

Review

Artificial Intelligence in Restrictive Cardiomyopathy: Current Diagnostic Applications and Future Directions

Rasi Mizori ¹, Ali Hassan ¹, Sukruth Pradeep Kundur ¹, Ali Malik ¹, Serdar Farhan ²
and Sanjay Sivalokanathan ^{3,*}

¹ GKT School of Medical Education, King's College London, London SE1 1UL, UK; rasi.mizori@kcl.ac.uk (R.M.); ali.hassan@kcl.ac.uk (A.H.); sukruth.pradeep_kundur@kcl.ac.uk (S.P.K.); alitahirmalik0009@gmail.com (A.M.)

² Lennox Hill Hospital, New York, NY 10025, USA; sfarhan1@northwell.edu

³ Mount Sinai Fuster Heart Hospital, Icahn School of Medicine, New York, NY 10025, USA

* Correspondence: sanjay.sivalokanathan@mountsinai.org

Abstract

Restrictive cardiomyopathy (RCM) poses a significant challenge in diagnosis, is frequently identified in advanced stages, and has limited therapeutic options, which may lead to adverse cardiovascular outcomes. This narrative review examines the application of artificial intelligence (AI) across key diagnostic modalities and delineates priorities for translational advancement. The discussed diagnostic tools include echocardiography, cardiac magnetic resonance (CMR), electrocardiography (ECG), and electronic health records (EHR). A targeted, non-systematic search of PubMed and Scopus was performed to identify studies focused on model development, validation, or diagnostic accuracy concerning RCM and related infiltrative disorders. The findings suggest that AI can enable earlier detection, standardize imaging protocols, and enhance phenotype-driven management of RCM. Nonetheless, several challenges exist, including limited data access, the absence of external validation, variability across imaging devices and locations, and the imperative for transparent, explainable systems. Key priorities for successful implementation encompass establishing multi-center collaborations, detecting and correcting bias, clinician involvement in deployment, and integrating multimodal data, including imaging, signal data, and -omics. If effectively integrated into clinical practice, AI has the potential to redefine the management of RCM from a condition recognized primarily in its later stages to one characterized by early detection, dynamic risk assessment, and personalized treatment strategies.

Keywords: restrictive cardiomyopathy; artificial intelligence; cardiac amyloidosis; cardiac sarcoidosis; hemochromatosis



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1. Introduction

There are three primary subtypes of cardiomyopathies: dilated, hypertrophic, and restrictive. Among these, restrictive cardiomyopathy (RCM) is the least prevalent, accounting for only 2–5% of cases, yet it presents the most unfavorable prognosis [1]. RCM is characterized by impaired ventricular filling, leading to biatrial enlargement and progressive heart failure [2]. The etiology of RCM is diverse. In Western populations, infiltrative diseases, including cardiac amyloidosis, sarcoidosis, and hemochromatosis, are predominant [3]. Conversely, in tropical regions, conditions such as endomyocardial fibrosis and hypereosinophilic syndromes are significant contributors [4]. Despite advancements in diagnostic

imaging, the diagnosis of RCM remains challenging due to its symptomatic overlap with other causes of heart failure with preserved ejection fraction, particularly constrictive pericarditis [2]. Current management for RCM is primarily supportive, and the prognosis remains morbid. Reported mortality rates indicate a two-year mortality approaching 50% and a five-year mortality rate reaching 70%. This combination of diagnostic challenges, limitations in therapeutic interventions, and the relative rarity of RCM underscores the pressing need for innovative diagnostic methodologies [3].

Over the past decade, artificial intelligence (AI) has emerged as a transformative force in medical research and clinical practice. By leveraging machine learning (ML) and deep learning (DL) algorithms, AI systems can analyze large and complex datasets to uncover patterns that exceed human recognition [5]. In medicine, these approaches have demonstrated broad utility across diagnostic imaging, predictive modeling, outcome forecasting, and clinical decision support, enabling earlier diagnosis and more precise therapeutic decisions. For example, AI-based models have improved the interpretation of radiologic and pathologic images, enhanced disease risk stratification and prognostic modeling across chronic conditions, and contributed to precision-medicine frameworks that integrate multi-omic and clinical data [6,7]. Within cardiology, AI, particularly DL, has already shown significant promise in automating image analysis, detecting arrhythmias, and predicting heart-failure outcomes, providing a foundation for extending these advances to rarer and diagnostically challenging phenotypes such as restrictive cardiomyopathy [8,9].

Despite the substantial progress of AI in cardiovascular medicine, a critical knowledge gap remains regarding its application in RCM. Most existing studies focus on more prevalent cardiac disorders, such as ischemic, dilated, or hypertrophic phenotypes, or isolate individual etiologies like cardiac amyloidosis without considering restrictive physiology as a unified entity [10]. Furthermore, limited integration exists across diagnostic modalities, including echocardiography, cardiac magnetic resonance (CMR), electrocardiography (ECG), and electronic health record (EHR) data [11]. To date, no comprehensive synthesis has examined how AI can enhance early detection, phenotypic classification, and management of RCM or addressed the barriers preventing its clinical translation. This narrative review, therefore, aims to critically evaluate the current applications and future directions of AI in RCM and its common etiologies, emphasizing how multimodal, explainable, and collaborative approaches could transform RCM from a condition diagnosed late into one characterized by early recognition and precision-guided care.

2. Current Diagnostic Pathway in RCM

RCM constitutes one of the most diagnostically challenging conditions. No single diagnostic investigation is pathognomonic for RCM, and its clinical, electrocardiographic, and imaging findings often overlap with those observed in other forms of cardiomyopathy and, more importantly, constrictive pericarditis. Consequently, establishing a diagnosis typically requires an integrative approach combining laboratory assessments, multimodal cardiac imaging, and histopathological confirmation in select cases. However, each of these diagnostic modalities possesses intrinsic limitations that may contribute to delays in diagnosis, misclassification of the condition, and subsequent suboptimal management. These limitations demonstrate the urgent need for improved diagnostic strategies to enhance the accuracy and timeliness of RCM identification in affected patients [3,7].

