Correlation between Pre-Operative Myocardial Fibrosis and Early Post CABG Dysrhythmia

Abstract

Background: Cardiac magnetic resonance (CMR) imaging combines the assessment of both the functional and structural aspects of the heart in order to identify the existence, timing, and intensity of ischemic heart disease by analyzing the function of the myocardium and the movement of the heart wall. This study aimed to investigate whether preoperative myocardial fibrosis, measured byCMRimaging, may be used to predict the incidence of rhythm disturbances in the early postoperative phase after coronary artery bypass grafting (CABG) surgery.

Methods: Two groups of 92 patients who had CABG procedures performed were studied in this retrospective observational single site cohort study: There were 43 patients in Group A who had atrial or ventricular arrhythmia, and 49 patients in Group B who did not.

Results: There was no correlation between arrhythmia and non-arrhythmia group and age, sex, body mass index, risk factor, CMR timing before surgery, cross clamp time, bypass time, left ventricular end-diastolic volume index (LV EDVI), LV end-systolic volume index(ESVI), SVI, LV ejection fraction (EF) and territory of scar and were positive correlation between both groups and scar (P <0.001). Scar% was an independent predictor of occurrence of rhythm disturbance (P=0.002) while LV EDVI, LV EF, LV ESVI, SVI, and presence of scar were not. Group A had a statistically significantly lowered LV-EF% and lower LV-SVI compared to Group B respectively. GroupA had a higher scar percentage compared with group B and this was statistically significant (P <0.001).Scar (%) can significantly predict the occurrence of rhythm disturbance (P=0.0002 and AUC = 0.708) at cut-off >14.8%.

Conclusions:CMR has evolved as a gold standard non-invasive imaging tool in cardiovascular medicine, promising tool for predicting postoperative cardiac arrhythmia after CABG.

Keywords: Myocardial Fibrosis, CABG, Dysrhythmia, CMR, EF

Introduction:

In both developing and developed countries, coronary artery disease (CAD)ranks high among the leading causes of mortality. The American Heart Association estimates that 16.2 million Americans, defined as those aged 20 and above, suffer from cardiovascular disease. More than one-third of all deaths in adults over the age of 35 are caused by CAD. Over the last several decades, our understanding of CAD has made great strides[1].

In recent decades, advancements in technology have strengthened the significance of noninvasive imaging in identifying, categorizing the risk, and treating individuals with ischemic heart disease. Cardiac magnetic resonance (CMR) imaging combines the assessment of heart function and structure to identify the presence, timing, and severity of ischemic heart disease. It evaluates factors such as myocardial function, wall motion, the occurrence and extent of myocardial ischemia, edema, and scar formation. The diagnostic and prognostic significance of currently established clinical procedures has been shown[2].

Correctly determining the presence or absence of viable myocardial muscle is crucial for effectively managing individuals with cardiac dysfunction. Viable muscle has the potential for contractile restoration. Consequently, a patient suffering from ischemic cardiomyopathy and ventricular dysfunction may see an enhancement in their functional capacity after cardiac revascularization. This improvement may lead to an increased chance of survival. Accurate detection of necrotic muscle, especially in cases of asymptomatic infarction (occult infarction), is crucial due to the potential for this tissue to serve as a foundation for ventricular tachyarrhythmia, a major contributor to sudden death[3].

This study aimed to investigate whether preoperative myocardial fibrosis, as measured by CMR, may be used to predict the incidence of rhythm disruption in the early postoperative period after undergoing CABG surgery.

Patients and Methods:

This research was a retrospective observational cohort study conducted at a single site. It included 92 patients of both sexes, aged between 20 and 75 years, who had undergone coronary artery bypass graft (CABG) surgery. The research was conducted between 2014 and 2022, after clearance from the Ethical Committee of Tanta University Hospitals and Aswan Heart Center in Egypt. The patient or the patient's family provided a well-informed written consent.

Exclusion criteria were any preoperative rhythm abnormality and If the CMR exam was incomplete or aborted.

According to occurrence of arrythmia during the hospital stay, patients were subdivided into two groups: Group A: patients who had arrhythmia either atrial or ventricular (n=43) and Group B: patients who did not have arrhythmia (n=49).

