

The impact of clinical and angiographic factors on percutaneous coronary angioplasty outcomes in patients with acute ST-elevation myocardial infarction

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Abstract

Introduction: Percutaneous coronary intervention (PCI) outcomes are dependent on certain clinical and angiographic factors. The impact of modifiable cardiovascular disease (CVD) risk factors on PCI outcomes is still controversial. The aim of the study was to evaluate the impact of clinical and angiographic factors on PCI outcomes for patients with acute ST-elevation myocardial infarction (STEMI).

Material and methods: Age, gender, CVD risk factors, Killip class and culprit coronary artery (CA) localization, total CA occlusion, initial and post-procedural thrombolysis in myocardial infarction (TIMI) flow grade, and thrombus aspiration characteristics were assessed retrospectively in 188 consecutive patients with STEMI who underwent primary PCI. Spearman's rho test was performed to assess hospital stay correlations, and logistic regression was applied to identify predictors of distal embolization (DE), in-hospital worsening of heart failure (WHF), and in-hospital mortality rate. Local ethics committee approval was obtained for the study.

Results: DE occurred in 12 (6.4%) patients. In-hospital WHF was diagnosed in 16 (8.5%) patients. Twelve (6.4%) patients died in hospital. Age had a positive weak correlation with hospital stay and was an independent predictor of distal embolization, in-hospital worsening of heart failure, and in-hospital mortality rate. Killip class, left main CA stenosis (> 50.0%), and post-procedural TIMI flow grade 1-2 were other predictors of death in hospital.

Conclusions: Age was an independent predictor of distal embolization, in-hospital worsening of heart failure, and in-hospital mortality. Other independent predictors of in-hospital mortality rate were Killip class, left main CA stenosis (> 50.0%), and post-procedural TIMI flow grade 1-2. The present analysis highlighted the "cholesterol paradox" with respect to in-hospital worsening of heart failure and mortality in hospital.

Key words: ST-elevation myocardial infarction, percutaneous coronary intervention, predictors, distal embolization, in-hospital worsening of heart failure, in-hospital mortality rate.

Introduction

Cardiovascular disease (CVD) is the most common cause of death among Europeans. The mortality from coronary heart disease (CHD) in Lithuania is one of the highest in Europe, and both Lithuanian males and females are

on the list of the first 10 European countries with the highest CHD mortality rates in 2013. Despite the improvement in the diagnosis and treatment, acute myocardial infarction (MI) occurs in about 20 people, 3 of whom die, in Lithuania each day [1, 2]. Previous studies revealed that percutaneous coronary intervention (PCI) outcomes are dependent on clinical variables (the most important of them are age, renal function, and left ventricular function) and anatomical complexity of coronary artery disease [3]. Halkin *et al.* developed the first risk score (the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications [CADILLAC]) for predicting mortality after PCI, which included both clinical and angiographic variables [4]. However, the impact of modifiable CVD risk factors on PCI outcomes is still not clear due to the existence of the phenomenon “obesity, smoking, and cholesterol paradox”, when the mortality rate after PCI is lower in these CVD risk groups. Meta-analysis of 100 studies revealed that diabetes, hypertension, and metabolic syndrome are independent predictors of adverse outcomes after PCI. Unexpectedly, smoking and obesity again showed a paradox after PCI [5]. According to the guidelines for PCI (2014), adverse outcomes after PCI are more common in patients with advanced age, diabetes, congestive heart failure (HF), chronic kidney disease, acute coronary syndromes and multi-vessel coronary artery (CA) disease [6]. Although previous studies analyzed predictors of PCI outcomes earlier, the results might differ among countries due to different access to healthcare centers and procedural techniques. Moreover, identification of the risk factors of adverse outcomes after PCI may help physicians to identify high-risk patients, who then may receive specific management, and thus prevent serious complications after the procedure.

The purpose of this study was to evaluate the impact of clinical and angiographic factors on PCI outcomes for patients with acute STEMI.

Material and methods

Study population

The study included consecutive patients who were hospitalized because of acute STEMI and PCI was performed within 24 h of the initial symptoms. All the investigated patients were treated in the Lithuanian University of Health Sciences, Kaunas Clinics Department of Cardiology from March 2, 2012 to November 29, 2012. Patients who had thrombolysis performed before their transfer to Kaunas Clinic are not included in the study.

