Native T1 Mapping in Non-Ischaemic Cardiomyopathy Using 3.0 Tesla MRI: A Single Centre Study

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ABSTRACT

INTRODUCTION: Heart failure is a global concern, with non-ischaemic cardiomyopathy (NICMP) contributing significantly. Myocardial fibrosis is a hallmark feature, and early detection is crucial for management and prognosis. Endomyocardial biopsy is the gold standard but invasive. Cardiac MRI offers a non-invasive alternative; however, late gadolinium enhancement (LGE) is limited in detecting diffuse fibrosis and unsuitable for chronic kidney disease. Native T1 mapping enhances tissue characterization. This study evaluates native T1 values in NICMP patients, comparing them with published reference values and LGE findings. **MATERIALS AND METHODS:** This retrospective study analysed 34 NICMP patients who underwent 3.0T cardiac MRI between January 2021 and October 2023. Mid-ventricular septal native T1 values were measured by two blinded readers and compared to a normal reference (1097 ms). Statistical analysis included one-sample T-tests for reference comparison and independent T-tests for differences between LGE-positive and LGE-negative groups. Inter-observer agreement was assessed using the intraclass correlation coefficient (ICC). **RESULTS:** The cohort (mean age 45.09 years) showed a mean native T1 value of 1307.97 ± 68.99ms, significantly higher than the reference ($p<0.001$). Inter-observer agreement was excellent (ICC: 0.98). Twelve patients (35.3%) were LGE-positive. No significant difference in native T1 values was observed between LGE-negative (1291.68 ms) and LGE-positive (1337.83 ms) groups. **CONCLUSION:** Native T1 values are significantly elevated in NICMP, potentially detecting diffuse fibrosis missed by LGE. T1 mapping shows promise as a non-invasive, gadolinium-free tool for diagnostic assessment and may contribute to risk stratification. Larger studies are needed to establish local reference values and validate these findings.

KEYWORDS: Non-ischaemic dilated cardiomyopathy, cardiac magnetic resonance, late gadolinium enhancement, native T1 mapping

INTRODUCTION

As the population ages, heart failure (HF) has become a leading cause of global morbidity and mortality. Cardiomyopathy (CMP), a group of disorders affecting heart muscle structure and function, is a primary driver of HF. Examples include hypertrophic, restrictive, dilated, arrhythmogenic right ventricular, and nonclassified cardiomyopathies.[1,2] Among over 60 million Asians, CMP prevalence ranges from 1.3% to 6.7%, with non-ischaemic CMP (NICMP) accounting for up to 40% of cases. This creates a significant socioeconomic burden and reduces patient quality of life.[3]

The hallmark of CMP and HF is myocardial fibrosis, categorised into reactive interstitial, infiltrative perivascular, and replacement fibrosis. Early detection is vital for lifestyle modifications and medical interventions to slow HF progression. While histological analysis via endomyocardial biopsy is the gold standard, it is primarily reserved for post-transplant rejection surveillance due to its invasive nature.[1,4]

Cardiac magnetic resonance (CMR) imaging is now a crucial non-invasive tool for assessing cardiac morphology. Conventionally, the late gadolinium enhancement (LGE) sequence detects myocardial tissue abnormalities such as replacement fibrosis and inflammation. LGE patterns can help identify the underlying aetiology of cardiomyopathy (Figure 1). However, LGE is an "all-or-none" technique that identifies focal replacement fibrosis but often misses diffuse interstitial fibrosis, which is common in NICMP.[1] Furthermore, gadolinium (Gd)-based contrast is contraindicated in many HF patients who also suffer from advanced chronic kidney disease (CKD) due to the risk of nephrogenic systemic fibrosis.[5]

