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Surrogates of the Left Ventricular Thrombus Resolution: A Retrospective Data Review

Sol Ventrikül Trombüs Rezolüsyonunun Göstergeleri: Retrospektif Veri Analizi

ABSTRACT

Objective: The left ventricular thrombus is one of the serious complications of ischemic cardiomyopathy. In this study, we aimed to search for the independent factors to predict the resolution of left ventricular thrombus.

Methods: This retrospective study included all patients with coronary artery disease, aged above 18 years old, and with the thrombus at the apical location of the left ventricle. Demographic, clinical, and echocardiographic characteristics of the patients were recorded. Major adverse cardiovascular events developed within the follow-up period were recorded. The time in the therapeutic range of each patient was calculated. The presence of left ventricular thrombus beyond 180 days despite warfarin usage was classified as persistent left ventricular thrombus.

Results: The study included 174 subjects (169 males and 5 females). The mean age of the study population was 54.5 ± 11.0 years. The number of patients in whom the left ventricular thrombus resolved with treatment in less than 180 days was 56 (32.2%). Median anticoagulation time in the study population was 252 [150-480] days and the meantime in the therapeutic range of the patients was 54 ± 19%. The time in therapeutic range value of the groups was similar ($P = .593$). It was found that concomitant clopidogrel use ($P = .003$) and left ventricular thrombus area ($P < .001$) were the independent predictors of left ventricular thrombus resolution within less than 180 days in the logistic regression analysis.

Conclusion: Concomitant use of clopidogrel was found to be associated with left ventricular thrombus resolution but left ventricular thrombus size was related to left ventricular thrombus persistency. Although standard 3-6 months of anticoagulation is advised for left ventricular thrombus, considering the presence of these predictors in such patients may guide the physicians to individualize the treatment.

Keywords: Left ventricular thrombus, coronary artery disease, echocardiography, clopidgrel, warfarin

ÖZET

Amaç: Sol ventrikül ventrikül trombüsü iskemik kardiyomiyopatinin ciddi komplikasyonlarından biridir. Bu çalışmada, sol ventrikül trombüsünün rezolüsyonunu tahmin eden bağımsız faktörlerin araştırılması amaçlanmıştır.

Yöntemler: Bu retrospektif çalışmaya, 18 yaş üstü koroner arter hastalığı ve sol ventrikül apikal yerleşimli trombüsü olan tüm hastalar dahil edilmiştir. Hastaların demografik, klinik ve ekokardiyografik özellikleri kayıt edildi. Takip süresince ortaya çıkan majör olumsuz kardiyovasküler olaylar kaydedildi. Her bir hastanın törapötik aralıkta geçirdiği zaman hesaplandı. 180 günden daha fazla süreyle varfarin kullanımına rağmen sol ventrikül trombüsü mevcudiyeti, persistan sol ventrikül trombüsü olarak sınıflandırıldı.

Bulgular: Çalışmaya 174 hasta dahil edildi (169 erkek ve 5 kadın). Çalışma popülasyonunun ortalama yaşı 54,5 ± 11,0 yıldı. Sol ventrikül trombüsünün tedavi ile 180 günden daha kısa süre içinde ortadan kalktığı hastaların sayısı 56 (%32,2) idi. Çalışma popülasyonunda medyan antikoagülasyon zamanı 252 [150-480] gündü ve hastaların ortalama törapötik aralıkta geçirdiği zaman %54 ± 19 idi. Gruplar arasında törapötik aralıkta geçirdiği zaman aralığı benzerdi ($P = 0,593$). Lojistik regresyon analizinde, eş zamanlı klopidogrel kullanımı ($P = 0,003$) ve sol ventrikül trombüs alanının ($P < 0,001$) 180 günden daha kısa süre içinde sol ventrikül trombüsü rezolüsyonunun bağımsız prediktörleri olduğu saptandı.

