Differences in Symptomatology and Clinical Course of Acute Coronary Syndromes in Women ≤45 Years of Age Compared to Older Women

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Abstract: Acute coronary syndromes (ACS) in young people are rare. The data regarding differences in symptoms in relation to age are scarce, which may have an influence on outcomes. The aim of this study was to evaluate the differences in the clinical course of ACS between younger women (≤45 years old) and older women (63-64 years old). We compared 7481 women with ACS from the Polish Registry of ACS between 2007 and 2014 (1834 women aged ≤45 years and 5647 women aged 63-64 years). The predominant symptom of ACS in both groups was chest pain, with a higher incidence occurring in younger women (90.4% vs 88.5%, $P = 0.025$). Prehospital cardiac arrest

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occurred more often in younger women (2.1% vs 0.8%, $P < 0.001$), and onset-to-balloon time was shorter (8.9 vs 15.2 hours, $P < 0.0001$) in this group. Younger women presented with a lower Killip class at admission (class I at admission: 92.7% vs 86.2%, $P < 0.001$). The dominant type of ACS in the younger cohort was ST-segment elevation myocardial infarction (STEMI) (42% vs 26.1%), localized mainly in the anterior wall (47.7% vs 36.1%, $P < 0.001$), with a higher percentage of total occlusion of infarct-related artery (TIMI 0, 45.2% vs 36.1%) and left anterior descending artery engagement for all (33.5% vs 26.5%, $P < 0.001$). Drug-eluting stents were often used in the younger patients (43.3% vs 38.2%, $P = 0.003$) without significant differences in percutaneous coronary intervention numbers. Pharmacotherapy was used less in younger women. The 30-day and 2-year mortality in young women was lower than in the older cohort. The clinical course of ACS in younger women differed in comparison to older women. Younger women had a higher occurrence of typical chest pain, STEMI, and left anterior descending artery engagement. Except STEMI patients young women received faster revascularization, however with no significant differences in invasive treatment. Pharmacotherapy was inadequate in younger women and that resulted in a lower usage of the beta-blockers, angiotensin-converting enzyme inhibitors, and statins in that group. Short- and long-term mortality was low, regardless of the type of ACS. (Curr Probl Cardiol 2021;46:100508.)

Introduction

Acute coronary syndromes (ACS) are uncommon among young people. Women ≤45 years old constitute <1% of all cases, but incidence of myocardial infarction in this population is rising.[1,2] Moreover, ACS may exert a significant influence on patients' life expectancies and quality of life, including their ability to work. Differences in the clinical course between sexes are well documented, and women seem to be a population at particular risk.[3-11] However, data comparing

symptomatology and course of ACS in younger and older women are scarce. The aim of this study was to evaluate the differences in the clinical course and mortality in women aged ≤45 years and 63-64 years.

Patients and methods

We analysed data of 7481 women with ACS from the Polish Registry of ACS (PL-ACS) from 2007 to 2014. We compared 1834 women aged ≤45 years (24.5%) with 5647 women aged 63-64 years (75.5%) who were hospitalized due to ACS. The analysis included symptoms, vital signs, onset-to-emergency room and onset-to-balloon time, angiographic findings, in-hospital treatment (invasive and pharmacological), left ventricular ejection fraction, complications, and mortality. Mortality rate data were obtained from the Polish National Universal Electronic System for Registration of Population (PESEL), which provided full results for 100% of the study population.

The PL-ACS registry is an ongoing, nationwide, multicentre, prospective, observational, mandatory registry of all consecutive ACS cases in Poland. This database is based on a standardised questionnaire completed at the time of ACS treatment in invasive cardiology units. Briefly, the ACS diagnosis is made by the attending physician based on the clinical presentation, electrocardiogram (ECG) findings, and biomarkers of myocardial necrosis. According to the European Society of Cardiology guidelines for ACS patients, the following were adopted as inclusion criteria for a diagnosis of ACS: increase and/or decrease of a cardiac biomarker, preferably high-sensitivity cardiac troponin, with at least one value above the 99th percentile of the upper reference limit and at least one of the following: (1) symptoms of ischemia; (2) new or presumed new significant ST-T wave changes or left bundle branch block on 12-lead ECG; (3) development of pathological Q waves on ECG; (4) evidence of new or presumed new loss of viable myocardium or regional wall motion abnormality in imaging techniques; (5) intracoronary thrombus detected on angiography or autopsy. Additionally, ST-segment elevation myocardial infarction (STEMI) patients required the following for diagnosis: ST elevation ≥2 mm in adjacent precordial leads and/or ≥1 mm in at least 2 adjacent limb leads, or newly diagnosed left bundle branch block. The details of registry design and selection criteria were reported elsewhere.[12]

Defining the upper limit of the younger cohort of women with ACS as 45 years reduced the likelihood of any impact of hormonal imbalances associated with menopause on the incidence of ACS in this population.

The estimated average age at menopause of women in the Polish population is 51.25 years (range of age at menopause is 45-56 years).

