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An Egyptian study for standardization of myocardial T1 mapping values on a 3 Tesla MRI machine

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ABSTRACT

Objective: of this study is to set standard values for the native T1 values in both normal and diseased myocardium on a 3 tesla MRI machine.

Methodology: this study was carried out in Misr Radiology Center. 31 patients were divided into normal group (control) including 10 patients and diseased group including 21 patients.

Result: The native T1 values on the healthy myocardium ranged from 1110 to 1300 msec, with ECV values ranging from 25 to 33 % with variable elevations of the native T1 and ECV values according to the pathology affecting the myocardium. We concluded that the above values are the reference values for the 3 T MRI machine.

Keywords: Cardiovascular Magnetic Resonance (CMR), Extra-cellular Volume (ECV), Late Gadolinium Enhancement (LGE).

INTRODUCTION

In the heart, diffuse interstitial fibrosis plays an essential role in the development of a variety of cardiomyopathies and is associated with increased mortality. Previously, endomyocardial biopsy was the principle method used to diagnose myocardial fibrosis. Currently, T1 mapping is a novel and expanding application of cardiac MR imaging and has the potential to depict diffuse interstitial fibrosis in a variety of cardiac diseases [(1)].

Rapid innovations in CMR now permit the routine acquisition of quantitative measures of myocardial and blood T1 which are key tissue characteristics. T1 quantification requires the acquisition of multiple images to derive the T1 recovery curve which is governed by the exponential time constant for MR longitudinal relaxation, T1. This parameter can be displayed as a pixelwise "T1 map" whereby an estimate of T1 is encoded in the intensity of each pixel. Its quantitative nature permits establishing normal T1 ranges, and T1 values can be assigned colors to simplify visual interpretation [(2)].

Native T1-mapping as well as ECV mapping is currently being explored as a diagnostic tool for a wide range of cardiomyopathies. Native T1 changes are detectable in both acute and chronic MI. Elevated native T1 has been reported in a number of diseases with cardiac involvement: myocarditis, amyloidosis, lupus and decrease in native T1 have been associated with Anderson Fabry disease, and high iron content [(3)].

In chronic MI, there is replacement of myocardial cells by scarring or fibrosis with an increase in extracellular collagen. Importantly, there is no edema, as this has resolved in the initial weeks after MI. Therefore, T1 values are higher than in normal myocardium, but not as high as in acute MI [(4)].

Native T1-mapping can display the typical non-ischemic patterns in acute myocarditis, similar to LGE imaging without the need for contrast agents. T1-mapping also detected additional areas of myocardial involvement and identified extra cases beyond T2W and LGE imaging [(5)].

A relatively higher pre-contrast T1 value and ECV, and lower post-contrast T1 value were found with T1 mapping in the myocardium of HCM patients, which suggested T1 mapping is better in the evaluation of myocardial fibrosis [(6)].

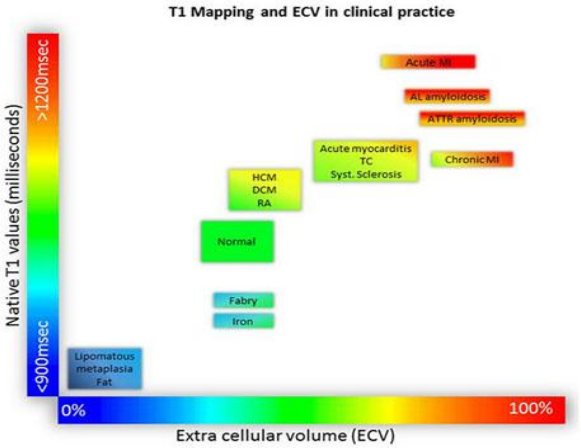

Figure (1): Tissue characterization using native T1 and extracellular volume fraction (ECV). Absolute values for native T1 depend greatly on field strength (1.5 T or 3 T), pulse sequence (MOLLI or ShMOLLI), scanner manufacturer and rules of measurements [(7)].