Research

Clinical (age, gender, CVD risk factors, Killip functional class) and angiographic (culprit CA lo-

calization, total CA occlusion, initial and post-procedural thrombolysis in myocardial infarction [TIMI] flow grade, thrombus aspiration) data were obtained retrospectively, analyzing medical case histories and quantitative coronary angiography recordings of CA. We analyzed data of 188 patients, ranging in age from 37 to 90 years. The existence of risk factors was identified from medical records and clinical test results performed in the Department of Cardiology. We assessed the degree of antegrade arterial flow recovery after the procedure, according to the classification of TIMI and distal embolization after PCI. Angiographically visible thrombus or plaque debris embolization distally from the target lesion was considered as distal embolization (DE). Also, we evaluated length of hospital stay (LOS), and outcomes such as stent thrombosis, strokes, cardiovascular deaths, and worsening of HF (WHF) rate during the hospitalization period. All stent thrombosis cases were confirmed by angiography. Natriuretic peptides were not measured for study patients; thus in-hospital WHF was defined as an increase of Killip class IV. Local ethics committee approval was obtained for the study.

Statistical analysis

The data were analyzed using the SPSS statistical package (version 20.0 for Windows). Categorical data are presented as numbers and percentages, and descriptive statistics are presented as mean \pm SD or medians (minimum; maximum). The Mann-Whitney test was applied for the statistical comparison of descriptive variables. The χ^2 test was used for the comparison of categorical values. ANOVA test was used to evaluate LOS in different groups and Spearman's rho test to assess hospital stay correlations. Binomial logistic regression was performed to identify clinical predictors of distal embolization, in-hospital WHF, and in-hospital mortality rate. The level of significance was considered as 0.05.

Results

Study population

Average age of patients was 65.32 ± 12.33 years. Those older than 65 years made up 51.1%. The majority of patients were male (70.2%). The CVD risk factor frequencies were as follows: 79.3% of patients had arterial hypertension, 14.9% diabetes, 78.2% dyslipidemia, and 35.6% smoked. In the dyslipidemia group, 51 (34.7%) patients used statins previously and average total cholesterol level in this group was 6.1 mmol/l. During and after hospitalization for STEMI, all patients received statins according to acute coronary syndromes guidelines. The majority of patients were in Killip

Table I. Clinical and angiographic characteristics of study patients

Clinical data	
Age [years]	65.32 ±12.33
Age groups:	
≤ 65	92 (48.9%)
> 65	56 (51.1%)
Gender:	
Female	56 (29.8%)
Male	132 (70.2%)
Arterial hypertension	149 (79.3%)
Diabetes	28 (14.9%)
Dyslipidemia	147 (78.2%)
Smoking	67 (35.6%)
Killip class:	
I	22 (11.7%)
II	131 (69.7%)
III	21 (11.2%)
IV	14 (7.4%)
Angiographic data	
Total coronary artery occlusion	132 (70.2%)
Left main coronary artery stenosis (> 50.0%)	12 (6.4%)
Initial TIMI flow grade:	
0	130 (69.2%)
1	23 (12.2%)
2	20 (10.6%)
3	15 (8.0%)
Post-procedure TIMI flow grade:	
0	2 (1.1%)
1	6 (3.2%)
2	30 (16.0%)
3	150 (79.8%)
Thrombus aspiration	36 (19.1%)
Age groups:	
≤ 65	15 (16.3%)
> 65	21 (21.9%)
Coronary artery occlusion groups:	
Total	33 (25.0%)
Non-total	3 (5.4%)
In-hospital outcomes	
Distal embolization	12 (6.4%)
Stent thrombosis	1 (0.5%)
Worsening of heart failure	16 (8.5%)
Stroke	2 (1.1%)
Death	12 (6.4%)
Data are presented as mean ± SD, n (%)	

class II (69.7%). Total coronary artery occlusion was diagnosed in 70.2% of patients. 92.0% of patients had initial TIMI flow grade ≤ 2. Post-procedural TIMI flow grade 3 was observed in 79.8% of patients. Thrombus aspiration was performed in 19.1% of patients. Clinical and angiographic characteristics of patients are summarized in Table I.

