2021

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Recommended Citation

Niazi, Azmat Khadija; Kassem, Hoda; Shalaby, Ghada; Khaled, Sheeren; Alzahrani, Muhannad Saleh; Ali, Hassan Mohammad; and Aboulenein, Fatima (2021) "Incidence and Predictors of Left Ventricular (LV) Thrombus after ST-Elevation Myocardial Infarction (STEMI) in the Holy Capital of Saudi Arabia," *Journal of the Saudi Heart Association*: Vol. 33 : Iss. 1 , Article 14.
Available at: <https://doi.org/10.37616/2212-5043.1243>

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Incidence and Predictors of Left Ventricular (LV) Thrombus after ST-Elevation Myocardial Infarction (STEMI) in the Holy Capital of Saudi Arabia

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Abstract

Background: Patients with acute myocardial infarction (AMI) especially those with large MI (myocardial infarction) as identified by ST elevation in multiple contiguous ECG leads or anterior MI, may suffer significant myocardial damage leading to impaired wall motion and contractility which may lead to the formation of left ventricular thrombus (LVT) in the patient. This study was aimed to establish the incidence of LV thrombus and determine the predictors associated with the formation of LV thrombus in patients with AMI.

Methods: This retrospective study was held at the only cardiothoracic centre of Makkah, which provides tertiary level cardiac services. A total of 3084 consecutive patients with acute MI between 2016 and 2019 were identified and divided into two groups i.e. group I (with LVT) and group II (without LVT). The case notes, echocardiography data and cardiac catheterization lab records were reviewed to identify patients with LV thrombus. Regression analysis was employed to evaluate the predictors responsible for the formation of LV thrombus.

Results: The overall incidence for LV thrombus was determined as 8.4% ($n = 260/3084$), while in the subpopulation of pilgrims, it was 8.2% ($83/1001$). Mean age for patients with and without LVT was 54 ± 11 years vs 56 ± 12 years ($p < 0.003$), respectively. There was no significant difference between the two groups with respect to gender, diabetes, hypertension, smoking, Arabic speaking or BMI > 30 . Coronary thrombus aspiration was utilized in 17% vs 12% ($p < 0.023$) patients with LVT and without LVT, respectively. It was observed that the patients with cardiac arrest tend to develop more LVT i.e. 8.5% vs 5.2% ($p < 0.033$). However, LV thrombus formation was significantly associated with anterior STEMI with incidence of LVT reaching 13.4% and low ejection fraction (all MI types) i.e. $32 \pm 9\%$ vs $42 \pm 11\%$, with $p < 0.000$ for both independent predictors.

Conclusions: LV thrombus is a relatively common occurrence in patients with acute MI, especially those with anterior STEMI and low ejection fraction $< 30\%$. Appropriate imaging studies are required for all acute MI patients in order to ascertain the presence or absence of LV thrombus as it has major influence on further management.

Keywords: Left ventricular thrombus (LVT), ST-Elevation myocardial infarction (STEMI), Acute myocardial infarction (AMI), Myocardial infarction (MI), Congestive heart failure (CHF), Primary percutaneous coronary intervention (PPCI), Left main stem disease (LMSD), Triple vessel coronary artery disease (TVCAD)

1. Introduction

According to reports from the World Health Organization (WHO), non-communicable diseases are one of the annual major causes of

death globally. Cardiovascular diseases are the second most common non-communicable diseases and one of the major causes of death i.e. 37% deaths caused by cardiovascular diseases in Kingdom of Saudi Arabia [1]. The development of

Received 2 October 2020; revised 27 February 2021; accepted 2 March 2021.
Available online 30 April 2021

