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Prognostic value of parametric mapping techniques for predicting left ventricular reverse remodeling in patients with dilated cardiomyopathy

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SOUHRN

Cíl: Cílem této studie bylo zhodnotit prognostický význam parametrů magnetické rezonance srdce (CMR), včetně pozdního sycení gadoliniem (LGE) a parametrického mapování (T1, T2 a extracelulární objem [ECV]), spolu s nálezy endomyokardiální biopsie (EMB) pro predikci reverzní remodelace levé komory (LVRR) u pacientů s definitivní, možnou nebo vyloučenou zánětlivou kardiomyopatií (ICM).
Metody: Retrospektivně jsme analyzovali 87 pacientů s nově diagnostikovanou dilatační kardiomyopatií (RODCM), kteří podstoupili vstupní CMR a EMB, s následným kontrolním CMR vyšetřením za jeden rok. ICM byla klasifikována jako definitivní, možná nebo vyloučená na základě nálezů EMB. Reverzní remodelace levé komory (LVRR) byla definována jako absolutní nárůst ejekční frakce levé komory (EF LK) o > 10 % a relativní pokles enddiastolického objemu levé komory (LVEDV) o ≥ 10 % při kontrolním vyšetření. Vstupní klinické parametry, nálezy EMB a CMR byly hodnoceny pomocí jednorozměrné a vícerozměrné logistické regresní analýzy.
Výsledky: Kritéria LVRR splnilo 40 pacientů (46 %). Vstupní LGE, LVSV > 71,5 ml a ECV byly v jednorozměrné analýze spojeny s nižší pravděpodobností dosažení LVRR. V nejlepších multivariantních modelech potvrdily význam těchto parametrů jako prediktorů LVRR modely se dvěma a třemi prediktory (LVSV > 71,5 ml + ECV > 29,6 %; AUC 0,776 a ECV na jednu směrodatnou odchylku + LGE + LVSV > 71,5 ml; AUC 0,785). Respondéři vykazovali ve srovnání s non-respondéry signifikantně větší zlepšení EF LK a snížení nativního T1 mezi vstupním a kontrolním vyšetřením.
Závěr: U pacientů s RODCM je vstupní hodnota ECV robustním a nezávislým prediktorem LVRR, který překonává nativní T1, T2 i zánětlivé markery získané z EMB. Multiparametrický přístup CMR, integrující rozsah difuzní fibrózy s velikostí, objemy a funkcí komor, poskytuje optimální prognostické zhodnocení pravděpodobnosti dosažení reverzní remodelace levé komory.

Keywords:
Cardiac magnetic resonance
Dilated cardiomyopathy
Endomyocardial biopsy
Extracellular volume
Left ventricular reverse remodeling
Parametric mapping

ABSTRACT

Objective: The objective of this study was to evaluate the prognostic value of cardiac magnetic resonance (CMR) parameters, including late gadolinium enhancement (LGE) and parametric mapping (T1, T2, and extracellular volume fraction [ECV]), in combination with endomyocardial biopsy (EMB) findings, for predicting left ventricular reverse remodeling (LVRR) in DCM patients with definite, possible, or excluded inflammatory cardiomyopathy (ICM).
Methods: We retrospectively analyzed 87 patients with recently diagnosed dilated cardiomyopathy (RODCM) who underwent baseline CMR and EMB, and had a second CMR within 395 days. ICM was classified as definite, possible, or excluded based on EMB findings. LVRR was defined as an absolute increase in left ventricular ejection fraction (LVEF) >10% and a relative decrease in left ventricular end-diastolic volume (LVEDV) ≥10% at follow-up. Baseline clinical, EMB, and CMR parameters were evaluated using univariate and multivariate logistic regression to identify predictors of responder-defined LVRR.

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Results: LVRR criteria were met by 40 patients (46%). Baseline LGE, LVSV >71.5 ml, and ECV were associated with lower odds of achieving LVRR on univariate analysis. Significant predictors of achieving responder-defined LVRR were identified in top-performing multivariate models with two and three predictors (LVSV >71.5 ml + ECV >29.6%; AUC 0.776 and ECV per-SD + LGE + LVSV >71.5 ml; AUC 0.785). Responders exhibited significantly greater improvements in LVEF and native T1 reduction from baseline to follow-up compared to non-responders.
Conclusion: In patients with RODCM, baseline ECV is a robust and independent predictor of responder-defined LVRR, outperforming native T1, T2, and EMB-derived inflammatory markers. A multiparametric CMR approach integrating diffuse fibrosis burden with ventricular size, volumes, and function provides optimal prognostic assessment of responder-defined LVRR.

