



Editorial Review

What Did We Learn about VADs in 2020?

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Abstract

This is our 7th annual literature review on mechanical circulatory support (MCS) devices.

Our previous reports were well received by the readers. The full text of the reviews for [2014](#), [2015](#), [2016](#), [2017](#), [2018](#), [2019](#)¹⁻⁶ were downloaded 807, 843, 638, 827, 841, and 199 times, respectively.

In this review, we summarized the most interesting and important, from our standpoint, publications covering MCS from 2020. There may be some slight overlap with the end of 2019 because some papers were published online first, and the year of the publication changed when they became available in print.

For the fourth time this year, we added a section on extracorporeal membrane oxygenation (ECMO), which primarily addresses new developments in veno-arterial (V-A) ECMO.

Readers who wish to supplement this review, argue with the author's statements, or express their opinions are encouraged to do so by sending letters to the editor at mguglin@iu.edu.

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Outcomes

In 2020, the focus of the annual report from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) was on the comparison of major outcomes between the axial-flow HeartMate II (HMII) (Abbott Laboratories, Abbott Park, IL), the centrifugal-flow Heartware (Medtronic, Minneapolis, MN), and the centrifugal-flow with full magnetic levitation HeartMate 3 (HM3) (Abbott Laboratories, Abbott Park, IL) devices. There has been a massive shift in the type of pumps used. While in 2014, 70.1% of implants were axial flow devices, their share was reduced to 2.1% in 2019.⁷

The overall survival with current-generation left ventricular assist devices (LVADs) continues to be favorable, with a 30-day mortality of only 5% and 1-year survival of 82%. No differences in 2-year survival (72% vs. 74%) were noted between those who received LVADs from 2014-2016 and those implanted between 2017-2018.⁷

There was no significant difference in survival between the HMII and Heartware, but the HM3 had a 1-year survival of 87%, which was significantly higher in an unadjusted comparison with the Heartware (79%, $P < .001$).⁷

Importantly, apart from right heart failure (HF), the HM3 had a lower complication risk. Freedom from the first stroke at 1 year, regardless of severity, was 88% for HMII, 84% for Heartware, and 93% for HM3. The gastrointestinal (GI) bleeding rate was 25% for HMII, 20% for Heartware, and 12% for HM3 for the first year post-implant. Beyond the first year, centrifugal-flow devices had a lower incidence of GI bleeding as compared to axial flow devices. Major infection was the most common adverse event, with only 60% of HMII, 57% of Heartware, and 67% of HM3 implantations being free of a major infection at 1 year. Freedom from right HF at one year was higher in HMII (71%) than in Heartware (62%) or HM3 (66%). The authors of the report underscored that the analysis coming from a non-randomized registry should be taken with caution.⁷

In addition, there was a major change in the balance between bridge-to-transplant (BTT) and destination therapy (DT) strategies. In 2014, less than half (46.6%) of the LVADs were implanted as DT; the share increased to 70.2% by 2019.⁷ This may reflect the change in the organ allocation system implemented by United Network for Organ Sharing (UNOS) in October of 2018 that made it increasingly difficult to transplant candidates who are stable on LVAD support and are without any major complications.

For those who received the LVAD as a BTT strategy, 33% received a transplant by 1 year, 50% by 2 years, and 61% by 5 years. In contrast, for those whose LVAD was implanted as DT, fewer than 20% received a transplant by 5 years.⁷

Two smaller-scale analyses compared the outcomes of patients with Heartware and HM3s.

The first was a single-center, retrospective study where higher-risk patients (INTERMACS level I-II) received Heartware (73%) versus HM3 (57%, $P = .018$). Patients with HVADs were more likely to experience cerebral bleedings (hazard ratio [HR] 6.79 [1.43-32.20], $P = .016$). Also, the incidence of hemocompatibility-related adverse events was significantly higher in the HVAD group (1.28 vs. 0.7 events per



patient-year, $P < .001$). The 1-year survival was similar in the HVAD and HM3 groups (62.2% vs 66.7%, respectively).⁸

In the second single-center study, patients were retrospectively matched by several major clinical parameters including age, sex, and the INTERMACS profile. During a median follow-up at 15.3 months, 29.1% and 24.1% of patients died in the HVAD and HM3 groups, respectively. The HR for mortality was 0.84 (nonsignificant). Freedom from cerebrovascular events did not differ between study groups. The risk of driveline infection was significantly lower in the HM3 than in the HVAD group (HR = 0.54; 95% CI: 0.35-0.84; $P = .006$). In addition, 8 patients with an HVAD and 0 with HM3 developed a pump thrombosis during follow-up ($P = .148$).⁹

