

Akut Anterior Miyokard İnfarktüsü Geçiren ve Primer Perkütan Koroner Girişim Uygulanan Hastalarda Sol Ventrikül Apikal Trombüs Oluşumunun Öngördürücüleri: SYNTAX Skorunun Önemi

Predictors Of Left Ventricular Apical Thrombus Formation in Patients With Acute Anterior Myocardial Infarction and Treated Primary Percutaneous Coronary Intervention: Importance of Syntax Score

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Özet

Amaç: Sol Ventrikül (SV) apikal trombüs oluşumu Anterior Miyokard İnfarktüsü (AMİ) geçiren hastalarda SV apikal anevrizma ve sistolik disfonksiyonun eşlik ettiği önemli bir istenmeyen olaydır. SYNTAX skoru koroner arter hastalarında kardiyovasküler mortalite ve morbiditenin önemli bir belirteçidir. Çalışmamızda AMİ geçiren hastalarda SV apikal trombüs oluşumu ile SYNTAX skoru ve diğer risk faktörleri arasındaki ilişkiyi araştırdık.

Gereç ve Yöntemler: AMİ geçiren ve primer perkütan koroner girişim uygulanan ardışık 205 hasta çalışmamıza dahil edildi (Kadın:35/Erkek:170, ortalama yaş: 55,8 ± 9,6 yıl). Koroner arter hastalığının ciddiyeti SYNTAX skoru ile değerlendirildi. Hastalar apikal trombüs varlığı (n=19) veya yokluğuna (n=186) göre iki gruba ayrıldı.

Bulgular: Apikal trombüs olan grupta sistolik ve diyastolik kan basıncı daha düşük olarak bulundu (p<0,001 her ikisi için). Apikal trombüs saptanan hastalarda SYNTAX skoru daha yüksek Sol Ventriküler Atım Oranı (SVAO) daha düşük olarak saptandı (p<0,001 her ikisi için). Çok değişkenli analizde SYNTAX skoru (p=0,003), düşük sistolik kan basıncı varlığı (p=0,006) ve düşük SVAO (p=0,001)'in SV apikal trombüs oluşumunu bağımsız olarak öngördüğünü saptadık.

Sonuç: Çalışmamızda azalmış SVAO, düşük sistolik kan basıncı ve yüksek SYNTAX skorunun (>18,25) perkütan koroner girişim uygulanan AMİ hastalarında SV trombüs oluşumu açısından yakın takip edilmesinin akılcı bir yaklaşım olabileceği sonucuna vardık.

Anahtar Kelimeler: Sol Ventrikül, Trombüs, SYNTAX skoru

Abstract

Objective: Left ventricular (LV) apical thrombus development is one of the important adverse events in patients with anterior ST elevation myocardial infarction (STEMI) and accompanies with LV apical aneurysm and systolic dysfunction. SYNTAX score is an important determinant of cardiovascular morbidity and mortality in patients with coronary artery disease. We aimed that the relationship between LV apical thrombus and SYNTAX score and other clinical risk factors patients with anterior STEMI.

Material and Methods: A total of 205 consecutive anterior STEMI patients undergoing primary PCI (35 female/ 170 male mean age: 55.8 ± 9.6 years) were included in our study. We assessed the severity and complexity of coronary artery disease by using SYNTAX score. The patients were divided into two groups; patients with apical thrombus (n=19) and patients without apical thrombus (n=186).

Results: We found that systolic and diastolic blood pressure were lower patients with apical thrombus groups. (p<0.001 for both). Syntax score was higher and LV ejection fraction (LVEF) is lower in patients with apical thrombus (p<0.001 for both). We also showed that LV apical thrombus formation was independently associated with lower systolic blood pressure (p=0.006), SYNTAX score (p=0.003), and depressed LVEF (p=0.001).

Conclusion: In this study, impaired LVEF, lower systolic blood pressure and SYNTAX score have been found to be predictors of LV thrombus generation. Patients presenting with anterior myocardial infarction who have high SYNTAX scores (> 18.25) at PPCI should be followed up closely.