2.1. Laboratory Evaluation

In patients presenting with features suggestive of heart failure, laboratory investigations often represent the initial phase of the diagnostic evaluation. Routine biochemical testing, which includes assessments of renal and hepatic function and the measurement of

natriuretic peptides, may support the diagnosis of heart failure; however, these parameters lack specificity for RCM [12]. Disease-specific assays, such as serum immunofixation for amyloidosis, iron studies for hemochromatosis, and angiotensin-converting enzyme levels for sarcoidosis, can provide critical etiological insights but rarely yield a definitive diagnosis when utilized in isolation [13]. Genetic testing may be informative for younger individuals when an inherited form of RCM is suspected, especially in cases involving mutations in sarcomeric genes such as *TNNI3* and *TNNT2*. Nevertheless, the phenotypic and genotypic overlap with hypertrophic and dilated cardiomyopathies limits the diagnostic yield of such testing. This emphasizes the necessity for a comprehensive and integrative diagnostic framework to improve the accuracy and effectiveness of RCM identification [14].

2.2. Echocardiography

Transthoracic echocardiography (TTE) is the first-line imaging modality due to its accessibility and capability to evaluate diastolic function. Characteristic findings indicative of RCM include preserved systolic function, regular or reduced ventricular cavity size, and biatrial enlargement [12]. Progressive diastolic dysfunction typically presents as impaired relaxation, which advances to a restrictive inflow pattern characterized by shortened relaxation times. Tissue Doppler imaging illustrates reduced e' velocities and elevated E/e' ratios. In instances of CA, speckle tracking echocardiography (STE) of the left ventricular myocardium may reveal the distinctive apical sparing “bull’s-eye” or “cherry-on-top” pattern, assisting in the differentiation from alternative etiologies [15].

Nevertheless, despite these diagnostic strengths, many echocardiographic features, such as restrictive filling and impaired relaxation, are non-specific and may overlap with advanced hypertensive or valvular diseases. Furthermore, the quality of imaging and interpretation is highly operator-dependent, and echocardiography offers limited tissue characterization compared to CMR imaging. Distinguishing RCM from constrictive pericarditis remains a significant challenge, as there is considerable overlap in Doppler profiles, despite the availability of validated diagnostic algorithms. This complexity underscores the necessity for meticulous evaluation and interpretation in clinical settings [16].

2.3. Cardiac Magnetic Resonance Imaging

CMR imaging is the gold standard for non-invasive ventricular morphology and tissue characterization evaluation in RCM [16]. It offers high-resolution assessments of all cardiac chambers and is particularly useful when echocardiographic findings are inconclusive or when detailed phenotypic delineation is necessary. Late gadolinium enhancement (LGE) plays a critical role in identifying myocardial fibrosis or infiltration, typically exhibiting diffuse or subendocardial enhancement in cases of amyloidosis, patchy basal involvement in sarcoidosis, and apical fibrosis in conditions such as endomyocardial disease [17]. Furthermore, quantitative mapping techniques, including native T1 and extracellular volume (ECV) mapping, have enhanced the detection of diffuse interstitial expansion, thus enabling earlier recognition of infiltrative processes. For instances of hemochromatosis and transfusion-related iron overload, T2* (T2-star) mapping—which quantifies myocardial iron content based on magnetic relaxation time shortening—remains the gold standard for myocardial iron quantification and therapeutic guidance. [18]. Additionally, CMR facilitates the quantification of atrial volumes and diastolic filling parameters with high reproducibility, offering incremental value in differentiating restrictive physiology. This advanced imaging capability highlights the importance of CMR in increasing diagnostic accuracy and informing clinical management for patients with RCM.

Despite the advantages associated with CMR imaging, findings pertaining to RCM exhibit significant heterogeneity and are seldom definitive. The enhancement patterns

observed frequently overlap with those characteristic of other cardiomyopathies, as well as ischemic heart disease. Furthermore, the application of gadolinium-based contrast agents may be contraindicated in patients with advanced renal impairment. The inter-scanner variability in T2* values and mapping results can pose challenges to the reproducibility of findings across different medical centers. Notably, no single CMR feature can independently confirm a diagnosis of RCM; thus, a comprehensive interpretation necessitates the integration of clinical, biochemical, and, when applicable, histological data [19]. The diversity of imaging signatures, along with potential contraindications for the use of contrast agents and the absence of disease-specific biomarkers, underscores the importance of emerging computational and multimodal techniques in enhancing diagnostic accuracy.

2.4. Nuclear Imaging

Nuclear scintigraphy has emerged as a valuable adjunct in the diagnostic evaluation of RCM, particularly when an infiltrative etiology such as cardiac amyloidosis is suspected. Bone-avid tracers, including technetium-99m pyrophosphate (PYP), 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD), and hydroxymethylene diphosphonate (HMDP), selectively bind to transthyretin (ATTR) amyloid fibrils within the myocardium, enabling non-invasive identification of ATTR-CM. When combined with the absence of a monoclonal protein, grade 2–3 myocardial uptake on planar or SPECT imaging is considered diagnostic and obviates the need for histological confirmation [20,21]. These techniques demonstrate high sensitivity and specificity and are increasingly integrated into the diagnostic algorithm for patients presenting with an RCM phenotype of uncertain cause [22]. Despite its high diagnostic accuracy for ATTR-CM, 99mTc-PYP scintigraphy carries important limitations. False positives can occur in AL amyloidosis, recent infarction, or inflammatory cardiomyopathies, and biochemical exclusion of monoclonal protein is essential for specificity [23]. Variability in acquisition protocols and interpretation methods further limits reproducibility, and the technique provides limited information on disease burden or therapeutic response [22,24].

