

Outcomes of invasive treatment in very elderly Polish patients with non-ST-segment-elevation myocardial infarction from 2003–2009 (from the PL-ACS registry)

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Abstract

Background: *Elderly patients with non-ST-segment elevation myocardial infarction (NSTEMI) are rarely included in randomized trials due to concomitant diseases. As a result, invasive treatment and aggressive pharmacotherapy are used less frequently in this group. The aim of the study was to analyze the impact of invasive treatment used for elderly patients (≥ 80 years) with NSTEMI from 2003–2009 and its impact on 24-month outcomes.*

Methods: *We performed analysis of 13,707 elderly patients, out of 78,422 total NSTEMI patients, enrolled in the prospective, nationwide, Polish Registry of Acute Coronary Syndromes (PL-ACS) from 2003 to 2009.*

Results: *The percentage of elderly NSTEMI population was 17.5%. Invasive treatment received 24% of them. In-hospital complications (stroke, reinfarction and death) were significantly less frequent in the invasive group, with the exception of major bleeding, which occurred almost three times more frequently (2.9% vs. 1.1%, $p < 0.0001$) in the invasive group. The 24-month mortality was lower (29.4% vs. 50.4%, $p < 0.0001$) in the invasive group and remained so after matching patients by the propensity score method (31.1% vs. 40.9%, $p < 0.0001$). From 2003 to 2009 the use of thienopyridines, beta-blockers and statins rose significantly. The frequency of invasive strategy increased significantly, from 10% in to over 50% in 2009. The frequency of major bleeding increased twofold, however a significant reduction in the 24-month mortality was observed over the years.*

Conclusions: *Elderly patients with NSTEMI benefit significantly from invasive strategies and modern pharmacotherapy recommended by treatment guidelines. Nevertheless, this approach is associated with an increased incidence of major bleeding. (Cardiol J 2013; 20, 1: 34–43)*

Key words: NSTEMI, elderly, percutaneous coronary intervention, mortality, temporal trends

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Introduction

Nineteen of the twenty countries with the highest worldwide percentages of elderly citizens are European [1]. In 2009, 13% of the Polish population was ≥ 65 years of age, and 3.3% were ≥ 80 years of age [2]. In people ≥ 40 years of age, an age at which there is a real risk of myocardial infarction (MI), 29% of the Polish population was ≥ 65 years of age, and 7% were ≥ 80 years of age. The prognosis for the near future foresees further significant aging of the Polish population [3]. Ischemic heart disease remains the main cause of death among the elderly and is responsible for approximately 50% of deaths among people ≥ 80 years of age [1]. Elderly patients are rarely included in randomized trials due to concomitant diseases and concerns relating to complications, especially bleeding. As a result, invasive treatment and aggressive pharmacotherapy are used less frequently in this group [4, 5], even though it is these high-risk patients that could potentially benefit the most from modern treatment methods [6]. Managing ST-segment-elevation MI (STEMI) raises fewer questions [7, 8], as confirmed in the Polish population [9, 10]. Although non-ST-segment-elevation MI (NSTEMI) is characterized by long-term mortality similar to that of STEMI [11], the choice of treatment strategies is usually more challenging. Registries complement randomized trials and may provide preliminary answers regarding the effectiveness of invasive treatments in elderly MI patients. Therefore, the role of registries has become essential. Using the data obtained from the Polish Registry of Acute Coronary Syndromes (PL-ACS), we analyzed the treatment methods used for elderly Polish patients (≥ 80) with NSTEMI from 2004–2009 and their impact on 24-month outcomes.

Methods

We used data from the PL-ACS registry. The registry's methodology and an analysis of the first 100,193 patients have been previously described [12]. In brief, the PL-ACS registry is an ongoing, nationwide, multicenter, prospective, observational study of consecutively hospitalized Polish patients due to the entire acute coronary syndrome (ACS) spectrum. The registry is a joint initiative of the Silesian Centre for Heart Diseases and the Polish Ministry of Health. The National Health Fund, a nationwide public health insurance institution in Poland, provides logistical support. All Polish citizens are required to have a National Health Fund

insurance policy. The pilot phase of the registry commenced in October 2003 in the Silesia region. In the following months, all the other regions were included.

Hospitals were invited to enter the registry if they had one of the following units: coronary care, cardiology, cardiac surgery, internal medicine, and intensive care. They were also invited to join if they admitted at least 10 ACS patients per year.