Length of hospital stay

Median hospital stay was 8.95 (1; 34) days. In the age > 65 years group LOS was statistically significantly longer than in the ≤ 65 years group (9.0 [1; 34] vs. 8.0 [2; 20], $p = 0.016$). The LOS was also significantly longer in the group of STEMI duration > 12 h until PCI (9.96 [1; 34] vs. 8.59 [1; 24], $p = 0.035$). The longest duration of hospitalization was in the group of > 65 years old and > 12 h until PCI (10.41 ±5.82 days), while the shortest hospitalization was in the group of ≤ 65 years old and ≤ 12 h until PCI (7.79 ±1.76 days). The LOS had a positive weak correlation with age ($r = 0.256$, $p = 0.001$), while the very weak correlation between hospitalization and time to PCI was not statistically significant ($r = 0.085$, $p > 0.05$).

Predictors of distal embolization

Twelve (6.4%) patients had DE. The DE was more frequent in the total CA occlusion group (9.1% vs. 0.0%, $p = 0.020$), and was also more frequent (of borderline significance) in the inferior STEMI group than in anterior STEMI group (10.0% vs. 3.1%, $p = 0.052$). Frequency of DE in age, gender, and CVD risk factor groups was without significant differences ($p > 0.05$). Predictors of DE are listed in Table II. Only age was a significant DE predictor in bivariate analysis. On multivariate analysis, surprisingly, age > 65 years and total CA occlusion were associated with lower risk of DE.

Predictors of in-hospital worsening of HF

In-hospital WHF was diagnosed in 16 (8.5%) patients. WHF was higher in the age of > 65 than in the ≤ 65 years group (12.5% vs. 4.3%, $p = 0.045$), and in the female than in the male group (17.9% vs. 4.5%, $p = 0.003$). Unexpectedly, WHF was less frequent in smokers (1.5% vs. 12.4%, $p = 0.010$) and in the dyslipidemia group (4.1% vs. 24.4%, $p < 0.001$). However, both smokers and the dyslipidemia group were younger than non-smokers and patients with a normal lipidogram (61.25 ±11.86 vs. 67.58 ±12.05, $p = 0.001$; 64.28 ±11.99 vs. 69.07 ±12.93, $p = 0.027$). Patients with post-procedural TIMI flow grade 0-1 (100.0%, 33.3%) had the highest rate of in-hospital WHF. All 12 patients who died in hospital had WHF. Predictors of in-hospital WHF are summarized in Table III. Only age was an independent predictor of WHF in all univariate,

Table II. Independent predictors of distal embolization on binomial logistic regression

Variable	Odds ratio	95% CI	P-value
Univariate predictors:			
Age	1.039	0.988–1.093	0.137
Age > 65 years	2.000	0.581–6.884	0.272
Bivariate predictors:			
Age	1.035	0.985–1.088	0.178
Inferior myocardial infarction	3.312	0.861–12.748	0.082
Age	0.948	0.928–0.969	< 0.001
Total coronary artery occlusion	2.901	0.692–12.162	0.145
Multivariate predictors:			
Age > 65 years	0.272	0.122–0.607	0.001
Inferior myocardial infarction	0.455	0.200–1.035	0.060
Total coronary artery occlusion	0.242	0.119–0.496	< 0.001

Table III. Independent predictors of in-hospital worsening of heart failure on binomial logistic regression

