ischemic cardiomyopathy (Tables 3 and 4). The ability for non-ischemic cardiomyopathy patients to be placed on an LVAD for an extended amount of time without compromising survival may justify long-term mechanical support for these specific patients.

On the other hand, ischemic cardiomyopathy patients displayed a lower rate of cardiac recovery with the use of an LVAD, which may be due to the irreversible scarring that occurs as a result of myocardial infarction [26]. In a prospective study performed with 154 subjects, it was observed that there was a significant increase in LVEF with 1 month of mechanical support for non-ischemic cardiomyopathy patients. However, for ischemic cardiomyopathy subjects, it took approximately 6 months

**Table 4** Duration of mechanical support and long-term outcomes for ischemic/non-ischemic cardiomyopathy patients

| | Type of cardiomyopathy | Average duration of mechanical support | Long-term outcomes |
|---|---|---|---|
| Tchantchaleishvili et al. (2016) [25] | 37.5% (ischemic CM)/50% (NICM)/12.5% (Mixed) | 870 days | HF-free at 276 days (avg.) = 75% |
| Maybaum et al. (2007) [30] | 45% (ischemic CM)/55% (NICM) | 134 ± 109 days | HF-free at 1 year = 67% |

**Table 5** Clinical characteristics of cardiac recovery in LVAD patients

| | #LVAD explants/ Total LVAD patients | Mean age of patient (years) | Sex | LVAD type | Heart failure type |
|---|---|---|---|---|---|
| Birks et al. (2006) [28] | 11/15 | N/A | N/A | N/A | NICM |
| Birks et al. (2011) [22] | 12/20 | 35.2 | 80%(M)/ 20% (F) | Continuous | NICM |
| Birks et al. (2018) [23] | 18/36 | 35.1 | 67.5% (M)/ 32.5%(F) | Continuous | NICM |
| Boehmer et al. (2012) [16] | 8/14 | 30 | 57% (M)/ 43% (F) | 71% pulsatile/29% continuous | Recent onset CM (myocarditis/IDCM) |
| Dandel et al. (2005) [18] | 32 Explanted | 47.6 (HF recurrence) 36.8 (no HF recurrence) | 94%(M)/ 6% (F) | N/A | IDCM |
| Dandel et al. (2008) [19] | 35/81 | 40.8 | 94% (M)/ 6% (F) | 88% pulsatile/12% continuous | IDCM |
| Dandel et al. (2012) [10] | 53/96 | 42.5 | 86.8% (M)/ 13.2% (F) | 60% pulsatile/34% continuous/6% biventricular | NICM |
| Farrar et al. (2002) [9] | 22 Explanted | 32 | 45% (M)/ 55% (F) | N/A | 55% (Myocarditis)/32% (NICM)/13% (myocarditis & NICM) |
| Frazier et al. (2015) [24] | 27/30 | 39 | 59% (M)/ 41% (F) | Continuous | 93% (NICM)/7% (ischemic CM) |
| Goldstein et al. (2012) [3] | 20/1108 | 33 | 45% (M)/ 55% (F) | Continuous | 90% (NICM) |
| Hetzer et al. (1999) [6] | 19 Explanted | 45.6 | 95% (M)/ 5% (F) | Pulsatile | IDCM |
| Krabatsch et al. (2011) [34] | 34/387 | 37.9 | 85% (M)/ 15% (F) | 37% pulsatile/63% continuous | IDCM |
| Maybaum et al. (2007) [30] | 6/67 | N/A | N/A | N/A | 55% (NICM)/45% (ischemic CM) |
| Tchantchaleishvilli et al. (2016) [25] | 8/223 | 43 | 13%(M)/ 87% (F) | Continuous | 37.5% (ischemic CM)/50% (NICM)/12.5% (mixed) |
| Wever-Pinzon et al. (2016) [26, 27] | 192/15,631 | 45 | 59.4% (M)/ 41.6% (F) | 15.1% pulsatile/84.9% continuous | 84.4% (NICM)/14.1% (ischemic CM) |

