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RESEARCH ARTICLE

Distribution of Left Ventricular Thrombus among Patients with Significantly Impaired Systolic Function

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Abstract:

Background:

The prevalence of Left Ventricular (LV) thrombus as well as the distribution among patients with a variable degree of left ventricular systolic function impairment due to various etiologies is not well known.

Objectives:

To describe the distribution of left ventricular thrombus in relation to the underlying pathology, *i.e.*, ischemic versus non-ischemic cardiomyopathy with Ejection Fraction (EF) below 45%.

Methods:

All echocardiography studies performed between January 2013 and September 2017 were reviewed, and only those with confirmed LV thrombus were included. The patient's demographic, clinical characteristics, cardiac history, and echocardiographic parameters were obtained. The cohort was divided into 4 subgroups: 22 patients with EF of 36 - 45% (A), 114 with 26% - 35% (B), 99 with 16 - 25% (C) and 48 with 15% or less (D).

Results:

A total of 63,732 echocardiography study results were reviewed. Only 282 patients were proved to have LV thrombus with EF less than 45%. 217 (77%) patients had previous myocardial infarction, of which 212 (97.7%) were presented with anterior regional wall motion abnormality. 90 (32.7%) patients were found to have dilated left ventricle, and 41 (14.5%) with dilated cardiomyopathy (DCM). 37 (13.2%) patients had moderately severe to severe mitral regurgitation. It was observed that the highest distribution of LV thrombus was seen in group B (40.3%).

Conclusion:

The majority of LV thrombus distribution was seen in patients with EF between 26% to 35% due to ischemic cardiomyopathy. Conversely, in the cohort of non-ischemic cardiomyopathy, the majority were observed in those with severely impaired LV function.

Keywords: LV thrombus, Ejection fraction, Myocardial infarction, Mitral regurgitation, Transthoracic echocardiography.

Article History

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1. INTRODUCTION

The Left Ventricular (LV) thrombus is a well-known devastating cardiac problem that needs special attention. The precise incidence of this problem is not clearly known due to the heterogeneity of the underlying problems. Most commonly encountered LV thrombi are found in patients with anterior Myocardial Infarction (MI) and low Ejection Fraction (EF) [1 - 5]. Although the exact mechanism by which the LV thrombus is formed is not well known yet, there are some hypotheses that may explain this process, like blood stasis, hypercoagulable state, and myocardial injury [10]. For confirming the presence

of LV thrombus, echocardiography is the modality of choice with acceptable sensitivity and specificity [15 - 17]. In this retrospective study, we described the distribution of LV thrombus in relation to the underlying pathology, *i.e.*, ischemic versus non-ischemic cardiomyopathy with EF less than 45%.

2. METHODS

2.1. Study Design and Population

The investigators retrospectively reviewed the echocardiographic studies in a specialized tertiary hospital in Riyadh, Saudi Arabia, from January 2013 to September 2017. Echocardiography review was done using the Philips IntelliSpace Cardiovascular (Koninklijke Philips N.V., USA) in order to determine patients with impaired left ventricular

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systolic function and LV thrombus. Patients with confirmed LV thrombus and left ventricular ejection fraction $\leq 45\%$ were included in the analysis.

2.2. Data Collection

Medical records and echocardiography studies were reviewed, and the patients who were confirmed to have LV thrombus were identified. Those with insufficient data were excluded from the study. Patients demographics, clinical characteristics, cardiac history, medications history, and echocardiographic parameters were collected. The cohort was divided into two groups: group A (ischemic cardiomyopathy) and group B (non-ischemic cardiomyopathy).

2.3. Transthoracic Echocardiography

Patients underwent Trans-Thoracic Echocardiography (TTE), and the echocardiographic measurements were obtained following the updated recommendations from the American Society of Echocardiography and the European Association of Cardiovascular Imaging 2015. A contrast echocardiogram was needed in some patients to confirm the diagnosis. Patients with a left ventricular internal diastolic diameter of more than 60 mm were considered to have dilated LV.

