ORIGINAL ARTICLE

INCIDENCE OF MYOCARDIAL FIBROSIS ON CARDIAC MAGNETIC RESONANCE IMAGING IN PATIENTS WITH ATYPICAL ELECTROCARDIOGRAPHY CHANGES

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Objectives: Ventricular fibrosis evaluation by cardiac magnetic resonance imaging (CMR) has been proposed as a risk factor for developing cardiomyopathies, arrhythmias and a potential indicator for sudden cardiac death (SCD). The objective of the study was to determine the incidence of myocardial fibrosis on CMR in patients who had normal invasive and/or non-invasive cardiology investigations but had subtly abnormal ECGs.

Methodology: Study was conducted at Cardiac MRI department of AFIC after the approval of ethical board. One hundred and thirty patients, between the ages of 20 to 55 years, presenting for the evaluation of chest pain, shortness of breath, palpitations and atypical changes on ECG, were included in the study while patients with acute LVF, myocardial infarction, infiltrative disorders and cardiomyopathies were excluded. Myocardial fibrosis was evaluated on CMR with a variety of sequences like steady state free precession (SSFP), parametric T1 and T2 mapping and late gadolinium enhancement (LGE). Data was stored and analyzed on SPSS-23.

Results: The mean age of the patients was 34.2 ± 9.65 years among which 127 (97.7%) were males while 3 (2.3%) were females. Fifteen (11.5%) patients were hypertensive while 5 (3.8%) patients were diabetic. The incidence of myocardial fibrosis among our study sample was 43.1% as 56 patients had confirmed LGE or raised parametric T1 map times on CMR.

Conclusion: CMR late gadolinium enhancement (LGE) and T1 mapping can pick myocardial fibrosis in patients with abnormal ECGs and it can help in identifying patients susceptible to cardiomyopathies and arrhythmias at an early stage for better future risk stratification.

Keywords: myocardial fibrosis, sudden cardiac death, T1 mapping, late gadolinium enhancement

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INTRODUCTION

Myocardial fibrosis can be demarcated by a significant rise in collagenous fibrous tissue in the myocardium. While some degree of fibrosis in the myocardium always exists in end-stage heart failure, some patients can have 'silent' myocardial fibrosis in otherwise healthy heart. Myocardial fibrosis can lead to impaired cardiac ventricular function. Various pathophysiological mechanisms can cause myocardial fibrosis including myocardial infarction, cardiomyopathies and hypertension etc. Among various types of myocardial fibrosis, the common types are, reactive interstitial fibrosis,[1] replacement fibrosis, infiltrative interstitial fibrosis and endo-myocardial fibrosis. In a broad variety of cardiomyopathies, diffuse replacement and interstitial fibrosis is a common feature.[2]

No specific therapeutic approach is present in guidelines for heart failure due to cardiomyopathy based on tissue composition.[3] This deficiency of definite diagnosis might lead to inapt therapy leading to amplified illness and supplementary financial burden to health care services.

The benefits of using non-invasive imaging technique like MRI has been established by many recent reports. The extent of fibrosis has been well categorized by CMR and may have extrapolative worth in various cardiomyopathies.[4] This myocardial fibrosis may lead to persistent ventricular tachycardia or fibrillation by slow and heterogeneous conduction that may favor the genesis of reentry mechanism.[5] Therefore, the estimation of ventricular fibrosis by late gadolinium enhancement (LGE) on CMR has been proposed as an indicator for sudden cardiac death (SCD) risk stratification.[6] In the past decade, the cardiac magnetic resonance imaging has appeared as a non-invasive diagnostic modality used to assess cardiac morphology, function and various cardiac pathologies like myocardial perfusion, viability, cardiomyopathies, infective, infiltrative disorders and cardiac masses. MRI produces high resolution images

without the use of ionizing radiation with minimal deterministic effects.[7] It has a unique property to differentiate the composition with the vast range of protocols that helps in the assessment of morphology without contrast administration. LGE sequence aids in the differential diagnosis of pathologies. Steady state free precession (SSFP) is the bread and butter of CMR image protocol, as it aids in the assessment of both cardiac morphology and function with high spatial resolution. Parametric mapping is a new emerging research technique in CMR for the quantitative analysis of fibrosis and edema.[8] T1 relaxation time is measured by native T1 map of the myocardium.[9] Tissue characterization is done after the administration of gadolinium-based contrast agent that works on the principle of T1 shortening. LGE corresponds to myocardial fibrosis indicates poor long-term cardiac outcomes including sudden cardiac death.[10]

In this study we have focused on the CMR identifications of fibrosis in myocardium through LGE and parametric T_1 mapping in young patients reporting with atypical thoracic pain, subtle non-specific ECG changes, apprehensions and palpitations etc. The rationale of this study is that myocardial fibrosis has diagnostic value in early stages of disease which can predict future adverse cardiac events like arrhythmias, overt heart failure and cardiomyopathies. It has a strong prognostic value with high morbidity and mortality. With early diagnosis, we can prevent future cardiac events in vulnerable populations. Therefore, the objective of this study was to determine the frequency of myocardial fibrosis on CMR in patients who had normal invasive and/or non-invasive cardiology investigations but had subtly abnormal ECGs.