Key Words: Left Ventricul, Thrombus, SYNTAX score

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INTRODUCTION

Primary percutaneous coronary interventions (PPCI) is the important reperfusion strategy in patients with ST segment elevation myocardial infarction (STEMI) (1) and many adversely factors may contribute to patients outcomes such as delaying time, accompanied comorbidities and hemodynamic status (2). It is well known that co-existence with obstructive coronary artery disease apart from the infarct related artery have realated with poor prognosis following PPCI (3). In addition to the other complications, left ventricular (LV) apical thrombus formation is the one of the major complication of anterior STEMI and usually accompanies with left ventricular apical aneurysm and systolic dysfunction (4). Presence of left ventricular thrombus formation is also linked with the arterial and cerebrovascular embolic complications (5). Previous studies have showed that endothelial damage, hypercoagulability, infarct size, left ventricular aneurysm and anterior myocardial infarct localization are the major risk factors of the thrombus development (6, 7). SYNTAX (Between PCI With TAXUS™ and Cardiac Surgery) score is an also key determinant of cardiovascular morbidity and mortality in patients with STEMI (8). Since we have no clear data, we aimed to investigate that the relationship between the frequency of LV apical thrombus formation and SYNTAX score and other clinical risk factors.

MATERIAL AND METHODS

Two hundred and five consecutive patients with Anterior STEMI who underwent PPCI were included in this study and then patients were divided into the two groups according to left ventricular thrombus presence. Patients with a history of coronary intervention or coronary artery bypass surgery, history, previous myocardial infarction, cardiac failure or valvular heart disease, history of end stage renal failure, active infection, cancer, hematological diseases, autoimmune diseases, pregnancy, anemia, recent blood transfusion and patients with atrial fibrillation were excluded from the study. All demographic and clinical data were prospectively collected and patients were followed by outpatients clinic for 3 months. Informed consent was obtained from all patients and study was also approved by our local ethical committee.

Anterior STEMI, Hypertension (HT), Diabetes mellitus (DM), Atrial fibrillation (AF) and Hyperlipidemia (HPL) were defined according to previously published guidelines (9-11). Patients with baseline hematocrit levels <39% for males and <36% for females were accepted anemia patients. All echocardiographic measurements were performed using Vivid 4 GE Medical System (Horten, Norway) with a 2.5 - 3.5MHz transducer in accordance with the modified Simpson's method before the PPCI, and after 24 hours from the PPCI, and before the hospital discharging and finally after 1 months (12).

According to previous descriptions, SYNTAX scores were calculated by two experienced invasive cardiologists blinded to the study protocol (13). PPCI was performed by ex-

perienced interventional cardiologists according to current guidelines. Periprocedural antiaggregant and anticoagulant treatment were administered to the all patients according to guidelines directions (9). Since our hospital had no Prasugrel and Ticagrelor due to insurance restrictions, patients received Clopidogrel as a P2Y12 inhibitor during this study. Venous blood was sampled from a peripheral vein prior to PPCI and during hospitalization. Blood samples were drawn into standardized tubes and assayed using routine laboratory techniques. Hematological measurements were performed using the aid of an XT-2000i analyzer (Sysmex America Inc., Long Grove, IL, USA). Routine biochemical measurements [e.g. creatinine (Cr)] were made using an automated biochemistry analyzer (Abbott Aeroset, Minneapolis, MN, USA).

Statistical Analysis

Analyses were performed using SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Numerical variables are presented as means \pm standard deviations, and nominal variables as percentages. Kolmogorov-Smirnov testing was used to determine whether variables were normally distributed. The independent samples t-test or Mann-Whitney U test were used to compare the values of continuous variables between the two groups. To evaluate the effects of various factors on left ventricular thrombus development, we performed multivariate regression analyses using logistic regression method. The model was adjusted using various candidate factors, such as blood pressure, killip status, heart rate, body surface area and SYNTAX score. A receiver operator characteristic (ROC) curve was constructed to determine the predictive value of SYNTAX score on left ventricular thrombus development. Coefficients with 95% confidence intervals (CIs) were presented. A p-value <0.05 was considered significant.

RESULTS

A total of 205 anterior STEMI patients undergoing primary PCI (35 female/ 170 male mean age: 55.8 ± 9.6 years) were included in our study. Patients with LV thrombus groups (9.2%) had lower pre-PCI TIMI, Left ventricular ejection fraction (LVEF), systolic blood pressure (SBP) and diastolic blood pressure (DBP) than patients without LV thrombus groups. However, killip class status, Brain natriuretic peptide (BNP) levels, SYNTAX score, apical aneurysm incidence were higher in patients with LV thrombus groups. We also found that patients with LV thrombus groups had higher furosemide and spironolactone usage ratios than the other group (**Table 1**).

According to multivariate regression analyses which was constructed using various candidate factors, SBP (OR; 0.938, P=0.006), SYNTAX score (OR;1.414, P=0.003) and LVEF (OR;0.767, P=0.001) were independent predictors of LV thrombus development (**Table 2**).