The determination of the age range of 63-64 years for the older ACS group was the result of several factors, firstly by need to exclude women older than 65 years old, because that is the age the World Health Organization uses to define "old age." As is known, the incidence of various diseases increases with age, so by choosing a group aged less than 65 years. The authors' concept was to show differences between various influences on the course of ACS. The impact of concomitant diseases on ACS is well documented in the literature, where the increasing number of loads and severity increases the frequency of ACS and worsens its course. Exclusion of a patient in old age (in our case >65 years of age—according to the WHO definition) allows for a better demonstration of the impact of the patient's age on the course of ACS, and not the effect of associated diseases. In addition, strict age restriction of 63-64 years resulted from the group size. Adoption of a lower age range, between 60 and 64 years, would have significantly increased the population number, and would have also increased the disproportion between the size of this group and the studied younger group (≤45 years with ACS). What is more, this strict limitation of age range reduce the probability of the effect of hormone replacement therapy (HRT) on outcomes. The data about HRT usage were not taken into account in the PL-ACS registry. General recommendations for the duration of HRT suggest that therapy should not be prolonged for more than 5-6 years due to a significant increase in the risk of breast and uterine cancers. Estimated age of menopause in Poland varies between 45-56 years, so it is possible that women aged 60-62 years could be using HRT. Due to this, we set the age limits for this group at 63-64 years.

Analysis

Depending on the compatibility of the distribution of continuous data with the normal distribution verified by the Shapiro-Wilk test, the quantitative variables are described as mean values with their corresponding standard deviation or as median values and corresponding 25th and 75th percentiles, as appropriate. Categorical variables are reported as absolute number and percentages. To evaluate the differences in baseline characteristic, angiographic finding, and pharmacological treatment, chi-square independence tests were applied. Student's t test was used for comparison of mean values of vital signs at admission. Since our hypothesis for normal and log-normal distribution of treatment delay (onset-to-emergency room time) had to be rejected, the Wilcoxon-Mann-Whitney U test was performed to test for

differences between groups. The Cochran Mentel-Haenszel Modified Ridit Scores was used to analyze the significance of the upward trend in the applicability of drug-eluting stents (DES) stents in subsequent years. To minimize differences in baseline characteristics between the groups of women who had an implanted DES and Bare metal stent (BMS), patients were matched in a 1 to 1 manner on the basis of propensity scores, which were calculated for each women using a logistic regression model that included baseline and angiographic parameters. According to the propensity score, patients were selecting using the nearest neighbour method. The probabilities of all-cause mortality were estimated by means of the Kaplan-Meier method and were compared with the use of log-rank test. Adjustment for multiple testing was performed. *P* values for 2-sided tests of <0.05 were considered statistically significant. Statistical analysis was performed with SAS 9.4 software (SAS Institute Inc, Cary, NC, 2008).

Results

We evaluated 7481 women with ACS: 1834 women at the age of ≤45 years (median 42) and 5647 women at the age of 63-64 years (median 63).

Symptoms, overall conditions, diagnosis

Baseline characteristics of the study groups are shown in Table 1.

The predominant symptom of ACS in both groups was chest pain, with a higher incidence in younger women (90.4% vs 88.5, $P = 0.025$) who also reported less dyspnoea (1.9% vs 5.3%, $P< 0.001$). In the younger group, prehospital cardiac arrest occurred more often as a first manifestation of ACS (2.1% vs 0.8%, $P< 0.0001$). Younger women had shorter onset-to-emergency room time (5.7 vs 7.8 hours, $P< 0.0001$). Most of the younger women were in good, overall condition at admission, expressed by a higher occurrence of Killip class I (92.7% vs 86.2%, $P< 0.0001$) in comparison to the older group; however, there was no significant difference in incidence of cardiogenic shock between the studied populations. The dominant type of ACS in the younger group was STEMI (42% vs 26.1%, $P< 0.0001$), as opposed to older women, in whom unstable angina (UA) occurred more often (28.3% vs 43.5%, $P< 0.0001$). There was no difference for non-ST segment elevation myocardial infarction (NSTEMI). In the younger women, ACS involved the anterior wall relatively often (47.7% vs 36.1%, $P< 0.0001$), with a statistically lower localization in the inferior wall for both groups.

Table 1. Baseline characteristics of the study groups: symptoms, vital signs at admission; type of ACS and its location.

