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POSITION PAPER

Evaluation and management of recent onset cardiomyopathy in the current era of heart failure therapeutics: a clinical consensus statement of the Heart Failure Association of the ESC

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Abstract

Recent-onset cardiomyopathy represents a clinically dynamic and potentially reversible clinical framework of non-ischaemic cardiomyopathy, characterized by high variability in left ventricular (LV) function and arrhythmic risk. This clinical consensus statement provides a structured diagnostic and therapeutic approach based on two prognostic axes: the potential for LV

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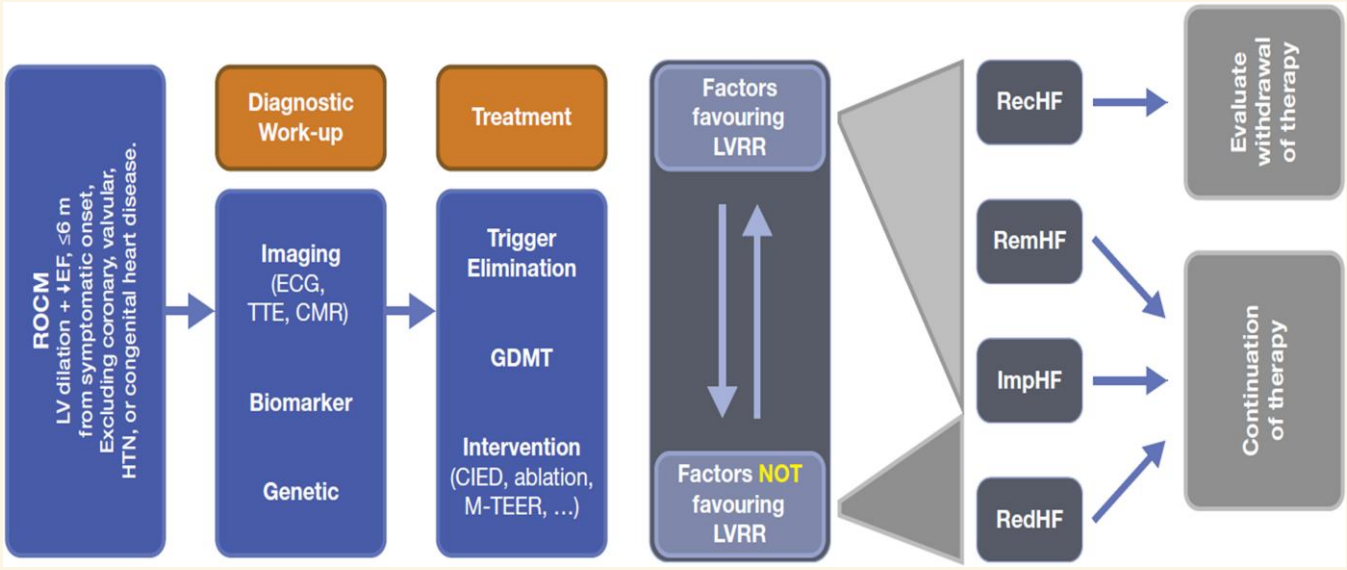
reverse remodelling (LVRR) and the risk of sudden cardiac death (SCD). We operationalize four trajectories in the LV evolution, ranging from recovered LV ejection fraction (LVEF) to persistently reduced LVEF. Multimodal stratification including echocardiography, cardiac magnetic resonance, genetic profiling, biomarkers, and early treatment response allows tailored decision-making on pharmacological and device-based therapies. We propose a unified management algorithm emphasizing early initiation of guideline-directed medical therapy, structured reassessment at 3 and 6 months, and individualized consideration of defibrillators, resynchronization therapy, arrhythmia ablation, transcatheter valve leaflet edge-to-edge repair, and advanced heart failure assessment. This document aims to support clinicians in risk stratification and timely management or referrals.

Graphical Abstract



The trajectory of recent-onset cardiomyopathy (ROCM). The ROCM framework complements existing phenotype-based cardiomyopathy classification and is intended as a practical approach to early evaluation and management. ROCM, recent-onset cardiomyopathy; LV, left ventricular; EF, ejection fraction; HTN, hypertension; ECG, electrocardiogram; TTE, transthoracic echocardiography; CMR, cardiac magnetic resonance; GDMT, guideline-directed medical therapy; CIED, cardiac implantable electronic device; M-TEER, mitral transcatheter edge-to-edge repair; LVRR, LV reverse remodelling; RecHF, recovered EF; RemHF, remission of EF; ImpHF, improved EF; RedHF, reduced EF; SCD, sudden cardiac death.

Keywords Recent-onset cardiomyopathy • Contemporary heart failure management • Guideline-directed medical therapy • Risk stratification • Reverse cardiac remodelling • Sudden cardiac death prevention

Introduction

Non-ischaemic cardiomyopathies comprise a heterogeneous group of conditions with diverse aetiologies and clinical outcomes.[1] Recent-onset cardiomyopathy (ROCM) constitutes a particularly dynamic and prognostically relevant time-sensitive early clinical framework for the evaluation and management of patients with newly diagnosed non-ischaemic LV systolic dysfunction.[2,3] Recent-onset cardiomyopathy is characterized by newly diagnosed (recent-onset symptoms or incidental finding) left ventricular systolic dysfunction (LVEF <40%) of non-ischaemic, non-valvular, and non-congenital aetiology, with an estimated onset since diagnosis of <6 months, frequently with reversible or treatable causes.[3] We do not propose ROCM as a novel phenotype in the sense of the European Society of Cardiology (ESC) cardiomyopathy classification, but rather to compliment as a clinically useful early-phase construct to guide diagnostic and therapeutic decision-making during the vulnerable early period.

The management of heart failure (HF) has been revolutionized over the past two decades.[4–6] Pharmacological and device therapies have impacted symptoms, quality of life (QoL), hospitalization, and survival rates.[4,5,7] Heart failure therapy has benefited non-ischaemic cardiomyopathy patients more than those with ischaemic cardiomyopathy in terms of response to therapy, LVEF improvement, and recovery.[8] Recent-onset cardiomyopathy presents a window of opportunity where rapid initiation of therapy and close follow-up can significantly alter disease trajectory. This clinical consensus statement aligns decision-making on two axes—the likelihood of left ventricular reverse remodelling (LVRR) and the risk of sudden cardiac death (SCD)—using three trajectories and time-bound reassessment (3 and 6 months) to translate multimodal markers into therapy timing. We adopted and extended the HF trajectory terminology established in the 2025 European Journal of Heart Failure expert consensus,[9] including improved HF (impHF), HF in remission (remHF), and recovered HF (recHF) to describe LVRR/SCD axes in determining short- and long-term therapies. Recent-onset cardiomyopathy is positioned within this improvement–remission–recovery continuum as a distinct, time-sensitive, and potentially reversible phenotype, which emphasizes diagnostic urgency, early aetiological clarification, and timely initiation and optimization of guideline-directed therapy to avoid adverse remodelling and maximize the chance

Table 1 List of pathophysiologic aetiology and causes of reversible cardiomyopathies

Aetiology	Causes	Aetiology	Causes
Tachycardia/ arrhythmias	Supraventricular • Sinus tachycardia • Atrial fibrillation/flutter • Supraventricular tachycardia: • Atrial tachycardia (junctional ectopic) • AV node re-entrant tachycardia • Dual (not circling) AV node tachycardia • AV re-entrant tachycardia Ventricular • Frequent premature ventricular contractions • Idiopathic ventricular tachycardia • Fascicular tachycardia	Sympatho-excitation/ stress	Takotsubo[a] (mental stress; physical stress; perioperative stress; Guillain–Barre syndrome; Pheochromocytoma; thyroid crisis) Autonomic dysfunction Medication induced
Immune/ inflammatory/ infectious	Viral, bacterial, protozoal/parasitic myocarditis (e.g. Chagas, Trichinella), as well as autoimmune/ immune-mediated myocarditis	Toxins/drugs	Marijuana Methamphetamine Sibutramine Alcohol Anthracyclines Sunitinib, sorafenib, trastazumab; rituximab; Adrenaline, dobutamine overdose Scorpion sting, jelly fish sting
Metabolic	Hyperthyroid Hypothyroid Hypocalcaemia Sheehan's syndrome Cushing syndrome Secondary adrenal insufficiency Beriberi Acromegaly Anabolic steroid Hypo parathyroid	Infiltration/storage	Siderotic or iron-induced Glycogen Storage disease Fabry's Loeffler's syndrome
Chronic disease	Obesity Liver cirrhosis Uraemia	Abnormal conduction	LBBB Chronic RV pacing Pre-excitation syndrome AV block (third-degree complete)

List of reversible cardiomyopathies divided into eight groups based on the pathophysiological mechanism. Treating the cause in most cases will result in significant improvement in EF (LVRR) that may lead to recHF or remHF.
[a]Stress-related (Takotsubo) cardiomyopathy may enter the differential diagnosis of recent-onset LV dysfunction but is not considered a cardiomyopathy phenotype within this framework.

of recovery. This clinical consensus statement is providing a complimentary platform to the published 2023 ESC cardiomyopathy guidelines.

Definition and aetiology of recent-onset cardiomyopathy

The 2023 ESC Guidelines for the Management of Cardiomyopathies define cardiomyopathy as a myocardial disorder characterized by structural and functional abnormalities of the heart muscle in the absence of significant coronary artery disease, primary valvular pathology, uncontrolled hypertension, or congenital heart disease sufficient to explain the observed phenotype.[1]

Recent-onset cardiomyopathy is characterized by newly detected structural and functional cardiac abnormalities—most often left ventricular (LV) dilation and reduced ejection fraction (EF)—diagnosed within 6 months of symptom onset or incidental first recognition of LV systolic dysfunction, excluding significant coronary, valvular, hypertensive, or congenital causes.[2,3] Recent-onset cardiomyopathy mandates a comprehensive diagnostic evaluation to identify potentially reversible aetiologies that can alter the clinical course and enable partial or full recovery of LV function. Differentiating ROCM from chronic cardiomyopathy is challenging especially that ROCM may be discovered incidentally in asymptomatic individuals or present acutely following a triggering event. This relies on clinical history, prior investigations, and the tempo of symptom development, although overlap remains common.

Aetiologies (*Table 1*) include but not limited to acute or subacute myocarditis (viral, autoimmune, or immune checkpoint inhibitor–related),[3,9–11] toxic or metabolic insults,[12] and tachyarrhythmia-induced LV dysfunction.[13,14] Stress-related (Takotsubo) cardiomyopathy[15] may enter the

differential diagnosis of recent-onset LV dysfunction but is not considered a cardiomyopathy phenotype within this framework, although it may relapse despite guideline-directed medical therapy (GDMT), which is advised with limited evidence. Genetic predisposition is increasingly recognized and should be evaluated to refine risk stratification and prognosis.[11] Toxic cardiomyopathies (e.g. alcohol- or chemotherapy-related) may recover fully or partially after removal of the offending agent and sustained abstinence.[12] Tachyarrhythmia-induced cardiomyopathy is another potentially reversible form that can mimic idiopathic dilated cardiomyopathy.[14] Persistent LV dysfunction despite optimized GDMT in patients with electrical dyssynchrony may improve with cardiac resynchronization therapy (CRT).[16] Thus, premature ventricular contraction (PVC) burden, right ventricular (RV) pacing, and tachyarrhythmias should be systematically assessed in all patients with ROCM, as they represent potential reversible contributors.[14,16] Peripartum cardiomyopathy is another important cause of ROCM, typically associated with high recovery rates, albeit with notable regional variation.[17–22]

The natural history of ROCM is challenging to delineate because subclinical disease may precede symptom onset by months or years. Contemporary cohorts demonstrate dynamic recovery patterns, with LV EF (LVEF) normalization in up to 70% of patients in Intervention in Myocarditis and Acute Cardiomyopathy-2 trial (IMAC-2) and 88% 4-year transplant-free survival—outcomes markedly better than earlier reports.[3]

Within the conceptual framework of Hulot *et al.*,[9] no single definition of LV reverse remodelling (LVRR) is universally accepted. LVRR has been described as either (i) an absolute LVEF increase ≥10% or to >50% and/or (ii) a reduction in LV end-diastolic diameter to ≤33 mm/m^2 or by ≥10% relative decrease.[23–28] In this document, LVRR refers to an LVEF increase to >40%—either spontaneous or therapy-related—accompanied by LV volume reduction. Patients with ROCM display a higher probability of LVRR and EF improvement than those with ischaemic or chronic non-ischaemic cardiomyopathies.[8] Some achieve spontaneous recovery following removal of the trigger, while others reach a state of remission without complete recovery. In contrast, a subset will deteriorate or remain stable despite GDMT and device therapy.[2,29]

Left ventricular ejection fraction trajectories in ROCM can be categorized into four dynamic phases of disease evolution, adapted from Hulot *et al.*,[9] each with specific therapeutic implications (*Graphical Abstract*; *Table 2*): (*recHF*) sustained normalization of LVEF (≥50%), functional status, LV volume, and biomarkers [N-terminal pro-B-type natriuretic peptide (NT-proBNP), global longitudinal strain (GLS)] with absence of late gadolinium enhancement (LGE). In this group, cautious and individualized tapering of GDMT may be appropriate.[30] (*RemHF*): recovery of LVEF ≥50% with persistent minor structural or biomarker abnormalities (incomplete normalization of LV volumes, GLS, or residual LGE). These patients remain at higher risk of remodelling or relapse, particularly after GDMT withdrawal or during new stressors and (*impHF*)—partial recovery of LVEF to >40% but <50%, fulfilling ESC criteria for HF with mildly reduced EF. Under contemporary GDMT, many patients with ROCM should potentially progress to full recovery over time. Persistent reduced EF (*redHF*) and absence of LVRR (LVEF ≤40%) despite optimized therapy, associated with adverse outcomes, including higher mortality and HF hospitalization.

Recognition of these functional trajectories facilitates risk-adapted management, guiding timely consideration of device implantation or advanced HF referral.