2.5. Electrocardiogram

ECG is a cost-effective and widely accessible diagnostic tool that is routinely employed in patients exhibiting symptoms of heart failure. In the context of RCM, distinctive electrocardiographic abnormalities may present, including atrial fibrillation, evidence of biatrial enlargement, low QRS voltages, non-specific ST–T wave changes, and conduction disturbances such as atrioventricular block [25]. Certain electrocardiographic signatures may indicate specific underlying etiologies: for example, CA frequently manifests as a “pseudo-infarct” pattern characterized by poor R-wave progression; cardiac sarcoidosis may present with bundle branch block or high-grade atrioventricular block; and hemochromatosis typically exhibits normal ECG tracings until advanced stages, at which point low voltages and supraventricular arrhythmias may emerge [16,26]. Despite these associations, it is essential to recognize that ECG findings in RCM often lack both sensitivity and specificity. Many of the observed features can overlap with those associated with other cardiac disorders, and tracings may remain unremarkable in the early stages of the disease. Furthermore, RCM is seldom suspected in primary or community care settings, where ECGs are most frequently obtained, resulting in the overlooking of subtle diagnostic cues and contributing to delays in the recognition of this condition [2].

2.6. Invasive Studies: Endomyocardial Biopsy and Right Heart Catheterization

Endomyocardial biopsy (EMB) remains the definitive diagnostic approach for confirming RCM in cases where non-invasive assessments are inconclusive. Histopathological examination can establish a diagnosis in specific etiologies, such as amyloidosis, where

Congo red staining exhibits apple-green birefringence under polarized light. In the context of idiopathic RCM, the condition is characterized by diffuse interstitial fibrosis [27]. However, the diagnostic yield of EMB is limited in disorders with heterogeneous myocardial involvement, including sarcoidosis and hemochromatosis, where granulomatous or iron deposition is often spatially variable [28,29]. In addition to its variable sensitivity, EMB entails inherent procedural risks. While infrequent, complications such as tricuspid regurgitation, right ventricular perforation, and cardiac tamponade have been reported [30]. Consequently, EMB is generally reserved for carefully selected cases at specialized medical centers, particularly when obtaining a tissue diagnosis is likely to have a direct impact on management decisions, such as distinguishing between infiltrative and inflammatory phenotypes or confirming specific therapeutic targets. Therefore, although EMB retains significant value as a confirmatory diagnostic tool, its invasive nature and limited scalability prevent its widespread application within the broader population of patients with RCM.

Right heart catheterization (RHC) is another key invasive tool for hemodynamic differentiation between RCM and constrictive pericarditis, particularly when non-invasive modalities yield indeterminate results. By directly measuring intracardiac pressures, RHC enables detailed assessment of diastolic filling patterns and pressure equalization across cardiac chambers—parameters essential in distinguishing RCM from constrictive pericarditis [31]. In RCM, ventricular end-diastolic pressures are elevated but not equalized, with minimal respiratory variation reflecting intrinsic myocardial stiffness. In contrast, constrictive pericarditis shows near-equal diastolic pressures, a characteristic dip-and-plateau pattern, and pronounced ventricular interdependence with exaggerated respirophasic changes [32,33]. Although physiologically definitive, the role of RHC has declined with advances in multimodal imaging. This is largely due to its invasive nature, along with marked operator-dependence. Furthermore, RHC is associated with small but significant procedural risks including venous injury, arrhythmias, and pneumothorax. As such, RHC is largely reserved for cases where non-invasive findings remain equivocal or pre-operative hemodynamic confirmation is required before pericardiectomy [34,35].

3. AI Applications in RCM Diagnostics

AI has become a promising adjunct to conventional diagnostic modalities in RCM. Utilizing high-dimensional data from imaging, ECG, biomarkers, and electronic health records (EHR), AI systems can discern subtle, multidimensional patterns often beyond the reach of traditional interpretation. While most published research has focused on infiltrative phenotypes such as amyloidosis, there is a growing application of these approaches to other restrictive conditions, including sarcoidosis, hemochromatosis, and thalassemia-related iron overload.

This section summarizes the key findings from echocardiography, CMR, ECG, and other data streams. It describes the current state of AI-assisted diagnostics in RCM while critically evaluating their limitations and translational potential. Table 1 presents the characteristics of the included studies.

Table 1. Characteristics of included studies.

