

Rate of Detection of Left Ventricular Thrombi on Cardiac Magnetic Resonance Viability Studies- A Single Center Study

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Abstract

Background: Left ventricular (LV) thrombus is a complication of acute Myocardial Infarction (MI) and is associated with systemic thromboembolism. Although standard trans-thoracic echocardiogram (TTE) is commonly used for screening, it is limited by low sensitivity for detection of LV thrombus. Magnetic resonance imaging has a high yield in detection of these thrombi. **Objective:** To determine rate of detection of left ventricular thrombi on magnetic resonance cardiac viability studies. **Design:** Retrospective, observational. **Setting:** Department of Radiology at a Hospital in Dhahran from April 2013 to April 2018. **Patients and Methods:** All recently reperfused ST Segment Elevation MI (STEMI) patients who were referred for MR cardiac viability studies with negative TTE (for LV thrombi) were evaluated. Patients with limited or incomplete studies, previously known MI or cardiac surgeries, and those contraindicated to MRI were excluded. An area of low signal intensity with no late gadolinium enhancement (LGE) was defined as thrombus on MR imaging, and two radiologists made consensus reporting for the diagnoses. Patients with anterior or non-anterior wall MI were documented, and their ejection fractions were recorded. The percentage estimation for positive LV thrombi cases was made. Any complications (like stroke or death) that occurred within one year of diagnoses were documented. A Chi-square and t-test determined the association. **Main Outcome Measures:** Detection of LV thrombi. **Sample size:** 125 patients. **Results:** Of the 125 patients, most were men (71.2%) with a mean age of 56.78 years. Eleven patients had left ventricular thrombi (8.8%), and most of these were anterior wall infarctions with low ejection fractions (<40%). Three out of 11 patients with LV thrombi developed complications versus 3 out of 114 without LV thrombi. **Conclusion:** Cardiac MR viability studies can detect LV thrombi in recently reperfused echo-negative STEMI patients. **Limitations:** Retrospective, small sample, single center, use of non-contrast echocardiography.

Keywords: Magnetic Resonance Imaging, Cardiac imaging, Left ventricular thrombus.

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INTRODUCTION

Acute myocardial infarction (AMI) is one of the leading causes of death in the developed world, and it affects nearly 3 million people worldwide and accounts for more than a million deaths annually in the United States [1]; 70% of victims have occlusions from atherosclerotic plaques. Acute MI can be either a non-ST-segment elevation MI (NSTEMI) or ST-segment elevation MI (STEMI). Treatment for STEMI includes immediate reperfusion i.e., emergent percutaneous

coronary intervention (PCI) within 48 hours of admission. This may reduce in-hospital mortality and decrease the length of stay [2]. Acute MI continues to have a high mortality out of the hospital [3]. The risks of cardiovascular events, stroke, and death increase after the acute myocardial event [4], and may be multifactorial [5].

A number of techniques have been available to assess myocardial viability including echocardiography, fluoro-2-deoxyglucose (FDG) positron emission

tomography (PET), and ^{201}Tl single-photon emission computed tomography (SPECT) [6]. More recently, cardiac computed tomography has also been used to identify coronary artery disease (myocardial perfusion imaging), evaluate global LV function and regional wall motion (multi-phase cine imaging), and to detect myocardial scar in myocardial infarction (delayed enhancement imaging) [7]. However, MRI remains the gold standard with its unique capability to provide quantitative information on cardiac function, perfusion and viability [8]. Unlike echocardiography, magnetic resonance imaging (MRI) has no technical limitations due to acoustic window or artifacts related to chest wall with its multiplanar acquisition. MRI also offers more spatial and temporal resolution than nuclear medicine modalities and better tissue characterization.⁷ In addition, MRI does not use ionizing radiation, this is another advantage with respect to other imaging modalities such as computed tomography (CT) or nuclear medicine.

Left ventricular (LV) thrombus is a complication of acute MI and is associated with systemic thromboembolism. Although standard transthoracic echocardiogram (TTE) is commonly used for screening, it is limited by low sensitivity for detection of LV thrombus [9]. Magnetic resonance imaging has a high yield in detection of these thrombi. Anatomic (morphologic) assessment by dark blood and bright blood sequences as well as cardiac function (motion) assessment by Steady-State Free Precession (SSFP)-based bright-blood images of the beating heart are useful for diagnosis. Perfusion imaging (also known as first-pass images) and myocardial viability (or myocardial enhancement study) can add insight [10]. Pre-contrast images are first obtained with first-pass perfusion imaging following injection of a half-dose of gadolinium. After injecting an additional half-dose of gadolinium, delayed images are obtained at 10 and 20 minutes. Ischemic myocardium typically shows delayed enhancement due to increased accumulation of contrast agent in combination with delayed washout over time [11]. Delayed enhancement identifies infarction or fibrotic tissue, while the absence of enhancement indicates viable myocardium, which is likely to improve following revascularization [8].

