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Comparison between native T1 mapping and late gadolinium enhancement in ischemic cardiomyopathy

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Abstract
Background: Ischemic cardiomyopathy continues to be a principal contributor to early morbidity and mortality. The formation of myocardial scar tissue, secondary to ischemic events, is linked with alterations in ventricular remodeling. The aim of the current study is to investigate the native T1 mapping and late gadolinium enhancement (LGE) to identify myocardial fibrosis in patients with ischemic cardiomyopathy.
Methods: This prospective center study was conducted on 87 patients that proved to have ischemic cardiomyopathy who were admitted to Benha University Hospital& national heart institute (NHI), Egypt from March 2022 to April 2023. Patients were subjected to a CMR viability evaluation, which included an analysis of ventricular function alongside an assessment of LGE for the identification of myocardial fibrosis and T1 mapping procedures. Also, 2D speckle tracking & GLS were done for all patients.
Results: The mean T1 mapping among patients with Late gadolinium enhancement was higher compared with patients who didn't show Late gadolinium enhancement (1131.7 Vs 983.0 respectively, moreover patients who has > 70% significant fibrosis had a higher T1 mapping compared with patients with lower grades of fibrosis (p<0.001). With studying each cardiac segment separately, surprisingly significantly mean T1 mapping was higher in late gadolinium enhancement segments compared with non-enhanced areas (p<0.001). Roc curve had proven that T1 mapping is an excellent discriminative tool to diagnose enhancement as a There was also a highly statistically significant positive association between GLS and T1 mapping. A notable negative association was detected between strain and T1 mapping across various myocardial segments.
Conclusion: T1-mapping & GLS proved to be effective tools in identifying patients with fibrosis compared with the gold standard method (late gadolinium enhancement).

Keywords: T1 Mapping, late gadolinium, GLS, ischemic cardiomyopathy, CMR Speckle tracking echocardiography

Introduction
Cardiovascular disease persists as a predominant cause of mortality in industrialized countries, with ischemic heart disease (IHD) and its complications being the primary contributors. In the past decade, advancements in technology have significantly enhanced the utility of noninvasive cardiovascular imaging modalities for the detection, quantification, and risk stratification of both acute and chronic IHD. Among these modalities, two-dimensional speckle tracking echocardiography (2D-STE) is particularly pivotal in evaluating global and regional myocardial function, thereby facilitating the diagnosis of ischemic origins [1].
In conjunction with echocardiography, nuclear medicine, and computed tomography, cardiac magnetic resonance (CMR) has emerged as a pivotal modality in the intricate characterization of IHD [2, 3]. CMR affords the capability to conduct objective quantifications of LV morphology and functionality, while also facilitating the visualization of myocardial ischemia, the ensuing acute insult, and the prospective evolution of chronic replacement fibrosis.
Hence, a thorough assessment of the localization and transmural extent of post- MI scar tissue is crucial for optimal clinical management and precise risk stratification. Presently, late gadolinium enhancement (LGE) imaging, conducted via CMR approximately 10 minutes

following the administration of gadolinium contrast, is regarded as the *in-vivo* gold standard for the detection and quantification of myocardial infarction [4].

Nonetheless, this technique possesses several significant limitations. The administration of gadolinium contrast is contraindicated in individuals with both acute and chronic renal insufficiency. It is noteworthy that approximately 20% of patients presenting with MI are afflicted with renal insufficiency [5].

Furthermore, the administration of gadolinium contrast carries a minor risk of adverse reactions. The duration of CMR imaging with LGE is prolonged, presenting difficulties in imaging this patient population. Native T1 mapping, a cutting-edge technique, enables quantitative characterization of the myocardium without requiring gadolinium contrast. Therefore, T1 mapping may serve as an appropriate and safer alternative for patients with ischemic cardiomyopathy who also have renal insufficiency [5].

Aim

The objective of the present study is to explore the utility of native T1 mapping in conjunction with LGE for the identification of myocardial fibrosis in individuals diagnosed with ischemic cardiomyopathy.

