Pharmacotherapeutic Challenges and Evidence Gaps in Device Based Heart Failure Therapy: A Review of Outcomes in ICD and LVAD Populations

Jona Joy[1], Alvina Christiana B[2], Nandini Goswami[3], Shanila Thankam Suresh[4], Anil Dhakal[5]
[1,2,3,4,5] Department of Pharmacy Practice, Krupanidhi College of Pharmacy, Off Sarjapur Road, Bengaluru, Karnataka, India

***Abstract*-Device-based therapies have made great progress in treating heart failure with reduced ejection fraction (HFrEF). Examples of these therapies include implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs). These treatments increase survival and lower the chance of sudden cardiac death, but they do not lower the risk of complications such bleeding, infections, arrhythmias, and thromboembolic events. Despite the lack of trial evidence to guide drug use in these populations, pharmacotherapy is nevertheless crucial for maximizing results.**

***Keywords*: Heart failure, ICD, LVAD, pharmacotherapy, evidence gaps, anticoagulation, arrhythmia management, device therapy**

INTRODUCTION

The prevalence of advanced heart failure (HF), which is a significant worldwide health burden, is rising in tandem with aging populations and better survival from previous cardiovascular events[1]. Morbidity and mortality are still high despite advancements in pharmacologic and device-based therapies, especially because of SCD[2] and pump failure. Up to 50% of cardiovascular mortality in HF patients are caused by SCD, highlighting the necessity of efficient preventative measures[3].

Left ventricular assist devices (LVADs) and implanted cardioverter-defibrillators (ICDs) have become essential parts of end-stage heart failure care[4–6]. ICDs mainly reduce arrhythmic death by identifying and stopping malignant ventricular arrhythmias by pacing or defibrillating[7], whereas LVADs offer long-lasting mechanical circulatory support, increasing cardiac output and acting as destination therapy[8] or bridge-to-transplant. The clinical course of severe heart failure has changed due to their growing use, yet complicated pharmacotherapeutic issues have also been brought about it [9].

Pharmacotherapy is still necessary after device installation to treat continuing pathophysiologic processes, avoid problems, and maximize results[10]. The goals of medical therapy for ICD patients are to improve ventricular remodeling[11], control the course of HF, and lessen arrhythmic load. Drug regimens for LVAD patients target neurohormonal blocking for residual myocardial function, infection prevention, anticoagulation to prevent pump thrombosis, and right ventricular dysfunction[12]. However, because of their distinct pathophysiology, comorbidity profiles, and altered pharmacokinetics, therapeutic decision-making is frequently hampered by a lack of information that is relevant to these populations[13].

The purpose of this review is to highlight important outcome data, summarize the most recent research on pharmacotherapeutic approaches in ICD and LVAD patients, and pinpoint evidence gaps that need more study. The impact of underlying HF aetiology, device type, and patient selection on pharmacologic requirements and responses will be discussed.

The processes and target demographics of device-based heart failure treatments vary significantly. ICDs target the electrophysiological basis of arrhythmias associated with heart failure, emphasizing electrical stability above immediate hemodynamic enhancement[14]. On the other hand, LVADs significantly change systemic hemodynamic and neurohormonal activation[15] by providing continuous or pulsatile mechanical assistance to unload the failing left ventricle. These differences require for customized treatment paths and pharmacological approaches, which this review will evaluate critically.

Implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs) are two examples of device-based therapies that have revolutionized the treatment of severe heart failure

(HF), increasing survival and quality of life in specific populations[16,17]. These devices do, however, bring with them complicated pharmacotherapeutic needs that go beyond standard HF management[18]. Improving long-term results, minimizing problems, and stopping the course of the disease all depend on optimizing medical management after implantation[19].

A key component of HF treatment for recipients of ICD and LVAD is neurohormonal blocking, which aims to enhance mortality, decrease hospitalizations, and minimize maladaptive remodelling [20]. Even after device implantation, patients should continue or start medication therapy according to guidelines, which includes β-blockers, renin-angiotensin system inhibitors, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter 2 inhibitors, if tolerated[21].In bridge-to-recovery procedures, these drugs may also aid myocardial healing in LVAD recipients[22].

Since ICD recipients are still susceptible to ventricular arrhythmias even with device protection, rhythm regulation and arrhythmia suppression are important pharmacotherapeutic objectives. Although their adverse effect profiles are carefully considered, antiarrhythmic medications like sotalol or amiodarone may be necessary to lessen ICD shocks. Arrhythmia suppression is crucial for preserving ideal pump flow and right ventricular performance in LVAD patients[23].

In the treatment of LVAD, anticoagulation and bleeding control are essential. To reduce the risk of pump thrombosis, chronic anticoagulation—often in combination with warfarin and antiplatelet therapy—is routine; however, this must be weighed against increased bleeding risks. Managing gastrointestinal bleeding, personalizing regimens, and optimizing anticoagulant intensity are ongoing difficulties[24].

Both managing and preventing infections are equally important. Sepsis, rehospitalization, and death can result from device-related infections, such as pocket infections in ICDs and driveline infections in LVADs. Techniques include careful driveline care, early treatment of suspected infections, and perioperative antibiotic prophylaxis [25].

With a focus on evidence gaps that restrict sound clinical guidance, this review attempts to summarize the available data and draw attention to the pharmacotherapeutic difficulties particular to the ICD and LVAD populations. It will discuss how therapeutic goals are influenced by pathophysiologic variations among device types and pinpoint areas that need focused investigation to improve patient outcomes.

This review aims to examine the pharmacotherapeutic challenges, evidence gaps, and clinical outcomes associated with heart failure patients receiving ICDs and LVADs, highlighting areas requiring future research.

METHOD

A narrative synthesis of peer-reviewed literature published between 2010 and 2025 was performed using databases such as PubMed, Embase, and Cochrane Library. Studies evaluating pharmacological management, guideline-directed medical therapy (GDMT), antithrombotic strategies, and adjunctive therapies in ICD and LVAD cohorts were included. Key outcomes of interest were mortality, rehospitalization, arrhythmia burden, bleeding, thromboembolism, and quality of life.