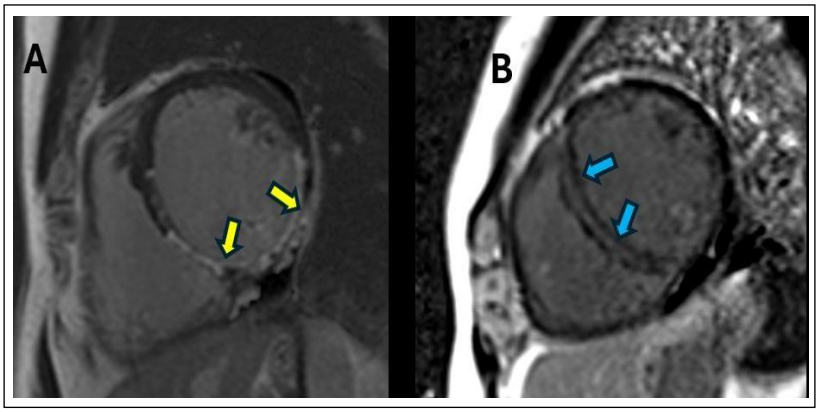

Figure 1: LGE image in short axis plane at mid ventricle demonstrates two enhancement patterns
(A) Transmural enhancement of inferior and inferoseptal wall consistent with right coronary artery territory infarction (yellow arrows). (B) Mid-myocardial enhancement at the septum (blue arrows), typical of nonischaemic cardiomyopathy, which may be seen in idiopathic dilated cardiomyopathy or myocarditis.

Native T1 mapping has emerged as a tissue-specific sequence that measures intrinsic myocardial relaxation times (ms) without contrast.[6,7] Unlike LGE, which requires a visual comparison between normal (nonenhanced) and abnormal (enhanced) fibrotic tissue, T1 mapping provides pixelated parametric maps that reflect both intracellular and extracellular properties. Studies suggest native T1 mapping is more sensitive than LGE for identifying diffuse fibrosis.[8-11] Detecting myocardial fibrosis is critical for prognostication, as its presence without timely intervention increases the risk of arrhythmia, heart failure progression, and premature mortality. Among various acquisition techniques, Modified Look-Locker Inversion recovery (MOLLI) is preferred for its high reproducibility and signal-to-noise ratio. Other techniques, such as Shortened MOLLI (ShMOLLI) and Saturation-recovery single-shot acquisition (SASHA), are comparatively less precise.[12]

Despite its potential, several knowledge gaps remain regarding native T1 mapping. There is a notable lack of standardisation, as values vary across scanner vendors, field strengths, and protocols. Currently, Malaysian reference values exist only for 1.5T systems, leaving the 3.0T range unestablished for the local population.[13] Additionally, limited research exists within the Malaysian population, as most findings are derived from Western cohorts. Finally, the specific relationship between native T1 values and LGE in NICMP remains poorly established, a critical consideration for CKD patients who cannot receive Gd-based contrast agents.

This study measures native T1 values in NICMP patients at a tertiary centre using a 3.0T system. We compare these values against the published normal mean and analyze the relationship between LGE findings and native T1 values. This research aims to benefit CKD patients by potentially eliminating the need for intravenous Gd and reducing reliance on invasive endomyocardial biopsies for diagnosing or quantifying myocardial fibrosis.

MATERIALS AND METHODS

Data Collection

This is a retrospective study conducted in the Radiology Department of a tertiary hospital. We collected images of 34 patients who underwent cardiac MRI (Philips Achieva 3.0T Tx) from January 2021 to October 2023. We included all studies that contained a native (non-enhanced) T1 map sequence, were reported as NICMP, and had left ventricular (LV) ejection fraction less than 50% and patients aged 18 years or older. Patients with poor image quality and without the T1 map sequence were excluded from this study.