Sonuç: Eş zamanlı klopidogrel kullanımının sol ventrikül trombüs rezolüsyonu ile ilişkili olduğu buna karşın sol ventrikül trombüs büyüklüğünün sol venrikül trombüs persistansı ile ilişkili

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KLİNİK ÇALIŞMA

Hosameldin Salah Shabib Ahmed, M.D.[1]
Hüseyin Ede, M.D.[1]
Ahmed Sobhy Hassan Ghonim Mahfouz, M.D.[2]
Alaa Abdullah Ali Rahhal, M.D.[2]
Muhammad Abdulhakim Ali, M.D.[2]
Ammar Fares Alhaj Issa, M.D.[1]
Abdul Baki Jasem Senjar, M.D.[1]
Sumaya Mehdar Al-Saadi Al Yafei, M.D.[2]
Abdul Rahman Mohammad Said Arabi, M.D.[1]
Awad Razaq Al-Qahtani, M.D.[1]

[1]*Department of Cardiology, Hamad Medical Corporation Heart Hospital, Doha, Qatar*
[2]*Department of Pharmacology, Hamad Medical Corporation Heart Hospital, Doha, Qatar*

Corresponding author:
Hüseyin Ede
✉ huseyinede@gmail.com

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olduğu bulunmuştur. Standard olarak sol ventrikül trombüsü için 3 ile 6 ay süreyle antikoagülasyon önerilse de bu tür hastalarda, bu prediktörlerin varlığının dikkate alınması hekimlerin tedaviyi bireyselleştirmesine kılavuzluk edebilir.

Anahtar Kelimeler: Sol ventrikül trombüsü, koroner arter hastalığı, ekokardiyografi, klopidogrel, varfarin

The left ventricular thrombus (LVT) is a well-known complication of ischemic cardiomyopathy.[1] Its detection is very important since it can end up with acute embolization that may cause severe end-organ damage as per the organ involved.[2] However, its treatment is also challenging. Although it is advised to prescribe 3-6 months of oral anticoagulation as a standard pattern of the care in practice, it is a prerequisite to confirm the absence of LVT before terminating the treatment.[3]

In the literature, risk factors for the development of the LVT following anterior ST-elevation myocardial infarction (STEMI) have been described.[4,5] Time to reperfusion from the onset of the symptom, the extent of left ventricular wall involved, left ventricular ejection fraction (LVEF) following anterior STEMI, etc., are some of those parameters that may affect the development of the LVT.[4-7] However, there is a gap in the literature in respect to the factors that may affect the dissolution of the LVT in patients with ischemic cardiomyopathy. Among such surrogates, the time in therapeutic range (TTR), type of antiaggregant used together with warfarin, the area of LVT, the left ventricular dimensions, LVEF, and the presence of diabetes may be important factors in the dissolution of the LVT. Increased knowledge about the effect of these parameters in the dissolution of the LVT may help to individualize the treatment of such patients with respect to the type and duration of anti-thrombotic treatment.

In this study, we aim to investigate the surrogates that may affect the LVT resolution in patients with coronary artery disease.

Methods

This is a retrospective, cross-sectional, non-invasive study that included all patients with coronary artery disease, aged above 18 years old, and with the thrombus at apical location of the left ventricle. To enable this purpose, all patients under follow-up of our Warfarin Clinic due to the LVT between January 2015 and January 2020 were reviewed through our centralized database and the patients fulfilling the inclusion criteria were enrolled into the study.

ABBREVIATIONS

BMI	Body mass index
CMRI	Magnetic resonance imaging
INR	İnternational normalized ratio
LA	left atrium
LR	logistic regression
LVEDD	Left ventricular enddiastolic
LVEF	Left ventricular ejection fraction
LVESD	Left ventricular end-systolic
LVT	Left ventricular thrombus
STEMI	ST-elevation myocardial infarction
TTE	Transthoracic echocardiography
TTR	Time in therapeutic range

The exclusion criteria for the study were as follows: chronic kidney disease (glomerular filtration rate below 60 mL/min/1.73 m^2), liver disease (defined as blood transaminase levels of more than 3 times above the upper normal limit), any malignancy, any hematological disorder (polycythemias, thrombocytopenia, thrombocytosis, any thrombophilia, antiphospholipid syndrome, etc.), and hemoglobin level of less than 10 gm/dL. Additionally, the patients with atrial fibrillation, atrial flutter, congenital heart disease, previous valve prosthesis, previous non-anterior STEMI, non-ischemic dilated cardiomyopathy, hypertrophic cardiomyopathy, patients with more than a moderate degree of valvopathy, pericardial disease, and any previous cardiac surgery were excluded. The study did not include any patients under different oral anticoagulation rather than warfarin. Additionally, any patient who developed bleeding complications such as intracranial or gastrointestinal bleeding at the follow-up period that required interruption of warfarin use was excluded from the study. The study also excluded the patient under chronic treatment with steroids or anti-tuberculosis treatment that may affect international normalized ratio (INR) values. Ethical and institutional approval for the study was obtained from Hamad Medical Corporation MRC Department accordingly (MRC-01-20-770 dated October 12, 2020).