All patients were subjected to: history taking, clinical examination, operative and anesthesia notes regarding cardiopulmonary bypass, and cross clamp time) and standard resting 12 lead ECG for rhythm analysis was done during the early post-operative course, daily in the first three days then every other day during hospital admission. The ECG analysis was mainly for arrhythmia detection either atrial or ventricular.

CMR

Ventricular volumes and function: Siemens Medical Systems' 1.5- T MRI scanner, the Siemens Magnetom Aera type, was used to carry out the CMR operation. Pictures were taken within one day after right cardiac catheterization (RHC). A retrospective electrocardiogram-gated steady-state free precession sequence was used to measure the systolic and diastolic volumes while the subject held their breath. Horizontal long-axis (2- and 4-chamber) and short-axis (12-14 consecutive slice) pictures were acquired. Beginning from the base of the heart and reaching to its apex, these slices enveloped both ventricles. The parameters for the scan were as follows: a repeat time ranging from 3.2 to 3.8 ms, an echo length from 1.6 to 1.9

ms, a flip angle from 50 to 70°, a matrix size of 160 by 256, a field of view from 350 to 400 mm, a temporal resolution of around 25 ms, and a slice thickness of 6 to 8 mm without a gap between the slices.

Delayed Contrast-Enhanced Magnetic Resonance Imaging: Following the injection of a gadolinium-based contrast agent (Magnevist, Schering AG, Berlin, Germany; 0.2 mmol/kg) in the same direction as the cine short-axis images, dynamic contrast-enhanced (DCE) images were obtained for a period of ten to fifteen minutes. The images were captured by using a segmented inversion-recovery gradient-echo pulse sequence with the following parameters: repetition time / echo time = 4.01 / 1.25 milliseconds, flip angle = 15 degrees, matrix = 208 x 256, and a mean voxel size of 1.6 x 1.3 x 5.0 millimeters. 180-200 milliseconds was used as the inversion time (T1) for this experiment.

CMR analysis

On an Intel desktop computer, each and every image was examined. For the purpose of evaluating the biventricular systolic function and the two-dimensional flow, the software tool known as Intellispace Portal, developed by Philips, was applied. In order to evaluate the biventricular systolic function, the endocardial contours of the left ventricle (LV) and the right ventricle (RV) were outlined in all cine short-axis data sections. This was done during both the end-diastolic and end-systolic phases of the heart's contractions. The measurements of end-diastolic and end-systolic volumes (EDV) were collected and then adjusted for body surface area (BSA) by using the Mosteller formula, which is as follows: (√Height [cm] × weight [kg]/3600). The end-systolic volume (ESV) was subtracted from the end-diastolic volume (EDV) in order to arrive at the indexed ventricular stroke volume (SVI). After dividing the SV by the end diastolic volume (EDV), the ejection fraction (EF) was determined according to the formula.**Figure 1**

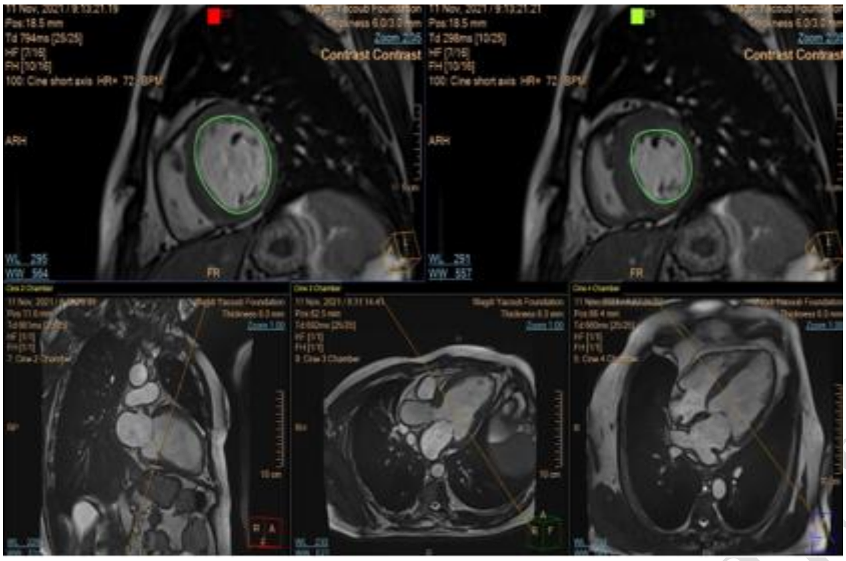

Figure 1: CMR volumeanalysis

Fibrosis: The level of fibrosis in each of the 16 myocardial segments was measured as part of the left ventricular global efficiency (LGE) evaluation. This was done by two experienced observers using the application (Segment CMR - Medviso). **Figure 2**

