Determinants of Coronary Angiography in Non-ST-elevation Myocardial Infarction with Low Ejection Fraction

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ABSTRACT

Objective: To investigate the clinical and demographic factors affecting the selection of angiography in patients with severe left ventricular systolic dysfunction (SLVSD, ejection fraction lower than 30%) developing non-ST-segment elevation (NSTEMI).

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Cardiology, School of Medicine, Izmir Katip Celebi University, Izmir, Turkey, between March 2018 and March 2021.

Methodology: Patients with SLVSD (Ejection fraction <30%) developing Clinical and demographic factors were compared between the patients who were or were not decided for angiography. Associated factors for the decision of angiography were evaluated.

Results: Overall, 68 (46%) out of 147 patients underwent coronary angiography. Angiography led to coronary artery bypass grafting (CABG) in 14 (21%), percutaneous coronary intervention (PCI) in 30 (44%), and medical treatment in 24 (35%). Among the patients who decided for CABG, 10 (71%) underwent surgery. In multivariate analysis; Killip score ≥2 [Odds ratio (OR) :33.85, 95% Confidence Interval (CI): 5.03-227.405 p<0.001], lower education level (OR: 17.66, 95% CI: 2.25-138.44, p=0.006), anaemia (OR: 10.60, 95% CI: 2.07-54.28, p=0.005), age ≥65 years (OR: 7.124, 95% CI: 1.33-38.12, p=0.02), and PCI history (OR: 0.132, 95% CI: 0.02-0.84, p=0.032) were associated factors with the decision of only medical treatments instead of angiography.

Conclusion: Demographic factors such as age and education level and clinical factors such as decompensation, PCI history, and anaemia significantly affect the decision of angiography in the patients with SLVSD and NSTEMI.

Key Words: *Heart failure, NSTEMI, Revascularisation, Severe left ventricular systolic dysfunction, Ejection fraction.*

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INTRODUCTION

Heart failure (HF) is still having high mortality despite state-of-the-art treatments. One of the common causes of mortality in HF is recurrent hospitalisations.[1] Although many clinical factors can lead to hospitalisations in HF, ischemic factors such as acute coronary syndrome have a major role in decompensation or deterioration during disease.

Acute coronary syndrome increases mortality in HF and *vice versa*. Unquestionably, revascularisation is essential irrespective of having heart failure by the time ST-segment elevation myocardial infarction is detected (STEMI).[2-5]

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However, there is still controversy about which group of the patients with NSTEMI and HF may highly benefit from revascularisation.[6,7]

Severe left ventricular dysfunction (SLVSD) further complicates the prognosis of the patients with NSTEMI. Therefore, clinicians may avoid invasive treatment in these patients for fear of increasing in-hospital mortality. Besides, additional comorbidities may affect the decision of only medical treatment instead of angiography. Based on these data, the aim of this study was to investigate the factors that influence clinicians to choose coronary angiography in patients with NSTEMI and SLVSD.

METHODOLOGY

This retrospective descriptive study included 147 patients with SLVD (ejection fraction <30%) who were hospitalised due to the NSTEMI at the School of Medicine, Izmir Katip Celebi University, Izmir, Turkey, between March 2018 and March 2021. This study was approved by the Ethical Committee (Approval No. 357) and it was consistent with the principles of the Helsinki Declaration.

The data of the patients were collected from the hospital records. Patients' demographic factors including age, gender, body mass index (BMI: weight divided by the square of height as Kg/m^2), education level, clinical findings (cardiovascular risk factors, clinical disease and other chronic diseases), Killip score, electrocardiography, echocardiography, and laboratory findings were recorded. Echocardiographic imaging was obtained before the patients underwent coronary angiography. Patients were divided into two groups based on undergoing angiography. Angiographic results were recorded as medical treatment, percutaneous coronary intervention (PCI), and coronary artery bypass grafting. Coronary stenosis was accepted as significant if the corresponding coronary artery had ≥ 50% stenosis.

Inclusion criteria was EF <30%, NSTEMI, and age >18 years. NSTEMI was defined if chest pain or electrocardiographic changes were present in addition to troponin elevation. Myocardial infarction was defined based on the universal definition of myocardial infarction. In this context, high sensitive troponin elevation at least one above 99th percentile limits in addition to either symptoms of myocardial ischemia, or non-ST elevation myocardial infarction-related electrocardiographic features including transient ST elevation of lower than 20 minutes, transient ST depression, T- wave changes, or normal.[6] Exclusion criteria was patients under 18 years of age, STEMI or unstable angina, ischemia-related mechanical complication, acute cerebrovascular event, severe dementia, refused guideline-recommended treatment or non-adherent to the medical treatment, severe frailty, tachycardiomyopathy, hypertensive emergency, myocarditis, aortic dissection, pulmonary embolism, anaphylaxis history to contrast medium, major bleeding, or platelets lower than 20 x 10^3/µL.

