Journal of Cardiac Failure 00 (2024) 1–17

JCF
Journal of Cardiac Failure

Review Article

HFSA Scientific Statement: Update on Device Based Therapies in Heart Failure

JERRY D. ESTEP, MD[1] HUSAM M. SALAH, MD[2] SAMIR R. KAPADIA, MD[3]
DANIEL BURKHOFF, MD, PhD[4] ANURADHA LALA, MD[5] JAVED BUTLER, MD, MPH, MBA[6,7]
SHELLEY HALL, MD[8] and MARAT FUDIM, MD, MHS[2,9]

Weston, FL; Durham, NC; Cleveland, OH; New York, NY; Dallas, TX; and Jackson, MI

ABSTRACT

Heart failure (HF) is 1 of the major challenges of our time, given its increase in prevalence and related mortality rates. Foundational pharmacological therapies, including angiotensin receptor neprilysin inhibitors (ARNIs), beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose co-transporter inhibitors (SGLTis), have been established for HF with reduced ejection fraction (HFrEF). Moreover, recent trials have established the role of SGLTis in patients with HF with preserved ejection fraction (HFpEF). However, even with these therapies, a substantial residual risk persists in both HFrEF and HFpEF. Alongside pharmacological advancements, device-based therapies have shown efficacy in HF management, including implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT). More recently, devices such as cardiac contractility modulation (CCM) and baroreflex activation therapy (BAT) have been approved by the FDA, although they lack comprehensive guideline recommendations. This scientific statement outlines the unmet needs in chronic HF, reviews contemporary data and provides a framework for integrating novel device-based therapies into current clinical workflows. It emphasizes the importance of early diagnosis and phenotyping, proper patient stratification and a personalized approach to combining pharmacological and device therapies. The document also highlights the need for further research into device interactions and patient selection to optimize outcomes, while recognizing the need for a more integrated approach to treatment so as to address the unmet needs and residual risks in HF management. (*J Cardiac Fail 2024;00:1–17*)

Despite recent advancements, heart failure (HF) remains common and is associated with significant adverse events, impaired quality of life and mortality.[1] New drugs and devices have been developed for the the management of HF. Currently 4 drugs are considered foundational medicines for patients with HF and reduced ejection fraction (HFrEF), including angiotensin receptor neprilysin inhibitors (ARNIs), beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium glucose co-transporter inhibitors (SGLTis). Similarly, recommendations for the use of established devices, including implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) are well established.[2] Other, more recently approved devices by the Food and Drug Administration (FDA), such as cardiac contractility modulation (CCM) and baroreflex activation therapy (BAT), lack society-based use recommendations. This consensus document defines the unmet need in chronic HF and the role of novel device

From the [1]Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic Florida, Weston, FL; [2]Division of Cardiology, Department of Medicine, Duke University School of Medicine, Durham, NC; [3]Department of Cardiovascular Medicine, Heart, Vascular and Thoracic Institute, Cleveland Clinic Foundation, Cleveland, OH; [4]Cardiovascular Research Foundation, New York, NY; [5]Zena and Weil Cardiovascular Institute, Mount Sinai Hospital, Icahn School of Medicine, New York, NY; [6]Baylor Scott and White Research Institute, Dallas, TX; [7]Department of Medicine, University of Mississippi School of Medicine, Jackson, MI; [8]Baylor University Medical Center, Dallas, TX and [9]Duke Clinical Research Institute, Durham, NC.

Manuscript received April 16, 2024; revised manuscript received July 16, 2024; revised manuscript accepted July 16, 2024.

Reprint requests: Marat Fudim, MD, MHS, Division of Cardiology, Department of Medicine, Duke University School of Medicine, Durham, NC. E-mail: Marat.fudim@duke.edu

See page 16 for disclosure information.

1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2024.07.007

therapies in bridging current HF gaps, provides categories of HF device therapy and reviews contemporary outcome data and guideline recommendations of selected FDA-approved devices (CCM, BAT, valve interventions with transcatheter aortic valve replacement, mitral valve edge-to-edge repair, tricuspid repair, CardioMEMS pulmonary artery pressure monitoring, and HeartMate [HM] 3 left ventricular assist device [LVAD]). In addition, we propose a clinical pathway to implement FDA-approved device-based therapies that align with current HF management workflow and define device HF technology under current clinical investigation. Established device therapies, such as CRT and ICD, are not discussed in this consensus document, because the recommendations related to the indications and timing of implantation of these devices are well described in contemporary HF guidelines.

Unmet Need and Residual Risk an Chronic Heart Failure

Guideline-directed medical therapy (GDMT) with the use of ARNI/ACE inhibition/ARB, beta blockers, MRAs, and SGLTis can reduce the relative risk of cardiovascular death risk by almost 75% and translate into an absolute risk reduction of approximately 25% with treatment over 2 years. These data translate into a number needed-to-treat of only 4 for patients with HFrEF.[3] Moreover, after decades without new successful therapies, 2 recent trials with SGLTis have been shown to reduce the risk of hospitalization due to HF and, to a lesser degree, cardiovascular death in patients with HF and mildly reduced EF (HFmrEF) and HF with preserved EF (HFpEF).[4,5] In parallel, there have been advances with device-based therapies for HFrEF as well, including ICDs and CRT in indicated patients.

It is important to note upfront that the *M* in GDMT accounts for drug- and device-based therapies, and both classes of therapy are to be considered synergistic rather than in competition with each other. Although implementation efforts for existing GDMT are important, many patients are unable to tolerate some drugs, rendering them at higher risk. Even if medication therapies were provided, unacceptably high residual risks remain, underscoring the need for ongoing research, including the development of novel device-based therapies.

In the DAPA-HF (Dapagliflozin and Prevention of Adverse-outcomes in Heart Failure) trial, 4744 patients with HFrEF were enrolled in the outpatient setting, and approximately 70% had New York Heart Association (NYHA) class II symptoms.[6] Patients with an estimated glomerular filtration rate (eGFR) of < 30 mL/min/1.73 m^2 were excluded. Importantly, these patients were exceptionally well treated at baseline, with 94% of patients taking an ACEi/ARB/ARNI, 96% taking a beta-blocker and 71% taking an MRA. Also, patients were receiving protocol-driven follow-up in a clinical trial setting. Despite having characteristics of being very well managed, the annualized event rate for HF hospitalization or cardiovascular death for patients in the dapagliflozin arm was 11.6 per 100 person-years. The EMPEROR-Reduced (Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction) trial had a patient population similar to that of DAPA-HF, including baseline medical therapy, yet allowed modestly higher natriuretic peptide levels and lower kidney function enrollment criteria of eGFR $\geq$ 20 mL/min/1.73m.[7] These modest changes were associated with an incidence of cardiovascular mortality or hospitalization for HF that was about $\sim$ 40% higher, with an annualized event rate of 15.8 per 100 person-years in the empagliflozin group.

Based on contemporary medication-management data, and despite the availability of newer drug therapies for HF, there is a need for further innovation in treatment. The residual risk for patients receiving optimized GDMT remains on par with or worse than other major cardiovascular diseases. Even the "lower-risk" subsets of patients with HF have adverse event rates higher than thresholds referenced as being high or very high risk for cholesterol guidelines for the management of atherosclerotic cardiovascular disease, as an example.[3] Importantly, it should be noted that the use of evidence-based GDMT is lower in patients with higher-risk HF, in part due to higher rates of absolute or relative contraindications (such as renal disease) and/or intolerance for GDMT in patients with advanced HF symptoms.[8] Currently, several therapies either are contraindicated or have little to no randomized data in populations with eGFR < 30 mL/min/1.73 m^2.

Role of Device Therapies in Bridging Current Gaps in Chronic HF

Alongside pharmacological treatment and prevention of HF, a number of device-based therapies have emerged to show efficacy. These range from implantable defibrillators for the prevention of sudden cardiac death, to pulmonary artery sensor monitors to reduce HF hospitalizations, to more structural interventions, such as transcatheter edge-to-edge repair devices and durable left ventricular assist devices and beyond.[9] Clinical trial designs that compare device-based therapies to pharmacological therapy alone have contributed to biases in choosing 1 therapeutic approach vs another, when, in fact, integrated strategies incorporating a combination of pharmacological and device-based therapies often allow for tailored optimal treatment of HF. Broadly, device-based therapies may be divided into 7 categories, summarized in Table 1.

Table 1 Categories of device-based therapies for heart failure

Categories of device therapies for HF	Example
Remote monitoring devices	Continuous pulmonary artery pressure monitoring
Valvular device-based therapies	Transcatheter edge-to-edge repair of the mitral valve
Autonomic modulators	Baroreflex activation therapy, vagus nerve stimulation, splanchnic nerve modulation
Electrophysiological modulators	Cardiac resynchronization therapy, cardiac contractility modulation
Respiratory modulators	Asymptomatic diaphragmatic stimulation, phrenic nerve stimulation
Structural device-based interventions	Interatrial shunt devices, basilar ventriculoplasty, LV reconstruction
Left ventricular assist devices (LVADs)	HeartMate3

Timing, Screening, and Referral Process for Novel Device-Based Therapies and the Role of the Heart Team

Despite the growing evidence of success of novel device-based therapies in the management of HF, evidence-based, standardized approaches to their implementation (akin to GDMT) are lacking, resulting in their delayed use or under use.