The researcher traced MRI reports in Viarad5 and retrieved images from PACS. Images were analysed using the Philips IntelliSpace Portal v.12.0 and a PHILIPS viewing monitor 3MP 1536 x 2046 matrix. Cine, LGE (10 minutes post-gadolinium injection), and T1 map (MOLLI technique) sequences were acquired. Left ventricular (LV) volumes and ejection fraction were determined using the modified Simpson technique by drawing the endocontour at end diastole and end systole. Indexed end diastolic and indexed end systolic volumes were calculated using the patient's body surface area (BSA) from the DuBois method. LV ejection fraction was obtained using the following formula: [End diastolic volume – End systolic volume / End diastolic volume] x 100. Subjects with an LV ejection fraction of less than 50% were selected since it is one of the features seen in cardiomyopathy. The presence and absence of a non-ischaemic LGE pattern were identified and documented. Non-ischaemic LGE patterns include mid-myocardial, subepicardial, or nonterritorial subendocardial involvement. For the T1 map, the researcher was blinded to the reported native T1 values. A motion-corrected native T1 map was generated using post-processing. Matching between pre- and post-motion-correction maps of more than 80% was accepted for native T1 analysis. Epicardial and endocardial contours were drawn, and papillary muscles were excluded from the blood pool. A region of interest (ROI) was drawn at the mid-ventricular septum to avoid the blood pool and papillary muscles (Figure 2). Native T1 relaxation time of the drawn ROI was automatically calculated and presented in the table (Figure 3). Mean native T1 values of NICMP were compared with the normal reference (1097ms from the previous study) based on a similar MRI vendor (Philips), magnetic strength (3T), and acquisition technique (MOLLI).[14] Mean native T1 values were also compared between the negative LGE group and the positive LGE group (non-ischaemic pattern).

Data analysis .

All data from the data collection sheet were entered and analysed using IBM SPSS Statistics 27.[15] Descriptive statistics were used to describe patient characteristics; mean and standard deviation (SD) were used for numerical data, while percentages were used for categorical data. Descriptive analysis was used to express the mean native T1 value of the mid-ventricular septum. Intraclass correlation coefficient analysis was used to analyse inter-observer agreement between the researcher and one cardiac radiologist. A one-sample T-test

was used to compare the mean native T1 value with the normal reference. An independent T-test was used to compare the mean native T1 value between negative and positive LGE groups.

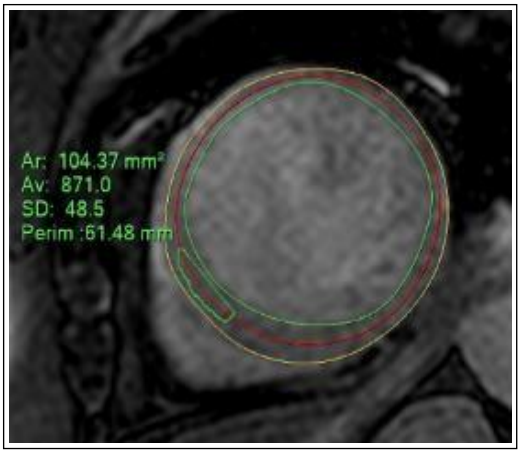

Figure 2: Contouring of myocardium and drawing of ROI on native T1 map at mid ventricle in short axis plane
Ar: area of small green circle; SD: standard deviation of signal intensity
Av: mean signal intensity within the small green circle; Perim: perimeter of the small green circle.
Note: Endocardium (green line), epicardium (yellow line), and a small green circle at the septal myocardium (ROI)

	T1 Native: Regional Result-1901, Slice No.: 2	
	Segment 1	Summary
T1 Native	1375±123 ms	1375±123 ms
R1 Native	0.73±0.06 Hz	0.73±0.06 Hz
T1 Enhanced	N/A ms	N/A ms
R1 Enhanced	N/A Hz	N/A Hz
ε	N/A	N/A
ROI Area Native	1461 mm²	1461 mm²
ROI Area Enhanced	N/A mm²	N/A mm²
Hematocrit	N/A %	N/A %
Field Strength	3 T	3 T

Figure 3: Native T1 relaxation time of the drawn ROI

RESULTS

Characteristics of the study population

50 cases were diagnosed with NICMP. 16 patients were excluded due to LVEF >50% (n=10), absent of T1 map sequence (n=5) and age less than 18 years old (n=1). Therefore, 34 patients were selected. The mean age was 45.09 (17.34) years, with 22 males and 12 females. Late gadolinium enhancement was present in 12 patients (35.3%). Mean T1 values of the mid-ventricular septum were 1307.97 (68.99) ms (Table I). 22 patients (64.7%) had dilated LVs, and 12 patients (35.3%) had normal LV size. The identified aetiologies of the NICMP patients were myocarditis, found in 10 patients (29.4%). Myocarditis was diagnosed based on a mid-myocardial or subepicardial enhancement pattern, correlated with the relevant clinical and laboratory findings.

