Angiographic predictors of left ventricular thrombus after anterior myocardial infarction

Abstract

Aim: Left ventricular thrombus (LVT) formation after anterior acute myocardial infarction (AMI) leads to increased morbidity and mortality rate. Therefore, a variety of studies were performed to find the predictors of LVT formation. However, the relationship between full angiographic features and LVT was not comprehensively investigated. The goal of the study is to assess the relationship between angiographic variables and LVT formation.

Material and Methods: A total of 87 patients with AMI were enrolled in the study. Patients who met exclusion criteria were excluded, and 75 patients were included in the final statistical analysis. Full angiographic data such as antegrade and retrograde filling, right-left coronary dominance, no-reflow phenomenon, and syntax (SX) score were obtained from all patients in both baseline and during the primary percutaneous coronary intervention (PCI). Then, two multivariate analysis models were created to find the angiographic predictors of LVT. Baseline angiographic findings were analyzed by Model 1 and data associated with PCI were used in Model 2.

Results: Primary PCI was performed in sixty-four patients (85.3%) and 57 patients (89%) were successfully revascularized. LVT developed in 18 (24%) patients (Group 1) and did not develop in 57 (76%) patients (Group 2). The prevalence of RCA ectasia, total occlusion, and baseline syntax (SX) score was higher in Group 1 than Group 2. Other angiographic features were similar in both groups. In multivariable models, RCA ectasia and baseline SX score were found to be independent angiographic predictors of LVT formation.

Discussion: The presence of right coronary artery ectasia and baseline SX score are independent angiographic predictors of LVT formation in patients with first anterior AMI. They can be used as simple and practical tools to predict the development of LVT.

Keywords

Ventricular thrombus; Myocardial infarction; Coronary angiography

DOI: 10.4328/ACAM.20152  Received: 2020-03-07  Accepted: 2020-04-02  Published Online: 2020-04-11  Ann Clin Anal Med 2020;11(5):479-484

Corresponding Author: Zeydin Acar, Department of Cardiology, Medicalpark Karadeniz Hospital, 61040, Trabzon, Turkey.

E-mail: drzeydin@yahoo.com  T: +90 462 2297070

Corresponding Author ORCID ID: https://orcid.org/0000-0002-0288-7499
Angiographic predictor of thrombus formation

Introduction
Left ventricular thrombus (LVT) formation is a major complication of acute myocardial infarction (AMI) because it is associated with higher mortality and morbidity due to systemic embolism. Therefore, a large number of studies were performed to find the factors associated with LVT formation during the last three decades. Initially, the effects of anticoagulant and fibrinolytic therapy on LVT formation were investigated in various studies [1-3]. Later, echocardiographic and biochemical predictors of LVT formation were sought [4-7]. In the last decade, the effect of primary percutaneous coronary intervention (PCI) on the development of LVT was specifically examined in five studies [8,9].

The extent of myocardial damage is an important predictor of LVT formation [5,8,10]. It was reported that some angiographic features may be associated with myocardial damage. For example, coronary artery ectasia (CAE) leads to the impairment of coronary flow reserve [11], ischemia [12] and left ventricular (LV) dysfunction [13]. Similarly, the presence of retrograde coronary collateral circulation reduces the myocardial damage in patients with AMI [14]. In addition, some other angiographic features such as thrombolysis in myocardial infarction (TIMI) frame count and syntax (SX) score were suggested to be associated with no-reflow phenomenon mortality in patients with AMI [15,16]. Thus, we hypothesized that angiographic features such as presence of ectatic vessel, SXscore, and retrograde filling of infarct-related artery may affect the extent of myocardial damage and may contribute to the LVT formation.

To date, although the relationship between LVT formation and some angiographic parameters such as door-to-balloon time and TIMI flow grade were evaluated in prior studies, full angiographic data has not been evaluated [9]. Therefore, in this prospective observational study, we aimed to comprehensively assess the relationship between angiographic findings and LVT formation.