We propose the following pathway to implement the FDA approved novel device-based therapies in the workflow of HF management (Fig. 1):

1. Following a diagnosis of HF, special attention should be paid to appropriate characterization and classification, with timely initiation and up-titration of relevant GDMT. In addition, identification of the etiology of HF (eg, coronary artery disease, hypertension, valvular heart disease, arrhythmia, left bundle branch block) and proper management of these etiologies should be considered (eg, revascularization, ambulatory blood pressure monitoring). Also, those who meet the guideline criteria for CRT should be referred for CRT implantation. Depending on the severity of disease, risk profile and setting (hospitalized vs at home), patients may be seen by a general cardiologist, cardiology practitioner or advanced HF specialist.
2. At follow-up visits, providers should aim to evaluate symptoms burden, functional status (eg, NYHA class hospitalizations for HF, associated structural abnormalities, and the response to GDMT and its tolerability. The persistence of NYHA class II or above symptoms following 3–6 months after initiation of pharmacological GDMT and CRT (where applicable) should result in consideration of device-based therapies for HF. Further, progressive disease, such as low blood pressure, escalating diuretics, need for inotropes, end-organ dysfunction, defibrillator shock, recurrent HF hospitalizations, imaging features suggestive of worsening disease (eg, worsening LV dilation, LA dilation, MR, or TR), and worsening biochemical markers (eg, NT-proBNP) should lead to a referral to an advanced HF specialist for consideration of advanced HF therapies, such as LVAD and heart transplantation.[10]

Integral to the evaluation for device-based therapies is the identification of the ideal patient population for each therapy, so as to improve the benefit-risk ratio of these therapies. The currently approved and investigational device-based therapies for HF generally target similar and broad patient populations, and as more device-based therapies are approved, more patients may be eligible for more than 1 device-based therapy (Fig. 2). The potential eligibility for multiple device-based therapies in 1 patient underscores the need for dedicated studies to examine the comparable and additive effects of device-based therapies as well as possible multidevice interactions. It is important to better understand multidevice interactions, because pathophysiological pathways may be altered in different ways, even though patients share common etiologies of HF and/or pathophysiological features. Developing tools to assess pathophysiological interactions may improve patient selection for various device-based therapies (eg, patients with greater degrees of baroreflex dysfunction may experience more benefits from BAT compared with other patients who have lesser degrees of baroreflex dysfunction). In addition, given that 1 patient may be a candidate for more than 1 device therapy, fiscal responsibility needs to be addressed. Based on recent evidence, invasive hemodynamic phenotyping may be needed to identify those who would benefit from certain device-based therapies and to exclude those who may experience harm.[11] These observations highlight the importance of early clinical, hemodynamic, structural, proteomic, and radiomics phenotyping to better direct the delivery of HF therapies.

Last, the current conventional approach to using device-based therapies in the management of HF focuses primarily on optimizing pharmacological GDMT before considering device-based therapies; this approach is based mainly on the design and conduct of the clinical trials that led to approval of device-based therapies as well as the temporal development and approval of drug therapies that preceded the development of device-based therapies. However, this approach has several shortcomings, many of which stem from the high prevalence of patients with HF not on pharmacological GDMT (eg, due intolerance, nonadherence, chronic recurrent cost).[12] The undermedicated population may be overlooked when being evaluated for device-based therapies or may experience significant delays when being treated by the

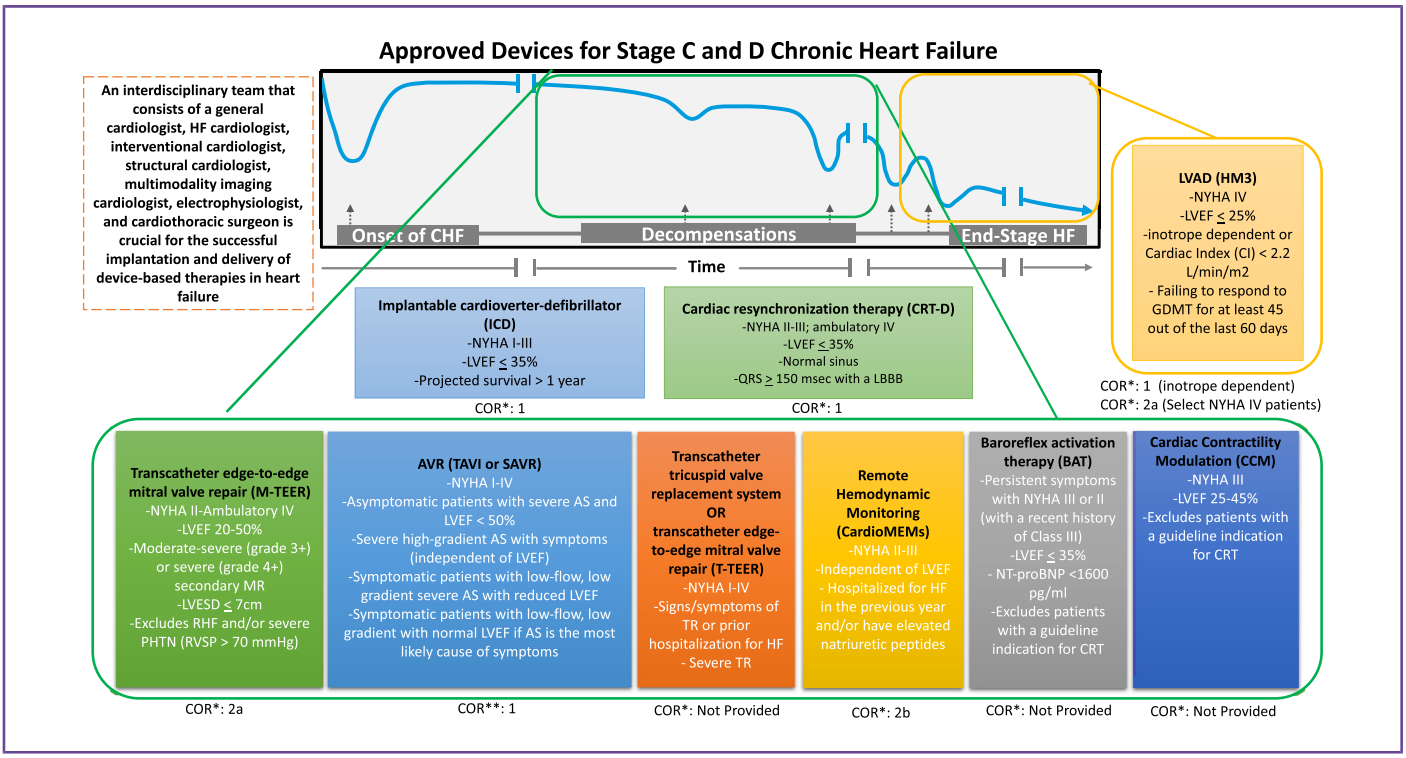

Fig. 1. Conceptual framework of device therapy in the management of heart failure.

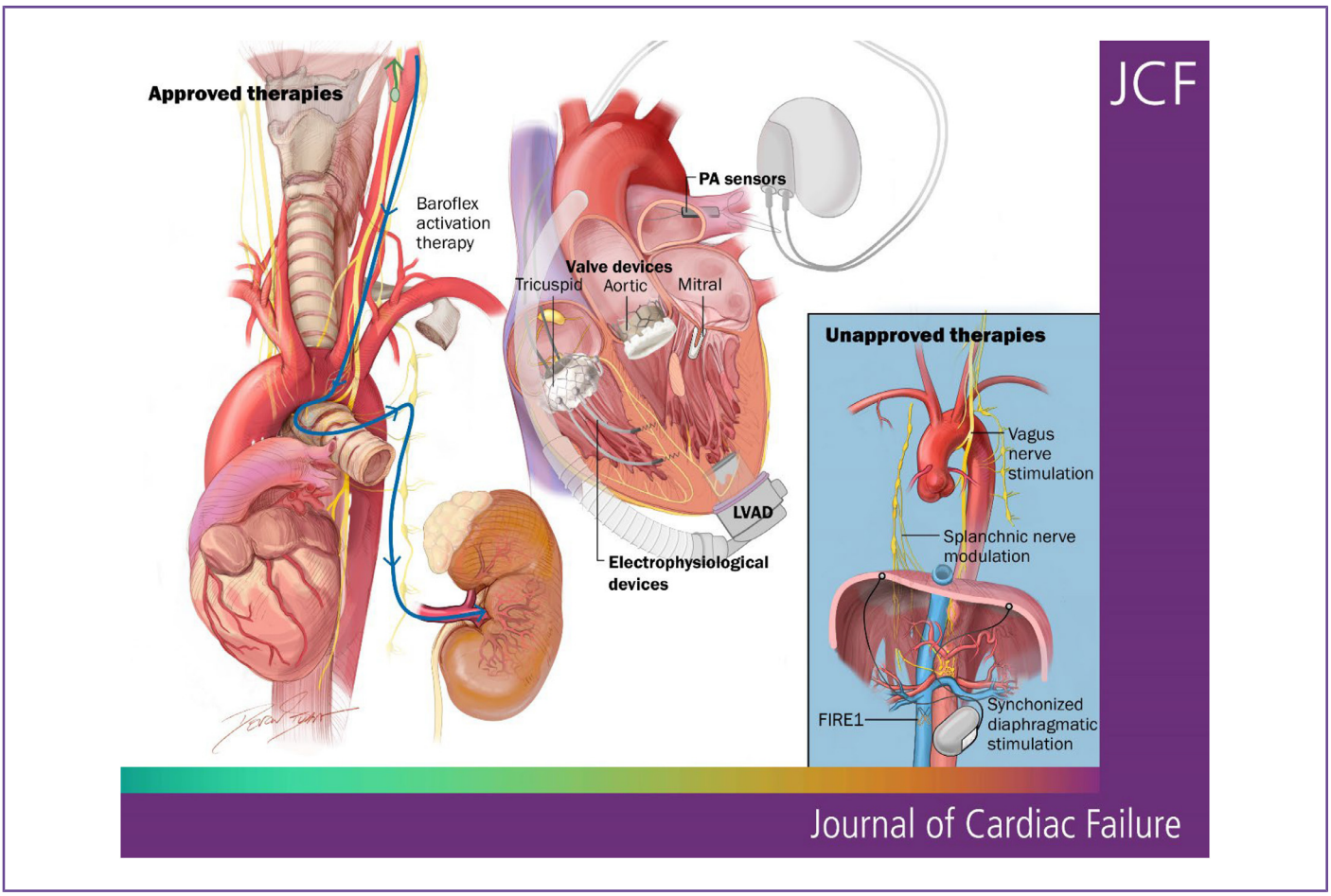

Fig. 2. Device-based options: approved and in the pipeline.

conventional approaches. It is also important to note that device therapy can facilitate the introduction and up-titration of drug therapy in a certain population of patients with HF (eg, patients with bradycardia). A personalized approach to sequencing HF therapies (both pharmacological and device-based therapies) may accelerate the delivery of the full potential of these therapies and should be investigated.[13]

Approved Devices for the Treatment of HF

Cardiac Contractility Modulation

Cardiac contractility modulation (CCM) using the IMPULSE Optimizer (Impulse Dynamics, Mount Laurel, NJ) provides relatively high voltage, nonexcitatory electrical impulses that generate long-acting stimulation of the right ventricle (RV) interventricular septum during the absolute refractory period in diastole.[14] CCM drives normalization of the expression of genes, including proteins involved with calcium cycling and the myocardial contractile machinery.[15,16] This novel mechanism improves contractility via alterations in calcium handling without increasing myocardial oxygen requirements.[17] Device implantation resembles a traditional transvenous pacemaker system but uses 2 RV lead (Fig. 3).