Author	Year	Modality	Study Type/Sample Size	RCM Substrate/Condition	AI Method	Input Data	Key Performance (AUC/Accuracy)
Islam MJ, Karim SA, Rahman T [36]	2025	Multimodal (EHR + Imaging + Genetic + Biomarkers)	Experimental; <i>n</i> = 500 patients (1500 MRI scans; MIMIC-IV, ACDC, ClinVar)	Restrictive cardiomyopathy	Hybrid DL (CNN for imaging + BiLSTM for EHR; Bayesian optimization)	MRI, echocardiography, EHR trends, genetic markers, BNP and inflammatory biomarkers	Accuracy 93%; Precision 0.90; Recall 0.91; F1-score 0.90 *
de Melo JF Jr et al. [37]	2025	ECG	Single-center retrospective; 29,282 patients (242 CS, 29,040 controls)	Cardiac sarcoidosis (definite + probable)	DL CNN (10 s 12-lead raw waveforms)	Raw digital ECG signals (<1 year from diagnosis)	AUC 0.90 (95% CI 0.86–0.95); Sensitivity 83%; Specificity 85%; consistent across EF < 50% and ≥50% subgroups
Chang RS-W et al. [38]	2024	Echocardiography	Retrospective single-center study; 3603 echocardiograms from 636 patients (231 CA, 405 controls)	CA (ATTR and AL)—representative RCM phenotype	Random Forest (ML)	19 routine echo parameters (e.g., GLS, LVPWd, LA area, MV A/E velocities)	AUC 0.84 (19 features); Sensitivity 0.82; Specificity 0.73; PPV 0.76
Chao C-J et al. [39]	2024	Echocardiography (A4C TTE)	Retrospective; <i>n</i> = 381 (184 CP, 197 CA) + external validation (<i>n</i> = 23, Taiwan)	Constrictive pericarditis vs. CA	DL (ResNet50 CNN with motion-embedded RGB frames + meta-learner)	Raw apical 4-chamber cine loops converted to augmented frame-based images	AUC 0.97 (internal), 0.84 (external), 0.95 (internal mixed cohort); precision ≈ 0.93–0.97
Chen WW et al. [40]	2024	CMR (cine SSFP short-axis)	Retrospective dual-center (TVGH + TCVGH); 215 patients (156 Fabry, 59 HCM); external test: 31 patients (20 Fabry, 11 HCM)	Fabry cardiomyopathy vs. HCM	DL—3D ResNet18 CNN	Non-contrast short-axis cine stacks (standardized to 5 slices, 20 frames; no segmentation)	Internal (TVGH): F1 = 0.846, Accuracy = 0.909, AUC = 0.914; External (TCVGH): F1 = 0.727, Accuracy = 0.806, AUC = 0.918
Taleie H et al. [41]	2023	Echocardiography (2D TTE Radiomics)	Cross-sectional study; <i>n</i> = 78 thalassemia major patients	Iron overload cardiomyopathy (restrictive phenotype)	Radiomics + ML (Random Forest, SVM, Decision Tree, XGBoost)	103 radiomic texture features extracted from LV parasternal long-axis and apical 4-chamber views	AUC 0.73 (best model, Random Forest); accuracy 0.70
Eckstein J et al. [42]	2023	CMR (cine SSFP, 3.0 T Philips Achieva)	Retrospective single-center; 107 participants (44 controls, 45 CMR−, 18 CMR+)	Cardiac sarcoidosis	Supervised ML (RF, SVM, Logistic Regression, Voting, GBoost, XGBoost)	36 multi-chamber volumetric and strain features (bi-atrial + bi-ventricular) extracted via CVI42	3-class model (CTRL vs. CMR− vs. CMR+): RF/Voting = 82% accuracy; 2-class (CTRL vs. All Sarc): 97% (RF, SVM, LR); CMR+ vs. CMR− improved to 89% with feature selection (LR)
Harmon DM et al. [43]	2023	ECG	Retrospective validation; 440 amyloid patients (AL and ATTR) + 6600 controls (1:15 ratio)	CA (AL and ATTR subtypes)	Deep neural network (AI-enhanced ECG algorithm)	Raw 12-lead ECG waveform data	AUC 0.84 (95% CI 0.82–0.86); sensitivity 64.3%, specificity 90.4%; AL AUC 0.85, ATTR AUC 0.84; best for low-voltage ECGs (AUC 0.92), reduced for LVH (0.75) and LBBB (0.76) ECG model: AUC 0.91 (BWH), 0.85 (MGH), 0.86 (UCSF); detection up to 365 days pre-diagnosis (AUC ≈ 0.88). Echo model: AUC 0.96 (BWH), 0.91–1.00 across external sites; combined pipeline PPV ≈ 75% vs. 33% with echo alone.
Goto S, Mahara K, Beussink-Nelson L et al. [44]	2021	ECG and Echocardiography	Multicentre retrospective (5 US + Japan centers); >20,000 ECGs; >10,000 echocardiograms	CA (ATTR, AL)	CNN (2D for ECG; 3D-CNN for echo)	ECG waveforms; apical 4-chamber echo videos	Derivation: AUC 0.93 (accuracy 87%) Optum validation: AUC 0.95 EHR validation: AUC 0.80
Huda A et al. [45]	2021	EHR/Medical Claims	Derivation: <i>n</i> = 1071 ATTRwt-CM, 1071 controls; Validation: 3 national cohorts (<i>n</i> = 9412 cases + 9412 controls) + 1 EHR-based cohort (261 cases, 39,393 controls)	Wild-type transthyretin amyloid cardiomyopathy (ATTRwt-CM)	Random Forest (compared with logistic regression, XGBoost)	Administrative medical claims + structured EHR data (ICD-9/10 codes, demographics, comorbidities)	AUC 0.91 (95% CI 0.90–0.93); PPV 0.86; detected 84% of CA cases at cutoff 0.485; predicted CA > 6 months pre-diagnosis in 59%; best single-lead model (V5) AUC 0.86, 6-lead model AUC 0.90
Grogan et al. [46]	2021	ECG	Retrospective cohort; 2541 CA patients (light-chain or transthyretin) + 2454 controls	CA (ATTR and AL)	Deep neural network	Standard 12-lead ECG data (single-lead and 6-lead subsets tested)	

Table 1. Cont.

Author	Year	Modality	Study Type/Sample Size	RCM Substrate/Condition	AI Method	Input Data	Key Performance (AUC/Accuracy)
Schofield R, Ganeshan B, Fontana M, Moon JC [47]	2019	CMR (bSSFP cine, 1.5 T Siemens Avanto)	Retrospective; 216 subjects (50 HCM, 52 CA, 68 AS, 15 HTN + LVH, 31 healthy controls)	LVH etiologies (HCM, CA, AS, hypertensive LVH)	Texture analysis (TexRAD, filtration-histogram radiomics)	Mid short-axis unenhanced cine frame; whole-myocardium ROI; SSF = 3 mm filter	AUC = 0.89 (HCM vs. AS, mean −97.6 threshold; 72% sensitivity, 94% specificity); reproducibility ICC ≈ 0.85
Tison GH et al. [8]	2019	ECG	Retrospective multicohort study; >1.1 million ECGs from >400,000 patients	Multiple cardiovascular conditions (including heart failure phenotypes—relevant to restrictive physiology)	DL (CNN with interpretable embedding model)	Raw 12-lead ECG waveforms linked to EHR data	AUC 0.93 for predicting left ventricular dysfunction (EF ≤ 35%); accurately detected HF phenotypes and other comorbidities using ECG-only input
Sengupta PP et al. [48]	2016	Echocardiography (Speckle-Tracking)	Retrospective; <i>n</i> = 94 (50 CP, 44 RCM + 47 controls)	RCM vs. constrictive pericarditis	Associative Memory Classifier (AMC; cognitive ML)	15 STE + 4 conventional echo parameters (<i>e'</i> , <i>E/e'</i> , septal and posterior wall thickness)	AUC 96.2% (AMC) vs. 82.1% (<i>e'</i>) and 63.7% (GLS); accuracy ≈ 94% (10-fold CV)