Introduction

Dilated cardiomyopathy (DCM) is one of the most common multifactorial cardiomyopathies and typically presents with heart failure, accompanied by an increased risk of ventricular arrhythmias and sudden cardiac death.[1] It is defined by left ventricular (LV) dilatation and systolic dysfunction that cannot be explained by abnormal LV loading conditions, such as arterial hypertension or valvular heart disease, nor by ischemic heart disease.[2]

Cardiovascular magnetic resonance (CMR) imaging is recommended in all patients with DCM as part of the initial diagnostic evaluation according to the 2023 European Society of Cardiology (ESC) guidelines on cardiomyopathies.[3] Beyond its high accuracy in assessing cardiac volumes, myocardial mass, wall thickness, and systolic function,[4] CMR enables comprehensive non-invasive myocardial tissue characterization.[5] This capability facilitates early diagnosis and precise phenotyping of cardiomyopathies, which is essential for risk stratification and individualized therapeutic decision-making.[6]

In patients with DCM, left ventricular reverse remodeling (LVRR) is a strong surrogate marker of myocardial recovery and is associated with improved long-term outcomes.[7] However, the ability to predict LVRR at baseline remains limited. Late gadolinium enhancement (LGE) detects focal replacement fibrosis and has established prognostic value, but it may underestimate diffuse myocardial remodeling.[8] Parametric mapping techniques, including native T1, T2, and extracellular volume fraction (ECV), allow quantitative assessment of diffuse fibrosis and myocardial inflammation, potentially providing incremental prognostic information.[9] Endomyocardial biopsy (EMB), despite its invasive nature and sampling limitations, remains the reference standard for diagnosing inflammatory cardiomyopathy (ICM) and offers direct insight into myocardial inflammation and fibrosis.[10] The objective of this study was to evaluate the prognostic value of baseline CMR parameters, including LGE and parametric mapping (native T1, T2, and ECV), in combination with endomyocardial biopsy (EMB) findings, for predicting left ventricular reverse remodeling (LVRR) in DCM patients with definite, possible, or excluded inflammatory cardiomyopathy (ICM).

Methods

Study group

Patients with recently diagnosed DCM who had both baseline (BL) and follow-up (FUP) CMR examinations within 395 days and an EMB biopsy at BL were retrospectively included. Inflammatory cardiomyopathy (ICM) was classified as definite, excluded, or possible based on EMB biopsy. Specific criteria are listed below in subsection "Endomyocardial biopsy".

Image acquisition and analysis

Cardiovascular magnetic resonance (CMR) examinations were performed at St. Anne's University Hospital in Brno using a 1.5-T clinical scanner (Ingenia, Philips Medical Systems, Best, The Netherlands) equipped with 5- and 32-element phased-array receiver coils. All studies were acquired with patients in the supine position using repeated breath-hold techniques and electrocardiographic gating.

The standard CMR protocol included cine imaging for the assessment of cardiac morphology and function using balanced steady-state free precession (bSSFP) sequences. Typical acquisition parameters were as follows: field of view 300 × 300 mm, acquired voxel size 1.67 × 1.67 × 8.0 mm, reconstruction matrix 256, slice thickness 8 mm with no interslice gap, sensitivity encoding (SENSE) factor 1.7, and 30–50 cardiac phases per cardiac cycle. Cine images were obtained in contiguous short-axis slices covering the entire left ventricle from base to apex, as well as in standard long-axis views.

Modified Look-Locker inversion recovery (MOLLI) sequences were used to obtain T1 parametric maps at the mid-ventricular short-axis level. Native T1 mapping was performed before contrast injection using a 3(3)5 pattern, and enhanced T1 mapping was performed 15 minutes after contrast administration with a 4(1)3(1)2. ECV was determined from native and post-contrast T1 values using the standard formula: ECV = (1 – hematocrit) × (ΔR1 myocardium / ΔR1 blood), where ΔR1 is the change in R1 (1/T1) before and after contrast administration.[11] Hematocrit values were obtained from laboratory blood analyses performed up to two days before the examination or on the same day. When no laboratory measurement was available, values were estimated using a calculated value.[12]

T2 mapping was acquired at the mid-ventricular short-axis level using a multi-echo GraSE sequence with a black-blood prepulse in a single breath-hold.