The safety and efficacy of CCM has been examined in several studies.[18–21] The randomized FIX-HF-5 trial (Evaluate Safety and Efficacy of the OPTIMIZER System in Subjects With Moderate-to-Severe Heart Failure) did not meet its primary endpoint, based on ventilatory anaerobic threshold, but it did show a benefit for CCM over optimal medical therapy regarding peak oxygen consumption (pVO_2) and quality-of-life measures at 6 months.[21] The FIX-HF-5 confirmatory study (FIX-HF-5C) was designed to confirm the positive subgroup analysis from the prior FIX-HF-5 trial[20] by prospectively testing the efficacy and safety of CCM in patients with NYHA functional class III or IV symptoms and LVEF ranging from 25%–45%. A total of 160 patients with QRS duration < 130 msec were randomized to continued medical therapy (control, n = 86) or CCM (treatment, n = 74, unblinded) for 24 weeks. Peak VO_2 (primary endpoint), Minnesota Living With Heart Failure questionnaire (MLWHFQ), NYHA functional class, and 6-minute hall walk were measured at baseline and at 12 and 24 weeks. The difference in peak VO_2 between groups was 0.84 (95% Bayesian credible interval: 0.123–1.552) mL O_2/kg/min, satisfying the primary endpoint. MLWHFQ ($P < 0.001$), NYHA functional class ($P < 0.001$), and 6-minute hall walk ($P = 0.02$) were all better in the treatment vs the control group. Overall, CCM proved to be safe, to improve exercise tolerance and quality of life in the specified group of patients with HF, and to lead to fewer hospitalizations due to HF.[20]

Impulse Dynamics received FDA approval in 2019 for patients with NYHA class III symptoms, despite GDMT, who do not have indications for CRT, including a narrow underlying QRS along with an LVEF between 25% and 45%. In the 2022 AHA/ACC/HFSA guidelines, it is stated, "Four RCTs have shown benefits in exercise capacity and quality of life (QOL) but, as of yet, no benefits in death or hospitalizations."[2] A specific use recommendation is not provided. The 2021 ESC HF guideline states CCM use "was associated with a small improvement in exercise tolerance and QOL"; however, like the 2022 AHA/ACC/HFSA guideline document, a specific guideline recommendation was not provided.[22] It is important to note that despite its FDA approval, the device currently has a Current Procedural Terminology (CPT) category III code that typically precludes reimbursement from non-Medicare plans, because these plans.

The potential roles of CCM in the settings of HFmrEF and HFpEF populations (NCT05064709) and in combination with ICD therapy (NCT05855135) are currently under investigation.

Baroreflex Activation Therapy

Sympatho-vagal imbalance is well known to predict adverse prognoses and symptoms in HFrEF. Baroreflex activation therapy (BAT) is delivered by a pacemaker-like device (Barostim Neo System, CVRx, Minneapolis, MN) that generates electrical stimulation of the carotid sinus with the intent of limiting sympathetic nervous system activation and enhancing parasympathetic nervous system effects. The system consists of an infraclavicular, subcutaneously implanted pulse generator connected to a 2 mm electrode placed on the carotid sinus that stimulates the baroreceptors, creating a signal that dampens sympathetic activity and boosts parasympathetic activity (Fig. 3, B).[23–25]

The BeAT-HF (Baroreflex Activation Therapy for Heart Failure) trial was a multicenter, prospective, randomized, controlled trial. Subjects were randomized 1:1 to receive either BAT plus optimal medical management (BAT group) or optimal medical management alone (control group).[26] Four patient cohorts were created from 408 randomized patients with HFrEF by using the following enrollment criteria: current NYHA functional class III or II with a recent history of class III; EF ≤ 35%; stable medical management for ≥ 4 weeks; and no class I indication for CRT.[26]

The intended-use population (1 of the 4 patient cohorts) that reflected the U.S. FDA-approved instructions for use (enrollment criteria plus NT-proBNP < 1600 pg/mL) consisted of 245 patients followed-up for 6 months (120 in the BAT group and 125 in the control group). BAT proved to be safe, with a major adverse neurological or cardiovascular system or procedure-related free event rate of 97% (95% CI: 93%–100%; $P < 0.001$). In the BAT group vs the control group, QOL score using MLWHFQ improved ($\Delta = -14.1$; 95% confidence interval [CI]: -19 to

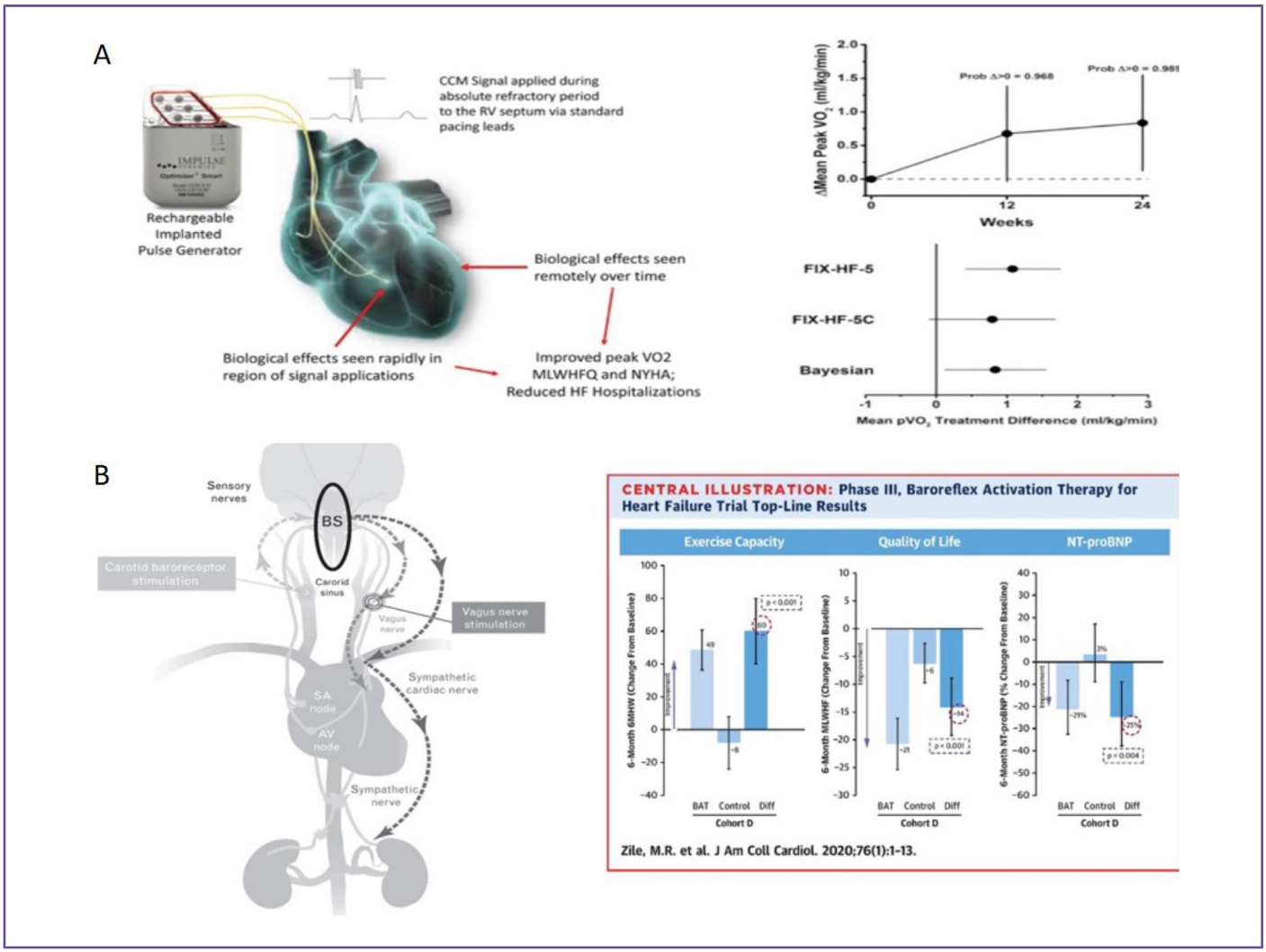

Fig. 3. A, Cardiac contractility modulation therapy delivers biphasic electrical signals to the septum of the right ventricle during the absolute refractory period, which results in myocardial changes with enhancement of contractility. B, Baroreflex activation therapy activates baroreceptors, which inhibits the rostral ventrolateral medulla with subsequent decrease in the sympathetic output.

-9; $P < 0.001$), 6MHW distance increased (Δ = 60 m; 95% CI: 40−80 m; $P < 0.001$), NT-proBNP levels decreased (Δ = -25%; 95% CI: -38% to -9%; $P = 0.004$).[26]

Based on the BeAT-HF study, the FDA granted premarket approval in 2019 to the Barostim Neo activation therapy to improve symptoms of HF, QOL, 6-minute hall walk, and functional status for patients who remain symptomatic (NYHA class III or II with recent histories of NYHA class III) despite GDMT and have an LVEF ≤ 35% with NT-proBNP < 1600 pg/mL and excluding patients indicated for CRT. This was the first FDA-approved neuromodulation technology for HFrEF, and the FDA required the manufacturer to continue the randomized BeAT-HF study to examine mortality and HF hospitalization rates after BeAT-HF. The results of the extended BeAT-HF were recently presented at the Technology and Heart Failure Therapeutics 2023 meeting, which showed no statistical difference in the primary endpoint (ie, composite of cardiovascular mortality and HF morbidity) between the 2 groups (relative risk: 0.94 [95% CI: 0.57−1.57]; $P = 0.82$) or in the individual components of the primary endpoint.[27] In a prespecified win ratio analysis using a hierarchical composite of cardiovascular mortality, LVAD/heart transplant, HF hospitalizations, and quality of life using MLWHF, the results were in favor of BAT (win ratio: 1.26 [95% CI: 1.02−1.58]; $P = 0.04$).[27] An additional analysis was performed by Coates et al., who performed an individual patient data meta-analysis on the 2 trials that randomized 545 HFrEF patients to BAT and GDMT or GDMT alone (open label).[28] In all patients, BAT provided a significant improvement in the 6-minute walk distance of 49 m (95% confidence interval [CI] 33, 64), MLWHF QOL of -13 points (95% CI -17, -10), and 3.4 higher odds of improving by at least 1 NYHA class (95% CI 2.3, 4.9) when compared to baseline and 6-month metrics.