2.4. Statistical Analysis

The demographic and clinical characteristics of patients were summarized using descriptive statistics. The continuous variables were expressed as mean \pm standard deviation, whereas the categorical variables were presented as frequencies and percentages. For assessing the difference between groups, independent samples student's T-test was used for continuous variables, and Pearson's Chi-square or Fisher's exact test was considered appropriate for categorical variables. All statistical

tests were considered statistically significant when the result of the p-value was < 0.05 . IBM SPSS Statistics Version 25.0 (IBM Corp. Armonk, New York.) was used for all analyses. Retrospective analysis of this study was approved by our institution's research ethics committee, where the patient consent was waived.

3. RESULTS

From January 2013 to September 2017, a total of 41,438 patients underwent 63,732 echocardiographic studies in our center. After a thorough review and filtering, we identified that 7,138 (17.2%) patients had impaired LV systolic function (EF $\leq 45\%$), among which 288 (4%) patients were identified to have confirmed LV thrombus. Five patients were excluded due to missing data, therefore, only 282 (3.9%) patients were included in the final analysis.

3.1. Demographic and Clinical Characteristics

The mean age was 58 ± 15.1 years old, and 262 (92.6%) patients were male. 217 (77%) patients had a previous myocardial infarction, of which 212 (98.2%) patients were presented with anterior regional wall motion abnormality. Implantable cardioverter-defibrillator was found in 41 (14.5) patients, while 4 (1.4%) patients had a permanent pacemaker. 90 (32.7%) patients were found to have dilated left ventricle, while 41 (14.5%) were found to have Dilated Cardiomyopathy (DCM). Ischemic Cardiomyopathy (ICM) patients were significantly older than non-ICM patients (60.7 ± 13.8 vs. 46.8 ± 16.6 years old, $p < 0.001$). All DCM patients were having heart failure symptoms with variable classes compared to 68.5% in the ICM group ($p < 0.001$). Stroke occurred in 33 patients (13.7%) in the ICM group and 6 (14.6%) patients in the DCM group ($p = 0.810$). Table 1 summarizes the demographic and clinical characteristics of the patients.

Table 1. Patient's demographic and clinical characteristics.

	All	ICM n = 241	Non-ICM n = 41	P-value
Age, years	58.7 \pm 15.1	60.7 \pm 13.8	46.8 \pm 16.6	< 0.001
Male, n (%)	261 (92.6)	227 (94.2)	34 (82.9)	0.011
Female, n (%)	21 (7.4)	14 (5.8)	7 (17.1)	
Weight, kg	78.5 \pm 15	78.5 \pm 14.7	78.5 \pm 16.7	0.979
Height, m	1.7 \pm 0.08	1.7 \pm 0.08	1.7 \pm 0.09	0.643
Body Mass Index, kg/m ²	28.4 \pm 5.5	28.4 \pm 5.2	28.7 \pm 5.2	0.735
Body Surface Area, m ²	1.9 \pm 0.2	1.9 \pm 0.2	1.9 \pm 0.2	0.775
Diabetes, n (%)	148 (52.5)	132 (55)	16 (39)	0.058
Hypertension, n(%)	152 (53.9)	132 (55)	20 (58)	0.460
Congestive Heart Failure, n (%)	206 (73)	165 (68.5)	41 (100)	< 0.001
Atrial fibrillation, n (%)	21 (7.4)	19 (7.9)	2 (4.9)	0.294
Previous PPM, n (%)	4 (1.4)	3 (1.2)	1 (2.4)	0.469
Previous ICD, n (%)	41 (14.5)	33 (13.7)	8 (19.5)	0.328
Location	212 (98.1)	-	-	
Anterior, n (%)	3 (1.4)	-	-	
Inferior, n (%)	2 (0.9)	-	-	
Posterior, n (%)				
Previous CVA, n (%)	39 (13.8)	33 (13.7)	6 (14.6)	0.810
Previous TIA, n (%)	7 (2.5)	5 (2.1)	2 (4.9)	0.270

Table 2. Echocardiographic parameters.