T1 mapping is hypothesized to contribute to the characterization of cardiac masses based on the spectrum of T1 relaxation times in tissue consisting of fat, calcium, melanin, blood and simple fluid. Thrombi and myxomas showed

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intermediate and relatively long T1 times, respectively [8].

Broadly, T1 mapping sequences have three parts: (1) the T1 magnetization preparation pulse, (2) a single image acquisition (readout) after a variable delay, and (3) variable repetitions of (1) and (2) to sample the longitudinal magnetization recovery curve after the magnetization preparation. Raw images are then reconstructed by post-processing into a single T1 map using a theoretical model of the expected signal intensity [9].

A T1 map is a two-dimensional (usually brightly colored) slice image where each image pixel displays the T1 relaxation time (ms) using a color look-up table to facilitate visual assessment [10].

Pixel-wise T1-mapping first appeared on the scene with the introduction of the MOLLI imaging strategy, which propelled the use of T1-mapping in CMR and inspired many new methods. MOLLI is widely used today with some protocol optimization and other adaptations [11].

Table (1): Summary of pros and cons of various T1 mapping methods [12].

Point of comparison	MOLLI	SHMOLLI	SASHA
Short breath hold	Poor	Fair	Fair
HR insensitivity	Poor	Fair	Fair
Absolute accuracy	Poor	Poor	Good
Signal to noise ratio	Good	Good	Poor

AIM OF THE WORK

We aim to determine the standard native T1 values specific to the Siemens 3 Tesla machine in both normal and diseased myocardia in an Egyptian population.

PATIENTS AND METHODS

Patients:

During a period of 12 months' duration from May 2017, thirty-one patients were enrolled in the study. Patients with clinical symptoms suggestive of underlying cardiac condition (e.g., dyspnea, chest pain or easy fatigability); whether suspected by another imaging modality (e.g., echo-cardiographs) or not.

Inclusion Criteria: All Patients asked to do Cardiac MRI; normal and diseased. Both sexes will be included. Adults and children.

Exclusion Criteria: Contraindications to MRI such as claustrophobia, pacemakers, cochlear implants, etc. Patients with degenerative neurological disorders that makes them unstable during the test. Patients with bad general condition needing life support.

MRI imaging: The study was performed with a 3-T MR system (Magnetom TIM TRIO, Siemens, Erlangen, Germany).

T1 mapping study: In addition to the routine CMR sequences; Modified Look-Locker. Inversion recovery pulse sequence is used. For T1 mapping, data were acquired in basal, midventricular, and apical SAX planes before and 10 - minutes after administration of 0.3 mmol/kg i.v. gadobutrol (Gadovist®, Bayer Healthcare Germany). Data were obtained in end-diastole using a cardiac gated, SSFP-based modified look-locker inversion recovery (MOLLI) technique.

MRI data analysis: Multiple parameters were measured: End-diastolic and end-systolic left ventricle volumes, ejection fraction, stroke volume and left ventricle mass for assessment of the ventricular function. Assessment of any anatomical variants or pathologies within the cardiac chambers e.g., masses or thrombi. Wall motion of the left ventricle is assessed at each myocardial segment: Normal, hypokinetic, akinetic, or dyskinetic. Detection if any late gadolinium enhancement was present throughout any of the 17 heart segments based on the 17-segment model recommended by the AHA (American Heart Association). Pixel wise illustration of the absolute T1 relaxation times on a map was done, color-coded maps were obtained. Then the ROI was placed over the 17 heart segments in both pre and post contrast images according to the AHA; that are 6 basal segments, 6 mid ventricular segments and 4 apical segments in addition to the blood itself in order to obtain the pre and the postcontrast T1 values in each of these segments. Extra-Cellular Volume is then calculated according to specific equation:

$$ECV = (1-\text{hematocrit})x$$

$$\frac{\frac{1}{postcontrast\ T1\ myocardium} - \frac{1}{Native\ T1\ myocardium}}{\frac{1}{Post\ contrast\ T1\ Myocardium} - \frac{1}{Native\ T1\ blood}}$$

IBM SPSS statistics (V. 25.0, IBM Corp., USA, 20172018) was used for data analysis. Date were expressed as mean±SD for quantitative parametric measures in addition to both number and percentage for categorized data. Crosstabulation was used to describe the categorized data.