A specific recommendation regarding BAT use for HF is not addressed in the 2022 AHA/ACC/HFSA guidelines.[2] In the 2021 ESC guidelines for the diagnosis and

treatment of HF, the following was stated: "Technologies that involve modification of the activity of the autonomic nervous system, e.g. baroreflex activation therapy, have also been shown to offer a modest improvement in effort capacity and QOL. However, currently, the evidence is considered insufficient to support specific guideline recommendations for a reduction in mortality or hospitalization for these and a variety of other implantable electrical therapeutic technologies."[22]

An additional effort to enhance the adoption of BAT is based on the use of a novel and less invasive interventional implantation technique than the standard surgical carotid sinus approach. This minimally invasive technique using a BAT wire Implant Kit and ultrasound guidance to place the stimulation lead near the carotid baroreceptors is currently under investigation (NCT04600791), with enrollment planned in 100 subjects at up to 35 U.S. sites.

Valve Device Interventions for the Treatment of HF

In patients with HF and valvular heart disease, it is recommended (class 1) that management be directed by a multidisciplinary team in accordance with clinical practice guidelines to prevent worsening of HF and adverse clinical outcomes.[2,29] In patients with valvular heart disease, HF is multifactorial, HF-related events are prevalent, and morbidity and mortality can be significantly improved by valve interventions.[30]

Devices to Treat Aortic Stenosis

In patients with aortic stenosis (AS) and HFrEF, a surgical risk assessment guides team decision making on surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR). Anatomy of the valve is the most important determinant in decision making, along with lifetime management of aortic stenosis. Although surgical risk can be defined as low, intermediate-to-high or prohibitive, TAVR can be considered across all risk profiles in anatomically appropriate candidates.[30,31] There are 3 valves that are currently approved by the FDA for TAVR: the EvolutFX TAVR system (Medtronic, Minneapolis, MN), which is supra-annular and self-expandable, and Sapien S3 Ultra valve system (Edwards Lifesciences, Irvine, CA), which is a balloon-expandable transcatheter heart valve, and Navitor valve (Abbott Industries, Abbott Park, IL), which is a self-expanding intra-annular device. All 3 device types have evolved; they are easier to use, have fewer complications and have favorable short- and long-term outcomes when compared with SAVR in randomized clinical trials.

There are very few randomized head-to-head trials that permit comparing device technologies, and despite inherent differences in expansion mode, stent frame and leaflet characteristics in the device types, clinical outcomes and, particularly, mortality rates have been considered comparable. There are no data to suggest a more favorable safety and effectiveness profile in a particular device type in patients with underlying HF.

In patients with HFrEF, moderate AS has been associated with a marked incremental risk of mortality.[32,33] The TAVR UNLOAD (NCT02661451) is an international, multicenter, randomized, open-label, clinical randomized control trial comparing the efficacy and safety of TAVR with the Edwards SAPIEN 3 Transcatheter Heart Valve in addition to optimal GDMT vs GDMT alone in patients with moderate AS.[34] In this study, moderate AS was defined by a mean transaortic gradient $\geq$ 20 mmHg and $<$ 40 mmHg, and an aortic valve area $>$ 1.0 cm^2 and $\leq$ 1.5 cm^2 at rest or after dobutamine stress echocardiography and reduced ejection fraction. The results are expected to be presented soon.

Transaortic Valve Intervention in Aortic Regurgitation

Severe aortic regurgitation (AR) associated with symptoms (stage D) or asymptomatic AR combined with a LVEF $<$ 55% or undergoing another cardiac surgery is a class 1 recommendation for SAVR.[29] Transcatheter aortic valve implantation (TAVI) for isolated chronic AR is challenging for multiple reasons, including dilation of the aortic annulus and aortic root and lack of sufficient leaflet calcification.[35] Risks of TAVI for treatment of AR include transcatheter valve migration and significant paravalvular leak.

TAVI maybe considered in carefully selected patients with severe AR and HF who have prohibitive surgical risks and in whom valvular calcification and annular size are appropriate for a transcatheter approach.[29] Two transcatheter valves designed to treat AR are the J-Valve (JC Medical, Pawtucket, RI) and the JenaValve (JenaValve Technology, Irvine, CA).[35,36] The J-Valve has unique self-aligning anchor rings combined with a self-expanding valve that directly grasps the aortic valve leaflets and provides solid anchoring to minimize the issue of valve embolization.[35] The JenaValve (JenaValve Technology, Irvine, CA) is a porcine root self-expanding valve on a nitinol frame with 3 integrated locators similar to the J-Valve.[36] The locators align the device with the native valve leaflet anatomy and act as a strut onto which the nitinol frame is expanded to ensure clipping of the device to the native leaflets. This engagement mechanism allows anchoring of the valve independent of cusp calcification, making it an ideal design for treatment of pure AR.

These devices have not been approved by the FDA; however, the J Valve is available under "expanded access" for compassionate use (NCT03876964), and the JenaValve is under investigational device exemption evaluation in a clinical trial (NCT02732704), both only as trans-

femoral devices. The Jena Valve has completed the trial, and the findings are under FDA review for the approval process.

Devices to Treat Mitral Regurgitation

Transcatheter Mitral Valve Edge-to-Edge Repair. Optimizing GDMT and reassessing MR severity remains critically important, because GDMT can improve secondary MR in those with left ventricular (LV) dysfunction and obviate the need for surgical or device intervention.[2] Two RCTs of transcatheter mitral valve edge-to-edge repair (mTEER) in patients with HFrEF and severe secondary MR have been performed.[37,38] The principle of MitraClip device (Abbott Vascular, Santa Rosa, CA) is based on the Alfieri edge-to-edge repair, where the anterior and the posterior leaflets are grasped and attached at the location of the regurgitation jet, thus creating a double orifice (Fig. 4, A, B).

The MITRA-FR (Multicentre Study of Percutaneous Mitral Valve Repair MitraClip Device in Patients With Severe Secondary Mitral Regurgitation) showed no benefit of mTEER over GDMT in reducing death or hospitalization.[38] In contrast, the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial showed significant reduction in HF and all-cause mortality in patients treated with mTEER and GDMT compared with GDMT alone.[37] Data from a 5-year follow-up of outcomes in the COAPT trial have been published and highlight a continued lower rate of hospitalization for HF and lower all-cause mortality through 5 years

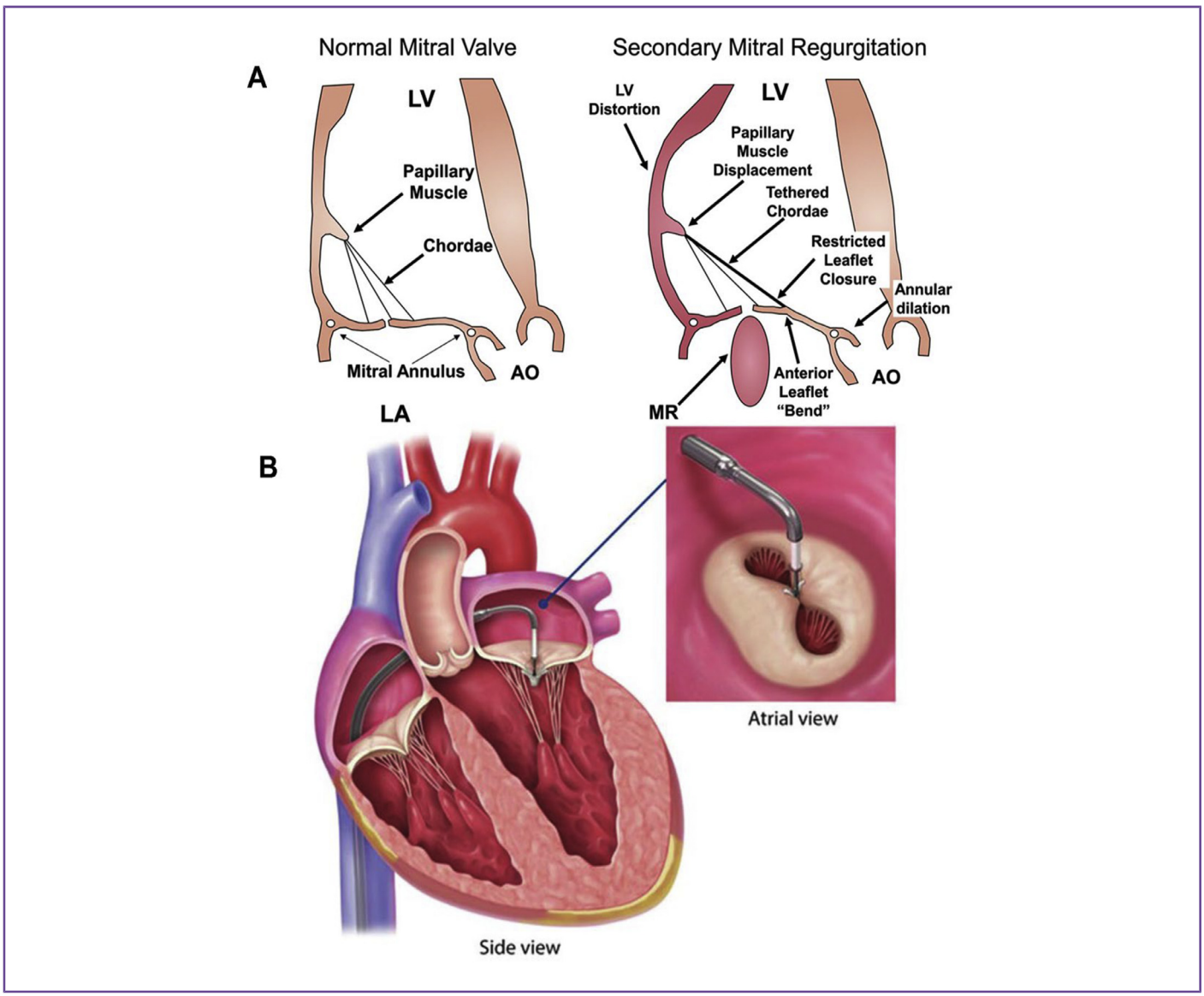

Fig. 4. Annular dilation, leaflet tethering, papillary muscle desynchrony, and valve tenting in heart failure can result in the development of secondary mitral regurgitation. Transcatheter edge-to-edge repair of the mitral valve can reduce mitral regurgitation and improve outcomes in patients with heart failure and secondary mitral regurgitation.