Epidemiology of recent-onset cardiomyopathy

The epidemiology of ROCM reflects complex interactions among demographic factors, regional risk profiles, and healthcare access, resulting in significant global heterogeneity. Accurate epidemiological data remain challenging to ascertain due to variability in diagnostic criteria and reporting.[2] Non-ischaemic cardiomyopathies account for 30%–40% of HF cases across all LVEF categories,[10] with geographical disparities—rising to 60% in patients with heart failure eith reduced ejection fraction (HFrEF).[10] Among non-ischaemic aetiologies, hypertension predominates (~50%), followed by idiopathic causes (up to 30%), valvular disease, and rarer subtypes.[11]

Regional registry data (ESC-HF-LT,[12] IMPROVE-HF,[13] ASIAN-HF,[14] and INTER-CHF[15]) highlight striking variations that maybe resource related: non-ischaemic HFrEF constitutes 35% of cases in North America but up to 80% in Africa.[16] Contemporary HFrEF trials (DAPA-HF,[31] PARADIGM-HF,[32] EMPEROR-Reduced,[17] GALACTIC-HF,[18] and VICTORIA[19]) report non-ischaemic aetiologies in 40%–47% of participants. The Swedish Heart Failure Registry (Swede-HF)[20–22] further delineates non-ischaemic cardiomyopathy epidemiology, with 51%–57% of HFrEF cases presenting within 6 months of symptom onset[23]—a proportion that has increased in recent years. Only a subset of non-ischaemic cases (30%) fulfils strict ROCM criteria; reported proportions vary with diagnostic stringency and access to imaging/genetics. Silent pre-symptomatic phases likely lead to under-recognition.[2]

Role of diagnostics in risk stratifying patients with recent-onset cardiomyopathy

Imaging studies, biomarkers, and genetic testing in addition to clinical evaluation are mainstay for risk stratifying patients with ROCM to predict LVRR and risk of SCD and thus for selecting patients for devices and advanced HF therapies (*Figure 1*; Supplementary Table S1). Note that most of the below diagnostics are recommended in any cardiomyopathy workup with few specificities to ROCM. Discussing diagnostics in this clinical consensus statement is in the context of LVRR–SCD axes.

The role of electrocardiogram in recent-onset cardiomyopathy

As a first-line assessment, electrocardiogram (ECG) detects abnormalities that guide further diagnostics, risk stratification, and therapeutic decisions, though its findings are often non-specific and must be integrated with imaging and clinical context.[24,25] Electrocardiogram provides prognostic insights by identifying high-risk features. Some electrocardiographic features should raise the suspicion of specific aetiologies.[1,24] In addition to arrhythmias [atrial fibrillation (AF) and ventricular tachycardia (VT)], depolarization/repolarization abnormalities, atrioventricular (AV)/intraventricular conduction disorders, and P-wave morphology alterations are important.[24] First-degree and advanced AV block are present in some genetic forms [e.g. involving lamin A/C (*LMNA*) gene] and other laminopathies, desminopathies, etc.[1,24] Moreover, extremely low QRS amplitude can suggest the diagnosis of aggressive genetic forms [e.g. phospholamban (PLN) gene variants] with a high risk of arrhythmias and SCD.[26–28] Left bundle branch block (LBBB), commonly observed at the time of diagnosis, may either contribute to or result from the disease and is associated with a lower likelihood of LVRR[27] and predict long-term mortality.[24] Furthermore, new-onset LBBB during follow-up has been identified as a strong independent predictor of major adverse cardiovascular events.[29] The presence of fragmented QRS complexes is another significant marker, linked to higher rates of all-cause mortality and ventricular tachyarrhythmias compared with patients without this finding.[30,33,34] High burden of PVCs, AF with rapid ventricular rate, and presence of new bundle branch block or high-degree AV block may signify a new onset of cardiomyopathy.

Specific arrhythmia may point towards specific aetiologies, such as tachycardia-induced cardiomyopathy or genetic cardiomyopathies. Some genetic defects, such as, *LMNA*, *FLNC*, RNA-binding motif-20 (*RBM20*), and PLN mutations, are associated with both LV dysfunction and polymorphic ventricular arrhythmias, with an increased risk of

Table 2 Nomenclature, types and characteristics of the clinical trajectories in recent-onset cardiomyopathy

Term	Definition	EF range	Structural/functional recovery[a]	Clinical implication	Clinically[b] (NYHA FC)	LV size	LGE	GLS	NT-proBNP[c]	Stability
Recovered EF (RecHF)	Full recovery of LVEF and cardiac structure/function	EF ≥50%	Normal LV size, normal LA, no significant diastolic dysfunction, no fibrosis on CMR, biomarkers normalized	May consider GDMT down-titration in selected cases, low SCD risk	I	Normal	Absent	Normal	Normal	>12 months
Remitted EF (RemHF)	Preserved or normalized EF but with residual structural or functional abnormalities	EF ≥50%	Abnormal GLS, persistent LV dilation, LGE, or elevated biomarkers (e.g. NT-proBNP)	Continue full GDMT, monitor closely; SCD risk may persist	I–II	Normal to mild dilation	Present	Abnormal	Normal to mildly elevated	< 12 months
Improved EF (ImpHF)	Partial EF recovery but remains <50%	EF 40%–49%	Some reduction in LV volume or NP, often symptomatic improvement	Maintain GDMT, reassess for ICD/CRT depending on fibrosis/genotype	Any class	Normal to moderate dilation (often dilated)	May be present	Mild to moderate ↓	Normal to mildly elevated—decreasing but still high	<12 months
Reduced EF (RedEF)	No EF improvement but clinical stabilization	EF <40%	Persistent dilation or dysfunction; stable symptoms, no progressive HF	Evaluate for device therapy; monitor LVRR or deterioration over time	Any class	Often moderate to severe dilation	Often present	Moderate to severe ↓	Persistently elevated	<3–6 months

The ROCM framework complements existing phenotype-based cardiomyopathy classification and is intended as a practical approach to early evaluation and management.
FAC, fraction area change; GLS, global longitudinal strain; LGE, late gadolinium enhancement; MR, mitral regurgitation; NP, natriuretic peptide; RVEF, right ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion.
[a]LV dysfunction: any of the following is still present: LV volume increase (LV dilated), increase left ventricular mass index (LVMi), increase left atrial (LA) size (≥moderate; low RVEF <50%; low FAC <35%; low TAPSE <17 mm; LV diastology >Grade 1; MR≥+2; GLS > −18%; LGE present); FAC, GLS, LGE, MR, RVEF, TAPSE.
[b]≥ New York Heart Association Functional Class (NYHA FC) 2.
[c]In addition, any positive troponin is considered abnormal and applies to all terms except RecHF.

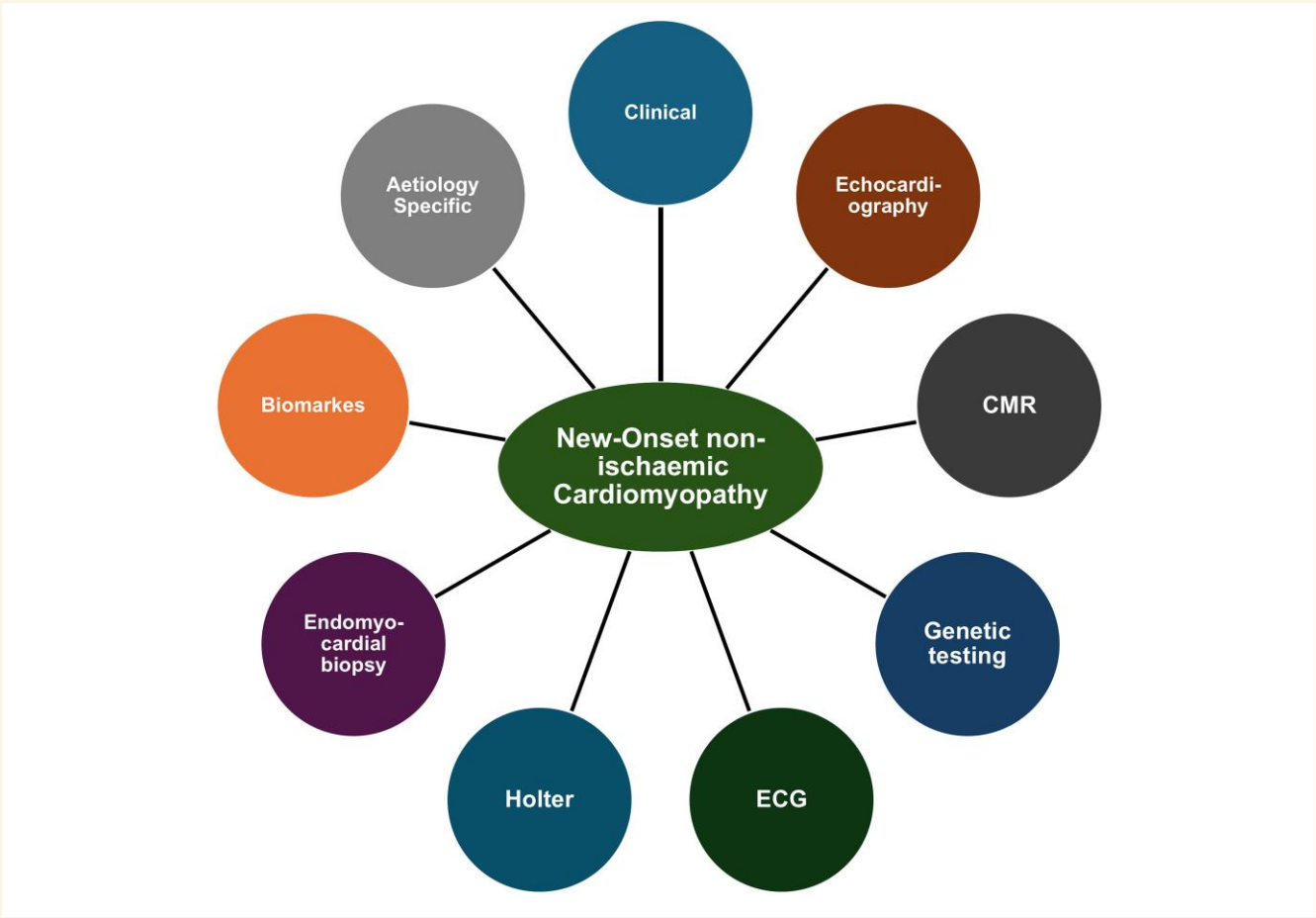


Figure 1 Diagnostic modalities used in diagnosis and risk stratification in new-onset non-ischaemic cardiomyopathies

SCD.[34,35] Carriers of *LMNA* and *SCN5A* mutations show a high prevalence of atrial arrhythmias mainly AF.[36–38] When combined with other imaging biomarkers—such as LGE on cardiac magnetic resonance imaging (MRI)—ECG findings enhance risk stratification, serving as a powerful predictor of mortality and SCD in ROCM patients.[24,35]

Holter monitoring (24–48 h ambulatory ECG) and implantable loop recorders (ILRs) enable prolonged rhythm assessment, detecting intermittent arrhythmias like AF, non-sustained ventricular tachycardia (NSVT), and conduction blocks that may contribute to or complicate the condition.[39,40] In the 2023 ESC cardiomyopathy guidelines, ECG Holter monitoring is part of multi-parametric assessment for DCM, revealing rhythm abnormalities in up to 40% of cases.[1] The 2018 ESC guidelines on syncope and the 2017 International Society for Holter and Noninvasive Electrocardigraphy and the Heart Rhythm Society (ISHNE-HRS) consensus endorses ILRs when non-invasive monitoring fails to diagnose aetiology of syncope or palpitations in HF.[40,41] In peripartum cardiomyopathy (PPCM), arrhythmias detected by ILR correlate with poor prognosis (80% adverse events vs 20% without), including death or transplantation.[39] In ROCM, detecting such arrhythmias early with timely intervention may lead to remission–recovery clinical trajectory.

Echocardiography in recent-onset cardiomyopathy

Transthoracic echocardiography (TTE) is a first-line, non-invasive tool for the comprehensive assessment of ROCM, providing valuable insights into aetiology, prognostic stratification, and serial evaluation of reverse remodelling.[42–46] Beyond diagnostic features, multiple echocardiographic parameters—including 2D/3D cardiac volumes, Doppler imaging, tissue Doppler, and strain analysis—hold prognostic significance and are used to monitor LVRR[42,43] (Supplementary Table S2).

Left ventricular size, wall thickness, and absence of atrial enlargement may reflect a new onset and potentially reversible cardiomyopathy. Conventional measures such as LVEF and left atrial volume remain strong predictors of transplant-free and left ventricuar assist devices (LVAD) -free survival, while Doppler-derived diastolic function indices (e.g. E/e′ ratio) correlate with filling pressures and long-term outcomes.[47] Global longitudinal strain is a key prognostic marker for LVRR, with higher GLS values indicating better reverse remodelling—even in cases with similar LVEF.[48] During follow-up, serial strain imaging quantifies the degree of reverse remodelling in response to guideline-directed therapy, where improvements in longitudinal strain often precede overt LVEF recovery and predict sustained clinical benefit.[43,48]

Additionally, 3D echocardiography offers reproducible volumetric measurements, enabling more accurate tracking of remodelling dynamics compared with 2D techniques and allowing timely adjustments to medical or device-based interventions.[47] When integrated with laboratory biomarkers and CMR findings, echocardiographic indices create a comprehensive framework for personalized ROCM management, guiding both therapeutic decisions and the monitoring for myocardial recovery.[42–44]

Cardiac magnetic resonance

Cardiac magnetic resonance (CMR) with tissue characterization plays a pivotal role in determining the underlying aetiology of

cardiomyopathies in general and in the framework of ROCM in specific, particularly through LGE imaging (Supplementary Table S1). This is crucial, as various conditions may present clinically overlapping features yet require distinct therapeutic approaches. Importantly, LGE patterns help identify or exclude ischaemic aetiology as a cause of LV dysfunction. The absence of LGE is associated with a more favourable prognosis.[49] While coronary angiography is regarded as the gold standard for distinguishing ischaemic from non-ischaemic causes, a notable limitation is that myocardial infarction may still occur despite unobstructed coronaries—due to spontaneous recanalization, coronary spasm, or embolic events.[50] The pattern and distribution of LGE, combined with advanced tissue characterization techniques (T1 and T2 mapping), aid in differentiating dilated cardiomyopathy (DCM)/nonischemic cardiomyopathy (NICM) mimics, such as acute/chronic myocarditis and sarcoidosis. Elevated T2 signal indicates myocardial oedema or inflammation, characteristic of acute phases in these conditions, while T2* imaging helps exclude iron overload in haemochromatosis.[51,52] This may reflect timing or duration of the cardiomyopathy.