Statistical analysis

RESULTS

The tables below show that most of our study population were males representing about 83.8% as well as the sex distribution among the control and the diseased.

Table (2): Shows the mean age of the control group and the standard deviation as well as the sex distribution among the group.

		Control group
		No. = 10
Age	Mean ± SD	45.20 ± 18.86
	Range	12 – 78
Sex	Female	2 (20.0%)
	Male	8 (80.0%)

Table (3): Shows the mean age of the diseased group and the standard deviation as well as the sex distribution among the group.

		Patients group
		No. = 21
Age	Mean ± SD	52.67 ± 15.70
	Range	28 – 77
Sex	Female	3 (14.3%)
	Male	18 (85.7%)

So among 10 patients who underwent cardiac MRI and were found to have healthy myocardium; we calculated the mean native T1 value and standard deviation from the mean value.

Table (4): Shows the mean native, postcontrast T1 values as well as ECV values in the control group.

	Control group	**Control group**	**Control group**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**
	Native T1	**Post Contrast T1**	**ECV**
Basal			
Ant	1198.80 ± 39.22	527.10 ± 80.21	28.80 ± 6.66
AS	1224.40 ± 76.58	519.30 ± 76.78	30.30 ± 7.75
IS	1221.30 ± 63.96	517.40 ± 90.64	30.50 ± 8.28
Inf	1243.40 ± 65.62	491.80 ± 90.85	33.70 ± 7.80
IL	1192.30 ± 40.69	505.70 ± 81.31	31.50 ± 8.03
AL	1215.20 ± 40.72	528.60 ± 74.77	29.00 ± 7.10
Mid Ventricle			
Ant.	1190.50 ± 73.12	535.20 ± 79.38	27.80 ± 5.63
AS	1210.60 ± 43.83	528.90 ± 79.82	29.00 ± 6.86
IS	1210.80 ± 42.15	532.10 ± 82.27	28.50 ± 5.48
Inf.	1220.80 ± 25.05	533.00 ± 92.41	28.60 ± 6.26
IL	1161.90 ± 52.38	526.40 ± 81.13	28.00 ± 6.57
AL	1209.50 ± 40.90	538.80 ± 78.76	27.90 ± 6.44
Apex			
Ant	1202.80 ± 58.39	523.50 ± 74.39	29.60 ± 9.78

Sept	1189.70 ± 51.20	527.60 ± 74.05	28.90 ± 7.88
Inf.	1229.40 ± 55.22	550.40 ± 57.89	27.70 ± 8.15
Lat.	1177.70 ± 55.49	524.40 ± 79.90	29.20 ± 8.02

From the above tables; we can say that a native T1 ranging from 1110 msec to 1300 msec usually denotes a healthy myocardium with no scarring, fibrosis or infiltration on the 3 tesla MRI machine.

And that healthy myocardium usually shows ECV values ranging from 25% to 35%.

Then, we classify our diseased patients according to the myocardial pathology as described in the table below:

Table (5): Describes the percentage of the diseased patients according to the myocardial pathology in the diseased group.

Type of diseased	No.	%
Amyloidosis	1	4.8%
HOCM	4	19%
Infarction	9	42.9%
Masses	6	28.6%
Myocarditis	1	4.8%
Total	21	100.0%

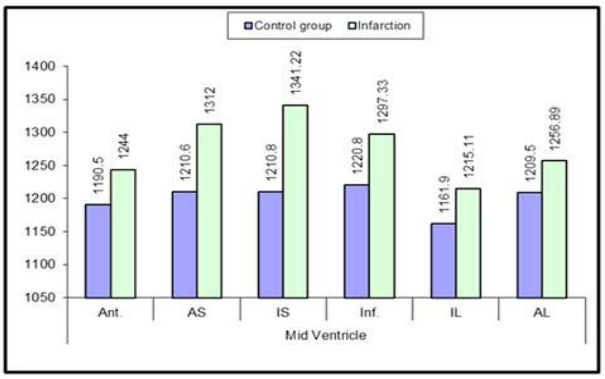

Figure (2): Shows elevated native T1 values in the patient's group compared to the healthy population.