Although various studies in the literature have focused on the sensitivities and specificities of both TTE and CMR in the detection of LV thrombi after recent acute MI [12], none of these have described ability of CMR to individually identify LV thrombi in patients with negative initial TTE. Therefore, we aim to highlight rate of detection of LV thrombi on contrast enhanced CMR in patients who presented to our cardiac unit with acute MI and had a negative initial TTE.

METHODS

This retrospective observational study was conducted in the Radiology Department at our Hospital

in Dhahran from April 2013 to April 2018. All patients (N=125) who had recent acute myocardial infarctions and negative standard TTEs (for LV thrombi), and who underwent subsequent cardiac MR viability studies (performed within 2 weeks) were evaluated. Patients were referred from the cardiology department and included those with recent STEMI (treated with percutaneous coronary intervention/ PCI) and on dual anti-platelet therapy (Aspirin 100 mg plus Clopidogrel 75 mg once daily). Patients with incomplete or limited MR studies (with artifacts), those with previous cardiac surgeries (or CABG), documented previous history of MI, non-vascularized patients, and those contraindicated to MRI and contrast were excluded. As the study was retrospective and did not involve disclosure of any patient information and privacy, the ethics committee of our Hospital waived the need for patient consent. The study was conducted in accordance with the Helsinki Declaration. All clinical and radiologic information were kept strictly confidential. Literature review was performed through electronic search (Google Scholar, PubMed).

Demographic information about age and gender of all patients was collected. Clinical information and radiographic/ imaging findings were acquired through patients' clinical notes/ Hospital Information System (HIS) and Radiology Information System/ Picture Archiving and Communication System (RIS/ PACS). Information about ejection fractions and type of STEMI (anterior wall or non-anterior wall) were recorded from the clinical notes and echocardiographies. Cardiac MR imaging studies were performed on a 1.5 Tesla scanner machine (General Electric/ GE, Optima 450 W GEM, 2013, Florence, South Carolina, USA), using gadolinium-based contrast agent (Dotarem, 0.2 mmol/kg; Guerbet, France). Imaging included FIESTA (Fast Imaging Employing Steady-state Acquisition) cine, 2 and 4 Chamber (CH) FIESTA sequences (TR/TE, 3.0/1.5 msec; flip angle, 60 degrees), cine IR (inversion recovery, two R-R intervals), single shot (SSh)- early and delayed, phase sensitive (PS) myocardial delayed enhancement (MDE) short axis (SA), 2CH and 4CH 3D MDE images, besides acquiring reformatted (magnitude) SA, 2CH and 4CH MDE images. Images were acquired up to 10 minutes after injection. Total imaging time was about 45-60 minutes.

Cardiac MR imaging studies were interpreted by two readers, one an expert thoracic radiologist and other an experienced general radiologist (each having more than 7 years of experience). The LV thrombus was identified on cardiac MR as a low-signal intensity mass surrounded by high-signal intensity structures such as intracavitary blood or hyper-enhanced (infarcted) myocardium, typically adherent to regions of abnormal wall motion (as seen on cine and confirmed by late DE). Left ventricular thrombus was carefully distinguished from microvascular obstruction (MVO),

which also appears as a dark area in the site of infarction; LV thrombi not completely encompassed by surrounding hyperenhanced myocardium, located adjacent to LV cavity and remain stable size on early and late gadolinium enhancement in contrast to MVO that are seen completely encompassed by hyperenhanced myocardium, located within myocardium, and shrinks with contrast fill-in on gadolinium enhancement [9]. Good inter-observer agreement was noted (with Cohen's kappa value of 0.69), and subsequent consensus reading was done by these two radiologists.

Complications like stroke and death within a period of one year after detection of thrombi were documented. Stroke was defined as new onset focal neurologic deficit caused by ischemia or hemorrhage as seen on imaging (either CT or MRI). Percentage

estimation for detection of LV thrombi on CMR was made. The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS, version 22). Chi-square test and t-test were used to determine association, and p-values less than 0.05 were considered significant.

RESULTS

Out of 125 patients, 89 (71%) were males and 36 (29%) were females, aged between 40-78 years (mean age, 56.78; standard deviation, 8.42).

