Factors Affecting Early Mortality and 1-Year Outcomes in Young Women With ST-Segment-Elevation Myocardial Infarction Aged Less Than or Equal to 45 Years

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Abstract: Given that up to 2% of patients with myocardial infarction (MI) are young women, the purpose of this study was to evaluate factors affecting outcomes in young women with ST-segment-elevation myocardial infarction (STEMI) aged less than or equal to 45 years. We evaluated 796 women with STEMI aged less than or equal to 45 years between 2007 and 2014, and mortality was 4.0%. Death occurred more often in women with prehospital sudden cardiac arrest, and severe symptoms of heart failure; less commonly, the women were subjected to percutaneous coronary intervention (PCI), with a higher rate of incomplete revascularization. Beta blockers (BB) and angiotensin converting enzyme inhibitors were frequently used in the survivor group. The independent predictor of 30-day mortality was as follows: inability to undergo PCI (odds ratio [OR] 4.6, 95% confidence interval [CI]

* All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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1.45-14.76, P = 0.009), sudden cardiac arrest (OR 4.5, 95% CI 1.5-18.3, P = 0.04). An increase in systolic blood pressure for every 5 mm Hg was associated with lower mortality, OR 0.90, 95% CI 0.76-0.97 in patients without cardiogenic shock (CS) and OR 0.69, 95% CI 0.61-0.78, $P < 0.0001$ in the group with CS. Predictors for 1-year mortality were the inability to undergo PCI (hazard ratio [HR] 84, 95% CI 1.6-43.1, P = 0.01) and CS (HR 6.97, 95% CI 1.39-34.7, P = 0.01). An increase of 5% in left ventricular ejection fraction reduced the mortality rate for 60% (HR 0.40, 95% CI 0.26-0.63, $P < 0.0001$) and an increase in systolic blood pressure for every 5 mm Hg reduced mortality for 34% (HR 0.66, 95% CI 0.52-0.84, P = 0.02). Both short- and long-term outcomes in young women aged less than or equal to 45 years with STEMI are good. The strongest predictor for both 30-day and 1-year mortality was the inability to undergo PCI. Suboptimal use of beta blockers and angiotensin converting enzyme inhibitors affect the outcomes in young women. Hypotension in the acute phase of MI increased mortality in young women, independent of coexisting CS. (Curr Probl Cardiol 2021;46:100419.)

Introduction

In the era of interventional cardiology development, the prognosis of patients with ST-elevation acute myocardial infarction (STEMI) has significantly improved. In developed countries, in-hospital mortality does not usually exceed 5% and 1-year mortality ranges between 7% and 13% of the patient population and is related to age and gender.[1-3] A particular group of patients are young people with myocardial infarction (MI) in whom often atypical symptomatology and nonatheromatous etiology of myocardial ischemia may have an impact on prognosis.

About 0.1%-2% of the MI population are young women.[4] Recent population data from the nationwide database showed that women and men with STEMI under 45 years of age accounted for 3.9% of all patients with STEMI with a predominance of men (84.7% vs 15.3%), which means that 0.6% of all STEMI patients are young women.[5] According to

existing data, both short- and long-term outcomes in young STEMI patients seem to be favorable.[6-8]

Unfortunately, the literature on this subject is scarce. There are only a few published studies that pertain to young women. This may be due to: (1) the difficulty in gathering the right number from the population; and (2) an unspecified, often controversial definition of "youth." In the available literature regarding young women with STEMI, the ages range from 35 to 60 years, which can generate significant discrepancies in results.

The purpose of this study was to evaluate the possible factors influencing 30-day and 1-year mortality in young women with STEMI aged less than or equal to 45 years.

Patients and Methods

We analyzed data from the period 2007-2014 of young women hospitalized with STEMI who were aged less than or equal to 45 years. The data came from the Polish Registry of Acute Coronary Syndromes,[9] an ongoing, nationwide, multicenter, prospective, observational, and mandatory registry of all consecutive acute coronary syndrome (ACS) cases in Poland. From among all Polish hospitals, a total of 535 centers were selected to be invited to enter the registry, based on the following conditions: (1) the center contains one of the following wards in its structure: coronary care unit, cardiology, cardiac surgery, internal medicine, or intensive care unit; or (2) the center does not have any of these wards but hospitalizes at least 10 ACS patients per year. This database is based on a standardized questionnaire completed at the time of ACS treatment in invasive cardiology units. At the time of analysis, the registry included 585,474 records. Briefly, the ACS diagnosis was made by the attending physician based on the clinical presentation, ECG findings, and biomarkers of myocardial necrosis. According to the ESC guidelines for STEMI patients, the following criteria were adopted: (1) ST-elevation $\geq$2 mm in adjacent precordial leads and/or $\geq$1 mm in at least 2 adjacent limbs leads, or newly diagnosed left bundle branch block; and (2) elevated concentrations of myocardial necrosis markers.[10] According to the protocol, all admitted patients with suspected ACS were screened to be eligible to enter the registry, but the patients were not enrolled until ACS was confirmed. Short stays for observation in the admission room before transfer to another hospital for management were not registered. Units without a catheterization laboratory had to transfer patients to the other units in case the patient was referred by the treating physician for angiography. If the patient was hospitalized during the same ACS in more than

1 hospital (transferred patient), all hospitals were required to complete the registry data. These hospitalizations were linked together during data management and were analyzed as 1 ACS case. The details of the registry design and selection criteria are reported elsewhere.[9]

The analysis included the following: major coronary artery disease risk factors, symptoms, onset-to-hospital and onset-to-balloon time, angiographical findings, in-hospital percutaneous coronary intervention (PCI) and pharmacological treatment, left ventricular ejection fraction (LVEF), and complications.