of follow-up when compared to medical therapy alone (death or hospitalization for HF within 5 years occurred in 73.6% of the patients in the device group and in 91.5% of those in the control group [hazard ratio, 0.53; 95% CI, 0.44−0.64]).[39] Significant differences between these 2 studies have been reported and include that enrolled patients in the MITRA-FR trial had greater degrees of LV enlargement and less severe MR compared to those in COAPT.[40]

Eligible patients in COAPT had ischemic or nonischemic cardiomyopathy with LVEFs of 20%−50%, moderate-to-severe (grade 3+) or severe (grade 4+) secondary MR, and remained in NYHA class II, III or ambulatory IV despite GDMT and CRT, where appropriate. Important exclusion criteria included the following: anatomy on transesophageal echocardiography that precluded device placement, stage D HF, LV end-systolic dimension > 7 cm, severe pulmonary hypertension, defined as a systolic pulmonary artery pressure > 70 mmHg, moderate or severe symptomatic RV failure, and hypotension requiring inotrope or temporary mechanical support use.[37]

Efforts to further reduce MR and optimize procedural outcome in challenging mitral valve anatomies include third-generation MitraClip devices. The Global EXPAND (Siponimod versus Placebo in Secondary Progressive Multiple Sclerosis) study (NCT03502811) is a post-market, prospective, observational, multicenter study of the commercially available third-generation MitraClip NTR and XTR M-TEER system. The MitraClip NTR (Abbott Industries, Abbott Park, IL) has a 9 mm arm length and a 5 mm width, and the MitraClip XTR a 12 mm arm length and a 5 mm width, which permits easier grasp and better reach.[40] Although MR reduction was comparable between NTR-only vs XTR-only treated patients, fewer XTR clips were required for achieving significant MR reduction.[40] mTEER carries a 2a recommendation in selected patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF < 50%) who have persistent symptoms (NYHA class II, III or IV) while on optimal GDMT, based on the 2022 AHA/ACC/HFSA and most recent valve guidelines.[2,29] MV (mitral valve) surgery is recommended for those with severe MR and LVEF > 50% and for those with contraindications to mTEER as a 2b recommendation.[2] There is an evolving body of data that examines mTEER in patients with secondary severe MR and more advanced HF profiles than that supported by COAPT inclusion and exclusion criteria.[41,42] Although mTEER has been associated with significantly lower all-cause mortality and a composite of mortality or HF admissions compared to medical therapy in those with cardiogenic shock, the data remain limited, and 1-year outcomes remained poor (~ 35%) in those treated with mTEER coded with underlying cardiogenic shock and/or supported by inotrope and/or temporary mechanical support based on an analysis from The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry.[41]

It remains important to highlight that in patients with symptomatic severe primary MR, regardless of LV function, MV surgery is a class 1 indication, with MV repair recommended in preference to MV replacement when the anatomical cause of MR is degenerative disease, and if a successful and durable repair is possible.[29] mTEER with the MitraClip system (Abbott) was approved by the FDA for commercial use in patients with severe symptomatic, primary MR who are at prohibitive surgical risk; this is a Class 2a recommendation.[2] The ongoing PRIMARY (Percutaneous or Surgical Mitral Valve Repair) and REPAIR MR (Percutaneous Mitra- Clip Device or Surgical Mitral Valve REpair in Patients With PrImaRy MItral Regurgitation Who Are Candidates for Surgery) clinical trials will be crucial in comparing the safety and effectiveness of mTEER to surgical mitral valve repair for treatment of primary MR with contemporary techniques and treatment strategies.[43]

Devices to Treat Tricuspid Regurgitation

Severe or progressive tricuspid regurgitation (TR) is a complex disease that results in RV volume overload, leading to RV failure, and is associated with poor long-term outcomes. Most cases of severe TR are secondary to left-sided heart disease, pulmonary hypertension and/or a dilated RV. Current transcatheter treatment options include leaflet approximation, direct annuloplasty, transcatheter valve replacement, and heterotopic caval valve implantation. The field of transcatheter tricuspid valve replacement (TTVR) continues to evolve with systems using orthotopic valve implantation with the recent FDA approval of the EVOQUE valve (Edwards Lifesciences, Irvine, CA).[44]

Two separate trials, TRILUMINATE Pivotal and TRISCEND II, add to the growing body of evidence surrounding TV repair in patients with severe TR. TriClip, similar to the MitraClip, is based on TEER (leaflet approximation) and is a minimally invasive system. The TRILUMINATE Pivotal Trial (NCT03904147) was a randomized, open-label trial of 350 subjects that investigated the effectiveness and safety of the TriClip device in symptomatic patients with severe TR and NYHA class II or more despite optimal medical therapy. Tricuspid TEER was safe for patients with severe TR, reduced the severity of TR, and was associated with an improvement in QOL. However, the incidence of death or tricuspid-valve surgery and the rate of hospitalization due to HF did not differ between the groups.[45] Based on the results of the TRILUMINATE Pivotal Trial, the FDA approved TriClip in April 2024 for patients with symptomatic severe TR who are on optimal medical therapy, are at intermediate or high risk for surgery, and in whom TEER is expected to reduce severity of TR to moderate or less, as determined by a multidisciplinary team in April 2024.

The TRISCEND II trial examined the safety and effectiveness of TTVR in the EVOQUE system based on the first

150 patients enrolled in the trial. While the rate of major adverse events was less than the expected rate (27.4% vs 43.8%), early findings showed TTVR with EVOQUE effectively eliminated TR in a vast majority of patients, despite more than 55% having massive or torrential TR and the remainder being categorized as severe.[46] The FDA approved this device as the first transcatheter tricuspid valve-replacement device based on results from the TRISCEND II trial. In patients with severe TR, the device significantly improved TR grade and led to meaningful improvements in functional status and symptoms. The EVOQUE system received CE Mark in 2023 and FDA approval in 2024, making it the world's first transcatheter valve-replacement therapy to receive regulatory approval to treat TR. Careful decision making is key for patients being considered for TTVR, because it may have implications for future transvenous devices.

Valve guidelines focus largely on surgical TV interventions, given the paucity of data concerning transcatheter TV repair and/or replacement and that the 2 studies discussed above were completed only recently. The 2021 Valvular Heart Disease guidelines of the European Society of Cardiology give a 2b, level C recommendation for transcatheter treatment of severe symptomatic TR in inoperable patients.[31] Contemporary outcome observations will likely influence future guideline recommendations.

Remote Monitoring Devices in Heart Failure

It is well established that elevated cardiac ventricular filling pressures at rest and with changes over time are associated with the morbidity and mortality rates that define HF, regardless of underlying LVEF.[47–49] Examples of device technologies for remote monitoring of HF include devices to monitor weights and vital signs, multiparameter scoring of risk through implanted rhythm ICD and CRT devices, lung congestion based on dielectric sensing through vest devices, radiofrequency through adhesive patch technology, thoracic impedance through device leads, and direct measurement of cardiac pressures by left atrial and pulmonary artery (PA) sensors.[49] PA pressure monitoring is the device technology with the most robust evidence for monitoring patients with HF.[49,50]

CardioMEMS HF System

CardioMEMS (CardioMEMS HF System, Abbott, Sylmar, CA) is the most extensively studied system among remote monitoring devices to guide HF management and prognosis.[47–49] It is currently the only invasive HF remote monitoring sensor with FDA approval and CE mark. The CardioMEMS device is an implantable wireless sensor that is placed in the left lower lobe pulmonary artery (through a 12-Fr catheter-delivery system) and is capable of measuring pulmonary artery pressure.[47] There have been 3 RCTs testing the safety and efficacy of this system.[47,49,51] The CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA functional class III patients with HF (CHAMPION) trial was an RCT conducted in 64 centers in the U.S.[47] Trial investigators found that hemodynamic-guided pharmacotherapy reduced HF hospitalization risk in outpatients (rate of HF related hospitalizations at 6 months: 0.32 vs 0.44; HR: 0.72; 95% CI 0.60–0.85; $P < 0.01$).[47]

The randomized arm of the hemodynamic-guided management of Heart Failure (GUIDE-HF) trial was a multicenter, single-blind study at 118 centers in the U.S. and Canada.[51] Patients with NYHA functional class II–IV chronic HF, all ejection fractions, and either a recent hospitalization due to HF or elevated natriuretic peptide levels were randomly assigned (1:1) to either hemodynamic-guided HF management or a usual-care control group. The primary endpoint was a composite of all-cause mortality and total HF events (HF hospitalizations and urgent HF hospital visits) at 12 months. The cumulative incidence of HF events was not reduced by hemodynamic-guided management (0.85, 0.70–1.03; $P = 0.096$) in the overall study analysis but was significantly decreased in the pre-COVID-19 impact analysis (0.76, 0.61–0.95; $P = 0.014$).[51] As in the CHAMPION trial, freedom from device- or system-related complications was excellent, with 1014 (99%) of 1022 patients free of device- or system-related complications. The pre-COVID-19 impact analysis indicated a possible benefit of hemodynamic-guided management on the primary outcome in the pre-COVID-19 period, driven primarily by a lower HF hospitalization rate compared with the control group.[51] Based on a more recent analysis of the Guide-HF study's patients, hemodynamically-guided HF management decreases HF-related endpoints across the EF spectrum in an expanded patient population of patients with HF, including those with NYHA class II–IV with either previous hospitalizations or natriuretic peptide elevations.[48] Research findings led to the expansion of the 2014 approval of this device, issued by the FDA for patients meeting the CHAMPION study criteria and extended to patients with NYHA class II or elevated natriuretic peptide levels.