Patients and Methods

This prospective study was conducted on 87 patients aged between 18 to 65 years old that were diagnosed with ischemic Cardiomyopathy and admitted to Benha University Hospital & NHI, Egypt during the period from March 2022 to April 2023. Patients with incomplete limited studies (either due to arrhythmia or missed T1 mapping sequence) were excluded from the study. All patients were subjected to history taking, complete examination included general and local examination, and full laboratory investigations. The inpatient management of the study cohort was meticulously analyzed, encompassing the spectrum of pharmacological interventions administered during hospitalization, the reperfusion techniques utilized, and the execution of coronary angiography. Each patient underwent coronary angiographic assessment, with significant stenosis being delineated as a luminal diameter reduction of ≥50% in the left main (LM) artery or ≥75% in the epicardial coronary arteries.

Trans-Thoracic 2D Echo Doppler and speckle tracking protocol

A comprehensive full-volume scan was procured via harmonic imaging from an apical approach, utilizing a frame rate surpassing 40% of the patient's heart rate to optimize the detection of "speckles" across successive frames. Accordingly, four electrocardiogram-gated consecutive cardiac cycles were captured during end-expiratory breath-hold. The integrity of the acquired data was rigorously verified in each subject prior to data storage by employing a 12-slice display modality available on the imaging apparatus, thereby ensuring the entire LV cavity and myocardial wall were encompassed within the full-volume dataset.

The peak systolic longitudinal strain values for each segment of the 17-segment LV model were autonomously computed by the algorithm. GLS was then derived by calculating the mean of the strain measurements obtained from each of the 17 individual segmental strain values.

CMR Protocol

All patients were subjected to cardiac MRI using a 1.5-Tesla scanner (Siemens Healthcare). The CMR protocol encompassed localizing white and black blood sequences in axial, coronal, and sagittal planes, cine imaging, native T1 mapping, and late gadolinium enhancement sequences. Cine imaging of the LV was executed with a steady-state free precession (SSFP) sequence, incorporating 4-chamber, 3-chamber, and 2-chamber long-axis views, along with 12 to 14 evenly spaced short-axis slices to encompass the entirety of the LV, maintaining a slice thickness of 6 mm and inter-slice gaps of 4 mm.

Cine images were obtained utilizing specific parameters: repetition time and echo time were set at 3.31 ms and 1.31 ms, respectively; the flip angle was calibrated to 62°; the imaging process captured 25 phases per cardiac cycle; the field of view was established at 240 × 300 mm²; the matrix resolution was 256 × 150; and the (GRAPPA) acceleration factor was applied.

T1 mapping was executed employing a single-breath-hold LLI sequence across three short-axis slices—basal, mid-cavity, and apical regions. The scanning parameters for the Look-Locker protocol included a FOV ranging from 360 to 290 mm; matrix sizes varied from 192×72 to 192×93; slice thickness was maintained at 6 mm; TR and TE were approximately 2.2 ms and 1.1 ms respectively; the phase interval spanned 23 to 25 ms; the flip angle was set at 50°; a turbo-factor of 8; and an acquisition window of 35 ms, capturing 22 to 30 phases across two RR intervals, which were adjusted according to HR.

Native T1 mapping was initially conducted, succeeded by the administration of a gadolinium-based contrast agent, Magnavist, at a dosage of 0.1–0.2 mmol/kg, which was immediately followed by a 30-ml isotonic saline flush. LGE images were then acquired in both long axis and short axis imaging planes, utilizing a breath-hold segmented inversion recovery sequence approximately 10 minutes post-contrast injection. The imaging parameters were set as follows: matrix size at 154 × 256, field of view at 28 × 34 cm, repetition time roughly 2.5 ms, echo time at 4.9 ms, flip angle at 30°, slice thickness at 6 mm, inter-slice gap at 1.6 mm, and in-plane image resolution at 1.7 × 1.3 mm. The inversion time was adjusted to optimally nullify the appearance of normal myocardium, typically ranging between 250 and 350 ms.