Left ventricular thrombi were seen in 11 patients (8.8%), of these 9 were having anterior wall infarctions (Table-1). No significant association of LV thrombi with type (location) of infarctions was observed (p value, .36).

Table-1: Distribution of patients with type (location) of infarctions and presence or absence of LV thrombi
Left ventricular thrombi were seen mainly at the apex or along the wall of aneurysm (Figures 1 & 2)

		LV Thrombus		Total number, percentage
		Not Present	Present	
Location	Anterior Wall	78, 89.7%	9, 10.3%	87, 100.0%
	Non-anterior Wall	36, 94.7%	2, 5.3%	38, 100.0%
Total		114, 91.2%	11, 8.8%	125, 100.0%

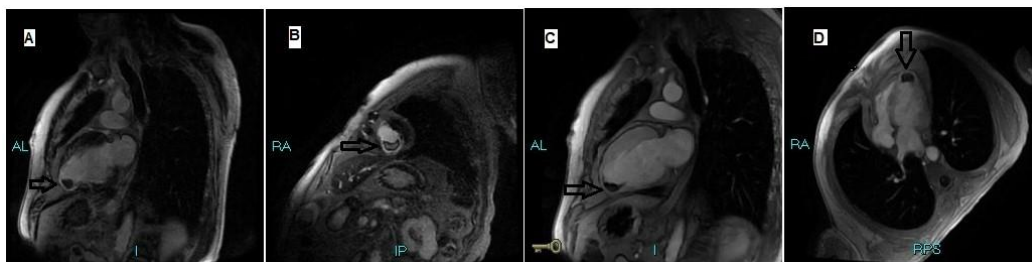


Fig-1: Selected images of CMR in a 62 years old patient showing low intensity LV thrombus at the cardiac apex. A) Long axis vertical 2CH (DGE) view. B) Short axis MDE (DGE) view. C) Long axis vertical 2CH (EGE) view, long inversion time (TI). D) Long axis horizontal 4CH (EGE) view, long inversion time (TI)

Where,

CMR- Cardiac Magnetic Resonance
LV- Left Ventricular
CH- Chamber
MDE- Myocardial Delayed enhancement
DGE- Delayed Gadolinium Enhancement
EGE- Early Gadolinium Enhancement
TI- Time to Inversion

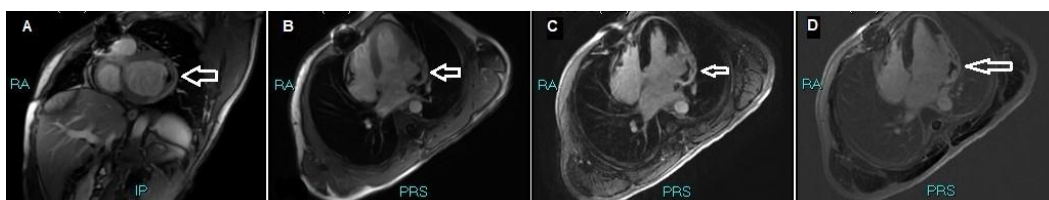


Fig-2: Selected images of CMR in a 40 years old patient showing low intensity LV thrombus along the wall of aneurysm. A) Short axis (EGE) view. B) Long axis horizontal 4 CH (EGE) view. C) Long axis horizontal 4CH MDE (DGE) view. D) Long axis horizontal 4CH (DGE) view, PS

Where,

CMR- Cardiac Magnetic Resonance
LV- Left Ventricular

CH- Chamber
 MDE- Myocardial Delayed enhancement
 DGE- Delayed Gadolinium Enhancement
 EGE- Early Gadolinium Enhancement
 PS- Phase Sensitive

Ejection fractions of less than 40 were observed to be associated with anterior wall location of infarctions (p-value, .0005), while these were not seen significantly associated with LV thrombi (Tables 2 & 3).

Table-2: Distribution of patients by ejection fractions and location of infarctions

		Location of infarction		Total number, percentage
		Anterior wall	Non anterior wall	
		number, percentage	number, percentage	
Ejection Fraction	Less than 40	59, 100.0%	0, 0.0%	59, 100.0%
	41 and above	28, 42.4%	38, 57.6%	66, 100.0%
Total		87, 69.6%	38, 30.4%	125, 100.0%

Table-3: Distribution of patients by ejection fractions and presence of LV thrombi

		LV thrombus		Total number, percentage
		Not present	Present	
		number, percentage	number, percentage	
Ejection Fraction	Less than 40	51, 86.4%	8, 13.6%	59, 100.0%
	41 and above	63, 95.5%	3, 4.5%	66, 100.0%
Total		114, 91.2%	11, 8.8%	125, 100.0%

Complications (stroke, death) were seen significantly associated in patients with LV thrombi patients (p-value, .0005) [Table 4].

