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Original Article

Predictors of acute myocardial infarct size in STEMI patients receiving thrombolytic therapy: A delayed contrast enhanced cardiac MRI study

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ABSTRACT

Introduction: Delayed contrast enhanced Cardiac MRI has been accepted as a standard tool worldwide for determination of infarcted myocardium and viability. Infarct size as determined by cardiac MRI has important therapeutic and prognostic information.
Methods: Twenty six STEMI patients who had received thrombolytic therapy were subjected to cardiac MRI assessment at 5–7 day of admission. Base line variables of the study population were compared with the acute infarct size as determined by the Cardiac MRI.
Results: The mean acute infarct size in our study population was 27.2 ± 17.4% of LV. We found through univariate analysis that final infarct size was dependent on time to thrombolysis ($p = 0.04$), Status of Thrombolysis ($p = 0.01$), smoking status ($p = 0.02$), location of infarct ($p < 0.00001$), presence of microvascular obstruction ($p = 0.01$) and viability status ($p = 0.0004$). Thus, larger acute infarct size was seen in delayed time to thrombolysis, failed status of thrombolysis, smokers, anterior location of the infarct, presence of microvascular obstruction and non viable myocardial status.
Conclusion: Infarct size as determined by Cardiac MRI has been shown to carry important therapeutic and prognostic information. We have tried to evaluate predictors of acute infarct on cardiac MRI in STEMI patients during their initial hospital stay. Knowing the predictors of acute infarct size can help in early intervention and provide prognostic information for future cardiac events.

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1. Introduction

Cardiovascular MR (CMR) imaging has become a practical, clinically useful tool for the non-invasive evaluation of ischemic heart disease providing both structural and functional information.[1]

It has also been shown that reversibly injured myocardium does not result in increased myocardial gadolinium concentrations and, therefore, does not enhance whereas regions of hyperenhancement accurately quantify nonviable myocardium.[2]

Many studies have shown that infarct size correlates with the remodeling, ejection fraction and future cardiac events and determination of infarct size by cardiac MRI gives important prognostic and therapeutic information.

Present study was done to the predictors of acute infarct size in STEMI patients receiving thrombolytic therapy.

2. Study population

The study was carried out in all consecutive patients of STEMI who had received thrombolytic therapy admitted in the Department of Cardiology over a period of one year.

3. Cardiac MRI examination

Cardiac MRI examination was conducted in the following manner. Cardiac Cine MRI was performed on 1.5 T Siemens Somatom machine using dedicated phased array chest coil after 5–7 days of hospital stay. Patient position was kept supine. Prospective ECG gating was used in all the patients. Pre contrast ECG gated GRE true FISP images in short axis, vertical long axis planes and horizontal long axis were acquired. Various imaging parameters were slice thickness = 8 mm, contiguous sections with no spacing; TE = 1.33, TR = 859.20, FOV = 340, Flip angle = 40° and image matrix of 101 × 92. T1 scout images were acquired by selecting the slice at mid cavity level and the appropriate myocardial nulling time was found in each patient by both visual inspection and mean curve method. Each patient was given 0.2 m mol/kg intravenous Gadolinium followed by 20 ml saline at a rate of 3 ml/s using a pressure injector. ECG gated Dynamic post contrast images were obtained with immediate and 20 min delayed acquisitions using inversion recovery 3D GRE sequences and using the appropriately selected time to inversion. Cine images were acquired in the corresponding short-axis, vertical long-axis views and horizontal long axis views. The acquisition of short-axis views were started 1 cm below the level of the mitral–valve–insertion plane and continued in 8 mm increments through the left ventricle.

Twelve equal circumferential segments were analyzed in each short-axis view.

Delayed hyper enhancement was observed after 20 min on post-contrast images. Enhanced area was defined as that showing signal intensity at least 2 SD greater than normal myocardium. The area of the infarction as depicted by delayed contrast enhancement was calculated in each segment as:

Area showing enhancement = a

Area unenhanced = b

Percentage of area enhanced in each segment = $a/(a + b) \times 100$.