Variable	All n = 282	ICM n = 241	Non-ICM n = 41	p-value
LV EF (%)	26.6 ± 8.3	28.0 ± 7.9	18.2 ± 5.1	< 0.001
< 15%	48 (17%)	29 (12%)	19 (46.3%)	< 0.001
16% - 25%	99 (35.1%)	79 (32.8%)	20 (48.8%)	
26% - 35%	113 (40.1%)	111 (46.1%)	2 (4.9%)	
36% - 45%	22 (7.8%)	22 (9.1%)		
LV EDD, mm (n = 275)	56.3 ± 9	54.6 ± 7.8	66.4 ± 9.0	< 0.001
LV ESD, mm (n = 274)	44.8 ± 11.1	42.3 ± 9.5	58.5 ± 9.5	< 0.001
Dilated LV n, (%) (n = 275)	90 (31.9%)	57 (23.6%)	33 (80.5%)	< 0.001
PASP, mmHg (n = 162)	44.7 ± 15.5	43.7 ± 16.0	48.6 ± 12.9	0.122
Mitral Regurgitation (n = 282)				0.009
No	91 (32.2%)	83 (34.7%)	8 (19.5%)	
Mild	89 (31.5%)	80 (33.4%)	9 (22%)	
Moderate	63 (22.3%)	49 (20.5%)	14 (34.1%)	
Moderately-severe	20 (7.1%)	13 (5.4%)	7 (17%)	
Severe	17 (6%)	14 (5.8%)	3 (7.3%)	

Table 3. Regional wall motion abnormalities distribution according to the EF.

Variable	N (%)	EF < 15%	EF 16 - 25%	EF 26 - 35%	EF 36 -45%	p-value
Anterior	213 (97.7%)	22	68	104	19	< 0.001
Inferior	3 (1.4%)	1	1	1	0	
Posterolateral	2 (0.9%)	1	1	0	0	

3.2. Echocardiographic Characteristics

The distribution of LV thrombus among different groups were as follows: 22 (7.8%) patients with EF of 36 - 45% (Group A), 114 (40%) with 26% - 35% (Group B), 99 (35%) with 16 - 25% (Group C), and 48 (17%) patients with EF less than 15% (Group D) (Fig. 1). The Mean left ventricular end-

diastolic diameter (LVEDD) was 56.3 ± 9 mm, while the LV end-systolic diameter was 44.8 ± 11.1 mm. The mean pulmonary artery systolic pressure was 44.7 ± 15.5 mmHg, whereas 37 (13.2%) patients had moderately severe to severe mitral regurgitation (Fig. 2). Table 2 summarizes the echocardiographic findings.