Beyond LV dysfunction, RV dysfunction and the extent of LGE detected by CMR are independent predictors of reduced likelihood of functional recovery.[49] Moreover, across multiple cardiomyopathies, the presence of fibrosis on LGE is associated with worse outcomes, including higher risks of major/fatal arrhythmias, HF events, and mortality. These findings provide incremental prognostic value over LVEF, which may be a less reliable predictor in this patient population.[53–55]

Several ongoing randomized trials (e.g. CMR-GUIDE and BRITISH) are evaluating whether LGE can guide patient stratification for implantable cardioverter-defibrillator (ICD) placement vs medical therapy alone. Until these results are available, LGE should not be used as the sole decision-making criterion but may assist in risk assessment for 'grey zone' cases.

Blood biomarkers in recent-onset cardiomyopathy

Circulating biomarkers can provide crucial diagnostic and prognostic information in ROCM and may provide its acuteness/duration. Cardiac-specific biomarkers like troponins (cTnI, cTnT) reliably detect myocardial injury, with elevated levels indicating active damage regardless of ischaemic or non-ischaemic aetiology.[56] Natriuretic peptides (BNP, NT-proBNP), well-established markers of haemodynamic stress, not only aid in HF diagnosis but also help assess disease severity. Recent advances include age-adjusted NT-proBNP thresholds that facilitate earlier HF detection when clinical symptoms appear.[57] Serial NT-proBNP measurements are particularly valuable, as decreasing levels correlate with LVRR, functional improvement, and better prognosis.[58–60] NT-proBNP and troponin trends are primary decision points. Failure of NT-proBNP to fall meaningfully by 3 months—or recurrent troponin positivity—should prompt absence of LVRR and repeat imaging (echocardiography ± CMR), device/ablation review, and consideration of endomyocardial biopsy (EMB) if inflammation remains suspected is to be considered in cases of myocarditis.[61]

Inflammatory markers like high sensitivity C-Reactive Protein (hs-CRP) offer clinically accessible insights into systemic inflammation, potentially guiding immunomodulatory therapy; however, their role alongside that of immunomodulatory therapies is yet to be established.[57] Among emerging biomarkers, soluble ST2 (IL1RL1) demonstrates promise, with elevated levels predicting worse outcomes in young male myocarditis patients—underscoring the need for sex- and age-specific biomarker interpretation.[62]

Future diagnostic innovations may incorporate liquid biopsy technologies and next-generation sequencing to detect novel biomarkers, including DNA methylation patterns, microRNA signatures, and exosome-derived proteins.[63–65] These advanced approaches could revolutionize ROCM management by enabling more precise diagnosis, accurate prognosis prediction, and personalized treatment monitoring—ultimately improving outcomes for this complex condition.

Endomyocardial biopsy in recent-onset cardiomyopathy

Endomyocardial biopsy, despite its limitation mainly regarding to sampling, remains the in vivo gold standard for aetiological diagnosis and risk stratification in cardiomyopathies including those with recent onset (particularly fulminant or acute myocarditis cases). Prospective studies demonstrate that EMB performed within 48 h of intensive care unit admission for suspected fulminant myocarditis significantly improves 1-year transplant-free and LVAD-free survival, particularly in lymphocytic myocarditis cases.[66] While non-invasive imaging cannot reliably differentiate infectious from non-infectious aetiologies, a critical distinction for selecting immunosuppressive vs immunomodulatory therapies, EMB provides definitive histopathological diagnosis to guide treatment decisions.[67] Endomyocardial biopsy is particularly crucial in patients presenting with cardiogenic shock or ventricular arrhythmias within 24–48 h from presentation.[61,68] In systemic sclerosis, EMB-quantified fibrosis extent correlates with major adverse cardiovascular events, including ventricular arrhythmias.[69] Biopsy most accurately assesses diffuse interstitial fibrosis (a common consequence of myocardial inflammation), while cardiac MRI with LGE better detects focal scarring.[70] Notably, combined evaluation of cardiomyocyte degeneration on EMB and LGE burden on CMR independently predicts LVRR response to guideline-directed therapy, highlighting the complementary prognostic value of multimodal tissue characterization in recent-onset scenarios.[71]

Genetic testing in recent-onset cardiomyopathy

Recent advances in next-generation sequencing and genome-wide association studies have significantly enhanced our understanding of the genetic basis of DCM, including those with recent onset. The genetic architecture of DCM is complex, exhibiting incomplete penetrance, variable expressivity, and poorly defined genotype–phenotype correlations. To date, over 50 genes have been associated with the disease. Genetic evaluation advised in ROCM patients presenting with arrhythmias.[1] While pathogenic variants are identified in ∼40% of familial DCM cases, the diagnostic yield is substantially lower in sporadic forms.[72] The inheritance is typically autosomal dominant in the adult population. Notably, 5%–15% of patients with acquired cardiomyopathies (including myocarditis, toxic exposures, cancer therapy-related cardiac dysfunction, endocrinopathies, and systemic diseases) harbour pathogenic or likely pathogenic variants.[73–75] The most prevalent genetic causes include *titin*-truncating variants (*TTNtv*) and *LMNA* accounting for up to 25% and 10% of all genetic causes, respectively.[76,77] Other clinically significant genes implicated in cardiomyopathy pathogenesis and associated arrhythmic manifestations include variants in the myosin heavy chain (MYH7), filamin C (FLNC), RBM20, Troponin-T (TNNT2), Troponin-C1 (TNNC1), PLN, desmoplakin (DSP), and BLC2-associated athanogene 3.[77]

In a recent prospective study of 386 ROCM patients, 25% were familial, 32% had variants of interests (VOIs), 18% had a single titin-truncating variant (TTNtv), and 14% had non-titin (non-TTN) genes VOIs.[76]

Lower probability of LVRR at 12 months occurred in patients with Class 4–5 non-TTN, genes coding nuclear envelops proteins VOIs, and family history of DCM.[77,78] Higher probability of death and fatal arrhythmias detected in non-TTN genes and in nuclear envelope proteins VOIs.[77] Genes coding cytoskeleton proteins were associated with an increased risk of life-threatening ventricular arrhythmias (*Figure 2*). On the other hand, negative result of genetic testing is a strong protective baseline variable against occurrence of life-threatening ventricular arrhythmias.[76] This emphasizes further that genotyping may improve early risk stratification at

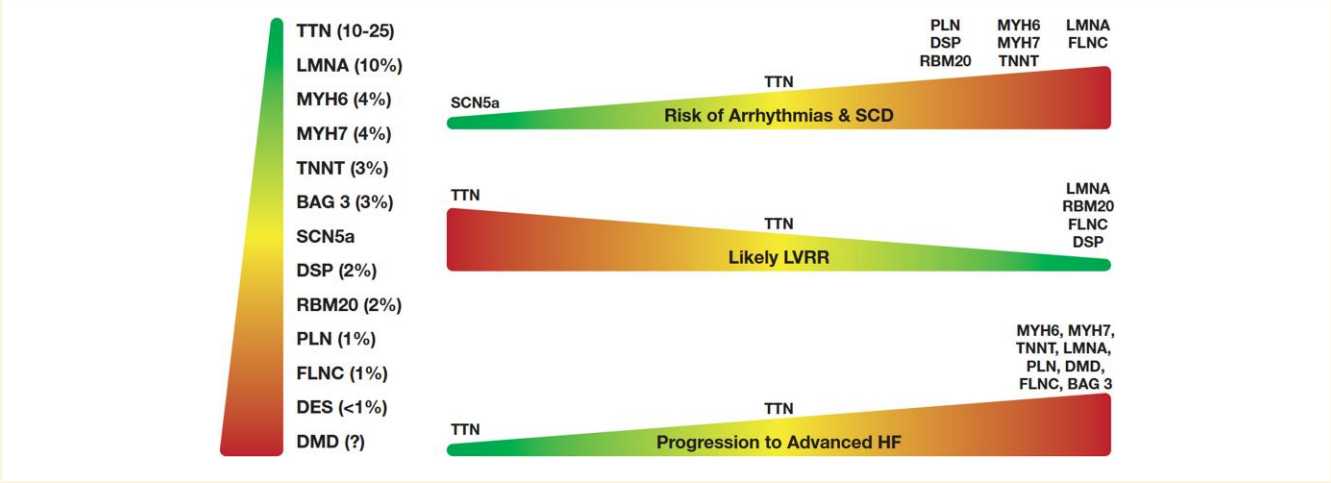


Figure 2 Most common genotypes and their relevance risk stratification in non-ischaemic cardiomyopathies

baseline assessment. In a large genetically and CMR characterized DCM/NDLVC cohort, arrhythmogenic (DSP, LMNA, FLNC, and RBM20) genotypes and LGE ring-like pattern demonstrate inverse relationships with LVRR, particularly in patients with LVEF <35%.[78] Emerging evidence supports the combined use of genotyping and cardiac MRI to identify high-risk DCM profiles, such as FLNC and DSP protein coding (DSP) variants with distinctive subepicardial LGE patterns are associated with NSVT.[79] This integrated approach enables more precise risk assessment and personalized management early in the disease course.Therefore, early genetic testing when indicated may provide additional LVRR–SCD axes information that will impact therapies.

Effect of guidelines-directed medical therapy on left ventricular reverse remodelling and sudden cardiac death

Left ventricular reverse remodelling with pharmacological therapy in HFrEF includes reduction of left ventricular end-diastolic volume (LVEDV) and/or left ventricular end-systolic volume (LVESV), reduction in mitral regurgitation (MR) grade, improvement in diastolic filling, reduction in left ventricular end-diastolic pressure (LVEDP), and/or improvement in LVEF.[80] Left ventricular reverse remodelling is an important therapeutic target as drugs that improve survival in HFrEF generally are associated with reverse remodelling effects.[81–84] Guideline-directed medical therapy in HFrEF is associated with reverse remodelling in a significant proportion of patients.[81] In a recent study of 598 *de novo* HF patients with LVEF <35%, almost half of the patients achieved LVEF >35% after 3 months.[85] The different classes of GDMT drugs have been reported to induce reverse remodelling to a varying degree. Recent data showing that sacubitril/valsartan demonstrated a pronounced effect on LVRR.[60,86,87] However, it is difficult to assess the relative importance of different drug classes on remodelling as smaller effect of newer drugs (e.g. SGLT2i) might reflect that patients in the relevant studies were already treated with Renin-Angiotensin-System (RAS) inhibitors and beta-blockers and as such the individual patient's potential for remodelling might already have mostly been obtained by the first drugs initiated.[88–90] Historic data seem to suggest that the largest effect on remodelling in HFrEF might be that caused by beta-blockade, though the results of beta-blockers should be revisited as studies had been conducted in patient with poor background therapy and therefore higher risk. In this context, it is evident that LV volumes are sensitive to heart rate, which may, in part, explain the results observed with beta-blockade and ivabradine.[91] In the current era of simultaneous initiation of several classes of GDMT, understanding individual drug effect on remodelling is difficult if not impossible.

An important question is if LVRR effect of GDMT is different in ROCM compared with chronic HF. Data suggest that different effects exist in two scenarios. In a recent study of 416 patients with an LVEF <35%, in whom treatment with sacubitril/valsartan was initiated, shorter duration of HF was among the most important predictors of LVRR.[92] Older data with angiotensin-converting enzyme inhibitor (ACEi) and beta-blockers alone in patients with non-ischaemic cardiomyopathies also support that shorter duration of HF predicts LVRR.[93] This relation between duration of HF and likelihood of LVRR is well known also after treatment with non-pharmacological treatment, i.e. mechanical unloading using LV assist devices.[94]

The time course of remodelling has been assessed in several studies. The positive effects of beta-blockers on remodelling are not apparent in the first month,[95] but effects of other drug classes or combinations have been observed after 3 months.[60] Continued improvement in LV structure and function with GDMT has been described over at least 12 months after therapy initiation. For sacubitril/valsartan, the effect between months 6 and 12 after initiation appears to be as large as the effect within the first 6 months.[92]

Guideline-directed medical therapy decreases not only the risk of HF progression but also the risk of SCD[7] (*Table 3*). This, obviously, has implications for timing of the decision to implant a prophylactic ICD in patients with HF, particularly those with ROCM treated with GDMT. There is a clear correlation between low LVEF as well as high left ventricular end-diastolic diameter (LVEDd) and the risk of SCD.[96,97] However, this does not necessarily imply that the improvement in LVEDd or LVEF ameliorates the risk of SCD. Importantly, a residual risk of SCD remains despite reverse remodelling, and it has been argued that even in patients with improvement in LVEF to a value >35% with GDMT, a prophylactic ICD may not be safely deferred in all patients.[98] Further studies and risk stratification, including genetic testing results, to define which patients with ROCM require a prophylactic ICD are clearly needed.