Device-Specific Outcomes

Total Artificial Heart

In a retrospective analysis of 217 patients who received a total artificial heart (SynCardia Systems, Tucson, AZ) at one of 6 high-volume, North American centers, 63.5% of patients later underwent cardiac transplantation, and 34.5% of recipients died. The mean time on support before the transplantation averaged 181 ± 179 days (range: 0-849). The overall survival in the entire cohort was 75%, 64%, and 58% at 1, 2, and 5 years, respectively.¹⁰

HeartMate 3 (HM3)

The prospective, observational, multi-national ELEVATE (Evaluating the HeartMate 3 with Full MagLev Technology in a Post-Market Approval Setting) registry was designed to study long-term outcomes of the HM3 in a real-world population in Europe and the Middle East. Survival at 2 years post-implant was 83%, with a favorable profile of adverse events. Specifically, the incidence of major complications was 10.2% for stroke, 9.7% for GI bleeding, and 1.5% for pump thrombosis. The outflow graft twists were found in 3.5% of patients.¹¹

As more and more evidence confirm a low rate of pump thrombosis in HM3, additional studies are being done to test the optimal level of anticoagulation in patients supported with this device. In a sub-study of the MOMENTUM 3 (Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3) trial, a comparison between 325 mg and 81 mg of aspirin a day revealed no difference in two-year survival, bleeding events, pump thrombosis, stroke, and peripheral arterial thromboembolic events. There were also no differences in survival free from hemorrhagic (usual-dose: 54.4% vs low-dose: 51.7%, $P = .42$) or thrombotic (usual-dose: 76.8% vs low-dose: 75.7%, $P = .92$) events.¹²

A new randomized controlled trial, The ARIES HM3 Pump IDE Study (The Antiplatelet Removal and Hemocompatibility EventS with the HeartMate 3 Pump IDE Study, [NCT04069156](https://clinicaltrials.gov/ct2/show/study/NCT04069156)) is poised to show whether aspirin at any dose has a role in HM3 management. Meanwhile, Lim et al.¹³ reported on the outcomes of patients who were given a choice of being on aspirin and warfarin or on warfarin only. Their study included 90 patients supported by a HM3. The majority (53/90) of subjects



opted out of aspirin after a median of 126 days post-implant, and 27/90 continued on both aspirin and warfarin. The median duration of warfarin monotherapy was 624 days, and 41/53 patients remained on warfarin alone for over a year. The 2-year survival for the whole cohort was 82%, and the 2-year survival conditional on hospital discharge was 93%. There was a total of 2 patients who had ischemic strokes after the division into aspirin or no aspirin, one per each arm. In other words, aspirin in HM3 patients seems to be unnecessary with a randomized study pending.

Imamura et al.¹⁴ studied the association of the geometry of the LVAD position with outcomes of patients. For HM3, a coronal angle (which is the angle between the axis of the inflow cannula and horizontal line, Figure 1) of ≤ 28 degrees was found to be the optimal placement. Such an angle, in comparison with angles of more than 28 degrees, was associated with better cardiac unloading and the following:

- lower central venous pressure (CVP) ($P = .030$)
- lower pulmonary capillary wedge pressure ($P = .027$)
- smaller left ventricular (LV) size ($P = .019$)
- smaller right ventricular (RV) size
- better RV function
- lower 1-year cumulative incidence of death or HF readmissions ($P = .008$).

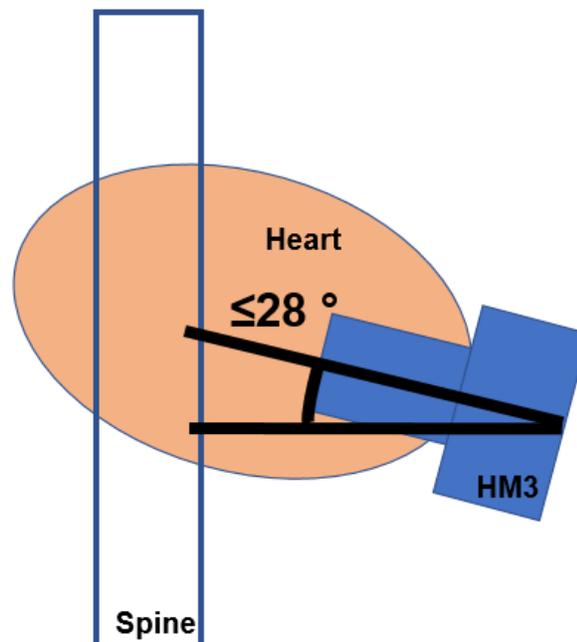


Figure 1. Coronal angle of HM3 cannula



Heartware Ventricular Assist Device

In terms of surgical placement of the device, for Heartware, the coronal angle less than 65 degrees was associated with better hemodynamics and fewer HF readmissions. The greater angle was associated with elevated intracardiac pressures, lower pulmonary artery pulsatility index ($P < .05$), and reduced RV function by echocardiography. Freedom from hemocompatibility-related events also tended to be lower in the wide-angle (>65 degrees) group (24% vs 62%; $P = .11$). The rate of GI bleeding was significantly higher in the wide-angle group (0.90 events/year vs 0.40 events/year; $P = .013$). The rates of stroke and pump thrombosis were statistically comparable.¹⁵