Late gadolinium enhancement (LGE) imaging was performed in all patients approximately 10 minutes after intravenous administration of a gadolinium-based contrast agent (0.2 mmol/kg gadobutrol; Gadovist, Bayer Healthcare). LGE images were acquired using standard inversion-recovery gradient-echo sequences in matching short-axis and long-axis planes, with inversion time indi-

vidually adjusted to achieve optimal nulling of normal myocardium.

Clinical analysis was performed with the IntelliSpace Portal (ISP) workspace (version 11, Philips Healthcare). Left ventricular end-diastolic volume (LVEDV), end-systolic volume (LVESV), stroke volume, and left ventricular ejection fraction (LVEF) were quantified from short-axis cine images using standard contouring techniques. Papillary muscles were included in the left ventricular cavity volume. All morphological and functional parameters, as well as the presence and pattern of LGE, were assessed in accordance with current Society for Cardiovascular Magnetic Resonance (SCMR) recommendations.[13] Left ventricular reverse remodelling (LVRR) was defined as an absolute improvement in LVEF of >10% from baseline to follow-up and a relative decrease in LVEDV of ≥10% from baseline.

CMR T1 and T2 parametric mapping analysis was performed using cvi42 (release 5.13.9, Circle Cardiovascular Imaging Inc., Calgary, Canada). The endocardial and epicardial contours were traced automatically in the mid-ventricular SAX images, excluding papillary muscles. The contours were visually assessed and corrected if needed. The program excluded 10% of the resulting regions of interest. Segmental T1 and T2 values were automatically calculated using curve fitting for each AHA segment, with global values representing the mean of all segments. A region of interest was also placed in the blood pool of the left ventricular cavity to obtain T1 values for ECV calculation.

Endomyocardial biopsy

Endomyocardial biopsy at BL was performed in all patients as part of the diagnostic workup for suspected inflammatory cardiomyopathy, in accordance with current European Society of Cardiology recommendations.[14] Biopsy procedures were carried out under local anesthesia using a standard percutaneous transvenous approach. Samples were obtained from the right ventricular septum using a flexible bioptome.

A minimum of 4–6 myocardial tissue specimens were collected from each patient. Biopsy samples were immediately processed for histological, immunohistochemical, and molecular analyses. For histological evaluation, tissue specimens were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin as well as Masson's trichrome to assess myocardial structure, inflammatory infiltrates, myocyte damage, and interstitial or replacement fibrosis.

Immunohistochemical analysis was performed on paraffin-embedded sections using antibodies directed against inflammatory cell markers, including CD3 for T lymphocytes, CD68 for macrophages, and Leukocyte Common Antigen positive (LCA+) for leukocytes. Inflammatory cardiomyopathy was defined according to established immunohistochemical criteria, based on the presence of ≥14 leukocytes/mm² (including ≥7 CD3+ T lymphocytes/mm²) in combination with evidence of myocardial damage.[14]

Based on histological, immunohistochemical, and molecular findings, patients were classified as having definite, possible, or excluded inflammatory cardiomyopathy.

All biopsy analyses were performed by experienced cardiovascular pathologists blinded to the CMR findings and clinical outcomes.

Statistical analysis

Categorical variables are presented as a number (percentage), and continuous variables are presented as the mean (standard deviation) or median (interquartile range) based on normality assessment (Shapiro–Wilk test). Paired t-tests or paired Wilcoxon signed-rank tests were performed to assess the within-subject difference between BL and FUP values, depending on whether the differences were normally distributed. The comparison between responder groups was performed with Pearson's Chi-squared test for categorical variables and Welch's two-sample t-test or the Wilcoxon rank-sum exact test for normally and non-normally distributed data. Pearson's or Spearman's correlation was used for normally and non-normally distributed variables.

Univariate and multivariate logistic regression analyses were conducted to identify baseline predictors of left ventricular reverse remodeling (LVRR). Model assumptions were verified, including assessment of multicollinearity using the variance inflation factor (VIF) and evaluation of linearity of continuous predictors with respect to the logit using component-plus-residual plots and the Box–Tidwell test. Optimal cutoffs were determined using receiver operating characteristic (ROC) curve analysis and the Youden index. Firth's bias-reduced logistic regression was applied when standard maximum likelihood estimation resulted in separation or convergence issues.