Table-4: Distribution of patients by LV thrombi and prognosis

		Prognosis		Total number, percentage
		No complication	Complication	
		number, percentage	number, percentage	
LV thrombus	Not present	11, 97.4%	3, 2.6%	14, 100.0%
	Present	8, 72.7%	3, 27.3%	11, 100.0%
Total		19, 95.2%	6, 4.8%	25, 100.0%

DISCUSSION

Coronary artery disease and MI remain a major cause of global morbidity and mortality, although the incidence of MI related complications has reduced since the introduction of coronary intervention [13]. Prompt identification of acute myocardial event and close monitoring may prevent associated complications. Detailed knowledge of complications and risk factors can help clinicians to adopt early management and better prognosis. Left ventricular (LV) thrombus is a serious complication of STEMI, that is proposed to result from blood stasis after LV dysfunction and altered configuration (aneurysm formation) [14]. The LV thrombi continues to occur in a small but substantial number of such patients especially with anterior wall infarctions. The presence of the thrombus can provide an embolic substrate for future embolic events [3, 4]. Standard TTE has traditionally been used for initial evaluation in these patients. However, echo can be limited or technically difficult for assessment of thrombi at the apex (i.e., close to chest wall) and are usually suspected [15], although contrast enhanced echo has recently been in practice for suspected cases. Nevertheless, an additional modality like cardiac magnetic resonance imaging (CMRI) is still needed to confirm diagnosis.

We used both early and delayed myocardial enhancement (EMR and DME) in cardiac magnetic resonance (CMR) imaging for discerning viable from the infarcted tissue, and also for identification of thrombus (by absence of contrast uptake). Several studies have validated yield of CMR versus echocardiography in terms of improved diagnostic performance [8, 11, 12]. It should be emphasized that improved detection of LV thrombi by DE-CMR over contrast-echo and even cine-CMR is largely attributable to intrinsic feature of imaging technique, evaluating tissue characterization rather than only tissue morphology. In our study, we found an 8.8% incidence of cardiac thrombus on such cardiac MRI studies. Weinsaft JW *et al.*, showed a similar percentage of 8% for MR detected LV thrombi, and observed a high yield of improved thrombus detection by the MRI when compared to echocardiography [15]. They also proposed that apical wall motion and ventricular dysfunction on echocardiogram can be an effective stratification tool for identification of patients to be assessed for contrast enhanced cardiac MRI. Since the introduction of percutaneous coronary intervention (PCI) and more aggressive anticoagulation, the incidence of LV thrombi has reduced from less than

46% to between 4-15% [9], though some studies have seen unchanged incidence even after PCI. Pöss J *et al.*, found an overall prevalence of LV thrombi to be 3.5% among 795 patients who underwent cardiac MRI, and 7.1% in anterior STEMI that correlated with our study results [16]. Meurin P *et al.*, found a 26% incidence of thrombi in 100 patients, 19 of these were seen on MRI, but they included patients with positive transthoracic echocardiography (TTE) as well [9], which we did not include. We also did not document details of PCI or anticoagulation regimes in our patients, however, Meurin P *et al.*, observed LV thrombi in 22.7% of patients who underwent primary PCI versus 50% in others (on anticoagulation). In our study, most of the thrombi were found to be at the apex and along the wall (mural), that are usually missed by echocardiography due to technical reasons of proximity to chest wall and echotextural characteristics respectively. These observations were also highlighted by Meurin P *et al.* in their prospective study, and matched with our findings. It should be noted that we only included (TTE) echo-negative patients, hence could only estimate FN for TTE in our selected subset of patients considering detection of thrombi on repeat echo after the MRI in 60 patients (48%).