Speaking of broader outcomes, in a multicenter, prospective registry collecting post-approval data on Heartware as a BTT from several European and Australian centers, a Kaplan-Meier survival through 7 years was 51%. Through 6 years, freedom from any stroke was 82%, while freedom from severely disabling stroke was 89%.¹⁶

In a single-center study of 103 patients who received an HVAD, the mean survival was 2.05 ± 2.14 years.¹⁷ The Kaplan-Meier analysis showed an overall survival rate of 69.7%, 56.7%, 46.0%, and 25.0% at 1, 2, 4, and 8 years, respectively. Sub-analysis of the BTT patients showed a mean survival of 2.45 ± 2.29 years with a survival rate of 85.1%, 75.1%, 67.2%, and 44.8% at 1, 2, 4, and 8 years, respectively. For DT, mean survival was 2.18 ± 1.91 years with a survival rate of 67.9%, 49.0%, and 25.1% at 1, 2, and 4 years, respectively.¹⁷

Although HM3 can be used for biventricular support with one pump per side, there is more experience with the HVAD in this configuration. According to data from several centers, survival at 1 and 2 years was 56% and 47%, respectively, with no difference between the right atrial and RV implantation of the right-sided device.¹⁸ However, per systematic literature review, Kaplan-Meier analysis showed a higher 1-year survival with implantation in the right atrial than the RV (91.7% vs 66.2% $P = .036$). Pump thrombosis occurred at a similar rate of 30%.¹⁹

While the HM3 pump has a built-in pulsatility with the slight speed change every 2 seconds, the HVAD has a somewhat similar function, the Lavare cycle, which has to be activated. In essence, once a minute, the set speed decreases by 200 revolutions per minute (rpms) for 2 seconds, then it increases to 200 rpms above the set speed for one second, and then returns to the baseline (Figure 2). This cycle is designed to automatically increase both ventricular and pump washing to prevent thrombosis. In a non-randomized study, Lavare was activated in some patients and left inactive in the rest. Surprisingly, both the incidence and rate of pump thrombosis were significantly higher for the "Lavare On" group (incidence of 31.8 % vs 7.9%, $P = .02$). There was a non-significant trend to a higher rate of strokes in patients with the Lavare cycle, and the incidence of GI bleeds was similar. The authors hypothesized that late activation of Lavare disturbed a stable but potentially prothrombotic pannus at the inflow cannula; they concluded that this feature, if used at all, should be activated immediately after the HVAD implantation.²⁰

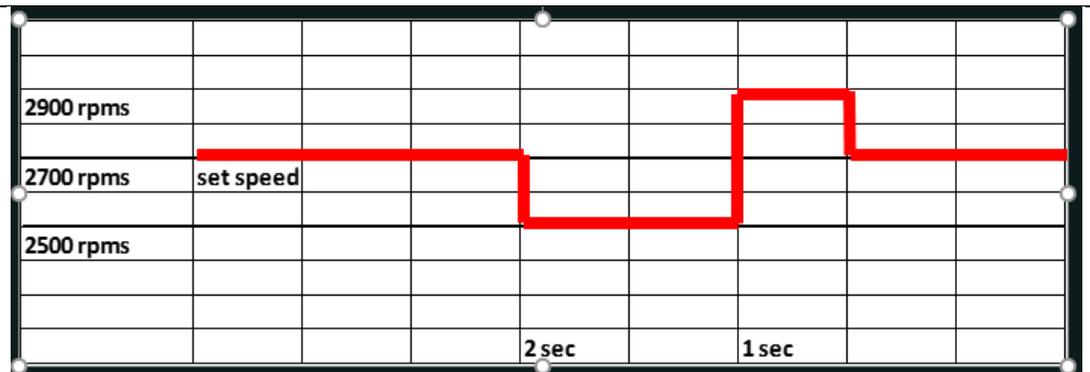


Figure 2. The Lavare cycle

Recovery

Cardiac recovery on LVAD support that allows for the LVAD to be inactivated via surgical removal or decommissioning percutaneously is one of the most popular topics in the MCS field, and there were major advancements in 2020. Percutaneous LVAD exclusion can be accomplished with the occluder deployed at both proximal and distal portions of the outflow graft or in the inflow graft, and patients usually continue to take warfarin for prevention of thromboembolism.²¹