More recently, MONITOR-HF (Monitoring of Pulmonary Artery Pressures in Patients With Chronic Heart Failure) was an open-label, randomized trial, completed in 25 centers in The Netherlands; it represents the first investigator-initiated study of remote pulmonary artery pressure monitoring performed in Europe.[49] The study randomized 348 patients to either the CardioMEMS-HF group (n = 176 [51%]) or the control group (n = 172 [49%]). Eligible patients had chronic HF of NYHA class III and a previous HF hospitalization, irrespective of ejection fraction. Hemodynamic monitoring substantially improved QOL (primary efficacy endpoint was the mean change in the Kansas City Cardiomyopathy Questionnaire) and reduced HF hospitalizations (secondary endpoint).[49] The between-group difference in 12-month KCCQ overall score changes was 7.1

Table 2 Approved and investigational devices for heart failure

Device categories	Mechanistic target	Device (company)	Suggested Solution	FDA Approval Status	Trial Leading to FDA Approval	Ongoing Trials
Remote monitoring devices	Increased intracardiac filling pressure	1. CardioMEMS system (Abbott) 2. Cordella system (Endotronix)	Continuous pulmonary artery pressure monitoring	Y	CHAMPION trial and GUIDE-HF for CardioMEMS; PROACTIVE-HF for Cordella	
		1. SAVE Sensor System (Acorai) 2. Cardiotag (Cardiosense)	Using seismocardiography, phonocardiography, photoplethysmography, and electrocardiograph data to noninvasively estimate intracardiac pressure	N	NA	
		Fire1 system	Inferior vena caval size monitoring	N	NA	1.FUTURE-HF (NCT04203576) 2. FUTURE-HF2 (NCT05763407)
	Surrogates of volume status (eg, third heart sound, thoracic dielectric sensing, and thoracic impedance) and other parameters (eg, resting heart rate, heart rate variability, respiratory rate statistics)	1. HeartLogic™ (Boston Scientific) 2. TriageHF™ (Medtronic) 3. HeartInsight (Biotronik)	Remote monitoring using cardiovascular implantable electronic devices	Y (approved for other inidcations but not for remote monitoring indication)	NA	
	Cardiac acoustic biomarkers, such as electromechanical activation time (the time from QRS onset to the first heart sound interval) and the third heart sound strength	Audicor (Inovise Medical)	Automated acoustic cardiography systems	N	NA	
	Radiofrequency to measure thoracic fluid for early detection of changes in pulmonary fluid levels assessed by a patch-based sensor	Zoll Heart Failure Management System	Wearable patch-based sensor	N (FDA cleared)	NA	
	Physiological parameters, such as weight, ECG, impedance plethysmography, and ballistocardiography signals assessed by standing on a scale	Bodyport Cardiac Scale	Weight scale with ability to measure multiple hemodynamic parameters	N (FDA cleared)	NA	

(*Continued*)

Table 2. (*Continued*)

Device categories	Mechanistic target	Device (company)	Suggested Solution	FDA Approval Status	Trial Leading to FDA Approval	Ongoing Trials
	Cardiopulmonary indicators, such as diastolic heart sound strength, heart sounds, heart rate, relative tidal volume, temperature, thoracic impedance, respiratory rate, body posture, and single-lead ECG assessed using a wearable sensor for cardiopulmonary monitoring	Sensinel Cardiopulmonary System	Wearable cardiopulmonary monitoring device	N (FDA cleared)	NA	
Valvular Device-Based Therapies	Left ventricular outflow obstruction due to aortic stenosis leading to adverse left ventricular remodeling	1. Evolut™ FX TAVR (Medtronic) 2. Sapien S3 Ultra valve (Edwards Lifesciences) 3. Navitor valve (Abbott)	Transcatheter aortic valve replacement	Y	PARTNER, PARTNER 2, and PARTNER 3 trials	1. Evolut™ EXPAND TAVR II (NCT05149755) 2. ENVISION (NCT05932615)
	Hypertrophy and dilatation of the left ventricle to allow for increased left ventricular stroke volume due to chronic aortic regurgitation	1. J-Valve (JC Medical) 2. JenaValve (JenaValve Technology)	Transcatheter aortic valve replacement	N	NA	1. JVTF EFS (NCT06034028) 2. J-Valve Compassionate Use (NCT03876964) 3. ALIGN-AR (NCT04415047) 4. ALIGN-AR EFS TRIAL (NCT02732704)
	Mitral annular dilatation, leaflet tethering, papillary muscle desynchrony, and valve tenting resulting in mitral regurgitation	MitraClip™ (Abbott)	Edge-to-edge mitral valve repair	Y	COAPT trial	1. Reshape-HF2 (NCT02444338) 2. EVOLVE-MR (NCT03891823)
		Carillon mitral contour system (Cardiac Dimensions)	Indirect mitral annuloplasty system.	N	NA	1. EMPOWER Trial (NCT03142152)
		1. Intrepid (Medtronic) 2. Tendyne (Abbott) 3. Sapien M3 (Edwards Lifesciences)	Transcatheter mitral valve replacement	N	NA	1. APOLLO (NCT03242642) 2. SUMMIT (NCT03433274) 3. ENCIRCLE (NCT0415329)
	Tricuspid regurgitation leading to progression of right heart failure and/or right heart failure leading to tricuspid regurgitation	TriClip™ (Abbott)	Edge-to-edge tricuspid valve repair	Y	TRILUMINATE Pivotal Trial	
		1. EVOQUE (Edwards Lifesciences) 2. Interpid TTVR (Medtronic)	Transcatheter tricuspid valve replacement system	Y (only EVOQUE)	TRISCEND II (for the EVOQUE system)	TTVR Early Feasibility Study (NCT04433065)

(*Continued*)

Table 2. (*Continued*)

Device categories	Mechanistic target	Device (company)	Suggested Solution	FDA Approval Status	Trial Leading to FDA Approval	Ongoing Trials
Autonomic Modulators	Overactivation of the sympathetic nervous system and decreased parasympathetic nervous system activity	Barostim neo System™ (CVRx, Inc)	Baroreceptor stimulation	Y	BeAT-HF	
		MobiusHD	Endovascular baroreflex amplification	N	NA	HF-FIM (NCT04590001)
	Overactivation of the sympathetic nervous system and decreased parasympathetic nervous system activity	VITARIA systems (LivaNova)	Vagus nerve stimulation	N	NA	
	Disrupted intravascular fluid distribution in heart failure	Satera Ablation Systems (Axon Therapies)	Splanchnic nerve modulation	N	NA	
Electrophysiological Modulators	Abnormal intracellular calcium handling of the cardiomyocyte	Optimizer Smart system (Impulse Dynamics)	Biphasic, long-duration, high-voltage electrical signal delivered to the septum of the right ventricle during the absolute refractory period	Y	FIX-HF-5C	PAS (NCT03970343)
	Remodeling of cardiomyocytes	Electrical microcurrent therapy with C-MIC system (Berlin Heals)	Microcurrent stimulation of cardiomyocytes resulting in intracellular and extracellular changes with reverse remodeling of cardiomyocytes	N	NA	
Respiratory Modulators	Alteration of intrathoracic pressure	VisONE asymptomatic diaphragmatic stimulation device (VisCardia)	Diaphragmatic stimulation pulses gated with cardiac cycles leading to modulation of intrathoracic pressure and enhancement of preload, afterload, and stroke volume	N	NA	
	Central sleep apnea in heart failure	remedē System (Respicardia)	Phrenic nerve stimulation	Y	The remedé System Pivotal Trial Study	remedē System Therapy Study (NCT03884660)

(*Continued*)

Table 2. (*Continued*)

Device categories	Mechanistic target	Device (company)	Suggested Solution	FDA Approval Status	Trial Leading to FDA Approval	Ongoing Trials
Structural device-based interventions	Increase in the left atrial filling pressures with exercise	InterAtrial Shunt Device (IASD, Corvia Medical) · V-Wave® interatrial shunt device · Occlutech AFR	Inter-atrial, left-right shunt	N	NA	1. RESPONDER-HF (NCT05425459) 2. Alleviant ALLAY-HF (NCT05685303)
	Increased basal left ventricle and mitral annular dimensions	· AccuCinch (Ancora Heart)	Transcatheter direct mitral valve annuloplasty and ventriculoplasty system	N	NA	CorCinch-EU Study (NCT03183895)
	Left ventricular remodeling in heart failure	ReVivent TC (BioVentrix)	Left ventricular reconstruction	N	NA	ALIVE (NCT02931240)
	Distribution of mitral valve geometry and left ventricle dilation	V-sling system (Cardiac Success Ltd)	Transcatheter ventricular repair system to reapproximates the papillary muscles	N	NA	
		Carillon mitral contour system	Transcatheter coronary sinus—based mitral annuloplasty	N	NA	EMPOWER (NCT03142152)
Durable mechanical circulatory support	End-stage left ventricular heart failure	1. First-generation devices: (Heartmate I) 2. Second-generation devices (Heartmate II) 3. Third generation devices (HeartWare and Heartmate 3	Left ventricular assist devices	Y	REMATCH trial (for HeartMate I); HeartMate II trial (for HeartMate II); ADVANCE trial (for HeartWare); and MOMENTUM 3 (for HeartMate 3)	
		Next-generation durable mechanical circulatory support devices (investigational devices): 1. BrioVAD: a compact LVAD with a centrifugal totally magnetically levitated long blade rotor, a flat HQ curve (ie, allows for intrinsic flow pulsatility), and a narrow and flexible driveline, and a small outflow cannula 2. BiVACOR: a compact continuous flow, electrically powered total artificial heart 3. FLOWMAKER (FineHeart): a fully implantable cardiac output management system 4. CorWave: a fully implanted LVAD that uses wave membrane technology to reproduce physiological flow pulsatility	Left ventricular assist devices and total artificial hearts	N	NA	

[95% confidence interval (CI), 1.5−12.8; $P = 0.013$], with a change from baseline of +7.0 in the CardioMEMS-HF group ($P = 0.0014$) and -0.1 in the control group ($P = 0.97$). Pulmonary artery pressure monitoring also reduced total HF hospitalizations by 44% compared with standard care (117 vs 212 events; hazard ratio, 0.56; 95% CI 0.38−0.84; $P = 0.0053$), with a concomitant reduction in mean pulmonary artery (PA) pressure values (33.3 mmHg at baseline vs 24.9 mmHg at 12-month follow-up; difference -8.4 mmHg; $P < 0.0001$).[49]