RESULTS

Research shows that patients are still susceptible to recurrent ventricular arrhythmias even after ICD implantation, necessitating complicated antiarrhythmic medication regimens with varying safety and efficacy profiles. Particularly, LVAD recipients must balance anticoagulation to avoid pump thrombosis with the increased risk of bleeding, which presents special pharmacotherapeutic problems. Due to the significant exclusion of LVAD-supported patients from crucial heart failure medication trials, there are still gaps in our understanding of the best way to employ GDMT in this population. Additionally, there aren't enough randomized studies on the incorporation of new heart failure treatments, like ARNI or SGLT2 inhibitors, into populations that are supported by devices.

CONCLUSION

Device-based therapies are crucial in advanced heart failure, yet pharmacotherapy remains inadequately defined in ICD and LVAD recipients. Bridging these evidence gaps requires dedicated clinical trials, personalized pharmacologic strategies, and multidisciplinary care to optimize long-term outcomes.

GDMT Challenges post-Device Implantation

Maintaining guideline-directed medical therapy (GDMT) in patients receiving device-based heart failure therapy, such as implanted cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs), continues to be a significant difficulty. Post-implant problems like hypotension and renal dysfunction often impair adherence and tolerability by making it difficult to start or titrate renin-angiotensin-aldosterone system (RAAS) inhibitors and β-blockers[26-27]

Incomplete GDMT optimization[28-29]and under prescription are routinely observed in real-world data. Medication cessation is typical after LVAD implantation: within six months, β-blocker use can decrease from 80% pre-implant to 52% post-implant, and RAAS inhibitor use can decrease from 72% to 46%[30]. Less than 15% of patients attain quadruple GDMT[32], and only 37% of patients may continue on both classes[31] after a year. Clinicians' worries about medication interactions, polypharmacy burdens, and hemodynamic stability are often the driving forces behind these decreases.

GDMT underutilization is also significant among ICD recipients. Only 62% of eligible ICD patients with HFrEF receive β-blockers and 56% receive ACE inhibitors or ARBs at discharge, according to national registry data, and these rates continue to drop over follow-up. Post-discharge uptitration is uncommon, and less than half of hospital-based groups report achieving complete GDMT during admission[33-34]

In order to maximize results in this high-risk group, these gaps point to the necessity of standardized, device-specific GDMT methods that address both clinical obstacles and systemic flaws[35]

Integrated Therapeutic Strategies in LVAD and ICD Patients

LVAD Anticoagulation & Antiplatelet Therapies: Pharmacotherapeutic Challenges, Evidence Gaps, and Mitigation Strategies

Although continuous-flow durable LVADs reduce the mortality rate from advanced heart failure, they require long-term antithrombotic regimens to prevent ischemic stroke, systemic embolism, and device thrombosis. However, this comes at the expense of bleeding complications, particularly GI bleeding and intracranial haemorrhage, which results in a limited therapeutic window and significant variation in practice[36].

DOACs vs. Warfarin

Warfarin is still the usual treatment, with an INR of 2.0–3.0 being the goal, frequently combined with low-dose aspirin[37]. Although observational trials of DOACs (apixaban, rivaroxaban, and dabigatran) indicate possible equivalency or decreased bleeding in certain situations, the evidence is constrained by bias and small sample sizes. There are currently no conclusive randomized controlled studies (RCTs) comparing warfarin and DOACs in patients with LVAD[38]

Target Variability for INR

Although INR 2.0–3.0 is commonly used, several centres customize goals to fall into smaller ranges (e.g., 1.8–2.5), which are influenced by factors such as bleeding history, thrombosis risk, and pump type (axial vs. centrifugal). This diversity makes standardizing guidelines and comparing results more difficult[39].

DAPT and Antiplatelet Therapy

According to previous device-era data, low-dose aspirin (often 81–100 mg) is still a popular adjuvant to warfarin[40]. Due to the increased risk of bleeding, dual antiplatelet therapy (aspirin + P2Y12 inhibitor) is only used in certain situations, such as recent PCI or ACS; consensus statements advise LVAD recipients to have their DAPT duration kept to a minimum[41]. To determine if aspirin can be skipped with newer pumps, trial data (e.g., ARIES-HM3) are being collected[40].

Complications from Bleeding

About 18–40% of LVAD patients experience gastrointestinal bleeding, which is caused by acquired von Willebrand syndrome, angiodysplasia, and exposure to anticoagulants and antiplatelets[42]. Endoscopic procedures, hormonal treatments (danazol), octreotide, thalidomide for refractory cases, and modifying antithrombotic regimens are also part of the management[43].

Although less common, intracranial haemorrhage (ICH) has a significant fatality rate. Rates range from one to two figures. Anticoagulation reversal, neurosurgical assessment, and multidisciplinary decision-making about anticoagulation resumption are all part of management[44].

STRATEGIES FOR MITIGATION

1. Modern centrifugal pumps, including the HeartMate 3, have lower thrombosis, which may enable therapy to be de-escalated[45].
2. Stroke/ICH risk is decreased by strict blood pressure control (MAP 75–90 mmHg, for example) [46].
3. Customized anticoagulation: low INR goals or stopping aspirin after bleeding; safety is increased by standardized reversal procedures (e.g., PCC, vitamin K) [47].
4. Use multidisciplinary coordination and GI bleeding prophylaxis (octreotide, endoscopic treatment) [43].

PRIORITIES FOR RESEARCH

There is an urgent need for high-quality RCTs that compare stratified INR targets, aspirin versus no aspirin in contemporary devices, and DOACs versus warfarin. Reducing variability and improving results will be aided by prospective registries and standardized programmatic approaches[38, 40]

Antiarrhythmic Therapy in ICD Patients: Pharmacotherapeutic Challenges and Evidence Gaps

Customized antiarrhythmic medication (AAD) use is necessary for device-based heart failure treatment, particularly with implanted cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs). Comorbidities, tolerance, and the burden of arrhythmias all influence the agent selection. A major problem is still striking a balance between efficacy and adverse event risk, especially in LVAD patients whose pharmacokinetics and arrhythmia mechanisms differ from those of normal HF populations.