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left ventricular thrombus (LVT) is a recognized complication in a variety of cardiac conditions and the highest rate is observed in acute myocardial infarction (AMI) and congestive heart failure (CHF) secondary to severe left ventricular systolic dysfunction [2, 3] (Figs. 1–3). If formation of LV thrombus leads to cerebrovascular events, then it is a severe and potentially fatal complication especially following ST-segment elevation myocardial infarction (STEMI). Mortality from acute myocardial infarction has decreased markedly since the beginning of primary percutaneous coronary intervention (PPCI) which has proven to be more effective than thrombolytic therapy by showing less mortality rates and lesser clinical adverse events. However, post-infarct complications still lead to morbidity and mortality in a large number of patients. The risk of LV thrombus formation is at its peak during the first 3 months following acute myocardial infarction. The incidence of LV thrombus has been reported to be in the range of 2.9%–15% in western regions [4]. Initial diagnostic modality was conducted using transthoracic echocardiography (TTE), but advances in non-invasive imaging techniques (contrast echocardiography, cardiac CT and cardiac MRI) have improved the sensitivity for diagnosis of LV thrombus. Once diagnosed, the initial management is anticoagulation with warfarin [5]. The prevalence of LV thrombus especially in primary PCI era is apparently reducing with the estimated prevalence rate ranging between 5% and 15% [6,7,9].

Fig. 1. LV Thrombus demonstrated by Transthoracic Echocardiography.

Fig. 2. LV Thrombus demonstrated by Echocardiography with IV contrast agents.

There is limited data available on the exact frequency of LV thrombus in primary PCI treated acute MI patients in Saudi Arabia. In the current retrospective study, we reviewed the incidence of LV thrombus and its associated risk factors in patients presented with acute myocardial infarction who were referred to King Abdullah Medical City (KAMC) Makkah. Because it is located at the holy capital Makkah, we had an opportunity to study the diverse but vulnerable, subpopulation of pilgrims in order to establish the incidence of LV thrombus in addition to the general population. The main objective of current study was to identify predictors so as to establish a strategy for vigilant surveillance of vulnerable groups with repeated screening for LV thrombus and its timely treatment.

Fig. 3. LV Thrombus demonstrated by Cardiac MRI.

2. Material and Methods

This retrospective study was held at the only public sector cardiothoracic centre of the Holy Makkah region which provided tertiary level cardiac services. A total of 3084 consecutive acute MI patients were identified during the period from 2016 to 2019.

2.1. Data Collection

The acute myocardial infarction patients are referred to this centre for further management. The patient's data comprised of those who sustained myocardial infarction and were brought for either primary PCI, post thrombolysis routine PCI (within 1 week of thrombolysis) or late presenter MI, i.e. those patients who presented more than 12 h after onset of symptoms and did not receive any reperfusion therapy. All patients did transthoracic echocardiography within 24–48 h up to 1 week during admission. The echocardiographic finding of LV thrombus refers to this initial echocardiogram conducted during the period of admission.

Demographic, clinical outcomes and echocardiographic data were obtained from the electronic and medical records. Patients with diabetes, hypertension or known smokers were identified from history and case notes. Anterior STEMI was defined as ST segment elevation in precordial leads on initial ECG (electrocardiogram). Left ventricular function was assessed using Simpson's method and 16-segment model was used to score the severity of wall motion abnormality by transthoracic echocardiography. The presence of LV thrombus was evaluated in apical 2 and 4 chamber views and off axis views. LV thrombus was classified into definite or probable types. Definite LV thrombus was defined as a discrete echodense mass in the left ventricular distinct from the endocardium and adjacent to an area of hypokinetic or akinetic myocardium. Probable thrombus was suspected when the images were technically challenging and an echodense mass could not be excluded. For probable thrombus patients, IV contrast echocardiography, cardiac CT or cardiac MRI were assigned and cases were identified as “with LVT” or “without LVT”. (The numeric data is not included in analysis for simplification of study). Coronary angiography, angioplasty and coronary thrombus aspiration were performed by interventional cardiologists as per standard protocols. The cardiac catheterization procedure logs and reports were reviewed for procedural findings and date of procedure. Anticoagulation therapy was initiated by the use of unfractionated heparin or low molecular weight heparin along with warfarin for

therapeutic anticoagulation to achieve the target INR range of 2–3.