Inability to undergo PCI was defined as a patient not selected by the treating physician for PCI. The decision about the method of treatment was made by the treating team. For the purposes of the register, no specific contraindications to withdraw from revascularization have been established. Cardiogenic shock was defined as IV degree of Killip-Kimball scale. All-cause mortality rate data at 30 days and 1 year following STEMI came from the official national database – PESEL (Universal Electronic System for Registration of the Population) and complete results were obtained for 100% of the study population.

Statistical Analysis

Depending on the distribution of continuous variables as assessed by the Shapiro-Wilk test, the results have been shown as arithmetic means with standard deviations or as median values and interquartile ranges. The significance of differences between the mean values of normally distributed variables in the study groups was evaluated using the Student's *t* test, and differences between non-normally distributed variables were evaluated using the nonparametric Mann-Whitney U test. Categorical variables have been shown as numbers and percentages (absolute and relative frequency). Comparison of categorical variables between the study groups was performed by the chi-square test with the Yates' correction for continuity, or Fisher's exact test if the minimum expected count in the cell was less than 5.

Univariable and multivariable binomial logistic regression with a combination of categorical and continuous predictors was used to determine early 30-day mortality. Initially, a series of single variable models was fitted to a developmental dataset in order to identify variables that were associated with mortality. To avoid overfitting for the multivariable models predicting 30-day and 1-year mortality, only variables with a univariate $P < 0.10$ were included in the first multivariable model, even if they were moderately correlated with one another (Pearson correlation or phi

coefficient < 0.85). Multiplicative interactions of systolic blood pressure (SBP), diastolic blood pressure (DBP), and hazard ratio (HR) with cardiogenic shock (CS) were tested. The stepwise selection method was applied based on likelihood ratio statistics comparing models with and without each variable and Akaike's information criterion, until well-fitting models were developed. A significance level of 0.05 (individual score test) was required to allow a variable into the model, and a significance level of 0.05 (Wald chi-square statistic) to stay in the model. The calibration of the predictive models was assessed by Hosmer-Lemeshow tests. Models and their improvements in predictive accuracy were evaluated by calculating the area under the receiver-operating characteristic curve (ROC, C-statistic). There were several models that fitted the data and gave similar predictions, and then, the final model was chosen on the basis of predictive accuracy (C = 0.9407). Odds ratios (OR) with a corresponding 95% confidence interval (CI) were assessed. Cox's proportional hazards regression was used to compute HR and two-sided 95% CI for the association between demographic and clinical characteristics and 1-year mortality. The proportional hazards assumption of the Cox model was verified by inspection of log-cumulative hazard plots. Multiplicative interactions of SSP, DBP, and HR with CS were tested, but none was significant in the Cox model. Based on the global score chi-square statistic, the best subset selection method was used among the variables indicated by univariate statistics. The 1-year mortality was summarized using the Kaplan-Meier method and evaluated using a stratified log-rank test. All tests were two-sided and a P value of <0.05 was considered statistically significant. All statistical analyses were performed using the SAS 9.2 (SAS Institute, Cary, NC) software.

Results

Analyses were performed on the data of the 796 women with STEMI. The median age in the study group was 42.0 years (interquartile range: 38.0-44.0). Group characteristics are shown in Table 1.

Early 30-day mortality was 3.0%. The women who died had a higher prevalence of prehospital sudden cardiac arrest (SCA), 20.8% vs 2.7%. They were in worse overall condition at admission with a higher prevalence of the following: pulmonary edema, 8.3% vs 0.39%; CS, 29.2% vs 0.52%; higher heart rate; and more frequent hypotension presence ($P < 0.0001$). Women who died had lower frequency of PCI: 66.7% vs 85.6%. The rate of complete revascularization, expressed by thrombolysis in myocardial infarction (TIMI) flow distribution, was also lower

Table 1. Baseline demographic and clinical characteristics of studied population.