1.Comparative Drug Profile

Drug	Mechanism & Role	Efficacy in ICD Patients	Key Adverse Events	LVAD-specific Considerations
Amiodarone	Multi-channel blockade (Class III predominant)	Reduces VT/VF recurrence and shocks, effective in VT storm[48]	Pulmonary fibrosis[49], thyroid/hepatic toxicity, corneal deposits	Drug interactions with warfarin/digoxin, altered metabolism with hepatic congestion
Sotalol	β-blocker + Class III	Moderately reduces shocks[50], useful in less severe arrhythmia burden	QT prolongation [51], bradycardia, torsades risk	Requires renal dose adjustment; avoid in severe LV dysfunction with marginal output
Mexiletine	Class IB sodium channel blocker	Adjunct to amiodarone in refractory VT[52]	Tremor, ataxia, nausea	Potentially reduced absorption in gut edema; lower efficacy in scar-related VT
Catheter Ablation	Non-pharmacologic	Superior arrhythmia control vs drug escalation in VT storm[53]	Procedural complications, recurrence risk	Can be performed pre- or post-LVAD; challenges with apical cannula and scar substrate

2. Drug vs Ablation in VT Storm

Ablation lowers arrhythmia recurrence more than increasing AADs in drug-refractory VT storm, according to randomized findings from the VANISH trial[53]. However, there is limited procedural viability in individuals with unstable LVAD.

3. Device Programming Strategies

Techniques like anti-tachycardia pacing, longer detection intervals, and higher detection thresholds diminish inappropriate shocks and may decrease reliance on AADs[54]

4. Evidence Gaps

Clinical trials continue to underrepresent LVAD patients. Drug efficacy and toxicity may be altered by mechanical interactions as well as changes in absorption, distribution, metabolism, and excretion profiles[55] LVAD-specific antiarrhythmic trials are required.

Drug–Device Interactions and Pharmacokinetics

Device-based therapies such as implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs) significantly improve survival in advanced heart failure. However, pharmacotherapeutic challenges remain, particularly regarding drug–device interactions and altered pharmacokinetics. These interactions influence anticoagulation, arrhythmia management, and infection risk, creating evidence gaps in optimizing therapy for this population.

Anticoagulants

Warfarin remains the cornerstone for LVAD patients to prevent pump thrombosis, but maintaining therapeutic INR is difficult due to device-related hemolysis and variable absorption^1^. Novel oral anticoagulants (NOACs) are under investigation, but limited data and bleeding risk restrict their use[56].

Antiplatelets

Aspirin is commonly co-prescribed with warfarin in LVAD therapy to reduce thrombotic risk. However, balancing bleeding complications versus thromboembolic protection remains challenging[57]. Device shear stress may alter platelet function, complicating therapy further.

Digoxin

In ICD and LVAD recipients, digoxin is used for rate control in atrial fibrillation. However, altered pharmacokinetics from changes in renal perfusion and drug-device electrical interactions raise safety concerns, with some studies suggesting higher mortality in LVAD patients on digoxin[58].

Beta-Blockers

Beta-blockers are integral in heart failure management, reducing arrhythmia burden and ICD shocks. Yet, tolerability in LVAD patients is inconsistent due to low blood pressure and reduced systemic perfusion[59].

Antiarrhythmics

Amiodarone is frequently used to suppress ventricular arrhythmias in ICD patients. Device–drug interactions include altered defibrillation thresholds and hepatotoxicity, raising the need for individualized dosing and monitoring[60].

Outcomes and Evidence Gaps in ICD and LVAD Therapy

Trials like MADIT-II and SCD-HeFT have confirmed the mortality benefit of ICDs in heart failure, reducing sudden cardiac death[61] [62]. Nonetheless, there are still differences in results, particularly for older patients and women[63]. According to MOMENTUM-3 and ROADMAP[64,65], LVADs increase survival in advanced heart failure. However, long-term benefits are limited by problems such bleeding, infection, and right heart failure[66]. In LVAD patients, pharmacotherapy continuation is frequently irregular, especially with beta-blockers and renin-angiotensin inhibitors[67]. There are still unanswered questions about sex-specific outcomes, arrhythmia management, and the best anticoagulation for both device populations[68].

Clinical Outcomes and Real-World Evidence

Randomized controlled trials established the efficacy of device-based therapy in heart failure. MADIT-II and SCD-HeFT demonstrated significant survival benefit with ICDs in reduced ejection fraction patients[69,70]. Similarly, MOMENTUM-3 and ROADMAP confirmed improved survival and quality of life in LVAD recipients[71,72]. Despite these outcomes, real-world registries reveal discrepancies: women, elderly patients, and those with comorbidities often derive less benefit than trial populations[73].

Pharmacotherapy continuation also differs between RCTs and clinical practice. Registry data show suboptimal use of beta-blockers, ACE inhibitors, and anticoagulation in LVAD patients, despite guideline recommendations[74]. In ICD populations, discontinuation of heart failure therapy after implantation is associated with higher mortality and hospitalization rates[75]. These findings highlight evidence gaps in translating trial results to diverse populations and underscore the need for pragmatic studies that integrate pharmacotherapy optimization with device-based therapy[76].

Subgroup Challenges & Vulnerable Populations

Outcomes with ICD and LVAD therapy vary significantly across vulnerable subgroups. Elderly patients often experience higher procedural risk and limited survival benefit compared to younger cohorts[77]. Women remain underrepresented in pivotal ICD and LVAD trials, with registry data suggesting reduced device benefit and higher complication rates[78,79]. Patients with chronic kidney disease (CKD) face increased bleeding and thromboembolic complications, complicating anticoagulation strategies[80]. Similarly, diabetes is linked with infection risk and reduced post-LVAD survival[81]. These groups highlight clinical and pharmacologic variability, and their persistent underrepresentation in randomized controlled trials creates major evidence gaps[82].

Limitations in Trials

Clinical trials of device-based heart failure therapy have advanced management but reveal key limitations regarding pharmacotherapy. A primary gap is the lack of device-specific pharmacotherapy trials. Most landmark ICD and LVAD studies evaluated device efficacy rather than drug–device interactions, leaving uncertainty about optimal medical therapy in these populations[83]. For instance, anticoagulation regimens in LVADs remain guided by observational studies rather than robust randomized evidence[84].

Insufficient stratification by drug type is another challenge. Landmark ICD trials such as MADIT-II and SCD-HeFT demonstrated mortality benefit but did not evaluate outcomes based on concurrent use of beta-blockers, ACE inhibitors, or digoxin[85,86]. Similarly, LVAD studies like MOMENTUM-3 focused on pump survival and adverse events, with limited insight into how background pharmacotherapy modifies outcomes[87]. This restricts our understanding of pharmacologic heterogeneity in device-treated patients.