There is also an association between LVRR and risk of SCD. The association between LVRR and life-threatening VAs has been reported in CRT studies, which justified the unique role of LVRR in SCD development.[99] Such associations were also confirmed in pharmacotherapy studies. Minami *et al.*[100] showed that, in patients with new-onset HFrEF treated with conventional HF medications, every 1% increase

Table 3 **Recent trials and impact on left ventricular reverse remodelling and sudden cardiac death**

Study name (author), no. of participants	Patient characteristics	Intervention	Background HF therapy	Follow-up (months)	Δ LVEF, LVV upon	Withdraw ICD indications, LVEF >35%
PROVE-HF, *N* = 794	HFrEF: NICM: 46%; new-onset: 10%; NYHA: II: 70%, NYHA III: 28%; NYHA IV: 2%; median LVEF 28%, (IQR: 24%–34%)	Switch to ARNI	ARNI ~100%; β-blockers ~95%; MRA ~35%	6 and 12	LVEF + mean 5.2% (4.8, 5.6); LVEDVi: −6.65 (−7; −6) (~8%) at 6 months: LVEF +9.4% (8.8; 9.9); LVEDVi −12.3 (−13; −12) (~15%) ml/m^2 at 12 months	32% at 6 months 62% at 12 months
Martens *et al.*[86] *N* = 151	HFrEF: NICM: 31%; NYHA: II: 68%, NYHA III: 30%; NYHA IV: 2%; median LVEF 29 ± 9%; duration of heart failure: 4.3 years (1.4–8.4)	Switch to ARNI	ARNI ~100% β-blockers ~95% MRA ~86%	12	LVEF +5% and above in 44% patients	No data
SAVE-ICD *N* = 230	HFrEF and LVEF ≤35%: NICM: 47% ; NYHA II: −55%, NYHA III: 42%; NYHA IV: −1%; median LVEF 28% ± 5.6%	ARNI initiation	ARNI ~100% β-blockers ~96% MRA ~73%	6	LVEF +3.9% Absolute increase in LVEF of ≥5 in 50%; 5%–7% in 26%; 8–10% in 14%; >10% in 11%	25% at 6 months
EMPA-TROPISM, *N* = 84	HFrEF, no diabetes: NICM: 50%; median LVEF 36.2% ± 8.2%	Empagliflozin 10 mg vs placebo	ACEIs/ARBs ~42%; ARNI ~43%; β-blockers ~88%; MRA ~31%	6	Empagliflozin vs placebo: LVEF +6% (+6 ± 4% vs −0.1 ± 3.9%), *P* = .001; LVEDV (−25.1 ± 26 vs −1.5 ± 25), *P* = .001	No data
SUGAR-DM-HF *N* = 105	HFrEF and LVEF ≤40% and diabetes: NYHA II: −77%, NYHA III: 23%; median EF 32% ± 10%; duration of heart failure, median (IQR), years, 2.1 (1.0–4.8)	Empagliflozin 10 mg vs placebo	ACEIs/ARBs ~61% ;ARNI ~34%; β-blockers ~90%; MRA ~60%	6	Empagliflozin vs placebo: LVEF +1.8 (5.7) vs 1.2 (3.8), *P* = .75; LVEDVi −9.0 (12.4) vs −0.4 (14.1), *P* = .004	No data
HF-OPT, *N* = 598	Newly diagnosed HFrEF and LVEF <35%; NICM: 58%; median LVEF 23 (IQR: 18–28)	GDMT + WCD	ACEI/ARBs:~68%; ARNI: ~25%; β-blockers: ~95%; MRA: 60%; ivabradine: 5.2%	12	Median LVEF improved from 23% (IQR 18%–28%) at index to 34% (IQR 28%–43%) at Day 90 and to 40% (IQR 33%–48%) at Day 180 (*P* < .001)	46% at 3 months 68% at 6 months 77% at 12 months

Continued

Table 3 *Continued*

Study name (author), no. of participants	Patient characteristics	Intervention	Background HF therapy	Follow-up (months)	Δ LVEF, LVV upon	Withdraw ICD indications, LVEF >35%
Tardif *et al.*[91] SHIFT (*N* = 411)	HFrEF <35%, sinus rhythm, and had resting heart rate ≥70 b.p.m. Duration of heart failure (years) 3.5 + 4.0 years NICM 33%	Ivabradine vs Placebo	ACEi/ARB: 97% (no ARNI) BB: 92% MRAs: 74%	8	Ivabradine reduced LVESVI vs placebo [−7.0 + 16.3 vs −0.9 + 17.1 ml/m^2; difference (SE), −5.8 (1.6), 95% CI −8.8 to −2.7, $P < .001$]. LV end-diastolic volume index (−7.9 + 18.9 vs −1.8 + 19.0 ml/m^2 $P < .002$) and LVEF (+2.4 + 7.7 vs −0.1 + 8.0%, $P < .001$). LVEF (%) 32.3+/−9.1 baseline to 34.7+/−10.2 at 8 months Change 2.4 +/−7.7 Change LVEF ≤5% = 36%	No data

ARNI, angiotensin receptor nepilysin inhibitor; BB, beta blockers; LVESVI, left ventricular end s-systolic volume index; LVEDVi, left ventricular end-diastolic volume index; MRA, mineralocorticoid receptor antagonist.

in LVEF was associated with a 22% decrease in the odds of SCD [odds ratio per 1% increase 0.78; 95% confidence interval (CI) (0.65–0.93)]. Martens *et al.*[86] found a significant reduction of NSVT episodes within a year following switching from ACEi/(Angiotension receptor blocker (ARB) to sacubitril/valsartan, with a greater decrease in VA episodes in those with pronounced LVRR. Moreover, a *post hoc* analysis of DAPA-HF reported a 14% risk reduction of composite serious ventricular arrhythmias (VA), resuscitated cardiac arrest, or SCD with every 5% increase in LVEF.[101]

Non-pharmacological therapy in recent-onset cardiomyopathy

Non-pharmacological interventions in ROCM play a critical role in optimizing LVRR and mitigating SCD risk. These approaches range from device-based therapies to targeted intervention-based strategies that have demonstrated substantial impact on prognosis in selected patients. They include ICDs, CRT, catheter ablation of arrhythmias, and transcatheter edge-to-edge repair for functional mitral regurgitation (M-TEER). Each intervention must be individually considered based on the likelihood of LVRR and arrhythmic risk.

Implantable cardioverter-defibrillator

While optimized medical therapy has reduced SCD incidence, it remains responsible for up to one-third of deaths in DCM.[98,102,103] Current guidelines[46] recommend ICD implantation for NICM patients with LVEF <35% despite optimal therapy as Class IIa, though recent evidence supports a more nuanced approach.[104] Primary prevention with ICD remains central in reducing SCD risk, especially in NICM as large registries (e.g. EU-CERT-ICD) and meta-analyses[105–107] confirmed significant reductions in both SCD and overall mortality—particularly in younger patients and those without CRT. Consequently, guidelines continue to recommend, as level of evidence IIa, ICDs for symptomatic NICM patients with LVEF <35% despite optimal medical therapy (OMT) with life expectancy exceeding one year.[35,46] However, LVEF alone is a limited risk prognosticator.[45,108–110] Myocardial fibrosis (usually higher LGE on CMR)[110] and high-risk genetic variants (LMNA, FLNC, RBM20)[111] identify patients who benefit from early ICD placement, even with subsequent LVEF improvement or prior to complete 3 months of GDMT.[53,108]

ESC guidelines suggest a 3-month period of OMT before ICD implantation to allow for potential LVEF improvement.[35] But data from the recent HF-OPT trials show that continued GDMT optimization beyond 90 days can further improve LVEF: nearly half of patients with initially low LVEF improved to >35% by 180 days, potentially avoiding unnecessary ICD implantation.[85] The dynamic nature of LVRR in ROCM suggests that delaying ICD decisions for 3–6 months of GDMT may allow significant functional recovery in many patients, potentially avoiding unnecessary device implantation in a substantial proportion of patients. For individuals with a high anticipated likelihood of LVRR, a wearable cardioverter-defibrillator (WCD) could serve as a useful bridging therapy.[112–114] This strategy provides protection from SCD while allowing continued GDMT during the critical waiting period prior to a final decision on permanent ICD implantation.

These findings support a more individualized approach to ICD timing, incorporating ongoing assessment of LV remodelling and arrhythmic risk markers to optimize outcomes.[115]

Cardiac resynchronization therapy

For patients with ventricular conduction delays (particularly LBBB with QRS ≥130 ms), CRT promotes substantial reverse remodelling, with ~30% of HF patients qualifying for this intervention.[116] CRT can lead to significant LVRR and improvement in LVEF, potentially reducing mortality risk, including the risk of SCD.[117] This has led to ongoing debate about whether adding a defibrillator to CRT therapy is necessary. In newly diagnosed cardiomyopathies, the choice between CRT-pacemaker (CRT-P) and CRT-defibrillator (CRT-D) should incorporate assessment of both remodelling potential and arrhythmic risk. Older patients with significant comorbidities and low arrhythmic risk may benefit from CRT-P alone, while those with extensive scarring or arrhythmogenic genotypes typically require CRT-D. Predictive models incorporating CMR findings (LGE quantification) and genetic data can optimize device selection as well as timing of CRT.[118,119]

Catheter ablation

Rhythm control through catheter ablation has emerged as a therapeutic strategy, particularly for tachycardia-mediated cardiomyopathy. Atrial fibrillation and HF frequently coexist and worsen each other's prognosis.[120,121] Atrial fibrillation impairs standard HF therapies, reduces CRT efficacy, and increases mortality.[120,122] Recent trials demonstrate ablation's superiority over rate control, with EAST-AFNET trial and CASTLE-AF showing significant mortality reduction and LVEF improvement in HFrEF patients.[123–125] Similarly, CAMERA-MRI reported a +18% LVEF increase post-ablation in patients with AF-induced cardiomyopathy.[126,127] The procedure is particularly effective for patients with high arrhythmia burden or LVEF <30%, with ESC guidelines now recommending ablation as first-line therapy for suspected arrhythmia-induced cardiomyopathy.[121] A recent meta-analysis of six randomized control trials (RCTs) confirmed that AF ablation in HFrEF reduces mortality, hospitalizations, and improves LVEF and QoL. Benefit was most pronounced in patients with LVEF <30%, NYHA ≥III, or high AF burden.[128]

In more advanced HF, CASTLE-HTx confirmed that ablation in end-stage HF patients reduced the combined risk of death, LVAD implantation, or heart transplantation by 76%. These benefits were maintained at 2-year follow-up.[124,129]

Frequent premature ventricular contractions (PVC) can cause arrhythmia-induced cardiomyopathy in patients without structural heart disease[130] and worsen LV function in the case of pre-existing LV systolic dysfunction. For PVC-induced cardiomyopathy, ablation achieves long-term success rates approaching 90%, making it the preferred intervention.

In summary, early rhythm control, when indicated, is advised in ROCM for significant LVRR and clinical outcome.

Transcatheter edge-to-edge repair

Functional MR (FMR) is the most common valvular disease in HF and is associated with worse symptoms, increased hospitalizations, and reduced QoL.[131] For patients with persistent symptomatic FMR despite GDMT and CRT, M-TEER offers symptomatic improvement and reduction in HF hospitalizations.[132] While M-TEER effectively reduces symptoms and HF hospitalizations in FMR, its impact on mortality remains uncertain. Current evidence supports its use in carefully selected ROCM patients where significant MR impedes reverse remodelling, particularly when persistent despite optimal medical and device therapy.[133–135] With the RESHAPE-2 trial, a broader application of M-TEER for HF patients with less-than-severe FMR may be appropriate, and further investigation is warranted including ROCM patients.[136] Ongoing research is evaluating its potential role in less severe MR cases.

These interventions collectively enable a precision medicine approach to ROCM management, where comprehensive assessment of remodelling potential and arrhythmic risk guides therapeutic decisions. The integration of advanced imaging, genetic testing, and continuous risk reassessment throughout the clinical course is essential for optimizing outcomes in this heterogeneous patient population.

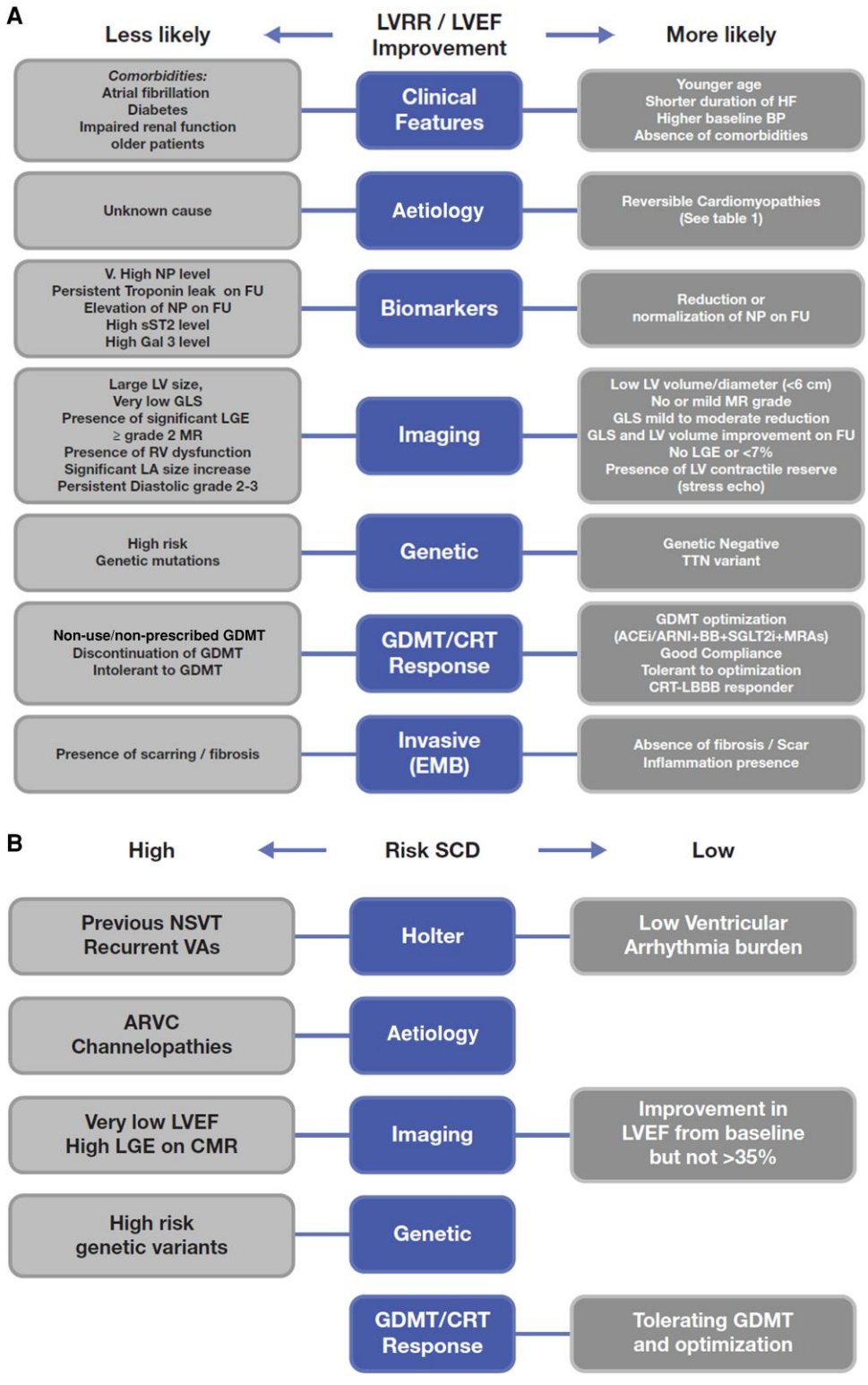


Figure 3 Factors favouring (*A*) left ventricular reverse remodelling and (*B*) sudden cardiac death risk

The relationship is not just correlational but causal and time dependent. The duration of HF is a critical determinant of the development, severity, and potential reversibility of FMR. Managing FMR effectively requires early intervention in the HF disease process to disrupt the self-perpetuating cycle of remodelling and regurgitation.