In our study, although we found a significant association (p value, .0005) of presence of LV thrombi to complications (like stroke and death) within one year of cardiac event when compared to those who were not having thrombi, yet we believe that such association should only be justified by a multivariate analysis which our study was lacking. Also, we observed a lower EF (less than 40) to be strongly associated with anterior wall infarctions (p value, .0005), but not the with presence of thrombi. Kim J and Weinsaft JW evaluated cardiac MRI studies in 738 patients with STEMI and found that patients with thrombi had lower LV ejection fraction and larger LV volumes [14, 15]. Also, they observed that thrombus related adverse events were strongly associated with heart failure rather than mortality. But they did not specifically mention thrombus location and aneurysmal dilatation. Merkler AE *et al.*, found a 9% short term risk of ischemic stroke in patients with LV thrombus detected on DE-CMR [17]. Takasugi J found prevalence of embolic stroke of undetermined source of about 22% in patients with myocardial infarction or LVEF less than 50; out of these nearly half of these were found to be cardioembolic in origin and 20% were having LV thrombus on cardiac MRI [18]. We found 2 of 3 patients with ischemic stroke and death in one patient within a year of LV thrombus detection. However, it should be noted that several other factors may also be related to such complications, and mere presence of LV thrombi and its correlation may not be over-emphasized. Follow up MRIs were performed in only a few of the survived patients (3 out of 8), that showed either regression or disappearance of thrombus with ongoing antiplatelet therapy. Pop C and his colleagues

observed reduction in ischemic events after dual antiplatelet anticoagulation in patients with acute coronary syndrome [19]. Rizas KD *et al.*, recently presented a novel electrocardiographic phenomenon called periodic repolarization dynamics (PRD) that they found to be a strong predictor of total and cardiovascular mortality in post-infarction patients [20]. Cambroner-Cortinas E *et al.*, found CMR to be helpful in both diagnosis and therapy by guiding the initiation or withdrawal of anticoagulants [21]. Also, they observed that the patients with simultaneous anterior wall infarctions and low EF (less than 50) were at the highest risk of developing LV thrombi, nearly similar to our study results.

Although we did not specifically document microvascular obstruction (MVO), however, we observed this phenomenon in few of the patients. We strongly feel that recognition of this entity by employing first pass (FP), early and late gadolinium enhancement (EGE and LGE) are important to differentiate MVO from thrombus. The hypoperfused area within the infarct seen after 1-2 minutes of contrast administration i.e., early MO has been found closely related to anatomic no-flow region but was smaller than pathologic region [22]. As gadolinium is not pure intravascular agent, it gradually diffuses into initially hypoperfused zone, hence the size of MVO decreases over time, being largest during first pass and smallest during late gadolinium enhancement (termed 'persistent' MO). First pass perfusion sequences (during first minute of gadolinium administration) suffer relatively low spatial resolution and reduced LV coverage resulting in reduced diagnostic sensitivity. Now, ultra-fast inversion-recovery (IR) gradient echo sequences are usually employed to assess MO on both EGE (between 2-4 minutes) and LGE, with the advantages of improved spatial resolution and complete LV coverage [23]. It should also be noted that temporal course of MO may vary in subsequent days to weeks of infarct healing, and may influence LV remodelling. Earlier resolution of MO appears to correlate with improved functional recovery after MI and outcome. Concept of functional (that may resolve more quickly) and structural no-flow (that requires prolonged infarct tissue healing) needs to be kept in mind for better understanding of pathophysiology and appearance on CMR [24]. We did not correlate MVO with clinical outcome, although it has been found to be predictive of clinical outcome [16], either independently or when adjusted with other parameters like infarct size and LV ejection fraction. Presence of hemorrhage (associated with reperfusion injury) with MVO has also been found to be highly correlated with pathologic infarct size [22-24]. Therefore, standardized approach and optimal CMR protocol are advised for acquiring detailed information from CMR.

Other limitations in our study included a small sample, retrospective, and a single center study. Echo-

positive LV thrombi patients were not routinely offered MRI for confirmation, therefore, were not included. Also, we did not mention any PCI in these patients. Follow up MRIs were not performed for every thrombus positive patient that could have documented benefit of on-going treatment plan. Also, catheter angiography (ventriculography) could not be offered or performed for most of our cases (due to patients' preferences and conditions), therefore, MRI sensitivity and specificity could not be specifically determined, and Receiver Operator Characteristic curve could not be plotted as well. We strongly feel that an early echocardiography in 1-2 weeks interval of an acute MI can be helpful in stratifying patients for DE-CMR by identification of apical wall motion, ventricular dysfunction or aneurysm. Such approach should be an essential part of management pathway in any cardiac center or Hospital dealing with MI patients. Documentation of any associated LV thrombus in such patients may help to modify anticoagulation/ treatment regimens and predict cardioembolic complications or death.

CONCLUSION

Left ventricular thrombi can be detected on cardiac MR viability studies in patients with reperfused STEMI and echo-negative patients.

Conflict of Interest

Authors declare that the research was conducted in absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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