The transmural extent of Infarction (TEI) within each segment (expressed as percentage of the total segmental area) was graded on a 5-point scale as follows:

Grade 0	no enhancement
Grade I	25% tissue involvement
Grade II	26–50%
Grade III	51–75%
Grade IV	76–100%

Total LV infarct size was calculated as Infarct size by DCE MRI (%LV) = [Sum of all TEI scores throughout LV (range, 0–4)]/(Total Number of segments × 4).

Microvascular obstruction was defined as any hypo-enhanced area present within the hyperenhanced infarcted region on delayed contrast images.

Left ventricular functional parameters were calculated using the Syngo Argus software and tracing the endocardial borders in each of the short axis cine images. Left ventricular ejection fraction, end diastolic and systolic volumes and stroke volume were calculated for each patient. For calculation purposes the papillary muscles were considered to be part of ventricular cavity.

All segments with enhancement in each patient were noted and patients were divided into two groups; viable and nonviable. The ratio of [Sum of all TEI scores throughout LV segments showing enhancement (range, 0–4)]/(Total Number of segments with enhancement) was noted in each patient.

Patients with score > 2 were considered to be having Non viable myocardium (Fig. 1 and 2).

Patients with score < 2 were considered to be having viable myocardium (Fig. 3).

4. Statistical analysis

Student's t test was used to compare the means of the continuous variables. Chi-square test was used to compare the discrete variables. All analysis were performed with Epi Info software. Univariate analysis was performed to see the association of variables with acute infarct size.

5. Results

Baseline characteristics of the study population is shown in Table 1.

Univariate analysis for infarct size is shown in Table 2.

The mean acute infarct size in our study population was 27.2 + 17.4% of LV. We found through univariate analysis that final infarct size was dependent on time to thrombolysis ($p = 0.04$), Status of Thrombolysis ($p = 0.01$), smoking status ($p = 0.02$), location of infarct ($p < 0.00001$), presence of

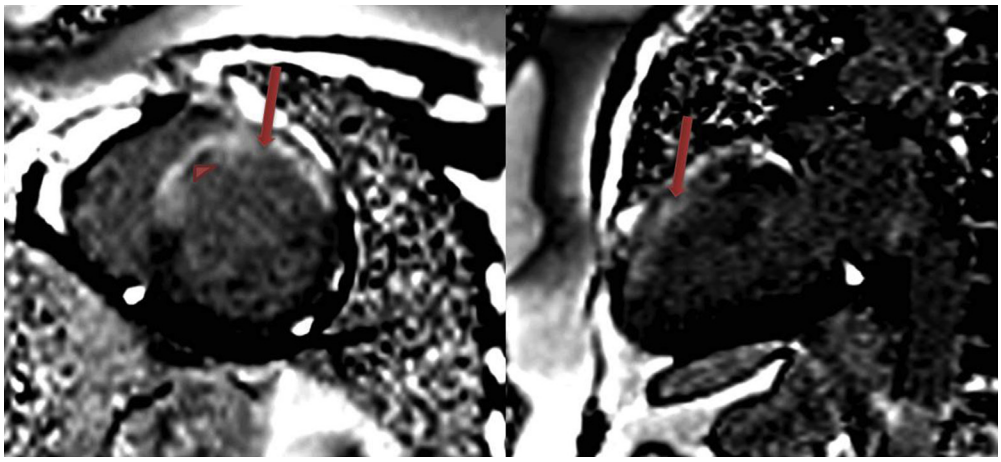

Fig. 1 – Short axis and vertical long axis delayed contrast enhanced images show anterior non viable infarct (red arrow). There are areas of non enhancement within the infarcted core suggestive of microvascular obstruction (arrow head).

microvascular obstruction ($p = 0.01$) and viability status ($p = 0.0004$). Thus, larger infarct size was seen in delayed time to thrombolysis, failed status of thrombolysis, smokers, anterior location of the infarct, presence of microvascular obstruction and non viable myocardial status.