	30-day follow-up survival N = 772	30-day follow-up died N = 24 (3%)	*P* Value	1-year follow-up survival N = 764	1-year follow-up died N = 32 (4%)	*P* Value
Overall conditions						
Age, years, mean (SD)	40.6 (4.2)	39.3 (4.8)	0.25	40.6 (4.2)	39.2 (4.7)	0.11
HR, bpm, mean (SD)	78.5 (16.1)	96.8 (28.3)	0.005	78.3 (15.8)	96.2 (28.4)	0.001
SBP, mm Hg, mean (SD)	130.9 (25.7)	92.0 (30.2)	<0.0001	131.1 (25.6)	97.8 (31.0)	<0.0001
DBP, mm Hg, mean (SD)	81.1 (15.5)	58.3 (19.7)	<0.0001	81.2 (15.4)	61.8 (20.2)	<0.0001
Pulmonary edema, n (%)	6 (0.39)	2 (8.3)	0.008	2 (0.3)	3 (9.4)	0.0006
Cardiogenic shock, n (%)	4 (0.52)	7 (29.2)	<0.0001	3 (0.4)	8 (25.0)	<0.0001
Prehospital SCA, n (%)	21 (2.7)	5 (20.8)	0.0007	19 (2.5)	7 (21.9)	<0.0001
Risk factors/comorbidities						
Smoking, n (%)	474 (61.4)	9 (37.5)	0.02	471 (61.6)	12 (37.5)	0.006
Arterial hypertension, n (%)	349 (45.2)	4 (16.7)	0.006	348 (45.5)	5 (15.6)	0.0008
Hypercholesterolemia, n (%)	265 (34.3)	6 (25.0)	0.34	265 (34.7)	6 (18.7)	0.06
Obesity, n (%)	181 (23.4)	3 (12.5)	0.21	181 (23.7)	3 (9.4)	0.06
Diabetes mellitus, n (%)	80 (10.4)	2 (8.3)	1.0000	80 (10.59)	2 (6.2)	0.76
History of myocardial infarction, n (%)	40 (5.2)	3 (12.5)	0.13	40 (5.2)	3 (9.4)	0.25
PAD, n (%)	9 (1.2)	0	1.000	9 (1.2)	0	1.00
CNS stroke, n (%)	9 (1.4)	0	1.000	9 (1.2)	0	1.00
Chronic kidney disease, n (%)	13 (1.7)	1 (4.2)	0.35	13 (1.7)	1 (3.1)	0.44
Chronic pulmonary disease, n (%)	5 (0.7)	1 (4.2)	0.17	5 (0.7)	1 (3.1)	0.22
Previous heart failure, n (%)	6 (0.8)	0	1.0000	6 (0.8)	0	1.00
MI localization						
Inferior wall, n (%)	341 (44.2)	5 (20.8)	0.06	328 (44.2)	8 (25.0)	0.10
Anterior wall, n (%)	362 (46.9)	15 (62.5)		357 (46.7)	30 (62.5)	
Others, n (%)	69 (8.9)	4 (16.7)		69 (9.0)	4 (12.5)	
Intervention						
Number of PCI, n (%)	661 (85.6)	16 (66.7)	0.02	655 (85.7)	22 (68.7)	0.02

(*continued on next page*)

Table 1. (*continued*)

	30-day follow-up survival N = 772	30-day follow-up died N = 24 (3%)	*P* Value	1-year follow-up survival N = 764	1-year follow-up died N = 32 (4%)	*P* Value
Onset-to-balloon time, hours, median (IQR)	3.6 (2.0-8.0)	2.8 (1.9-7.1)	0.47	3.6 (2.0-8.0)	2.8 (1.5-7.1)	0.17
Post-PCI TIMI flow, n (%)						
0	8 (1.3)	3 (20.0)	<0.0002	8 (1.3)	3 (15.0)	0.0003
1	6 (1.0)	0		6 (1.0)	0	
2	14 (2.3)	3 (20.0)		14 (2.3)	3 (15.0)	
3	576 (95.4)	9 (60.0)		571 (95.3)	14 (70.0)	
GP IIb /IIIa usage, n (%)	287 (43.4)	9 (56.2)	0.31	283 (43.2)	13 (59.1)	0.14
Bleeding (all), n (%)	9 (1.2)	0	1.000	7 (0.9)	2 (6.2)	0.05
Major bleeding, n (%)	5 (0.6)	0	1.000	3 (0.4)	2 (6.2)	0.01
Pharmacotherapy						
Beta blockers, n (%)	497 (64.4)	6 (25.0)	<0.0001	493 (64.5)	10 (31.2)	0.0001
ACE-I, n (%)	442 (57.2)	4 (16.7)	<0.0001	440 (57.6)	6 (18.7)	<0.0001
LVEF, %, mean (SD)	49.9 (9.2)	29.2 (12.4)	<0.0001	50.0 (9.1)	30.9 (9.6)	<0.0001

ACE-I, angiotensin converting enzyme inhibitors; CNS, central nervous system; DBP, diastolic blood pressure; HR, heart rate; LVEF, left ventricle ejection fraction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SCA, sudden cardiac arrest; TIMI, thrombolysis In myocardial infarction.

($P < 0.0002$). In the group of dead beta blockers (BB) and angiotensin converting enzyme inhibitors (ACE-I) were less frequently used (25.0% vs 64.4%), (16.7% vs 57.2%), respectively, in a hospital setting. In woman who died, heart failure occurred more often with reduced ejection fraction (HFrEF) with the average LVEF 29.2% vs 49.9%, at discharge in comparison with survivors. About 36% of early deaths occurred on the first day (1-day mortality rate: 1.1%; 2-30 days: 1.9%). Patients who died on the first day were classified as having had a poor general condition at admission. In nearly half of the cases, they were suffering from CS and 25% of them had prehospital SCA. PCI was less frequent in this group in comparison with survivors: 56% vs 85.4%; moreover, the final effect of PCI was worse 50% vs 1.5%, $P < 0.001$ (results for TIMI flow, 0).