Patients using antihypertensive treatment or consecutive blood pressure over 140/90 mmHg were defined as having hypertension.[8] Patients on antidiabetic treatment or fasting blood glucose >126 mg/dl or HgA1c >6.5 gr/dl were accepted as diabetes.[9] Dyslipidemia was defined if the patients on lipid treatment or cholesterol or triglyceride levels were above the limits according to the cardiac risk profile.[10] Glomerular filtration rate (GFR) lower than 60 ml/min/1.73 m^2 was recorded as chronic renal failure (CRF).[11] Patients with a history of cerebral ischemia, infarct or hemorrhage, and a history of central cerebral damage were included in the stroke group. The peripheral arterial disease was accepted if there was atherosclerotic stenosis of more than 50% on Doppler ultrasonography, computed tomography, magnetic resonance imaging, angiography, or ankle-brachial index under 0.9. Prior history of PCI, CABG, known heart failure, intracardiac defibrillator (ICD), and cardiac resynchronisation therapy (CRT) was documented. According to the Killip classification, provided that the patient had lung edema comprising more than half of the lung or cardiogenic shock defined as Killip 3 and 4, respectively.[12] Additional clinical diseases diagnosed by the other disciplines such as metastatic cancer, chronic obstructive chronic disease, duration of hospitalisation, and in-hospital mortality were evaluated.

Statistical analyses were performed using SPSS 23 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp). Continuous variables were demonstrated median ± interquartile range (Q1-Q3) after assessing normality distribution on the Kruskal-Wallis test. Categorical variables were demonstrated as percentages. Patients undergoing angiography or not were compared with Mann-Whitney U test. Categorical variables were compared using the chi-square test. Variables with a p-value <0.2 were put in univariate analysis. The factors associated with the decision of performing angiography in univariate analysis were put in multivariate logistic regression analysis. Associated factors were shown with odds ratio (OR) and 95% confidence interval (CI). A two-sided p-value <0.05 was accepted as statistically significant.

Table I: Baseline characteristics of the patients with severe heart failure and acute myocardial infarction without ST-segment elevation.

	Coronary angiography not performed 79 (54%)	Coronary angiography performed 68 (46%)	p
Age, years median (IQR)	69 (65-79)	60 (53-69)	<0.001
Female gender n (%)	35 (44%)	10 (15%)	<0.001
BMI kg/m^2 median (IQR)	29 (25-31)	27 (25-29)	0.01
Hypertension n (%)	45 (57%)	36 (53%)	0.62
Dyslipidemia n (%)	23 (29%)	24 (35%)	0.42
Diabetes Mellitus n (%)	47 (59%)	28 (41%)	0.03
Chronic renal failure n (%)	18 (23%)	6 (9%)	0.02
Smoking n (%)	8 (10%)	18 (26%)	0.01
Stroke n (%)	14 (18%)	6 (9%)	0.12
PAD n (%)	8 (10%)	10 (15%)	0.40
COPD n (%)	12 (15%)	18 (26%)	0.09
Malignity n (%)	4 (5%)	2(3%)	0.69
PCI history n (%)	12 (15%)	26 (38%)	0.001
CABG history n (%)	35 (44%)	8 (12%)	<0.001
ICD/CRT n (%)	14 (18%)	8 (12%)	0.31
Known heart failure n (%) n (%)	47 (59%)	24(35%)	0.003
Severe valvular disease	21 (27%)	8 (12%)	0.02
Atrial fibrillation n (%)	21 (30%)	6 (9%)	0.001
Nosocomial infection n (%)	2 (2,5%)	4 (5,9%)	0.42
Angina n (%)	29 (37%)	52 (76%)	<0.001
Killip Class >2 n (%)	60 (76%)	24 (35%)	<0.001
Malign arrhythmia n (%)	4 (5%)	4 (6%)	1
CPR n (%)	2(2%)	4 (6%)	0.42
Intubation n (%)	-	2(3%)	0.21
Heart rate median (IQR)	85(70-95)	82 (75-92)	0.74
LVEF(%) median (IQR)	25 (20-25)	25 (25-28)	0.002
Anaemia n (%)	55 (70%)	22 (32%)	<0.001
Platelet 10 ^{3} /µL median (IQR)	246(211-323)	230(195-301)	0.10
Peak troponin ng/L median (IQR)	228(91-2153)	599 (77-1864)	0.67
AST U/L median (IQR)	32(16-57)	28.5 (19-62)	0.86
ALT U/L median (IQR)	21 (11-43)	21 (15-35)	0.76
Creatinine mg/dl median (IQR)	1.32(0.95-1,78)	1.09(0.9-1.26)	0.001
GFR ml/min/1.73 m^2 median (IQR)	49 (35-65)	68 (59-80)	<0.001
CRP mg/dl median (IQR)	21 (8-76)	15 (6-37)	0.11
Low education level (Elementary school or less) n%	61(77%)	24 (35%)	0.002
Insurance n (%)	72(91%)	66 (97%)	0.18
Marital status, bachelor n (%)	35 (44%)	8 (12%)	<0.001
Duration of hospitalisation, days median(IQR)	5 (3-8)	4 (3-6)	0.61
Contrast nephropathy		2(3%)	
Stent thrombosis		2 (3%)	
In-hospital mortality	16 (20%)	2 (3%)	0.001