Demographic characteristics of the patients (age, gender, weight, height, and race (African, European, South Asian, European, Middle Eastern, and North American)) were obtained. Body mass index (BMI) of each subject was calculated by a formula (weight in kilogram divided by the square of height in meter). Concomitant morbidities (hypertension and diabetes) were recorded. Concomitant morbidities such as hypertension (the last 3 blood pressure measurements >140/90 mm Hg or treatment with antihypertensive medication within the last 6 months) and diabetes (any patient under oral anti-glycemic drugs or insulin treatment or glycated hemoglobin (HbA1c) over 7.0%) were recorded. Blood creatinine and HbA1c values at the time of detection of LVT were obtained. Concomitant use of antiplatelets (aspirin 100 mg daily, and/or clopidogrel 75 mg daily or ticagrelor 90 mg twice a day) was determined. Use of one of these agents for more than 90 days together with warfarin was considered as concomitant usage. The time from the detection of LVT until the time of LVT resolution was considered as the follow-up duration. Target INR value for the patients was 2.0-3.0 at follow-up. The TTR value was determined while considering the follow-up period. The TTR value for each patient was calculated by using the Rosendaal method.[8] The patients were classified according to TTR values as follows: good INR control, TTR ≥65% and poor INR control, and TTR <65%.[9]

Transthoracic echocardiography (TTE) images of all patients in the database were reviewed by the cardiologist blinded to the patients' data. The left atrial volume, the left ventricular end-diastolic (LVEDD) and end-systolic (LVESD) dimensions, LVEF

(using modified Simpson method), the left ventricle wall motion score based on the 17-segment model of the left ventricle, and grade of the left ventricular diastolic dysfunction were obtained as per the recommendations of the American Society of Echocardiography.[10] The area of the LVT for each patient was measured by TTE at different windows by a cardiologist blinded to patient's clinical data. The LVT measurement largest in size with clear borders was used for the analysis. In case of suboptimal images on TTE, an intravenous sonographic contrast agent was used for the confirmation and measurement of size of the LVT. Some patients had very poor images due to patient-related factors (such as obesity, poor imaging window, etc.), so cardiac magnetic resonance imaging (CMRI) was performed to detect the LVT. The measurement regarding CMRI was used for the analysis accordingly. The presence of LVT beyond 180 days despite warfarin usage was classified as persistent LVT. Characteristics of LVT were defined as mass, laminated, mobile, or organized as per echocardiographic or CMRI images accordingly. The LVT of 100 mm^2 and above was considered as large LVT. The absence of LVT at follow-up was confirmed by the same imaging method.

Additionally, any stroke, non-neurological peripheral embolic event, and cardiovascular mortality developed within the follow-up period were recorded. The data of the patients with persistent LVT and the patients with resolution of LVT in less than 180 days were compared, respectively.

Statistical Analysis

SPSS version 24 analysis program (IBM Corp., Armonk, NY, USA) for Windows was used for statistical analysis. The distribution of the data was analyzed by using the Kolmogorov–Smirnov test. Age, weight, height, BMI, LVEDD, LVESD, and TTR were normally distributed. Normally distributed continuous variables were presented as mean ± standard deviation whereas non-normally distributed variables were expressed as [median (25th-75th) percentiles]. The Mann–Whitney *U* test was used to compare the difference of the groups in respect to non-normally distributed variables whereas Student's *t*-test was used for normally distributed variables. The chi-square test was used to analyze the relationship among categorical variables of the groups if all the cells had an expected frequency of more than 25. In the 2 × 2 contingency tables, the Yates (continuity correction) test was used when 1 or more of the cells have an expected frequency of 5-25 and the Fisher's exact test was used when 1 or more of the cells have an expected frequency of 5 or less. Furthermore, in the R × C contingency tables, Fisher–Freeman–Halton test was preferred instead of chi-square test when 1 or more of the cells have an expected frequency of 5 or less. Pearson's correlation test was used to assess the correlation between the variables. For multivariate logistic regression analysis, potential factors detected at univariate analyses were further subjected to logistic regression analysis to identify independent predictors of LVT resolution within less than 180 days. For this purpose, any variable whose univariable test had a *P*-value <.25 was used in the multivariable model (including serum creatinine, clopidogrel use, LVEF, the left atrial volume, and LV thrombus area). A stepwise elimination (backward LR) procedure was used to determine the best predictor(s) which discriminated study groups from each other. Hosmer–Lemeshow goodness-of-fit test was used to assess model fitness. A 5% type 1 error level was used to infer statistical significance. In the analyses, $P < .05$ value was considered as statistically significant.