A detailed protocol with inclusion and exclusion criteria, methods and logistics, and definitions of all the fields in the registry dataset was prepared before the registry was started. The protocol was revised in May 2005 to be compatible with the Cardiology Audit and Registration Data Standards (CARDS) [13]. Nevertheless, the PL-ACS Registry case report form (CRF) covers only part of the CARDS dataset.

According to the protocol, all admitted patients with suspected ACS were screened for their eligibility to enter the registry, but they were not enrolled until ACS was confirmed. The patients were then classified as having unstable angina, NSTEMI, or STEMI. NSTEMI was defined as the presence of positive cardiac necrosis markers and the absence of all of the following: ST-segment elevation ≥ 2 mm in contiguous chest leads that is consistent with infarction, ST-segment elevations ≥ 1 mm in two or more standard leads, and a new left bundle branch block. If the patient was hospitalized in more than one hospital for the same ACS episode (i.e., if the patient was transferred), all the hospitals were required to complete the registry data. These hospitalizations were linked together during data management and were subsequently analyzed as a single ACS case.

The data were collected by skilled physicians who were attending the patients. The data were entered directly into an electronic CRF or temporarily printed on a CRF before being transferred to an electronic CRF. Internal checks for missing or conflicting data and values markedly outside of their expected ranges were implemented within the software. Further data checking was performed by the applied data management and analysis center of the Silesian Centre for Heart Diseases if necessary.

The exact dates of deaths from all causes were obtained from the official mortality records of the National Health Fund. The vital status at 24 months following the NSTEMI was available for all the patients who were included in the registry up to December 2009.

The analysis included all the NSTEMI patients ≥ 80 years of age. The clinical characteristics and

outcomes of the patients treated with invasive (coronary angiography during hospitalization) and conservative (no coronary angiography during hospitalization) methods were compared. The temporal trends from 2003–2009 were analyzed for clinical characteristics, methods of treatment, and early and long-term outcomes.

Statistical analysis

The continuous variables are expressed as the mean \pm standard deviation (SD) or the median (interquartile range). The significance of their differences between groups was evaluated using the Student's T-test or the Mann-Whitney test, depending on the data distribution. The categorical variables are expressed as percentages; the significance of their differences between groups was evaluated using the χ^2 test (with Yates' correction in cases where the expected value of a cell is < 5). A propensity score analysis was used to compensate for the nonrandomized design of the study. The propensity scores were calculated using a multiple regression model that included all of the covariates shown in Figure 2. The C-statistic for this model was 0.84. The 24-month mortalities of the studied groups and the propensity score-matched subgroups were evaluated using Kaplan-Meier analysis and the log-rank test. A multiple-factor Cox proportional hazards regression model was used to determine the factors affecting the 12-month mortality; the results are shown as relative risks (RR) and 95% confidence intervals (CI). The significance of temporal trends over the years in question was evaluated using the Cochran-Armitage test for categorical variables and the Jonckheere-Terpstra test for continuous variables. A two-tailed p value ≤ 0.05 was considered statistically significant. The calculations were performed using STATISTICA 10 (StatSoft Inc., Tulsa, OK, USA), MedCalc 11.5 (MedCalc Software, Belgium) and SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 78,422 patients were hospitalized due to NSTEMI in 460 hospitals throughout Poland (including 101 (22%) invasive cardiology centers), and registered in the PL-ACS Registry between October 2003 and December 2009. The percentage of admissions due to NSTEMI among all the ACS patients (a total of 244,870 patients) was 32%; this fraction increased from 20% in 2003 to 38% in 2009 (p for the trend < 0.0001). The percentage of elderly patients (≥ 80 years) with NSTEMI was 17.5%

(n = 13,707); this fraction increased from 12% in 2003 to 18% in 2009 (p for the trend < 0.0001).

Of the 13,707 NSTEMI patients ≥ 80 years of age, 3,288 (24%) received invasive treatment. The remaining 10,419 (76%) were treated conservatively. The differences in the baseline clinical characteristics between the patients treated invasively and those treated conservatively are shown in Table 1. The patients treated invasively were younger, less frequently female and significantly less frequently admitted with major hemodynamic disorders (pulmonary edema and cardiogenic shock). Patients with a history of hypertension, hypercholesterolemia, past coronary revascularization, sinus ECG rhythm and smoking were more frequent in this group. It is worth noting that invasive treatment was performed in only 52% the patients admitted to invasive cardiology wards (n = 5,859), with the remaining 48% being treated conservatively.