Post processing

LV function and volumetric analysis were meticulously evaluated utilizing the dedicated Argus software (Siemens Healthcare), which required precise manual delineation of the myocardial contours at both end-diastolic and end-systolic phases along the endocardial boundaries.

All parameters were adjusted for body surface area, calculated utilizing the Mosteller equation. Aortic blood flow measurements were examined using Argus Flow software through the manual segmentation of the respective vessels throughout the entire cardiac cycle. For the assessment of myocardial native T1 to identify fibrosis or scar tissue, ROIs were manually placed on 16 myocardial segments per patient in the pre-contrast images to derive segmental myocardial T1 values.

The ROIs were defined with sizes exceeding 12 pixels. These ROIs deliberately excluded the LV cavity and epicardial fat and were delineated independently of the corresponding LGE images.

Ethical consideration

The investigation received approval from the Ethics Committee of the Faculty of Medicine at Benha University Hospitals and the NHI.

Statistical analysis

Statistical analysis and data management were executed using SPSS version 28 (IBM, Armonk, New York, USA). The normality of quantitative data was assessed utilizing the Kolmogorov–Smirnov test in conjunction with direct data visualization techniques. Quantitative data, conforming to normal distribution principles, were represented as means and standard deviations. Categorical data were summarized using frequencies and percentages. For comparative purposes, the independent t-test was applied to evaluate differences between two groups, whereas a one-way ANOVA was employed for comparisons among three groups. Categorical data were compared using the Chi-square test. ROC analysis was done for T1 mapping and strain to diagnose late gadolinium enhancement. The optimal cut-off points, diagnostic indices, and areas under the curve with 95% confidence intervals were determined. Strain correlations with GLS and T1 mapping were assessed using Pearson's correlation. All statistical analyses employed two-tailed tests. Significance was ascribed to P-values less than 0.05.

Results

Regarding patients' demographics**,** the mean age of the studied patients was 51 ±7 years. There was a male predominance (90.8%). Table 1

Table 1: Baseline characteristics of the studied groups

Variables		Total (n=87)
Age (years), mean ± SD		51.0±7.0
Sex, No (%)	Male	79 (90.8)
	Female	8 (9.2)

SD = Standard deviation.

T1 mapping was significantly higher in those with late gadolinium enhancement (1131.7 ±106.9) than in those without late gadolinium enhancement (p< 0.001). Table 2

Table 2: T1 mapping according to late gadolinium enhancement

Variables		Late gadolinium enhancement		
		Yes (N = 623)	No. (N = 769)	P-value
T1 mapping	Mean ±SD	1131.7 ±106.9	983 ±47.1	<0.001*

*Significant P-value

Moreover, T1 mapping significantly differed according to fibrosis grade (P < 0.001). It was significantly lower in segments with fibrosis of less than 50% (1064.2 ±59.2) than in segments with fibrosis of 50-70% (1122.4 ±109.1) and more than 70% (1190.3 ±102.6). Additionally, it was significantly lower in segments with 50-70% fibrosis than in segments with more than 70% fibrosis. Figure 1.