2.2. Statistical Analysis

The statistical analysis was performed using SPSS version 20. Data were presented as mean, standard deviation for continuous data and percentages for categorical variables. Baseline and in-hospital characteristics were compared in both groups according to the echocardiographic findings. Univariate analysis was done using *t*-test and chi-squared test for continuous and categorical variables, respectively. A *p* value < 0.05 was considered significant. Regression analysis was applied to determine the predictors for the formation of LV thrombus. Variables with *p* values < 0.1 were retained in the multivariable model.

3. Results

3.1. Key Results

A total of 3084 consecutive patients who met the criteria were included in the analysis. The LV thrombus was detected in 8.4% patients in general, whereas in sub population of pilgrims, the incidence of LV thrombus was established as 8.2%. Anterior STEMI and poor ejection fraction < 30 were recognized as independent and significant predictors associated with the formation of LV thrombus.

3.2. Demographics

Other than age (*p* < 0.003), gender, diabetes, hypertension and smoking were found to be statistically non-significant in both groups. The incidence of LV thrombus in males turned out to be 9% vs 6.2% in female population (*p* < 0.05). There was no major difference of incidence between general population vs pilgrims i.e. 8.2% vs 8.4%. However, it was slightly higher in non-Arabic speakers vs Arabic speakers i.e. 9.3% vs 7.9%. There were no pre-hospital clinical characteristics that differed among the groups. Baseline characteristics in patients with LVT and without LVT are shown in [Table 1](#).

3.3. Infarct Related Characteristics

The prevalence of anterior STEMI for group I and group II was 86.6% vs 52.1% (*p* < 0.001), respectively. Incidence of LV thrombus in patients with anterior STEMI was ascertained as 13.4% (*p* < 0.001). Significantly lower mean LV ejection fraction such as $32 \pm 9\%$ vs $42 \pm 11\%$ was observed (*p* < 0.001) for

Table 1. Baseline clinical characteristics, Infarct related characteristics and Procedure related data in patients With and Without LV Thrombus.

Variables	With LVT n = 260	Without LVT n = 2824	p-value
Age years			
Mean $\pm$ SD	54 $\pm$ 11	56 $\pm$ 12	<0.003
Gender male	229 (88%)	2338 (84%)	<0.053
Arabic speaking	102 (57.3%)	1183 (62%)	0.260
Pilgrims	83 (32.2%)	918 (33.2%)	0.403
Co-morbidities			
DM	146 (56.2%)	1517 (54.1%)	0.289
HTN	137 (52.7%)	1498 (53.5%)	0.431
Smoking	89 (34.2%)	922 (33%)	0.679
BMI <30	72 (27.8%)	790 (29%)	0.399
Infarct Related Characteristics			
Thrombolysis	53 (20.4%)	512 (18.3%)	NS
Late presenting STEMI	29 (11.2%)	345 (12.3%)	NS
Anterior	222 (86%)	1435 (52.1%)	<0.001
2 nd max Trop	115 $\pm$ 199	94 $\pm$ 230	NS
Mean $\pm$ SD			
Procedural Data			
Trans radial	212 (81.5%)	2149 (76.6%)	NS
LMS	10 (3.9%)	79 (2.9%)	NS
TVCAD	39 (15.1%)	437 (15.8%)	NS
Tirofiban	69 (26.6%)	677 (24.3%)	NS
Aspiration	44 (17%)	333 (12%)	NS
Number of stents	1.2 $\pm$ 0.8	1.3 $\pm$ 0.8	NS
Mean $\pm$ SD			

LVT = left ventricular thrombus, SD = standard deviation, NS = non significant, DM = diabetes mellitus, HTN = hypertension, BMI = body mass index, STEMI= ST-elevation myocardial infarction, Trop = Troponin, LMS = left main stem, TVCAD = triple vessel coronary artery disease.

group I as compared to group II, respectively. In a subpopulation of patients with anterior MI and poor EF which comprises of 60% of anterior MI patients, we found out that 25.6% had developed LVT.