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, CABG: Coronary artery bypass grafting, COPD: Chronic obstructive pulmonary disease, CPR: Cardiopulmonary resuscitation, CRP: C-reactive protein, CRT: Cardiac resynchronisation therapy, GFR: Glomerular filtration rate, ICD: Intracardiac defibrillator, LVEF: Left ventricle ejection fraction, PAD: Peripheral arterial disease. IQR: Interquartile range, and n: Number.

RESULTS

The number of patients undergoing angiography was 68 (46%). Baseline characteristics of the patients with or not undergoing angiography were shown in Table I. Patients, who didn't undergo angiography, were older and predominantly female. In addition, the rate of BMI, diabetes, CRF, smoking, CABG history, known HF, severe valvular disease, atrial fibrillation, Killip score >2, anaemia, lower education level, and being a bachelor was higher in those who were considered ineligible for angiography. However, the presence of angina, PCI history, and ejection fraction was higher in the angiography group.

Angiography results were: 44% PCI, 35% medical treatment, and 21% CABG. Among patients who decided on CABG, 71% underwent surgery. Significant coronary stenosis was present at 68%, 62%, 56%, and 3% in the left anterior descending artery, right coronary artery, circumflex artery, and left main coronary artery, respectively. The rate of given standard medical treatment was higher in the patients undergoing angiography (Table II). Besides, the mortality rate was higher in the patients who didn't undergo angiography (20% *vs.* 3%, p=0.001).

Table II: Medication of heart failure during hospitalisation.

	Coronary angiography (-)	Coronary angiography (+)	p
Beta blocker	69 (87%)	68 (100%)	0.002
ACEi	38 (48%)	40 (59%)	0.194
Statin	34 (43%)	48 (71%)	0.001
MRA	22 (28%)	22 (32%)	0.552

ACEi: Angiotensin-converting enzyme inhibitor, MRA: Mineralocorticoid receptor antagonists.

Table III: Factors associated with the ineligibility to perform coronary angiography in univariate logistic regression analysis.

	Univariate logistic regression analysis		
	OR	95%CI	p
Killip 2 and more	(5.789)	2.828-11.854	<0.001
Low education level	(3.012)	1.482-6.123	0.002
Anaemia	(4.792)	2.383-9.636	<0.001
Age ≥65 years	(8.512)	3.972-18.240	<0.001
PCI history	(0.289)	0.132-0.634	0.002
Female gender	(4.61)	2.06-10.31	<0.001
BMI> 30 Kg/m^2	(2.767)	1.322-5.791	0.007
Diabetes mellitus	(2.098)	1.085-4.058	0.03
Chronic renal failure	(3.049)	1.134-8.200	0.03
Smoking	(3.195)	1.289-7.922	0.01
COPD	(2.010)	0.888-4.551	0.09
CABG history	(5.966)	2.552-14.112	<0.001
Known heart failure	(2.693)	1.378-5.263	0.004
Severe valvular disease	(2.716)	1.114-6.617	0.03
Atrial fibrillation	(4.509)	1.717-11.841	0.002
Angina	(0.178)	0.087-0.368	<0.001
EF<25%	(2.437)	1.169-5.084	0.02
Bachelor	(5.966)	2.522-14.112	<0.001

Statistical results after univariate and multivariate analyses were shown in Table III. In multivariate analysis; Killip score ≥2 (OR :33.85, 95% CI: 5.03-227.405 p<0.001), lower education level (OR: 17.66, 95% CI: 2.25-138.44, p=0.006), anaemia (OR: 10.60, 95% CI: 2.07-54.28, p=0.005), PCI history (OR: 0.132, 95% CI: 0.02-0.84, p=0.032), and age ≥ 65 years (OR:7.124, 95% CI:1.33-38.12, p=0.02) were associated factors with the decision of angiography instead of medical treatment (Table IV).

Table IV: Factors associated with the ineligibility to perform coronary angiography in multivariate logistic regression analysis.