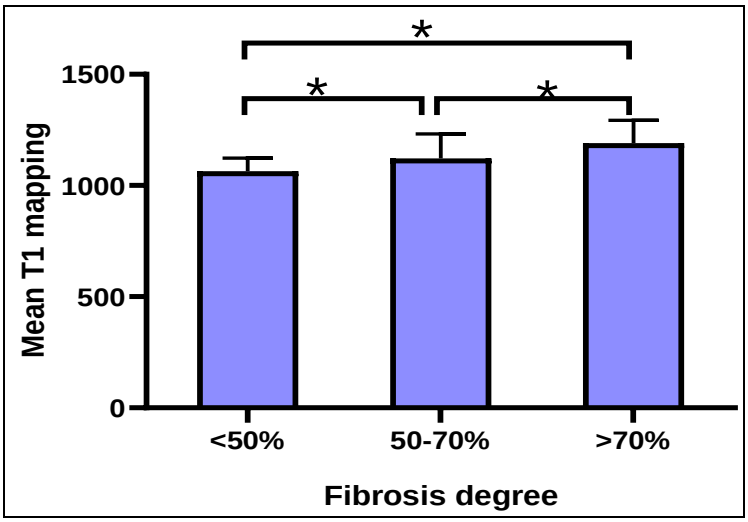

Fig 1: T1 mapping according to fibrosis degree in those with enhancement

T1 mapping was significantly higher in all tested segments with enhancement compared with those without enhancement (p < 0.001). Table 3.

Table 3: T1 mapping according to late gadolinium enhancement in different cardiac segments

Variables	Late gadolinium enhancement, Mean ±SD		
	Yes	No.	P-value
Apex anterior	1160.3 ±101.7	969.1 ±38.5	<0.001*
Apex inferior	1164 ±112.1	980.4 ±37.1	<0.001*
Apex lateral	1136.8 ±89.8	971.8 ±51.7	<0.001*

Apex septal	1185.3 ±103	958 ±49.5	<0.001*
Basal anterior	1122.7 ±115.4	982.2 ±47.5	<0.001*
Basal anterolateral	1099.6 ±110.7	978.9 ±39.6	<0.001*
Basal anteroseptal	1082.7 ±62.5	1001.3 ±43.9	<0.001*
Basal inferior	1081.1 ±184.1	980.2 ±51.7	0.006*
Basal inferior-septal	1099.4 ±70.3	990.6 ±45.8	<0.001*
Basal inferolateral	1137.6 ±83.6	978 ±57.6	<0.001*
Mid anterior	1132.4 ±90.9	981.3 ±38.8	<0.001*
Mid anterolateral	1086.7 ±111.7	984.2 ±42	<0.001*
Mid ateroseptal	1116.8 ±83.1	994.1 ±43.7	<0.001*
Mid inferior	1128.1 ±99.3	987.9 ±58	<0.001*
Mid inferior-septal	1108.3 ±88.4	991.7 ±45.8	<0.001*
Mid inferolateral	1141.8 ±139.3	981.8 ±43.5	<0.001*

*Significant P-value

ROC analysis was done for T1 mapping and GLS to predict late gadolinium enhancement. It revealed a significant area under the curve of 0.948 for T1 mapping and 0.942 for GLS ($P < 0.001$), indicating an excellent discrimination ability for both of them. The best cutoff point for T1 mapping was > 1020, and ≤ 20 for GLS. Table 4, Figure 2 & 3.

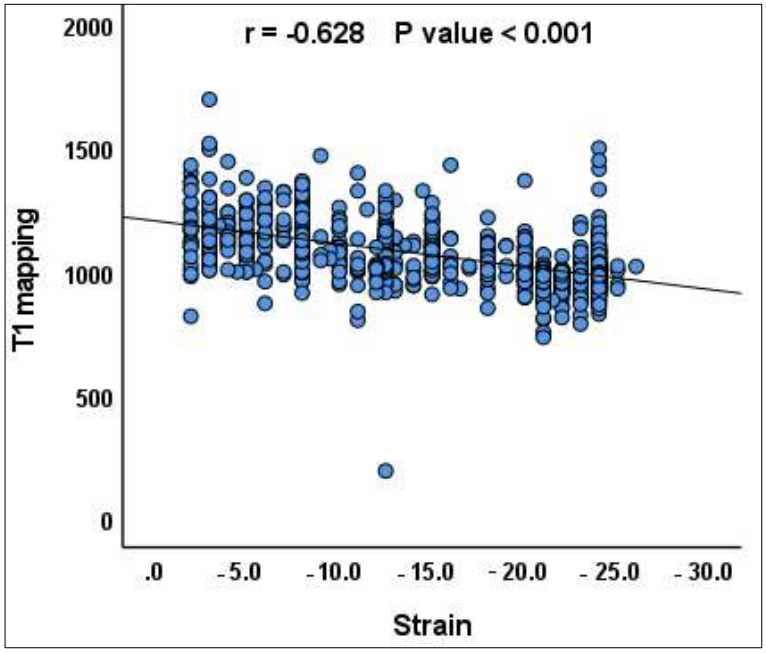

Fig 2: Correlation between strain and T1 mapping of different segment

A significant negative correlation was observed between strain and T1 mapping for different segments (r = -0.628, < 0.001).