In general, recovery remains rare with less than 5% of LVADs being explanted per the INTERMACS.⁷ In the European Registry for Patients with Mechanical Circulatory Support, successful LVAD explantation due to myocardial recovery occurred in 1.5% of patients.²² Patients who recovered, compared with those who did not, were younger (44 vs. 56 years, $P < .001$), had a shorter duration of HF ($P < .001$), and had a non-ischemic etiology (only 9% of recovered patients had ischemic cardiomyopathy vs. 41.8% in patients without recovery, $P < .001$).²²

It is widely known that when an LVAD unloads the LV, the ventricle decreases in size and left ventricular ejection fraction (LVEF) improves, which mostly occurs within the first 6-12 months after the implant.²³ On the tissue level, however, full recovery is uncommon. When cardiac specimens from patients without cardiac disease, with severe cardiomyopathy, and with cardiomyopathy on LVAD support were examined for cardiac fibrosis, the collagen content was significantly higher in failing hearts, both without mechanical unloading and on LVAD support, than in healthy hearts.²⁴

Historically, in two single-center studies, the rate of myocardial recovery was remarkably high. In the first study from 2006, which included young patients who received an LVAD for non-ischemic cardiomyopathy, 73% (11/15) of them later had the LVAD explanted due to recovery. All patients in that study were on a pulsatile-flow LVAD. The cumulative rate of freedom from HF was 100% and 88.9% at 1 and 4 years post-explantation, respectively. In addition to standard HF medications, patients received a beta2- adrenergic-receptor agonist and clenbuterol in hope of preventing myocardial atrophy.²⁵ However, high-dose clenbuterol, given to another group of patients on LVAD support, failed to produce any changes in the myocardium, although it resulted in an increase in skeletal muscle mass.²⁶



In the second study, published in 2011, a similar combination of angiotensine receptor enzyme inhibitors (ACE), angiotensine receptor blockers (ARBs), beta blockers (BB), aldosterone antagonists, and clenbuterol was given to 20 young (35.2 ± 12.6 years), non-ischemic patients on a continuous-flow LVAD. Explantation occurred in 63.2% of patients. Over a year later, LVEF in post-explant patients remained normal at $58.1 \pm 13.8\%$.²⁷

In 2020, results from the prospective, multicenter, non-randomized RESTAGE-HF study (Remission from Stage D Heart Failure) were published. In 40 non-ischemic patients (from six different clinical sites) on HMII support, the LVAD speed was optimized, and regular echocardiograms were performed at reduced LVAD speed (6000 rpms, no net flow) to test underlying myocardial function. Remarkably, cases of recovery occurred in all participating sites.²⁸ The patient group was relatively young (aged 35.1 ± 10.8 years). The medical regimen consisted of lisinopril (20 mg twice a day), carvedilol (50 mg twice a day), spironolactone (25 mg daily), digoxin (125 mcg daily), and losartan (150 mg daily). Unlike in the first two studies, clenbuterol was not used. The primary end point was the proportion of patients with sufficient improvement of myocardial function to reach criteria for explantation within 18 months with sustained remission from HF (freedom from transplant/VAD/ death) at 12 months. Overall 50% (18/36) of patients receiving the protocol were explanted within 18 months. For those that were explanted, the pre-explant LVEF was $57 \pm 8\%$; end-diastolic diameter was 4.81 ± 0.58 cm; end-systolic diameter was 3.53 ± 0.51 cm; pulmonary capillary wedge pressure was 8.1 ± 3.1 mm Hg; and pulmonary artery saturation was $63.6 \pm 6.8\%$ at 6000 rpms. Of note, 4 patients dropped out for unrelated reasons. After explantation, survival free from VAD or transplantation was 90% at 1-year and 77% at 2 and 3 years.