Variable	Odds ratio	95% CI	P-value
Univariate predictors:			
Age	1.068	1.017–1.121	0.008
Age 65 years	3.143	0.975–10.130	0.055
Bivariate predictors:			
Age	1.046	0.991–1.104	0.102
Female gender	2.767	0.831–9.217	0.097
Age	1.076	1.021–1.133	0.006
Anterior myocardial infarction	2.671	0.849–8.401	0.093
Age	1.056	1.005–1.109	0.030
Smoking	0.145	0.018–1.147	0.067
Age	1.068	1.018–1.121	0.008
Hypertension	0.504	0.158–1.607	0.247
Age	1.066	1.016–1.118	0.009
Diabetes	2.927	0.885–9.680	0.078
Age	1.054	1.004–1.108	0.034
Dyslipidemia	0.160	0.052–0.486	0.001
Age	1.066	1.015–1.119	0.010
TIMI grade	0.706	0.340–1.466	0.351
Multivariate analysis:			
Age	1.065	1.014–1.119	0.012
TIMI grade:			
1	1.283	0.149–11.038	0.821
2	0.871	0.068–11.208	0.915
3	0.000	0.000	0.998

bivariate and multivariate analyses. Surprisingly, dyslipidemia was associated with lower risk of in-hospital WHF in bivariate analysis.

Predictors of in-hospital mortality

Twelve (6.4%) patients died in hospital (6 patients died due to cardiogenic shock, 2 – cardio-

pulmonary insufficiency, 2 – cardiogenic shock and acute kidney failure, 1 – heart tamponade after rupture of myocardium, 1 – cardiopulmonary insufficiency and acute kidney failure). In-hospital mortality was more frequent in the age > 65 years than in the ≤ 65 years group (10.4% vs. 2.2%, $p = 0.021$), and in females than in males (16.1% vs. 2.3%, $p < 0.001$). Unexpectedly, frequency of

in-hospital mortality was lower in smokers (0.0% vs. 9.9%, $p = 0.008$), and in the dyslipidemia group (2.0% vs. 22.0%, $p < 0.001$). The highest in-hospital mortality rate was in patients with Killip class IV (50.0%), and in post-procedural TIMI flow grade 0-1 (50.0%, 33.3%). Predictors of in-hospital mortality are listed in Table IV. Age and age > 65 years were independent predictors of mortality in hospital in univariate analysis. In bivariate analysis, significant predictors of in-hospital mortality were age, Killip class, left main CA stenosis (> 50.0%), TIMI grade after PCI, and post-procedural TIMI flow grade 1. Also female gender was associated (at borderline significance) with higher risk of in-hospital mortality ($p = 0.051$). Surprisingly, dyslipidemia was associated with lower risk of death in

hospital. On multivariate analysis, Killip class and post-procedural TIMI flow grade 1-2 were independent predictors of in-hospital death, while dyslipidemia was still associated with lower death risk.

Discussion

The rate of PCI increased in the whole of Europe during the past decade [2]. However, despite the high success rate of PCI for STEMI patients (93.3%), serious complications may still be diagnosed after PCI. According to PCI guidelines (2014), major clinical in-hospital complications after PCI are defined as MI, stroke, emergency coronary artery bypass grafting (CABG), and death [6]. The National Cardiovascular Data Registry of United States (2012) reported that adverse events

Table IV. Independent predictors of in-hospital mortality on binomial logistic regression

Variable	Odds ratio	95% CI	P-value
Univariate predictors:			
Age	1.093	1.028–1.162	0.004
Age > 65 years	5.233	1.114–24.571	0.036
Bivariate predictors:			
Age	1.060	0.992–1.132	0.085
Female gender	4.408	0.994–19.545	0.051
Age	1.093	1.028–1.161	0.004
Hypertension	0.737	0.180–3.025	0.672
Age	1.090	1.027–1.158	0.005
Diabetes	1.833	0.428–7.848	0.414
Age	1.075	1.011–1.143	0.021
Dyslipidemia	0.093	0.023–0.378	0.001
Age	1.067	0.996–1.142	0.064
Killip class	5.829	2.580–13.171	< 0.001
Age	1.090	1.024–1.160	0.007
Left main coronary artery stenosis (> 50.0%)	4.983	1.058–23.481	0.042
Age	1.092	1.027–1.161	0.005
TIMI grade	0.886	0.423–1.855	0.748
Age	1.086	1.020–1.156	0.010
TIMI grade after PCI	0.350	0.165–0.740	0.006
Age	1.089	1.021–1.162	0.010
TIMI grade after PCI:			
1	35.870	1.596–806.219	0.024
2	7.754	0.949–63.338	0.056
3	1.982	0.446–8.811	0.369
Multivariate predictors:			
Dyslipidemia	0.113	0.018–0.720	0.021
Killip class	9.796	2.847–33.707	< 0.001
TIMI grade after PCI:			
1	185.520	3.739–9205.433	0.009
2	71.659	4.767–1077.249	0.002
3	2.953	0.340–25.647	0.326

after PCI occurred in 12.4% of STEMI patients. The incidence of in-hospital risk-adjusted mortality was 4.8%, heart failure 3.5%, stroke 0.6%, and emergency CABG from 0.05% to 0.87% [7].