Table 4: ROC analysis of T1 mapping and GLS to diagnose LGE

Variables	AUC	95% CI	Best cutoff point	Sensitivity	Specificity	PPV	NPV	P-value
T1 mapping	0.948	0.935 - 0.960	>1020	90.9%	87.8%	85.8%	92.2%	<0.001*
GLS	0.942	0.928 - 0.956	≤ 20	96.6%	88%	86.7%	97%	<0.001*

*Significant P-value; AUC: Area under the curve; PPV: Positive predictive value; NPV: Negative predictive value

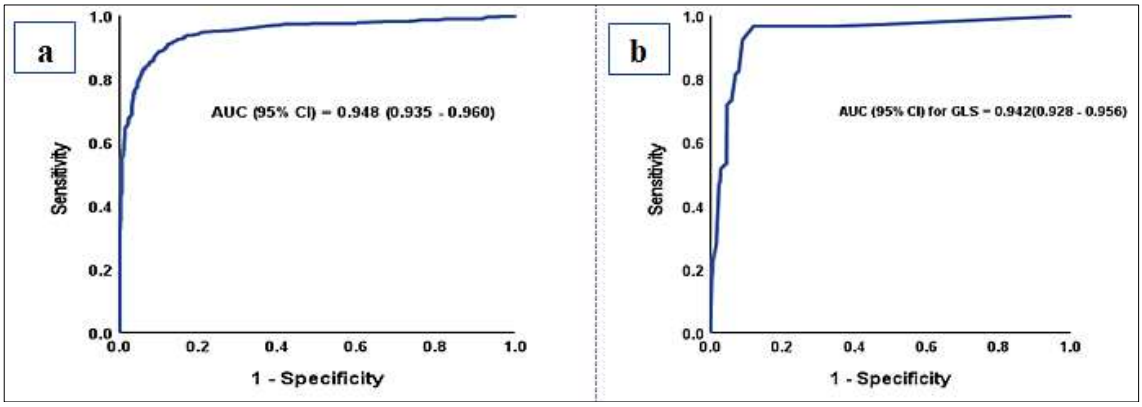

Fig 3: ROC analysis of T1 mapping to diagnose late gadolinium enhancement (a: T1 mapping, b: GLS)

Discussion

Cardiovascular Magnetic Resonance (CMR) is progressively being utilized to distinguish the aetiology of various cardiomyopathies. The modality's three-dimensional capability, coupled with exceptional spatial resolution and superior tissue contrast, allows for precise quantification of cardiac morphology and function [6]. The assessment of LV volumes, mass, and ejection fraction, alongside the evaluation of regional wall motion abnormalities, can be effectively conducted irrespective of body habitus or imaging windows, and without the risk of ionizing radiation exposure [7].

This study was designed to test the agreement between the native T1 mapping and LGE to identify myocardial fibrosis in patients with ischemic heart disease.

This study was conducted on 87 patients (1392 cardiac segments) scheduled for elective cardiac MRI.

In the current study, T1 mapping was significantly higher in segments with late gadolinium enhancement (1131.7 ±106.9) than in segments without late gadolinium enhancement (Table 2).

In alignment with our findings, Elsafty *et al*. [8] conducted a study examining the disparities in native T1 mapping results between cases exhibiting negative and positive fibrosis as identified by late contrast-enhanced imaging. Their study demonstrated that myocardial segments displaying late gadolinium enhancement had significantly higher native T1 values compared to those without enhancement.

