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ORIGINAL ARTICLE

Association between Left Ventricular Thrombus Formation and Adverse Outcomes in Acute Anterior Myocardial Infarction Patients who had Undergone Primary Percutaneous Coronary Intervention

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ABSTRACT

Aim: To investigate the association between left ventricular thrombosis (LVT) and adverse cardio-cerebrovascular events in anterior acute ST segment elevation myocardial infarction patients who had undergone primary percutaneous coronary intervention.
Study design: A retrospective study.
Study place and duration: From 22nd Oct 2020 to 22nd Oct 2021 at the Cardiology department of Ch.Pervaiz Elahi Institute of Cardiology Multan.
Methodology: The study included patients who were identified with anterior acute ST segment elevation myocardial infarction and received primary percutaneous intervention within the first 12 hours following onset. Patients were specifically evaluated for being treated with oral vitamin K antagonists (VKA) at discharge along with their assessment of the international normalized ratio (INR). The primary endpoint was considered as the occurrence of major cardio-cerebrovascular events, the secondary endpoint was the resolution of thrombus in LVT patients within 1 year.
Results: 4(6.6%) patients were diagnosed with LVT within a month after disease onset and 56(93%) without LVT. During one year follow up, 6(10%) patients without LVT and 1(22%) patient with LVT had gone through MACCE event at least once. According to univariate analysis, LVT is related to an increase in the risk of MACCE events. The rate of heart failure differed significantly (OR = 3.42, 95% CI (1.3-4.6)). Within a year of onset, LVT was an independent predictor of MACCE (HR =2.3, 95% CI (1.11-6.40)). Moreover, in patients with INR ≥ 2 risk of MACCE was less as compared to those with INR < 2.
Conclusion: LVT is an independent predictor of 1 year adverse cardio-cerebrovascular events in subjects with ant-AMI who had undergone PPCI. Within therapeutic range ≥2 treatment consists of triple therapy. It can potentially reduce the rate of MACCE events and increase the dissolution of the thrombosis.
Keywords: Left venous thrombosis, anterior myocardial infarction, adverse coronary outcomes, primary cutaneous infarction,

INTRODUCTION

Left ventricular thrombosis (LVT) commonly results from anterior acute ST segment elevation myocardial infarction (ant-AMI). According to the studies, 40% to 60% of patients with LVT had ant-AMI[1]. Although primary percutaneous coronary intervention (PPCI) greatly helps in the reduction of infarct area and development of LVT, 4-15% of cases with ant-AMI still report thrombus formation even after receiving PPCI[2,3,4].

Currently, molecular mechanisms underlying LVT formation are not known. Generally, abnormal blood flow stasis, endocardium injury, trigger in inflammatory reactions, and extended coagulation period during myocardial infarction (MI) are some of the major reasons that are associated with LVT. Even if the MI is treated, factors such as anterior wall MI and a larger infarct area continue to pose the risk of LVT[5,6]. The occurrence rate of LVT is higher in patients having left ventricular ejection fraction (LVEF) less than 40% when compared to those having normal LVEF. Moreover, ant-AMI patients with LVEF < 40% are at a greater risk of LVT formation as high as 17.8%[7].

Among the major hazards of LVT, systemic embolism is reported to cause serious disabilities and is even cause fatality without any prominent warning signs. According to a study,16.3% of LVT patients suffered from systemic embolism in a period of around 5-years[8]. Furthermore, more patients with LVT suffer from in-hospital mortality than those with cardiac diseases but no venous thrombosis[9].

Given the high complication and mortality rate associated with LVT, it is pertinent to explore the adverse events associated with LVT, so that on-time and effective management of patients. Therefore, the present study was designed to investigate the association between LVT and adverse cardio-cerebrovascular events in ant-AMI patients who had undergone PPCI.

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METHODOLOGY

This retrospective study was conducted from 22nd Oct 2020 to 22nd Oct 2021 at the Cardiology department of Ch.Pervaiz Elahi Institute of Cardiology Multan. The study included patients who were identified with ant-AMI and received primary coronary intervention within the first 12 hrs. following onset of infarction. An ant-AMI was characterized as the coexistence of characteristic chest pain with elevated ST segment and the presence of myocardial necrosis markers[10]. The LFT diagnosis was carried out independently by two trained cardiologists.