During hospitalization, the patients treated invasively received the drugs recommended by treatment guidelines, such as acetylsalicylic acid, thienopyridines, statins, beta-blockers and angiotensin converting enzyme inhibitors (Table 2), significantly more frequently. Heparins, nitrates and diuretics were used more frequently in patients treated conservatively. Table 3 shows the treatment details of the invasive group. Percutaneous coronary interventions (PCI) were performed in 70% of the patients; coronary artery bypass grafting was performed or planned in 13%. After receiving coronary angiography, almost 20% of patients were qualified to receive conservative treatment (without revascularization). Stents were used in 90% of the PCIs, of which 4% were drug-eluting stents.

The left ventricular ejection fraction (the last examination while hospitalized) was significantly higher among the patients treated invasively (Table 4). In-hospital complications (stroke, reinfarction and death) were less frequent in the invasive group, with the exception of major bleeding, which occurred almost three times more frequently (2.9% vs. 1.1%) in the invasive group. The length of hospital stay was three days shorter for the invasive patients. The 24-month mortality was high, but significantly lower (by almost half) in the invasive group (Fig. 1). After matching patients by the propensity score method, the prognosis in the invasive group was still significantly better (Table 5, Fig. 1). The multivariate analysis controlled for the differences in baseline characteristics and the pharmacotherapy used found that invasive treatment significantly decreased 24-month mortality in elderly

Table 1. The clinical characteristics of the elderly non-ST-segment elevation myocardial infarction patients, by treatment strategy.

	Invasive treatment (n = 3,288)	Conservative treatment (n = 10,419)	P
Age [years]: median (interquartile range)	82 (81–84)	83 (81–86)	< 0.0001
Age, range	80–99	80–105	–
Females	52.5%	62.8%	< 0.0001
Diabetes mellitus	30.9%	30.5%	0.65
Hypertension	78.6%	71.0%	< 0.0001
Hypercholesterolemia	36.3%	32.6%	< 0.0001
Current tobacco smoking	22.8%	9.6%	< 0.0001
Obesity (body mass index \geq 30)	14.8%	14.9%	0.84
Prior myocardial infarction	22.9%	22.2%	0.37
Prior percutaneous coronary intervention	5.7%	1.2%	< 0.0001
Prior coronary artery bypass grafting	3.2%	1.6%	< 0.0001
Cardiac arrest prior to admission	0.7%	1.4%	0.0010
Heart rate on admission	81 \pm 20	91 \pm 27	< 0.0001
ECG with no ST-T changes	13.0%	16.3%	< 0.0001
Heart rhythm other than sinus	15.7%	27.3%	< 0.0001
Systolic arterial pressure [mm Hg]	140 \pm 27	141 \pm 36	0.42
Killip 2 on admission	16.9%	28.0%	< 0.0001
Killip 3 on admission	4.5%	13.6%	< 0.0001
Killip 4 on admission	1.9%	4.5%	< 0.0001
Hospitalization in the invasive ward	100%	27.1%	< 0.0001

Table 2. The drugs used during hospitalisation in the elderly non-ST-segment elevation myocardial infarction patients, by treatment strategy.

	Invasive treatment (n = 3,288)	Conservative treatment (n = 10,419)	P
Aspirin	93.5%	89.2%	< 0.0001
Thienopyridines	88.2%	41.4%	< 0.0001
Glycoprotein IIb/IIIa inhibitors	4.6%	0.1%	< 0.0001
Heparins:	58.1%	80.1%	< 0.0001
Low-molecular-weight heparin	37.0%	67.8%	< 0.0001
Unfractionated heparin	27.0%	15.4%	< 0.0001
Beta-blockers	80.7%	71.1%	< 0.0001
Angiotensin-converting enzyme inhibitors	80.6%	72.3%	< 0.0001
Statins	84.9%	69.3%	< 0.0001
Calcium antagonists	10.1%	8.9%	0.029
Nitrates	34.5%	59.0%	< 0.0001
Fibrates	0.7%	0.6%	0.39
Diuretics	35.9%	55.4%	< 0.0001

NSTEMI patients (RR 0.67, 95% CI 0.62–0.72, $p < 0.0001$) (Fig. 2).

Table 6 presents temporal trends in the clinical characteristics, treatment methods and out-

comes in the elderly NSTEMI patients. The mean age of the patients did not change over the period in question, whilst the incidence of diabetes and the percentage of patients with prior PCI increased sig-

Table 3. Invasive non-ST-segment elevation myocardial infarction treatments in elderly patients.