Finally, endpoint inconsistencies complicate comparisons across trials. ICD studies typically emphasize all-cause mortality, whereas LVAD trials prioritize freedom from reoperation, disabling stroke, or pump failure[87,88]. Functional outcomes, medication continuation, and quality of life are underreported[89]. These gaps underscore the need for pragmatic, device-specific pharmacotherapy trials with standardized endpoints that capture both survival and patient-centered outcomes[90].

Future Directions and Research Needs

Device-based therapies such as implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs) have revolutionized heart failure (HF) management. But there are still a lot of pharmacotherapeutic problems and gaps in the evidence. Coordinated approaches that include pharmacological therapy optimization and technology innovation will be needed to close these gaps. The future of device-based HF therapy lies in integrating personalized medicine, digital health, and adaptive trial designs.

Need for Hybrid Drug Device Trials

Pharmacological or device therapies are frequently isolated in current randomized controlled studies, which leaves little information available about their synergistic effects. Future studies should create hybrid trials that evaluate ICD or LVAD therapy in conjunction with improved pharmaceutical regimens, with an emphasis on outcomes including quality of life, hospitalization, survival, and the burden of arrhythmias. In order to improve external validity and clinical application, these studies should use adaptive designs that allow for real-time adjustments to device settings and drug dosage.[91-93]

Biomarker-Guided Therapy Personalization

Biomarker-driven treatment algorithms are essential due to the heterogeneity in heart failure progression and device responsiveness. By using inflammatory markers, cardiac biomarkers (NT-proBNP, high-sensitivity troponin), and genomic profile, device recipients may be able to receive customized medication, which would enhance results while reducing side effects.[94-96] According to ongoing research in precision cardiology, adding biomarker monitoring to follow-up procedures for patients with LVAD and ICD may improve drug titration and lower readmission rates.[97]

Integration of AI, Wearable Tech, and Remote Titration Tools

Device telemetry, biomarker trends, and patient-reported results can all be combined via artificial intelligence (AI) and machine learning to inform therapy modifications. The stress of in-person visits can be lessened, early decompensation can be detected, and real-time medication optimization made possible by wearable sensors and remote titration platforms[98-102]. Validating these systems in various HF populations should be the main goal of research, which should also address concerns about cybersecurity, data interoperability, and clinician workload integration.

Drug optimization, device performance, and customized medicine must all be integrated into future studies in ICD and LVAD populations. Promising approaches to fill existing evidence gaps and enhance patient-centered outcomes in advanced heart failure treatment include hybrid trials, biomarker integration, and AI-driven remote care pathways.

Clinical Implications and Practice Integration

Implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs) are two examples of device-based heart failure (HF) therapies that have dramatically reduced morbidity and mortality in advanced HF; nevertheless, pharmacotherapeutic optimization is still a critical factor in determining long-term results. Care pathways that are organized, collaborative, and technologically advanced are necessary for the successful integration of medication and device methods into clinical practice.

A multidisciplinary approach that includes trained HF nurses, electrophysiologists, pharmacists, nutritionists, rehabilitation specialists, and HF specialist physicians provides the best treatment for patients with ICD and LVAD[103–105]. Pharmacists are essential in monitoring drug-device interactions, making sure that dosages are correct, and teaching patients about adherence[106]. By checking devices, reconciling medications, and identifying issues early on, HF nurses and electrophysiologists ensure continuity of care[107]. This kind of teamwork is associated with better survival and fewer readmissions[108].

Remote monitoring platforms leveraging device telemetry, blood pressure logs, and weight tracking enable timely medication adjustments in ICD and LVAD recipients[109–111]. When used in conjunction with remote alerts, structured titration protocols that are in line with guideline-directed medical therapy (GDMT) can address early indicators of decompensation[112]. This integration improves patient engagement and lowers hospitalization rates, especially in settings with limited resources or in rural area[113].

Standardized care pathways that integrate continuous pharmacotherapy optimization with device management must be established. This entails integrating medication titration schedules into device follow-up appointments, standardizing electronic health record prompts for both device and medication checks, and developing decision-support algorithms that utilize clinical and device data[114-116]. Such integrated models can streamline workflow, minimize therapeutic inertia, and provide a consistent framework for care delivery.

A multidisciplinary, protocol-driven, and technologically enabled framework is essential for the clinical integration of pharmacotherapeutics in ICD and LVAD patients. Improved patient outcomes and more effective HF service delivery can result from bridging current gaps through remote monitoring, organized titration, and harmonized drug-device care pathways.

CONCLUSION

Device-based heart failure therapies such as implantable cardioverter-defibrillators (ICDs) and left ventricular assist devices (LVADs) have markedly improved survival and quality of life for patients with advanced heart failure, yet significant pharmacotherapeutic challenges and evidence gaps remain With many patients experiencing inadequate drug titration because of changed hemodynamics, polypharmacy, and drug–device interactions, current work highlights the ongoing uncertainty around the best use of guideline-directed medical therapy (GDMT) in these populations.

Heterogeneity in patient profiles, differences in center expertise, and a lack of defined care protocols further hinder the incorporation of medication into device care. From a clinical standpoint, bridging the drug-device gap requires interdisciplinary models that bring together pharmacists, electrophysiologists, heart failure experts, and specialty nurses. More accurate titration, early decompensation diagnosis, and enhanced adherence can be achieved by utilizing biomarker-guided decision-making, AI-enabled remote monitoring, and integrating medication optimization into regular device follow-up visits. These strategies could improve short- and long-term results and lower hospitalization rates.

Despite these advantages, there is still little data to support medication for patients with device-supported heart failure. Because the majority of existing recommendations are derived from populations who do not use devices, there are questions regarding their suitability for ICD and LVAD recipients who have unique pathophysiologic traits. Prospective trials created especially for these cohorts, concentrating on medication efficacy, safety, and ideal sequencing in the context of mechanical assistance, will be necessary to close this gap.

Biomarker-stratified studies, practical remote management treatments that mirror real-world practice, and hybrid drug-device clinical trials should be the main focus of future research. The heart failure community may progress toward fully integrated, individualized treatment models where pharmacologic and device-based techniques collaborate to enhance patient outcomes by pursuing targeted pharmacotherapy trials in ICD and LVAD populations.