The follow-up data of the patients were obtained from the hospital registry and the significant clinical consequences were confirmed by patients through phone calls. The patients with missing follow-up data were excluded from the study. All included participants were informed of study objectives and their consent was sought. Similarly, ethical consent was taken from the ethical committee of the hospital. Patients were specifically evaluated for being treated with oral vitamin K antagonists (VKA) at discharge along with their assessment of the international normalized ratio (INR). An INR value of 2 or above was considered normal as per guidelines[11]. A significant bleeding event was characterized as the one with following attributes: intraocular/ intracranial hemorrhage, fall in hemoglobin level by more than 4g/dl, hematoma of greater than 5cm, or the cases who required blood transfusion[12].

The primary endpoint was considered as the occurrence of major cardio-cerebrovascular events such as congestive heart failure, revascularization, non-fatal stroke, non-fatal myocardial reinfarction or all-cause death within one year after onset. Whereas, the secondary endpoint was the resolution of thrombus in LVT patients within 1 year.

Statistical analysis: SPSS version 21.0 was used for statistical analysis. Continuous variables were represented as median with interquartile range or mean along with standard deviation. Whereas, categorical variables were represented as frequency and percentages. The student's t-test was used for the univariate comparison of continuous variables while the χ 2 test was for used categorical variables. Association between LVT and adverse outcomes was assessed through logistic regression analysis. Independent risk factors of adverse cardio-cerebrovascular events were computed by applying a cox proportional hazard regression. The log-rank test was used to calculate differences in secondary and primary outcomes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The median age of the patients was 60 years. 35 subjects were male. 4(6.6%) patients were diagnosed with LVT within a month after disease onset. Upon first TTE examination, subjects with LVT had lower LVFF as compared to subjects without LVT, higher Killip classification, higher levels myocardial enzymes, and long ischemic duration (Table 1).

Moreover, subjects with LVT had more frequent lesions in the left anterior descending branch (LAD) and pre-angioplasty TIMI flow grade ≤ 1 as compared to those without LVT. Among subjects with LVT, 1 (25%) was given VKA therapy while 3(75%) were given "triple therapy" (VKA, clopidogrel, and aspirin) following or at the time of discharge. Non-VKA oral anticoagulants were not prescribed to any of the patients.

There was no difference in the prescription of an angiotensin converting enzyme inhibitor (ACEI), dual antiplatelet therapy, statins, and beta-blockers between the two groups. Patients were LVT were prescribed mineralocorticoid receptor antagonists more frequently (P<0.05). During one year follow up, 6(10%) patients without LVT and 1(22%) patient with LVT had gone through the cardio-cerebrovascular event at least once. In the LVT group, the incidence of MACCE was much higher as compared to the non-LVT group (Table I).

Major bleeding occurred in 1(25%) patient with LVT and 11(20%) patients without LVT. The incidence of major bleeding events did not differ significantly between both groups. However, in subjects with LVT, rate of major bleeding showed increasing trend.

Individual components of the cardio-cerebrovascular event were also examined. The rate of heart failure differed significantly (OR = 3.42, 95% CI (1.3-4.6)). However, other components of the cardio-cerebrovascular event did not differ significantly. Moreover, for those with LVT incidence of stroke showed an increasing trend (OR = 2.1, 95% CI (1.0-6.0) (Table II). Within a year of onset, LVT was an independent predictor of the cardio-cerebrovascular event (HR = 2.3, 95% CI (1.11-6.40). 24 hour LVEF, age, and peak value of creatine kinase were other independent predictors. (Table III)

Table I: Clinical features in patients with and without LVT (n=60)

Postangioplasty TIMI flow grade≤ 1	1 (25%)	7 (12%)	.19
Proximal left anterior descending coronary artery lesion	2 (62%)	28 (51%)	.03
Treatment at discharge			
Dual antiplatelet therapy	3 (75%)	40 (72%)	.56
Oral anticoagulant	2 (50%)	3 (5.3%)	<.001
Triple therapy	3 (75%)	3 (4.6%)	<.001
ACEI	1 (25%)	16 (28%)	.306
Beta blockers	2 (50%)	30 (52%)	.44
Statins	3 (75%)	43 (76%)	.56
MRA	1 (25%)	9 (16%)	<.001
Clinical results after a year			
MACCE	1 (25%)	6 (10%)	<.001
Congestive heart failure	2 (50%)	21 (38%)	.001
Reinfarctions	2 (50%)	26 (47%)	.723
Revascularization	1 (25%)	18 (32%)	1.00
Stroke	2 (50%)	14 (25%)	.125
Major bleeding	1 (25%)	11 (20%)	.055

Abbreviation: ACEI =angiotensin converting enzyme inhibitor, MACCE= major adverse cardio- cerebrovascular events, MRA=mineralocorticoid receptors antagonists, TIMI=thrombolysis in myocardial infarction.