	Invasive treatment (n = 3,288)
Multivessel coronary disease	70.0%
PCI:	70.0%
Stent implantation	89.9%
Drug-eluting stent	3.6%
Multivessel PCI	19.0%
Final TIMI 3 flow after PCI	90.7%
CABG during hospitalization	1.4%
CABG planned after discharge	11.8%
Without revascularization	19.5%

PCI — percutaneous coronary intervention; TIMI — Thrombolysis In Myocardial Infarction; CABG — coronary artery bypass grafting

nificantly. The incidence of major hemodynamic disorders on admission (pulmonary edema and cardiogenic shock) decreased. The use of drugs recommended by treatment guidelines, such as thienopyridines, beta-blockers and statins, rose significantly. There was a decreasing trend for nitrate and diuretic use. The frequency of invasive diagnostic methods increased significantly, from 10% in 2003/2004 to over 50% in 2009, which also caused an increase in the number of percutaneous and surgical revascularization procedures. The length of hospital stays decreased from 10 days in 2003/2004 to 6 days in 2009. The incidences of in-hospital stroke, myocardial reinfarction and death decreased. The frequency of major bleeding increased twofold. There was also a significant reduction in the 24-month mortality over the years.

Table 4. The in-hospital and long-term prognosis in elderly non-ST-segment elevation myocardial infarction patients, by treatment strategy.

	Invasive treatment (n = 3,288)	Conservative treatment (n = 10,419)	P
Left ventricular ejection fraction	46.3 ± 11.4	44.7 ± 13.5	< 0.0001
Major bleeding	2.9%	1.1%	< 0.0001
Stroke	0.4%	1.0%	0.0008
Myocardial reinfarction	1.6%	5.2%	< 0.0001
Death	5.0%	14.0%	< 0.0001
Length of hospitalization [days]: median (interquartile range)	6 (3–9)	9 (6–12)	< 0.0001
30-day mortality	8.4%	19.5%	< 0.0001
6-month mortality	16.2%	32.1%	< 0.0001
12-month mortality	21.4%	39.4%	< 0.0001
24-month mortality	29.4%	50.4%	< 0.0001

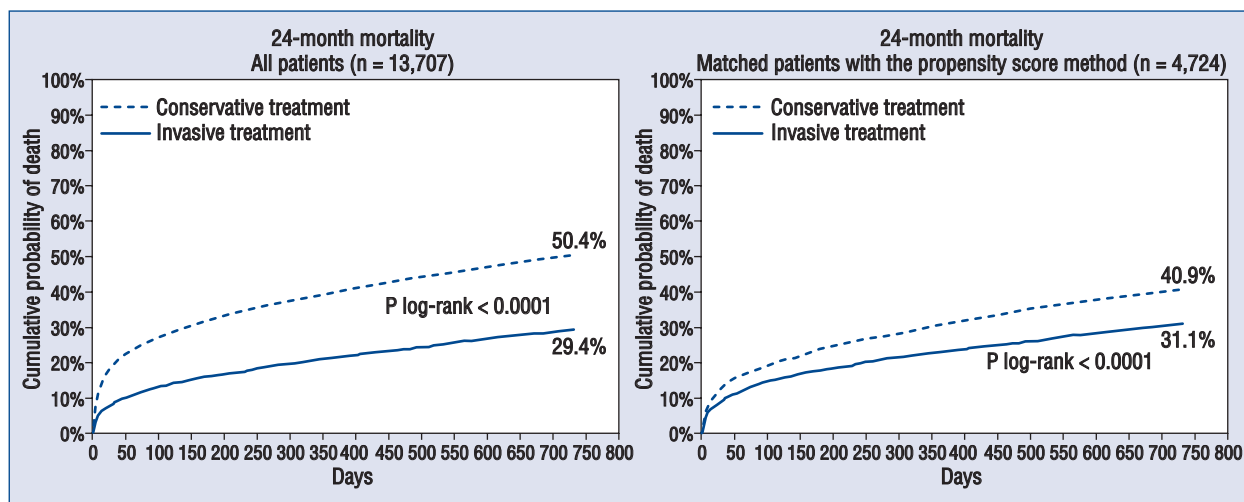


Figure 1. The 24-month mortality by treatment method for all of the elderly non-ST-segment elevation myocardial infarction patients and for the propensity score matched elderly non-ST-elevation myocardial infarction patients.

Table 5. The in-hospital and long-term prognosis in the propensity score-matched subgroups of elderly non-ST-segment elevation myocardial infarction patients, by treatment strategy.