6. Discussion

Determination of myocardial viability is of paramount importance. Multiple observational studies have suggested survival benefit in such patients if they are revascularized when myocardial viability is detected on imaging tests.

Wolfgang G. Rehwald et al[2] have compared delayed contrast enhancement with histopathological findings and found that it accurately differentiates viable and non viable regions.

Holger Thiele et al[3] studied 360 consecutive STEMI patients who were reperfused by primary PCI within 12 h after symptom onset through delayed contrast enhanced cardiac MRI performed 3.1 ± 4.1 days after the acute event. They found that predictors of final infarct size were pre-PCI TIMI-flow grade, infarct location, Killip class and 90 min ST-segment resolution. Like their results we also found that infarct size was larger when located anterior than inferior. Our study also correlated with their results that higher Killip class was associated with larger infarct size. They also found that final infarct size was inversely related to 90 min ST resolution which correlated with the status of thrombolysis assessed by us which included ST resolution as the marker for efficacy of thrombolysis. The mechanism of reperfusion was different in our study which included thrombolysis through streptokinase whereas in their study it was primary PCI. In contrast to our study the time-to-reperfusion did not affect infarct size in their study. It is probably reflected by the difference in the method of reperfusion between the two studies. They have also pointed out that the lack of relation between time to reperfusion and final infarct size in their study may be reflected by the selection bias in their study in which patients with larger infarct were treated earlier.

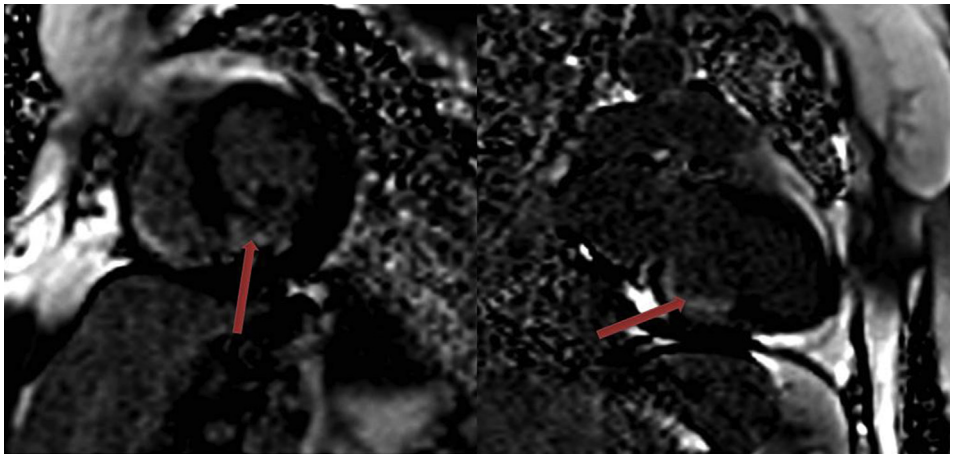

Fig. 2 – Delayed contrast enhanced short axis and vertical long axis images show non viable inferior wall infarct (red arrows).

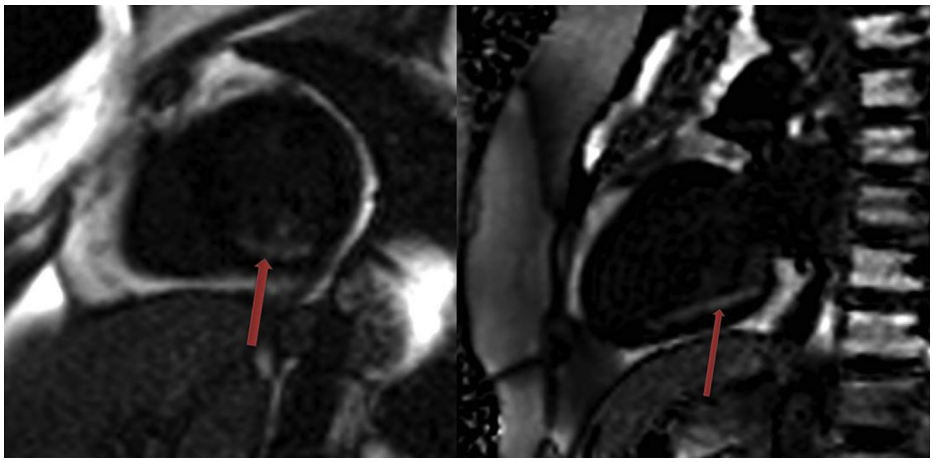

Fig. 3 – Delayed contrast enhanced short and vertical long axis images show evidence of viable inferior wall infarct with less than 50% transmural enhancement (red arrows).