	Group ≤45 y.o.N = 1834	Group 63-64 y.o.N = 5647	*P* value
Age [y]	42 [39-44]	63 [63-64]	<0.0001
BMI [kg/m^2]	26.7 ± 5.3	28.8 ± 5.5	<0.0001
Hypertension	966 (49.9%)	3340/4275 (78.1%)	<0.0001
Diabetes	203 (10.6%)	1255/4275 (28.9%)	<0.0001
Smoking	433 (22.2%)	949/4275 (22.2%)	<0.0001
Hypercholesterolemia	700 (36.1%)	1894/4275 (44.3%)	<0.0001
Average number of major risk factors	1.7 ± 1.2	2.0 ± 1.1	<0.0001
Peripheral artery disease	27 (1.4%)	153/4275 (3.6%)	<0.0001
Ischemic stroke	23 (1.2%)	121/4275 (2.8%)	<0.0001
Family history of CAD	339 (17.%)	492/4275 (11.5%)	<0.0001
Main symptom			
Chest pain	1656 (90.4%)	4993 (88.5%)	0.0256
Dyspnea	35 (1.9%)	299 (5.3%)	<0.0001
Weakness	11 (0.6%)	53 (0.9%)	0.1711
Syncope	13 (0.7%)	29 (0.5%)	0.3308
Cardiac arrest	38 (2.1%)	48 (0.8%)	<0.0001
Others	20 (1.1%)	45 (0.8%)	NS
Without any symptoms	59 (3.2%)	174 (3.1%)	0.7711
Onset-to-emergency room time [h]	5.7 (2.5-16.4)	7.8 (2.9-28.9)	<0.0001
Onset-to-balloon time [h]	8.9 (3.6-26.7)	15.5 (5.5- 52.0)	<0.0001
Vital signs:			
Heart rate [bpm]	78.2 ± 17.3	76.8 ± 17.0	0.0026
Systolic pressure [mm Hg]	133.1 ± 24.6	140.6 ± 13.8	<0.0001
Diastolic pressure [mm Hg]	81.7 ± 14.6	81.3 ± 13.8	0.3672
Killip-class			
I	1700 (92.7%)	4864 (86.2%)	<0.0001
II	92 (5.0%)	564 (10.0%)	<0.0001
III	5 (0.3%)	125 (2.2%)	<0.0001
IV	36 (2.0%)	88 (1.6%)	0.2394
Type of ACS			
STEMI	770 (42.0%)	1472 (26.1%)	<0.0001
NSTEMI	544 (29.7%)	1715 (30.4%)	0.5660
UA	519 (28.3%)	2456 (43.5%)	<0.0001
ACS localization			
Inferior wall	334 (43.4%)	777 (52.8%)	<0.0001
Anterior wall	367 (47.7%)	532 (36.1%)	<0.0001
Other	69 (9.0%)	163 (11.1%)	0.1189

Treatment

Percutaneous coronary intervention

Analysis showed that there were no significant differences between studied groups in the number of percutaneous coronary intervention

(PCI) or its final effect expressed by Thrombolysis In Myocardial Infarction (TIMI) flow (TIMI 3, 95.1% vs 94.4%, NS) (Table 2).

In the younger women, single-vessel disease occurred more often (55% vs 40.9%, $P< 0.0001$). Left anterior descending artery represented an infarct-related artery (IRA) in a higher percentage (33.5% vs 26.5%, $P< 0.0001$) in young, in contrast to older women where the occlusion of right coronary artery (22.9% vs 27.1%, $P = 0.0007$) and circumflex branch (11.3% vs 16.3%, $P< 0.0001$) occurred often. Interestingly, total occlusion of IRA was also more frequent in the younger women (TIMI 0, 45.2% vs 36.1%, $P< 0.0001$).

In non-IRA, in younger women, insignificant lesions were less frequent than in older one, however still mainly localized in the left anterior

Table 2. Table presenting angiographical findings.

	Group ≤45 y.o.N = 1665	Group 63-64 y.o.N = 4997	*P* value
ACS related artery			
Left ascending artery—LAD	558 (33.5%)	1323 (26.5%)	<0.0001
Right coronary artery—RCA	381 (22.9%)	1355 (27.1%)	0.0007
Left circumflex artery—Cx	188 (11.3%)	813 (16.3%)	<0.0001
Diagonal branch—D	49 (2.9%)	126 (2.5%)	0.3517
Left marginal artery—LM	37 (2.2%)	87 (1.7%)	0.2083
By-pass	5 (0.4%)	45 (0.9%)	0.0285
Indeterminate	446 (26.8%)	1248 (25.0%)	0.1415
Number of arteries with significant lesions	Group ≤45 y.o. N = 242	Group 63-64 y.o. N = 555	
0	64 (26.4%)	107 (19.3%)	<0.0001
1	133 (55.0%)	227 (40.9%)	
2	32 (13.2%)	138 (24.9%)	
3	13 (5.4%)	67 (21.1%)	
4	0	15 (2.7%)	
5	0	1 (0.2%)	
In-stent restenosis	29 (1.6%)	104 (1.8%)	0.4634
Number of PCI	1140 (62.2%)	3453 (61.2%)	0.4394
Bare metal stent (BMS)	518 (50.4%)	1796 (55.3%)	0.0069
Drug eluting stent (DES)	445 (43.3%)	1242 (38.2%)	0.0035
Balloon angioplasty	64 (6.2%)	212 (6.5%)	0.7405
Preprocedural TIMI flow			
0	470 (45.2%)	1184 (36.1%)	<0.0001
1	172 (16.5%)	638 (19.5%)	
2	182 (17.5%)	677 (20.7%)	
3	216 (20.8%)	780 (23.8%)	
Postprocedural TIMI flow			
0	17 (1.6%)	60 (1.8%)	0.8063
1	10 (1.0%)	33 (1.0%)	
2	24 (2.3%)	92 (2.8%)	
3	992 (95.1%)	3098 (94.4%)	