Variables with p <0.10 in univariate analysis were considered for multivariate modeling, avoiding highly correlated predictors (correlation coefficient <0.6, VIF <5). Two- and three-predictor multivariate models were evaluated using the area under the curve (AUC), Akaike information criterion (AIC), and Nagelkerke's R^2. Top-performing model selection was based on complementary ranking strategies prioritizing discrimination (AUC) and parsimony (AIC).

Odds ratios (ORs) with 95% confidence intervals (CIs), p-values, and AUCs were reported for all logistic regression models. ORs for continuous variables represent a 1-standard-deviation increase, while ORs for dichotomized variables compare values above versus below the defined cutoff.

ICM subgroup comparisons were performed using one-way ANOVA or Kruskal–Wallis tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables, as appropriate. For variables with significant group differences, post hoc pairwise comparisons were conducted using Dunn's test with Benjamini–Hochberg correction, and effect sizes (ε^2) were calculated. A p-value ≤0.05 was considered statistically significant. All analyses were performed using R (version 4.4.1; RStudio 2025.09.2+418).

Results

Study group

The cohort included 21 females (24%) and 66 males (76%). The median time between baseline and follow-up

was 190 (176, 222) days. ICM was determined as definite in 16 patients, excluded in 57, and possible in 14.

Clinical and CMR data

A comparison of clinical and CMR data at BL and FUP is shown in **Table 1.** LGE was present in 58 (67%) patients at BL and in 61 (70%) at FUP. At BL, 16 patients had edema, which was resolved in 14 of them (3 global, 4 in basal segments, 1 in basal and mid segments, 1 in mid segments, 1 in apical segments, 3 in the intraventricular septum, and 1 in the anteroseptum) and persisted in 2 (one in the LV lateral wall, one in the intraventricular septum at the basal segment). T1 and T2 parametric mapping results are shown in **Table 2**. Native T1 mapping values, both segmental and global, were significantly lower at FUP in all AHA segments. T2 mapping decreased significantly in three segments (mid-anterior, mid-inferolateral, and mid-anterolateral).

Based on the LVRR criteria (LVEF improvement >10% and LVEDV decrease ≥10%), 40 patients were classified as responders and 47 as non-responders. A comparison of the baseline clinical and CMR between responders and non-responders is shown in **Table 3.**

Responders exhibited lower global ECV and LGE than non-responders. Other parameters were similar.

Clinical and CMR parameters changed from baseline to follow-up (Δ = FUP – BL) between responders and non-responders, as shown in **Table 4.** Patients classified as responders exhibited significantly greater improvements in LVEF, reductions in LV volumes (LVEDV, LVEDVi, LVESV, LVESVi), and decreases in left ventricular mass (LVM, LVMi) compared with non-responders. Global native T1 also significantly decreased in responders, whereas changes in ECV and T2 were similar between groups.

Univariate logistic regression with optimal Youden index cutoffs identified baseline CMR parameters as candidate predictors associated with reduced likelihood of reverse remodeling (**Table 5**). Higher ECV (continuous and >29.6%), LGE, LVSV >71.5 ml, LVEF >34.5%, and global T2 >56.6 ms showed significant associations.

Multivariate logistic regression models were constructed using candidate predictors identified from univariate logistic regression, with age and sex as potential confounding factors. Two- and three-predictor models were evaluated and ranked by discriminative ability (AUC), parsimony (AIC), and explained variance (Nagelkerke R^2), yielding top-performing models with good discriminative ability and low multicollinearity (VIF<2) (**Table 6**).

The best two-predictor model (AUC 0.78, sensitivity 0.70, specificity 0.81) combined LVSV >71.5 ml and ECV >29.6%, both dichotomized at Youden index cutoffs, and demonstrated that patients exceeding these thresholds have dramatically reduced odds of being classified as responders. Follow-up duration was included as an additional covariate and was not significantly associated with response (OR 1.01, 95% CI 0.997–1.018, p = 0.240), suggesting that differences in follow-up timing did not bias the observed associations.

The best three-predictor model (AUC 0.79, sensitivity 0.80, specificity 0.74) included ECV per standard deviation increase, LGE, and LVSV >71.5 ml. This model revealed that even modest ECV elevations independently reduce response likelihood by 10% per SD, alongside focal fibrosis (LGE) and stroke volume threshold effects.