The mean value of 2nd maximum troponin I (signifying larger infarct size) was found to be slightly higher in patients with LVT compared to those without LVT (i.e. 115 $\pm$ 199 vs 94 $\pm$ 230, p < 0.184). Categorical analysis for both groups is shown in Table 1.

3.4. Procedural Characteristics

Transradial approach was the preferred approach for PCI in patients with LV thrombus i.e. 82% (p < 0.080). Incidence of LVT in tirofiban administered patients was 9.2%. Use of thrombus aspiration was noticed to be significantly higher in patients with LVT i.e. 17% vs 13% in those without LVT (p < 0.023). No significant association of LV thrombus was documented with mean value of number of stents, left main stem disease and triple vessel coronary artery disease (Table 1).

3.5. Outcomes Characteristics

There was a strong correlation of LV thrombus and the composite end point for major adverse

cardiovascular events (MACE) defined as a combination of cardiogenic shock, pulmonary oedema, intubation ventilation and cardiac arrest during in-hospital stay i.e. 13.4% vs 8.1%, p value < 0.005. To this end, a trend towards significance was observed in post procedural immediate in-hospital clinical outcomes, including cardiogenic shock, intubation ventilation and cardiac arrest. Patients with LV thrombus tend to have higher percentage of occurrence of cardiogenic shock i.e. 7% vs 4% (p < 0.036), pulmonary oedema 4.6% vs 3.4% (p < 0.290), intubation ventilation 7.3% vs 4% (p < 0.151) and cardiac arrest 8.5% vs 5.2% (p < 0.033). Length of stay was

Table 2. In-hospital outcome parameters.

Variables	With LVT n = 260	Without LVT n = 2824	p value
Pulmonary oedema	12 (4.6%)	95 (3.4%)	NS
Cardiogenic shock	18 (6.9%)	113 (4.0%)	<0.036
Intubated ventilated	19 (7.3%)	127 (4.5%)	NS
Cardiac arrest	22 (8.4%)	146 (5.2%)	<0.033
Post PCI EF(%)			
Mean $\pm$ SD	32 $\pm$ 9	42 $\pm$ 11	<0.001
Length of stay (days)	8 $\pm$ 7	5.4 $\pm$ 8	<0.001
Mean $\pm$ SD			

LVT = left ventricular thrombus, NS = non-significant, Post PCI EF = post percutaneous coronary intervention ejection fraction, SD = standard deviation.

Table 3. Independent predictors for LV Thrombus Formation.

Variables	p value
Post PCI_EF	<0.001
Anterior STEMI	<0.001

evaluated to be significantly higher in patients with LVT i.e. 8 ± 7 vs 5.4 ± 8 ($p < 0.000$) (Table 2).

3.6. Multivariate Logistical Regression Model

Regression analysis was performed to assess the formation of LV thrombus by independent predictors. After adjusting for diabetes mellitus, thrombolysis, late presenters and pilgrims, the clinical predictors for an increased risk of LV thrombus formation were recognized as poor EF<30% and anterior STEMI ($p < 0.000$) (Tables 3 and 4).

4. Discussion

The formation of left ventricular thrombus is a dreaded post myocardial infarction complication leading to high risk of thromboembolism especially cerebrovascular accidents [10]. The Virchow's triad is thought to be the main stay of pathogenesis behind formation of LV thrombus. This includes a vicious cycle starting after the combination of blood stasis, which is secondary to LV regional wall akinesia or dyskinesia along with subendocardial damage from prolonged ischemia and a hypercoagulable state which is a main factor of atherosclerosis [8].