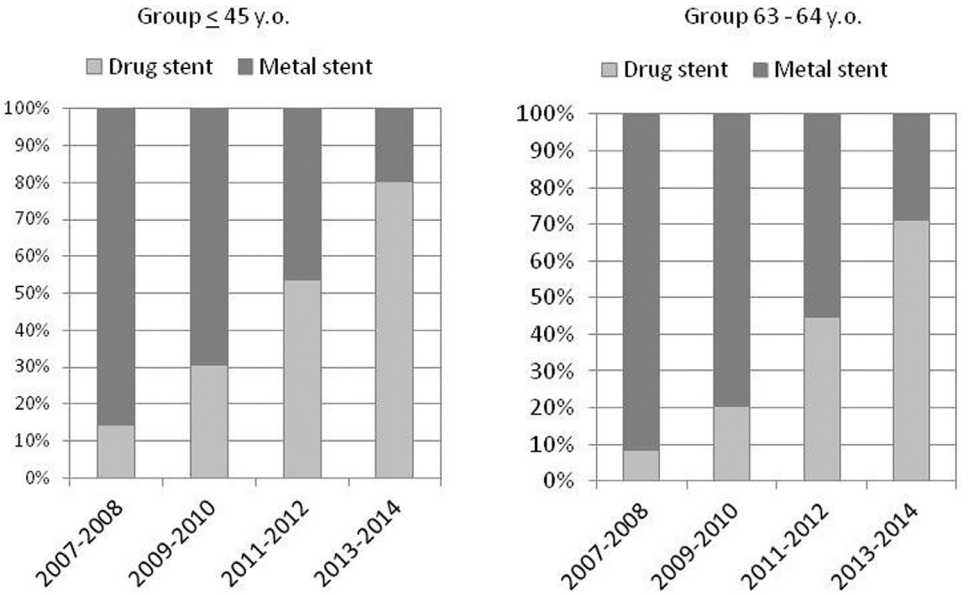
descending artery. GPIIb/IIIa inhibitors were administered more frequently during PCI, with no difference in the number of PCIs (62.2% vs 61.2%) (Table 2). In both groups an upward trend was observed in the use of DESover 7 years, ($P < 0.0001$), (Fig 1). The analysis showed that the factors affecting the more frequent use of DES vs BMS in young women were: younger age of the patient (40.8 years vs 41.1 years $P = 0.012$), higher incidence of diabetes (15.5% vs 10.2%, $P = 0.014$), previously diagnosed coronary artery disease (CAD) (8.55 vs 4.6%, $P = 0.013$), history of ACS (15.4% vs 5.8%, $P < 0.0001$).

Both in the younger and older population in the first days of observation showed a decreasing trend in mortality when using DES vs BMS, but no significant differences in mortality were observed during 24 months of follow-up. To minimize differences in the baseline characteristics between the DES and BMS groups, women were matched using the propensity score method. The area under the receiver operating characteristic curve was 0.772 (<45 years old) and 0.765 (63-43 years old). A total of 468 (<45 years old) and 1516 (63-64 years old) with matched baseline characteristic (for young: data of ACS episode, type of ACS, previous history of ACS, obesity, age; for older women: data of ACS episode, type of ACS, previous PTCA, diabetes, hypercholesterolemia) were identified. Among patients after propensity score matching we found that in older patients the type of stent affects mortality, which is lower in patients with DES. The above-mentioned analysis confirmed the lack of impact of the type of stent used (DES/BMS) on mortality in the population of young women with ACS (Fig 2A and B).

Surgical interventions - coronary artery bypass grafting (CABG) were used less often in the younger group (4.5% vs 9.1%).

Treatment delays. Significant differences were observed with delays in interventional treatment within groups. Young women with NSTEMI and UA compared to older ones faster received adequate interventional treatment respectively: (13.7 hours vs 15.8 hours $P = 0.014$); (22.7 hours vs 31.9 hours $P = <0.001$), which results both from a faster patient recruitment for help as well as faster percutaneous therapy (Table 3). A phenomenon absent for patients with STEMI, where times were similar between the study groups, and the only difference is shorter emergency-to-balloon time in the younger group.

Additional information was provided by the analysis including the transport mode of patients to the invasive centre (directly from home vs from another hospital). We found that for both younger and older group the mode of transport to the cathlab had an significant influence on onset-



N, % DES	2007-2008	2009-2010	2011-2012	2013-2014	P
≤45 y.o	17 (14.3%)	90 (30.7%)	208 (53.5%)	130 (80.2%)	<0.0001
63-64 y.o.	23 (8.6%)	165 (20.4%)	584 (44.8%)	470 (71.2%)	<0.0001

FIG 1. Trend in the use of different types of stents in the studied populations (DES vs. BMS).