METHODOLOGY

In this descriptive cross-sectional study, we enrolled 130 patients, held retrospectively, fulfilling inclusion criteria and underwent CMR from May 2020 to June 2021 at Armed Forces Institute of Cardiology and National Institute of Heart Diseases. After approval from IERB, study was conducted according to the Declaration of Helsinki and conversant consent was renounced by the institute due to the retrospective nature of the study. Non-probability consecutive sampling technique was used and sample size was calculated with WHO formula by taking 75% prevalence of myocardial fibrosis in asymptomatic patients with HCM with confidence interval of 95% and 8% margin of error. Patients with chest pain, shortness of breath and palpitations were initially assessed by ECG, Echocardiogram and Computed Tomographic coronary angiography. Patients with atypical presentation and insignificant diagnostic information on echo and CT angiography underwent CMR. Patients with acute LVF, old myocardial infarction and history of infiltrative disorder were excluded.

CMR scan was performed on Siemens Magnetom Skyra 3.0 Tesla. Dedicated 18 channel phased array surface coil is used to receive the echo signal. Protocols were applied with breath hold and ECG gating, both prospectively and retrospectively according to the sequence. Protocol was designed as steady state free precession (SSFP) cine, parametric T1 and T2 mapping, first pass perfusion and late gadolinium enhancement images, both magnitude and phase sensitive inversion recovery (PSIR). Contrast was administered at a mean dose of 0.15mmol/kg. On an average, one hour is required to complete the scan.

Cardiac anatomy and function were analyzed on SSFP cine images with single slice at 2-chamber, 3-chamber, 4-chamber and 10 slices at short axis (SAX) view. Volumetric analysis was done by Simpson's method on 25 images of each slice with complete cardiac cycle. Both T1 and T2 parametric maps are obtained on SAX view with 3 slices (base, mid and apex). Myocardium with a parametric T1 map value of more than 1300ms is considered as fibrotic and more than 45ms T2 time is labeled as edematous. Magnitude and PSIR late gadolinium enhancement images were obtained after 8-10 minutes of contrast and analyzed for myocardial fibrosis. All the images were viewed and analyzed on Syngo.via workstation.

Retrospective data was collected from cardiac MRI department during 13 months' time. Data was extracted from CMR database. The included variables were demographics (age, gender, height, weight, etc.), clinical variables (hypertension, diabetes mallitus, obesity, smoker, etc.), ECG changes (RBBB, inverted T-waves, ST seggs), and the important variable of this study is myocardial fibrosis (MF) 56 (43.1%) which was measured on CMR through LGE or raised parametric T1 map. MF is the indicator of high-risk morbidity and mortality.

Data analysis was performed on Statistical Package for Social Sciences version 23 (SPSS-23). Mean and standard deviation was used to expressed quantitative variables. Categorical variables were described in terms of frequency and percentages. To evaluate associations among categorical variables, chi square test was applied.

RESULTS

The study included 130 participants with an average age of 34.2 ± 9.65 years. 127 (97.7%) patients were males. Out of these 27 (20.8%) patients were obese. Patients had various reasons for undergoing cardiac MRI, most of them were chest pain 93 (71.5%) and ST seggs 81 (62.3%) on ECG as shown in Table 2. The incidence of myocardial fibrosis among our study population was 56 (43.1%).

Table 1: Baseline clinical parameters

Characteristics	Summary
Age (mean ± SD)	34.2 ± 9.65
Height (mean ± SD)	172.56 ± 6.4
Weight (mean ± SD)	71.62 ± 13.0
Gender	
Male	127 (97.7%)
Female	3 (2.3%)
Hypertension	15 (11.5%)
Diabetes mellitus	5 (3.8%)
Obesity	27 (20.8%)
Smoker	7 (5.4%)
Family history	14 (10.8%)
Chest pain	93 (71.5%)
Shortness of breath	31 (23.8%)
Palpitations	41 (31.5%)
ECG findings	
RBBB	36 (27.7%)
Inverted T-waves	63 (48.5%)
ST seggs	81 (62.3%)

Association of clinical variables and ECG changes with myocardial fibrosis on CMR is shown in Table 2. There was significant association between obesity and MF (p=0.056). Most of the variables mentioned in the table shows no statistical significance (p≥0.05).