Candidate Selection

Several tests, that are traditionally included in the panel of parameters checked before accepting a candidate for LVAD implant, may not be as helpful as assumed. The level of prealbumine before the LVAD implant was not associated with post-implant adverse events including bleeding, infection, stroke, renal failure, and RV failure. In addition, lower prealbumin did not impact risk-adjusted 1-year mortality when modeled either as a categorical or continuous variable.²⁹

Pre-VAD abnormal pulmonary functions overall were not associated with inferior outcomes, although patients in the lowest strata of forced expiratory volume in one second (FEV1) ($< 60\%$ predicted) and FEV1/forced vital capacity (< 0.5) had elevated risk-adjusted hazards for mortality (HR 2.63, 95% CI, 1.51-4.60 and HR 18.92, 95% CI, 2.10-170.40, respectively).³⁰

The impact of smoking on LVAD outcomes was examined in several studies in 2020. Former smokers had statistically comparable total readmission rates with never smokers (2.49 vs. 2.13 event/year), whereas current smokers had significantly higher rates compared to never smokers (2.81 events/year, $P < .05$). The rates of driveline infection, stroke, and hemolysis were statistically comparable between the never smokers and former smokers, while current smokers had significantly higher rates compared to never smokers ($P < .05$ for all).³¹



Additionally, active smoking was associated with higher rates of adverse events in males, while females had a high rate of adverse events irrespective of smoking status.³²

Interestingly, a survey of VAD implanting centers revealed that only a third of them (32%) consider smoking a deciding factor in destination therapy evaluations.³³

Psychosocial evaluation is easily one of the most subjective tests patients have to pass in order to become LVAD candidates. In the INTERMACS database, patients were determined to have psychosocial risk if they had one of the following: (1) limited social support; (2) limited cognition; (3) substance abuse (alcohol and drug); (4) severe psychiatric disease (including major depression and other major psychiatric diagnosis); and (5) repeated noncompliance. The most prevalent psychosocial risk factor was substance abuse in 12.6% of recipients. Patients with psychosocial risk were at increased hazards for device-related infection, GI bleeding, pump thrombosis, and readmission and reduced hazards for cardiac transplantation ($P < .05$ for all). However, the most important outcomes—survival on pump support or stroke—were unaffected.³⁴

Management of Patients on LVAD Support

Quality of Life

Patients on LVAD support have better hemodynamics and enjoy a better quality of life than pre-VAD, but many limitations remain. A recent study by Fujino et al.³⁵ showed that following LVAD implantation, pulmonary arterial pressure and pulmonary capillary wedge pressure decreased, and cardiac index increased significantly and then remained unchanged throughout follow-up. On the contrary, right atrial pressure decreased initially and then gradually increased to pre-implant values. The pulmonary artery pulsatility index (PAPI) decreased initially and returned to pre-implant values, then progressively decreased over longer follow-up. On cardiopulmonary stress test their peak VO_2 averaged 10.6 ± 3.1 ml/kg/min, indicating an inability to boost oxygen delivery to the muscles during exercise, which is consistent with severe impairment of exercise capacity.³⁶

In terms of emotional well-being, more patients with LVADs attempt or commit suicide than healthy individuals or those with chronic medical conditions in general. A study from the French registry, which has data on nearly 500 LVAD recipients, reported that 10 patients (2%) attempted or committed suicide either by unplugging/sectioning their LVAD cable or drug intoxication over 14 months of follow-up. Only 2 of these patients had a previous history of psychiatric disorder (depression with suicide attempt and schizophrenia). The variables associated with suicide/suicidal attempt were DT LVAD and follow-up at a center without an LVAD coordinator.³⁷

Medical Management

ACE/ARBs/BB

In the annual literature review from last year,⁶ we emphasized the importance of guideline directed medical therapy (GDMT) after the LVAD. The LVAD recipients



with optimized hemodynamics have lower mortality³⁸⁻⁴¹ and fewer complications. It is of particular interest that they had not only fewer HF readmissions, which would be intuitive, but also fewer hemocompatibility-related events such as bleeding and thrombosis.⁴¹ An effort should be made to maximize favorable effects of pharmacological management. Last year, another report demonstrated the advantages of GDMT for RV function reflected in PAPI. Over the first year after implant, patients who received BB and ACE/ARBs demonstrated higher PAPI than patients not managed with these drugs (3.3 vs 1.6, $P = .043$ for BB and 3.4 vs 2.1, $P = .03$ for ACE/ARBs). BB were also associated with reduced HF readmission, and ACE/ARBs⁴² with reduced HF readmission and GI bleeding ($P < .05$ for all).⁴²

Sacibutril/Valsartan

Reports on the use of sacibutril/valsartan in LVAD patients are of particular interest. Three reports were published last year. The first experience with sacibutril/valsartan was released and reviewed 5 patients. The tolerability of the drug was not very favorable, with 3 out of 5 patients discontinuing the medication due to hypotension-related symptoms.⁴³