| | Mean duration of HF symptoms | Mean LVEF (pre-implant) | Mean mechanical support duration | Max. LVEF (post-implant) | Long-term outcome |
|---|---|---|---|---|---|
| Birks et al. (2006) [28] | N/A | 12% | 320 ± 186 days | 64% | Survival rate: 1 year = 90.9%/4 years = 81.8% |
| Birks et al. (2011) [22] | 3.2 years ± 3.5 years | 14.6% | 286 ± 97 days | 70% | Survival rate (without HF recurrence): 83.3% at 1 and 3 years |
| Birks et al. (2018) [23] | N/A | 14.9± 5% | 351 ± 165 days | 55 ± 5% | Survival rate = 78% |
| Boehmer et al. (2012) [16] | 1.2 ± 1.2 months | 20% | 106 ± 44 days | 49% | Transplant-free:1 year = 78%, 2 years = 68%, 3 years = 68% |
| Dandel et al. (2005) [18] | 4.3 ± 3.7 years | 15% | 4.6 ± 4.4 months | 41.4% (HF)/ 49.4% (no HF) | Survival rate: 5 years = 78.3%/ HF-free at 3 years = 69.4% and 5 years = 58.2%/HF recurrence at 3 years = 31.3% |
| Dandel et al. (2008) [19] | 4 years | 15% | 4.3 months | 47% | Survival rate:5 years = 76.2% and 10 years = 70.7%/HF-free at 5 years = 61.3%/HF recurrence = 37.1 |
| Dandel et al. (2012) [10] | 4 years | N/A | 3.5 years | 47.5% | HF-free at 5 years = 61.1% |
| Farrar et al. (2002) [9] | N/A | N/A | 57 days (80% of patients supported for less than 90 days) | N/A | Survival rate: 1 year = 86% and 5 years = 77%/Heart transplant required = 14%/Death = 9% |
| Frazier et al. (2015) [24] | N/A | 20.3% | 533 ± 424 days | 46.9% | Death = 7.4% |

**Table 5** (continued)

| | Mean duration of HF symptoms | Mean LVEF (pre-implant) | Mean mechanical support duration | Max. LVEF (post-implant) | Long-term outcome |
|---|---|---|---|---|---|
| Goldstein et al. (2012) [3] | < 1 year for 61% of patients | 19% | 324 days | N/A | Survival rate: 1 year = 95% and 3.5 years = 85% |
| Hetzer et al. (1999) [6] | N/A | 15.8% | 187 days | 47.4% | HF recurrence: 26%/Death = 11% |
| Krabatsch et al. (2011) [34] | 2.34± 0.58 years | N/A | 0.3 ± 0.23 years | N/A | N/A |
| Maybaum et al. (2007) [30] | > 6 months for 70% of patients | 17% | 134 ± 109 days | LVEF > 40% (34%) | HF-free at 1 year = 67% |
| Tchantchaleishvilli et al. (2016) [25] | N/A | 17% | 870 days | 56% | HF-free at 276 days (avg.) = 75% |
| Wever-Pinzon et al. (2016) [26, 27] | > 2 years for 31.2% of patients | 10% | 323.3 days | LVEF > 40% (12.6%) | HF-free = 85.7% |

until there was significant improvement in LVEF [26]. The increase in length of time until myocardial recovery observed in ischemic cardiomyopathy patients is most likely due to the large amounts of myocardial scarring that occurs [26].

Though ischemic cardiomyopathy may have less viable myocardium, cardiac recovery can still be observed over a longer duration of mechanical support [15]. With this is in mind, ischemic cardiomyopathy may justify longer durations of mechanical support to wait for cardiac recovery. However, further research is needed to determine if the delay in cardiac recovery would also delay the negative consequences associated with prolonged mechanical support.

## Clenbuterol

Another factor that may justify longer mechanical support is the use of clenbuterol, which is a selective beta-2 receptor agonist. Clenbuterol has been shown to induce physiologic cardiac muscle hypertrophy [31, 32].