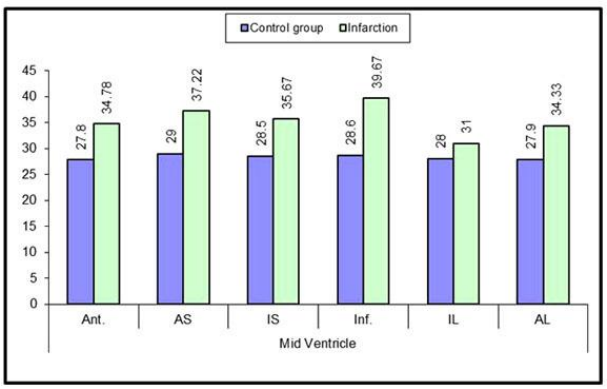

Figure (3): Elevated ECV values in those with myocardial infarctions compared to the control group in the mid myocardial segments.

The previous data can be made clearer by the following example of a 55 years old male patient with Ischemic heart disease and past history of PCI twice.

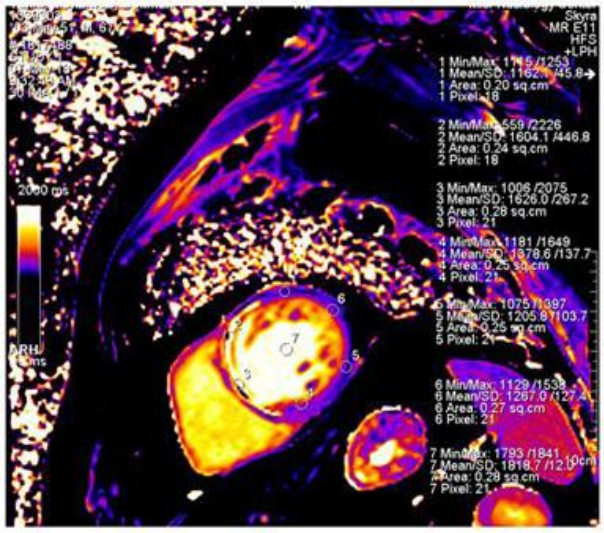

Figure (4): Delayed Post-contrast image in the mid ventricular region showing post contrast enhancement in the anterolateral, infero-septal and inferior mid ventricular walls.

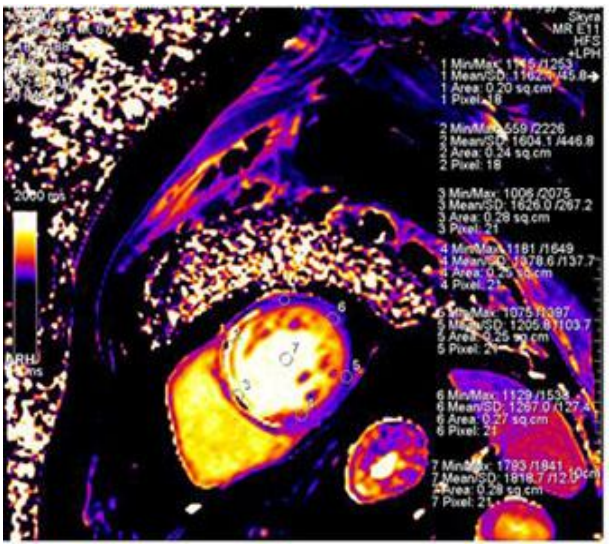

Figure (5): T1 colour coded images in mid ventricular region showing elevated native T1 values in the anterolateral, infero-septal and inferior mid ventricular segments.