Table 2: Association of ECG changes and symptoms of heart failure with myocardial fibrosis on CMR

Variables	Myocardial fibrosis	p-value
Total (N)	**56**	
Obesity	16 (28.6%)	0.056
Chest pain	39 (69.6%)	0.670
Palpitations	20 (35.7%)	0.373
RBBB	16 (28.6%)	0.846
Inverted T-waves	31 (55.4%)	0.171
ST depression	38 (67.9%)	0.256

Association of ejection fraction (EF) (p= 0.018) and parametric T1 map (p=0.001) with myocardial fibrosis is shown in Table 3.

DISCUSSION

In past decade, CMR is gradually becoming the modality of choice in diagnosing cardiac pathologies, even in those who don't have specific signs and symptoms but have some clue towards the possibility of having an underlying cardiac pathology, for diagnosis and management of patients with cardiomyopathies and heart failure. It can do so with its the unique ability to evaluate tissue characterization and cardiac function by LGE and SSFP sequences, respectively.[11,12] For diagnosis and treatment of cardiomyopathies and heart failure patients, it has been projected as a wide-ranging tool in the clinical arena. This study mainly focused in determining myocardial fibrosis in patients who had inconclusive Echocardiography and CT coronary angiography studies but had non-specific findings such as atypical chest pain, palpitations, shortness of breath and non-conclusive ECG changes, because studies have proven that patients with myocardial fibrosis are at risk of developing cardiomyopathies, heart failure and arrhythmias. Escorting in the progress of heart failure and death, fibrosis of myocardium is the concluding point of convergence for all heart muscle diseases.[13]

Table 3: Association of ejection fraction and T1 map with myocardial fibrosis

	LGE		P-value
	Yes	No	
T1 map			
<1100	0 (0%)	2 (2.7%)	0.001
1101-1250	9 (16.1%)	61 (82.4%)	
1251- 1400	45 (80.4%)	11 (14.9%)	
>1400	2 (3.6%)	0 (0%)	
Ejection Fraction			
<40	6 (85.7%)	1 (14.3%)	0.018
41-50	12 (75%)	4 (25%)	
51-60	16 (39%)	25 (61%)	
>60	22 (32.8%)	44 (66.7%)	

The current study reports several important observations such as very high prevalence of myocardial fibrosis assessed by late gadolinium enhanced images on CMR even without surface signs and symptoms of cardiac disease which is in line with previous studies. Kwong RY stated 28% having LGE on CMR.[14]

Gulati et al. conducted a study in 2013 for assessment of myocardial fibrosis and prognostic information beyond LVEF on CMR. The LGE-CMR sequence not only permit extra dependable risk stratification of patients but also enable recognition of high-risk patients for cardiomyopathies and arrhythmias who are routinely overlooked.[15] The advent of parametric maps further enhances our acquaintance and clinical evaluation of myocardial fibrosis and enhances the information provided by LGE-CMR. One of the most crucial and clinically related prognostic markers in present exercise is fibrosis which was autonomous of LVEF.[16] Another significant result of our study is the expression of high frequency of myocardial fibrosis (>80%) by CMR-LGE in subjects with low Ejection Fraction (Table 3). Parametric T1 mapping in

combination with LGE will be of great benefit for a more specific myocardial tissue characterization.

In our sample, many patients are often diagnosed when symptoms of heart failure develop. However, myocardial fibrosis is encountered at an early stage where signs and symptoms are not suggestive of cardiac pathology. CMR can help diagnose such patients at an early stage. 56 (43.1%) patients showed evidence of myocardial fibrosis on CMR without having any overt signs and symptoms of heart failure. According to Domenech-Ximenos B et al. 37.6% athletes show focal LGE suggesting myocardial fibrosis.[17] Our study has confirmed that CMR can help us better stratify patients with cardiovascular risk, sensing subclinical myocardial transformations before the start of evident cardiac symptoms.[18]

This can improve therapeutic strategies by employing them at an early stage, thus improving clinical outcomes.[19] By early detection of fibrosis, risk factor stratification and intervention, the progression of the diseased process can be de-escalated and burden on our health services system can be mitigated. This is a single center, retrospective study which does not take into account the effects of different co-morbidities. A multi-center prospective study including diverse population can be fruitful to evaluate incidence and effects of different co-morbidities.

CONCLUSION

LGE and parametric mapping on CMR helps in identifying patients at probability of evolving cardiomyopathies, cardiac arrhythmias and heart failure at an early stage which can have effect on future outcomes. The results show that patients with atypical presentation and insignificant changes on ECG with normal Echocardiography and CT coronary angiography can still have abnormal myocardium with fibrosis and CMR should be considered with possible serial monitoring to critically analyze the progress of any silent myocardial fibrosis.

AUTHORS' CONTRIBUTION:

AN, MZK, and NS: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. MS and WR: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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