Mortality in a 1-year follow-up slightly increased to 4.0%. The women who died had pulmonary edema more often: 9.4% vs 0.3%; CS: 25% vs 0.4%; and higher heart rate at admission. They also had significantly higher rates of SCA: 21.9% vs 2.5%. These women were less likely to undergo PCI: 68.7% vs 85.7%. They had lower numbers of complete revascularizations: 70.0% vs 95.3%. Their LVEF at discharge was significantly lower: 30.9% vs 50.0%. BB (31.2% vs 64.5%) and ACE-I (18.7% vs 57.6%) were significantly less frequently used in hospital. Women who died had more hemorrhagic complications: 6.2% vs 0.9%, including episodes of major bleeding. However, there was no association between bleeding episodes and implemented anticoagulant or thrombolytic therapy. The percentage of patients who received thrombolytic therapy was 0.3% (8) for the entire study population. Only 3.4% of non-PCI patients had thrombolysis, which accounted for half of all procedures. There were no relationships between number of in-stent restenosis and number of arteries with PCI between groups.

During the follow-up, no mortality rate trend was found. In the 30-day follow-up, the mortality rate was a minimum of 1.3% in 2009 year and a maximum of 4.0% in 2010 year. In the 1-year follow-up, it ranges from 1.3% in 2009 year to 6.1% in 2008.

For both the 30-day and 1-year observations, there was no relationship between prognosis and onset-to-hospital and onset-to-balloon time. Any of the coronary artery disease (CAD) risk factors were not significantly more common among the women who died. Surprisingly, the prevalence of arterial hypertension in their medical history and current smoking were less frequent in this group after the 30-day follow-up: 16.7% vs 45.2% for hypertension and 37.5% vs 61.4% for smoking, but also after the 1-year observation: 15.6% vs 45.5% and 37.5% vs 61.6%, respectively.

There were no statistical dependence between mortality and numbers of ACS. During the 7-year follow-up, 3.4% of patients had a second episode of ACS, where only in 0.16% occurred during the same hospitalization (without taking into account the type of ACS).

Through multivariate analysis, we showed that the independent predictors of 30-day mortality were the following: inability to undergo PCI (OR 4.6, 95% CI 1.45-14.76, $P = 0.009$), prehospital SCA (OR 4.5, 95% CI 1.5-18.3, $P = 0.04$). An increase in SBP for every 5 mm Hg was related with lower mortality in young MI women, depending on the CS occurrence (OR 0.90, 95% CI 0.76-0.97 for patients without CS and OR 0.69, 95% CI 0.61-0.78, $P < 0.0001$ in the group with CS). The strongest predictors of 1-year mortality were: inability to undergo PCI (HR 8.4, 95% CI 1.6-43.1, $P = 0.01$), prehospital CS (OR 6.97, 95% CI 1.39-34.7, $P = 0.01$). In young STEMI woman, each increase for every 5% in LVEF reduced the mortality rate for 60% (HR 0.40, 95% CI 0.26-0.63, $P < 0.0001$) and each increase in SBP for every 5 mm Hg reduced the mortality rate for 34% (HR 0.66, 95% CI 0.52-0.84, $P = 0.02$; Table 2, Fig 1).

Discussion

In recent years, a declining trend in ACS incidence and mortality rate in women has been observed.[11,12] However, many authors believe that this phenomenon occurs mainly in the population of older women, with a steady rate of morbidity and mortality among younger women. Female gender is an independent adverse prognostic factor in ACS, but the data regarding diversity and differences in the course of the ACS in young women are scarce.[13] Our analysis included only women with STEMI aged less than or equal to 45 years. Against the background of the available literature, this work distinguishes the unique, homogeneous population of young Caucasian women with large numbers and the age-appropriate standard.

In our study, 1-year mortality was low and did not exceed 4%. Due to the lack of a universally accepted definition of youth and the lack of unanimity among STEMI researchers studying young women, it is difficult to compare the results of studies aimed at mortality in young woman. Age limits that are accepted by different authors range between 35 and 60 years. Therefore, the mortality rates are different; they vary between 0.8% and 6.45% for 30-day mortality, up to 12.3% for in-hospital mortality and even up to 19.6% in long-term follow-up. Notably, young women in comparison with men may have more than a 2 times higher probability

Table 2. Impact of baseline and clinical characteristics on 30-day and 1-year overall mortality.