Gregg W. Stone et al[4] studied the determinates of infarct size in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention. They found that anterior infarction, time to reperfusion, epicardial infarct artery patency before and after reperfusion, male gender, previous AMI, and failed thrombolytic therapy were important predictors of infarct size after angioplasty in patients with AMI. We also found that anterior location of infarct, time to perfusion and failed thrombolysis were associated with larger infarct size. No correlation with male sex was found in our study like them probably due to the small sample size of the study group. Their study was different from our study as they took all patients of MI whereas our study was limited to STEMI patients with thrombolysis done with streptokinase. Infarct size estimation in their study was through SPECT.

Edmund T. Hasche et al[5] studied 61 patients who were thrombolysed. Infarct size was estimated from the 12-lead ECG according to a 32-point QRS score at day 7 post thrombolysis. They found through multivariate regression that size of risk region, duration of ischemia, and degree of initial ST-segment elevation were independent predictors of infarct size, of which the most important variable was ischemia time. Our study also shows that the infarct size is greater when time to thrombolysis is increased. Although the method of infarct determination between the two studies was different there is agreement that increased duration of ischemia results in larger infarct size.

Table 1 – Baseline characteristics of the study population ($n = 26$).

Risk factor		Frequency
Sex	Male	20 (76.9%)
	Female	6 (23.1%)
Smoking status	Smokers	21 (80.8%)
	Never smoked	5 (19.2%)
Diabetes	Yes	5 (19.2%)
Hypertension	Yes	9 (34.6%)
Dyslipidemia	Yes	9 (34.6%)
Killip class	Killip class I	12 (46.2%)
	Killip class II	14 (53.4%)
Status of thrombolysis	Successful	11 (42.3%)
	Partial	2 (7.7%)
	Failed	13 (50%)
Microvascular obstruction	Yes	(14) 53.8%
	No	(12) 46.2%
Infarcted region	Anterior	9 (34.6%)
	Lateral	4 (15.4%)
	Inferior	13 (50%)

E wu et al[6] studied 122 patients with STEMI following acute percutaneous reperfusion. They performed Cardiac magnetic resonance imaging within 1 week following STEMI in 122 subjects. They found that acute infarct size correlated linearly with the initial End systolic volume index (ESVI), end-diastolic volume index (EDVI) and EF. Our study also has shown the same relationship between these indices.

Pier Giorgio Masci et al[7] have demonstrated that the amount of necrotic myocardium strongly determines the pattern of infarct healing, and regional and global LV remodeling. E wu et al[6] had demonstrated that Infarct size, EF and ESVI can predict the development of future cardiac events. They found that acute infarct size, which is independent of LV stunning and loading, directly relates to LV remodeling and is a stronger predictor of future events than measures of LV systolic performance. Stijntje D. Roes et al[8] also found infarct size on contrast-enhanced MRI to be superior to LVEF and LV volumes for predicting long-term mortality in patients with healed myocardial infarction.

In our study we also demonstrated the presence of microvascular obstruction in 14 (53.8%) of our patients. Katherine C. Wu et al[9] studied 44 patients with acute MI 10 + 6 days after infarction. Microvascular obstruction was present in 11 (25%) of their patients. Our results correlated with their findings that microvascular obstruction was associated with larger infarct size.

Gadolinium-based enhancement imaging is neither necrotic nor fibrotic specific, and thus their concentration is influenced by any conditions altering extracellular volume such as myocardial edema. In a study Reimer et al demonstrated that 2–4 days after reperfusion in the infarcted

Table 2 – Univariate analysis for infarct size.

