INCIDENCE, PREDICTORS AND COURSE OF LEFT VENTRICULAR THROMBUS IN INDIAN PATIENTS SURVIVING TO DISCHARGE AFTER ANTERIOR WALL MYOCARDIAL INFARCTION

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ABSTRACT

BACKGROUND

To prospectively estimate the incidence of left ventricular (LV) thrombus over one-year follow-up in patients presenting with anterior wall myocardial infarction (AWMI) and to identify the predictors of LV thrombus, to study the course of LV thrombus including clinically evident thrombo-embolic manifestations over a one-year period in Indian population.

METHODS

Two hundred patients with first AWMI were prospectively and consecutively enrolled. At the time of hospitalization, key demographic and clinical characteristics were collected along with echocardiographic data. Patients were followed up for development or change in existing LV thrombus and thromboembolic event.

RESULTS

Incidence of LV thrombus was 6.5%. The mean platelet volume and LV wall motion score index (LVWMSI) were significantly higher in LV thrombus patients in comparison to non-LV thrombus patients. Baseline ejection fraction (EF), mean mitral E wave deceleration time (MDT) and mean mitral propagation velocity (MVP) were significantly lower in LV thrombus patients. At one-year follow-up, 30.76% patients showed disappearance of thrombus, 46.15% showed decrease in size and 23.07% showed no change in size while 15.38% patients showed embolic events.

CONCLUSIONS

High MPV at admission, low baseline EF, high LVWMSI, low baseline MDT and low MVP are independent predictors of LV thrombus. Moreover, patients undergoing primary PTCA have decreased risk of LV thrombus.

HOW TO CITE THIS ARTICLE: Sajeev CG, Kamra A, Vellani H. Incidence, predictors and course of left ventricular thrombus in indian patients surviving to discharge after anterior wall myocardial infarction. J. Evid. Based Med. Healthc. 2019; 6(15), 1213-1217. DOI: 10.18410/jebmh/2019/252

BACKGROUND

Cardiovascular disease has emerged as the leading cause of death of morbidity and mortality in India with coronary artery disease (CAD) being the major contributor.[1] Of the various presentations of CAD, the ST elevation myocardial infarction (STEMI) is associated with highest degree of morbidity and mortality. Formation of intramural thrombus and subsequent embolization, though rare, has been a significant complication after STEMI.

In STEMI, sub endocardial and endothelial injury along with increased concentration of pro coagulant factors occurs due to prolonged ischemia. On the other hand, blood stasis results due to the akinetic portions of necrotic myocardium. Such situation can be overcome with timely reperfusion which thereby improves myocardial savage, reduces the infarcted area, stimulates recovery of left ventricular (LV) systolic function, and theoretically reduces the risk of LV thrombus formation.[2] Majority of thrombi occur within the first week after STEMI but there are probabilities of significant incidences beyond this period also.[3,4] So, knowledge regarding the incidence of this problem in our population and the possible predictors will be helpful in planning optimal screening and judicious use of anticoagulation drugs.

All of the previous studies have shown consistently higher incidence of LV thrombi following anterior wall MI (AWMI) than inferior wall MI.[5,6] So a screening strategy may be practically more relevant in the selected AWMI patients. Ejection fraction (EF), left ventricular wall motion score index (LVWMSI) and the presence of apical aneurysm are the factors which have retained the predictive value across the studies after multivariate analysis.[7,8] Diastolic function assessed by mitral E wave deceleration time (MDT) has been described as a factor in a study.[9] Mitral valve propagation velocity (MVP) is another factor to look upon, whose effect on LV thrombus has been ambiguous. Effect of mean platelet volume (MPV) on mortality in patients with CAD was studied previously and found that the patients within the highest quintile of MPV had overall increased vascular mortality.[10] MPV has not been studied previously as a

Financial or Other, Competing Interest: None.
Submission 29-03-2019, Peer Review 04-04-2019,
Acceptance 10-04-2019, Published 15-04-2019.
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DOI: 10.18410/jebmh/2019/252

predictor of LV thrombus; this study has attempted to predict its importance.