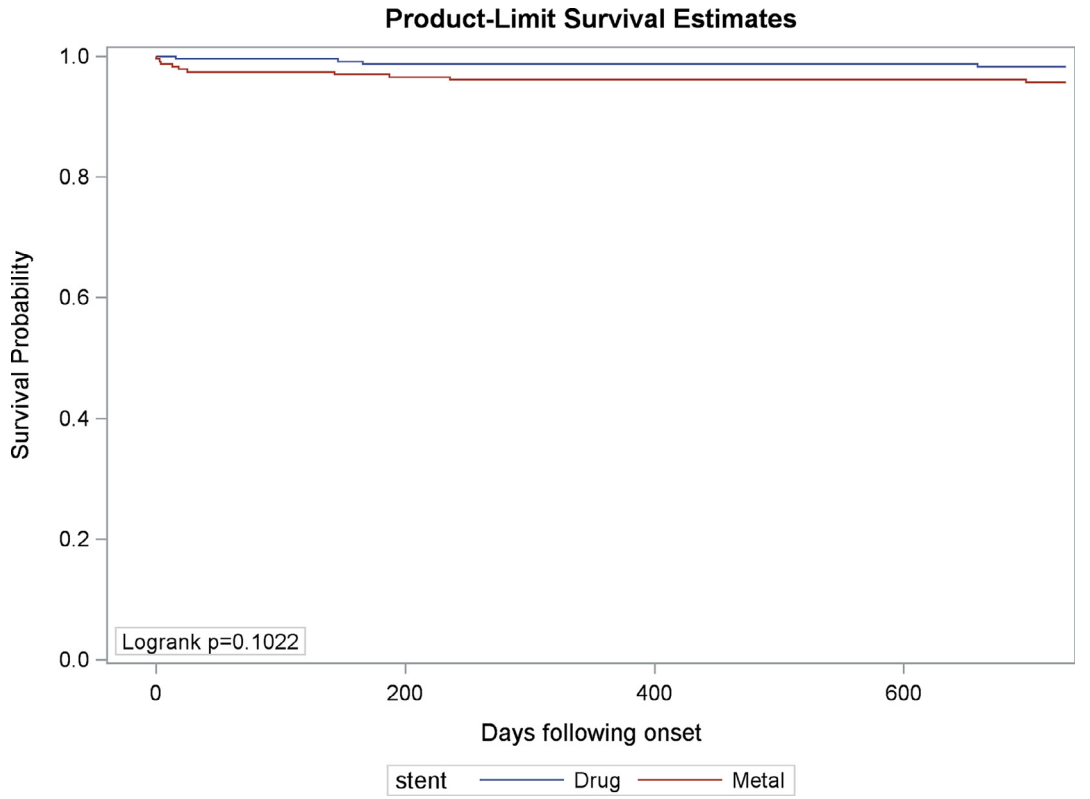


FIG 2. (A) Graph presenting the probability of survival of patients under or equal 45 years, depending on the type of stent DES vs. BMS. (B) Graph presenting the probability of survival of patients 63-64 years, depending on the type of stent DES vs. BMS.

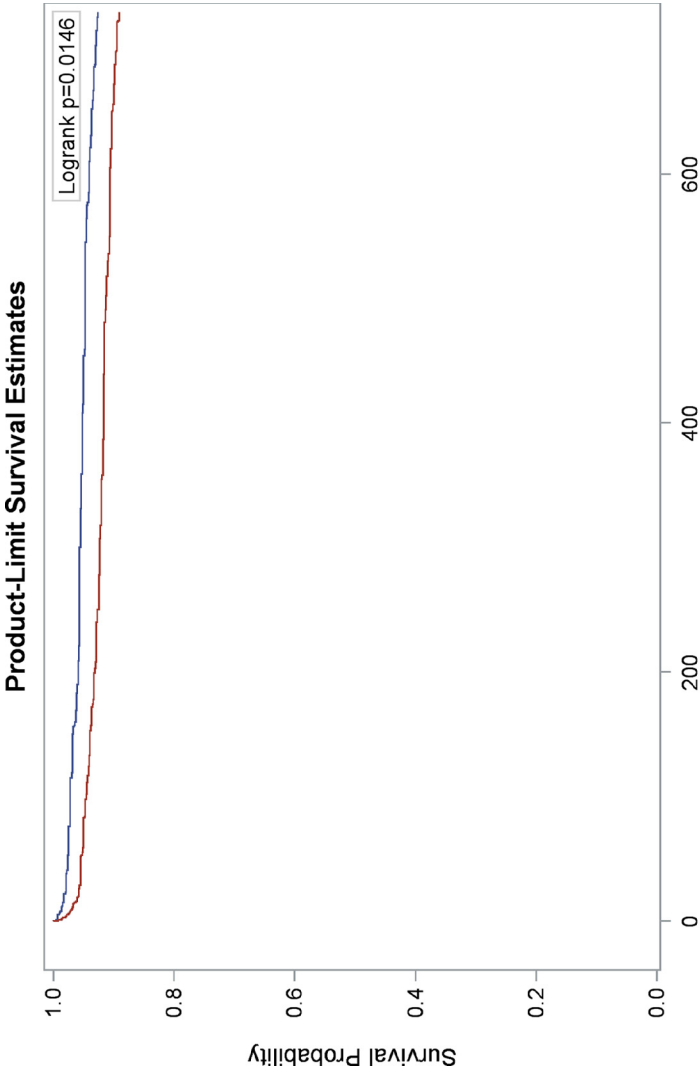


FIG 2 Continued.