	Invasive treatment (n = 2,362)	Conservative treatment (n = 2,362)	P
Major bleeding	2.9%	1.2%	< 0.0001
Stroke	0.4%	0.6%	0.41
Myocardial reinfarction	1.8%	4.2%	< 0.0001
Death	5.7%	8.5%	0.0002
30-day mortality	9.2%	13.1%	< 0.0001
6-month mortality	18.0%	23.9%	< 0.0001
12-month mortality	23.2%	30.5%	< 0.0001
24-month mortality	31.1%	40.9%	< 0.0001

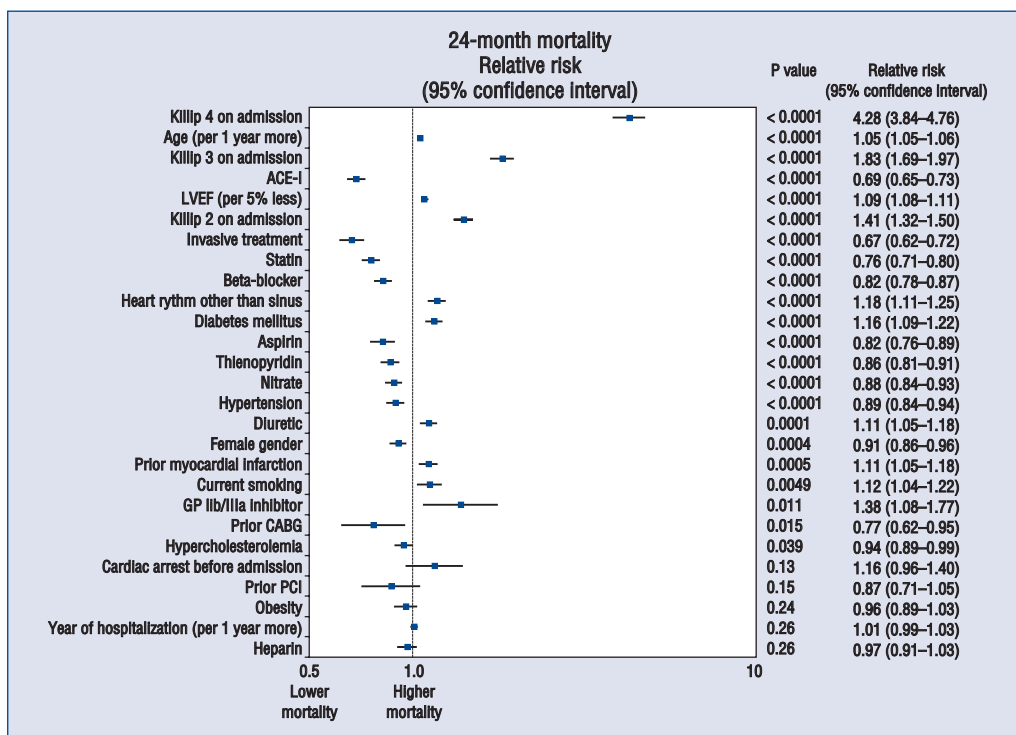


Figure 2. The multivariate analysis of the impact of selected parameters on 24-month mortality in elderly non-ST-segment elevation myocardial infarction patients; ACE-I — angiotensin converting enzyme inhibitors; CABG — coronary artery bypass grafting; GP — glycoprotein; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

Discussion

This study shows that implementing modern treatment methods, including invasive strategies and the pharmacotherapy recommended by treatment guidelines, improves the prognosis of NSTEMI patients ≥ 80 years of age. However, one side effect to this treatment approach is an increase in the incidence of major bleeding complications.

Over the years, an increased frequency of using both invasive treatments and the drugs recommended by treatment guidelines has been observed.

Despite numerous publications, which are summarized in the current treatment guidelines of the European Society of Cardiology [6, 7], our knowledge of the optimal treatment strategy in elderly NSTEMI patients is still insufficient [5], as elderly patients are rarely included in randomized cli-

Table 6. The temporal trends in the clinical characteristics, treatment methods and outcomes in elderly non-ST-segment elevation myocardial infarction patients from 2003–2009.