There are scarce studies looking at the natural history of LV mural thrombus following MI and give variable information regarding the clearance of thrombus on follow-up and also on the incidence of clinically manifested embolic phenomena.[11] The association of embolic phenomena with anticoagulation therapy is also important. Thus, the study aimed to prospectively estimate the incidence of LV thrombus over one-year follow-up in patients presenting with AWMI and to identify the predictors of LV thrombus, to study the course of LV thrombus including clinically evident thrombo-embolic manifestations over a one-year period in Indian population.

METHODS

Study Design and Patient Population

This prospective study included 200 consecutive patients who were admitted to the cardiology department at our Institute with diagnosis of first AWMI. An informed consent was obtained from all patients. Baseline data was collected regarding demographic characteristics, co-morbidities and method of revascularization.

Inclusion criteria were ST elevation in anterior leads within 48 hours before the inclusion, patients surviving beyond 48 hours after admission, echocardiographic examination performed within 5 days of MI. Patients were excluded if they had past history of documented STEMI of any territory, documented wall motion abnormalities, echocardiographically documented preexisting LV dysfunction, patients with documented preexisting intra cardiac thrombus or masses, known pro thrombotic disease state, inadequate transthoracic echo windows, unwillingness to give consent.

Primary outcome was the incidence of left ventricular mural thrombus at the end of one year. Secondary outcomes were incidence of possible embolic complications at the end of one year and disappearance rate of mural thrombi at the end of one year.

Procedure

All examinations were performed with the help of Echo vivid E9 (GE Healthcare, United States) using 2·5 MHz transducer, and stored in video tapes for later analysis. Echoes were acquired in standard parasternal short- and long-axis, apical 2-, 3-, and 4-chamber imaging planes in accordance with American Society of Echocardiography consensus guidelines(8).

Parameters assessed during baseline examination were EF by M mode in PLAX view, EF by Simpsons in apical view, LVWMS), MDT, MVP, presence or absence of left ventricular mural thrombi, site, size and mobility of thrombus.

All examinations were performed by either of the two investigators and recorded. All cases of definite or doubtful thrombi were examined by each other and arrived at consensus. If there was disagreement or doubt after this, images were reviewed by a third examiner and his decision was taken as final. At random, 20 cases were re-examined by another examiner at baseline to find out the inter observer variability.

Follow-Up

All patients clinically followed up for a period of one year, were subjected to trans thoracic examinations like two-dimensional and Doppler echocardiography at baseline (within 5 days of admission), at the end of three months, at the end of six months and one year. All patients were asked about possible embolic manifestations during follow up examinations or telephonically every three months till the end of one year. Any such event was verified by examination of hospital records. During the follow-up examinations, only the presence or absence of mural thrombus and the change in size of the preexisting thrombus was noted down.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation and categorical variables as counts and percentages. Student's t-test was applied to calculate the difference between the groups. All data were analysed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15.

RESULTS

Two hundred patients of AWMI included in the study, had mean age of 60 years. Of these total males were 149(74.5%) and females were 51(25.5%). Type 2 diabetes mellitus was found in 68 (34.0%) patients, hypertension in 70 (35.0%) patients and prevalence of smoking was found to be in 25.5% population (Table 1). LV thrombus was present in 13 of 200 patients accounting to 6.5%.

Variables	Patients (N = 200)
Age (Mean, Years)	60
Male, n (%)	149 (74.50%)
Diabetes Mellitus, n (%)	68 (34.00%)
Hypertension, n (%)	70 (35.00%)
Current Smoker, n (%)	51 (25.50%)
Presence of LV Clot, n (%)	13/200 (6.50%)
Table 1. Baseline Demographics of Patients	
LV- Left Ventricle	

Total 67 out of 200 patients underwent primary angioplasty out of which only 1 patient developed LV thrombus($p < 0.05$) which represent that patients undergoing primary angioplasty were on lower risk of LV thrombus.