Quite a wide range of studies have evaluated predictors of PCI success, but the results of these studies are controversial, especially concerning modifiable CVD risk factors' impact on PCI outcomes. Halkin *et al.* were the first to include both clinical and angiographic factors to predict mortality after PCI, and reported seven predictors of short- and long-term mortality (age > 65 years, anemia, Killip class II/III, left ventricular function at baseline, renal insufficiency, triple-vessel disease and post-procedural TIMI grade) [4]. However, PCI guidelines (2014) suggest different predictors of PCI outcomes, as mentioned in the introduction. Moreover, data about modifiable CVD factors' impact on PCI success are even more confusing. A meta-analysis of 100 studies was consistent with previous studies and still showed the cholesterol, smoking and obesity paradox [5]. Also, although previous studies assessed predictors of PCI outcomes earlier, the effectiveness of PCI strongly depends on the healthcare system and availability of emergency facilities. Therefore, our study provides important national data about predictors of PCI success in the Lithuanian healthcare system. We evaluated correlations to LOS and identified clinical and angiographic predictors of such PCI outcomes as DE, in-hospital WHF, and in-hospital death.

Previous studies revealed different predictors of prolonged hospital stay (> or ≥ 6 days): Schellings *et al.* showed that left ventricular ejection fraction, age, female sex, previous MI, HF on admission, and TIMI flow 0 before PCI were independent predictors of prolonged hospitalization [8]. Meanwhile, Isik *et al.* reported only three independent predictors for prolonged hospital stay (anterior STEMI, angiographic failure, peripheral vascular complications) [9]. Moreover, Agarwal *et al.* found out that long hospital stay is associated with increased long-term mortality [10]. Our study is consistent with the results indicating that older age is associated with longer stay (patients > 65 years had a significantly longer stay, and we observed a weak correlation between age and LOS). We also observed that hospital stay is longer in patients with time to PCI >12 h, although the correlation between these factors was not significant.

No-reflow (TIMI < 3) after PCI is caused by a combination of endothelial injury and DE of thrombus or atheromatous debris. Incidence of post-procedural TIMI < 3 varies from 11.0% to 41.0% in STEMI patients [11]. The DE obstructs blood flow to viable myocardium and induces necrosis, therefore leading to a poor in-hospital and long-term prognosis [12]. Previous studies revealed that the

major predictors of DE after PCI are female sex, high thrombus burden, long target lesion, and right CA as an infarct-related artery [13–15]. In our study, DE occurred in 6.4% of patients and was more common in patients with total CA occlusion and in inferior STEMI patients. These results are similar to previous studies, because total occlusions have higher thrombus and inferior STEMI is mostly due to right CA occlusions. Interestingly, our multivariate analysis showed that age > 65 years and total occlusions are related to lower risk of DE. We believe that these paradoxical results can be explained by certain factors. The group of > 65 years had fewer inferior STEMI patients (44.8% vs. 51.1%) than the group of ≤ 65 years, and thrombus aspiration was performed in 21.9% of > 65-year-old patients compared to 16.3% of ≤ 65-year-old patients. The total occlusion group also had more thrombus aspiration (25.0% vs. 5.4%). Previous studies showed that aspiration thrombectomy or distal protection devices had favorable effects in reducing thrombus or plaque embolization, especially in high-thrombus burden cases [15, 16].