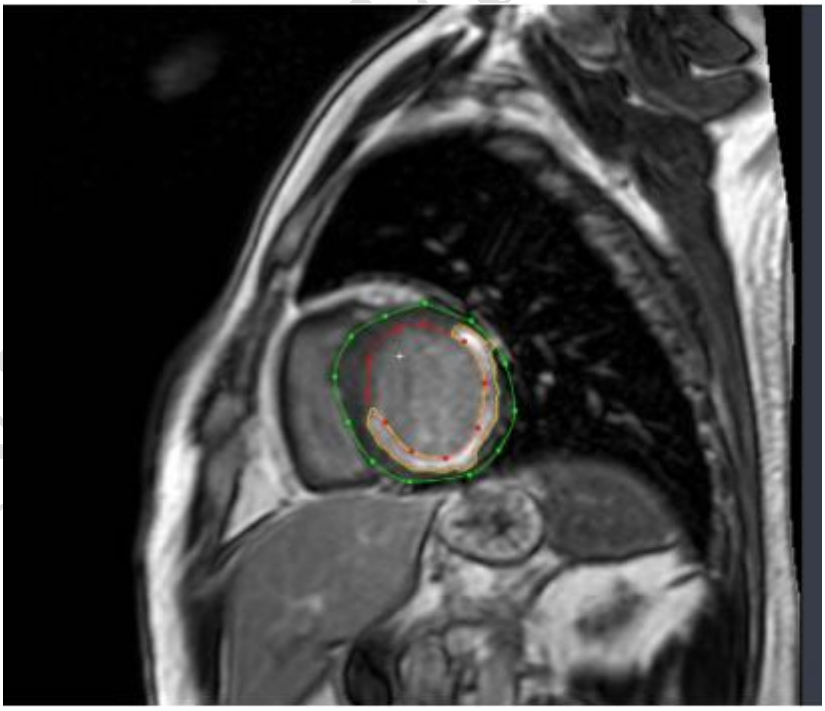

Figure 2: The area of fibrosis by segment CMR-Medviso software in LGE images

Sample Size Calculation:

The Epi-Info statistical software, produced by the World Health Organization and the Center for Disease Control and Prevention in Atlanta, Georgia, USA, was used to calculate sample size and power analysis. The precise version used was 2002. The criteria utilized for calculating sample size were as follows: 95% confidence interval. Preoperative myocardial fibrosis, as evaluated by CMR, may predict the occurrence of rhythm disturbance in the early postoperative period after CABG surgery. This prediction has a 70% sensitivity and a 10% margin of error (60-80%). The sample size, as calculated by the aforementioned criteria, was larger than 81. The sample size was increased to 96 patients to account for any missing data and improve data quality in the inquiry.

Statistical analysis

Utilizing the SPSS v26 program (IBM Inc., Chicago, Illinois, United States of America), the statistical analysis was carried out. Histograms and the Shapiro-Wilks test were used in order to ascertain whether or not the data are distributed in a normal fashion. The quantitative parametric data were evaluated using an analysis of variance (ANOVA) test, followed by a Tukey post hoc test. The results were given as the mean and the standard deviation (SD). The Kruskal-Wallis test with an adjusted Bonferroni correction was used to compare the quantitative non-parametric data. The data were provided as the median and the interquartile range (IQR). Additionally, the Chi-square test was used to analyze the qualitative variables, which were reported in the form of frequency and percentage (%). In order to highlight the significance of scar tissue (percentage) found by CMR in determining the likelihood of developing rhythm abnormalities, a Receiver Operating Characteristic (ROC) curve was developed specifically for this purpose. For statistical significance, a two-tailed P value of less than 0.05 was regarded to be significant.

Results:

Scar (%) can significantly predict the occurrence of rhythm disturbance (P=0.0002 and AUC = 0.708) at cut-off >14.8% with 69.77% sensitivity, 65.31% specificity, 68.9% PPV and 78.2% NPV.