30-day mortality	Logistic regression			
	Univariate		Multivariable*	
	Odds ratio (95% CI)	*P* Value	Odds ratio (95% CI)	*P* Value
HR, ↑5 bpm	**1.27 (1.15-1.40)**	**<0.0001**		
SBP, ↑5 mm Hg	**0.71 (0.64-0.79)**	**<0.0001**	**0.90 (0.76-0.97)**†	**<0.0001**
			0.69 (0.61-0.78)‡	**<0.0001**
DBP, ↑5 mm Hg	**0.61 (0.52-0.71)**	**<0.0001**		
Pulmonary edema, yes vs no	**23.3 (3.7-146.5)**	**0.0008**		
Cardiogenic shock, yes vs no	**79.1 (21.1-295.7)**	**<0.0001**		
Prehospital SCA, yes vs no	**9.4 (3.2-27.6)**	**<0.0001**	**4.5 (1.5-18.31)**	**0.04**
Risk factors/comorbidities				
Smoking, yes vs no	**0.38 (0.16-0.87)**	**0.02**		
Arterial hypertension, yes vs no	**0.24 (0.08-0.72)**	**0.01**		
Hypercholesterolemia, yes vs no	0.64 (0.25-1.63)	0.35		
Obesity, yes vs no	0.47 (0.14-1.58)	0.22		
Diabetes mellitus, yes vs no	0.79 (0.18-3.41)	0.75		
History of myocardial infarction, yes vs no	2.6 (0.75-9.13)	0.13		
Interventions				
Inability of PCI, yes vs no	**3.0 (1.24-7.12)**	**0.01**	**4.6 (1.45-14.76)**	**0.01**
Onset-to-balloon time	0.99 (0.97-1.02)	0.65		
Post-PCI TIMI flow, 0-1 vs 2-3	**10.5 (2.67-41.5)**	**0.0008**		
Pharmacotherapy				
Beta blockers, yes vs no	**0.18 (0.07-0.47)**	**0.0004**		
ACE-I, yes vs no	**0.15 (0.05 -0.044)**	**0.0006**		
LVEF, ↑5%	**0.33 (0.20-0.55)**	**<0.0001**		

1-year mortality	Cox's proportional hazards regression§			
	Univariate		Multivariable	
	Hazard ratio	*P* Value	Hazard ratio	*P* Value
HR, ↑5 bpm	**1.26 (1.17-1.37)**	**<0.0001**		
SBP, ↑5 mm Hg	**0.76 (0.71-0.82)**	**<0.0001**	**0.66 (0.52-0.84)**	**0.02**
DBP, ↑5 mm Hg	**0.70 (0.60-0.75)**	**<0.0001**		
Pulmonary edema, yes vs no	**23.3 (7.1-76.8)**	**<0.0001**		
Cardiogenic shock, yes vs no	**44.5 (19.7-100.9)**	**<0.0001**	**6.97 (1.39-34.7)**	**0.02**
Prehospital SCA, yes vs no	**9.2 (4.0-21.2)**	**<0.0001**		
Risk factors/comorbidities				
Smoking, yes vs no	**0.382 (0.187-0.782)**	**0.008**		

(*continued*)

Table 2. (*continued*)

1-year mortality	Cox's proportional hazards regression[§]			
	Univariate		Multivariable	
	Hazard ratio	*P* Value	Hazard ratio	*P* Value
Arterial hypertension, yes vs no	**0.228 (0.088-0.592)**	**0.002**		
Hypercholesterolemia, yes vs no	0.443 (0.182-1.077)	0.07		
Obesity, yes vs no	0.340 (0.104-1.117)	0.08		
Diabetes mellitus, yes vs no	0.578 (0.138-2.419)	0.45		
History of myocardial infarction, yes vs no	1.846 (0.562-6.059)	0.31		
Interventions				
Inability of PCI, yes vs no	**2.66 (1.26-5.61)**	**0.01**	**8.4 (1.6-43.1)**	**0.01**
Post-PCI TIMI flow, 0-1 vs 2-3	**7.0 (2.1-23.9)**	**0.002**		
Pharmacotherapy				
Beta blockers, yes vs no	**0.260 (0.121-0.542)**	**0.0004**		
ACE-I, yes vs no	**0.176 (0.072-0.427)**	**0.0001**		
LVEF, ↑5%	**0.36 (0.25-0.50)**	**<0.0001**	**0.40 (0.26-0.63)**	**<0.0001**

ACE-I; CNS; DBP; HR; LVEF; PCI; PAD; SBP; TIMI—see Table 1.
Results of binominal logistic regression and Cox's proportional hazards regression.
Bold values have statistical significance $P < 0.05$.

*C-statistic: 0.9364; Hosmer-Lemeshow goodness-of-fit test: $P = 0.9564$; LR test: $P < 0.001$.

†In patients without cardiogenic shock.

‡In a patient with cardiogenic shock.

§Likelihood ratio test, score test, and Wald test: $P < 0.001$.

of in-hospital mortality due to STEMI.[14-16] Our analysis does not show any significant, unfavorable impact of comorbidities on the mortality rate. Moreover, in both the 30-day and 1-year observations, women who died had a prevalence of arterial hypertension compared with survivors. Hypertension-adjusted analysis showed that higher mortality in the group with a lower prevalence of hypertension was due to a higher prevalence of hypercholesterolemia, more frequent MI in the past and a lower number of complete revascularizations in a 30-day follow-up. For the 1-year observation, mortality was related to a history of MI as well as a lower number of complete revascularizations. Moreover, hypotension in the acute phase of MI was correlated with higher mortality among women, both with and without co-existing CS; however, in the CS group, it was more strongly correlated (Figs 2A and 3). Some of the studies on the impact of SBP values on the prognosis describes adversely affect both low and high pressure values. In our observation, no inverted bell-shaped curve was observed for the pressure value. On the basis of nonlinear segment regression, the cut-off point was determined for the SBP value of