Table I: Characteristics of non-ischaemic cardiomyopathy patients (n=34)

Variables	Mean (SD)
Age	45.09 (17.34)
Gender*	
Male	22 (64.7)
Female	12 (35.3)
T1 relaxation time at mid septum, ms	1307.97 (68.99)
LGE status*	
Negative	22 (64.7)
Positive	12 (35.3)
Indexed LV EDV, ml/m²	205.44 (82.85)
Indexed LV ESV, ml/m²	144.47 (82.64)
LV EF, %	31.12 (8.26)

*n(%)

Inter-observer variability for native T1 mapping measurement

An intraclass correlation analysis of a single-rating, absolute-agreement, two-way mixed-effects model with 2 readers (researcher and cardiac radiologist) across 18 native T1 measurements, which is appropriate for assessing agreement between fixed readers across multiple subjects (Table II).

Table II: ICC of inter-observer agreement

	Intraclass (95% CI)	F test (df1, df2)	p-value
Single measures	0.98 (0.94, 0.99)	84.13(17,17)	<0.001

*Single Rating, Absolute-Agreement, Two-Way Mixed Effects Model.

The inter-observer agreement between the researcher and cardiac radiologist is excellent, as indicated by the intraclass correlation coefficient of 0.98 (95% CI: 0.94 to 0.99). According to a previous study,[16] an ICC value greater than 0.90 indicates excellent reliability. The accompanying F-test result [$F(17,17=84.13$, $p<0.001$] further supports the statistical significance of the agreement between readers.

Relationship of T1 mid-ventricular septum values to the normal reference

Mean T1 mid-septal value 1307ms was higher than the population reference value of 1097ms, a statistically significant difference of 210.97 (186.90, 235.04) (Table III).

Table III: Comparison of mean native T1 values mid septum to normal reference (n=34)

	Mean (SD)	Mean of normal reference	t-stat (df)	pvalue*
T1 mid septum, ms	1307.97 (68.99)	1097	17.83 (33)	<0.001

*One-sample t-test

Native T1 values of the mid-ventricular septum among LGE-positive and LGE-negative patients

There were 12 subjects with LGE-positive and 22 with LGE-negative. The mean T1 mid-ventricular septum value in the LGE-positive group was 1337.83 ms (36.191), which was higher compared with the normal reference value of 1097 ms. The mean T1 mid-septal myocardium value in the LGE-negative group was 1291ms, which was also comparably higher than the population reference value of 1097ms. There was no

statistically significant difference in mean native T1 value between the LGE negative group (mean (SD) 1291.68 ms (77.50)) and the LGE positive group (mean SD 1337.83 ms (36.19)) (Table IV).

Table IV: Comparison of mean native T1 values mid septum to normal reference among LGE positive and LGE negative (n=34)

	Mean (SD)	Mean Difference (95% CI)	t-stat	p-value*
LGE Negative	1291.68(77.50)	-46.15(-94.59,2.29)	-1.941	0.061
LGE Positive	1337.83(36.19)			

*Independent T-test

DISCUSSION

The current study comprises 22 males and 12 female subjects. There is an established correlation whereby the female gender has higher native T1 values. A previous study of healthy populations demonstrated a global native T1 mean of 1124.9±55.2 ms, with women having a statistically higher value than men (1163±30.5 vs. 1077.9±39.5 ms, respectively; $p<0.001$).[17] However, the correlation between the genders was not assessed in the current study. Future studies examining correlations between age, gender, and ethnicity will require a more balanced demographic distribution to ensure representative results.