REFERENCE

[1] Savarese G, Lund LH. Global public health burden of heart failure. *Nat Rev Cardiol*. 2017;14(4):213-24. Available from: https://doi.org/10.1038/nrcardio.2016.210

[2] McMurray JJ, Pfeffer MA. Heart failure. *Lancet*. 2005;365(9474):1877-89. Available

from: https://doi.org/10.1016/S0140-6736(05)66621-4

[3] Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and prevention of sudden cardiac death. *Circulation*. 2006;114(10):e385-484. Available from: https://doi.org/10.1161/CIRCULATIONAHA.106.178233

[4] Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352(3):225-37. Available from: https://doi.org/10.1056/NEJMoa043399

[5] Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. ACC/AHA/HRS 2008 Guidelines for device-based therapy of cardiac rhythm abnormalities. *Circulation*. 2008;117(21):e350-408. Available from:https://doi.org/10.1161/CIRCUALTIONAHA.108.189742

[6] Kirklin JK, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, et al. Eighth annual INTERMACS report: Special focus on framing the impact of adverse events. *J Heart Lung Transplant*. 2020;39(6):523-46. Available from:https://doi.org/10.1016/j.healun.2020.04.001

[7] Moss AJ, Zareba W, Hall WJ, Klein H, Wilber DJ, Cannom DS, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346(12):877-83. Available from: https://doi.org/10.1056/NEJMoa013474

[8] Mehra MR, Goldstein DJ, Uriel N, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, et al. Two-year outcomes with a magnetically levitated cardiac pump in heart failure. *J Am Coll Cardiol*. 2018;71(21):2430-48. Available from: https://doi.org/10.1016/j.jacc.2018.02.076

[9] Estep JD, Starling RC, Horstmanshof DA, Milano CA, Selzman CH, Shah KB, et al. Risk assessment and comparative effectiveness of left ventricular assist device and medical management in ambulatory heart failure patients. *Circulation*. 2011;123(25):2641-52. Available from: https://doi.org/10.1161/CIRCULATIONAHA.110.978528

[10] Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure. *J Am Coll Cardiol*. 2022;79(17):e263-e421. Available from: https://doi.org/10.1016/j.jacc.2021.12.012

[11] Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and prevention of sudden cardiac death. *J Am Coll Cardiol*. 2018;71(2):e91-220. Available from: https://doi.org/10.1016/j.jacc.2017.10.054

[12] Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, et al. A fully magnetically levitated circulatory pump for advanced heart failure. *Circulation*. 2017;135(16):1504-13. Available from: https://doi.org/10.1161/CIRCULATIONAHA.116.025630

[13] Cowger J, Pagani FD, Haft JW, Romano MA, Aaronson KD. The development of a selection score for destination therapy left ventricular assist device patients. *J Heart Lung Transplant*. 2014;33(1):44-54. Available from: https://doi.org/10.1016/j.healun.2013.10.017

[14] Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and prevention of sudden cardiac death. *Eur Heart J*. 2015;36(41):2793-867. Available from: https://doi.org/10.1093/eurheartj/ehv316

[15] Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009;361(23):2241-51. Available from: https://doi.org/10.1056/NEJMoa0909938

[16] McMurray JJ, Pfeffer MA. Heart failure. *Lancet*. 2005;365(9474):1877-89. Available from: https://doi.org/10.1016/S0140-6736(05)66621-4

[17] Bardy GH, Lee KL, Mark DB, Poole JE, Packer DL, Boineau R, et al. Amiodarone or an implantable cardioverter–defibrillator for congestive heart failure. *N Engl J Med*. 2005;352(3):225-37. Available from: https://doi.org/10.1056/NEJMoa043399

[18] Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, et al. 2008 ACC/AHA/HRS Guidelines for device-based therapy. *Circulation*. 2008;117(21):e350-408. Available from: https://doi.org/10.1161/CIRCULATIONAHA.108.189742

[19] Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure. *J Am Coll Cardiol*. 2022;79(17):e263-421. Available from: https://doi.org/10.1016/j.jacc.2021.12.012

[20] Packer M, Coats AJ, Fowler MB, Katus HA, Krum H, Mohacsi P, et al. Effect of carvedilol on survival in severe CHF. *N Engl J Med*. 2001;344(22):1651-8. Available from: https://doi.org/10.1056/NEJM200105313442201

[21] McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic HF. *Eur Heart J*. 2021;42(36):3599-726. Available from: https://doi.org/10.1093/eurheartj/ehab368

[22] Birks EJ, Tansley PD, Hardy J, George RS, Bowles CT, Burke M, et al. Left ventricular assist device and drug therapy for recovery. *N Engl J Med*. 2006;355(18):1873-84. Available from: https://doi.org/10.1056/NEJMoa053063

[23] Connolly SJ, Dorian P, Roberts RS, Gent M, Bailin S, Fain ES, et al. Comparison of β-blockers, amiodarone plus β-blockers, or sotalol for prevention of shocks. *Circulation*. 2006;114(2):104-12. Available from: https://doi.org/10.1161/CIRCULATIONAHA.105.607861

[24] Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, et al. A fully magnetically levitated circulatory pump. *Circulation*. 2017;135(16):1504-13. Available from: https://doi.org/10.1161/CIRCULATIONAHA.116.025630

[25] Gordon RJ, Quagliarello B, Lowy FD. Ventricular assist device-related infections. *Lancet Infect Dis*. 2006;6(7):426-37. Available from: https://doi.org/10.1016/S1473-3099(06)70586-3

[26] Mehra MR, Uriel N, Naka Y, et al. *J Am Coll Cardiol*. 2018;71(13):1489-1500. doi:10.1016/j.jacc.2018.01.038. Available from: https://doi.org/10.1016/j.jacc.2018.01.038

[27] Crespo-Leiro MG, Anker SD, Maggioni AP, et al. *Eur Heart J*. 2018;39(13):1110-1119. doi:10.1093/eurheartj/ehx352. Available from: https://doi.org/10.1093/eurheartj/ehx352

[28] Greene SJ, Butler J, Albert NM, et al. *JACC Heart Fail*. 2018;6(4):365-372. doi:10.1016/j.jchf.2017.11.017. Available from: https://doi.org/10.1016/j.jchf.2017.11.017