According to the AHA/ACC/HFSA HF guideline, in selected adult patients with NYHA class III HF and histories of HF hospitalization in the past year or elevated natriuretic peptide levels, on maximally tolerated GDMT, the usefulness of wireless monitoring of PA pressure by an implanted hemodynamic monitor to reduce the risk of subsequent HF hospitalizations is uncertain (2b recommendation).[2] The 2021 ESC HF guideline provides a similar 2b recommendation, stating, "monitoring of pulmonary artery pressure using a wireless hemodynamic monitoring system may be considered in symptomatic patients with HF in order to improve clinical outcomes."[22] Based on the aggregate evidence to date (CHAMPION, GUIDE-HF, MONITOR-HF, and prior comparable device-based, pressure-monitoring strategies) a strategy targeting filling pressures represents a fundamental determinant of decreasing HF hospitalization risk; these data, taken together, are expected to influence a future higher guideline recommendation for use.[50,52]

Durable LVADs to Treat Advanced Heart Failure

LVADs are a safe and effective therapy to prolong survival and improve QOL and functional capacity for selected patients with advanced HF.[53,54] Currently, the HeartMate3 (HM3; Abbott) is the only FDA-approved durable LVAD for use in adults. Based on a randomized control trial (the Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HM3 (MOMENTUM 3) and registry data, HM3 mag-lev technology compared to older LVADs was associated with greater 1- and 5-year survival rates and greater freedom from hemocompatibility-related adverse events, including gastrointestinal bleeding, stroke and device malfunction/pump thrombus.[53,54] A reduction in bleeding events has been further observed with the avoidance of aspirin in addition to the use of vitamin-K antagonist (VKA), based on the international, randomized, double-blind, placebo-controlled study of aspirin (100 mg/d) vs placebo with VKA therapy in patients with advanced HF supported by the HM3.[55]

The current 1- and 5-year post-HM3 implant overall survival estimates are between 83% and 86% and 58% and 64%, respectively.[53,56,57] The HM3 risk score (HM3RS) developed and validated by incorporating preimplant factors (age, prior coronary artery bypass surgery or valve procedure, sodium, blood urea nitrogen, left ventricular end diastolic dimension, and RAP/PCWP ratio) to reliably predict 1-year and 2-year mortality post-HM3 implant permits successful stratification into tertiles, with higher-than-average (91% ± 2%), average (83% + 3%), and lower-than-average (68% ± 4%) 2-year survival rates.[58] Independent predictors of 5-year all-cause mortality conditional on discharge from the index hospitalization include postimplant index hospitalization hemocompatibility-related adverse events, postimplant index hospitalization, serious ventricular arrhythmias, and eGFR) < 60 mL/min/1.73 m^2 at discharge.[65] In patients without these post-implant risk factors plus 2 implant risk factors (prior CABG or valve procedure and elevated blood urea nitrogen) that constituted 35% of the examined cohort in the MOMENTUM 3 pivotal trial, 5-year survival was 77.4%, which was comparable to contemporary post-heart transplant 5-year survival.[65] Contemporary observations can be used to guide LVAD shared decision making in this population of patients.

Based on the AHA/ACC/HFSA HF guideline, in selected patients with advanced HFrEF and NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation was effective in improving functional status, QOL and survival (class 1 recommendation; level of evidence A).[2] In contrast, in select non-inotrope-dependent patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS can be beneficial to improve symptoms, improve functional class and reduce mortality rates (Class 2a recommendation; level of evidence: B-R).[2] Current recommendations are coupled with a value statement defined as uncertain (B-NR) with durable MCS devices associated with low to intermediate economic value based on current costs and outcomes.[2] Based on the ESC HF guidelines, LVAD use was deemed a class 2a recommendation as a bridge to heart transplant candidacy or use as destination therapy.[22] Several other novel devices are currently in various stages of investigation.[9,59]

Summary and Future Directions

Device-based therapies are becoming integral to managing HF, offering a promising avenue to address the high residual risk, overcome certain limitations of drug therapy (eg, adherence and tolerance), and effectively target some of the HF-related pathophysiological alterations that may not be amenable to pharmacological therapy. Despite the growing role of device-based therapies in HF, there exist gaps in the field that necessitate better identification of the ideal patient population by employing clinical, hemodynamic and structural phenotyping of HF. Additionally, establishing a systematic approach to integrate device interventions into the HF management

workflow through evidence-based sequencing strategies is crucial. A large number of device-based therapies are under investigation, and they target a myriad of intra- and extra-cardiac pathologies (Fig. 2). While some therapies may not be proven to be beneficial and safe, a significant number will likely be approved and join the ranks of a rapidly growing field of therapies for patients with HF. Several HF devices are currently being examined to address the unmet needs of patients with HF and to close the residual gap that exits despite use of GDMT; these devices are summarized in Table 2.

Marat Fudim

Disclosures

JDE reports being a consultant/advisor for Abbott, Getinge, Zoll, and the Cleveland Clinic/Amwell. JB reports grant support from Abiomed, Axon Therapies, Ancora Heart, Edwards Lifesciences. Consulting for Aquapass, Axon Therapies, Orchestra Biomedical, Corvia, Edward Lifesciences, Harvi Dynamics, IMPULSE Dynamics, and Zoll Medical. SH reports being a consultant/advisor for Abbott, Abiomed, Evaheart, CareDx, and Natera. MF is a consultant/has ownership interest in Abbott, Ajax, Alio Health, Alleviant, Artha, Audicor, AxonTherapies, Bayer, Bodyguide, Bodyport, Boston Scientific, Broadview, Cadence, Cardioflow, Coridea, CVRx, Daxor, Edwards LifeSciences, Echosens, EKO, Feldschuh Foundation, Fire1, FutureCardia, Galvani, Gradient, Hatteras, HemodynamiQ, Impulse Dynamics, Intershunt, Medtronic, Merck, NIMedical, NovoNordisk, NucleusRx, NXT Biomedical, Orchestra, Pharmacosmos, Presidio, Procyreon, Proton Intelligence, ReCor, Rockley, SCPharma, Shifamed, Splendo, STAT Health, Summacor, SyMap, Verily, Vironix, Viscardia, Zoll. All other authors report no disclosures.

CRediT authorship contribution statement

JERRY D. ESTEP: Writing – original draft, Writing – review & editing. **HUSAM M. SALAH:** Writing – review & editing. **SAMIR R. KAPADIA:** Writing – review & editing. **DANIEL BURKHOFF:** Writing – review & editing. **ANURADHA LALA:** Writing – review & editing. **JAVED BUTLER:** Writing – review & editing. **SHELLEY HALL:** Writing – review & editing. **MARAT FUDIM:** Writing – original draft, Writing – review & editing.

References

1. Bozkurt B, Ahmad T, Alexander KM, et al. Heart failure epidemiology and outcomes statistics: a report of the Heart Failure Society of America. J Card Fail 2023;29:1412–51. https://doi.org/10.1016/j.cardfail.2023.07.006.
2. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2022;145:e895–1032. https://doi.org/10.1161/CIR.0000000000001063.
3. Greene SJ, Butler J, Fonarow GC. Contextualizing risk among patients with heart failure. JAMA 2021;326:2261–2. https://doi.org/10.1001/jama.2021.20739.
4. Anker SD, Butler J, Filippatos G, et al. Empagliflozin in heart failure with a preserved ejection fraction. N Engl J Med 2021;385:1451–61. https://doi.org/10.1056/NEJMoa2107038.
5. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med 2022;387:1089–98. https://doi.org/10.1056/NEJMoa2206286.
6. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019;381:1995–2008. https://doi.org/10.1056/NEJMoa1911303.
7. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020;383:1413–24. https://doi.org/10.1056/NEJMoa2022190.
8. Lee DS, Tu JV, Juurlink DN, et al. Risk-treatment mismatch in the pharmacotherapy of heart failure. JAMA 2005;294:1240–7. https://doi.org/10.1001/jama.294.10.1240.
9. Salah HM, Fudim M, Burkhoff D. Device interventions for heart failure. JACC Heart Fail 2023;11:1039–54. https://doi.org/10.1016/j.jchf.2023.07.002.
10. Baumwol J. I Need Help"—A mnemonic to aid timely referral in advanced heart failure. J Heart Lung Transplant 2017;36:593–4. https://doi.org/10.1016/j.healun.2017.02.010.
11. Borlaug BA, Blair J, Bergmann MW, et al. Latent pulmonary vascular disease may alter the response to therapeutic atrial shunt device in heart failure. Circulation 2022;145:1592–604. https://doi.org/10.1161/circulationaha.122.059486.
12. McCullough PA, Mehta HS, Barker CM, et al. Mortality and guideline-directed medical therapy in real-world heart failure patients with reduced ejection fraction. Clin Cardiol 2021;44:1192–8. https://doi.org/10.1002/clc.23664.
13. Salah HM, Butler J, Fudim M. Rapid sequence initiation of device therapy in heart failure. JACC: Advances 2023;2:100316. https://doi.org/10.1016/j.jacadv.2023.100316.
14. Brunckhorst CB, Shemer I, Mika Y, Ben-Haim SA, Burkhoff D. Cardiac contractility modulation by non-excitatory currents: studies in isolated cardiac muscle. Eur J Heart Fail 2006;8:7–15. https://doi.org/10.1016/j.ejheart.2005.05.011.
15. Borggrefe M, Burkhoff D. Clinical effects of cardiac contractility modulation (CCM) as a treatment for chronic heart failure. Eur J Heart Fail 2012;14:703–12. https://doi.org/10.1093/eurjhf/hfs078.
16. Feaster TK, Ewoldt JK, Avila A, et al. Nonclinical evaluation of chronic cardiac contractility modulation on 3D human engineered cardiac tissues. J Cardiovasc Electrophysiol 2024. https://doi.org/10.1111/jce.16222. xx:xxx–x .
17. Butter C, Wellnhofer E, Schlegl M, Winbeck G, Fleck E, Sabbah HN. Enhanced inotropic state of the failing left ventricle by cardiac contractility modulation electrical signals is not associated with increased myocardial oxygen consumption. J Card Fail 2007;13:137–42. https://doi.org/10.1016/j.cardfail.2006.11.004.
18. Borggrefe MM, Lawo T, Butter C, et al. Randomized, double blind study of non-excitatory, cardiac contractility modulation electrical impulses for symptomatic heart failure. Eur Heart J 2008;29:1019–28. https://doi.org/10.1093/eurheartj/ehn020.
19. xxx Neelagaru SB, Sanchez JE, Lau SK, Nonexcitatory et al. cardiac contractility modulation electrical impulses: feasibility study for advanced heart failure in patients with normal QRS duration. Heart Rhythm 2006;3:1140–7. https://doi.org/10.1016/j.hrthm.2006.06.031.
20. Abraham WT, Kuck KH, Goldsmith RL, et al. A randomized controlled trial to evaluate the safety and efficacy of cardiac contractility modulation. JACC Heart Fail 2018;6:874–83. https://doi.org/10.1016/j.jchf.2018.04.010.
21. Kadish A, Nademanee K, Volosin K, et al. A randomized controlled trial evaluating the safety and efficacy of cardiac contractility modulation in advanced heart failure. Am Heart J 2011;161:329–37. e1-2. https://doi.org/10.1016/j.ahj.2010.10.025.
22. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599–726. https://doi.org/10.1093/eurheartj/ehab368.
23. Georgakopoulos D, Little WC, Abraham WT, Weaver FA, Zile MR. Chronic baroreflex activation: a potential therapeutic approach to heart failure with preserved ejection fraction. J Card Fai l 2011;17:167–78. https://doi.org/10.1016/j.cardfail.2010.09.004.
24. Gronda E, Seravalle G, Brambilla G, et al. Chronic baroreflex activation effects on sympathetic nerve traffic, baroreflex function, and cardiac haemodynamics in heart failure: a proof-of-concept study. Eur J Heart Fail 2014;16:977–83. https://doi.org/10.1002/ejhf.138.
25. Abraham WT, Zile MR, Weaver FA, et al. Baroreflex activation therapy for the treatment of heart failure with a reduced ejection fraction. JACC Heart Fail 2015;3:487–96. https://doi.org/10.1016/j.jchf.2015.02.006.