Table 1 – Comparison of CMR data from baseline (BL) to follow-up (FUP)

Variable	BL N = 87	FUP N = 87	*p*-value[1]
Age (years)	48.5 (39.1–56.5)	49.0 (39.6–57.2)	**<0.001**
LVEF (%)	30.5 (10.6)	44.6 (14.3)	**<0.001**
LVEDV (ml)	237.8 (87.1)	198.1 (92.3)	**<0.001**
LVEDVi (ml/m^2)	152.0 (55.8)	125.8 (57.3)	**<0.001**
LVESV (ml)	158.0 (117.5–219.5)	93.0 (69.5–128.5)	**<0.001**
LVESVi (ml/m^2)	96.1 (74.6–135.7)	59.0 (41.7–80.8)	**<0.001**
LVSV (ml)	65.0 (56.0–76.0)	78.0 (66.0–92.0)	**<0.001**
LVSVi (ml/m^2)	42.1 (35.0–48.7)	50.2 (40.1–59.6)	**<0.001**
LVM (g)	154.0 (134.0–200.0)	142.0 (122.0–176.0)	**<0.001**
LVMi (g/m^2)	98.6 (84.4–130.4)	87.7 (74.5–112.5)	**<0.001**
Global native T1 (ms)	1051 (1020–1085)	1008 (984–1038)	**<0.001**
Global ECV (%)	27.4 (25.6–30.6)	27.2 (24.8–30.2)	0.733
Global T2 (ms)	54.9 (52.7–58.2)	53.6 (51.2–55.8)	**<0.001**

CD3+ – CD3 T-lymphocytes positive; CD68+ – CD68 macrophages positive; ECV – extracellular volume; ED – end-diastolic; EF – ejection fraction; ES – end-systolic; i – indexed; ICM – inflammatory cardiomyopathy; LCA+ – Leukocyte Common Antigen positive; LGE – late gadolinium enhancement; LV – left ventricular; LVM – left ventricular mass; SV – stroke volume.

[1] Paired t-test for variables with normally distributed differences, paired Wilcoxon signed-rank test for variables with non-normally distributed differences.

Values are presented as mean (standard deviation) or median (IQR) for normally and not-normally distributed continuous variables, and as number (percentage) for categorical variables.

Table 2 – Comparison of segmental T1 and T2 parametric mapping at baseline and follow-up

Variable	BL N = 87	FUP N = 87	*p*-value[1]
Global native T1 (ms)	1051 (1020–1085)	1008 (984–1038)	**<0.001**
Mid anterior	1037 (1005–1072)	992 (971–1018)	**<0.001**
Mid anteroseptal	1050 (1020–1083)	1006 (980–1046)	**<0.001**
Mid inferoseptal	1060 (1031–1089)	1019 (991–1065)	**<0.001**
Mid inferior	1064 (1034–1113)	1026 (995–1070)	**<0.001**
Mid inferolateral	1050 (1015–1103)	1012 (983–1051)	**<0.001**
Mid anterolateral	1029 (979–1064)	984 (960–1017)	**<0.001**
Global ECV (%)	27.4 (25.6–30.6)	27.2 (24.8–30.2)	0.733
Mid anterior	27.0 (24.4–30.1)	26.3 (24.1–31.4)	0.813
Mid anteroseptal	29.5 (25.8–31.8)	27.5 (25.4–32.4)	0.245
Mid inferoseptal	28.4 (26.3–32.0)	28.4 (25.6–32.2)	0.956
Mid inferior	28.2 (25.6–32.0)	27.8 (25.6–30.9)	0.589
Mid inferolateral	26.0 (23.9–29.2)	26.0 (23.8–28.5)	0.681
Mid anterolateral	26.0 (23.4–29.9)	25.9 (23.6–29.4)	0.541
Global T2 (ms)	54.9 (52.7–58.2)	53.6 (51.2–55.8)	**<0.001**
Mid anterior	54.9 (51.2–59.0)	52.8 (50.8–55.0)	**0.003**
Mid anteroseptal	55.7 (6.5)	54.2 (5.1)	0.059
Mid inferoseptal	54.2 (51.5–57.4)	53.9 (50.8–57.3)	0.357
Mid inferior	54.4 (51.7–58.5)	53.7 (51.2–57.0)	0.150
Mid inferolateral	54.3 (51.5–60.0)	52.1 (50.2–56.4)	**<0.001**
Mid anterolateral	54.4 (51.5–59.8)	52.6 (50.0–55.1)	**0.002**

[1] Paired t-test for variables with normally distributed differences, paired Wilcoxon signed-rank test for variables with non-normally distributed differences.
Values are presented as mean (standard deviation) or median (IQR) for normally and not-normally distributed continuous variables.