	Multivariate logistic regression analysis		
	OR	95%CI	p
Killip 2 and more	(33.851)	5.039-227.405	<0.001
Low education level	(17.663)	2.253-138.449	0.006
Anaemia	(10.608)	2.073-54.283	0.005
Age ≥65 years	(7.124)	1.331-38.124	0.02
PCI history	(0.132)	0.021-0.842	0.03
Female gender	(1.414)	0.257-7.763	0.69
BMI> 30 Kg/m^2	(1.527)	0.308-7.560	0.60
Diabetes Mellitus	(2.855)	0.496-16.418	0.24
Chronic renal failure	(1.324)	0.111-15.773	0.82
Smoking	(1.157)	0.133-10,081	0.89
COPD	(5.395)	0.450-64.706	0.18
CABG history	(3.074)	0.555-17.014	0.20
Known heart failure	(2.802)	0.598-13.119	0.19
Severe valvular disease	(2.878)	0.492-16,838	0.24
Atrial fibrillation	(6.942)	0.715-67.358	0.09
Angina	(0.504)	0.116-2.186	0.36
EF<25%	(6.583)	0.981-44.178	0.052
Bachelor	(3.638)	0.512-25.858	0.20

DISCUSSION

To this knowledge, this is the first study to have investigated the associated factors including clinical and demographic variables with the decision of angiography in patients with SLVSD and NSTEMI. According to the results of this study, Killip score >2, low education level, anaemia, and age over 65 years were independent variables related to the decision of medical treatment instead of performing angiography.

Heart failure has been a disincentive factor with regard to the decision of angiography so far. Heart failure has been considered a strong mortality predictor in NSTEMI.[13] A study demonstrated that angiography and PCI rate were lower in NSTEMI patients with heart failure (57% *vs.* 47%).[14] Kaul *et al* also showed similar results that the patients with heart failure had a tendency to be followed without angiography (57% *vs.* 43%).[15] These findings consisted of the previous studies. More than half of the heart failure patients were refused angiography. Despite fear of mortality during angiography in LVSD and NSTEMI, early angiography within two weeks of hospitalisation in patients with ischemia-caused heart failure reduced all-cause mortality, heart failure caused mortality, and heart failure caused hospitalisation.[16]

Although revascularisation is strongly recommended within the time limits of ST-segment elevation in myocardial infarction diagnosis, the time of revascularization is determined based on the risk level in NSTEMI. However, some groups of the patients with certain risk levels may be neglected from angiography in clinical practice. Çakmak *et al*. reported that advanced age (>90 years) independently increases in-hospital mortality and major complications regardless of performing PCI or medical treatment.[17] Franco *et al.* showed higher Killip class and

advanced age were poor prognostic factors in HF patients with NSTEMI, and these factors were associated with the decision of non-invasive treatment.[18] In large cohort of the patients with HF, age, white race, dementia, COPD, CABG history, high creatinine level, atrial fibrillation, and unknown EF were the predictors in the decision of angiography. This study showed consistent results with previous studies that Killip score, anaemia, and advanced age were associated with the decision of angiography. Furthermore, low education is another factor related to the decision on non-invasive treatment. There are some main possible reasons. Firstly, patients with low education levels tend to non-adherence to the medication which may increase angiographic complications, particularly stent thrombosis. Secondly, low-educated people are mainly composed of elder people and they usually reside in the rural and pastoral areas. These people frequently need someone else or a caregiver to take pills and meet their daily needs. These factors might influence the clinician in performing angiography.

The rate of standard medical treatment was higher in the angiography group. These findings were consistent with the OPTIMISE-HF trial which showed an association between aspirin, statins, beta-blockers, Renin-angiotensin system (RAS) blockers, and in-hospital angiography in the patient with heart failure.[19] However, patients who refuted angiography had a higher rate of decompensation and renal failure which might preclude the use of beta-blockers and RAS- blockers.

This study was conducted at a single centre. Therefore, the results of this study cannot be generalised to the population. Although causes of troponinosis were excluded, operator bias cannot be ruled out in the diagnosis of NSTEMI due to the retrospective nature of the study. Although the mortality rate was higher in those patients who didn't undergo angiography, we couldn't deduce performing angiography would reduce mortality since those patients had a higher rate of mortality risks.

CONCLUSION

Coronary angiography decision in NSTEMI patients with SLVSD might be affected by clinical factors such as high Killip score, anaemia, PCI history, and advanced age and demographic factor such as low education level.

ETHICAL APPROVAL:

This study was approved by the Ethical Committee (Approval No. 357) and it was consistent with the principles of the Helsinki Declaration.

PATIENTS' CONSENT:

The study is retrospective study. For this reason, patient consent is not available.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

SVE: Substantial contributions to the conception or design of the work, acquisition, analyses and interpretation of data.
ZYE: Drafting the work and revising it critically for important intellectual content.
AE: Final approval of the version to be published.
OS: Drafting the work.
All the authors have approved the final version of the manuscript to be published.

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