Two patients with LVT had INR ≥ 2, among them 1 suffered from cardio-cerebrovascular events within a year. 2 patients with LVT had INR <2 and both of them suffered a cardio-cerebrovascular event within a year. In patients with INR ≥ 2 risk of the cardio-cerebrovascular event was less as compared to those with INR < 2. However, the incidence of stroke and major bleeding did not differ significantly.

Table II: Univariate Analysis for MACCE (N=60)

	MACCE event in pts with LVT	**OR**	**95% confidence interval**	***P*-value**
MACCE	1 (25%)	2.4	1.36-4.22	<.001
CI Congestive heart failure	2 (50%)	3.42	1.3-4.6	.001
Reinfarction	2 (50%)	1.34	.54-3.45	.724
Revascularization	1 (25%)	.92	.19-4.3	1.00
Stroke	2 (50%)	2.08	.81-5.6	.125

Table III: Multivariate analysis of predictors of MACCE in subjects with LVT (n=60)

	Hazard ratio	**95% Confidence interval**	***P-value***
LVT	2.30	2.11- 5.40	.020
LVEF	2.05	0.98-3.26	.013
Peak creatine kinase	2.1	1.06- 3.87	.005
Age	0.009	0.06- 2.05	.007

DISCUSSION

In this study, ant-AMI patients who were treated with PPCI were examined to analyze the incidence of LVT. Out of a total of 60 patients, 4 had LVT within a month of disease onset. In another study, 429 ant-AMI subjects who had undergone PPCI were analyzed, results showed that 18 patients had LVT within seven days of disease onset[3]. Another study was conducted on patients with AMI treated with PPCI, results showed a 15% incidence of LVT[4]. Studies have shown that during the PCI period prevalence of LVT is significantly lowered. In another study including 1734 patients with STEMI, the incidence of LVT lowered from 7.3% to 3.3% within ninety days[13].

In our study, subjects with LVT had greater ischemia time, greater values of myocardial enzymes, and worse cardiac functions as compared to those without LVT. Previous studies have also shown heart failure, longer duration between symptom onset and PPCI, and large infarct size are also related to greater risk of LVT[2]. Hypertension, left ventricular systolic dysfunction and flow grade ≤ 1 before angioplasty also are predictors of LVT[14].

STEMI results in myocardial ischemia, endocardium necrosis, endothelial injury, increase in coagulant stimulating factors, and intense inflammatory response. In necrotic myocardium, abnormal movement of the ventricular wall results in blood coagulation particularly left ventricular apex[15]. The risk of mural thrombus formation is increased by these factors. Myocardial blood supply is improved by emergency reperfusion, it also saves stunned myocardium, increases recovery of left ventricular systolic function, reduces infarct size, and decreases the risk of LVT.

Our study shows that subjects with LVT had 2.28 times greater risk of 1-year MACCE as compared to those without it. Moreover, the incidence of reinfarction and stroke was also noted in LVT patients, though it was not significant statistically. Lack of significance can be due to less follow-up period and low incidence. Among different adverse events, an increase in the rate of congestive heart failure is most prominent in subjects with LVT. There is doubt about the cause and effect relation between LVT and heart failure[16]. However, according to our study, LVT is suggestive of harmful events despite aggressive drug and reperfusion therapy.

Oral anticoagulants along with dual antiplatelet therapy are recommended for subjects with AMI having LVT. In the above study, 3 subjects with LVT were treated using VKA. 2 patients reached INR ≥ 2. The results revealed that patients with INR more

than 2 have less incidence of stroke than those with INR < 2. These results are also confirmed by 7 other studies that show that giving anticoagulant therapy for six months significantly reduces the risk of embolism[17], though few disadvantages may be seen. A study showed that patients receiving PCI along with triple therapy (dual- antiplatelet therapy and oral anticoagulation) had greater bleeding incidence within 1 year as compared to those receiving dual treatment (clopidogrel and oral anticoagulation)[18]. In patients with combined anti-platelet therapy and oral anticoagulants risk of bleeding events range from 4% to 16%. In our study, in patients with LVT having INR ≥ 2 incidence of bleeding is 7.7%. This result is following the prior studies.

CONCLUSION

LVT is an independent predictor of adverse cardio-cerebrovascular outcomes in subjects with ant-AMI who had undergone PPCI. Within therapeutic range ≥2 treatment consists of triple therapy. It can potentially reduce the rate of MACCE events and increase the dissolution of the thrombosis.