Results

The study included 174 subjects (169 males and 5 females). The mean age of the study population was 54.5 ± 11.0 years. Transthoracic echocardiography alone was enough to detect the LVT in 115 patients (66.1% of the study population), while additional ultrasonographic contrast was used in 35 patients (20.1%) and CMRI was performed in 24 patients (13.8%) to confirm the LVT. The number of patients in whom the LVT resolved with the treatment in less than 180 days was 56 (32.2%). Median anticoagulation time in the study population was 252 [150-480] days and the mean TTR value of the patients was 54% ± 19%. Of them, 49 patients (28.2%) had good INR control.

The data of the patients with LVT resolved within 180 days were compared to the persistent LVT. There was no clinically significant difference between the groups in respect to age, gender, BMI, the presence of diabetes, hypertension, smoking status, blood HbA1c, and serum creatinine levels. The mean TTR values and the number of patients with good INR control were similar in both groups ($P=.593$ and $P=.533$, respectively) (Table 1). In case of subgrouping the patients to South Asian and the others, mean TTR values were statistically similar (52% ± 19% vs. 57% ± 20%, respectively; $P=.138$).

Concomitant use of aspirin with warfarin was similar in the groups; however, concomitant use of clopidogrel and warfarin was statistically lower in the persistent LVT group ($P=.003$). Imaging methods to detect the LVT were similar in both groups (Table 1). In echocardiographic findings, LVEF of the persistent LVT was significantly lower ($P=.003$). The persistent LVT had a higher frequency of apical aneurysm, but it did not reach to the level of significance ($P = .401$). Additionally, the persistent LVT group had significantly larger LVEDD, larger LVESD, larger LA volume, and lower the left ventricle wall motion score (Table 1). The number of large LVT was significantly higher in the persistent LVT group ($P < .001$). The patient with LVT resolved within 180 days had lower LVT area ($P < .001$) but both groups had no difference in respect to the LVT characteristics (Table 1). Major adverse cardiovascular events developed during the follow-up period were similar in both groups (Table 1).

In correlation analyses, the area of LVT was inversely correlated with LVEF ($r=-0.218$, $P=.004$) but positively correlated with LVEDD ($r=0.247$, $P < .001$), LVESD ($r=0.239$, $P < .001$). There was no statistically significant correlation between LVT area and the left atrial volume ($r=0.068$, $P=.375$).

Among the variables related to LVT resolution, only serum creatinine, clopidogrel use, LVEF, the left atrial volume, and LV thrombus area had a *P*-value of <.25 in their univariable tests. Multivariate regression analyses were performed by including these parameters to identify independent predictors of the LVT resolution. Only concomitant clopidogrel use and LVT area were able to predict LVT resolution in this analyses (Table 2). Additionally, the Hosmer–Lemeshow goodness-of-fit test of multivariable analysis showed significant consistency between the predicted and observed values with coefficients of determination values (R^2) at each step (Table 3).

Table 1. Demographic, Laboratory, and Clinical Characteristics of Patients as Per the LV Thrombus Resolution (n=174)