Material and Methods

Patients Selection
The study population consisted of 87 consecutive patients with anterior AMI. The anterior AMI was diagnosed as the presence of anginal chest pain >30 min, ST segment elevation >2 mm in consecutive two derivations in electrocardiography (ECG) and/or cardiac-Troponin I (c-Trop I) elevation. Exclusion criteria were defined as the presence of in-hospital death, previous or emergency coronary artery by-pass graft operation (CABG-op) and inadequately echocardiographic follow-up. But, subjects with thrombus detected before elective CABG operation or in-hospital death were not excluded. The use of antihypertensive and antidiabetic drugs (or insulin) was accepted for the diagnosis of hypertension (HT) and diabetes mellitus (DM), respectively. The study was conducted in accordance with the guidelines in the Declaration of Helsinki. The Local Ethics Committee approved the study protocol. The informed consent was obtained for all of the study participants.

Coronary angiography and revascularization procedures
Selective coronary angiography (CA) was performed by the Judkins technique using right or left femoral artery. Primary percutaneous coronary intervention (PCI) was considered as the main treatment method for the patients who presented to our hospital with AMI. Before primary PCI, 600 mg clopidogrel and 300 mg acetylsalicylic acid were given to all patients. If a patient was not a candidate for primary PCI, fibrinolytic therapy was used for revascularization. Patients who were reperfused by fibrinolytic therapy in other centers underwent elective CA or rescue PCI according to clinical status. All angiographic records in both baseline and during PCI were assessed by two experienced interventional cardiologists who were blinded to the patient’s data. If there was a disagreement, the final decision was obtained by consensus with the third cardiologist’s assessment.

Antegrade filling and retrograde filling of infarct-related artery
Antegrade filling determined by thrombolysis in myocardial infarction (TIMI) flow grade was assessed using baseline CA records. TIMI flow grade was assessed using a predefined method [17]. The presence of TIMI flow grade 2 or 3 distal to the culprit lesion in the main branch of the left anterior descending artery (LAD) was accepted as antegrade filling (spontaneous revascularization). The presence of TIMI 0-1 flow was considered as total occlusion. Retrograde filling was evaluated using baseline CA records. The presence of collateral circulation from RCA or Cx to LAD artery was accepted as retrograde filling and was graded using a method predefined by Rentrop et al [18].

Right-left dominance of coronary circulation
Right or left dominance was assessed according to the origin of the posterior descending artery (PDA) and posterolateral artery (PLA). Right dominant circulation was considered if the PDA and PLA have originated from the RCA, and left dominant circulation was considered when they originated from Cx artery.

Coronary artery ectasia
The presence of localized or diffuse dilation of the coronary arteries with a luminal dilation exceeding the 1.5-fold of normal adjacent segment or vessel diameter has been accepted coronary artery ectasia (CAE) [19]. Cases that are not accompanied by critical stenosis (≥50%) have been considered as isolated ectasia. In this study, we accepted as CAE only isolated form because of two reasons that may lead to conflicting data about the impact of ectasia on LVT formation. First, the presence of critical stenosis in the ectatic vessel may influence the effect of ectasia on coronary flow and myocardial function. Secondly, critical stenosis in ectatic vessel also increases the SXscore. Thus, data overlapping may occur.

SYNTAX score
SX score was calculated using the SXscore algorithm [20] at two stages. According to this algorithm, each coronary stenosis (≥50%) in vessels (≥1.5 mm) was scored separately for LAD, RCA, and Cx artery. Then, they were added together to obtain the overall SXscore.

SXscore in baseline: It was obtained from baseline coronary anatomy. The presence of TIMI 0 or 1 flow in LAD was scored as a total occlusion (<3 months) with thrombus.

SXscore after wiring/ballooning: This score was computed using coronary anatomy after wiring/ballooning. If reperfusion was obtained, SXscore was computed according to new coronary anatomy. But, if there was no reperfusion, the lesion was scored
as a total occlusion (<3 months) with thrombus.

**Successful primary PCI, no-reflow phenomenon and TIMI frame count**

The presence of TIMI 3 flow grade and <30% residual lesion in LAD artery was accepted as successfully PCI; whereas, TIMI 0 or 1 flow grade in target vessel after PCI was considered no-reflow phenomenon. In addition, to obtain a more objective evaluation of coronary blood flow, TIMI frame count (TFC) after PCI was calculated using a method which was firstly described by Gibson et al [21]. TFC for LAD (corrected by dividing by 1.7), circumflex (Cx), and right coronary artery (RCA) were separately calculated. Then, the mean TFC was obtained by dividing the sum of TFC of three vessels by three in only patients with antegrade TIMI 2-3 flow after PCI.