On evaluating different parameters included in the study and their relationship with LV thrombus, it was observed that MPV was 10.55 fl in LV patients while it was 8.67 fl in non-LV thrombus patients ($p < 0.001$) which showed that high MPV was associated with increased risk of LV thrombus. Mean baseline EF was 34.23% in LV thrombus patients while it was 51.2% in non-LV thrombus patients ($p < 0.001$) which showed that baseline low EF was associated with increased risk of LV thrombus. Mean MDT and MVP in

LV thrombus patients were 134.69 m/s and 42.92 m/s, respectively while in non-LV thrombus patients mean MDT and MVP were 156.76 m/s and 52.32 m/s, respectively (p <0.001), showing that diastolic dysfunction was associated with increased chance of LV thrombus. Higher LVWMSI in LV thrombus patients (2.04) in comparison to non-LV thrombus patients (1.22) was statistically significant (p <0.001) suggesting that higher LVWMSI was associated with increased chance of LV thrombus (Table 2).

Parameters	Left Ventricular Thrombus		t Value	p Value
	Positive (n=13)	Negative (n=187)		
	Mean ± SD	Mean ± SD		
MPV	10.55 ± 1.82	8.67 ± 0.54	9.89	<0.001
EF (%)	34.23 ± 6.15	51.20 ± 7.80	7.67	<0.001
MDT (ms)	134.69 ± 13.47	156.76 ± 10.53	7.16	<0.001
MVP (m/s)	42.92 ± 4.92	52.32 ± 4.36	7.45	<0.001
LVWMSI	2.04 ± 0.36	1.22 ± 0.28	9.87	<0.001

Table 2. Assessment of Echocardiographic Parameters in All Patients

MPV- Mean Platelet Volume; EF- Ejection Fraction; MDT- Mitral E Wave Deceleration Time; MVP- Mitral Valve Propagation Velocity; LVWMSI- Left Ventricular Wall Motion Score Index

All 13 patients with LV thrombus were treated with oral anticoagulation together with dual antiplatelet therapy, bridging with heparin until a therapeutic international normalised ratio (INR) was reached. While assessing fate of LV thrombus, it was found that disappearance rate of LV thrombus within one year was 30.76%, while decrease in size was noted in 46.15% patients and no change in size of LV thrombus was noted in 23.07% (Table 3). In all patients with LV thrombus apex was either akinetic or dyskinetic with no patients having normal apex and in all patients LV thrombus was located at apex. In this study, two out of thirteen patients (15.38%) having LV thrombus developed embolic event with one patient having transient ischemic attack, while one patient had right sided cerebrovascular accident.

Outcomes	Patients with LV Thrombus (n = 13)
LV Thrombus Size (mean, mm)	22 x 12.9
Apical Site, n (%)	13 (100%)
Appearance of Thrombus in < 7 days, n (%)	11 (84.61%)
Disappearance within One Year, n (%)	4 (30.76%)
Decrease in Size Within One Year, n (%)	6 (46.15%)
No Change, n (%)	3(23.07%)
Embolic Events, n (%)	2 (15.38%)

Table 3. Course of Left Ventricular Thrombus During One Year

LV- Left Ventricle

DISCUSSION

Incidence

Previous studies show highly variable incidence of LV thrombi after STEMI.[7] Our study showed incidence of 6.5%. This is parallel with many previous post thrombolytic studies; in study done by Gianstefani S et al.[2] incidence was 4% while in contrary, in study done by Okuyan E, et al.,[12] the incidence was 42.85%. The variability of incidences poses to be depending on the geographical differences or various other environmental factors which might lead to such wide ranges of incidence on considering different population.

Predictors

Type 2 diabetes has been associated with endothelial dysfunction and increase in inflammatory markers,[13] so theoretically it seems to be a good predictor of occurrence of LV thrombus. Type 2 diabetes was studied in many previous studies to check its association with LV thrombus. In a study by Okuyan E, et al., type 2 diabetes was found to be statistically significant (p = 0.04) predictor of LV thrombus when compared to non-diabetics.[12] On contrary, in our study, it was found that role of type 2 diabetes was not statistically significant (p = 0.72) in predicting occurrence of LV thrombus. These results were consistent with study done by Gianstefani S et al. and Solheim S et al, both of those studies failed to show type 2 diabetes as a reliable predictor of LV thrombus.[2,14]