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve

All demographics, medical history, cross clamp, bypass time, showed insignificantly different between both groups.**Table 1**

Table 1: Data on demographics, risk factors, duration on cross clamp and bypass, total number of grafts between arrhythmia and non-arrhythmia groups, and combination surgery

		Arrhythmia group (n=43)	Non-arrhythmia group (n=49)	P
Age (years)		58.5(43 – 74)	47.5(20 – 75)	0.072
Sex	**Male**	35 (81.4%)	44 (89.8%)	0.248
	Female	8 (18.6%)	5 (10.2%)	
BMI (Kg/m^2)		29.14 ± 4.4	27.49 ± 3.98	0.062
Risk Factors	**DM+HTN**	21 (48.84%)	18 (36.73%)	0.184
	HTN	7 (16.28%)	6 (12.24%)	
	DM	8 (18.6%)	7 (14.29%)	
Cross clamp time (min)		90(67.5 – 105)	92(64 – 119)	0.991
Bypass time (min)		159(118 – 200)	150(121 – 180)	0.597

CMR parameters (LV EDV, LV SV, SVI and LVEF), presence of scar and territorial distribution of myocardial fibrosis showed no significant difference between both groups. The presence of scar showed significant difference between both groups (P<0.001). **Table 2**

Table 2: CMR, scar parameters by CMR parameters of arrhythmia group and non-arrhythmia group

		Arrhythmia group (n=43)	Non-arrhythmia group (n=49)	P
LV EDVI (ml/m^2)		111.17 ± 31.24	100.5 ± 30.54	0.106
LV ESVI (ml/m^2)		70.76 ± 31.35	59.54 ± 30.18	0.088
SVI(ml/m^2)		40.5 ± 11.64	40.73 ± 10.47	0.922
LV EF (%)		38.33 ± 12.56	43.33 ± 14.86	0.091
Presence of scar		40 (93.02%)	46 (93.88%)	0.868
Scar (%)		20.78 ± 12.72	12.43 ± 9.3	**<0.001***
Territory of scar	**LAD**	11 (25.58%)	13 (26.53%)	0.764
	LAD-LCX	6 (13.95%)	5 (10.2%)	
	LAD-LCX-RCA	1 (2.33%)	0 (0%)	
	LAD-RCA	12 (27.91%)	8 (16.33%)	
	LCX	1 (2.33%)	7 (14.29%)	

	RCA	6 (13.95%)	7 (14.29%)	
	RCA-LCX	3 (6.98%)	3 (6.12%)	

There was no correlation between (Arrhythmia and non-Arrhythmia group) and age, gender, BMI, risk factor, CMR time, cross clamp time, bypass time, LV EDVI, LV ESVI, SVI, LV EF and territory of scar and were positive correlation between (Arrhythmia and non-Arrhythmia group) and scar (%) (P <0.001). **Table 3**

Table 3: Relationship between (Arrhythmia and non-Arrhythmia group) and other parameters

	r	**P value**
Age	0.189	0.072
Sex	0.120	0.253
BMI	0.195	0.062
Risk Factor	0.141	0.181
CMR time (mon)	0.011	0.914
Cross clamp time (min)	-0.025	0.812
Bypass time	0.023	0.827
LV EDVI (ml/m^2)	0.172	0.106
LV ESVI (ml/m^2)	0.181	0.088
SVI (ml/m^2)	-0.010	0.922
LV EF (%)	-0.179	0.091
Scar (%)	0.364	**<0.001***
Territory of scar	-0.019	0.858

In Multivariate regression, scar% was independent predictors of occurrence of rhythm disturbance (P value =0.002) while LV EDVI, LV EF, LV ESVI, SVI and presence of scar were not. **Table 4**

Table 4: Multivariate regression of CMR parameters to predict the occurrence of rhythm disturbance

	Coefficient	Std. Error	**P**
LV EDVI (ml/m^2)	-0.36056	0.32948	0.2738
LV EF (%)	-0.021263	0.055788	0.7031
LV ESVI (ml/m^2)	0.35534	0.33324	0.2863
SVI (ml/m^2)	0.39274	0.32783	0.2309
Scar%	0.086844	0.028344	**0.002***
Presence of scar	-1.62121	0.98274	0.0990

Discussion

In our observational study we have demonstrated that the percentage of myocardial scarring is the predictor to occurrence of arrythmia in early post-operative period post GABG operation. The cut off point for occurrence of arrhythmia was at scar percentage of 18.8%**(P=0.0002 and AUC = 0.708)**. Lower EF % tends to be present in the arrhythmia Vs non-arrhythmia cohort but it is not statistically significant.