26. Zile MR, Lindenfeld J, Weaver FA, et al. Baroreflex activation therapy in patients with heart failure with reduced ejection fraction. J Am Coll Cardiol 2020;76:1–13. https://doi.org/10.1016/j.jacc.2020.05.015.
27. Zile M. BeAT-HF: long-term safety and outcomes. Paper presented at Technology and Heart Failure Therapeutics meeting, March 21, 2023. Accessed March 20, 2024. https://www.tctmd.com/slide/beat-hf-long-term-safety-and-outcomes
28. Coats AJS, Abraham WT, Zile MR, et al. Baroreflex activation therapy with the Barostim™ device in patients with heart failure with reduced ejection fraction: a patient level meta-analysis of randomized controlled trials. Eur J Heart Fail 2022;24:1665–73. https://doi.org/10.1002/ejhf.2573.
29. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2021;143:e35–71. https://doi.org/10.1161/cir.0000000000000932.
30. Steiner J, Rodés-Cabau J, Holmes Jr DR, LeWinter MM, Dauerman HL. Mechanical intervention for aortic valve stenosis in patients with heart failure and reduced ejection fraction. J Am Coll Cardiol 2017;70:3026–41. https://doi.org/10.1016/j.jacc.2017.10.040.
31. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2021;43:561–632. https://doi.org/10.1093/eurheartj/ehab395.
32. Ludwig S, Schofer N, Abdel-Wahab M, et al. Transcatheter aortic valve replacement in patients with reduced ejection fraction and nonsevere aortic stenosis. Circulation: Cardiovasc Intervent 2023;16:e012768. https://doi.org/10.1161/CIRCINTERVENTIONS.122.012768.
33. Jean G, Van Mieghem NM, Gegenava T, et al. Moderate aortic stenosis in patients with heart failure and reduced ejection fraction. J Am Coll Cardiol 2021;77:2796–803. https://doi.org/10.1016/j.jacc.2021.04.014.
34. Spitzer E, Van Mieghem NM, Pibarot P, et al. Rationale and design of the Transcatheter Aortic Valve Replacement to UNload the Left ventricle in patients with ADvanced heart failure (TAVR UNLOAD) trial. Am Heart J 2016;182:80–8. https://doi.org/10.1016/j.ahj.2016.08.009.
35. Costanzo P, Bamborough P, Peterson M, Deva DJ, Ong G, Fam N. Transcatheter aortic valve implantation for severe pure aortic regurgitation with dedicated devices. Interv Cardiol 2022;17:e11. https://doi.org/10.15420/icr.2021.19.
36. Poschner T, Werner P, Kocher A, et al. The JenaValve pericardial transcatheter aortic valve replacement system to treat aortic valve disease. Future Cardiol 2022;18:101–13. https://doi.org/10.2217/fca-2021-0065.
37. Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med 2018;379:2307–18. https://doi.org/10.1056/NEJMoa1806640.
38. Obadia J-F, Messika-Zeitoun D, Leurent G, et al. Percutaneous repair or medical treatment for secondary mitral regurgitation. N Engl J Med 2018;379:2297–306. https://doi.org/10.1056/NEJMoa1805374.
39. Stone GW, Abraham WT, Lindenfeld J, et al. Five-year follow-up after transcatheter repair of secondary mitral regurgitation. N Engl J Med 2023;388:2037–48. https://doi.org/10.1056/NEJMoa2300213.
40. Grayburn PA, Sannino A, Packer M. Proportionate and disproportionate functional mitral regurgitation: a new conceptual framework that reconciles the results of the MITRA-FR and COAPT trials. JACC Cardiovasc Imag 2019;12:353–62. https://doi.org/10.1016/j.jcmg.2018.11.006.
41. Godino C, Munafò A, Scotti A, et al. MitraClip in secondary mitral regurgitation as a bridge to heart transplantation: 1-year outcomes from the International MitraBridge Registry. J Heart Lung Transplant 2020;39:1353–62. https://doi.org/10.1016/j.healun.2020.09.005.
42. Simard T, Vemulapalli S, Jung RG, et al. Transcatheter edge-to-edge mitral valve repair in patients with severe mitral regurgitation and cardiogenic shock. J Am Coll Cardiol 2022;80:2072–84. https://doi.org/10.1016/j.jacc.2022.09.006.
43. McCarthy PM, Whisenant B, Asgar AW, et al. Percutaneous MitraClip device or surgical mitral valve repair in patients with primary mitral regurgitation who are candidates for surgery: design and rationale of the REPAIR MR trial. J Am Heart Assoc 2023;12:e027504. https://doi.org/10.1161/jaha.122.027504.
44. Maisano F, Hahn RT, Lurz P, et al. Transcatheter treatment for tricuspid valve disease. EuroIntervent 2021;17:791–808. https://doi.org/10.4244/eij-d-21-00695.
45. Sorajja P, Whisenant B, Hamid N, et al. Transcatheter repair for patients with tricuspid regurgitation. N Engl J Med 2023;388:1833–42. https://doi.org/10.1056/NEJMoa2300525.
46. Kodali S. TRISCEND II: a randomized trial of transcatheter tricuspid valve replacement in patients with severe tricuspid regurgitation. Presented at TCT 2023; 2023;
47. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet 2011;377:658–66. https://doi.org/10.1016/s0140-6736(11)60101-3.
48. Zile MR, Mehra MR, Ducharme A, et al. Hemodynamically-guided management of heart failure across the ejection fraction spectrum: the GUIDE-HF trial. JACC Heart Fail 2022;10:931–44. https://doi.org/10.1016/j.jchf.2022.08.012.
49. Brugts JJ, Radhoe SP, Clephas PRD, et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. Lancet 2023;401:2113–23. https://doi.org/10.1016/S0140-6736(23)00923-6.
50. Fudim M, Butler J, Kittipibul V. Implantable hemodynamic-GUIDE monitors: a CHAMPION among devices for heart failure. J Am Coll Cardiol 2024;83:695–8. https://doi.org/10.1016/j.jacc.2023.12.008.
51. Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. Lancet 2021;398:991–1001. https://doi.org/10.1016/s0140-6736(21)01754-2.
52. Lindenfeld J, Costanzo MR, Zile MR, et al. Implantable hemodynamic monitors improve survival in patients with heart failure and reduced ejection fraction. J Am Coll Cardiol 2024;83:682–94. https://doi.org/10.1016/j.jacc.2023.11.030.
53. Jorde UP, Saeed O, Koehl D, et al. The Society of Thoracic Surgeons Intermacs 2023 Annual Report: focus on magnetically levitated devices. Ann Thorac Surg 2024;117:33–44. https://doi.org/10.1016/j.athoracsur.2023.11.004.
54. Mehra MR, Uriel N, Naka Y, et al. A fully magnetically levitated left ventricular assist device: final report. N Engl J Med 2019;380:1618–27. https://doi.org/10.1056/NEJMoa1900486.
55. Mehra MR, Netuka I, Uriel N, et al. Aspirin and hemocompatibility events with a left ventricular assist device in advanced heart failure: the ARIES-HM3 randomized clinical trial. JAMA 2023;330:2171–81. https://doi.org/10.1001/jama.2023.23204.
56. Mehra MR, Goldstein DJ, Cleveland JC, et al. Five-year outcomes in patients with fully magnetically levitated vs axial-flow left ventricular assist devices in the MOMENTUM 3 randomized trial. JAMA 2022;328:1233–42. https://doi.org/10.1001/jama.2022.16197.
57. Nayak A, Hall SA, Uriel N, et al. Predictors of 5-year mortality in patients managed with a magnetically levitated left ventricular assist device. J Am Coll Cardiol 2023;82:771–81. https://doi.org/10.1016/j.jacc.2023.05.066.
58. Mehra MR, Nayak A, Morris AA, et al. Prediction of survival after implantation of a fully magnetically levitated left ventricular assist device. JACC Heart Fail 2022;10:948–59. https://doi.org/10.1016/j.jchf.2022.08.002.
59. Fudim M, Abraham WT, von Bardeleben RS, et al. Device therapy in chronic heart failure: JACC State-of-the-Art Review. J Am Coll Cardiol 2021;78:931–56. https://doi.org/10.1016/j.jacc.2021.06.040.