At the Cleveland Clinic, 10 patients with LVADs and hypertension tolerated sacibutril/valsartan for a median duration of 292 (141–422) days, and 4 of them tolerated the high dose. Although mean blood pressure decreased by 20.0 ± 14.0 mmHg ($P = .002$), the dosage had to be reduced due to hypotension in only one patient. As a result of being on sacibutril/valsartan, the daily diuretic requirement decreased: furosemide oral equivalents decreased from 220.0 ± 167.9 mg to 120.0 ± 94.3 mg, and N-terminal pro-B-type natriuretic peptide was reduced from 2929 pg/mL at baseline to 1530 pg/mL after a median of 19 (5–16) days of follow-up ($P = .36$).⁴⁴

In a retrospective study from several European countries, 22 LVAD (HM3 and HVAD) patients were treated with sacibutril/valsartan for approximately 2 months. Only a third of the patients had a mean arterial pressure > 90 mmHg. The moderate dose of 49/51 mg twice daily was achieved in 86% of the patients. Sacibutril/valsartan was effective in reducing the mean blood pressure (80 [73.5–92] mmHg vs 75 [70–84.5] mmHg, $P = .03$) and it was related to an increased pump flow (4.05 [3.57–4.52] vs 4.4 [3.70–4.65] liters per minute; $P = .01$). Left ventricular end-diastolic dimension, inferior vena cava diameter, and N-terminal pro-B-type natriuretic peptide decreased, as well as daily diuretic requirement. In addition, the functional status improved. The proportion of patients in New York Heart Association (NYHA) class I increased from 14.3% to 47.6% after sacibutril/valsartan initiation ($P = .002$).⁴⁵ Overall, the use of sacibutril/valsartan in the LVAD population looks tolerable and promising.

Sildenafil

Two conflicting studies on the role of sildenafil in post-LVAD management were published in 2020. According to the INTERMACS analysis, phosphodiesterase type 5 inhibitors in patients on LVAD support were associated with a lower rate of pump thrombosis (HR, 0.82; 95% CI, 0.74-0.90; $P < .001$) and ischemic stroke (HR, 0.85;



95% CI, 0.75-0.97; $P = .019$).⁴⁶ On the other hand, a systematic review and meta-analysis of published studies found that sildenafil was not associated with lower post-operative RV failure, GI bleeding, stroke, or pump thrombosis.⁴⁷

Obesity

Management of obesity in the LVAD population remains a hot topic because many patients need to lose weight in order to be listed for transplant. Bariatric surgery remains a valid and sometimes the only option leading to success. In a systematic review and meta-analysis on sleeve gastrectomy in LVAD recipients, it was found that both surgeries are performed simultaneously in 37% of cases, while the remaining cases were staged. The mean body mass index decreased from 46.7 kg/m² (95% CI: 42.9-50.6) to 33.4 kg/m² (95% CI: 30.2-36.6) ($P < .01$) over the follow-up of 12.7 months. Bariatric surgery resulted in 66% of patients to be listed for heart transplantation, including 33% (95% CI: 22-47) who were transplanted. The outcomes of simultaneous versus staged surgeries were comparable.⁴⁸ Similar results were reported from published literature by Aelst et al.⁴⁹ and deAbreu et al.⁵⁰

Arrhythmia

While the discussions about the need for an implantable cardioverter-defibrillator (ICD) in patients with an LVAD are ongoing, most patients have ICDs, and they need to be interrogated on a regular basis. The electromagnetic interference between the LVAD and ICD which prevents interrogation is not uncommon. In a retrospective, multicenter, observational study of LVAD recipients with a transvenous lead ICD, approximately 4% of patients' ICDs could not be interrogated because of interference. The interference occurred after a median of 19.0 (5.2 -88.0) days following LVAD implantation, and 6%, 2%, and 1.5% occurred in patients implanted with Abbott, Medtronic, and Biotronik devices, respectively ($P < .001$). In most cases, patients had an HMII pump. The issue could sometimes be remedied by placing a metal plate on the chest between the LVAD and ICD and placing a metal box above the LVAD. In half of the cases, however, this did not work, and ICDs had to be replaced.⁵¹ In another study, this type of interference was reported in 13% of the patients. They were implanted with HMII and HM3 pumps, and the interference usually occurred between an HMII and Abbott ICD and between the HM3 and Biotronik ICD; rarely was interference reported with Medtronic devices.⁵²

In one case, when an in-office interrogation was unsuccessful due to electromagnetic interference, the patient was instructed to extend his arm above his head on the ipsilateral side of the ICD, thereby increasing the distance between the LVAD and ICD. This eliminated the interaction and allowed for reprogramming of the device.⁵³

Subcutaneous ICDs have become a popular option for LVAD-supported patients. Because it does not have intracardiac leads, the risk of infection is lower than in transvenous defibrillators. In subcutaneous devices, sensing relies on good discrimination between P, R, and T waves, which can be altered after LVAD implantation. When tested for an adequate electrocardiogram signal, more than 70% of patients with an LVAD were eligible for a subcutaneous ICD.⁵⁴