Regional data regarding incidence of LVT formation following acute MI in the era of primary PCI is yet to be established. The prime objectives of this study were to identify the incidence and predictors for LV thrombus formation in patients with acute myocardial infarction. Current study which is part of an ongoing project also aimed to support the establishment of practical guidelines for

repeated screening of high-risk cases, utilizing serial echocardiography in post MI patients. The overall incidence of LV thrombus in the current study was 8.4%. Earlier studies from the pre-thrombolytic and thrombolytic eras suggested that LV thrombus had been present in up to 46% of acute MI patients [11]. In the present era, incidence of LV thrombus formation following acute MI is thought to be lower (5%–10%) owing to the widespread use of rapid mechanical reperfusion and potent anti-platelet and anti-thrombotic agents [8,12].

It is worth mentioning that while being located at the holy city of Makkah, pilgrims formed an integral part of our patient's population. The pilgrims are a vulnerable group comprising of participants from all over the world with different risk profiles. They perform religious rituals in highly stressful conditions and in a mass gathering of millions. Yet no specific studies had been carried out in the past to establish the incidence of LV thrombus in this diversified population of pilgrims of Makkah. Regarding our study, the incidence of LVT in pilgrims was determined as 8.2% which was almost similar to the overall incidence in the general population i.e. 8.4%.

Regarding incidence of LV thrombus, our results are in accordance with a recent study from Austin et al. where from an initial yield of 1144 studies, inclusion criteria was met by 19 studies including 10,076 patients across 27 centres in 9 countries. Rate of LV thrombi after all STEMI was 2.7% and 9.1% after anterior STEMI. Current study provided data of regional incidence for LVT based on the reality that although, primary PCI is considered the preferred method of revascularization in patients with myocardial infarction which leads to better salvage of the myocardium [12], there is however, limited data on the incidence of LVT in patients with myocardial infarction in the primary PCI era [14,15].

This study shows higher incidence than Zielinska et al. which diagnosed LV thrombus in 5.4% of acute

Table 4. Detailed regression analysis.

Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.forExp(B)	
							Lower	Upper
Step 1 ^a Age	−0.023	0.007	11.596	1	0.001	0.977	0.964	0.990
PostPCI_EF	−0.058	0.008	56.992	1	0.000	0.943	0.929	0.958
ANT_STEMI (1)	1.471	0.225	42.890	1	0.000	4.356	2.804	6.766
Cardiogenic Shock (1)	−0.019	0.364	0.003	1	0.958	0.981	0.481	2.001
MPV	0.022	0.041	0.286	1	0.593	1.022	0.944	1.107
HbA1C	0.006	0.026	0.052	1	0.820	1.006	0.956	1.059
Constant	−0.275	0.697	0.156	1	0.693	0.759		

Post PCI EF = post percutaneous coronary intervention ejection fraction, STEMI=ST-elevation myocardial infarction.

^a Variable(s) entered on step 1: Age, PostPCI_EF, ANT_STEMI, CardiogenicShock, MPV, HbA1C.

anterior wall MI patients and only 0.3% LV thrombus was diagnosed in non-anterior wall myocardial infarctions, whereas our study shows that the LV thrombus was diagnosed in 13.4% of patients with anterior MI [16].

The percentage of primary PCI was 71% of the patients with Solheim et al. whereas in the current study, PPCI was done in 80% (207/260) of LVT patients [17]. Similar results have been reported in a study that early LV thrombi were detected in 7.1% (21/297) acute anterior MI patients who had been treated with primary PCI [15]. One of the aspects of our study is that the incidence of LV thrombus did not vary significantly between patients treated with primary PCI, thrombolysis or conservatively, which is also endorsed by Solheim et al. Larger infarcts (depicted by higher 2nd Troponin I) are associated with more pronounced myocardial injuries, an increased inflammatory response, extensive wall motion abnormalities and a hypercoagulable state, thereby imposing an increased risk for the formation of mural thrombus [17,20,21].