**Echocardiography and Thrombus detection**

Echocardiographic evaluation was serially performed on 1,3,7 and 30 days according to the recommendations of the American Society of Echocardiography using a commercially available system (Vivid 3, GEMS Ultrasound, Tirtar, Carmel, Israel) [22]. LV dimensions were measured by two dimensional guided M mode echocardiography. LV function was assessed by left ventricular ejection fraction (LVEF) using the modified biplane Simpson’s rule. LVT was diagnosed by the presence of an echodense mass with a margin distinct from the LV wall. The wall motion score index (WMSI) was calculated using the 16 segments model [23]. The motion of each segment was coded as follows: 1=normal, 2=hypokinesis, 3=akinesis, 4=dyskinesis, and 5=aneurysmal. Then, WMSI was computed by dividing the sum of scores of all segments by sixteen.

**Statistical analysis**

Continuous variables were described as mean ± standard deviation (SD). Normal distributions of values were assessed using the Kolmogorov-Smirnov test and histogram. The Mann-Whitney U test was used for the analysis of continuous variables. Categorical variables were expressed as percentage values. They were analyzed using the Chi-squared or the Fischer’s exact test. A multivariable logistic regression analysis was performed to determine the independent predictors of LVT formation. The variables which have a p-value <0.1 in univariate analysis were included in the multivariable analysis. Two multivariable logistic regression models were created. Model 1 analyzed the baseline angiographic findings and model 2 used the angiographic data during PCI. A p-value <0.05 was considered statistically significant. All statistical analyses were performed by the SPSS software program (SPSS, 13.0, Inc, Chicago, Illinois).

**Results**

**Baseline Characteristics**

Eighty-seven consecutive patients were included in the study. Patients who met exclusion criteria (4 patients died in hospital, 3 patients underwent CABG-op, and 5 patients have insufficient echocardiographic follow-up) were excluded. Seventy-five subjects (mean age 59.6±12.7 years) were included in the statistical analysis. LVT was detected in 18 of 75 patients (24%, Group 1) and was not detected in 57 patients (76%, Group 2). Both groups had similar baseline demographic findings including age (61.3±14.2 vs 59.1±12.25, p=0.58), gender (male/female ratio =16/2 vs 45/12, p=0.5), smoking (55.6% vs 33.3%, p=0.09), rates of HT and DM (50% vs 42.1%, p=0.56 and 22.2% vs 12.3%, p=0.44, respectively). Systolic blood pressure was similar in both groups (112.8±21 mmHg vs 120.9±23.9 mmHg, p>0.05) but diastolic blood pressure was higher in Group 2 than Group 1 (77.1±15.3 vs 67.3±12.2, p=0.02).

**Angiographic features**

All angiographic findings of both groups were presented in Table 1. The primary PCI was performed to sixty-four patients (85.3%) and 57 patients (89%) were successfully revascularized.
Angiographic predictor of thrombus formation

Table 3. Univariate predictors and multivariable regression analysis for Model 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate</th>
<th>Multivariable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>95% CI</td>
<td>p</td>
</tr>
<tr>
<td>Age</td>
<td>0.968-1.062</td>
<td>0.56</td>
</tr>
<tr>
<td>Gender</td>
<td>0.385-8.978</td>
<td>0.42</td>
</tr>
<tr>
<td>HT</td>
<td>0.348-3.493</td>
<td>0.87</td>
</tr>
<tr>
<td>DM</td>
<td>0.580-9.423</td>
<td>0.23</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.870-9.226</td>
<td>0.08</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.317-44.041</td>
<td>0.02</td>
</tr>
<tr>
<td>Duration of chest pain</td>
<td>0.999-1.004</td>
<td>0.26</td>
</tr>
<tr>
<td>Right-left dominance</td>
<td>0.417-8.804</td>
<td>0.40</td>
</tr>
<tr>
<td>RCA ectasia</td>
<td>1.142-19.439</td>
<td>0.03</td>
</tr>
<tr>
<td>Cx ectasia</td>
<td>0.659-93.365</td>
<td>0.10</td>
</tr>
<tr>
<td>SXscore after wiring/ballooning</td>
<td>0.997-1.172</td>
<td>0.06</td>
</tr>
<tr>
<td>Door-to-balloon time</td>
<td>0.978-1.007</td>
<td>0.3</td>
</tr>
<tr>
<td>Success of PCI</td>
<td>0.024-1.066</td>
<td>0.06</td>
</tr>
<tr>
<td>TFC</td>
<td>0.974-1.163</td>
<td>0.17</td>
</tr>
<tr>
<td>Slow flow/no-reflow</td>
<td>0.494-29.959</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Cx: Circumflex artery, DM: Diabetes Mellitus, HT: Hypertension, PCI: Percutaneous coronary intervention, RCA: Right coronary artery, SXscore: Syntax score, TFC: TIMI frame count, WMSI: Wall motion score index