Interference also occurs between subcutaneous ICDs and LVADs and manifests in inappropriate shocks. In a study by Ishida et al., interference was reported in patients with HM3 and HVAD devices. In some patients, the problem could be resolved by reprogramming the ICD to an alternate vector, but some defibrillators had to be replaced.⁵⁵ Duke researchers found such interference to be quite common.⁵⁶

Another topic on the crossroads between MCS and electrophysiology is the relationship between arrhythmias and mechanical unloading. In the study from the Dresden Impella Registry, all 19 patients with cardiogenic shock and arrhythmias refractory to electrical defibrillation or antiarrhythmic drugs, were able to stop their arrhythmia after implantation of a micro-axial heart pump. This phenomenon was referred to as heart rhythm stabilization.⁵⁷

Although V-A ECMO does not treat ventricular tachycardia, it effectively provides a hemodynamic bridge to support patients until electrical instability is treated or subsides on its own, like in acute ischemic cardiomyopathy. In a retrospective study from two French centers, 83 patients were on ECMO for a treatment-refractory electrical storm. Of this cohort, 59% had acute ischemic cardiomyopathy and 66% underwent cardiopulmonary resuscitation prior to ECMO, with 18% cannulated during the procedure. Fifty patients (60%) had ventricular tachycardia and/or ventricular fibrillation alternating with short periods of sinus rhythm, and 33 (40%) had refractory ventricular tachycardia and/or ventricular fibrillation. Catheter ablation was performed in 15% of the patients, 45% were successfully weaned off, and 42% were alive 6 months post-admission. The median time on support was 3 days (1-13 days).⁵⁸

The most common procedure for termination of refractory ventricular tachycardia is ablation. Ablation procedures can be lengthy and cause myocardial stunning and hemodynamic compromise in already decompensated patients with severe cardiomyopathy. In a systematic review on MCS for life-threatening arrhythmia, Mariani et al.⁵⁹ found that survival after ablation for electrical storm is higher with prophylactic use of MCS for hemodynamic support. Patients with prophylactically used MCS also had higher rates of termination and non-inducibility of ventricular tachycardia after ablation.

Ablations are also performed in ventricular tachycardia in LVAD recipients. Grinstein et al.⁶⁰ used a composite outcome of adverse events to analyze the ablation procedure's impact. They found that 58% of patients who had ablation while on LVAD suffered an adverse event during a one-year follow up (11%--confirmed pump thrombosis; 41%--suspected pump thrombosis; 39%-- thromboembolic events including stroke). This rate was significantly higher ($P = .002$) than the 30% rate of adverse events in patients with an LVAD and ventricular tachycardia but treated without ablation.⁶⁰

Complications of the VADs

Stroke

Stroke is a devastating complication of an LVAD, and everything that may prevent it should be utilized. In a single-center, retrospective study, statins were associated



with a reduced rate of cerebrovascular accidents. In patients receiving statins, strokes occurred at the rate of 0.11 events per patient-year while the rate for those not on a statin was 0.22 events per patient-year (age-adjusted HR 0.46; 95% CI = 0.24-0.88; $P = .019$). The difference was determined by ischemic strokes, because the rate of hemorrhagic strokes was similar regardless of statin use.⁶⁰

Gastrointestinal Bleeding

Almost every year, there is a new report on a novel pharmacological therapy for prevention of GI bleeding in patients on LVAD support. In 2020, bevacizumab was found to be such a therapy. Patients were given 8-18 infusions intravenously during the study period. Median follow-up time after bevacizumab initiation was 21.7 months. Four out of five patients had a complete response, and the last patient achieved a partial response. Treatment with intravenous bevacizumab resulted in a significant reduction in the number of blood transfusions from the median 56.5 to 6.6 red blood cell units per year, $P = .035$. Similarly, the median number of bleeding-related hospitalizations decreased from 5.4 to 1.7 per year, $P = .041$. The requirements in endoscopic procedures were also reduced.⁶¹

In another series of 8 patients with frequent GI bleeding, success was achieved with the use of tamoxifen. Tamoxifen was associated with a significant decrease in major GI bleedings from a median of 3 (IQR 1.4-7) events/patient-year pre-tamoxifen initiation to 0 (IQR 0-0.9) events/patient-year post-tamoxifen initiation ($P = .02$). Transfusion of packed red blood cells also decreased from 16.8 (IQR 9.9-30.6) units/patient-year pre-tamoxifen initiation to 1.5 (IQR 0-7.5) units/patient-year post-tamoxifen ($P = .04$).⁶²