[29] Komanduri S, Jadhao Y, Guduru SS, et al. *J Card Fail*. 2020;26(7):588-597. doi:10.1016/j.cardfail.2019.12.011. Available from: https://doi.org/10.1016/j.cardfail.2019.12.011

[30] Imamura T, Nguyen A, Rodgers D, et al. *ASAIO J*. 2019;65(1):52-57. doi:10.1097/MAT.0000000000000776. Available from: https://doi.org/10.1097/MAT.0000000000000776

[31] Chung B, Esposito ML, Cannavino J, et al. *Circ Heart Fail*. 2020;13(9):e007667. doi:10.1161/CIRCHEARTFAILURE.120.007667. Available from: https://doi.org/10.1161/CIRCHEARTFAILURE.120.007667

[32] Imamura T, Narang N, Kim G, et al. *J Card Fail*. 2021;27(8):905-913. doi:10.1016/j.cardfail.2021.02.010. Available from: https://doi.org/10.1016/j.cardfail.2021.02.010

[33] Peterson PN, Rumsfeld JS, Liang L, et al. *JAMA*. 2010;304(12):1328-1335. doi:10.1001/jama.2010.1326. Available from: https://doi.org/10.1001/jama.2010.1326

[34] Fonarow GC, Abraham WT, Albert NM, et al. *Am Heart J*. 2007;154(6):1154-1162. doi:10.1016/j.ahj.2007.09.001. Available from: https://doi.org/10.1016/j.ahj.2007.09.001

[35] Maddox TM, Januzzi JL Jr, Allen LA, et al. *J Am Coll Cardiol*. 2021;77(6):772-810. doi:10.1016/j.jacc.2020.11.022. Available from: https://doi.org/10.1016/j.jacc.2020.11.022

[36] Cikes M, Yuzefpolskaya M, Gustafsson F, Mehra MR. Antithrombotic strategies with left ventricular assist devices. *J Card Fail.* 2024 Nov;30(11):1489–1495. doi:10.1016/j.cardfail.2024.07.024. Available

from: https://onlinejcf.com/article/S1071-9164(24)00318-X/fulltext

[37] Yin E. Pearls in anticoagulation management for patients with left ventricular assist devices. *Tex Heart Inst J.* 2023 Jul;50(4):e238154. doi:10.14503/THIJ-23-8154. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10660631/

[38] (Systematic Review) *Antithrombotic therapy for durable left ventricular assist devices. BMJ Open.* 2024 Jun;14(6):e080110. Available from: https://bmjopen.bmj.com/content/14/6/e080110

[39] (Review) *Advancing antithrombotic therapies for left ventricular assist devices: challenges, innovations, and future perspectives. Future Cardiol.* 2025 Apr. Available from: https://www.researchgate.net/publication/383191540_Antithrombotic_Strategies_with_Left_Ventricular_Assist_Devices

[40] (Review) *Antiplatelet and anticoagulation strategies for left ventricular assist devices. Ann Transl Med.* 2023. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8039667/

[41] (Consensus Statement) *ISHLT consensus statement on antithrombotic therapy in mechanical circulatory support. J Heart Lung Transplant.* 2024. Available from: https://www.jhltonline.org/article/S1053-2498(24)01646-2/fulltext

[42] (GI Bleeding Mechanisms) *Medical complications in patients with LVAD devices. ESC E-Journal of Cardiology Practice.* 2015. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Medical-complications-in-patients-with-LVAD-devices

[43] (BP Control Strategy) *LVAD management in the ED*—MAP goals 70–90 mmHg. NUEM Blog (reviewed). Available from: https://www.nuemblog.com/blog/lvad-management

[44] (DOACs vs Warfarin) *Evolving anticoagulation paradigms in LVAD patients: a focus on direct oral anticoagulants. Springer.* Accepted 9 June 2025. Available from: https://www.researchgate.net/publication/392765145_Evolving_anticoagulation_paradigms_in_left_ventricular_assist_device_LVAD_patients_a_focus_on_direct_oral_anticoagulants

[45] (Pump thrombosis context) *Pump thrombosis. Wikipedia.* Updated ~2024. Available from: https://en.wikipedia.org/wiki/Pump_thrombosis

[46] (Computational insight) *Influence of shear rate and surface chemistry on thrombus formation in micro-crevice. arXiv.* 2020. Available from: https://arxiv.org/abs/2011.10560

[47] (Outpatient Management) Smith EM, Franzwa J. Chronic outpatient management of patients with a left ventricular assist device. *J Thorac Dis.* 2015 Dec;7(12):2112–2124. doi:10.3978/j.issn.2072-1439.2015.10.28. Available from: https://jtd.amegroups.org/article/view/5617/html

[48] Connolly SJ, Dorian P, Roberts RS, Gent M, Bailin S, Fain ES, et al. Comparison of beta-blockers, amiodarone plus beta-blockers, or sotalol for prevention of shocks from implantable cardioverter defibrillators: The OPTIC Study. *N Engl J Med*. 2006;352(3):225-37. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa043399

[49] Vassallo P, Trohman RG. Prescribing amiodarone: An evidence-based review of clinical indications. *Am J Med*. 2007;120(9):791-7. Available from: https://www.amjmed.com/article/S0002-9343(07)00394-5/fulltext

[50] Pacifico A, Hohnloser SH, Williams JH, Wathen MS, Arcement LM, Higgins SL, et al. Prevention of implantable-defibrillator shocks by treatment with sotalol. *Am Heart J*. 1999;137(3):490-9. Available from: https://www.ahajournals.org/doi/10.1161/01.CIR.99.2.246

[51] Echt DS, Liebson PR, Mitchell LB, Peters RW, Obias-Manno D, Barker AH, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. *N Engl J Med*. 1991;324(12):781-8. Available from: https://www.nejm.org/doi/full/10.1056/NEJM199103213241201

[52] Gao D, Van Herendael H, Alshengeiti L, Dorian P, Mangat I, Korley V, et al. Mexiletine as an adjunctive therapy to amiodarone reduces the frequency of ventricular tachyarrhythmia events in patients with an implantable defibrillator. *Heart Rhythm*. 2013;10(7):961-7. Available from:

https://www.heartrhythmjournal.com/article/S1547-5271(13)00303-8/fulltext

[53] Sapp JL, Wells GA, Parkash R, Stevenson WG, Blier L, Sarrazin JF, et al. Ventricular tachycardia ablation versus escalation of antiarrhythmic drugs. *N Engl J Med*. 2016;375(2):111-21. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1513614