WHF is defined as symptoms and signs of HF that are deteriorating despite the initial therapy. To our knowledge, no studies have investigated predictors of WHF after PCI in patients with STEMI. There are studies only about predictors of HF occurrence after PCI. These studies revealed that independent predictors of post-procedural HF are female sex, age ≥ 60 years, diabetes, dyslipidemia, prior HF, prior MI, anterior STEMI, and baseline TIMI flow grade 0 [17, 18]. Cotter *et al.* reported that age, co-morbidities, and markers of HF severity were moderately predictive of WHF after admission for acute HF. Also, this study revealed that WHF is associated with longer hospital stay and increased mortality risk [19]. In our study, WHF was diagnosed in 8.5% of patients. Our results are similar to studies which evaluated predictors for HF occurrence. WHF was more common in older and female group patients, and was highest in patients with TIMI flow grade 0-1. The risk of mortality for these patients was increased, because all patients with WHF died in our study. However, only age was an independent predictor of WHF in logistic analysis. Interestingly, we found that WHF was less common in smokers, and moreover, dyslipidemia was associated with lower risk of WHF. We may explain this paradox with the fact that smokers and the dyslipidemia group were significantly younger.

The in-hospital mortality rate after PCI varies from 1.1 to 1.7% [20]. According to PCI guidelines (2014), advanced age, comorbidities such as diabetes, congestive HF, chronic kidney disease, multi-vessel CA disease, high-risk lesions, and the PCI type (urgent or emergency procedure) are all

factors associated with increased risk of death after PCI [6]. Saman *et al.* identified quite different predictors of 30-day and 1-year mortality after PCI in STEMI patients. In their study, strong mortality predictors were previous MI, diabetes, Killip class > II, post PCI-TIMI < 3, and left ventricular function less than 30% [21]. Benamer *et al.* reported that female gender is also an independent predictor of in-hospital mortality after PCI in patients with STEMI [22]. Previous studies revealed controversial data about the impact of modifiable CVD risk factors on mortality after PCI. Diabetes, hypertension, and metabolic syndrome are independent predictors of mortality after PCI in most studies. However, a lot of studies showed the smoking and obesity paradoxes, and a few studies showed the cholesterol paradox [5, 23]. In our study, rate of death in hospital was 6.4%. Our results are similar to previous studies. Independent predictors of in-hospital mortality rate were age, Killip class, left main CA stenosis (> 50.0%), and TIMI grade after PCI < 3. Also, female gender was a borderline predictor of mortality ($p = 0.051$). Although the mortality rate was lower in smokers and the dyslipidemia group, significantly lower risk of death was associated only with dyslipidemia, and thus our study highlighted the cholesterol paradox. Reasons for this phenomenon of modifiable risk factors are still not clear. The dyslipidemia paradox is explained mainly due to younger age of patients and earlier administration of lipid-lowering therapy [23]. In our study, the dyslipidemia group was also younger than the normal lipido-gram group, and 34.7% of patients used statins previously. The smoking paradox can be explained by younger age and more favorable clinical status for smokers. However, these results actually show that smokers require PCI at a much younger age than nonsmokers. Moreover, in these studies after adjustment of the analysis for age, no protective impact of smoking was seen. Chen *et al.* tested more than 19 000 patients and found that quitting smoking whether before or after PCI is related to significantly lower risk of death [5, 24, 25].

First, the number of patients included in the study was small. Moreover, the number of patients with adverse outcomes after PCI was even smaller. Second, the retrospective nature of data collection leads to the fact that potential predictors could not be recorded. Third, we did not include left ventricular function and kidney function in our analysis, although these are major predictors of PCI outcomes. And, finally, we evaluated only short-term outcomes that occurred in hospital. Further research about predictors of short- and long-term adverse outcomes after PCI is needed, especially with predictors such as left ventricular function and kidney function. Also, more studies about modifiable CVD

risk factors' impact on PCI success are needed in order to identify reasons for this phenomenon.

In conclusion, our study demonstrated that age correlates with length of hospital stay, and is an independent predictor of distal embolization, in-hospital worsening of heart failure, and in-hospital mortality rate. Other independent predictors of in-hospital mortality are Killip class, left main coronary artery stenosis (> 50.0%), and post-procedural TIMI flow grade 1-2. Furthermore, our study showed lower risk of in-hospital worsening of heart failure and in-hospital mortality in the dyslipidemia group.

Conflict of interest

The authors declare no conflict of interest.

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