Table 3. Table presenting differences in treatment delay in studied groups.

	Group <45 y.o.	Group 63-64 y.o.	*P*
Onset-to-balloon time [h]			
STEMI	4.25 [2.50-9.83]	4.67 [2.67-11.50]	0.051
NSTEMI	13.75 [6.50-31.20]	15.83 [7.46-42.08]	0.014
UA	22.75 [6.83-71.00]	31.19 [11.33-98.21]	<0.0001
Onset-to-emergency time [h]			
STEMI	3.62 [2.00-8.00]	3.83 [2.10-9.17]	0.093
NSTEMI	8.65 [3.58-19.43]	9.36 [3.77-27.58]	0.015
UA	9.50 [3.35-49.33]	15.30 [4.28-71.70]	0.0003
Emergency-to balloon time [h]			
STEMI	0.42 [0.23-0.79]	0.48 [0.25-1.00]	0.012
NSTEMI	1.47 [0.50-5.50]	2.00 [0.63-7.67]	0.009
UA	3.25 [1.32-16.07]	4.78 [1.98-20.47]	0.0001

to-balloon time extension, only in the case of STEMI patients, with no difference between study groups (Table 3A).

Pharmacological treatment. We found significant differences in pharmacological treatment between groups, with a lower usage of medications in the younger women. In-hospital treatment and recommendations at discharge for the younger women less often included beta-blockers (BB); angiotensin-converting enzyme inhibitors (ACE-I); angiotensin receptor blockers (ARB); statins; calcium channel blockers; and diuretics and hypoglycaemic medications. Moreover, enoxaparin and inotropes were used less in young during their hospital stays (14.4% vs 16.7% and 1.2% vs 2.0%, respectively) (Table 4). In the time related analysis of drug use, significant differences were shown only for in-hospital treatment. It is interesting that only for GPIIbIIIa inhibitors and tienopiridin has been shown more frequent use in young patients over 7 years, where for most drugs the opposite trend was found—less frequent use of BB, ACE-I, ARB, acidum acetylsalicylicum (ASA) diuretics, and statins in 2014 vs 2007. There were no differences for discharge drugs.

Complications, mortality

The incidence of all complications was low in both groups and did not exceed 4%, with no statistical differences. We found only a higher incidence of pulmonary oedema in older women (0.73% vs 0.27%, $P = 0.004$), with similar rates of bleeding, mechanical complications, sudden cardiac arrest, cardiogenic shock, and re-infarction. At 2-year follow-up,

Table 3A. Table presenting differences in treatment delay in studied groups depending on transport method to cathlab (directly from home vs via other hospital).

		Group <45 y.o.	Group 63-64 y.o.	*P*
Onset-to-balloon time [h]				
STEMI	From home	3.67 [2.25-8.95]	4.08 [2.37-9.83]	0.109
	From hospital	4.92 [3.12-11.2]	5.83 [3.17-13.92]	0.124
	*P*value	<0.0001	<0.0001	–
NSTEMI	From home	12.00 [5.83-32.83]	17.00 [8.00-42.17]	0.033
	From hospital	13.99 [7.46-30.39]	15.33 [7.13-41.88]	0.173
	*P*value	0.67	0.436	–
UA	From home	23.75 [8.00-77.5]	34.17 [12.75-102.6]	0.001
	From hospital	19.00 [6.25-56.00]	28.13 [9.46-85.25]	0.003
Onset-to-emergency time [h]				
STEMI	From home	3.00 [1.68-7.00]	3.33 [1.92-7.25]	0.123
	From hospital	4.46 [2.58-9.64]	4.90 [2.67-12.42]	0.222
	*P*value	<0.0001	<0.0001	–
NSTEMI	From home	6.78 [2.98-16.17]	7.50 [3.00-21.00]	0.171
	From hospital	10.33 [5.08-21.90]	12.50 [4.78-34.00]	0.063
	*P*value	<0.0001	<0.0001	–
UA	From home	8.43 [2.98-49.17]	13.63 [3.85-63.53]	0.012
	From hospital	11.25 [3.93-49.33]	21.06 [5.57-81.70]	0.002
Emergency-to balloon time [h]				
STEMI	From home	0.42 [0.25-0.83]	0.48 [0.25-1.00]	0.126
	From hospital	0.42 [0.22-0.68]	0.45 [0.25-1.00]	0.039
	*P*value	0.24	0.7	–
NSTEMI	From home	2.37 [0.65-16.3]	3.83 [1.00-18.07]	0.030
	From hospital	1.08 [0.42-2.42]	1.44 [0.50-4.08]	0.024
	*P*value	<0.0001	<0.0001	–
UA	From home	5.75 [1.77-21.82]	7.76 [2.58-25.11]	0.014
	From hospital	2.17 [0.92-5.75]	3.00 [1.27-6.42]	0.017

prognosis for younger women was better than for older women, with a lower mortality rate regardless of the type of ACS (Fig 3).