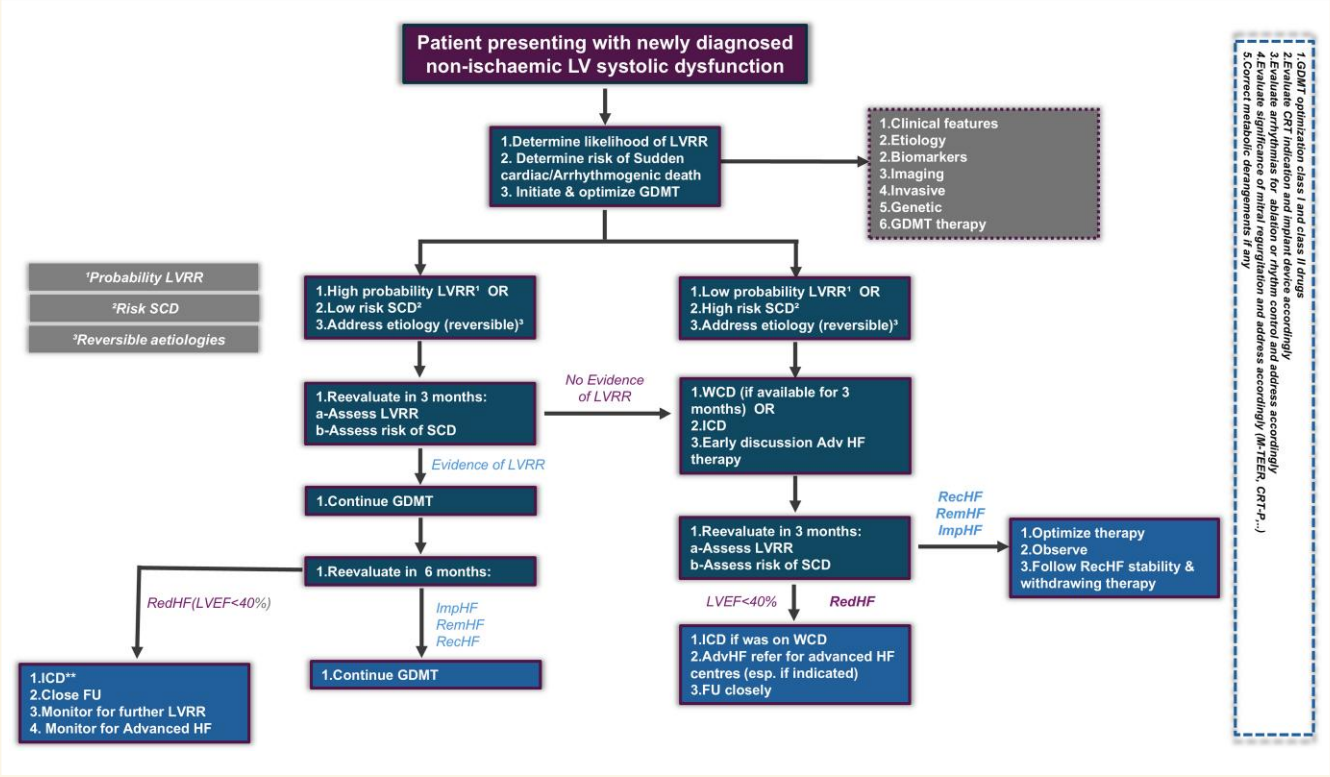


Figure 4 Proposed algorithm for the diagnosis and management of recently diagnosed non-ischaemic cardiomyopathies

Conditions to consider withdrawing therapy

Heart failure with improved EF (impHF) occurs in 10%–40% of HFrEF patients following GDMT, device therapy, or spontaneous recovery.[137] While improved EF is associated with better prognosis, it rarely represents full recovery and often is transient.[9,138]

Recent terminology of clinical trajectories distinguishes impHF, remHF, and recHF, though their long-term clinical course is not fully understood.[9] In clinical studies, predictors of LVRR include female sex, non-ischaemic aetiology, and low biomarker levels (NT-proBNP, troponin, and galactin-3).[139] Absence of high-risk genetic variants responsible of pathogenic mutations in cytoskeleton proteins (truncating titin mutations) was also associated to reverse remodelling.[140,141] Broader use of comprehensive HF therapy with full implementation of the four therapeutic pillars has increased impHF prevalence, but data guiding long-term management remain limited—especially in patients who normalize EF (LVEF ≥50%).[9]

The TRED-HF trial[142] addressed GDMT withdrawal in patients with recovered or partially recovered EF. Within 6 months, 44% relapsed after stopping therapy. Long-term follow-up (median 6 years) showed 65% relapsed, often due to therapy down-titration, triggers, or disease progression.[143] Similar risks were noted in post myocardial infarction and cancer treatment related cardiac dysfunction after stopping cardioprotective drugs, particularly in patients with baseline LVEF <45%.[144,145]

In contrast, limited data suggest that neurohormonal blockade withdrawal may be safe in carefully selected CRT responders, but evidence is scarce.[146] More recently, the Withdrawal of HF therapy after AF rhythm control with EF normalization (WITHJDRAW-AF) Trial have shown that withdrawal of HF therapy in AF cardiomyopathy with normalized EF following AF rhythm control was not associated with a decline in LVEF for most patients in the following 6 months.[147]

The clinical challenge remains balancing potential adverse effects of continued therapy against the significant relapse risk upon withdrawal, emphasizing the need for individualized decision-making guided by serial cardiac assessment.

Risk stratification in recent-onset cardiomyopathy

In ROCM, LVRR and SCD risk vary by aetiology, genetics, and treatment response (*Figure 3A and B*). Reversible conditions show high LVRR rates and low SCD risk. Despite response to GDMT and functional recovery, SCD risk persists in patients with high-risk genetic variants, significant myocardial fibrosis, or high arrhythmia burden necessitating ongoing risk stratification and primary prevention ICD/WCD (wearable cardioverter defibrillator).

Effective ROCM management relies on integrating clinical, imaging, biomarker, and genetic data to predict and assess LVRR potential and SCD risk and to guide therapeutic decisions. This multimodal, personalized approach optimizes outcomes by tailoring interventions and avoiding premature escalation to advanced therapies. Contemporary GDMT and CRT have been proven to enhance remodelling.

Systematic evaluation and longitudinal assessment of these predictors in patients with ROCM is paramount. There is always needed to evaluate eligibility of CRT and valvular TEER that help in LVRR, better use of GDMT, improve outcome, and delay progression to advanced HF (*Figure 4*; Supplementary Figure S1). Identifying factors favouring LVRR enables tailored risk stratification, potentially delaying advanced device therapy, while recognizing predictors of progression mandates early referral for advanced management. Similarly, high arrhythmic

risk may benefit from early ICD or WCD use, while others should be monitored on GDMT optimization with re-evaluation at 3 months intervals.

Future perspectives and conclusions

The evolving landscape of ROCM necessitates the strategic integration of circulating biomarkers with advanced imaging, histopathology, and continuous monitoring to refine risk stratification and optimize evidence-based HF therapy.[148] Prospective ROCM-focused registries, phenotype-stratified studies of recovery and relapse trajectories, and studies addressing optimal timing of device therapy are needed. In addition, Further research is needed to evaluate the combined impact of foundational therapy on LVRR and residual risk of SCD among patients with ROCM. AI has a great potential in ROCM to facilitate the generation of individualized risk scores for LVRR that outperform traditional criteria.[149] Optimizing the timing of device therapy (ICDs and CRT), while minimizing unnecessary interventions and maximizing the likelihood of durable cardiac recovery is one of AI broad applications.

A prioritization of serial, multi-marker panels to capture dynamic pathophysiological shifts in ROCM—integrating real-time biomarker trends with AI-driven algorithms that synthesize data streams from echocardiographic strain imaging, CMR tissue characterization, EMB histology, and continuous rhythm monitoring—should enhance our understanding, facilitating improved risk stratification and the development of personalized management approaches in ROCM.[150–153]

Prompt implementation and up-titration of GDMT will remain the cornerstone of ROCM management. Early initiation—ideally during the acute hospitalization phase—has been consistently associated with improved survival and enhanced LVRR.[46] Biomarker-guided therapy adjustments, such as escalating drug doses in the setting of persistently elevated NT-proBNP, can close treatment gaps and tailor pharmacotherapy intensity to individual risk profiles.[154,155] Moreover, biomarkers may inform the timing of advanced interventions: for instance, persistently elevated NT-proBNP despite optimal GDMT could indicate the need for early consideration of CRT or prophylactic ICD placement in high-risk ROCM subsets.[156,157] Ongoing clinical trials, including BRITISH CMR, GUIDE DCM, CMR-ICD, SPANISH-1, and PROFID, aim to investigate the efficacy of ICDs for primary prevention in HFrEF, including ROCM, in the context of contemporary GDMT, incorporating, genetic testing, CMR and electrophysiology studies for SCD risk stratification.[158–160]

In conclusion, ROCM represents a dynamic disease entity with substantial potential for recovery and variable risk of SCD. This clinical consensus statement provides a structured approach for diagnosis, stratification, and therapeutic management based on the likelihood of LVRR and arrhythmic risk. By integrating clinical, imaging, biomarker, and genetic data and by emphasizing the need for dynamic reassessment, this framework aims to help physicians with timely management and referrals.

Supplementary data

Supplementary data are available at *ESC Heart Failure* online.

Declarations

Disclosure of Interest

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References

1. Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, *et al.* 2023 ESC Guidelines for the management of cardiomyopathies. *Eur Heart J* 2023;**44**:3503–626. https://doi.org/10.1093/eurheartj/ehad194
2. Givertz MM, Mann DL. Epidemiology and natural history of recovery of left ventricular function in recent onset dilated cardiomyopathies. *Curr Heart Fail Rep* 2013;**10**:321–30. https://doi.org/10.1007/s11897-013-0157-5
3. McNamara DM, Starling RC, Cooper LT, Boehmer JP, Mather PJ, Janosko KM, *et al.* Clinical and demographic predictors of outcomes in recent onset dilated cardiomyopathy: results of the IMAC (Intervention in Myocarditis and Acute Cardiomyopathy)-2 study. *J Am Coll Cardiol* 2011;**58**:1112–8. https://doi.org/10.1016/j.jacc.2011.05.033
4. 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 heart failure. *Eur Heart J* 2021;**42**:3599–726. https://doi.org/10.1093/eurheartj/ehab368

5. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al.* 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2023;**44**:3627–39. https://doi.org/10.1093/eurheartj/ehad195
6. Tromp J, Ouwerkerk W, van Veldhuisen DJ, Hillege HL, Richards AM, van der Meer P, *et al.* A systematic review and network meta-analysis of pharmacological treatment of heart failure with reduced ejection fraction. *JACC Heart Fail* 2022;**10**:73–84. https://doi.org/10.1016/j.jchf.2021.09.004
7. Shen L, Jhund PS, Petrie MC, Claggett BL, Barlera S, Cleland JGF, *et al.* Declining risk of sudden death in heart failure. *N Engl J Med* 2017;**377**:41–51. https://doi.org/10.1056/NEJMoa1609758
8. Sinner G, Omar HR, Lin YW, Elayi SC, Guglin ME. Response to cardiac resynchronization therapy in non-ischemic cardiomyopathy is unrelated to medical therapy. *Clin Cardiol* 2019;**42**:143–50. https://doi.org/10.1002/clc.23123
9. Hulot JS, Ter Maaten JM, Bayes-Genis A, Halliday BP, Metra M, Moura B, *et al.* Heart failure improvement, remission, and recovery: a European Journal of Heart Failure expert consensus document. *Eur J Heart Fail* 2025;**27**:1807–19. https://doi.org/10.1002/ejhf.3732
10. Joseph P, Roy A, Lonn E, Störk S, Floras J, Mienlniczuk L, *et al.* Global variations in heart failure etiology, management, and outcomes. *JAMA* 2023;**329**:1650–61. https://doi.org/10.1001/jama.2023.5942
11. Shore S, Grau-Sepulveda MV, Bhatt DL, Heidenreich PA, Eapen ZJ, Hernandez AF, *et al.* Characteristics, treatments, and outcomes of hospitalized heart failure patients stratified by etiologies of cardiomyopathy. *JACC Heart Fail* 2015;**3**:906–16. https://doi.org/10.1016/j.jchf.2015.06.012
12. Kaplon-Cieslicka A, Benson L, Chioncel O, Crespo-Leiro MG, Coats AJS, Anker SD, *et al.* A comprehensive characterization of acute heart failure with preserved versus mildly reduced versus reduced ejection fraction—insights from the ESC-HFA EORP Heart Failure Long-Term Registry. *Eur J Heart Fail* 2022;**24**:335–50. https://doi.org/10.1002/ejhf.2408
13. Fonarow GC, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, *et al.* Improving evidence-based care for heart failure in outpatient cardiology practices: primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). *Circulation* 2010;**122**:585–96. https://doi.org/10.1161/CIRCULATIONAHA.109.934471
14. Teng TK, Tromp J, Tay WT, Anand I, Ouwerkerk W, Chopra V, *et al.* Prescribing patterns of evidence-based heart failure pharmacotherapy and outcomes in the ASIAN-HF registry: a cohort study. *Lancet Glob Health* 2018;**6**:e1008–18. https://doi.org/10.1016/S2214-109X(18)30306-1
15. Dokainish H, Teo K, Zhu J, Roy A, AlHabib KF, ElSayed A, *et al.* Global mortality variations in patients with heart failure: results from the International Congestive Heart Failure (INTER-CHF) prospective cohort study. *Lancet Glob Health* 2017;**5**:e665–72. https://doi.org/10.1016/S2214-109X(17)30196-1
16. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *Eur J Heart Fail* 2020;**22**:1342–56. https://doi.org/10.1002/ejhf.1858
17. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, *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
18. Teerlink JR, Diaz R, Felker GM, McMurray JJV, Metra M, Solomon SD, *et al.* Cardiac myosin activation with omecamtiv mecarbil in systolic heart failure. *N Engl J Med* 2021;**384**:105–16. https://doi.org/10.1056/NEJMoa2025797
19. Armstrong PW, Pieske B, Anstrom KJ, Ezekowitz J, Hernandez AF, Butler J, *et al.* Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2020;**382**:1883–93. https://doi.org/10.1056/NEJMoa1915928
20. Savarese G, Bodegard J, Norhammar A, Sartipy P, Thuresson M, Cowie MR, *et al.* Heart failure drug titration, discontinuation, mortality and heart failure hospitalization risk: a multinational observational study (US, UK and Sweden). *Eur J Heart Fail* 2021;**23**:1499–511. https://doi.org/10.1002/ejhf.2271
21. Shahim A, Linde C, Savarese G, Dahlström U, Lund LH, Hage C. Implementation of guideline-recommended therapies in heart failure with reduced ejection fraction according to heart failure duration: an analysis of 55 581 patients from the Swedish Heart Failure (SwedeHF) Registry. *Eur J Heart Fail* 2025;**27**:421–31. https://doi.org/10.1002/ejhf.3565
22. Johansson I, Dahlstrom U, Edner M, Näsman P, Rydén L, Norhammar A. Prognostic implications of type 2 diabetes mellitus in ischemic and nonischemic heart failure. *J Am Coll Cardiol* 2016;**68**:1404–16. https://doi.org/10.1016/j.jacc.2016.06.061
23. Stolfo D, Lund LH, Benson L, Lindberg F, Ferrannini G, Dahlström U, *et al.* Real-world use of sodium-glucose cotransporter 2 inhibitors in patients with heart failure and reduced ejection fraction: data from the Swedish Heart Failure Registry. *Eur J Heart Fail* 2023;**25**:1648–58. https://doi.org/10.1002/ejhf.2971
24. Silvetti E, Lanza O, Romeo F, Martino A, Fedele E, Lanzillo C, *et al.* The pivotal role of ECG in cardiomyopathies. *Front Cardiovasc Med* 2023;**10**:1178163. https://doi.org/10.3389/fcvm.2023.1178163
25. Bozkurt B, Colvin M, Cook J, Cooper LT, Deswal A, Fonarow GC, *et al.* Current diagnostic and treatment strategies for specific dilated cardiomyopathies: a scientific statement from the American Heart Association. *Circulation* 2016;**134**:e579–646. https://doi.org/10.1161/CIR.0000000000000455
26. Gigli M, Merlo M, Graw SL, Barbati G, Rowland TJ, Slavov DB, *et al.* Genetic risk of arrhythmic phenotypes in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 2019;**74**:1480–90. https://doi.org/10.1016/j.jacc.2019.06.072
27. Merlo M, Zaffalon D, Stolfo D, Altinier A, Barbati G, Zecchin M, *et al.* ECG in dilated cardiomyopathy: specific findings and long-term prognostic significance. *J Cardiovasc Med (Hagerstown)* 2019;**20**:450–8. https://doi.org/10.2459/JCM.0000000000000804
28. Valentini F, Anselmi F, Metra M, Cavigli L, Giacomin E, Focardi M, *et al.* Diagnostic and prognostic value of low QRS voltages in cardiomyopathies: old but gold. *Eur J Prev Cardiol* 2022;**29**:1177–87. https://doi.org/10.1093/eurjpc/zwaa027
29. Aleksova A, Carriere C, Zecchin M, Barbati G, Vitrella G, Di Lenarda A, *et al.* New-onset left bundle branch block independently predicts long-term mortality in patients with idiopathic dilated cardiomyopathy: data from the Trieste Heart Muscle Disease Registry. *Europace* 2014;**16**:1450–9. https://doi.org/10.1093/europace/euu016
30. Basaran Y, Tigen K, Karaahmet T, Isiklar I, Cevik C, Gurel E, *et al.* Fragmented QRS complexes are associated with cardiac fibrosis and significant intraventricular systolic dyssynchrony in nonischemic dilated cardiomyopathy patients with a narrow QRS interval. *Echocardiography* 2011;**28**:62–8. https://doi.org/10.1111/j.1540-8175.2010.01242.x
31. Butt JH, Nicolau JC, Verma S, Docherty KF, Petrie MC, Inzucchi SE, *et al.* Efficacy and safety of dapagliflozin according to aetiology in heart failure with reduced ejection fraction: insights from the DAPA-HF trial. *Eur J Heart Fail* 2021;**23**:601–13. https://doi.org/10.1002/ejhf.2124
32. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, *et al.* Angiotensin-neprilysin inhibition versus Enalapril in heart failure. *N Engl J Med* 2014;**371**:993–1004. https://doi.org/10.1056/NEJMoa1409077
33. Sha J, Zhang S, Tang M, Chen K, Zhao X, Wang F. Fragmented QRS is associated with all-cause mortality and ventricular arrhythmias in patient with idiopathic dilated cardiomyopathy. *Ann Noninvasive Electrocardiol* 2011;**16**:270–5. https://doi.org/10.1111/j.1542-474X.2011.00442.x
34. Chrispin J, Merchant FM, Lakdawala NK, Wu KC, Tomaselli GF, Navara R, *et al.* Risk of arrhythmic death in patients with nonischemic cardiomyopathy: JACC review topic of the week. *J Am Coll Cardiol* 2023;**82**:735–47. https://doi.org/10.1016/j.jacc.2023.05.064
35. Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Blom NA, *et al.* 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J* 2022;**43**:3997–4126. https://doi.org/10.1093/eurheartj/ehac262
36. Hasselberg NE, Haland TF, Saberniak J, Brekke PH, Berge KE, Leren TP, *et al.* Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation. *Eur Heart J* 2018;**39**:853–60. https://doi.org/10.1093/eurheartj/ehx596
37. Olson TM, Michels VV, Ballew JD, Reyna SP, Karst ML, Herron KJ, *et al.* Sodium channel mutations and susceptibility to heart failure and atrial fibrillation. *JAMA* 2005;**293**:447–54. https://doi.org/10.1001/jama.293.4.447
38. Tayal U, Newsome S, Buchan R, Whiffin N, Walsh R, Barton PJ, *et al.* Truncating variants in titin independently predict early arrhythmias in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 2017;**69**:2466–8. https://doi.org/10.1016/j.jacc.2017.03.530
39. Hoevelmann J, Sliwa K, Briton O, Ntsekhe M, Chin A, Viljoen C. Effectiveness of implantable loop recorder and Holter electrocardiographic monitoring for the detection of arrhythmias in patients with peripartum cardiomyopathy. *Clin Res Cardiol* 2023;**112**:379–91. https://doi.org/10.1007/s00392-022-02101-3
40. Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, *et al.* 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. *Heart Rhythm* 2017;**14**:e55–96. https://doi.org/10.1016/j.hrthm.2017.03.038
41. Brignole M, Moya A, de Lange FJ, Deharo J-C, Elliott PM, Fanciulli A, *et al.* 2018 ESC guidelines for the diagnosis and management of syncope. *Eur Heart J* 2018;**39**:1883–948. https://doi.org/10.1093/eurheartj/ehy037
42. Pender A, Lewis-Owona J, Ekiyoyo A, Stoddard M. Echocardiography and heart failure: an echocardiographic decision aid for the diagnosis and management of cardiomyopathies. *Curr Cardiol Rep* 2025;**27**:64. https://doi.org/10.1007/s11886-025-02194-y
43. Trasca L, Popescu MR, Popescu AC, Balanescu SM. Echocardiography in the diagnosis of cardiomyopathies: current status and future directions. *Rev Cardiovasc Med* 2022;**23**:280. https://doi.org/10.31083/j.rcm2308280
44. Chaudhari M, Ashwath ML. Cardiac imaging in the diagnosis and management of heart failure. *J Clin Med* 2025;**14**:5002. https://doi.org/10.3390/jcm14145002
45. Brown PF, Di Marco A, Tsoumani Z, Reid A, Bradley J, Nucifora G, *et al.* Predictive value of a comprehensive atrial assessment with cardiac magnetic resonance in nonischemic cardiomyopathy: keep it simple. *Int J Cardiovasc Imaging* 2024;**40**:557–67. https://doi.org/10.1007/s10554-023-03024-4
46. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al*; ESC Scientific Document Group. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology

(ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2022;**24**:4–131. https://doi.org/10.1002/ejhf.2333
47. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, *et al.* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2015;**16**: 233–70. https://doi.org/10.1093/ehjci/jev014
48. Jung IH, Park JH, Lee JA, Kim GS, Lee HY, Byun YS, *et al.* Left ventricular global longitudinal strain as a predictor for left ventricular reverse remodeling in dilated cardiomyopathy. *J Cardiovasc Imaging* 2020;**28**:137–49. https://doi.org/10.4250/jcvi.2019.0111
49. Gulati A, Japp AG, Raza S, Halliday BP, Jones DA, Newsome S, *et al.* Absence of myocardial fibrosis predicts favourable long-term survival in new-onset heart failure. *Circ Cardiovasc Imaging* 2018;**11**:e007722. https://doi.org/10.1161/CIRCIMAGING.118.007722
50. Assomull RG, Shakespeare C, Kalra PR, Lloyd G, Gulati A, Strange J, *et al.* Role of cardiovascular magnetic resonance as a gatekeeper to invasive coronary angiography in patients presenting with heart failure of unknown etiology. *Circulation* 2011;**124**: 1351–60. https://doi.org/10.1161/CIRCULATIONAHA.110.011346
51. Gravina M, Casavecchia G, Mangini F, Mautone F, Ruggeri D, Guglielmi G, *et al.* Magnetic resonance mapping for the assessment of cardiomyopathies and myocardial disease. *Int J Cardiol* 2024;**415**:132440. https://doi.org/10.1016/j.ijcard.2024.132440
52. Forleo C, Carella MC, Basile P, Mandunzio D, Greco G, Napoli G, *et al.* The role of magnetic resonance imaging in cardiomyopathies in the light of new guidelines: a focus on tissue mapping. *J Clin Med* 2024;**13**:2621. https://doi.org/10.3390/jcm13092621
53. Eichhorn C, Koeckerling D, Reddy RK, Ardissino M, Rogowski M, Coles B, *et al.* Risk stratification in nonischemic dilated cardiomyopathy using CMR imaging: a systematic review and meta-analysis. *JAMA* 2024;**332**:1535–50. https://doi.org/10.1001/jama.2024.13946
54. Gulati A, Jabbour A, Ismail TF, Guha K, Khwaja J, Raza S, *et al.* Association of fibrosis with mortality and sudden cardiac death in patients with nonischemic dilated cardiomyopathy. *JAMA* 2013;**309**:896–908. https://doi.org/10.1001/jama.2013.1363
55. Nikolaidou C, Ormerod JOM, Ziakas A, Neubauer S, Karamitsos TD. The role of cardiovascular magnetic resonance imaging in patients with cardiac arrhythmias. *Rev Cardiovasc Med* 2023;**24**:252. https://doi.org/10.31083/j.rcm2409252
56. Ammirati E, Moslehi JJ. Diagnosis and treatment of acute myocarditis: a review. *JAMA* 2023;**329**:1098–113. https://doi.org/10.1001/jama.2023.3371
57. Bayes-Genis A, Docherty KF, Petrie MC, Januzzi JL, Mueller C, Anderson L, *et al.* Practical algorithms for early diagnosis of heart failure and heart stress using NT-proBNP: a clinical consensus statement from the Heart Failure Association of the ESC. *Eur J Heart Fail* 2023;**25**:1891–8. https://doi.org/10.1002/ejhf.3036
58. Daubert MA, Adams K, Yow E, Barnhart HX, Douglas PS, Rimmer S, *et al.* NT-proBNP goal achievement is associated with significant reverse remodeling and improved clinical outcomes in HFrEF. *JACC Heart Fail* 2019;**7**:158–68. https://doi.org/10.1016/j.jchf.2018.10.014
59. Weiner RB, Baggish AL, Chen-Tournoux A, Marshall JE, Gaggin HK, Bhardwaj A, *et al.* Improvement in structural and functional echocardiographic parameters during chronic heart failure therapy guided by natriuretic peptides: mechanistic insights from the ProBNP Outpatient Tailored Chronic Heart Failure (PROTECT) study. *Eur J Heart Fail* 2013;**15**:342–51. https://doi.org/10.1093/eurjhf/hfs180
60. Januzzi JL Jr, Prescott MF, Butler J, Felker GM, Maisel AS, McCague K, *et al.* Association of change in N-terminal pro-B-type natriuretic peptide following initiation of sacubitril-valsartan treatment with cardiac structure and function in patients with heart failure with reduced ejection fraction. *JAMA* 2019;**322**:1085–95. https://doi.org/10.1001/jama.2019.12821
61. Schulz-Menger J, Collini V, Groschel J, Adler Y, Brucato A, Christian V, *et al.* 2025 ESC Guidelines for the management of myocarditis and pericarditis. *Eur Heart J* 2025;**46**: 3952–4041. https://doi.org/10.1093/eurheartj/ehaf192
62. Coronado MJ, Bruno KA, Blauwet LA, Tschöpe C, Cunningham MW, Pankuweit S, *et al.* Elevated sera sST2 is associated with heart failure in men ≤50 years old with myocarditis. *J Am Heart Assoc* 2019;**8**:e008968. https://doi.org/10.1161/JAHA.118.008968
63. Ammirati E, Veronese G, Bottiroli M, Wang DW, Cipriani M, Garascia A, *et al.* Update on acute myocarditis. *Trends Cardiovasc Med* 2021;**31**:370–9. https://doi.org/10.1016/j.tcm.2020.05.008
64. Benincasa G, Mansueto G, Napoli C. Fluid-based assays and precision medicine of cardiovascular diseases: the 'hope' for Pandora's box? *J Clin Pathol* 2019;**72**:785–99. https://doi.org/10.1136/jclinpath-2019-206178
65. Kennel PJ, Saha A, Maldonado DA, Givens R, Brunjes DL, Castillero E, *et al.* Serum exosomal protein profiling for the non-invasive detection of cardiac allograft rejection. *J Heart Lung Transplant* 2018;**37**:409–17. https://doi.org/10.1016/j.healun.2017.07.012
66. Huang F, Ammirati E, Ponnaiah M, Montero S, Raimbault V, Abrams D, *et al.* Fulminant myocarditis proven by early biopsy and outcomes. *Eur Heart J* 2023;**44**:5110–24. https://doi.org/10.1093/eurheartj/ehad707
67. Tschope C, Ammirati E, Bozkurt B, Caforio ALP, Cooper LT, Felix SB, *et al.* Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. *Nat Rev Cardiol* 2021;**18**:169–93. https://doi.org/10.1038/s41569-020-00435-x
68. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, *et al.* Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2013;**34**:2636–48, 2648a-2648d. https://doi.org/10.1093/eurheartj/eht210
69. Mueller KA, Mueller II, Eppler D, Zuern CS, Seizer P, Kramer U, *et al.* Clinical and histopathological features of patients with systemic sclerosis undergoing endomyocardial biopsy. *PLoS One* 2015;**10**:e0126707. https://doi.org/10.1371/journal.pone.0126707
70. Jellis C, Martin J, Narula J, Marwick TH. Assessment of nonischemic myocardial fibrosis. *J Am Coll Cardiol* 2010;**56**:89–97. https://doi.org/10.1016/j.jacc.2010.02.047
71. Ishii S, Inomata T, Fujita T, Iida Y, Ikeda Y, Nabeta T, *et al.* Clinical significance of endomyocardial biopsy in conjunction with cardiac magnetic resonance imaging to predict left ventricular reverse remodeling in idiopathic dilated cardiomyopathy. *Heart Vessels* 2016;**31**:1960–8. https://doi.org/10.1007/s00380-016-0815-0
72. Heymans S, Lakdawala NK, Tschope C, Klingel K. Dilated cardiomyopathy: causes, mechanisms, and current and future treatment approaches. *Lancet* 2023;**402**:998–1011. https://doi.org/10.1016/S0140-6736(23)01241-2
73. Lota AS, Hazebroek MR, Theotokis P, Wassall R, Salmi S, Halliday BP, *et al.* Genetic architecture of acute myocarditis and the overlap with inherited cardiomyopathy. *Circulation* 2022;**146**:1123–34. https://doi.org/10.1161/CIRCULATIONAHA.121.058457
74. Garcia-Pavia P, Kim Y, Restrepo-Cordoba MA, Lunde IG, Wakimoto H, Smith AM, *et al.* Genetic variants associated with cancer therapy-induced cardiomyopathy. *Circulation* 2019;**140**:31–41. https://doi.org/10.1161/CIRCULATIONAHA.118.037934
75. Stroeks S, Henkens M, Dominguez F, Merlo M, Hellebrekers DMEI, Gonzalez-Lopez E, *et al.* Genetic landscape of patients with dilated cardiomyopathy and a systemic immune-mediated disease. *JACC Heart Fail* 2024;**13**:133–45. https://doi.org/10.1016/j.jchf.2024.08.011
76. Kubanek M, Binova J, Piherova L, Krebsova A, Kotrc M, Hartmannova H, *et al.* Genotype is associated with left ventricular reverse remodelling and early events in recent-onset dilated cardiomyopathy. *ESC Heart Fail* 2024;**11**:4127–38. https://doi.org/10.1002/ehf2.15009
77. Jordan E, Peterson L, Ai T, Asatryan B, Bronicki L, Brown E, *et al.* Evidence-based assessment of genes in dilated cardiomyopathy. *Circulation* 2021;**144**:7–19. https://doi.org/10.1161/CIRCULATIONAHA.120.053033
78. Setti M, Iseppi M, Verdonschot JAJ, Rizzi JG, Paldino A, Pio Loco Detto Gava C, *et al.* Integrated role of cardiac magnetic resonance and genetics in predicting left ventricular reverse remodelling in dilated and non-dilated cardiomyopathy. *Eur J Heart Fail* 2025; **27**:2571–81. https://doi.org/10.1002/ejhf.3671
79. Pirruccello JP, Bick A, Wang M, Chaffin M, Friedman S, Yao J, *et al.* Analysis of cardiac magnetic resonance imaging in 36,000 individuals yields genetic insights into dilated cardiomyopathy. *Nat Commun* 2020;**11**:2254. https://doi.org/10.1038/s41467-020-15823-7
80. Kubanek M, Sramko M, Maluskova J, Kautznerova D, Weichet J, Lupinek P, *et al.* Novel predictors of left ventricular reverse remodeling in individuals with recent-onset dilated cardiomyopathy. *J Am Coll Cardiol* 2013;**61**:54–63. https://doi.org/10.1016/j.jacc.2012.07.072
81. Bao J, Kan R, Chen J, Xuan H, Wang C, Li D, *et al.* Combination pharmacotherapies for cardiac reverse remodeling in heart failure patients with reduced ejection fraction: a systematic review and network meta-analysis of randomized clinical trials. *Pharmacol Res* 2021;**169**:105573. https://doi.org/10.1016/j.phrs.2021.105573
82. Savage P, Watson C, Coburn J, Cox B, Shahmohammadi M, Grieve D, *et al.* Impact of SGLT2 inhibition on markers of reverse cardiac remodelling in heart failure: systematic review and meta-analysis. *ESC Heart Fail* 2024;**11**:3636–48. https://doi.org/10.1002/ehf2.14993
83. Correale M, D'Alessandro D, Tricarico L, Ceci V, Mazzeo P, Capasso R, *et al.* Left ventricular reverse remodeling after combined ARNI and SGLT2 therapy in heart failure patients with reduced or mildly reduced ejection fraction. *Int J Cardiol Heart Vasc* 2024; **54**:101492. https://doi.org/10.1016/j.ijcha.2024.101492
84. Cintron G, Johnson G, Francis G, Cobb F, Cohn JN. Prognostic significance of serial changes in left ventricular ejection fraction in patients with congestive heart failure. The V-HeFT VA Cooperative Studies Group. *Circulation* 1993;**87**:VI17–23. https://doi.org/10.1161/01.CIR.87.6.17
85. Veltmann C, Duncker D, Doering M, Gummadi S, Robertson M, Wittlinger T, *et al.* Therapy duration and improvement of ventricular function in de novo heart failure: the Heart Failure Optimization study. *Eur Heart J* 2024;**45**:2771–81. https://doi.org/10.1093/eurheartj/ehae334
86. Martens P, Nuyens D, Rivero-Ayerza M, Van Herendael H, Vercammen J, Ceyssens W, *et al.* Sacubitril/valsartan reduces ventricular arrhythmias in parallel with left ventricular reverse remodeling in heart failure with reduced ejection fraction. *Clin Res Cardiol* 2019;**108**:1074–82. https://doi.org/10.1007/s00392-019-01440-y
87. Guerra F, Ammendola E, Ziacchi M, Aspromonte V, Pellegrino PL, Del Giorno G, *et al.* Effect of SAcubitril/Valsartan on left vEntricular ejection fraction and on the potential indication for implantable cardioverter defibrillator in primary prevention: the