Variable	Coefficient	Correlation coefficient	f-test	*p* Value
Age	0.262 ± 0.342	0.02	0.58	0.45
sex	3.36 ± 8.2	0.01	0.16	0.68
Smoker	−18.611 ± 7.9	0.18	5.4	0.02
Diabetic	2.24 ± 8.8	0.00	0.06	0.8
Hypertension	−2.130 ± 7.3	0.00	0.08	0.7
Dyslipidemic	9.14 ± 10.0	0.03	0.83	0.37
DBP	0.195 ± 0.27	0.02	0.51	0.48
SBP	0.004 ± 0.15	0.00	0.0006	0.98
RBS	0.11 ± 0.07	0.09	2.3	0.14
HR	−0.30 ± 0.28	0.05	1.2	0.28
Status of thrombolysis	8.7 ± 3.1	0.24	7.5	0.01
Time to thrombolysis	2.7 ± 1.3	0.15	4.3	0.04
Killip class	12.7 ± 6.4	0.14	3.85	0.06
Infarct location	−14.3 ± 2.49	0.58	33.0	0.000007
MO	16.0 ± 6.1	0.22	6.76	0.01
Viability status	−23.1 ± 5.6	0.42	17.0	0.0004
Dysfunctional myocardium	0.6 ± 0.07	0.74	66.9	0.000000
Dysfunctional but viable	0.20 ± 0.42	0.01	0.24	0.62
LVEF	−1.17 ± 0.1	0.73	65.7	0.000000
LVESV	0.20 ± 0.05	0.35	13.1	0.001
LVEDV	0.18 ± 0.06	0.25	8.0	0.009
SV	−1.7 ± 0.29	0.58	33.5	0.000007

myocardium there is a 25% increase in water content in conjunction with inflammation and hemorrhage.[10] Thus this technique may overestimate myocardial necrosis in the very early phase when the volume of the infarcted tissue tends to increase due to phenomena other than myocytes necrosis, such as hyperemia, edema and inflammation cells infiltration. Recent studies have shown a significant decrease in extent of enhancement between day 1 and day 7 post-infarction, suggesting an overestimation of the extent of irreversible damage at very early imaging. These findings need to be considered when performing late gadolinium, technique for necrosis quantification in the early post-infarction phase.[11]

There were certain drawbacks in our study. The sample size was small as it included STEMI patients receiving thrombolytic therapy who were willing to participate in the study. Only patients who were stable and could withstand the cardiac MRI examination were included. The infarct size was estimated within a week of myocardial infarct and may represent an overestimation of the final infarct size due to edema. Final infarct size can be assessed on follow up imaging as initially there is infarct shrinkage. T2w imaging and myocardial tagging in the patients could have added by estimating the myocardium at risk. We did not incorporate these as limited sequences were taken to reduce the time of acquisition of relatively sick MI patients in MR gantry. Further these sequences could have more relevant if follow up was done. The interpretation of delayed gadolinium enhanced cardiac MRI was done by a single observer and interpretation by another observer could have reduced observer bias. The wall motion abnormalities were visually assessed and could be subjected to observer bias. Follow up of the patients could not be taken due to financial constraints to the patients and difficult geographical terrain in this part of the country, thus estimation of final infarct size was not taken. This study was intended as a preliminary study to evaluate various parameters which can predict the size of acute infarct size on cardiac MRI as evaluated on thrombolysed STEMI patients. The infarct size estimated may represent overestimation as could have been seen on follow up imaging however we had put an effort to evaluate all these factors in acute STEMI patients with imaging done during their initial hospital stay. Further studies evaluating these parameters with follow up of the patients to determine the final infarct size are required.

To conclude, delayed contrast enhanced cardiac MRI examination can give both morphological and functional information which have important therapeutic as well as prognostic implications. We have tried to determine the factors influencing the acute infarct size in STEMI patients during their initial hospital stay as determined by cardiac MRI which can carry prognostic and therapeutic implications.

Conflicts of interest

All authors have none to declare.

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