Table (6): Native T1 and ECV values in a patient with infarctions involving the anterolateral, infero-septall and inferior mid ventricular segments.

Myocardial Segment	Native T1 values	ECV values
1-Anterior 2-Anteroseptal	1= 1162 2= 1604	1= 28 2= 47
3-Inferoseptal 4-Inferior	3= 1626 4= 1379	3= 45 4= 36
5-Inferolateral 6-Anterolateral	5= 1206 6 = 1267	5= 33 6= 33

Also, significantly higher native T1 and ECV values were reported in patients with hypertrophic cardiomyopathies entailing scarring or fibrosis of one or more of the myocardial segments.

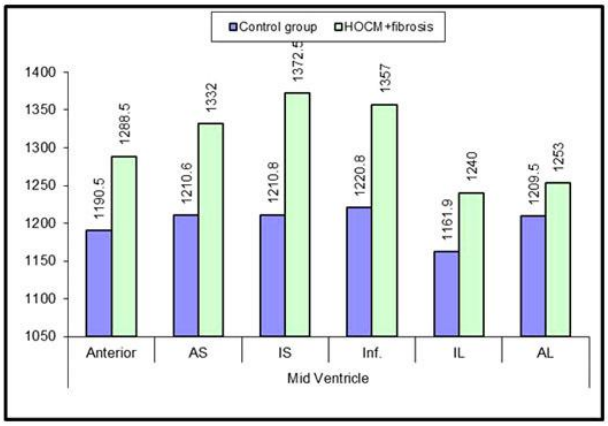

Figure (6): Significantly elevated T1 values in those with myocardial scarring duo to HOCM compared to the normal population.

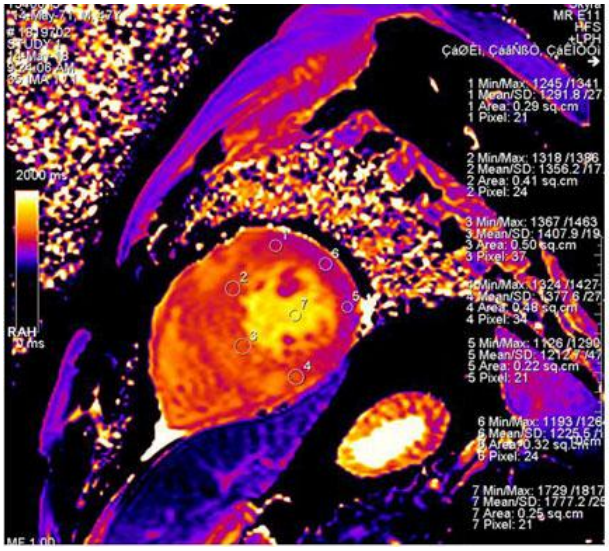

Figure (7): Color coded map representing the elevated native T1 values in the scarred myocardial segments in a patient of HCM.

Our study included one patient with cardiac amyloidosis and one patient with chronic myocarditis Elevations of the native T1 values and ECV values were noted all over most of the myocardial segments compared to the control group.

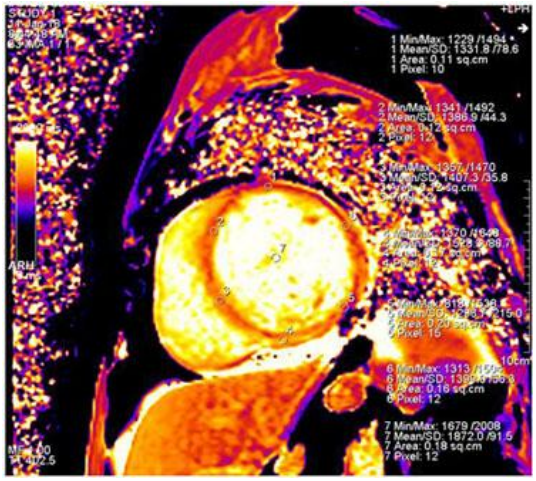

Figure (8): Color coded T1 image of the mid ventricular myocardium showing diffuse elevation of the native T1 values in patent with chronic myocarditis.