Among the LGE-positive subjects, 10 out of 12 (83.3%) subjects had dilated LV. This is parallel to the heart failure process, in which cardiac remodeling has failed, and the heart begins to dilate. Many previous studies have shown that LGE is a strong prognostic indicator of poor outcome.[18] It is associated with increased adverse cardiac events and mortality, such as hospitalisation due to heart failure, ventricular arrhythmias, and death. Based on our results, the native T1 value of 1338 ms (36.19) may serve as a guide to indicate the presence of LGE in future non-contrast cardiac MRI examinations, which may reflect a poor-prognosis group in heart failure risk stratification. However, this finding needs to be verified with a larger sample size.

Ten patients (29.4%) were confidently diagnosed with myocarditis in the current study. Other diagnoses include drug-induced cardiomyopathy (n=1), arrhythmogenic right ventricular cardiomyopathy (n=1), post-partum cardiomyopathy (n=1), COVID-related cardiomyopathy (n=1), and nonspecific aetiology in 20 patients. The nonspecific aetiology group required further clinical information. Histological confirmation was not performed in the current study. It is acknowledged that correlation with histological diagnosis is necessary; however, given the invasive nature of specimen collection, histological data are sparse. A recent study revealed a significant association between CMR and histological features of dilated cardiomyopathy.[19] It indicates that these imaging features have the potential to capture histological information.

The inter-observer agreement between the researcher and the cardiac radiologist was excellent. It is partly due to the similar software platforms used and the feasibility of the ROI placement at the midventricular septum. Further strengthening of the ROI placement method shall increase the accuracy of the measurements. This includes standardizing the ROI size, which was not done in this study. Our study, however, ensured the ROI was not smaller than 40 mm^2 while avoiding the blood pool and papillary muscles.

The present study demonstrated that 1) the native T1 values of 1307 ms in NICMP are higher than the reference value of 1097 ms, 2) there was no significant difference in the native T1 values of the NICMP

patients between the positive and negative LGE groups. It is important to note that the 1097 ms was derived from studies conducted in different parts of the world. Despite the similarity between the MR scanner and acquisition technique, it may not reflect the true native T1 mean of our local population.

Previous studies using a 3T MR scanner reported 1341.31±41.48ms in DCM subjects, significantly higher than the normal subjects in the same study (1186.47±45.67ms). 20 These previous studies included a control group of healthy subjects, which can be readily used as reference values within the study.[20] Our study lacked native T1 values from healthy subjects due to a lack of healthy volunteers, budget constraints, and grant limitations. We do recognise that, although the small sample size, studying healthy subjects would serve as an initial step toward establishing a cumulative local reference for native T1 values in this centre.

Even though there is a significant difference in native T1 values between NICMP patients and the normal reference, we were still unable to determine a cutoff threshold for clinical use to accurately diagnose myocardial fibrosis, as there was no local control group. However, the higher mean native T1 value (1292 ms) in our results compared with the normal reference may suggest the possible presence of myocardial fibrosis in our NICMP patients despite negative LGE. This finding will be beneficial for NICMP patients with CKD, as they may undergo follow-up CMR by monitoring native T1 values without the need for Gd. Increasing native T1 values at subsequent CMR visits may indicate progressive disease. A previous study on hypertrophic cardiomyopathy and DCM at a 3T scanner revealed native T1 values of 1254 ms and 1239 ms, respectively.[21]

The positive and negative LGE groups were determined by the cardiac radiologist who reported the CMR. Presence of hyperenhancement on LGE sequence of non-ischaemic patterns anywhere in the myocardium was grouped as positive LGE, while absence of hyperenhancement was grouped as negative LGE. Both groups, positive and negative LGE, showed increased native T1 values of 1338 ms and 1292 ms, respectively, with no significant difference between them. Among the 12 subjects with positive LGE, 8 had mid-wall midventricular septum enhancement. The remaining 4 subjects showed subepicardial enhancement at different sites. None of the LGE-positive subjects had hyperenhancement at the right ventricular insertion point. It is of note that hyperenhancement at the right ventricular insertion point carries a better prognosis in nonischaemic dilated cardiomyopathy, and a previous study suggested the right ventricular insertion point enhancement is benign in nature.[22]