Discussion

ACS manifest with different symptoms depending on age, sex, and comorbidities. The reasons for this differences may be complex and are related to anatomy, pathophysiology, and psychological aspects.[13-15] Infarction in the absence of significant atherosclerotic lesions is more common among younger women in comparison to older patients. In such cases, ischemia results from vascular dissection, myocardial bridges, congenital or acquired anatomical changes of the vessels, vascular spasms, thromboembolism or substance misuse.[16,17] Generally, women have less favourable outcomes than men, which to some extent is caused by atypical symptoms and under treatment.[3-9]

Table 4. Differences in pharmacological treatment in studied women during in-hospital phase and at discharge.

	In-hospital treatment			Discharge recommendation	
	Group ≤45 y.o.N = 1834	Group 63-64 y.o.N = 5647	*P* value	Group ≤ 45 y.o.N = 1834	Group 63-64 y.o.N = 5647
Anticoagulants	782 (42.7%)	2552 (45.2%)	0.0545		
UFH	468 (25.5%)	1419 (25.2%)	NS	–	–
LMWH	264 (14.4%)	941 (16.7%)	0.0213	66 (3.6%)	257 (4.6%)
Fondaparinux	10 (0.55%)	27 (0.5%)	NS	N/A	N/A
Bivalirudin	1 (0.05%)	3 (0.05%)	1.000	N/A	N/A
GPIIb/IIIa blocker	364 (19.9%)	675 (12.0%)	<0.0001	N/A	N/A
Inotropes	23 (1.2%)	111 (2.0%)	0.0459	N/A	N/A
Acetylsalicylic acid	1590 (86.7%)	4958 (87.8%)	0.2142	1636 (89.2%)	5071 (89.8%)
Clopidogrel	1718 (93.7%)	5333 (94.4%)	0.2217	1345 (73.3%)	4071 (72.1%)
Prasugrel	24 (1.3%)	85 (1.5%)	0.5415	15 (0.8%)	42 (0.74%)
Beta-blockers	1204 (66.6%)	4079 (72.2%)	<0.0001	1436 (78.3%)	4605 (81.5%)
ACE-I	1033 (56.3%)	3738 (66.2%)	<0.0001	1259 (68.6%)	4246 (75.2%)
ARB	34 (1.8%)	199 (3.5%)	0.0003	35 (1.9%)	252 (4.5%)
Fibrates	18 (0.98%)	56 (0.99%)	0.9694	23 (1.25%)	56 (0.99%)
Statins	1266 (69.0%)	4321 (76.5%)	<0.0001	1509 (82.3%)	4820 (85.4%)
Calcium blockers	133 (7.2%)	649 (11.5%)	<0.0001	170 (9.3%)	705 (12.5%)
Nitrats	196 (10.7%)	962 (17.0%)	<0.0001	165 (9.0%)	775 (13.7%)
Diuretics	159 (8.7%)	1138 (20.2%)	<0.0001	199 (10.9%)	1327 (23.5%)
Oral hypoglycemic agents	45 (2.4%)	546 (13.4%)	<0.0001	63 (3.4%)	721 (12.8%)
Insulin	89 (4.8%)	756 (13.4%)	<0.0001	90 (4.9%)	696 (12.3%)

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

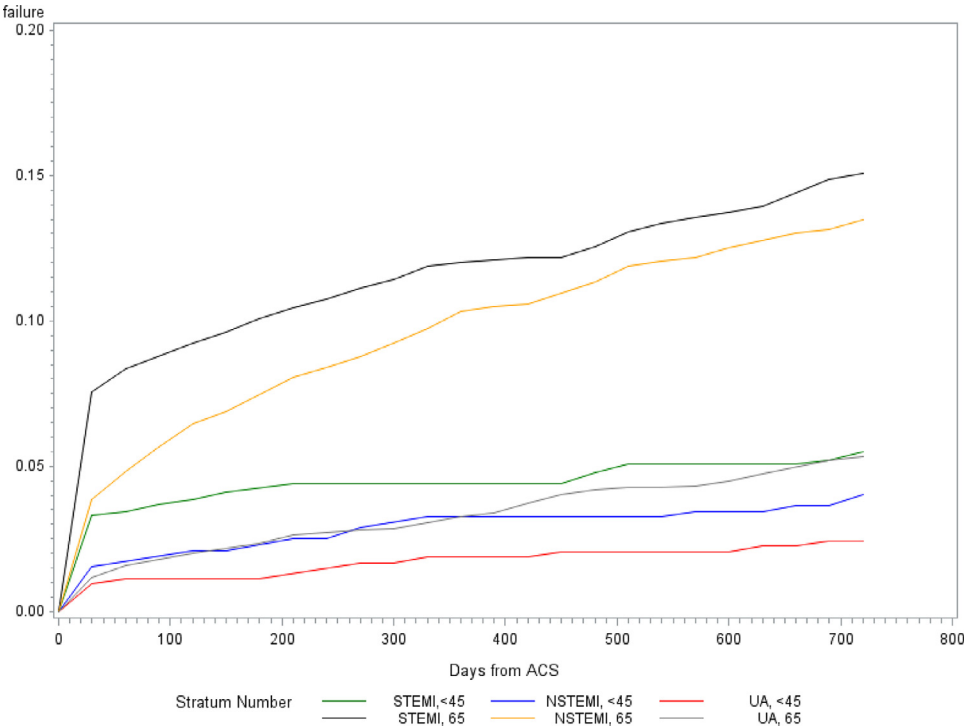


FIG 3. Kaplan-Meier curves comparing all-cause mortality in the study groups.