by primary PCI. Six patients (8%) received fibrinolytic therapy and 2 patients (2.7%) underwent rescue PCI. No-reflow phenomenon developed in 4 of 75 patients (5.3%). There was no difference between both groups for the development of no-reflow (14.3% vs 5.8%, respectively, p=0.19). TIMI frame counts were similar in both groups. The rate of total occlusion in baseline was higher in Group 1 than Group 2; but, retrograde filling and right-left dominance were similar in both groups. The prevalence of coronary ectasia in LAD and Cx artery was similar in both groups. But, the prevalence of both overall and isolated RCA ectasia was higher in Group 1 than Group 2. Baseline SXscore was higher in Group 1 than Group 2. But, SXscore after wiring/ballooning was similar in both groups.

Parameters of Echocardiography

There were significant differences in baseline echocardiographic parameters of both groups. Systolic and diastolic diameters were higher in Group 1 than Group 2 (38.6±8.9 mm vs 31.7±4 mm, p=0.002 and 53.1±7 mm vs 47.9±4.8 mm, p=0.003, respectively). WMSI also were higher in Group 1 than Group 2 (1.86±0.37 vs 1.5±0.37, p=0.005). But, ejection fraction was lower in Group 1 compared with Group 2 (32.8±9.4 vs 42.8±10.1, p=0.002).

Relationship between LVT formation and other factors

This relationship was assessed with two different models. Model 1 was created using the baseline angiographical data obtained from all patients (Table 2). In this model, smoking, LVEF, the presence of total occlusion in presentation, RCA ectasia and baseline SXscore were associated with LVT formation in univariate analysis. RCA ectasia, SXscore, smoking, and WMSI were found to be an independent predictor of LVT by multivariable analysis. In addition, RCA ectasia and baseline SXscore were similarly found to be independent predictors when data of patients who underwent only PCI were analyzed in this model.

In model 2, the data of patients who underwent PCI were analyzed (Table 3). Smoking, WMSI, RCA ectasia, SXscore after wiring/ballooning and the success of PCI were related to LVT formation in univariate analysis. However, only RCA ectasia was independently associated with LVT formation in multivariable analysis.

Discussion

In this study, angiographic factors associated with LVT formation comprehensively were firstly investigated in patients with anterior AMI. RCA ectasia and baseline SXscore were found to be independent predictors of LVT formation. However, other angiographic data were not related to the LVT. LVT is an important complication of AMI which leads to morbidity and mortality because of embolism. Therefore, factors associated with LVT formation have always been the focus of attention and a large number of studies were performed to find these factors. Initially, the effects of acetylsalicylic acid, heparin, streptokinase or tissue plasminogen activator on LVT formation were investigated in various studies [1-3]. Later, many of biochemical and echocardiographic parameters such as LV wall motion score and C-reactive protein were found to be associated with LVT formation [4-7]. In the last decade, primary PCI was the first-line therapy for AMI and its effect on the development of LVT was sought by five studies [8,9]. According to the results of these studies, the extent of myocardial damage and regional inflammation are the most important predictors of LVT formation [4-7,10]. It has been reported that some angiographic features such as presence of retrograde filling and CAE have affected the myocardial damage [11-14]. SXscore has also recently raised as a predictor of no-reflow phenomenon and mortality in ST segment elevation myocardial infarction [16]. However, to date, all angiographic data were not evaluated, although the relationship between LVT formation and some angiographic factors such as door-to-balloon time and TIMI flow grade were evaluated in prior studies [9]. Therefore, we comprehensively assessed the relationship between LVT formation and all angiographic data which may affect the extent of myocardial damage in this study.