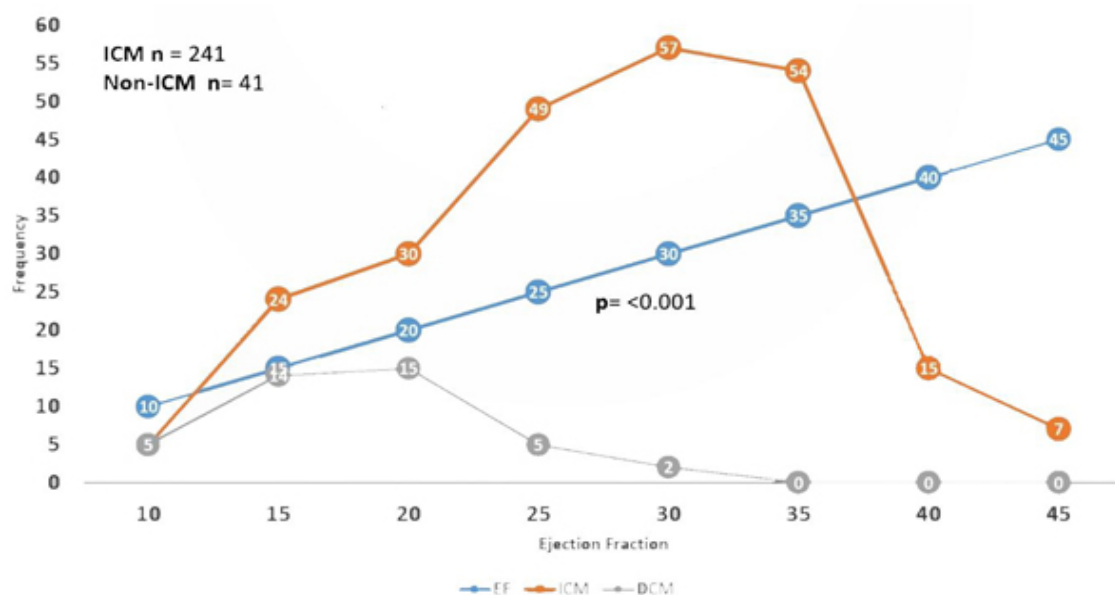


Fig. (1). Distribution of patients with Left Ventricular (LV) thrombus according to LV Ejection Fraction (EF) This figure shows the distribution of patients with Left Ventricular (LV) thrombus according to LV Ejection Fraction (EF) in patients with ischemic cardiomyopathy (ICM) and Dilated cardiomyopathy (DCM). The majority of the distribution of LV thrombus was observed in patients with ICM and EF between 25 - 35%. Of note, patients with DCM and EF above 20% have minimal distribution.

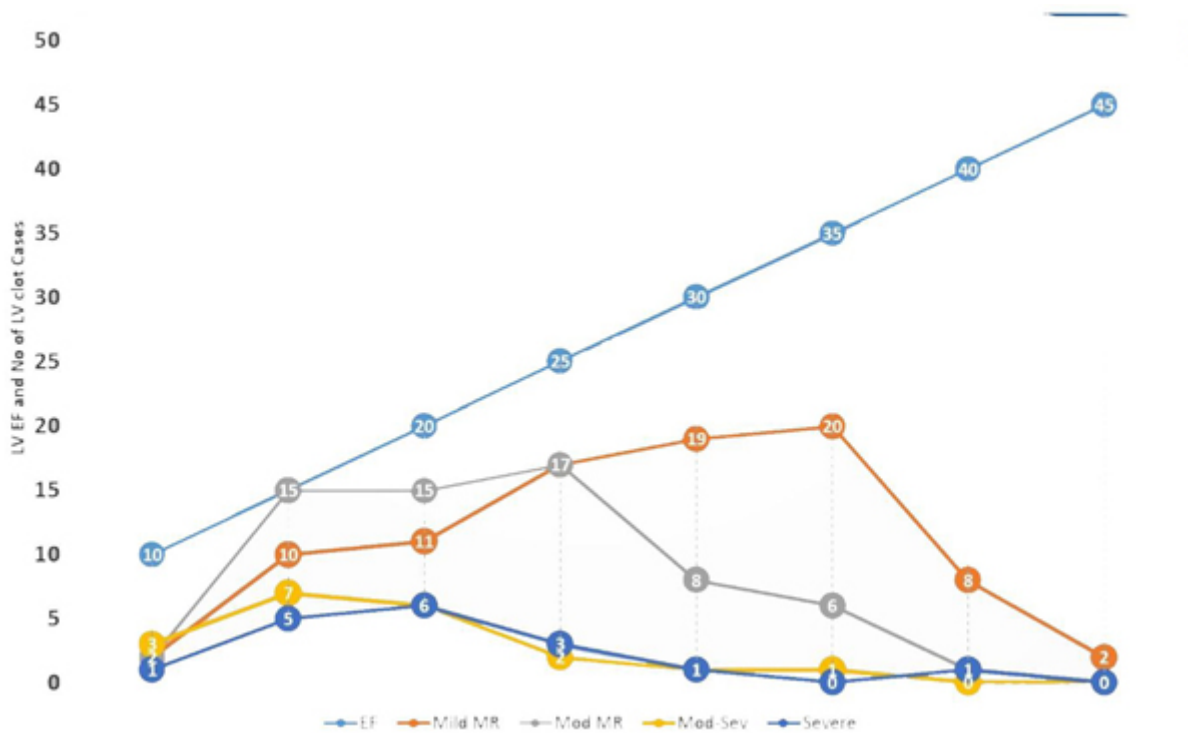


Fig. (2). Relationship between the Mitral Regurgitation (MR) severity and the distribution of LV thrombus. This figure represents the relationship between the Mitral Regurgitation (MR) severity and the distribution of LV thrombus. The patients with moderately severe and severe MR have minimal distribution, especially when their EF is greater than 20%.