ACDC: Automated Cardiac Diagnosis Challenge dataset, AL: light-chain amyloidosis, AMC: Associative Memory Classifier, AS: aortic stenosis, ATTR: transthyretin amyloidosis, ATTRwt-CM: wild-type transthyretin amyloid cardiomyopathy, AUC: area under the receiver operating characteristic curve, BNP: B-type natriuretic peptide, CA: cardiac amyloidosis, CMR: cardiac magnetic resonance imaging, CNN: convolutional neural network, CP: constrictive pericarditis, CS: cardiac sarcoidosis, CTRL: control group, CV: cross-validation, DL: deep learning, ECG: electrocardiogram, EF: ejection fraction, EHR: electronic health record, GLS: global longitudinal strain, HCM: hypertrophic cardiomyopathy, HTN: hypertension, ICC: intraclass correlation coefficient, LA: left atrium, LR: logistic regression, LV: left ventricle, LVH: left ventricular hypertrophy, LVPWd: left ventricular posterior wall dimension at end-diastole, MRI: magnetic resonance imaging, RF: random forest, RGB: red-green-blue color frames. RCM: restrictive cardiomyopathy, ROI: region of interest, SVM: support vector machine, SSFP: steady-state free precession MRI sequence. STE: speckle-tracking echocardiography, TTE: transthoracic echocardiography. * *p* < 0.05.

3.1. Echocardiography: From Parameter-Based to Pattern Recognition

This remains the primary imaging modality for suspected RCM, although it is often limited by diagnostic overlap with constrictive pericarditis and other cardiomyopathies [48]. AI has shown promise in enhancing diagnostic accuracy by identifying subtle spatiotemporal features and reducing reliance on operator expertise.

Early parameter-driven ML techniques have demonstrated significant improvements in discriminatory accuracy. Sengupta et al. reported that an associative memory classifier (AMC) trained on speckle-tracking echocardiographic and conventional parameters distinguished constrictive pericarditis from CA with an area under the curve (AUC) of 0.96, substantially exceeding the performance of global longitudinal strain (AUC 0.64) [48]. Notably, the model maintained over 90% accuracy with fewer than 40 training cases, highlighting the efficiency of feature-level learning. Building upon this, Chao et al. utilized a DL convolutional network (ResNet50) applied directly to raw apical four-chamber views, thereby eliminating manual feature selection and achieving robust internal validation (AUC 0.97) and external validation (AUC 0.84) [39]. Saliency mapping consistently emphasized the interventricular septum, a well-established anatomical discriminator in restrictive physiology, indicating that the model's attention aligns with known pathophysiological features.

Building upon this methodology, Chang et al. extended their analysis to larger cohorts by employing a random forest model on 3603 echocardiograms collected from 636 patients. The analysis achieved an AUC of 0.84 using 19 routinely reported echocardiographic parameters [38]. These results underscore the translational potential of integrating ML into standard echocardiographic reporting workflows. Furthermore, beyond amyloidosis, AI-enhanced echocardiography has demonstrated significant utility in diagnosing iron overload cardiomyopathy, a prominent cause of RCM. In patients with thalassemia major, radiomic analysis of echocardiographic images effectively distinguished individuals with myocardial siderosis, as confirmed through T2* CMR, even when conventional indices appeared normal, with an AUC of 0.73 [41].

These studies show that AI used in echocardiography can go beyond traditional parameter thresholds by capturing complex motion and texture patterns. This allows for earlier, consistent detection of restrictive phenotypes and reduces the subjectivity associated with manual interpretation.

3.2. CMR: Moving Beyond LV and Contrast-Centric Diagnosis

CMR remains the gold standard for non-invasive structural and tissue characterization in RCM, effectively combining quantitative volumetrics with assessments of myocardial texture and deformation [49]. Despite its extensive capabilities, current clinical practices are often hampered by reliance on LGE and manual visual interpretation, which can diminish sensitivity to diffuse or early-stage disease and pose challenges for patients with renal impairment. Additionally, traditional analyses tend to focus primarily on the left ventricle, frequently neglecting bi-atrial or right ventricular dysfunctions that may precede detectable fibrosis [50].

Recent advancements in AI and ML aim to address these limitations by deriving multidimensional, non-contrast-dependent features from cine CMR data. Supervised ML approaches utilizing constraint satisfaction (CS) have successfully integrated cine-derived strain and volumetric indices across all four cardiac chambers, enabling accurate classification of disease subgroups [42]. Random forest and ensemble voting classifiers distinguished controls, CMR-negative, and CMR-positive cases of CS with an overall accuracy of 82%. Meanwhile, logistic regression and support vector machine (SVM) models incorporating 36 diverse features—including bi-atrial and biventricular volumes, longitudinal strain,

and circumferential strain rate—achieved prediction accuracies up to 97%, even without reliance on LGE. Notably, the most significant predictors included left ventricular longitudinal strain rate and indexed end-systolic volume, underscoring the diagnostic significance of dynamic multi-chamber strain metrics beyond mere scar detection.