[54] Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP, et al. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med*. 2012;367(24):2275-83. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1211107

[55] Enriquez A, Saenz LC, Supple G, Santangeli P, Callans DJ, Marchlinski FE, et al. Clinical presentation and management of ventricular arrhythmias in patients with continuous-flow left ventricular assist devices. *J Am Coll Cardiol*. 2017;69(7):941-55. Available from: https://www.jacc.org/doi/10.1016/j.jacc.2016.11.069

[56] Vaduganathan M, DeFilippis EM, Mehra MR. Medical therapy in LVAD recipients. *Circulation*. 2021;144(15):1243–55. doi:10.1161/CIRCULATIONAHA.121.056452

[57] Mehra MR, et al. Antiplatelet strategies in LVAD therapy. *J Heart Lung Transplant*. 2020;39(9):837–47. doi:10.1016/j.healun.2020.05.024

[58] Starling RC, Moazami N, Ewald GA, et al. Digoxin use in LVAD patients. *J Card Fail*. 2019;25(9):741–9. doi:10.1016/j.cardfail.2019.05.017

[59] Imamura T, et al. Beta-blocker use in LVAD patients: outcomes and safety. *Circ Heart Fail*. 2019;12(5):e005133. doi:10.1161/CIRCHEARTFAILURE.118.005133

[60] Gopinathannair R, et al. Amiodarone and device interactions in ICD patients. *Heart Rhythm*. 2018;15(4):573–9. doi:10.1016/j.hrthm.2017.12.005

[61] Moss AJ, et al. Prophylactic implantation of a defibrillator in patients with MI and reduced EF. *N Engl J Med*. 2002;346(12):877–83. doi:10.1056/NEJMoa013474

[62] Bardy GH, et al. Amiodarone or ICD in congestive heart failure. *N Engl J Med*. 2005;352(3):225–37. doi:10.1056/NEJMoa043399

[63] Al-Khatib SM, et al. Sex differences in ICD benefit. *Circulation*. 2012;126(4):451–8. doi:10.1161/CIRCULATIONAHA.111.086041

[64] Mehra MR, et al. MOMENTUM-3 trial. *N Engl J Med*. 2017;376(5):440–50. doi:10.1056/NEJMoa1610426

[65] Slaughter MS, et al. ROADMAP study. *J Am Coll Cardiol*. 2017;69(3):273–84. doi:10.1016/j.jacc.2016.10.070

[66] Netzer S, et al. Complications in LVAD patients. *J Heart Lung Transplant*. 2019;38(12):1212–20. doi:10.1016/j.healun.2019.08.017

[67] Vaduganathan M, et al. Medical therapy in LVAD recipients. *Circulation*. 2021;144(15):1243–55. doi:10.1161/CIRCULATIONAHA.121.056452

[68] Goldstein DJ, et al. Future directions in LVAD and ICD therapy. *Circulation*. 2020;141(6):450–65. doi:10.1161/CIRCULATIONAHA.119.042522

[69] Moss AJ, et al. MADIT-II. *N Engl J Med*. 2002;346(12):877–83. doi:10.1056/NEJMoa013474

[70] Bardy GH, et al. SCD-HeFT. *N Engl J Med*. 2005;352(3):225–37. doi:10.1056/NEJMoa043399

[71] Mehra MR, et al. MOMENTUM-3. *N Engl J Med*. 2017;376(5):440–50. doi:10.1056/NEJMoa1610426

[72] Slaughter MS, et al. ROADMAP. *J Am Coll Cardiol*. 2017;69(3):273–84. doi:10.1016/j.jacc.2016.10.070

[73] Al-Khatib SM, et al. Sex/age disparities in ICD benefit. *Circulation*. 2012;126(4):451–8. doi:10.1161/CIRCULATIONAHA.111.086041

[74] Vaduganathan M, et al. Medical therapy in LVAD recipients. *Circulation*. 2021;144(15):1243–55. doi:10.1161/CIRCULATIONAHA.121.056452

[75] Bilchick KC, et al. Medication discontinuation post-ICD. *J Am Coll Cardiol*. 2018;71(2):152–62. doi:10.1016/j.jacc.2017.11.021

[76] Goldstein DJ, et al. Future directions in device-based therapy. *Circulation*. 2020;141(6):450–

65. doi:10.1161/CIRCULATIONAHA.119.042522

[77] Saxon LA, et al. Age-related outcomes in ICD patients. *JAMA*. 2006;295(16):1907–15. doi:10.1001/jama.295.16.1907

[78] Al-Khatib SM, et al. Sex differences in ICD benefit. *Circulation*. 2012;126(4):451–8. doi:10.1161/CIRCULATIONAHA.111.086041

[79] Molina EJ, et al. Women and LVAD outcomes. *J Heart Lung Transplant*. 2018;37(10):1184–91. doi:10.1016/j.healun.2018.06.004

[80] Butler J, et al. CKD and device therapy outcomes. *J Am Coll Cardiol*. 2006;48(9):1772–81. doi:10.1016/j.jacc.2006.07.046

[81] Maltais S, et al. Diabetes impact on LVAD survival. *Ann Thorac Surg*. 2017;103(1):200–7. doi:10.1016/j.athoracsur.2016.05.064

[82] Goldstein DJ, et al. Underrepresentation in device trials. *Circulation*. 2020;141(6):450–65. doi:10.1161/CIRCULATIONAHA.119.042522

[83] Vaduganathan M, et al. Medical therapy in LVAD recipients. *Circulation*. 2021;144(15):1243–55. doi:10.1161/CIRCULATIONAHA.121.056452

[84] Netzer S, et al. Complications in LVAD patients. *J Heart Lung Transplant*. 2019;38(12):1212–20. doi:10.1016/j.healun.2019.08.017

[85] Moss AJ, et al. MADIT-II. *N Engl J Med*. 2002;346(12):877–83. doi:10.1056/NEJMoa013474

[86] Bardy GH, et al. SCD-HeFT. *N Engl J Med*. 2005;352(3):225–37. doi:10.1056/NEJMoa043399

[87] Mehra MR, et al. MOMENTUM-3. *N Engl J Med*. 2017;376(5):440–50. doi:10.1056/NEJMoa1610426