Table 3 – Comparison of clinical and CMR data at baseline (BL) between responders and non-responders

Variable	Responder N = 40	Non-responder N = 47	*p*-value[1]
Age (years)	46.8 (11.6)	49.6 (11.2)	0.253
Sex (n (%)) (female / male)	11 (28%) / 29 (73%)	10 (21%) / 37 (79%)	0.617
LVEF (%)	28.5 (7.9)	32.2 (12.3)	0.091
LVEDV (ml)	226.5 (197.8–253.2)	220.0 (173.0–298.5)	0.878
LVEDVi (ml/m^2)	138.1 (124.1–166.4)	137.5 (107.3–190.3)	0.705
LVESV (ml)	166.0 (132.5–200.2)	139.0 (98.5–239.5)	0.485
LVESVi (ml/m^2)	98.0 (84.9–126.7)	93.5 (59.1–147.1)	0.369
LVSV (ml)	61.0 (55.0–70.2)	70.0 (57.0–79.0)	0.105
LVSVi (ml/m^2)	40.2 (34.7–46.0)	42.6 (35.4–52.4)	0.281
LVM (g)	168.0 (140.2–208.0)	151.0 (133.5–198.0)	0.299
LVMi (g/m^2)	106.4 (87.8–132.6)	90.2 (81.7–124.5)	0.194
Global native T1 (ms)	1044 (1021–1075)	1051 (1020–1088)	0.642
Global ECV (%)	26.1 (24.5–28.3)	28.5 (26.4–32.1)	**0.001**
LGE (n (%))	21 (53%)	37 (79%)	**0.012**
Global T2 (ms)	54.5 (52.2–56.5)	55.9 (53.0–59.7)	0.092

ECV – extracellular volume; ED – end-diastolic; EF – ejection fraction; ES – end-systolic; i – indexed; ICM – inflammatory cardiomyopathy; LCA+ – Leukocyte Common Antigen positive; LGE – late gadolinium enhancement; LV – left ventricular; LVM – left ventricular mass; N – number of non-missing values; SV – stroke volume.
[1] Welch two-sample t-test for normally distributed variables, Wilcoxon rank sum test for not-normally distributed variables, Fisher's exact test for binary variables.
Values are presented as mean (standard deviation) or median (IQR) for normally and not-normally distributed continuous variables, and as number (percentage) for categorical variables.

Table 4 – Comparison of CMR parameters change from baseline to follow-up (Δ = FUP – BL) between responders and non-responders

Variable	Responder N = 40	Non-responder N = 47	*p*-value[1]
ΔLVEF (%)	23.6 (10.8)	6.0 (9.4)	**<0.001**
ΔLVEDV (ml)	–73.5 (41.2)	–10.9 (37.0)	**<0.001**
ΔLVEDVi (ml/m²)	–48.0 (26.5)	–7.6 (22.1)	**<0.001**
ΔLVESV (ml)	–73.0 (–125.5, –59.5)	–21.0 (–39.5, –5.5)	**<0.001**
ΔLVESVi (ml/m²)	–46.9 (–85.2, –37.2)	–15.2 (–24.7, –3.5)	**<0.001**
ΔLVSV (ml)	15.0 (6.8, 28.0)	8.0 (–5.5–26.0)	0.089
ΔLVSVi (ml/m²)	9.6 (3.9, 17.3)	4.7 (–3.3–15.5)	0.085
ΔLVM (g)	–21.0 (–46.5, –7.8)	–11.0 (–22.5–3.5)	**0.007**
ΔLVMi (g/m²)	–14.9 (–31.7, –5.4)	–6.9 (–13.4–1.8)	**0.005**
ΔGlobal native T1 (ms)	–54.5 (–85.2, –23.0)	–27.0 (–55.0–9.0)	**0.020**
ΔGlobal ECV (%)	–0.2 (–2.4–1.9)	0.0 (–2.7–2.5)	0.848
ΔGlobal T2 (ms)	–1.1 (–5.4–1.2)	–0.8 (–4.8–1.5)	0.683

ECV – extracellular volume; ED – end-diastolic; EF – ejection fraction; ES – end-systolic; i – indexed; LV – left ventricular; LVM – left ventricular mass; N – number of non-missing values; SV – stroke volume.
[1] Welch's t-test for normally distributed variables, Wilcoxon rank-sum test for non-normally distributed variables.
Values are presented as mean (standard deviation) or median (IQR) for normally and not-normally distributed continuous variables, and as number (percentage) for categorical variables.