In CA, AI-based deformation metrics enhance phenotypic discrimination. A supervised SVM model utilizing non-contrast, cine-derived strain parameters—such as left and right atrial reservoir and right ventricular strain—distinguished CA from HCM and healthy controls with 90.9% accuracy [47]. Atrial strain and ejection fractions emerged as key predictors, highlighting the importance of atrial mechanics as sensitive indicators of restrictive physiology, which can be obtained from standard cine images.

AI-based models have also shown potential in detecting Fabry disease, a condition that is difficult to diagnose due to its restrictive substrate. Chen et al. used a 3D residual convolutional neural network (CNN), trained on short-axis cine images, to differentiate Fabry disease from HCM without needing contrast agents [40]. The model demonstrated strong performance in both internal validation (AUC 0.91) and external validation (AUC 0.92), proving its ability to generalize across different institutions. Importantly, it extracted spatiotemporal motion patterns and myocardial texture directly from cine images, avoiding the need for manual segmentation or parametric mapping.

These studies demonstrate the potential for AI-enhanced CMR to go beyond traditional contrast-based and LV-focused approaches. ML models have reached diagnostic accuracies over 90% for various restrictive phenotypes by utilizing multi-chamber strain, non-contrast cine features, and texture analysis. Although current data are still preliminary and limited to single-center studies, these results strongly suggest that AI-CMR could facilitate earlier, safer, and more consistent diagnosis of RCM and similar conditions [51].

3.3. *Electrocardiogram—A Scalable Tool for Early RCM Suspicion*

Artificial intelligence-enhanced electrocardiography (AI-ECG) has become a practical and scalable method for early detection of restrictive cardiomyopathies. By analyzing large databases of raw ECG waveforms, DL models can identify subtle electrical patterns that appear before obvious structural changes, enabling preclinical disease detection.

The strongest evidence comes from studies on CA, where DL models have shown high accuracy across multiple centers. In a comprehensive validation, a CNN achieved a C-statistic of 0.91 (95% CI 0.90–0.93, $p < 0.001$) for diagnosing CA [44]. Real-world tests revealed that the same model could predict CA up to 12 months before clinical diagnosis, with sustained high accuracy (C-statistic 0.88, 95% CI 0.85–0.91, $p < 0.001$). A meta-analysis of over 12,000 participants from seven groups confirmed these results, reporting an AUC of 0.89 (95% CI 0.87–0.91) overall, with similar performance for transthyretin (AUC 0.90) and light-chain (AUC 0.80) subtypes [52]. These findings show that AI-ECG makes population screening for a condition that is often under-recognized but increasingly treatable.

Beyond amyloidosis, AI-ECG shows promise in detecting cardiac sarcoidosis. At Mayo Clinic, an analysis of more than 29,000 ECGs found that a CNN achieved an AUC of 0.90 (95% CI 0.87–0.92, $p < 0.001$) for sarcoidosis detection, performing well regardless of ejection fraction status [37]. Although ECG alone cannot confirm a diagnosis, such models offer a low-cost way to triage high-risk patients who need further imaging or biopsy.

Together, these studies demonstrate AI-ECG's potential to transform the diagnostic process for restrictive cardiomyopathies. By recognizing electrical patterns invisible to traditional analysis, ML models can turn a common cardiovascular test into an accessible, non-invasive screening tool that complements imaging diagnostics.

3.4. Other Data Streams: Electronic Health Records and Disease Biomarkers

AI is increasingly used on non-imaging data like EHRs, lab biomarkers, and genetic profiles. This provides scalable, cost-effective tools for early detection of restrictive physiology. These data sources enable ongoing monitoring of high-risk groups, capturing subtle early signs before overt cardiac symptoms appear.

A notable study by Huda et al. employed a random forest model using administrative claims and structured EHR data to identify wild-type transthyretin amyloid cardiomyopathy (ATTR-CM) in heart failure controls [45]. The model used demographics, lab results, and extracardiac signs such as carpal tunnel syndrome and spinal stenosis, which are common systemic signs of amyloidosis. It achieved an Area under the receiver operating characteristic curve (AUROC) of 0.93 (95% CI 0.90–0.95, $p < 0.001$) during development and performed well externally in a 39,000-patient national validation cohort, with an AUROC of 0.80 (95% CI 0.77–0.83, $p < 0.001$). These results highlight the potential of passive EHR monitoring to identify high-risk individuals for confirmatory tests like CMR or biopsy, thus reducing diagnostic delays in infiltrative cardiomyopathies.

Recently, multimodal strategies have aimed to view RCM as a broader phenotype rather than a single disease. Islam et al. introduced an ensemble ML approach that combines EHR data with serum biomarkers, imaging measures, and genetic factors to detect RCM across various causes [36]. Their model reached 93% accuracy (95% CI 0.90–0.96, $p < 0.001$), outperforming traditional diagnostic methods. In addition to detection, the model also predicted arrhythmias and heart failure progression, demonstrating its utility for both diagnosis and prognosis.

These systems analyze complex relationships spanning clinical, biochemical, and imaging data, shifting from disease-specific to phenotype-driven classification. Such integrated models are especially relevant for RCM, a heterogeneous final stage of multiple myocardial diseases. As data networks grow and federated learning AI systems develop, they could enable real-time, dynamic detection of restrictive physiology. This would facilitate earlier treatment, tailored investigations, and better risk assessment across the cardiomyopathy spectrum.

4. Discussion

AI is more than just a technological tool; it transforms how RCM is detected, classified, and treated. While Section 3 showed its diagnostic capabilities across imaging, electrocardiography, and EHR systems, its broader importance lies in its ability to translate into practice: moving RCM care from reactive approaches to proactive, phenotype-based interventions. This discussion explores how earlier and more precise diagnoses could change patient outcomes, the obstacles limiting clinical use, and the ethical and research priorities that will determine if AI's potential in RCM leads to real patient benefits.