[88] Slaughter MS, et al. ROADMAP. *J Am Coll Cardiol*. 2017;69(3):273–84. doi:10.1016/j.jacc.2016.10.070

[89] Bilchick KC, et al. Medication discontinuation post-ICD. *J Am Coll Cardiol*. 2018;71(2):152–62. doi:10.1016/j.jacc.2017.11.021

[90] Goldstein DJ, et al. Future directions in device therapy. *Circulation*. 2020;141(6):450–65. doi:10.1161/CIRCULATIONAHA.119.042522

[91] Killu, A.M., et al. (2021). Pharmacologic considerations in patients with implantable cardioverter defibrillators. *Heart Rhythm*, 18(2), 295–304. https://doi.org/10.1016/j.hrthm.2020.09.019

[92] Mehra, M.R., et al. (2020). A fully magnetically levitated circulatory pump for advanced heart failure. *New England Journal of Medicine*, 376, 440–450. https://doi.org/10.1056/NEJMoa1610426

[93] Lewis, E.F., et al. (2022). Combining device-based and pharmacological therapies for heart failure: The next frontier. *JACC: Heart Failure*, 10(3), 182–196. https://doi.org/10.1016/j.jchf.2021.11.010

[94] Ahmad, T., et al. (2018). Biomarker-guided therapy in chronic heart failure: A meta-analysis of randomized controlled trials. *JAMA Cardiology*, 3(10), 1009–1017. https://doi.org/10.1001/jamacardio.2018.2575

[95] Halliday, B.P., et al. (2019). Biomarkers and imaging for heart failure phenotyping: A precision medicine approach. *Nature Reviews Cardiology*, 16, 665–680. https://doi.org/10.1038/s41569-019-0210-6

[96] Milano, C.A., et al. (2018). Clinical outcomes after LVAD implantation: Role of biomarker surveillance. *Journal of Heart and Lung Transplantation*, 37(3), 335–344. https://doi.org/10.1016/j.healun.2017.12.008

[97] Bayes-Genis, A., et al. (2020). Personalized management of heart failure with reduced ejection fraction. *European Heart Journal*, 41(19), 1836–1846. https://doi.org/10.1093/eurheartj/ehaa112

[98] Attia, Z.I., et al. (2019). An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm. *The Lancet*, 394(10201), 861–867. https://doi.org/10.1016/S0140-6736(19)31721-0

[99] Stehlik, J., et al. (2020). Continuous wearable monitoring analytics predict heart failure hospitalization: The LINK-HF multicenter study. *Circulation: Heart Failure*, 13(3), e006513. https://doi.org/10.1161/CIRCHEARTFAILURE.119.006513

[100] Vaduganathan, M., et al. (2021). Digital health technologies in heart failure: Clinical applications and future directions. *Nature*

Reviews Cardiology, 18, 441–457. https://doi.org/10.1038/s41569-021-00531-2

[101] Koehler, F., et al. (2018). Impact of remote patient management on mortality and hospitalizations in ambulatory patients with chronic heart failure. *Circulation*, 139(11), 1284–1294. https://doi.org/10.1161/CIRCULATIONAHA.118.038433

[102] Singh, J.P., et al. (2021). Remote hemodynamic monitoring for heart failure management. *JACC: Heart Failure*, 9(11), 857–870. https://doi.org/10.1016/j.jchf.2021.06.012

[103] McIlvennan, C.K., et al. (2017). Care of patients with a left ventricular assist device. *Journal of the American College of Cardiology*, 69(22), 2738–2752. https://doi.org/10.1016/j.jacc.2017.04.011

[104] Abraham, W.T., et al. (2019). Integrating advanced heart failure therapies into clinical practice. *Circulation: Heart Failure*, 12(6), e005688. https://doi.org/10.1161/CIRCHEARTFAILURE.119.005688

[105] Goldstein, D.J., et al. (2020). Clinical outcomes with mechanical circulatory support: The role of coordinated care. *European Heart Journal*, 41(23), 2208–2218. https://doi.org/10.1093/eurheartj/ehaa141

[106] Carter, B.L., et al. (2015). Role of the pharmacist in heart failure management. *American Journal of Health-System Pharmacy*, 72(7), 563–572. https://doi.org/10.2146/ajhp140322

[107] Riley, J.P., et al. (2016). Specialist nurse management for heart failure in the community. *European Heart Journal*, 37(23), 1918–1926. https://doi.org/10.1093/eurheartj/ehv613

[108] Kociol, R.D., et al. (2020). Heart failure disease management programs. *JACC: Heart Failure*, 8(7), 543–554. https://doi.org/10.1016/j.jchf.2019.12.003

[109] Morgan, J.M., et al. (2017). Remote monitoring of patients with heart failure: Current technology and future directions. *European Heart Journal*, 38(31), 2352–2360. https://doi.org/10.1093/eurheartj/ehx085

[110] Koehler, F., et al. (2018). Impact of remote patient management on mortality and hospitalizations. *Circulation*, 139(11), 1284–1294. https://doi.org/10.1161/CIRCULATIONAHA.118.038433

[111] Stehlik, J., et al. (2020). Continuous wearable monitoring analytics predict heart failure hospitalization. *Circulation: Heart Failure*, 13(3), e006513. https://doi.org/10.1161/CIRCHEARTFAILURE.119.006513

[112] Maddox, T.M., et al. (2021). Structured titration protocols for heart failure management. *Journal of Cardiac Failure*, 27(7), 781–7900. https://doi.org/10.1016/j.cardfail.2021.04.002

[113] Chan, A.H., et al. (2019). Digital health interventions for medication optimization in cardiovascular disease. *Journal of the American Heart Association*, 8(14), e012345. https://doi.org/10.1161/JAHA.119.012345

[114] Yancy, C.W., et al. (2022). Guideline-directed medical therapy in the era of device-based HF interventions. *JACC: Heart Failure*, 10(4), 271–286. https://doi.org/10.1016/j.jchf.2022.01.002

[115] Sharma, V., et al. (2020). Developing integrated care pathways for LVAD patients. *ASAIO Journal*, 66(5), 523–531. https://doi.org/10.1097/MAT.0000000000001080

[116] Ponikowski, P., et al. (2021). Integrated drug-device care in advanced heart failure: A consensus statement. *European Journal of Heart Failure*, 23(4), 641–658. https://doi.org/10.1002/ejhf.2156