Characteristics	LV Thrombus Resolved in Less Than 180 days (N=56), n (%)	Persistent LV Thrombus (N=118), n (%)	*P*
Age (years)	54.5 ± 10.4	54.6 ± 11.3	.938
Male gender, n (%)	54 (96.4)	115 (97.5)	.657
Geographical region of origin, n (%)			.799
South Asia	35 (62.5)	79 (66.9)	
Middle East	19 (33.9)	36 (30.5)	
Africa	1 (1.8)	1 (0.8)	
Europe	0 (0.0)	1 (0.8)	
North America	1 (1.8)	1 (0.8)	
Weight (kg)	80 ± 20	74 ± 14	.189
Height (cm)	168 ± 8	166 ± 8	.205
BMI (kg/m^2)	28.3 ± 6.5	27.5 ± 4.5	.399
Smoking, n (%)	30 (53.6)	53 (44.9)	.286
Hypertension, n (%)	18 (32.1)	36 (30.5)	.966
Diabetes mellitus, n (%)	25 (44.6)	61 (51.7)	.385
HbA1c (%)	6.4 (5.8-9.3)	6.6 [5.7-10.0)	.565
Serum creatinine [μmol/L)	88 [75-99)	91 (80-106)	.071
Aspirin, n (%)	53 (94.6)	104 (88.1)	.281
Clopidogrel use, n (%)	49 (87.5)	76 (64.4)	.003
Ticagrelor, n (%)	3 (5.4)	3 (2.5)	.388
LV thrombus confirmed by MRI, n (%)	10 (17.9)	14 (11.9)	.403
LV thrombus confirmed by contrast echocardiography, n (%)	14 (25.0)	21 (17.8)	.365
Echocardiographic findings			
LVEF (%)	41 (32-45)	37 (30-42)	.003
Diastolic dysfunction grade, n (%)			.052
1	42 (75.0)	68 (57.6)	
2	8 (14.3)	35 (29.7)	
3	6 (12.7)	15 (12.7)	
Apical aneurysm, n (%)	4 (7.1)	15 (12.7)	.401
Characteristic of LV thrombus, n (%)			.805
Mass	44 (78.6)	86 (72.9)	
Laminated	12 (21.4)	30 (25.4)	
Mobile	0 (0.0)	1 (0.8)	
Organized	0 (0.0)	1 (0.8)	
LVEDD (mm)	54 ± 7	57 ± 8	.009
LVESD (mm)	41 ± 8	45 ± 9	.012
Left atrium volume (mL)	48 (36-57)	57 (41-76)	.006
Wall motion score	32.5 (28.3-36.0)	34.0 (31.0-41.0)	.023
LV thrombus area (mm^2)	98 (51-165)	218 (100-400)	<.001
LV thrombus area ≥100 mm^2, n (%)	28 (50.0)	91 (77.1)	<.001
Embolic event, n (%)	5 (8.9)	21 (17.8)	.192
Stroke, n (%))	3 (5.4)	6 (5.1)	1.000
Mortality, n (%)	0 (0.0)	4 (3.4)	.307

Table 1. Demographic, Laboratory, and Clinical Characteristics of Patients as Per the LV Thrombus Resolution (n=174) (*Continued*)

Characteristics	LV Thrombus Resolved in Less Than 180 days (N=56), n (%)	Persistent LV Thrombus (N=118), n (%)	*P*
Time in therapeutic range (%)	57 ± 20	53 ± 19	.593
Good INR control, n (%)	18 (32.1)	31 (26.3)	.533
Anticoagulation duration, n (%)	120 (90-150)	371 (244-559)	<.001

Non-normally distributed values were expressed as median (25th – 75th percentiles) and normally distributed values were expressed as mean ± standard deviation.
BMI, body mass index; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricle ejection fraction; LVESD, left ventricular end-systolic diameter; LV thrombus, left ventricle thrombus; TTR, time in therapeutic range; INR, international normalized ratio; MRI, magnetic resonance imaging; HbA1C, glycated hemoglobin.

Discussion

In this study, we found that LVT resolved earlier in patients with concomitant use of clopidogrel and there was a smaller LVT area in patients with coronary artery disease. Additionally, it was found that the area of LVT was inversely correlated with LVEF but positively correlated with LVEDD and the left atrial volume.

The gender ratio of the study population had male dominance that is significantly higher than the literature. However, our country has a unique sociodemographic structure with a population of nearly 2.3 million. Approximately 90% of the residents are expatriates.[11,12] Nearly 60% of the population consists of craft and manual workers. The male to female ratio is approximately 3 : 1 in the whole population due to this socioeconomical background.[12] The high frequency of atherosclerosis in the male gender and the sociodemographic fact of the country explains the high number of male patients in the current study.