We also found that the cut-off value of SYNTAX score >18.25 was predicted LV thrombus development with a sen-

Table 1. Patients Characteristics Based On LV Thrombus Presence

Variables	Group 1 Without LV thrombus n=186	Group 2 With LV thrombus n=19	P
Age (years) mean \pm st dev	55.2 \pm 11.2	57.4 \pm 8.9	NS
Male gender n,	157	13	NS
DM n, (%)	40 (21,5)	6 (31,5)	NS
HT n, (%)	78 (42)	9 (45)	NS
HPL n, (%)	63 (33,5)	3 (20)	NS
Smoking n, (%)	141 (75,8)	16 (85)	NS
BMI kg/m ²	27.5 \pm 4.1	28.1 \pm 4.1	NS
SBP, mmHg	132 \pm 25.1	103 \pm 16.7	<0.001
DBP mmHg	82.2 \pm 15.4	68.2 \pm 11.7	<0.001
Killip class 2-4, (%)	13 (7)	7 (37)	<0.001
Haemoglobin, gr/dL	14.5 \pm 1.5	13.6 \pm 1.8	0.015
WBC,	12.7 \pm 3.9	13.6 \pm 4.6	NS
LDL, mg/dL	138 \pm 28.7	146 \pm 36	NS
TG, mg/dL	172 \pm 116	139 \pm 69	NS
Kreatinin, mg/dL	0.94 \pm 0.58	0.93 \pm 0.2	NS
BNP, pg/ml	687 \pm 1041	1926 \pm 2018	<0.001
Time onset to chest pain, (hours)	4.2 \pm 2.9	5.6 \pm 1.9	NS
SYNTAX score	15.2 \pm 4.3	22.1 \pm 3.9	<0.001
Implanted stent number	1.26 \pm 0.52	1.26 \pm 0.45	NS
Door to baloon time dk	24.3 \pm 6.0	27.0 \pm 9.3	NS
Contrast volume (ml)	241 \pm 73	286 \pm 73.6	0.009
Pre-PCI TIMI	0.45 \pm 0.75	0.05 \pm 0.22	<0.001
Post PCI TIMI	2.89 \pm 0.42	2.84 \pm 0.68	NS
LVEF (%)	45.2 \pm 7.1	32.1 \pm 4.3	<0.001
Apical aneurysm n, (%)	15 (%8)	15 (79)	<0.001
ASA, (%)	181 (97,3)	19 (100)	NS
BB, (%)	176 (94)	17 (89,4)	NS
ACEİ - ARB, (%)	168 (90.0)	16 (84)	NS
GP2B3A, (%)	30(16.1)	4(21.0)	NS
Furosemid, (%)	73 (39)	17 (89)	<0.001
Spiranolactone, (%)	33 (18)	14 (73)	<0.001
Statin, (%)	168 (90)	16 (84)	NS
CCB, (%)	15 (8)	0 (0)	NS
Peak CK-MB	86.4 \pm 97.5	115.6 \pm 124.6	NS
Peak troponin, ng/mL	1424 \pm 2475	1690 \pm 2468	NS

DM: Diabetes Mellitus, HT: Hypertension, BMI:Body Mass Index, SBP:Systolic Blood Pressure, DBP: Diastolic Blood Pressure, WBC: White Bool Cell, LDL: Light density Lipoprotein, TG: Triglyceride, BB: Beta Blocker, CCB: Calcium Channel Blocker

Table 2. Predictors of LV thrombus development.

Variables	OR	CI, 95%	P value
SBP mmHg	0.938	0.897 – 0.982	0.006
SYNTAX score	1.414	1.122 – 1.782	0.003
LVEF, %	0.767	0.660 – 0.892	0.001

sitivity of 84.25% and specificity of 75.80% (AUC 0.889, 95% CI 1.122 to 1.782, $p=0.001$) (**Figure 1**).

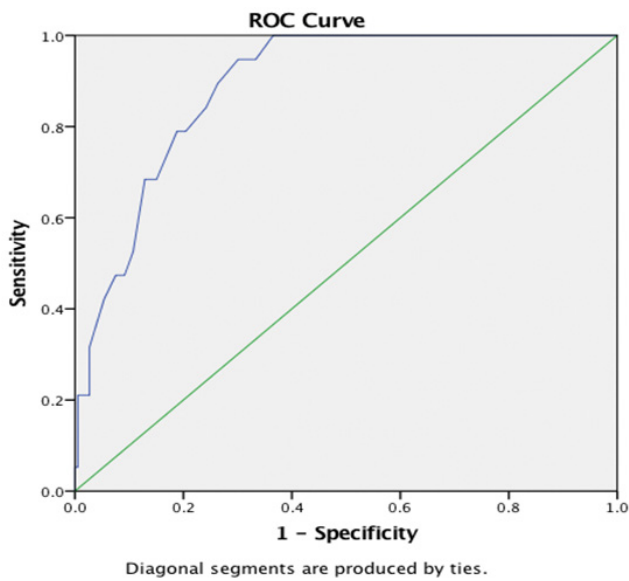


Figure 1. Relationship the Between Syntax Score and LV thrombus Development.