Conflict of interest: Nil

Authors contribution: MHA conceived, designed and did statistical analysis, **MSA** did data collection and manuscript writing, **HAS** did review and final approval of manuscript, **AMS** did editing of manuscript

REFERENCE

1. Lee SH, Lee S-R, Rhee K-S, Chae J-K, Kim W-H. Usefulness of myocardial longitudinal strain in prediction of heart failure in patients with successfully reperfused anterior wall ST-segment elevation myocardial infarction. Korean Circulation Journal. 2019;49(10):960-72.
2. Mao TF, Bajwa A, Muskula P, Coggins TR, Kennedy K, Magalski A, et al. Incidence of left ventricular thrombus in patients with acute ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. The American journal of cardiology. 2018;121(1):27-31.
3. Bulluck H, Chan MH, Paradies V, Yellon RL, Ho HH, Chan MY, et al. Incidence and predictors of left ventricular thrombus by cardiovascular magnetic resonance in acute ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention: a meta-analysis. Journal of Cardiovascular Magnetic Resonance. 2018;20(1):1-10.
4. Ram P, Shah M, Lo KB, Figueredo V. Reply: surprisingly low incidence of left ventricular thrombosis in anterior ST-segment elevation myocardial infarction. Clinical Cardiology. 2018;41(10):1298.
5. Caro-Dominguez P, Yoo S-J, Seed M, Grosse-Wortmann L. Magnetic resonance imaging of cardiovascular thrombi in children. Pediatric Radiology. 2018;48(5):722-31.
6. Chaosuwannakit N, Makarawate P. Left Ventricular Thrombi: Insights from Cardiac Magnetic Resonance Imaging. Tomography. 2021;7(2):180-8.
7. Weinsaft JW, Kim HW, Crowley AL, Klem I, Shenoy C, Van Assche L, et al. LV thrombus detection by routine echocardiography: insights into performance characteristics using delayed enhancement CMR. JACC: Cardiovascular Imaging. 2011;4(7):702-12.
8. Maniwa N, Fujino M, Nakai M, Nishimura K, Miyamoto Y, Kataoka Y, et al. Anticoagulation combined with antiplatelet therapy in patients with left ventricular thrombus after first acute myocardial infarction. European heart journal. 2018;39(3):201-8.
9. McCarthy CP, Vaduganathan M, McCarthy KJ, Januzzi JL, Bhatt DL, McEvoy JW. Left ventricular thrombus after acute myocardial infarction: screening, prevention, and treatment. JAMA cardiology. 2018;3(7):642-9.
10. Aguilera-Alvarez V, Odeyinka O, Lopez A. Role of thrombotic thrombocytopenic purpura in myocardial infarction for elevation of ST segment. Journal of Advanced Medical and Dental Sciences Research. 2021;9(10):62-6.
11. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology. 2014;64(21):e1-e76.
12. Ozaki Y, Hara H, Onuma Y, Katagiri Y, Amano T, Kobayashi Y, et al. CVIT expert consensus document on primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) update 2022. Cardiovascular intervention and therapeutics. 2022:1-34.
13. Garber AM, Mentz RJ, Al-Khalidi HR, Shaw LK, Fiuzat M, O'Connor CM, et al. Clinical predictors and outcomes of patients with left ventricular thrombus following ST-segment elevation myocardial infarction. Journal of thrombosis and thrombolysis. 2016;41(3):365-73.
14. Rodriguez JBC, Okajima K, Greenberg BH. Management of left ventricular thrombus: a narrative review. Annals of Translational Medicine. 2021;9(6).
15. Li XY, Su GH, Wang GX, Hu HY, Fan CJ. Switching from ticagrelor to clopidogrel in patients with ST-segment elevation myocardial infarction undergoing successful percutaneous coronary intervention in real-world China: occurrences, reasons, and long-term clinical outcomes. Clinical cardiology. 2018;41(11):1446-54.
16. Gianstefani S, Douiri A, Delithanasis I, Rogers T, Sen A, Kalra S, et al. Incidence and predictors of early left ventricular thrombus after ST-elevation myocardial infarction in the contemporary era of primary percutaneous coronary intervention. The American journal of cardiology. 2014;113(7):1111-6.
17. Vaitkus PT, Barnathan ES. Embolic potential, prevention and management of mural thrombus complicating anterior myocardial infarction: a meta-analysis. Journal of the American College of Cardiology. 1993;22(4):1004-9.
18. Smits PC, Frigoli E, Tijssen J, Jüni P, Vranckx P, Ozaki Y, et al. Abbreviated antiplatelet therapy in patients at high bleeding risk with or without oral anticoagulant therapy after coronary stenting: an open-label, randomized, controlled trial. Circulation. 2021;144(15):1196-211.