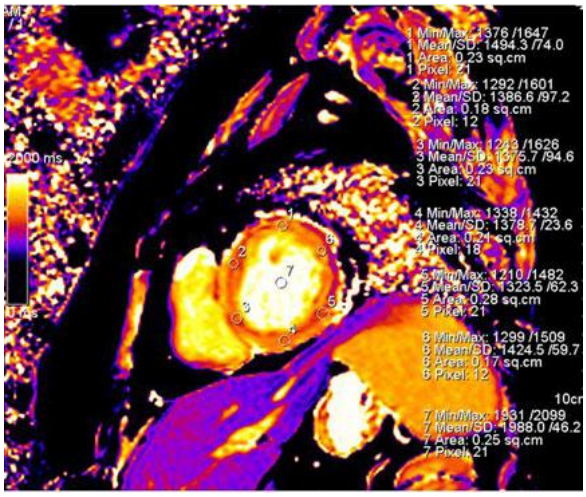

Figure (9): Color coded T1 image of the mid ventricular myocardium showing diffuse elevation of the native T1 values in patent with cardiac amyloidosis.

Our study included 6 patients with cardiac masses representing 28.6% of the patients group.

These masses included cardiac thrombi and neoplastic masses.

i- Cardiac thrombi:

One of the two patients that were referred to us with cardiac thrombi detected on echocardiography was not injected contrast agent duo to the elevated kidney functions. So, post contrast T1 value was not obtained.

The mean native T1 value of the cardiac thrombus was 1065.5 msec.

ii- Cardiac neoplastic masses:

Three patients with neoplastic masses or thrombi were referred to us. They showed variable native and post contrast T1 values.

Mean native T1 value= 1035 msec.

Mean post contrast T1 value=541.6 msec.

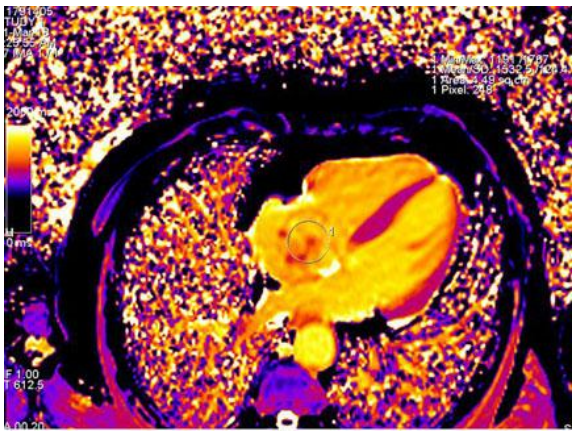

Figure (10): Color coded T1 image showing elevated native T1 value of the lesion.

DISCUSSION

Cardiovascular magnetic resonance (CMR) provides techniques for non-invasive myocardial tissue characterization. T1 mapping of the left ventricular myocardium, i.e. quantification of the myocardial T1 relaxation time, as well as the T1-derived extracellular volume fraction have been demonstrated to add valuable information [(13)].

The differences in acquisition schemes have a direct effect on the range of normal and abnormal T1 with a given technique, which means that absolute T1 values can only be directly compared when they were obtained with the same acquisition scheme at the same field strength using the same post-processing methods. Thus, reports on T1 values should always include the T1 mapping technique that was used and the site-specific normal range for T1 [(14)].

Our main finding on the normal population were: T1 mapping achieved a high degree of diagnostic image quality. Observer dependency of T1 relaxation time quantification was very low. Mean values of myocardial T1 relaxation times are presented per segment and per slice and can be used as reference values in the next CMR examination entailing the use of T1 mapping sequences. An inter-subject variation of the T1 values is present and this can be a limiting factor to establishment of standard cut-off values. The myocardial T1 relaxation times reported here can be regarded as reference values specific only for this cohort, time point, mapping technique, type and dosage of contrast media. Further comparisons with other published results are difficult unless an identical study design is used.