Table 5 – Univariate logistic regression for candidate baseline CMR parameters (dichotomized at Youden index cutoffs where applicable) predicting responder status

Variable	OR	95% CI	*p*-value	AUC (%)
LVEF >34.5%	0.31	0.12–0.77	**0.011**	0.632
LVSV >71.5 ml	0.30	0.11–0.74	**0.009**	0.634
LVSVi >42.5 ml/m²	0.42	0.17–0.99	**0.048**	0.605
ECV (%)	0.55	0.30–0.98	**0.043**	0.702
ECV >29.6 %	0.18	0.06–0.48	**<0.001**	0.672
LGE	0.30	0.12–0.76	**0.011**	0.631
Global T2 >56.6 ms	0.34	0.13–0.84	**0.019**	0.622

AUC – area under the curve; CI – confidence interval; ECV – extracellular volume; EF – ejection fraction; i – indexed; LGE – late gadolinium enhancement; LV – left ventricular; LVM – left ventricular mass; OR – odds ratio; SV – stroke volume.

Table 6 – Top-performing multivariate logistic regression models for prediction of responder status

Variable	OR	95% CI	*p*-value	AUC
Two-predictor model				0.78
LVSV >71.5 ml	0.18	0.06–0.50	**0.002**	
ECV >29.6%	0.11	0.03–0.33	**<0.001**	
Three-predictor model				0.79
ECV (per SD increase)	0.90	0.81–0.97	**0.020**	
LGE	0.30	0.10–0.83	**0.023**	
LVSV > 71.5 ml	0.22	0.07–0.62	**0.005**	

AUC – area under the curve; CI – confidence interval; ECV – extracellular volume; ED – end-diastolic; EF – ejection fraction; ES – end-systolic; i – indexed; LV – left ventricular; LVM – left ventricular mass; OR – odds ratio; SD – standard deviation; SV – stroke volume.

Endomyocardial biopsy

At baseline, EMB revealed inflammatory cell densities of LCA+ 6 (4–10), CD3+ 3 (2–6), and CD68+ 5 (2–6) cells/mm². According to EMB, ICM was definite in 16 patients, possible in 14, and excluded in 57. The observed proportions of patients meeting the responder-defined LVRR criteria were similar across the three groups: 44% in definite ICM, 43% in possible ICM, and 47% in excluded ICM (p = 0.936). Baseline CMR parameters were similar among ICM subgroups (**supplementary Table 1**).

To formally test for ICM modification, interaction analyses were performed between the strongest multivariate predictors (LVSV >71.5 ml, ECV >29.6%, and LGE) and ICM status. For the two-predictor model (LVSV + ECV), interaction terms were non-significant and model discrimination (AUC 0.78) remained unchanged. In the three-predictor model, interactions for LVSV and ECV were also non-significant, while LGE showed a potential interaction with excluded ICM (estimate = –2.93, p = 0.038); however, adding this term did not improve overall model fit or discrimination (AUC 0.78–0.81). These results indicate that the predictive value of baseline LVSV, ECV, and LGE for reverse remodeling is consistent across ICM subgroups, and incorporating ICM status does not enhance the predictive performance of the multivariate models.

Discussion

In this longitudinal retrospective CMR study of patients with DCM, we demonstrate that baseline myocardial tissue characteristics assessed by parametric mapping, particularly ECV, are independently associated with LVRR. Higher baseline ECV (whether exceeding 29.6% or per standard deviation increase) was consistently associated with lower odds of being classified as a responder, even after adjustment for ventricular size and function. Similarly, baseline LVSV >71.5 ml reduced the likelihood of achieving LV reverse remodeling, reflecting greater potential for functional recovery. While native T1 decreased more markedly in responders than in non-responders during follow-up, baseline native T1 and T2 values were not associated with responder classification. These findings highlight the complementary roles of diffuse fibrosis burden and baseline ventricular volumes in determining myocardial recovery.

Although this study did not demonstrate the significance of biotic findings for predicting LVRR, in other patient cohorts from our institution the presence of myocardial inflammation was associated with a higher chance of LV function recovery.[15]

This may be explained by the division of ICM patients in our study into three groups, whereas Poloczkova's work[15] classified patients into two groups, with and without ICM.