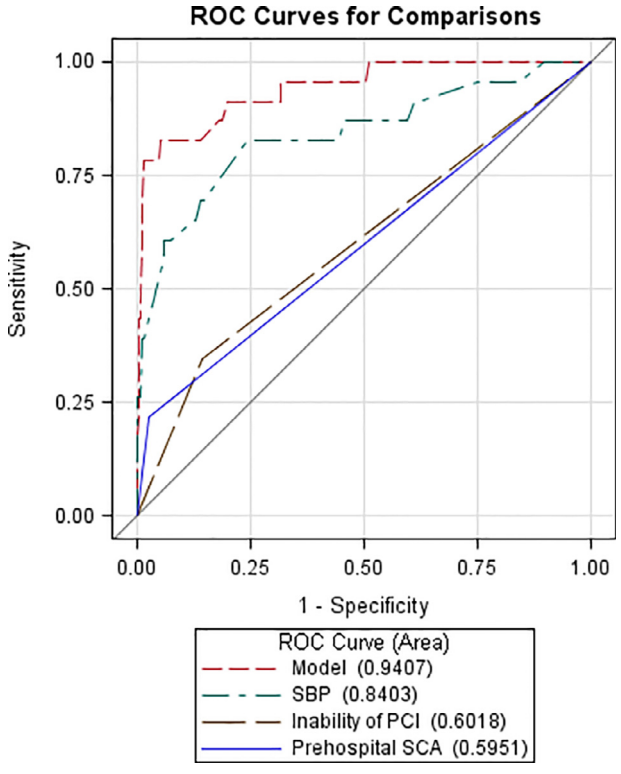

FIG 1. C-statistics of logistic regression model predicting 30-day mortality.

≤113.5 mm Hg. Below this value, the death probability is described by the quadratic function (decreasing part of the function – the death probability decreases with increasing pressure because of the continuity of the function at the junction point of 2 segments – the square and linear functions, there is no growth segment). For higher values, the probability of death is constant and amounts to 0.74 (Fig 4).

Interestingly, significantly more women who smoked were in the survivor group. Similar observations have been made by other authors, where the mechanism of pseudo-protective effects of smoking in MI has been explained by the fact that smokers develop an increase in blood thrombogenicity and, consequently, excessive stimulation of the fibrinolytic system.[15]

Many authors emphasize the role of the lack of awareness of being at CAD risk as a factor worsening the prognosis. Unfortunately, that is still a major social problem, especially in the young female population.[17] As reported in the VIRGO study, women had less awareness about being at

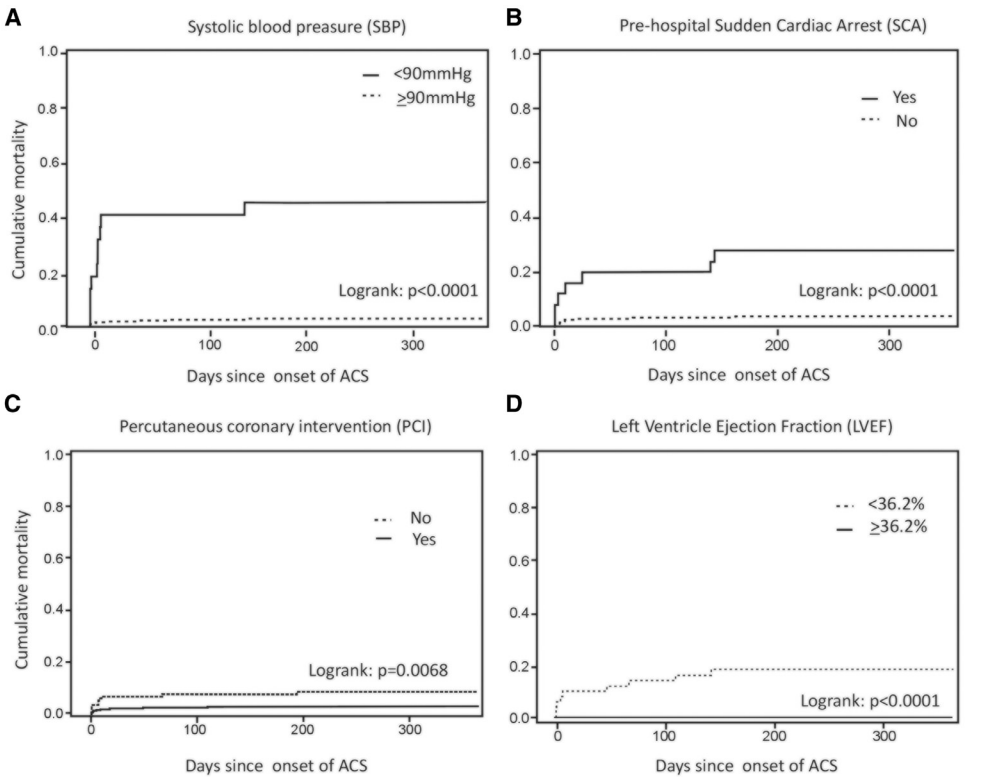

FIG 2. Kaplan-Meier curves for cumulative mortality for women with ST-segment elevation myocardial infarction aged less than or equal to 45 years. (A) Mortality rate depending on systolic blood pressure value (90 mm Hg vs ≥90 mm Hg). (B) Mortality rate depending on sudden cardiac arrest occurrence. (C) Mortality rate depending on percutaneous coronary interventions. (D) Mortality rate depending on ejection fraction value at discharge (<36.2% vs ≥36.2%).