Checking gender as a predictor of LV thrombus we found that it was not associated with increased risk of LV thrombus (p = 0.835). It was consistent with previous studies done by Okuyan E, et al.,[12] Gianstefani S, et al.[2] and Solheim S, et al.[14]

While studying effect of thrombolysis on formation of LV thrombus we found that thrombolysis with SK failed to decrease the risk of LV thrombus formation, it was found to be not statistically significant when compared to patients who were not thrombolysed. It was consistent with the work done by Vaitkus and Barnathan, they were not able to demonstrate a statistical difference in the incidence of LV thrombus formation.[15] We found that patients who underwent primary PCI had significantly less chance of development of LV thrombus (p <0.05). There is no head to head comparison in literature between patients undergoing PCI or not undergoing but studies in which patients who underwent PCI showed less incidence as compared to non PCI studies.[16]

While assessing different echocardiographic parameters as predictors of LV thrombus, it was found that diastolic dysfunction i.e. decreased MDT and MVP was associated with increased risk of LV thrombus (p <0.001). Deceleration time was previously studied by Okuyan E, et al., they found that Doppler-derived MDT was significantly lower in patients with LV thrombus than without LV thrombus (127.34 ± 39.07 vs. 155.26 ± 44.61 ms; p = 0.007).[12] The MVP has not been studied as a predictor of LV thrombus in previous studies.

In this study we found that higher LVWMSI was associated with increased chance of LV thrombus. The

results of present study have been in persistence with results of previous studies stating the association of WMSI with LV thrombus formation.[9,17] The WMSI shows severity of LV systolic dysfunction, so it is reasonable to see high incidence of LV thrombus in patients with low EF. In present study, mean baseline EF was significantly lower in LV thrombus patients ($p < 0.001$). This factor has also been consistently shown to be associated with increased risk of LV thrombus in most of previous studies on LV thrombus.[2,12]

Literature states that platelet size and activity are correlated, and mean platelet volume (MPV) increases before acute myocardial infarction.[14] However, association of this factor with LV thrombus has not been studied previously. Thus, to the best of our knowledge, this is the first study to assess the association of higher MPV with LV thrombus. It was found that MPV was higher in LV thrombus patients than in non-LV thrombus patients ($p < 0.001$) which depicted that high MPV was associated with increased risk of LV thrombus.

Characteristics and natural history of LV thrombus

In this study mean size of LV thrombus was 22 X 12.9 mm, most of thrombus appeared within 7 days of myocardial infarction (11/13) and it is consistent with previous study which stated that maximum incidence of LV thrombus occurred within one week (>75%) after MI.[18]

In present study, LV thrombi in all patients were located at the apex. But, in general, the site of thrombus formation has been widespread and not exclusively located apically; approximately 11% occurs at the septal wall and 3% at the inferoposterior wall.[19]

While checking the fate of LV thrombus it was observed that disappearance rate of LV thrombus within one year was 30.76%, while decrease in size was noted in 46.15% patient and no change in size of LV thrombus was noted in 23.07% patients. Study done by Stratton JR, et al., stated that among 60 patients, LV thrombi were unchanged in 24 (40%), completely resolved in 24 (40%), decreased in size in four (7%), increased in size in five (8%), and decreased and then increased in size in three (5%) patients.[7]

In this study, two out of thirteen patients (15.38%) having LV thrombus developed embolic event with one patient having TIA while another patient had right sided CVA. In a study by Keren A, et al.,[6] systemic embolism was found in six (17%) out of the 35 patients with thrombus, while study by Stratton JR, et al., reported that among 60 patients of LV thrombi, definite systemic emboli occurred in seven patients (12%).[7]

CONCLUSIONS

In light of results of the study, parameters like MPV at admission, baseline EF, LVWMSI, baseline MDT and MVP have been the independent predictors of LV thrombus while patients undergoing primary PTCA had decreased risk of LV thrombus. Thus, assessment and thereby consideration of these parameters might pose a good prognostic effect on patients after first anterior wall myocardial infarction.

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