SAVE-ICD study. *Eur J Clin Pharmacol* 2021;**77**:1835–42. https://doi.org/10.1007/s00228-021-03189-8
88. Santos-Gallego CG, Vargas-Delgado AP, Requena-Ibanez JA, Garcia-Ropero A, Mancini D, Pinney S, *et al.* Randomized trial of empagliflozin in nondiabetic patients with heart failure and reduced ejection fraction. *J Am Coll Cardiol* 2021;**77**:243–55. https://doi.org/10.1016/j.jacc.2020.11.008
89. Lee MMY, Brooksbank KJM, Wetherall K, Mangion K, Roditi G, Campbell RT, *et al.* Effect of empagliflozin on left ventricular volumes in patients with type 2 diabetes, or prediabetes, and heart failure with reduced ejection fraction (SUGAR-DM-HF). *Circulation* 2021;**143**:516–25. https://doi.org/10.1161/CIRCULATIONAHA.120.052186
90. Usman MS, Januzzi JL, Anker SD, Salman A, Parikh PB, Adamo M, *et al.* The effect of sodium-glucose cotransporter 2 inhibitors on left cardiac remodelling in heart failure with reduced ejection fraction: systematic review and meta-analysis. *Eur J Heart Fail* 2024;**26**:373–82. https://doi.org/10.1002/ejhf.3129
91. Tardif JC, O'Meara E, Komajda M, Böhm M, Borer JS, Ford I, *et al.* Effects of selective heart rate reduction with ivabradine on left ventricular remodelling and function: results from the SHIFT echocardiography substudy. *Eur Heart J* 2011;**32**:2507–15. https://doi.org/10.1093/eurheartj/ehr311
92. Mohebi R, Liu Y, Felker GM, Prescott MF, Piña IL, Butler J, *et al.* Prediction of left ventricular ejection fraction change following treatment with sacubitril/valsartan. *JACC Heart Fail* 2023;**11**:44–54. https://doi.org/10.1016/j.jchf.2022.09.009
93. Kawai K, Takaoka H, Hata K, Yokota Y, Yokoyama M. Prevalence, predictors, and prognosis of reversal of maladaptive remodeling with intensive medical therapy in idiopathic dilated cardiomyopathy. *Am J Cardiol* 1999;**84**:671–6. https://doi.org/10.1016/s0002-9149(99)00414-2
94. Birks EJ, Drakos SG, Patel SR, Lowes BD, Selzman CH, Starling RC, *et al.* Prospective multicenter study of myocardial recovery using left ventricular assist devices (RESTAGE-HF [Remission from Stage D Heart Failure]): medium-term and primary end point results. *Circulation* 2020;**142**:2016–28. https://doi.org/10.1161/CIRCULATIONAHA.120.046415
95. Hall SA, Cigarroa CG, Marcoux L, Risser RC, Grayburn PA, Eichhorn EJ. Time course of improvement in left ventricular function, mass and geometry in patients with congestive heart failure treated with beta-adrenergic blockade. *J Am Coll Cardiol* 1995;**25**:1154–61. https://doi.org/10.1016/0735-1097(94)00543-y
96. Narayanan K, Reinier K, Teodorescu C, Uy-Evanado A, Aleong R, Chugh H, *et al.* Left ventricular diameter and risk stratification for sudden cardiac death. *J Am Heart Assoc* 2014;**3**:e001193. https://doi.org/10.1161/JAHA.114.001193
97. Solomon SD, Zelenkofske S, McMurray JJ, Finn PV, Velazquez E, Ertl G, *et al.* Sudden death in patients with myocardial infarction and left ventricular dysfunction, heart failure, or both. *N Engl J Med* 2005;**352**:2581–8. https://doi.org/10.1056/NEJMoa043938
98. Leyva F, Israel CW, Singh J. Declining risk of sudden cardiac death in heart failure: fact or myth? *Circulation* 2023;**147**:759–67. https://doi.org/10.1161/CIRCULATIONAHA.122.062159
99. Barsheshet A, Wang PJ, Moss AJ, Solomon SD, Al-Ahmad A, McNitt S, *et al.* Reverse remodeling and the risk of ventricular tachyarrhythmias in the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy). *J Am Coll Cardiol* 2011;**57**:2416–23. https://doi.org/10.1016/j.jacc.2010.12.041
100. Minami Y, Kikuchi N, Shiga T, Suzuki A, Shoda M, Hagiwara N. Incidence and predictors of early and late sudden cardiac death in hospitalized Japanese patients with new-onset systolic heart failure. *J Arrhythm* 2021;**37**:1148–55. https://doi.org/10.1002/joa3.12618
101. Curtain JP, Docherty KF, Jhund PS, Petrie MC, Inzucchi SE, Køber L, *et al.* Effect of dapagliflozin on ventricular arrhythmias, resuscitated cardiac arrest, or sudden death in DAPA-HF. *Eur Heart J* 2021;**42**:3727–38. https://doi.org/10.1093/eurheartj/ehab560
102. Beggs SAS, Jhund PS, Jackson CE, McMurray JJV, Gardner RS. Non-ischaemic cardiomyopathy, sudden death and implantable defibrillators: a review and meta-analysis. *Heart* 2018;**104**:144–50. https://doi.org/10.1136/heartjnl-2016-310850
103. Weintraub RG, Semsarian C, Macdonald P. Dilated cardiomyopathy. *Lancet* 2017;**390**:400–14. https://doi.org/10.1016/S0140-6736(16)31713-5
104. Kober L, Thune JJ, Nielsen JC, Haarbo J, Videbæk L, Korup E, *et al.* Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med* 2016;**375**:1221–30. https://doi.org/10.1056/NEJMoa1608029
105. Schrage B, Uijl A, Benson L, Westermann D, Ståhlberg M, Stolfo D, *et al.* Association between use of primary-prevention implantable cardioverter-defibrillators and mortality in patients with heart failure: a prospective propensity score-matched analysis from the Swedish heart failure registry. *Circulation* 2019;**140**:1530–9. https://doi.org/10.1161/CIRCULATIONAHA.119.043012
106. Zabel M, Willems R, Lubinski A, Bauer A, Brugada J, Conen D, *et al.* Clinical effectiveness of primary prevention implantable cardioverter-defibrillators: results of the EU-CERT-ICD controlled multicentre cohort study. *Eur Heart J* 2020;**41**:3437–47. https://doi.org/10.1093/eurheartj/ehaa226
107. Barakat AF, Saad M, Elgendy AY, Mentias A, Abuzaid A, Mahmoud AN, *et al.* Primary prevention implantable cardioverter defibrillator in patients with non-ischaemic cardiomyopathy: a meta-analysis of randomised controlled trials. *BMJ Open* 2017;**7**:e016352. https://doi.org/10.1136/bmjopen-2017-016352
108. Argentiero A, Carella MC, Mandunzio D, Greco G, Mushtaq S, Baggiano A, *et al.* Cardiac magnetic resonance as risk stratification tool in non-ischemic dilated cardiomyopathy referred for implantable cardioverter defibrillator therapy-state of art and perspectives. *J Clin Med* 2023;**12**:7752. https://doi.org/10.3390/jcm12247752
109. Klem I, Klein M, Khan M, Yang EY, Nabi F, Ivanov A, *et al.* Relationship of LVEF and myocardial scar to long-term mortality risk and mode of death in patients with nonischemic cardiomyopathy. *Circulation* 2021;**143**:1343–58. https://doi.org/10.1161/CIRCULATIONAHA.120.048477
110. Becker MAJ, Cornel JH, van de Ven PM, van Rossum AC, Allaart CP, Germans T. The prognostic value of late gadolinium-enhanced cardiac magnetic resonance imaging in nonischemic dilated cardiomyopathy: a review and meta-analysis. *JACC Cardiovasc Imaging* 2018;**11**:1274–84. https://doi.org/10.1016/j.jcmg.2018.03.006
111. Escobar-Lopez L, Ochoa JP, Mirelis JG, Espinosa MÁ, Navarro M, Gallego-Delgado M, *et al.* Association of genetic variants with outcomes in patients with nonischemic dilated cardiomyopathy. *J Am Coll Cardiol* 2021;**78**:1682–99. https://doi.org/10.1016/j.jacc.2021.08.039
112. Kutyifa V, Moss AJ, Klein HU, McNitt S, Zareba W, Goldenberg I. One-year follow-up of the prospective registry of patients using the wearable defibrillator (WEARIT-II Registry). *Pacing Clin Electrophysiol* 2018;**41**:1307–13. https://doi.org/10.1111/pace.13448
113. Masri A, Altibi AM, Erqou S, Zmaili MA, Saleh A, Al-Adham R, *et al.* Wearable cardioverter-defibrillator therapy for the prevention of sudden cardiac death: a systematic review and meta-analysis. *JACC Clin Electrophysiol* 2019;**5**:152–61. https://doi.org/10.1016/j.jacep.2018.11.011
114. Duncker D, Marijon E, Metra M, Piot O, Fudim M, Siebert U, *et al.* Sudden cardiac death in newly diagnosed non-ischaemic or ischaemic cardiomyopathy assessed with a wearable cardioverter-defibrillator: the German nationwide SCD-PROTECT study. *Eur Heart J* 2025;**46**:4597–606. https://doi.org/10.1093/eurheartj/ehaf668
115. Cleland JGF, Halliday BP, Prasad SK. Selecting patients with nonischemic dilated cardiomyopathy for ICDs: myocardial function, fibrosis, and what's attached? *J Am Coll Cardiol* 2017;**70**:1228–31. https://doi.org/10.1016/j.jacc.2017.07.748
116. Abdin A, Kondo T, Bohm M, Jhund PS, Claggett BL, Vaduganathan M, *et al.* Effects of dapagliflozin according to QRS duration across the spectrum of left ventricular ejection fraction: an analysis of DAPA-HF and DELIVER. *Eur J Heart Fail* 2024;**26**:1952–63. https://doi.org/10.1002/ejhf.3350
117. Killu AM, Mazo A, Grupper A, Madhavan M, Webster T, Brooke KL, *et al.* Super-response to cardiac resynchronization therapy reduces appropriate implantable cardioverter defibrillator therapy. *Europace* 2018;**20**:1303–11. https://doi.org/10.1093/europace/eux235
118. Mullens W, Auricchio A, Martens P, Witte K, Cowie MR, Delgado V, *et al.* Optimized implementation of cardiac resynchronization therapy: a call for action for referral and optimization of care. *Europace* 2021;**23**:1324–42. https://doi.org/10.1093/europace/euaa411
119. Maass AH, Vernooy K, Cramer MJ, Vos MA, Rienstra M, Van Gelder IC. Refining success of cardiac resynchronization therapy using a simple score predicting the amount of reverse ventricular remodelling: results from the MARC study—authors reply. *Europace* 2018;**20**:393. https://doi.org/10.1093/europace/eux169
120. Khazanie P, Liang L, Qualls LG, Curtis LH, Fonarow GC, Hammill BG, *et al.* Outcomes of medicare beneficiaries with heart failure and atrial fibrillation. *JACC Heart Fail* 2014;**2**:41–8. https://doi.org/10.1016/j.jchf.2013.11.002
121. Van Gelder IC, Rienstra M, Bunting KV, Casado-Arroyo R, Caso V, Crijns HJGM, *et al.* 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2024;**45**:3314–414. https://doi.org/10.1093/eurheartj/ehae176
122. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, *et al.* A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;**347**:1825–33. https://doi.org/10.1056/NEJMoa021328
123. Kirchhof P, Camm AJ, Goette A, Brandes A, Eckardt L, Elvan A, *et al.* Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med* 2020;**383**:1305–16. https://doi.org/10.1056/NEJMoa2019422
124. Sohns C, Fox H, Marrouche NF, Crijns HJGM, Costard-Jaeckle A, Bergau L, *et al.* Catheter ablation in end-stage heart failure with atrial fibrillation. *N Engl J Med* 2023;**389**:1380–9. https://doi.org/10.1056/NEJMoa2306037
125. Marrouche NF, Brachmann J, Andresen D, Siebels J, Boersma L, Jordaens L, *et al.* Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med* 2018;**378**:417–27. https://doi.org/10.1056/NEJMoa1707855
126. Prabhu S, Taylor AJ, Costello BT, Kaye DM, McLellan AJA, Voskoboinik A, *et al.* Catheter ablation versus medical rate control in atrial fibrillation and systolic dysfunction: the CAMERA-MRI study. *J Am Coll Cardiol* 2017;**70**:1949–61. https://doi.org/10.1016/j.jacc.2017.08.041
127. Sugumar H, Prabhu S, Voskoboinik A, Young S, Gutman SJ, Wong GR, *et al.* Atrial remodeling following catheter ablation for atrial fibrillation-mediated cardiomyopathy: long-term follow-up of CAMERA-MRI study. *JACC Clin Electrophysiol* 2019;**5**:681–8. https://doi.org/10.1016/j.jacep.2019.03.009