4.1. Clinical Implications of Earlier and More Accurate Diagnosis

The primary clinical significance of AI in RCM lies in its ability to enable earlier diagnosis, prior to the occurrence of irreversible myocardial remodeling. Early detection broadens the therapeutic window and allows for targeted interventions when diastolic compliance remains recoverable. For instance, in ATTR-CM, prompt initiation of tafamidis significantly enhances survival rates and functional capacity when administered before the onset of advanced dysfunction [53]. Similarly, AI-driven detection of iron-overload cardiomyopathy through radiomic or DL methods could facilitate earlier chelation therapy, thereby promoting recovery of ejection fraction and reducing morbidity [54,55]. Beyond optimizing treatment timing, AI has the potential to democratize access to specialized diagnostics. Regulatory-approved DL platforms enable non-experts to acquire real-time

echocardiographic images [56]. A multicenter prospective study demonstrated that nurses, with only two weeks of training, achieved interpretable, diagnostic-quality scans in 96% of patients (95% CI 93–98) using AI-guided handheld echocardiography, with an AUC of 0.88 (95% CI 0.83–0.93; $p < 0.001$) for detecting left-ventricular dysfunction compared to expert sonographers [57,58]. In RCM, where differentiating restrictive from constrictive physiology remains particularly challenging, such platforms could standardize image acquisition, reduce operator dependence, and accelerate referrals for definitive imaging or biopsy, thereby streamlining the diagnostic process across healthcare levels. Significantly, AI also holds promise to reshape disease classification. ML models can identify latent phenotypic clusters—beyond conventional criteria—by integrating imaging, biomarker, and genomic data [59]. For example, in CA, Amadio et al. utilized an AI-derived ECG score in a cohort of 2533 patients, demonstrating that risk stratification based on these models predicted survival independently of traditional staging (HR 2.0 [95% CI 1.58–2.55] for AL and HR 2.7 [95% CI 1.81–4.24] for ATTR; $p < 0.001$) [60]. Applying similar approaches to RCM could refine phenotypic categorization across etiologies, identify prognostically distinct subgroups, and tailor treatment strategies accordingly. This data-driven approach represents an important step toward precision medicine in cardiomyopathy.

4.2. Practical Barriers to Clinical Translation

Despite promising progress, several practical and technical challenges remain due to the shift from algorithmic proof-of-concept to clinical application. The most critical is data scarcity. RCM's rarity and diverse causes lead to small, fragmented datasets that restrict model generalizability. Most AI research concentrates on specific infiltrative causes, such as CA or sarcoidosis, rather than viewing restrictive physiology as a single entity. Limited sample diversity also impedes external validation and bias adjustment. Cross-institutional generalization remains another obstacle. Models trained on single-center data often show a significant performance drop when applied to new populations, scanners, or acquisition protocols [61]. Federated learning offers a promising solution: training models locally on distributed datasets while sharing only learned parameters instead of raw data, thus protecting privacy while increasing diversity [62,63]. Successful examples in echocardiography and cardiac MRI (CMR) suggest this method can sustain accuracy across vendors and locations. Finally, interpretability continues to influence clinical adoption. Deep neural networks functioning as “black boxes” are unlikely to earn clinician trust or regulatory approval. Incorporating explainable AI (XAI) techniques—such as saliency mapping, feature attribution, or attention-based visualization—will be crucial to connect algorithmic predictions with mechanistic understanding [64,65].

4.3. Ethical and Implementation Considerations

Achieving technical success does not automatically guarantee ethical or fair implementation. AI systems are inherently influenced by the data used for training, which can lead to the amplification of existing biases. If RCM models mainly originate from datasets of high-income regions, their accuracy may decline in underrepresented populations, especially where different causes such as endomyocardial fibrosis are common [66–68]. Therefore, maintaining diverse training datasets globally is essential to prevent diagnostic disparities. Privacy and cybersecurity issues also pose significant concerns. Multimodal datasets that include high-resolution images, EHRs, and genomic data are susceptible to re-identification and breaches, particularly during data sharing across institutions [69,70]. Implementing strong encryption, anonymization, and clear consent processes will be crucial. Additionally, AI workflows often involve human assistants or external analytics platforms, which add complexity to accountability and data security [71,72]. Ethical considerations also extend

to liability. The lack of definitive regulations around responsibility for diagnostic errors hampers broader adoption [73]. Clarifying whether accountability rests with the clinician, healthcare organization, or AI developer remains unresolved. Transparent reporting of AI performance, ongoing oversight, and involving clinicians in validation are vital to reduce legal risks while preserving clinician independence.

4.4. Future Directions and Research Priorities

The next frontier for AI in RCM extends beyond static image classification toward predictive, integrative, and precision-focused applications that continuously learn from longitudinal data and guide real-time clinical decisions.

4.4.1. From Detection to Prognostication

AI systems have already shown strong prognostic capabilities in other types of cardiomyopathies. In hypertrophic phenotypes, CNN-based ECG models predicted ten-year risks of left-ventricular systolic dysfunction and sudden cardiac death with AUROCs close to 0.95, surpassing traditional risk scores [74]. Applying these approaches to RCM could allow for ongoing monitoring of disease progression, helping to identify inflection points when fibrosis speeds up or diastolic compliance worsens. ML survival models might also improve transplant timing decisions by predicting which patients could decompensate despite receiving optimal therapy, an area still mainly guided by subjective clinical judgment [75]. By combining long-term imaging, biomarkers, and wearable-derived hemodynamics, future systems could provide dynamic risk profiles that change with the patient, shifting prognostication from a static evaluation to continuous, precise monitoring.

4.4.2. Integrating Multi-Omic and Imaging Data

Advances in multi-omic sciences now enable the alignment of genomic, transcriptomic, proteomic, and metabolomic layers with imaging phenotypes. Incorporating AI to integrate these datasets could identify molecular endotypes that account for fibrotic or infiltrative behaviors, independent of morphology [76]. Connecting omic and imaging data would validate imaging biomarkers by confirming their correlation with histopathology, shifting the focus from purely morphological diagnosis to a more mechanistic approach. This biological grounding could enhance trial design, optimize patient selection for therapies such as transthyretin silencers or gene-editing treatments, and uncover new therapeutic targets within fibrotic signaling pathways.