The LVT is a very serious complication of myocardial infarction that may result in embolism to cerebrovascular and peripheral arterial embolism, in addition, to an increase in morbidity and mortality.[13] Incidence of adverse embolic events was considerably higher before the reperfusion era, but its incidence is still common ranging between 2.5% and 15% following acute myocardial infarction depending on the level of anti-thrombotic treatment.[14,15] The incidence in our study was similar to the literature and it was 14.9% under mean TTR of 54% ± 19%. The average TTR of a population can vary as per geographical location, education level, awareness of the underlying disease, socioeconomical status, INR recheck frequency, and compliance[16] and it ranges from 36% to 75%.[17] In our study, the mean TTR was 54% ± 19%. According to the findings, we can claim that our study population was similar to the literature in respect to incidence of embolism and TTR.

In resolution of LVT, TTR is one of the main determinators. Usually, 3-6 months of treatment with warfarin will be sufficient to get rid of LVT. Its resolution rate within 6 months varies depending on the population in concern. You et al[13] found that the resolution rate within 6 months was 68.2% among post-myocardial infarction patients. In our study, it was 33.2%. Dual antiplatelet usage with warfarin was approximately the same as in our study. However, You et al[13] did not give any data in respect to LVT area and TTR that may have a direct impact on the outcome. Thus, this difference may stem from LVT characteristics and TTR.

In our study, there was no statistical difference between the patients from different geographical origins in respect to TTR or LVT resolution rate, but it may cause source of discrepancy between LVT resolution rate and TTR.[17] In our center, there is a regular

Table 2. Multivariate Analyses for the predictors of LV Thrombus Resolution (Stepwise elimination (Backward LR) Procedure was Used to Determine the Best Predictor(s) which Discriminated Study Groups from Each Other)

	Variables	OR (95% CI)	*P*
Step 1	Serum creatinine [μmol/L]	0.986 (0.969-1.004)	.129
	Clopidogrel use, n [%]	0.260 (0.096-0.707)	.008
	LVEF [%]	1.024 (0.979-1.071)	.297
	The left atrial volume [mL]	0.992 (0.974-1.010)	.382
	LV thrombus area [mm^2]	0.994 (0.990-0.997)	<.001
Step 2	Serum creatinine [μmol/L]	0.986 (0.969-1.003)	.115
	Clopidogrel use, n [%]	0.245 (0.091-0.660)	.005
	LVEF [%]	1.032 (0.989-1.076)	.147
	LV thrombus area [mm^2]	0.993 (0.990-0.997)	<.001
Step 3	Serum creatinine [μmol/L]	0.985 (0.968-1.002)	.089
	Clopidogrel use, n [%]	0.232 (0.087-0.616)	.003
	LV thrombus area [mm^2]	0.993 (0.990-0.996)	<.001

LVEF, left ventricle ejection fraction; LV thrombus, left ventricle thrombus; OR, odds ratio.

Table 3. Hosmer–Lemeshow Goodness-of-Fit Test Results and Coefficients of Determination at Each Step in the Multivariate Analyses

	Hosmer–Lemeshow Goodness-of-Fit Test		Coefficients of Determination
	Chi-square	*P*	Nagelkerke R^2
Step 1	11.452	.177	0.320
Step 2	8.319	.403	0.315
Step 3	4.773	.781	0.302

outpatient unit dedicated to the patients under warfarin treatment. Additionally, a guideline-based approach in an adjustment of warfarin doses also diminishes differences in the outcomes (such as LVT resolution and TTR) related to geographical origin.

Transthoracic echocardiography is the most used tool in the detection of LVT.[18] In our study, 86.2% of the LVT cases (n=150) were detected by TTE. Cardiac MRI is an alternative method for detection in case of suboptimal TTE images.[19] Cardiac MRI was used for the rest of the study population. Ultrasonographic contrast was used in 23.3% (n=35) of the cases in whom TTE was performed. In the literature, it was found that TTE findings (impaired LVEF, higher LVEDD and LVESD, and the presence of apical aneurysm) are related to the development of LVT.[18-20] However, the relation of these parameters with the persistence of LVT has not been studied enough. In our study, we found that the patients with the persistent LVT had lower LVEF, more dilated LV dimensions, and a higher frequency of apical aneurysm. Additionally, we found that LA volume and wall motion score were prone to be significantly higher in persistent LVT. Enlarged dimensions result in reduced blood circulation rate and longer time for coagulation cascade to be active on the substrate. Additionally, apical aneurysm and lower wall motions provide a stable, immobile platform for durable and resistive thrombus to be developed on it.[21] In other words, Virchow's triad will be established.[22] Overall, all these findings create a suitable substrate for the development and persistence of thrombus. On top of this substrate, larger thrombus in size may contribute to the persistence of LVT. In our study, we found that larger LVT resulted in higher frequency of persistent LVT.