The differences between patients of the same sex in relation to age are less clear. In our study, chest pain and cardiac arrest occurred more often in younger women, while dyspnoea was a more frequent symptom of ACS in older women. This suggests that symptoms become more atypical with ageing. The percentage of chest pain in both our groups was high, but with a higher incidence in younger women which was consistent with previous studies, however in Canto et al study chest pain was recorded less often in both younger and older group, (74% vs 53%); of cases with myocardial infarction, respectively.[18] In the more recent VIRGO study, 87% of women complained of chest pain.[19] In about 90% of all women, regardless of age, chest pain was the most common symptom of ACS, hence, despite the statistical difference between the groups, it does not seem to have a significant clinical significance—in ACS differentiation between groups. However, this fact clearly shows that chest pain is typical symptom of ACS in young woman and which makes diagnosis easier. What is more during the diagnosis of chest pain in women, young age should not be a disparaging factor, delaying the implementation of appropriate treatment. Nevertheless, time to intervention in our population was significantly longer in younger women. The probability of ACS in women ≤45 years old seems to be low, which may be very misleading. For this reason, campaigns raising the awareness of symptoms of ACS and emphasizing the need for urgent healthcare consultation, particularly in younger patients, are required.[15] Interestingly, the incidence of pulmonary oedema in both populations is very small with a significant difference in favour of young women. Nevertheless, with such a relatively small population size, this difference does not seem to have a significant impact in clinical practice.

The major type of ACS in young women was STEMI, with involvement of the anterior wall due to single-vessel stenosis, usually the left ascending artery. On the other hand, multivessel disease was more prevalent in the older women, and the most common type of ACS in that group was UA. The predominance of a single-vessel disease among younger women compared to older women in our study is consistent with the results of the Coronary Artery Surgery Study registry, but the distribution of lesions in the latter was independent of age.[20] This may be explained not only by age, but also by distribution of risk factors. The prevalence of risk factors for ACS in young women with ACS is different to those in healthy women and to those in older women. In our previous publication we found that in older women included in the PL-ACS registry, hypertension, hypercholesterolemia, and diabetes were the main risk factors of coronary artery disease, while women aged ≤45 years smoked twice as

much as women aged 63-64 years and the strongest predictor of ACS in women ≤45 years of age was diabetes, with a 6-fold increase in risk.[21] The trend towards higher incidence of STEMI in ACS in a younger population was also observed in other studies.[22] However, Davis et al reported a higher incidence of UA in women aged ≤ 55 years than in older women with comparable rates of STEMI.[23]

PCIs were performed in a similar percentage of patients in both groups, but pharmacotherapy was underused in the younger population. It was valid for BB, ACE-I, ARB, and statins. What is more in previous study it was shown that suboptimal pharmacotherapy in young women with STEMI worsened their prognosis.[24] Such phenomenon has been reported in literature primarily for people ≥80 years old.[25] Davis et al observed more prevalent usage of BB after ACS in a population of women >55 years old, without significant differences in the treatment with ACE-I and lipid-lowering drugs.[23]

We conclude that both older and younger women are prone to receive fewer medications strongly recommended by International Societies of Cardiology. However, outcomes in younger women with ACS in our study were favourable. This is similar to the observations of other authors, who reported lower mortality in younger patient with ACS than in older patients.[26,27] This suggests that age represents a very strong risk factor for overall mortality. Painless presentations of ACS may also contribute to higher mortality in older women.[28] Interestingly, the mortality rate from ACS after 2 years was highest for STEMI. This contrasts with some previous data, which indicated that STEMI is associated with higher short-term mortality than NSTEMI, but in regards to long-term follow-up, the proportion was inverted or nearly equal.[29,30]

Limitations

The main limitation of this study was its retrospective design, especially since the questionnaire was filled in during 3 stages, which may affect its accuracy. The analysis did not include patients who died during the prehospital period. Due to the design of the study, the authors did not have data on the pharmacological treatment used in the posthospital period, which could have an influence on long-term prognosis A matter of discussion was the age limit of patients. The study was aimed at younger women; however, “youth” is not precisely defined. In our study, we included women aged under and equal to 45 years. This limit reduced the probability of the impact of menopausal (including premature) hormonal imbalances on the incidence of MI in this population. Estimated mean

age of menopause for women in the Polish population is 51.25 years (range from 45 years-56 years).

Conclusion

In conclusion, women ≤45 years old, when compared to those aged 63-64 years, present more typical symptoms of ACS, with a higher proportion of STEMI and single-vessel disease. In young women delay between onset of symptoms and emergency room is shorter. The frequency of invasive treatment is independent of age. Younger patients less frequently receive the drugs which are recommended in evidence-based medicine. In-hospital and 2-year survival in younger women with ACS is better than in the older population.

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