The clinical relevance of each arrhythmia is contingent upon several parameters, such as the underlying cardiac function, comorbidities of the patient, length of the arrhythmia, and the velocity of ventricular response. POAs may be well-tolerated in some individuals, whereas in others they might contribute to both morbidity and death, depending on the interplay of these variables [4]. Tachycardia-induced rapid ventricular rates may lead to both diastolic and later systolic dysfunction, resulting in a decrease in cardiac output and potentially causing hypotension or myocardial ischemia. Bradyarrhythmia, especially when accompanied by the impairment of atrial function, may significantly impact individuals with either systolic or diastolic ventricular failure[5].

It's important to use imaging techniques to accurately diagnose, measure, and put these patients into risk groups, especially now that there are effective but expensive implantable devices [6]. There have been huge improvements in CMR's ability to meet many of these needs and give a full review in the last 5 years[7]. Because of improvements in both technology and software, a current CMR scanner can give information about the structure and function of the myocardium, as well as the tissue's survival, circulation, and flow, all in a single 45–60 minute study[8].

While most images are taken without the need for contrast chemicals, the use of Gd-CA, like Gd-DTPA (gadolinium diethylenetriamine penta-acetic acid), to show circulation flaws, microvascular ischemia, and areas of scar tissue/fibrosis is a big step forward [9]. Because Gd-CA is paramagnetic, it gives off a bright light when it is scanned. It doesn't change metabolism and is safe to give through a peripheral line as a single bolus. There is a very small chance that it will hurt the kidneys, so people who already have serious kidney damage should avoid getting it. Gd-CA can't get through the entire myocyte membrane because of how it is chemically made and how big its molecules are. It can, however, slowly spread and build up in the space between muscle cells or in myocytes where the cell membrane has been damaged. Most of the time, 0.1 to 0.2 mmol/kg (12 to 40 ml) is given[6].

Some of the most common problems that can happen after a CABG surgery are supraventricular (especially atrial fibrillation) and ventricular tachyarrhythmias (VT). Postoperative conduction disturbances also happen a lot, and sometimes a permanent pacemaker is needed to fix the problem [10]. A number of studies have shown a strong link between atrial rhythms and both valve and nonvalvular CABG surgery[11, 12].

Atrial fibrillation is the most prevalent kind of supraventricular tachyarrhythmias that may arise following CABG, with a reported incidence ranging from 5% to 40% [13]. There has been a rise in the occurrence of atrial fibrillation after CABG, even though there have been ongoing advancements in cardiac surgical methods. This tendency seems to be influenced, at least in part, by the introduction of cold potassium cardioplegia in the mid- to late 1970s for CABGprocedures. The precise prevalence of postCABG atrial flutter is uncertain due to its typical co-occurrence with atrial fibrillation. Post-coronary artery bypass graft (CABG) atrial fibrillation often develops within a timeframe of 24 to 72 hours after the surgery, with the highest occurrence seen on the second day after the operation[10]. Andreini et al. [14] stated that Ventricular arrhythmias of diverse causes were detectable on CMR imaging in a significant proportion of individuals who had no abnormalities on echocardiography. Also, Rizvi et al. [15] documented that Among the 90 patients who had CABG and had no previous history of heart failure (HF) or atrial fibrillation (AF), 34 patients (37.7%) experienced postoperative atrial fibrillation (PoAF) before being discharged from the hospital.

Noordman et al. shown that in individuals who have survived a myocardial infarction, the extent of the scar's "border zone" area serves as an indicator for predicting ventricular arrhythmic episodes and long-term mortality.[16] study. Appropriate ICD shocks were associated with a higher event-free survival rate in patients with smaller overall scar masses compared to those with larger masses (>49.0 g).

Similarly, Buxton et al. [17] documented that total mortality and arrhythmic deaths/cardiac arrests occurred more frequently in patients with EF<30% than in those with EF of 30% to 40%.

Limitations of this study included that the sample size was relatively small. The retrospective nature of the study gave weak evidence conclusions.

Conclusions:

CMR has developed into a non-invasive imaging technique that shows great promise for the prediction of postoperative cardiac arrhythmia after CABG.

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