Different Devices

Intra-Aortic Balloon Pump

A new organ allocation system for heart transplantation favors patients on short- and intermediate-term MCS, and several studies reported an increase of temporary MCS use in listed patients since the end of 2018 when the new policy came into effect.⁶³ Since the goal is to keep patients ambulatory while they wait for the donor heart, use of the axillary artery as a site of implantation is very attractive for clinicians. However, positioning the balloon pump at this site is prone to complications. Bhimaraj et al.⁶⁴ published a paper about their experience with axillary intra-aortic balloon pumps. The procedure was successful in 68% of their 195 cases; 120 patients were BTT and 13 patients received LVADs. The pump required frequent bedside repositioning, and 37% of the pumps had to be replaced for malfunction. The rate of complications was quite high. Specifically, 15.8% required 1 exchange, 8.7%-2 exchanges, 4.6%-3 exchanges, 3%- 4 exchanges, 1% -5 exchanges, and 1 patient needed 7 exchanges.⁶⁴

Impella

For the same reasons, axillary Impella (Abiomed, Danvers, MA) is increasingly being used. In a cohort of 40 patients with cardiogenic shock, the duration of



support on this device was 21.05 ± 17 days. Half of the patients died during the same admission, and 17% had complications from the Impella including right arm ischemia or neuropathy (7.5%) and pump malfunction requiring device replacement (10%).⁶⁵

What is New in V-A ECMO World?

In the V-A ECMO world, the issue of venting the LV for prevention or treatment of LV distension and pulmonary edema continues to be an actively discussed topic. While V-A ECMO is a life-saving method for patients with low-output failure surgery, this therapy may increase LV afterload due to retrograde blood flow in the aorta, which may lead to progression of pulmonary congestion.

Prognostic significance of this complication is not well established. In our paper about “white lungs” on V-A ECMO, we showed that in patients who did not have severe pulmonary congestion, survival to weaning off V-A ECMO and survival to hospital discharge were 91.7% and 66.7%, respectively. In those with white lungs, the corresponding values were 50.0% and 26.5%, respectively ($P = .019$ for discharged alive).⁶⁶

In 2020, Distelmaier et al.⁶⁷ examined the predictive value of pulmonary congestion in patients that need V-A ECMO support after cardiovascular surgery.

When evaluated progressively during ECMO support, pulmonary edema on the first day was not associated with poor prognosis, but if the congestion was present on the 3rd or the 5th day of support, it was significantly associated with survival (adjusted HR 2.81; 95%-CI 1.76-4.46, $P < .001$, and HR 3.01; 95%-CI 1.84-4.93, $P < .001$, respectively). Linear regression revealed that only ECMO output (not LV function, cardiac output, central venous saturation, maximum dobutamine, and norepinephrine dose or fluid balance) was associated with the evolution of pulmonary congestion ($P = .007$).⁶⁷

There are multiple ways to unload (vent) the LV. We gave a detailed review of different solutions for this problem in 2018.⁴ In 2020, different methods were compared with the use of a mock circulatory loop with simulated acute LV failure on ECMO support. A surgically placed LV vent and temporary LVAD provided the most complete unloading in terms of reduction of LV diastolic volume. The temporary VAD was also the best for reduction in left atrial pressure from 13.3 to 4.4 mm Hg. The pulmonary artery surgical vent was the most effective at reducing mean pulmonary arterial pressure from 21.0 to 10.6 mm Hg.⁶⁸ In another model, Impella has a higher capability of LV unloading than atrial septal defect.⁶⁹

The Impella device increases the forward flow from the LV into the aorta and remains one of the most popular ways to unload the LV. In an international, multicenter cohort study, LV unloading with Impella, which was used in 49% of patients on V-A ECMO due to cardiogenic shock, was associated with a lower 30-day mortality (HR, 0.79 [95% CI, 0.63-0.98]; $P = .03$), despite higher complication rates.⁷⁰

One of the ideas brought up in 2020 was inserting an additional catheter into the pulmonary artery and connecting it to the venous arm of V-A ECMO.⁷¹



Although there is no universal age limit for initiation of V-A ECMO, most programs put arbitrary restrictions because of lower survival in older age groups. However, ECMO may be an option for elderly patients. The analysis of three age groups (70-74, 75-79, and ≥ 80 years of age) showed that in the whole cohort, 46.7% were weaned off ECMO. Overall in-hospital mortality was estimated at 68.3% with highest crude mortality rates observed in the 75-79 year-old subgroup (70.1%). Characteristically, nearly 100% mortality was observed when ECMO was used for sepsis.⁷²

Overall, 2020 was a productive year with many new developments. We hope to expand on them in 2021.

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