128. Pasqualotto E, Ternes CMP, Chavez MP, Polanczyk CA, Ferreira ROM, Nienkötter T, *et al.* Catheter ablation for atrial fibrillation in heart failure with reduced ejection fraction patients: a meta-analysis. *Heart Rhythm* 2024;**21**:1604–12. https://doi.org/10.1016/j.hrthm.2024.04.098
129. Sohns C, Moersdorf M, Marrouche NF, Bergau L, Costard-Jaeckle A, Crijns HJGM, *et al.* Catheter ablation in patients with end-stage heart failure and atrial fibrillation: two-year follow-up of the CASTLE-HTx trial. *Circulation* 2024;**150**:1904–6. https://doi.org/10.1161/CIRCULATIONAHA.124.071517
130. Latchamsetty R, Bogun F. Premature ventricular complex-induced cardiomyopathy. *JACC Clin Electrophysiol* 2019;**5**:537–50. https://doi.org/10.1016/j.jacep.2019.03.013
131. Sannino A, Smith RL 2nd, Schiattarella GG, Trimarco B, Esposito G, Grayburn PA. Survival and cardiovascular outcomes of patients with secondary mitral regurgitation: a systematic review and meta-analysis. *JAMA Cardiol* 2017;**2**:1130–9. https://doi.org/10.1001/jamacardio.2017.2976
132. Writing Committee Members; Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, *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. *J Am Coll Cardiol* 2021;**77**:450–500. https://doi.org/10.1016/j.jacc.2020.11.035
133. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, *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
134. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, *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
135. Anker MS, Porthun J, Bonnet G, Schulze PC, Rassaf T, Landmesser U. Percutaneous transcatheter edge-to-edge repair for functional mitral regurgitation in heart failure: a meta-analysis of 3 randomized controlled trials. *J Am Coll Cardiol* 2024;**84**:2364–8. https://doi.org/10.1016/j.jacc.2024.08.026
136. Anker SD, Friede T, von Bardeleben RS, Butler J, Khan M-S, Diek M, *et al.* Transcatheter valve repair in heart failure with moderate to severe mitral regurgitation. *N Engl J Med* 2024;**391**:1799–809. https://doi.org/10.1056/NEJMoa2314328
137. Ghimire A, Fine N, Ezekowitz JA, Howlett J, Youngson E, McAlister FA. Frequency, predictors, and prognosis of ejection fraction improvement in heart failure: an echocardiogram-based registry study. *Eur Heart J* 2019;**40**:2110–7. https://doi.org/10.1093/eurheartj/ehz233
138. Florea VG, Rector TS, Anand IS, Cohn JN. Heart failure with improved ejection fraction: clinical characteristics, correlates of recovery, and survival: results from the valsartan heart failure trial. *Circ Heart Fail* 2016;**9**:e003123. https://doi.org/10.1161/CIRCHEARTFAILURE.116.003123
139. Aimo A, Gaggin HK, Barison A, Emdin M, Januzzi JL Jr. Imaging, biomarker, and clinical predictors of cardiac remodeling in heart failure with reduced ejection fraction. *JACC Heart Fail* 2019;**7**:782–94. https://doi.org/10.1016/j.jchf.2019.06.004
140. Herman DS, Lam L, Taylor MR, Wang L, Teekakirikul P, Christodoulou D, *et al.* Truncations of titin causing dilated cardiomyopathy. *N Engl J Med* 2012;**366**:619–28. https://doi.org/10.1056/NEJMoa1110186
141. Wilcox JE, Fang JC, Margulies KB, Mann DL. Heart failure with recovered left ventricular ejection fraction: JACC scientific expert panel. *J Am Coll Cardiol* 2020;**76**:719–34. https://doi.org/10.1016/j.jacc.2020.05.075
142. Halliday BP, Wassall R, Lota AS, Khalique Z, Gregson J, Newsome S, *et al.* Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial. *Lancet* 2019;**393**:61–73. https://doi.org/10.1016/S0140-6736(18)32484-X
143. Cheng L, Hammersley D, Ragavan A, Javed S, Mukhopadhyay S, Gregson J, *et al.* Long-term follow-up of the TRED-HF trial: implications for therapy in patients with dilated cardiomyopathy and heart failure remission. *Eur J Heart Fail* 2025;**27**:113–23. https://doi.org/10.1002/ejhf.3475
144. Lee SH, Rhee TM, Shin D, Hong D, Choi KH, Kim HK, *et al.* Prognosis after discontinuing renin angiotensin aldosterone system inhibitor for heart failure with restored ejection fraction after acute myocardial infarction. *Sci Rep* 2023;**13**:3539. https://doi.org/10.1038/s41598-023-30700-1
145. Park H, Lee N, Hwang CH, Cho S-G, Choi GH, Cho JY, *et al.* Prognosis after withdrawal of cardioprotective therapy in patients with improved cancer therapeutics-related cardiac dysfunction. *JACC CardioOncol* 2024;**6**:699–710. https://doi.org/10.1016/j.jaccao.2024.07.018
146. Nijst P, Martens P, Dauw J, Tang WHW, Bertrand PB, Penders J, *et al.* Withdrawal of neurohumoral blockade after cardiac resynchronization therapy. *J Am Coll Cardiol* 2020;**75**:1426–38. https://doi.org/10.1016/j.jacc.2020.01.040
147. Segan L, Kistler PM, Nanayakkara S, Taylor A, Hare J, Costello B, *et al.* Withdrawal of heart failure therapy after atrial fibrillation rhythm control with ejection fraction normalization: the WITHDRAW-AF trial. *Eur Heart J* 2026;**47**:250–62. https://doi.org/10.1093/eurheartj/ehaf563
148. Fatakdawala MM, Ryoo Ali HJ, Song J, Irizarry-Caro JA, Faiz SA, Kumar S, *et al.* Correlation of natriuretic peptides with invasively measured intracardiac filling pressures in patients with cancer. *JACC CardioOncol* 2025;**7**:448–50. https://doi.org/10.1016/j.jaccao.2025.03.006
149. Xie X, Yang M, Xie S, Wu X, Jiang Y, Liu Z, *et al.* Early prediction of left ventricular reverse remodeling in first-diagnosed idiopathic dilated cardiomyopathy: a comparison of linear model, random forest, and extreme gradient boosting. *Front Cardiovasc Med* 2021;**8**:684004. https://doi.org/10.3389/fcvm.2021.684004
150. Lai C, Yin M, Kholmovski EG, Popescu DM, Lu D-Y, Scherer E, *et al.* Multimodal AI to forecast arrhythmic death in hypertrophic cardiomyopathy. *Nat Cardiovasc Res* 2025;**4**:891–903. https://doi.org/10.1038/s44161-025-00679-1
151. Cau R, Pisu F, Suri JS, Montisci R, Gatti M, Mannelli L, *et al.* Artificial intelligence in the differential diagnosis of cardiomyopathy phenotypes. *Diagnostics (Basel)* 2024;**14**:156. https://doi.org/10.3390/diagnostics14020156
152. Kolk MZH, Ruiperez-Campillo S, Allaart CP, Wilde AAM, Knops RE, Narayan SM, *et al.* Multimodal explainable artificial intelligence identifies patients with non-ischaemic cardiomyopathy at risk of lethal ventricular arrhythmias. *Sci Rep* 2024;**14**:14889. https://doi.org/10.1038/s41598-024-65357-x
153. Fatkin D, Calkins H, Elliott P, James CA, Peters S, Kovacic JC. Contemporary and future approaches to precision medicine in inherited cardiomyopathies: JACC focus seminar 3/5. *J Am Coll Cardiol* 2021;**77**:2551–72. https://doi.org/10.1016/j.jacc.2020.12.072
154. Januzzi JL Jr, Richards AM. Natriuretic peptide-guided heart failure therapy after the GUIDE-IT study. *Circulation* 2018;**137**:2101–3. https://doi.org/10.1161/CIRCULATIONAHA.118.033853
155. Januzzi JL Jr, Ahmad T, Mulder H, Coles A, Anstrom KJ, Adams KF, *et al.* Natriuretic peptide response and outcomes in chronic heart failure with reduced ejection fraction. *J Am Coll Cardiol* 2019;**74**:1205–17. https://doi.org/10.1016/j.jacc.2019.06.055
156. Asgardoon MH, Vasheghani-Farahani A, Sherafati A. Usefulness of biomarkers for predicting response to cardiac resynchronization therapy. *Curr Cardiol Rev* 2020;**16**:132–40. https://doi.org/10.2174/1573403X15666191206163846
157. Russo AM, Desai MY, Do MM, Butler J, Chung MK, Epstein AE, *et al.* ACC/AHA/ASE/HFSA/HRS/SCAI/SCCT/SCMR 2025 appropriate use criteria for implantable cardioverter-defibrillators, cardiac resynchronization therapy, and pacing. *J Am Coll Cardiol* 2025;**85**:1213–85. https://doi.org/10.1016/j.jacc.2024.11.023
158. Shchendrygina A, Yehya A, Skouri H. The timing for primary prevention for ICD in the current era of pharmacotherapy. *Card Fail Rev* 2025;**11**:e14. https://doi.org/10.15420/cfr.2025.05
159. Yehya A, Lopez J, Sauer AJ, Davis JD, Ibrahim NE, Tung R, *et al.* Revisiting ICD therapy for primary prevention in patients with heart failure and reduced ejection fraction. *JACC Heart Fail* 2025;**13**:1–13. https://doi.org/10.1016/j.jchf.2024.09.014
160. Selvanayagam JB, Hartshorne T, Billot L, Grover S, Hillis GS, Jung W, *et al.* Cardiovascular magnetic resonance-GUIDEd management of mild to moderate left ventricular systolic dysfunction (CMR GUIDE): study protocol for a randomized controlled trial. *Ann Noninvasive Electrocardiol* 2017;**22**:e12420. https://doi.org/10.1111/anec.12420