In the Harefield protocol, clenbuterol is used in conjunction with a beta blocker, angiotensin converting enzyme (ACE) inhibitor, angiotensin-1 receptor antagonist, and an aldosterone antagonist. However, clenbuterol is not administered until after maximal cardiac recovery has occurred in LVAD patients, most often indicated by the LVEDD [22, 29, 34]. The use of clenbuterol as part of the Harefield protocol has shown adequate cardiac recovery for LVAD explantation in over 60% of patients [22, 29]. This is suggested to be due to the induction of physiologic cardiac muscle hypertrophy that may prevent cardiac atrophy from occurring while on mechanical support [21]. The ability of clenbuterol to counteract myocardial atrophy may allow for extended duration of mechanical support.

Although the Harefield studies showed promising results of clenbuterol use, it is not currently available in the United States. A US multicenter study that utilized the Harefield protocol was unable to reproduce the same results, with only 1 of 17 patients able to be explanted from mechanical support [17]. Different etiologies of heart failure, duration of mechanical support, and medication dosage have been suggested for the discrepancy in results of the Harefield protocol [15]. As a result, the current literature does not support the use of clenbuterol as the sole reason for prolonged mechanical support beyond 6 months.

## Optimal medical therapy

Various medications have been suggested for LVAD patients with potential for myocardial recovery. RESTAGE-HF (Remission from Stage D Heart Failure) is a current multi-center prospective non-randomized study that is investigating a standardized pharmacological protocol that works in conjunction with prolonged LVAD support in order to promote cardiac reverse remodeling.

The pharmacological regimen includes lisinopril 40 mg, spironolactone 25 mg, digoxin 125 mcg, losartan 150 mg, and carvedilol 25 mg bid. The goal of the medical therapy in this study is to increase the rate of LVAD explantation and decrease the rate of heart failure recurrence after explantation. Forty patients with non-ischemic cardiomyopathy were enrolled into this study from six different centers. Recently published primary endpoint results of RESTAGE-HF have showed successful cardiac recovery for LVAD patients, with 50% of patients having been explanted thus far [23].

# Conclusion

For all the studies mentioned in this review, the average duration of mechanical support for LVAD patients varies widely. There are many factors that may account for the variability of mechanical support duration between studies. Differences in etiology of heart failure, age, comorbidities, duration of heart failure diagnosis, device flow type, medical treatment, weaning protocol, or patient selection criteria are some of the factors that may play a role in the mechanical support duration [19, 26].

Additionally, the variability of length of mechanical support for patients that experienced cardiac recovery may also be due to the small sample sizes in most studies. Cardiac

recovery due to mechanical support is still a rare occurrence; only 1.3% of all patients on the INTERMACS registry have undergone cardiac recovery [27] (Table 5).

Given the variability in duration of mechanical support until maximum cardiac recovery and the potential negative consequences of prolonged LVAD use, it has been suggested that there would be a 6-month waiting period for cardiac reverse remodeling monitoring before weighing options such as transplant [7]. However, there may be circumstances that justify an extended waiting period for cardiac recovery such as patients using a continuous-flow LVAD, diagnosed with a certain type of cardiomyopathy, or using maximal pharmacological therapy [27]. Furthermore, it must also be considered that many patients that may experience cardiac recovery adequate for device explantation may be susceptible to HF recurrence regardless of the amount of cardiac recovery achieved due to length of pre-implant heart failure history, persistent LV dilation, low off-pump LVEF, and/or type of cardiomyopathy [11]. As a result, the length of mechanical support for each patient must be made on an individualized basis with consideration of risks/benefits based on cardiac function and history.

## Compliance with ethical standards

For this type of study (meta-analysis), formal consent is not required.

**Conflicts of interest** Mr. Binh Pham has no conflict of interest or financial ties to disclose. Dr. Sandra Chaparro has received research grants from Abbott, Amgen, Mesoblast, and Medtronic.

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