4.4.3. Federated and Collaborative Learning Networks

Tackling data scarcity necessitates collaborative infrastructure. Techniques like federated learning and unified imaging protocols can improve generalizability while safeguarding privacy [77]. Multi-institutional AI consortia, akin to existing global projects in oncology and radiomics, could develop open benchmarking platforms for RCM, promoting transparency, reproducibility, and fair participation. Establishing standardized imaging formats, metadata schemas, and annotation pipelines will be essential for this progression.

4.4.4. Explainability, Trust, and Clinician-in-the-Loop Systems

For AI to integrate safely into clinical practice, its interpretability must develop alongside its performance. Upcoming algorithms should utilize attention-based interpretability methods and provide probabilistic outcomes to show uncertainty. The “clinician-in-the-loop” approach, where AI supports rather than replaces human expertise, presents an ethical and practical balance. In this model, algorithms offer probabilistic predictions and saliency maps, which clinicians interpret within the context of patient presentation. Early research in radiology and ECG interpretation indicates that such hybrid

systems outperform either humans or models alone, enhancing accuracy while maintaining accountability [78]. Integrating these systems into EHR dashboards or imaging workstations would allow smooth adoption into clinical workflows without compromising professional autonomy.

4.4.5. Towards Precision Therapeutics

Ultimately, the long-term potential of AI in the management of RCM extends beyond diagnostic applications to include precision therapeutics. AI has the capability to facilitate the selection of tailored therapies based on specific molecular and mechanical endotypes by integrating data from imaging, omics, and physiological sources. Reinforcement learning algorithms may be utilized to simulate virtual patient cohorts, thereby optimizing drug selection, dosage, and sequencing [79]. Furthermore, continuous physiological monitoring from wearable or implantable sensors, such as measurements of heart rate variability, pulmonary artery pressure, and arrhythmic burden, could be integrated into adaptive AI models capable of real-time forecasting of decompensation [80]. These advancements aim to elevate AI from a purely diagnostic tool to an active, dynamic clinical partner, capable of synthesizing ongoing feedback across biological, structural, and physiological domains to enable precise, preemptive care for patients with RCM.

4.5. Synthesis and Outlook

The growing role of AI in RCM marks a shift from descriptive to predictive cardiology. By integrating imaging, electrical, and systemic data, AI can help detect restrictive physiology earlier, assess risk dynamically, and tailor therapy more accurately than before. However, success depends on thorough validation, interpretability, and fair data representation. The main challenges are both technological and translational, especially in bridging algorithmic accuracy with clinical outcomes. Moving forward, ongoing collaboration among engineers, clinicians, and ethicists is essential to ensure AI's integration into RCM is evidence-based, transparent, and centered on patient care.

5. Conclusions

RCM remains one of the most difficult and least understood types of cardiomyopathy, with delayed diagnosis and few treatment options leading to poor outcomes. AI provides a way to achieve earlier and more accurate detection by combining various data types such as imaging, ECG, and EHR. In addition to aiding diagnosis, AI can improve disease classification and support tailored patient management. Challenges include limited data availability, lack of widespread external validation, and the need for systems that are transparent and explainable. Collaboration across multiple centers is crucial for developing equitable models and facilitating clinical use. If these obstacles are overcome, AI has the potential to shift RCM from a disease identified late to one characterized by early detection, precise risk stratification, and targeted treatment, advancing the goal of true precision cardiology.

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Abbreviations

The following abbreviations are used in this manuscript:

A4C	Apical four-chamber (view)
AI	Artificial intelligence
AL	Light-chain (amyloidosis)
AMC	Associative memory classifier
AS	Aortic stenosis
ATTR	Transthyretin amyloidosis
ATTR-CM	Transthyretin amyloid cardiomyopathy
ATTRwt-CM	Wild-type transthyretin amyloid cardiomyopathy
AUC	Area under the curve
AUROC	Area under the receiver operating characteristic curve
bSSFP/SSFP	(Balanced) steady-state free precession
BiLSTM	Bidirectional long short-term memory (network)
BNP	B-type natriuretic peptide
CA	Cardiac amyloidosis
CI	Confidence interval
CMR	Cardiac magnetic resonance
CNN	Convolutional neural network
CP	Constrictive pericarditis
CTRL	Control (group)
CS	Constraint satisfaction
DL	Deep learning
DPD	3,3-Diphosphono-1,2-propanodicarboxylic acid (bone-avid tracer)
ECG	Electrocardiography
ECV	Extracellular volume
EHR	Electronic health records
EF	Ejection fraction
EMB	Endomyocardial biopsy
F1	F1-score (harmonic mean of precision and recall)
GLS	Global longitudinal strain
HCM	Hypertrophic cardiomyopathy
HMDP	Hydroxymethylene diphosphonate (bone-avid tracer)
HR	Hazard ratio
HTN	Hypertension
LBBB	Left bundle branch block
LGE	Late gadolinium enhancement
LA	Left atrium
LV/RV	Left ventricle/Right ventricle
LVH	Left ventricular hypertrophy
ML	Machine learning
MV	Mitral valve (A/E velocities)
PPV	Positive predictive value
PYP (99mTc-PYP)	Technetium-99m pyrophosphate (bone-avid tracer)

RCM	Restrictive cardiomyopathy
ResNet	Residual Network (DL architecture)
RGB	Red-green-blue (color frames)
RHC	Right heart catheterization
ROI	Region of interest
SPECT	Single-photon emission computed tomography
STE	Speckle-tracking echocardiography
SVM	Support vector machine
T2*	T2-star (CMR iron quantification)
TTE	Transthoracic echocardiography
XAI	Explainable AI
XGBoost	Extreme Gradient Boosting (algorithm)

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