4. DISCUSSION

Although its precise incidence among different cardiac pathologies is not well known, LV thrombus is more often seen among patients with anterior wall myocardial infarction [1, - 3], especially when the ejection fraction is less than 50% [4, 5]. The development of the LV thrombus is usually seen during the first month of the onset of the myocardial infarction [6 - 8]. Factors that may contribute to the formation of LV thrombus include large infarct size, severe apical asynergy, LV aneurysm, anterior myocardial infarction, age more than 50, male gender, or EF less than 40% [10, 11]. One study conducted at the University of Maiduguri Teaching Hospital, Nigeria, showed that the highest prevalence of the LV thrombus was seen among patients with dilated cardiomyopathy (39.29%), followed by myocardial infarction (29.76%). Peripartum cardiomyopathy accounted for 21.43%, while hypertensive cardiomyopathy was the cause in only 7.14% of the patients. The lowest prevalence was seen in patients with rheumatic heart disease (2.38%) [13]. In takotsubo cardiomyopathy, the prevalence of ventricular thrombus was around 1.3% [14]. Another study showed that the prevalence of LV thrombus in dilated cardiomyopathy was around 2.1%, and was observed more in younger patients with lower EF, higher regional wall motion score, higher velocity of early diastolic filling, and greater left ventricular diastolic dimension [12]. The combination of blood stasis, endothelial injury, and hypercoagulable state (Virchow’s triad) is thought to be the underlying mechanism for the formation of the LV thrombus [10]. In contrast, the vast majority of our patients

with LV thrombus formation were those with ischemic cardiomyopathy (85.5%), and the anterior location of the regional wall motion abnormalities was the commonest distribution (97.7%), followed by the inferior wall (1.4%) Table 3, while the non-ischemic cardiomyopathy accounted for only (14.5%). LV thrombus was found in the apical location in most of our patients. Among patients with ischemic cardiomyopathy, the majority were with EF between 26 - 35% (Group B), while in the non-ischemic cardiomyopathy group, the EF was mostly below 20%. These findings may suggest that patients with non-ischemic cardiomyopathy are less likely to develop LV thrombus if the EF is above 20%. Anterior wall hypokinesia was seen in the majority of patients with EF ranging between 26 - 35% (Group B), while global hypokinesia was found in patients who have EF between 15 - 20%. The presence of ischemic wall injury may play a more critical role in the formation of thrombus than stasis of blood due to global hypokinesia. Male gender was more prominent in our study, probably due to the fact that males are at higher risk of developing MI, which is the most common underlying cause of LV thrombus in our study. Ozdemir N *et al.* found that the presence of severe mitral regurgitation may protect against the formation of the LV mural thrombus in patients with ischemic dilated cardiomyopathy [9]. In our study, moderately severe to severe MR was found in 37 patients (13.2%), of which the majority [33 patients (11.7%)] had severely impaired LV EF (15 - 20%). This low distribution of thrombus in association with significant MR may imply a protective mechanism imposed by MR against LV thrombus formation, especially in those with EF more than 20%. The detection of LV thrombus

might be challenging as the sensitivity and specificity of routine TTE are 33% and 91%, respectively [15 - 17], but the sensitivity may be increased to 60% if the imaging was performed when LV thrombus is clinically suspected [15]. Therefore, patients with anterior MI and reduced EF need to be screened for LV thrombus. Being a retrospective study is one of the limitations of our study. Furthermore, we did not look for specific hematological disorders, which may play a role in thrombus formation. We also did not encompass and analyze the influence of LV diameter. Further studies are needed to assess the impact of these disorders on the formation of LV thrombus.

CONCLUSION

The majority of LV thrombus distribution was seen in patients with EF between 30% to 35% due to ischemic cardiomyopathy. Conversely, in the cohort of non-ischemic cardiomyopathy, the majority were observed in those with severely impaired LV function. This indicates that mural injury is probably a more important factor in thrombus formation than blood stasis.

LIST OF ABBREVIATIONS

LV	=	Left Ventricular
MI	=	Myocardial Infarction
EF	=	Ejection Fraction
TTE	=	Trans-Thoracic Echocardiography
ICM	=	Ischemic Cardiomyopathy
DCM	=	Dilated Cardiomyopathy
LVEDD	=	Left Ventricular End-Diastolic Diameter
MR	=	Mitral Regurgitation

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Retrospective analysis of this study was approved by the research ethics of Prince Sultan Cardiac Center, Saudi Arabia.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Informed consent was waived.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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