The lack of a significant difference in mean native T1 values between the positive and negative LGE groups may reflect diffuse myocardial fibrosis in both groups, with negative LGE subjects already having early myocardial fibrosis that LGE does not capture. It is worth noting that negative LGE in NICMP patients does not necessarily indicate diffuse or very early myocardial fibrosis. Many other mechanisms impair myocardial contractility, including myocyte contractile abnormalities (mitochondrial dysfunction), early-stage metabolic disorders (diabetes mellitus), inflammation (transient myocarditis), valvular heart disease, and inherited disorders (sarcomere dysfunction). In this group of diseases, native T1 values may still fall within the normal reference range despite reduced myocardial function.

In the current study, we chose the single ROI method at the mid-ventricular septum, given the thickest myocardial tissue in that region. It provides a relatively homogeneous tissue sample with minimal artifacts

from surrounding structures such as blood vessels or epicardial fat. Drawing a single ROI in the septum is also less time-consuming than segmenting the entire myocardium into multiple regions, especially when assessing diffuse disease. There is a suggestion that the single ROI method may not fully represent the whole myocardium. A previous study examined structural heart disease, compared T1 values using the single-septal ROI method and the 16-segmental ROI method, revealing similar performance.[23] Another recent study in 2023 also applied the single ROI method at the mid-ventricular septum, focusing on diffuse myocardial disease (DM) and DCM, and correlated native T1 values and ECV with the histological diagnosis.[19] Hence, drawing a single ROI at the mid-ventricular septum to measure the native T1 value of diffuse myocardial tissue is sufficient and less time-consuming than a 16-segment analysis in a relatively healthy patient.

Study limitations

This study has several limitations. First, the small sample size consisted of 34 NICMP subjects; however, the single-ROI method at the mid-ventricular septum remains appropriate for assessing diffuse myocardial disease.[23] Second, T1 values are highly dependent on MR strength, protocols, and software, limiting extrapolation to other institutions. Third, the lack of a healthy control group and local 3.0T reference values necessitated the use of a pooled mean of 1097ms,[14] though inter-center variability in techniques and demographics often precludes using external values as standards.[24-26] Fourth, while prognosis was not directly evaluated, more LGE-positive patients exhibited LV dilation, a known independent predictor of outcomes in NICMP.[18] Fifth, no histological correlation was performed. Finally, demographic associations were not examined, a challenge previously noted in local research due to imbalanced sample distributions.[13]

CONCLUSION

This study shows significantly elevated native T1 values in NICMP patients (mean 1307 ms) compared to the reference (1097 ms). The lack of a significant difference in native T1 values between the LGE-positive (1338 ms) and LGE-negative (1292 ms) groups suggests that native T1 mapping may reflect diffuse myocardial fibrosis despite negative LGE. Utilising a single-septal ROI approach proved practical and reliable, yielding excellent inter-observer agreement. While limited by a small sample size and lack of histological correlation, these findings establish a foundation for native T1 mapping at 3.0T MRI in Malaysia. This technique offers a promising, contrast-free alternative for myocardial evaluation, particularly when Gd is contraindicated. Future larger-scale studies are essential to establish local reference values and promote the clinical utility of T1 mapping.

FUTURE RECOMMENDATION

Future research should focus on establishing local reference values for T1 and T2 maps and the extracellular volume fraction. Larger cohorts are needed to strengthen comparisons between LGE groups, while the influence of age, gender, and ethnicity on T1 values warrants further investigation. Additionally, prospective studies should evaluate the prognostic relationship between native T1 values and NICMP outcomes.

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The study did not receive any research grant.

CONFLICT OF INTEREST

There were no conflicts of interest between the contributors of this research.

INSTITUTIONAL REVIEW BOARD (ETHICS COMMITTEE)

The study protocol was approved by the Human Research Ethics Committee, USM on 23rd October 2025, JEPeM code: USM/JEPeM/22060370

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