A study performed on 2016 by ***Weingartner et al.,*** on 20 healthy subjects on a 3 T MRI machine concluded that the mean native T1 value using MOLLI technique was 1182.6 +/-35.8 msec., however the post contrast T1 value was 541.1 +/-33.8 msec and ECV values 27.5 +/-3.1 % [(15)].

Among the healthy population of **our study**; our mean precontrast T1 value is = 1209 msec among all the myocardial segments, while the mean postcontrast T1 value =525.6 msec. and the mean ECV was 29.3%.

Dall'Armellina et al. conducted a study published in 2012 aiming to define the native T1

values in cases of myocardial infarctions. They reported a mean precontrast T1 value of 1257 msec. for infarcted segments compared to 1196 msec for normal unaffected segments at 3 T MRI **(16)**.

In our study; we reported a mean precontrast T1 value of 1369 msec for the infarcted myocardial segments compared to 1209 for the normal unaffected segments.

Liu et al. stated that in patients with HOCM; the pre-contrast T1 value was 1217.3 ± 97.4 msec. with an ECV 25.7 ±3.6%.

In our study; the findings are higher than the above study; as we reported a mean native T1 in HCM patients of 1339 msec and mean ECV of 38%; this is duo to the fact that our study was conducted over a 3T MRI machine which resulted in higher T1 values.

In a study performed by ***Lin et al.*** in 2018 on 82 patients with cardiac amyloidosis and 20 healthy subjects on a 3T scanner; the patients demonstrated an increase in native T1 of 1438 ± 120 ms vs. 1283 ± 46 ms for the control group and ECV of 43.9 ± 10.9% vs 27.0 ± 1.7% for the healthy controls **(17)**.

In our study; we got similar measurements of the native T1 and the ECV values among the patient of myocarditis reaching 1384.5 msec. and 44% respectively.

In patients with myocarditis, we found in **our study** that segments with LGE had significantly higher T1 and ECV values, and patient segments without LGE had less elevated T1 values but still above the normal range, suggesting that areas without apparent LGE were also involved.

In a study done by ***Casper et al.*** in 2017 on 19 patients with cardiac masses; both myxomas and neoplastic masses showed relatively long native T1 values measuring 1316±71 msec and 1333±101 msec respectively **(18)**.

Our results in both benign (myxoma) and malignant cardiac masses are much less than the above-mentioned values as they showed T1 values of 253 msec and 1035 msec respectively; this is mostly duo to small number of the cases or in-appropriate defining of the lesions on the color-coded maps.

CONCLUSION

Tissue characterization by native T1 mapping may serve as an important source of diagnostic, therapeutic and prognostic decision making in various cardiac diseases. An advantage of a non-invasive method for the assessment of fibrosis is the potential to follow changes in the myocardium over time as in patients with cardiomyopathies Patients with poor renal function (or on dialysis) precluding gadolinium-based contrast injection may benefit from using native T1 mapping instead of LGE imaging. Clinically, several studies have shown that T1 mapping with ECV is particularly useful in the assessment of cardiac diseases with diffuse fibrosis. Furthermore, T1 mapping with ECV might be helpful as an adjunct in cases with ambiguous LGE. Beyond differential diagnosis of cardiomyopathies, tissue characterization with T1 mapping can be very useful in differentiating between pericardial fat vs. LGE as well as in tissue characterization of various cardiac tumors.

Although tissue characterization with native T1 and ECV has been shown to have incremental diagnostic benefit even in very early disease stages (e.g. diffuse fibrosis not detectable by LGE), there is an overlap between different cardiomyopathies and some overlap with normal T1 values. Like all medical parameters, abnormalities in native T1 and ECV need to be interpreted within their clinical context and pre-test probabilities and in conjunction with established CMR techniques such as LGE. Elevations and reductions of T1 and ECV are not specific and can be caused by various disease processes. In some instances, these processes can even cancel each other out (e.g., pseudonormalization in Anderson-Fabry disease when replacement fibrosis exceeds the fatty-related T1 decrease).

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