In accordance with our results, Osheroov et al. also found no difference in the frequency of LVT in patients treated with thrombolysis compared to primary PCI [16]. Similarly, Zielinska et al. also could not prove any influence of the use of glycoprotein IIb/IIIa receptor blockers on the occurrence of mural thrombosis [16,17]. Similarly, Adam et al. identified cardiac arrest as a clinical characteristic independently associated with the development of LV thrombus. The patients with cardiac arrest may have larger infarcts due to proximal vessel location, lack of preconditioning or potentiation of transmural injury due to hypotension. In addition, the transient stasis of blood associated with cardiac arrest may also predispose patients to thrombosis in the arterial system [22,23].

The current study also detected poor ejection fraction <30% and anterior wall MI as a strong predictor of LVT similar to those studies, stating that larger infarcts are associated with more marked myocardial injuries, extensive wall motion abnormalities and a hypercoagulable state so that there is an increased risk for the formation of mural thrombus [12,13,18,19]. Our observation suggests that such patients are a potential risk group for cardio-embolic complications in the primary PCI era [22]. In a similar study by Khouri et al. LVT was diagnosed in second echocardiography and in patients with reduced ejection fraction, $\leq 40\%$ had a repeat test before hospital discharge (days 5–7) [24]. This strategy needs more attention and testing in our centre.

5. Study Limitations

We acknowledge the limitations of this retrospective study regarding selection bias especially referral bias because data comprised of acute myocardial infarction patients who were referred to this cardiac centre for further management. Patients were mainly diagnosed with transthoracic echocardiography, but some cases were also confirmed by IV contrast echocardiography, cardiac CT or cardiac MRI. The data is not comprehensive, therefore, further analysis is required. Another limitation might be the lack of more frequent echocardiographic examinations, including pre-discharge echo (24 h, 5–7 days, and 1 month after acute MI) which may miss about 15%–30% of late LV thrombus formation, occurring at 1–3 months after onset of acute MI [4]. Further studies are required for the use of anticoagulation and outcomes in patients with LV thrombus.

5.1. Suggestions

Delayed LV thrombus formation in patients with myocardial infarction has been demonstrated when echocardiography is performed just prior to discharge or 1–3 months after discharge, so the diagnosis of LV thrombus should be considered during follow-up visits as well. Although, current guidelines state that the need for serial echocardiography in patients with acute myocardial infarction still remains controversial. Routine use of contrast echocardiography in severely reduced ejection fraction may lead to more frequent diagnosis of LV thrombus cases.

5.2. Benefits of this Study/What Does This Study Add to What We Already Know?

First, this study corroborates earlier studies by confirming that the LV thrombus is still a well-known complication in patients with myocardial infarction, despite the use of mechanical reperfusion therapy, potent anti-platelet and antithrombotic therapy. The predictors include poor ejection fraction and anterior STEMI so serial echocardiographic examination is recommended in such cases especially for the diagnosis of LV thrombus cases.

Finally, this study draws attention towards the fact that LV thrombus remains an important complication of myocardial infarction in the contemporary era. In order to prevent potentially devastating thromboembolic complications, this study reminds us to remain vigilant and actively seek LV thrombus, particularly in high risk patients presenting with STEMI prior to hospital discharge.

Author Contribution

Azmat Khadija Niazi: Conception, Supervision, Data Collection And/Or Processing, Analysis And/Or Interpretation, Writer, Critical Review, **Hoda Kassem:** Materials, Data Collection And/Or Processing, **Ghada Shalaby:** Design, **Sheeren Khaled:** Design, Literature Review, **Muhannad Saleh Alzahrani:** Materials, Data Collection And/Or Processing, **Hassan Mohammad Ali:** Supervision, **Fatima Aboulenein:** Conception, Formal analysis And/Or Interpretation, Critical Review.

Conflicts of interest

This study did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors. No conflict of interest was encountered.

Acknowledgement

The author acknowledges the contribution (technical support) of Dr. Javaid Iqbal & Mr. Bilal Munir Ahmad.

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