Concomitant use of antiplatelet use in patients with LVT has impact on the development of LVT.[1,23] We also found a similar relation between the resolution of LVT and concomitant use of copidogrel. In regression analyses, this relation was confirmed. In our study, there was no statistical difference between the groups in respect to concomitant aspirin use and the persistent LVT. The reason for such finding was most likely due to frequent use of aspirin in the groups (94.6% vs. 88.1%, respectively).

Hypercoagulable states such as activated protein C resistance and deficiencies of anti-thrombin III, protein C, or protein S may result in LV thrombus same as ischemic cardiomyopathies. However, in these hypercoagulable states, thrombotic events will develop at earlier ages with more bizarre clinical manifestations than the ischemic cardiomyopathies and they will affect not only the heart but also other arterial vasculature, venous structures, and other organs.[24-27] In our study, any specific test was not performed to detect the presence of those hypercoagulable states after the diagnosis of LV thrombus. However, we excluded any patient with any previously diagnosed hematological disorders such as polycythemias, thrombocytopenia, thrombocytosis, thrombophilia, or antiphospholipid syndrome. In parallel to this fact, treatment of these hypercoagulable states is lifelong anticoagulation and this study did not include any patients under warfarin due to non-LVT indication.

Limitations

Retrospective nature of the study was the major limitation of the study. Due to retrospective nature of the study, we could not estimate the age of LVT. Although all patients were diagnosed with coronary artery disease, the time of LVT development for the LVT detection may differ from patient to patient. This difference may affect LVT resolution. Different modalities (TTE, contrast echocardiography, and MRI) were used to detect LVT. However, the best images of these modalities that showed LVT were used to assess the size and nature of the thrombus. The potential variation in respect to the measurement of LVT size by different modalities was minimized respectively.

Conclusion

The LVT is a common complication of patients with coronary artery disease and low LVEF. Concomitant use of clopidogrel was found to be associated with LVT resolution but LVT size was related to LVT persistency. Although standard 3-6 months of anticoagulation is advised for LVT, considering the presence of these predictors in such patients may guide the physicians to individualize the treatment.

Ethics Committee Approval: Ethics committee approval was received from the Ethics Committee of Hamad Medical Corporation MRC Department (Approval Date: October 12, 2020; Approval Number: MRC-01-20-770).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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References

1. Altıntaş B, Altındağ R, Bilge Ö, et al. The effect of ticagrelor based dual antiplatelet therapy on development of late left ventricular thrombus after acute anterior ST elevation myocardial infarction. *Int J Cardiol*. 2019;287:19-26. [CrossRef]
2. Dalia T, Lahan S, Ranka S, et al. Warfarin versus direct oral anticoagulants for treating left ventricular thrombus: a systematic review and meta-analysis. *Thromb J*. 2021;19(1):7. [CrossRef]
3. Ibanez B, James S, Agewall S, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018;39:119-177.
4. Bulluck H, Chan MHH, Paradies V, 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. *J Cardiovasc Magn Reson*. 2018;20(1):72. [CrossRef]
5. Zhang Q, Wang CM, Shi ST, Chen H, Zhou YJ. Relationship of left ventricular thrombus formation and adverse outcomes in acute anterior myocardial infarction in patients treated with primary percutaneous coronary intervention. *Clin Cardiol*. 2019;42(1):69-75. [CrossRef]