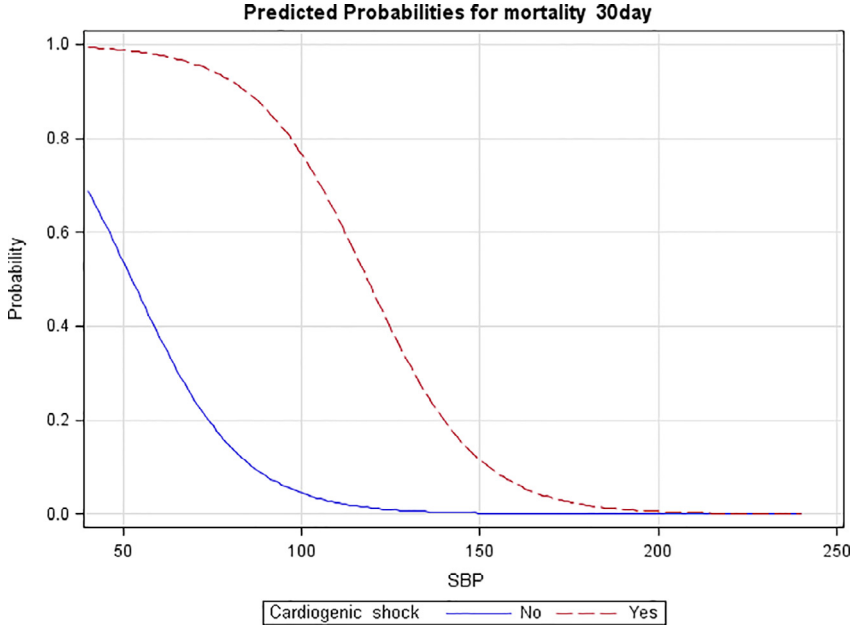

FIG 3. Estimated probability of 30-day mortality depending on the systolic blood pressure and cardiogenic shock interaction based on the logistic regression model.

risk (RR 0.89) due to being a lower risk for CAD than men.[18] In the last decade, in the Polish population, the knowledge and awareness of cardiovascular risk factors have advanced significantly. Up to 30% of the people who declared their awareness were shown to be unaware of their own CAD risk factors.[19] What is more the prevalence of risk factors for ACSs in young women with ACS is different to those in healthy women and to those in older women with higher prevalence of smoking. The strongest predictor of ACS in women ≤45 years of age was diabetes, with a 6-fold increase in risk.[20]

In our study, we found a strong correlation between the patient's overall condition at admission and mortality. One-dimensional analysis showed that mortality rates increase along the severity of acute heart failure occurrence both for 30-day and 1-year follow-up. For 30-day follow-up, it was strongly correlated with the occurrence of SCA (Fig 2B) but only for the 1-year follow-up was CS an independent predictor of mortality, which is in accordance with the results of other studies.[15] In 23 patients (1.2%) during the treatment, pressure amines were used with no difference between studied groups survival vs death.

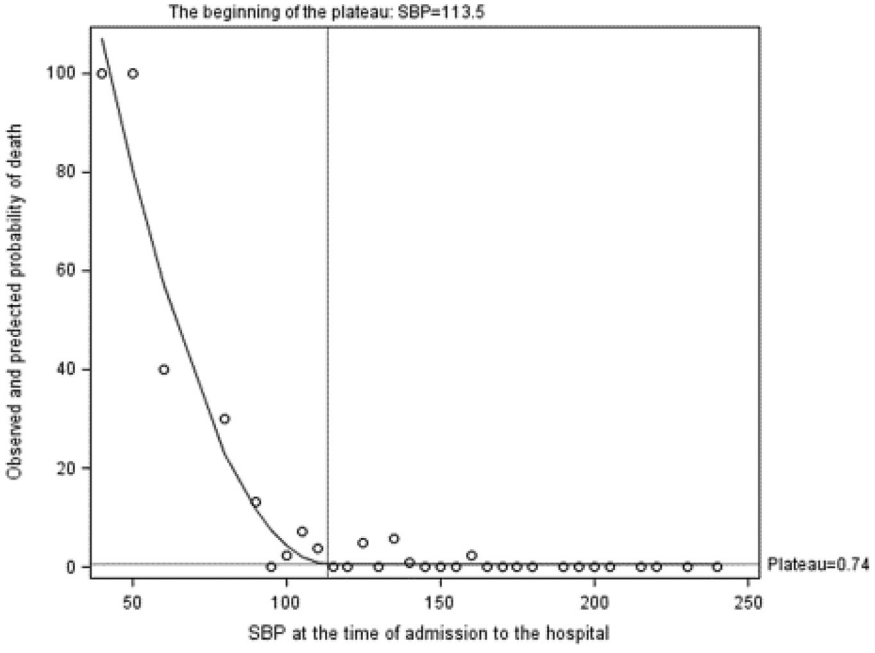

FIG 4. A curve showing death probability depending on the SBP value determined by the nonlinear segment regression method. Coefficient of determination R = 0.976 (comment: curve defined by the SAS program).

In the present study, we demonstrated the differences in in-hospital treatment (interventional, pharmacologic) and their influence on prognosis. Women who died were less frequently treated by BB and ACE-I in hospital and less often underwent PCI, which significantly worsened their prognosis (Fig 2C). Moreover, in women treated with PCI, the rate of incomplete revascularizations was greater.