Based on the in hospital and 3 months follow up results we also found that ventricular fibrillation ($p=0.001$), contrast-induced nephropathy development ($p=0.016$), stent thrombosis ($p=0.012$), symptomatic HF development ($p<0.001$), stroke ($p=0.011$) and mortality ($p=0.006$) ratios were higher in patients with LV thrombus groups than without thrombus groups (**Table 3**).

data about STEMI and LV thrombus development. Studies showed that LV thrombus development incidence 5.1% - 7.1% in patients with anterior STEMI underwent PPCI (6, 16). However, both studies are retrospective and have limited echocardiographic assessment. Our patient's groups were followed 30 days with adequate echocardiographic study for thrombus development and we also found that 9.2% of patients had LV thrombus development. Although having limited and selective patients data, Solheim *et al.* also showed that patients underwent PPCI due to STEMI had 9.2% LV thrombus development (7). In our study we found lower LV thrombus incidence. In addition to respective design, bigger sample size can contribute this results, so we think our results might reflect more truthful LV thrombus incidence in patients with anterior STEMI underwent PPCI.

In our study, we assessed CAD complexity and severity with SYNTAX score which predict major adverse cardiac events such as no-reflow and 30 days mortality (17, 18). Although SYNTAX score have predictive importance, we have no clear data about relationship with SYNTAX score and LV thrombus incidence up to now. According to our results SYNTAX score predicted LV thrombus development. First, bigger SYNTAX score may be related more ischemic burden and gained infarct size. It is well known that large infarct size and lower LV EF predicted LV thrombus development (6, 19). Another reason of this result is as a SYNTAX score increased catecholamine levels also increased which closely related to expanded microvascular resistance (20). This expanded resistance may be contribute LV blood stasis and thrombus development.

Table 3. 3 months follow up results according to LV thrombus presence.

Variables	Group 1 Without LV thrombus n=186	Group 2 With LV thrombus n=19	P value
AF, n (%)	2 (1)	0 (0)	0.8
VF, n (%)	12 (6,5)	7 (37)	0.001
HF, n (%)	85(46)	19 (100)	< 0.001
Stent thrombosis, n (%)	12 (6,5)	5 (26)	0.012
CIN, n (%)	13 (7)	5 (26)	0.016
Stroke, n (%)	3 (1,6)	3 (15,7)	0.011
Mortality, n (%)	2 (1)	3 (15,7)	0.006

DISCUSSION

In our prospective study, we found that SYNTAX score is one of the independent predictors of LV thrombus development. Hypercoagulability, endothelial impairment and blood stasis are important traditional pathophysiologic factors for LV thrombus development in patients with STEMI (14). Though first 24 hours are important, studies have shown that LV thrombus development may be seen within 14 days due to LV remodeling (15). In PPCI area, we have limited

There are conflicting results between medical therapy and LV thrombus development. GISSI-2 claimed that no association between beta blocker therapy and LV thrombus development, but another study showed early IV beta blocker administration is related to LV thrombus development (21, 22). In our study we didn't use early IV beta blocker and show association between LV thrombus formation and beta blocker usage. Discordant to previous studies, we found that GPIIb/IIIa usage, older age and hypertension did not affect LV thrombus development (6, 23,24). In our opinion smaller

sample size might be contribute this result.

Although prospective design and relatively large sample size our study have some limitations. First we didn't evaluate inflammatory parameters such as hs-CRP, IL-6 and TNF- α that may related more accurate results. Second none of our patients did not use more aggregation inhibitors such Prasugrel and/or Ticagrelor due to health insurance restrictions and local availability. Using Prasugrel and Ticagrelor might be related lower LV thrombus development and more contemporary results. Third, we used traditional transthoracic echocardiographic study for detecting LV thrombi. However Cardiac MRI studies showed that MRI more sensitive technique to evaluate LV thrombus (6, 25).

As a conclusion, In this study, higher SYNTAX score, lower LVEF and SBP have been found to be predictors of LV thrombus generation. We think that patients presenting with anterior myocardial infarction who have high SYNTAX scores (> 18.25) at PPCI should be followed up closely for LV thrombus formation and take strict antithrombotic medication. For clear explanation of in this issue further randomized controlled studies are to be needed.

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