We found only two independent angiographic predictors for LVT: the presence of RCA ectasia and baseline SXscore. Coronary ectasia has some adverse effects on coronary circulation and myocardium. For example, Akyürek et al. [11] reported impaired coronary flow in patients with diffuse coronary artery ectasia. Markis et al. [12] suggested myocardial ischemia caused by CAE. In addition, Ceyhan et al. [13] have recently shown that CAE leads to the impairment of LV myocardial performance in patients without critical stenosis. In our study, the prevalence of RCA ectasia was higher in Group 1 than Group 2. Also, there was a relationship between CAE and RCA TIMI frame count (B=0.73, 95% CI=1.023-1.131, p=0.004, not given in results) which suggests impaired coronary flow and myocardial ischemia in non-infarcted RCA area. Ventricular remodeling results from the loss of the necrotic myocardial tissue and myocardial disruption within the non-infarcted area. Therefore, it has been proposed that the presence of RCA ectasia may contribute to LVT formation by means of myocardial ischemia.
and accelerated remodelling.

SXscore is a scoring system which suggests lesion complexity based on anatomical and functional characteristics of each critical coronary stenosis (>50%) in the vessel larger than 1.5 mm. Basically, this system was developed to choose the optimal treatment strategies in elective patients who have three-vessel or left main artery disease. To date, the relationship between SXscore and LVT formation in patients with ST-elevation MI has not been assessed. This relationship was firstly evaluated in this study and baseline SXscore was found to be an independent predictor for LVT. In our study, the baseline SXscore was significantly correlated with LVEF ($r = -0.40$, $p<0.001$) and LVESD ($r=0.28$, $p=0.014$). Therefore, we considered that baseline SXscore may affect the ventricular remodelling and LVT formation. On the other hand, SXscore after wiring/ballooning was not an independent predictor for LVT formation in our study. A possible explanation of this situation is that SXscore after wiring/ballooning may not affect the remodelling process, because, we could not find any relationship between SXscore after wiring/ballooning and LV function or diameters in this study.

Smoking, is another independent predictor of LVT in this study, has a variety of the adverse effects on the cardiovascular system such as increased levels of adhesion molecules, fibrinogen and homocysteine and endothelial dysfunction [24]. Additionally, Zornoff et al. reported that smoking has aggravated the ventricular remodelling after myocardial infarction [25]. They also reported that the loss of anti-thrombotic property of the surface of the infarcted region and ventricular remodelling are two main mechanisms for LVT formation. Therefore, it has been considered that smoking may affect the LVT formation by means of both changing the surface of the infarcted area to a thrombogenic layer and aggravating the ventricular remodelling. On the other hand, we could not find a relationship between LVT formation and other angiographic data such as antegrade and retrograde filling, TIMI flow grade, TIMI frame count, successful primary PCI, door-to-balloon time. Actually, some angiographic findings including the success of the primary PCI and door-to-balloon time were found to be unrelated to LVT in previous studies. However, other angiographic findings including the presence of total occlusion and retrograde filling in baseline, right-left dominance of coronary circulation, coronary ectasia, TIMI frame count and no-reflow were firstly evaluated in our study and they were not related to LVT.

Our results are consistent with and support previous studies. Additionally, our results may suggest that the presence of a pathology that leads to more globally affected myocardium plays a role in the development of LVT after AMI. For example, RCA ectasia may affect a non-infarcted region of myocardium and may lead to more global impairment of ventricle in anterior AMI. Similarly, overall SXscore accounts the effect of all vessel. Therefore, it may suggest a more globally affected myocardium.

The indexes of globally myocardial dysfunction such as myocardial performance (Tei) index and WMSI were found to be associated with LVT formation in previous echocardiography studies supports this consideration.

### Study Limitation

The small sample size is the main limitation of our study. However, our study has some advantages. First, our study was performed prospectively. Secondly, the study population consisted of consecutive patients instead of selective patients. Therefore, the results of this study may reflect the real world.

### Conclusion

The presence of RCA ectasia and baseline SXscore are associated with LVT formation in patients with anterior AMI. Both can be easily assessed using coronary angiography and they can be used as a practical tool for determining patients at a higher risk of developing LVT.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

### Funding:

None

### Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

### References