Results of previous studies show that young women are less likely to undergo PCI than young men and older women.[8,21,22] The main reason for this is the unusual and diverse ischemia symptoms in women, which delay the patient's request for help and, ultimately, the PCI procedure. Interestingly, in our study, there was no relationship between prognosis and onset-to-hospital and onset-to-balloon time for either the 30-day or the 1-year observations.

In our study, BB and ACE-I were less frequently used in the mortality group, due to the higher incidence of acute heart failure with accompanying hypotension, pulmonary edema, or shock. The propensity-matched analysis does not show the effect of low LVEF and higher heart rate on the frequency of BB use. A similar observation for STEMI patients was

made by Young et al, who showed a 59% reduction in cardiovascular mortality in the BB group.[23] LVEF had prognostic value in the present study. A cut-off point of 36.2% for the LVEF value was determined by one-dimensional logistic regression and the ROC curve, which best discriminated against the analyzed patients in terms of the endpoints (Fig 2D). LVEF is a parameter that does not provide information about myocardial perfusion, so some authors prefer magnetic resonance imaging as a more reliable tool for assessing LV function, myocardial salvage index or microvascular obstruction, which correlate better with prognosis.[24] However, the basic evaluation of LVEF in echocardiography remains a primary method for assessing the risk of death in patients with ACS.

Over the years, the location of MI has been considered as one of the major prognostic factors in ACS patients. Most authors agree on the unfavorable location of myocardial infarction at anterior wall, which is associated with occlusion of the left anterior descending or left main coronary artery − regardless of the type of ACS (NSTEMI vs STEMI). This is mainly due to myocardial ischemia/necrosis and significant decrease in LVEF.[26,27] Another explanation is the greater propensity to ventricular fibrillation (VF) in patients with left anterior descending involvement.[28,29] Our study did not show a significant effect of the location of ACS on patient mortality, although a trend toward greater mortality in the anterior MI was observed. Similarly to other studies, in our population, this was only due to a larger area of necrosis in relation to patients with inferior wall MI and lower LVEF (47.4% vs 51.6%, $P < 0.0001$), with no difference in pharmacotherapy, clinical condition at admission, prehospital SCD, or final PCI effect. The only significant difference in treatment was the higher number of PCIs performed in patients with ACS of the anterior wall (87.8% vs 85.5%, $P < 0.0001$), which does not explain higher mortality. Interestingly, relationship between ACS location and prognosis is variable over time, where anterior location significantly worsens the very early (VF) and late (HFrEF) prognosis, while the inferoposterior location increases long-term mortality due to a higher probability of a high degree of atrioventricular conduction disturbances, which was not observed in our population.[29]

Limitations

The main limitation of the study is its retrospective design: the questionnaire was completed over 3 stages, which may affect its accuracy. The analysis does not include patients who died during a prehospital period. Due to design of the study, the authors did not have data on the

pharmacologic treatment used in the posthospital period, which could have an influence on long-term observation. Study analyzed only all-cause mortality. A matter of discussion was the age limit of patients. The study was aimed at young women; however, the definition of "youth" is not precisely specified. In our study, we included women less than or equal to 45 years of age. This limit reduces the probability of the impact of menopausal (including premature) hormonal imbalances on the incidence of MI in this population. The estimated mean age of menopause for women in the Polish population is 51.25 years (the age range is 45-56 years).[25]

Moreover, study suffers from low event rate. In case of mortality rate and CS, they mostly occurred in 30-day follow-up. Due to this fact, these results are in a wide confidence intervals.

The analysis included a relatively long period, from 2007 to 2014, in which there was considerable progress in the techniques of interventional cardiology and the standards of treatment for STEMI patients changed, which may affect the results. However, the use of such a lengthy period allowed us to assemble a large number of individuals from a closely selected population and to obtain statistically significant results.

The strength of our study includes its national and population-based design. The analyzed population was selected and strictly limited to young women from urban and rural areas. Nevertheless, due to the large sample size, the study was unique on a European scale. The issue of coronary disease in young women has been addressed in few scientific reports globally. Moreover, there are very few similar studies that analyze factors influencing STEMI mortality in woman aged less than or equal to 45 years in countries from Central and Eastern Europe, which are undergoing rapid socioeconomic transformations. It is well known that the organization and financing of the health care system, the accessibility of intervention cardiology centers, as well as the health literacy of the patients and the population in general could have significant influence. Thus, we believe that our research will contribute to a better understanding of this significant problem, and our findings may substantially contribute to development of new strategies of ACS treatment and a reduction of the mortality rates for women.

Conclusions

Both the 30-day and 1-year prognosis in young women with STEMI aged less than or equal to 45 years were favorable and did not exceeded 4%. The strongest predictors of 30-day and 1-year mortality were the

inability to undergo PCI. Suboptimal pharmacotherapy, that is, the lower use of BB and ACE-I, worsened the prognosis in young women. Hypotension in the acute phase of MI increased mortality in young women, independent of co-existing CS.

Contribution Statement

All authors contributed to: (1) conceiving and designing the study, or acquiring the data, or analyzing and interpreting the data; (2) drafting the article or revising it critically for important intellectual content; and (3) giving final approval of the version to be submitted.

Competing Interests

All authors declare they have no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

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