Contrasted to our results, Youn, *et al*., [9] showed that the T1value had no significant different between LGE (+) and LGE (−) groups (1328.5 ± 83.5 ms vs 1321.3 ± 105.4 ms).

With testing T1 mapping according to late gadolinium enhancement in each segment separately, this current study found that the mean T1 mapping was significantly higher in all tested segments with LGE (+) compared with LGE (-) (Table 3).

Elsafty *et al*., [8] expressed that the mean Native T1 mapping was significantly higher in LGE (+) compared with LGE (-) in anterior segment (1120.88 ± 84.99 vs 1041.13 ± 58.76), Antero-septal (1130.85 ± 79.79 vs 1047.74 ± 42.74), Inferior (1100.07 ± 62.86 vs 1055.95 ± 59.87), Infero-lateral (1121.07 ± 82.75 vs 1051.75 ± 56.23), and antero-lateral (1123.60 ± 55.72 vs 1042.60 ± 47.87), however Elsafty and his colleagues didn't find significant difference in infero-septal segment (p=0.138).

In our study, T1 mapping significantly differed according to fibrosis grade. It was significantly lower in segments with fibrosis of less than 50% than in segments with fibrosis of 50-70% and more than 70%. Additionally, it was significantly lower in segments with 50-70% fibrosis than in segments with more than 70% fibrosis (Figure 1).

Our study exhibited highly statistically significant negative association between strain and T1 mapping (r=-0.628, p<0.001; Figure 2).

Conversely, Rutherford, *et al*., [10] did not find any significant correlation between GLS and T1 mapping. They posited that it remains uncertain whether their study lacked sufficient power to discern a relationship between the two measures or if these measures represent subtly different aspects of cardiac pathological processes. Regardless, each has distinct merits: GLS is a dynamic indicator, while T1 time is arguably a more constant parameter.

In the present study, ROC analysis was done for T1 mapping and GLS to diagnose late gadolinium enhancement & showed an excellent discrimination ability. The best cutoff point for T1 mapping was > 1020, and ≤ 20 for GLS (Table 4, Figure 3).

Similarly, Elsafty *et al*., [8] found that T1-mapping has shown to be significantly an excellent diagnostic tool to diagnose fibrosis but with lower area-under-the-curve (AUC= 0.721) compared to our current study. They used a cut-off point >1070 which showed sensitivity 66.0%, specificity 68.51%, PPV=38.7%, and PVN=87.3%.

Also, Cui, *et al*., [11] found AUC= 0.84 and used a cutoff point of 1220.22 ms at which the sensitivity and specificity were 77.8% and 88.9%

In this context, Puntmann *et al*. [12] demonstrated that in NIDCM, native T1 mapping can quantitatively characterize diffuse myocardial abnormalities, particularly diffuse fibrosis, which may not be visible on LGE images. This method exhibits high diagnostic accuracy, with a sensitivity of 100%, specificity of 96%, and an area under the curve of 0.99, all without the necessity for gadolinium contrast.

Chen *et al*., [13] reported that strain indices demonstrated strong diagnostic performance in detecting early LV dysfunction in patients with preserved EF myocarditis and healthy controls. ROC curve analysis revealed that PSC was the most effective strain parameter, with a cutoff value of -19.72%, achieving a sensitivity of 68% and a specificity of 88%.

Our present study is relatively a small study which tested only 87 patients which was considered one of the main limitations of study. Moreover, the patients were chosen by non-probability sampling technique which make the results unsuitable for generalizability.

Conclusion

T1-mapping offers superior diagnostic value compared to late gadolinium enhancement in patients with cardiomyopathy. T1 mapping was higher in patients with late gadolinium enhancement and the mean T1 mapping level increases with increased fibrosis level. It had proven its efficiency in all cardiac segments when tested separately. GLS had also been proven as an effective tool in identifying patients with fibrosis compared with gold standard method (late gadolinium enhancement).

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Conflict of Interest: Nil.

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