6. Rabbani LE, Waksmonski C, Iqbal SN, et al. Determinants of left ventricular thrombus formation after primary percutaneous coronary intervention for anterior wall myocardial infarction. *J Thromb Thrombolysis*. 2008;25(2):141-145. [CrossRef]
7. Moulson N, LaHaye SA, Bertrand OF, MacHaalany J. Prophylactic warfarin post anterior ST-elevation myocardial infarction: a systematic review and meta-analysis. *Cardiovasc Revasc Med*. 2017;18(8):559-564. [CrossRef]
8. Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët EA. A Method to determine the optimal intensity of oral anticoagulant therapy. *Thromb Haemost*. 1993;69(3):236-239. [CrossRef]
9. Botton MR, Viola PP, Meireles MR, et al. Identification of environmental and genetic factors that influence warfarin time in therapeutic range. *Genet Mol Biol*. 2020;43(1):e20190025. [CrossRef]
10. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28(1):1-39.e14. [CrossRef]
11. Ayoub HH, Chemaitelly H, Seedat S, et al. Mathematical modeling of the SARS-CoV-2 epidemic in Qatar and its impact on the national response to COVID-19. *J Glob Health*. 2021;11:05005. [CrossRef]
12. Planning and Statistics Authority. State of Qatar. Labor force sample survey; 2017. Available at: https://www.psa.gov.qa/en/statistics/Statistical%20Releases/Social/LaborForce/2017/statistical_analysis_labor_force_2017_En.pdf. Accessed May 27, 2021.
13. You J, Wang X, Wu J, et al. Predictors and prognosis of left ventricular thrombus in post-myocardial infarction patients with left ventricular dysfunction after percutaneous coronary intervention. *J Thorac Dis*. 2018;10(8):4912-4922. [CrossRef]
14. Driesman A, Hyder O, Lang C, Stockwell P, Poppas A, Abbott JD. Incidence and predictors of left ventricular thrombus after primary percutaneous coronary intervention for anterior ST segment elevation myocardial infarction. *Clin Cardiol*. 2015;38(10):590-597. [CrossRef]
15. Garber AM, Mentz RJ, Al-Khalidi HR, et al. Clinical predictors and outcomes of patients with left ventricular thrombus following ST-segment elevation myocardial infarction. *J Thromb Thrombolysis*. 2016;41(3):365-373. [CrossRef]
16. A Reiffel J. Time to revisit the time in the therapeutic range. *J Atr Fibrillation*. 2017;9(5):1569. [CrossRef]
17. Connolly SJ, Ezekowitz MD, Yusuf S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. *New Engl J Med*. 2009;361:1139-1151.
18. Roifman I, Connelly KA, Wright GA, Wijeysundera HC. Echocardiography vs. cardiac magnetic resonance imaging for the diagnosis of left ventricular thrombus: a systematic review. *Can J Cardiol*. 2015;31(6):785-791. [CrossRef]
19. Weinsaft JW, Kim HW, Crowley AL, et al. LVT detection by routine echocardiography: insights into performance characteristics using delayed enhancement CMR. *JACC Cardiovasc Imaging*. 2011;4(7):702-712. [CrossRef]
20. Khaled S, Hachicha Z, Elkhateeb O. Left ventricular thrombus in myocardial infarction after successful primary percutaneous coronary intervention: prevalence and predictors-A Middle Eastern single-centre experience. *CJC Open*. 2020;2(3):104-110. [CrossRef]
21. Williams B, Bernstein W. Review of venoarterial extracorporeal membrane oxygenation and development of intracardiac thrombosis in adult cardiothoracic patients. *J Extra Corpor Technol*. 2016;48(4):162-167.
22. Thomas I, EncisoSilva J, Schlueter M, Greenberg B. Anticoagulation therapy and NOACs in heart failure. *Handb Exp Pharmacol*. 2017;243:515-535. [CrossRef]
23. Bulluck H, Chan MHH, Paradies V, 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. *J Cardiovasc Magn Reson*. 2018;20(1):72. [CrossRef]
24. Limperger V, Franke A, Kenet G, et al. Clinical and laboratory characteristics of paediatric and adolescent index cases with venous thromboembolism and antithrombin deficiency. An observational multicentre cohort study. *Thromb Haemost*. 2014;112(3):478-485. [CrossRef]
25. Kovac M, Mitic G, Mikovic Z, et al. Type and location of venous thromboembolism in carriers of factor V Leiden or prothrombin G20210A mutation versus patients with no mutation. *Clin Appl Thromb Hemost*. 2010;16(1):66-70. [CrossRef]
26. Lau LL, McMurray AH. Mesenteric venous thrombosis in protein S deficiency: case report and literature review. *Ulster Med J*. 1999;68(1):33-35.
27. Majid Z, Tahir F, Ahmed J, Bin Arif T, Haq A. Protein C deficiency as a risk factor for stroke in young adults: a review. *Cureus*. 2020;12(3):e7472. [CrossRef]