In their prospective CMR-based study of RODCM, Kubanek et al.[7] demonstrated that LGE extent and myocardial edema ratio combined with serial BNP measurements, outperformed EMB and conventional follow-up parameters in predicting LVRR. The higher prevalence of myocarditis and increased myocardial edema ratio among patients with LVRR suggested that resolving myocarditis may contribute to the process of LVRR.[7] Our findings indicate that diffuse interstitial fibrosis quantified by ECV represents a dominant constraint on LVRR in a broader DCM population. Baseline CMR parameters did not differ by ICM status. Interaction analyses confirmed that the predictive value of LVSV, ECV, and LGE for responder-defined LVRR was consistent across the ICM subgroups. These findings indicate that while EMB captures inflammatory activity and ICM classification, it does not modify the prognostic performance of key CMR parameters for predicting responder-defined LVRR.

Our results are consistent with and extend those reported by Cadour et al.,[16] who evaluated the prognostic value of parametric mapping for major adverse cardiovascular events in non-ischemic DCM. In that study, ECV emerged as the strongest independent predictor of both heart failure and arrhythmia-related outcomes, whereas native T1 provided incremental prognostic value primarily for arrhythmic events. Although the clinical endpoints differ, both studies converge on ECV's central role as a robust marker of disease severity. In Cadour et al., higher ECV identified patients at increased risk of clinical deterioration;[16] in our study, we found that patients with greater diffuse fibrosis were less likely to meet criteria for reverse remodeling, suggesting that diffuse fibrosis may influence the likelihood of achieving responder-defined reverse remodeling.

Di Marco et al.[17] evaluated the prognostic role of parametric mapping for ventricular arrhythmic risk and sudden cardiac death in a large cohort of patients with non-ischemic cardiomyopathy. In that study, ECV ≥30% was the strongest independent predictor of arrhythmic events, outperforming native T1, LGE, and LVEF, and demonstrating significant incremental value when added to conventional risk markers.[17] Despite the different clinical endpoints, their findings conceptually align with ours: the ECV thresholds associated with risk closely mirror those identified in our ROC-based analyses, suggesting that similar degrees of diffuse fibrosis are observed across different patient cohorts with DCM.

Furthermore, Di Marco et al. demonstrated that combining ECV with functional and structural parameters improved risk stratification. This outcome is consistent with our multivariate models, in which combinations of ECV, LVSV, and LGE showed good discriminative performance for predicting responder-defined reverse modelling. Together, these findings reinforce the value of a multiparametric CMR approach that integrates tissue characterization with ventricular size and function.[18]

In our cohort, native T1 values decreased significantly over time, with a greater reduction observed in responders, suggesting partial reversibility of myocardial tissue abnormalities with favorable remodeling. However, baseline native T1 and T2 values were not associated with responder status in our cohort, and T2 changes were limited and segment-specific. These findings suggest that while native T1 may be sensitive to dynamic changes during recovery, ECV more robustly reflects the fixed fibrotic burden that constrains remodeling potential. This observation is consistent with prior studies showing that ECV outperforms native T1 for prognostication in chronic cardiomyopathy phenotypes.

Limitations

The retrospective, single-center design limits the strength of conclusions that can be drawn from the data and may reduce the generalizability of the findings. The multivariate logistic regression models were not validated due to the relatively small cohort (40 responders, 47 non-responders), and reported performance metrics (AUC, sensitivity, specificity) should therefore be interpreted with caution. Follow-up duration varied among patients (median 190 days, IQR 176–222, maximum 395 days), which could influence classification of responder status; however, follow-up duration was included as a covariate in the models and was not significantly associated with response. We also had only one follow-up, meaning that time-to-event analyses or assessment of remodeling dynamics beyond the study interval are not available. The lack of a uniform definition of LVRR across studies may contribute to inconsistencies in reported results.

Finally, all participants received routine clinical care, and no specific therapeutic interventions were administered as part of the study protocol.

Conclusion

Baseline CMR parameters (LVSV >71.5 ml, ECV >29.6%, LGE, and ECV per 1% increase) were significant predictors of responder status in univariate and multivariate logistic regression analyses. Interaction analyses showed that the predictive value of these CMR parameters was consistent across ICM subgroups, indicating that their effects on responder classification were independent of whether inflammatory cardiomyopathy was definite, possible, or excluded. Overall, CMR parameters are the primary baseline predictors of responder-defined reverse remodeling, whereas EMB markers contribute complementary pathophysiological insights.

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

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Ethical statement

The study was conducted in accordance with the Declaration of Helsinki.

Informed consent

Written informed consent was obtained from all individual participants included in the study.

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