	2003/2004	2005	2006	2007	2008	2009	P for the trend
Age, years (median)	83	83	83	83	83	83	0.34
Female gender	59.9%	59.7%	61.5%	61.7%	59.6%	58.3%	0.25
Diabetes	28.3%	29.6%	28.9%	28.8%	33.0%	35.3%	< 0.0001
Prior MI	21.0%	27.4%	21.7%	22.9%	18.2%	21.1%	< 0.0001
Prior PCI	0.8%	0.9%	0.8%	1.8%	3.9%	5.8%	< 0.0001
Prior CABG	1.7%	2.6%	1.9%	1.6%	1.8%	2.3%	0.60
Killip 3 on admission	12.4%	13.2%	12.6%	11.3%	10.5%	8.0%	< 0.0001
Killip 4 on admission	6.5%	4.5%	4.2%	3.3%	3.5%	3.0%	< 0.0001
Cardiac arrest prior to admission	1.5%	1.8%	1.0%	1.1%	0.9%	1.4%	0.50
Aspirin	86.9%	91.4%	89.9%	90.3%	90.3%	90.6%	0.39
Thienopyridines	20.2%	28.3%	34.9%	54.5%	79.5%	90.7%	< 0.0001
Heparins	72.7%	78.3%	78.9%	77.6%	72.2%	64.4%	< 0.0001
GP IIb/IIIa inhibitors	1.4%	0.7%	0.5%	1.2%	1.5%	2.5%	< 0.0001
Beta-blockers	62.4%	71.2%	74.5%	75.5%	73.8%	75.1%	< 0.0001
Statins	58.5%	69.9%	72.5%	74.4%	76.0%	78.0%	< 0.0001
ACE inhibitors	71.3%	74.9%	74.8%	75.7%	74.0%	72.1%	0.29
Nitrates	70.5%	65.5%	59.8%	52.0%	45.5%	30.6%	< 0.0001
Diuretics	54.3%	54.5%	52.7%	52.0%	47.5%	43.3%	< 0.0001
Invasive treatment	9.8%	13.5%	14.9%	19.3%	33.2%	52.5%	< 0.0001
PCI	7.3%	8.7%	10.1%	13.0%	24.6%	37.3%	< 0.0001
CABG urgent or delayed	0.9%	3.0%	2.4%	3.3%	4.2%	5.6%	< 0.0001
Mean LVEF	44.8%	44.6%	45.3%	45.0%	45.9%	45.8%	0.033
Length of hospitalization, days (median)	10	9	8	8	7	6	< 0.0001
Stroke	1.2%	1.1%	0.7%	1.0%	0.8%	0.3%	0.0078
Major bleeding	1.6%	0.9%	0.9%	1.1%	2.8%	2.6%	< 0.0001
Myocardial reinfarction	5.4%	7.0%	5.6%	3.6%	2.3%	1.6%	< 0.0001
Death during hospitalization	15.1%	13.6%	11.9%	11.5%	11.4%	9.2%	< 0.0001
30-day mortality	20.9%	17.9%	16.5%	17.1%	16.5%	14.5%	0.0002
6-month mortality	30.9%	29.9%	28.9%	28.6%	27.4%	24.8%	< 0.0001
12-month mortality	37.7%	36.7%	35.5%	36.0%	34.5%	31.1%	< 0.0001
24-month mortality	47.5%	47.9%	45.2%	46.9%	43.3%	41.6%	< 0.0001

MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting; GP — glycoprotein; LVEF — left ventricular ejection fraction; ACE — angiotensin converting enzyme

nical trials. Furthermore, they are usually analyzed together with the unstable angina patients as non-ST-segment-elevation ACS (NSTEMI-ACS). The mean percentage of patients ≥ 75 years of age in the randomized NSTEMI-ACS trials from 1994–2000 was approximately 18% [14], whilst the percentage in clinical registries for that period was 38% [5]. The percentage of NSTEMI patients ≥ 75 years of age in the PL-ACS registry is 35%. Furthermore, the elderly patients included in randomized trials differ in clinical characteristics from those included in registries [15], as they are lower risk patients and consequently have lower 30-day mortalities than

registry patients [5]. This finding is consistent with our observations. Nevertheless, attention should be paid to analyzing the subgroups of elderly patients in those randomized trials where invasive NSTEMI-ACS treatment proved to be more beneficial than conservative treatment. In the TIMI IIIb (Thrombolysis In Myocardial Infarction) trial, the percentage of patients ≥ 75 years of age was only 3% [16]. An analysis of the subgroup of patients ≥ 65 years of age revealed that an early invasive strategy lowers the short-term RR of death or MI by 46%; the statistical significance of this difference remained for up to one year after the randomization [17]. The

FRISC-II (Fragmin during Instability in Coronary Artery Disease) trial was the first to demonstrate the supremacy of invasive strategies over conservative treatment in NSTEMI-ACS, though no patients ≥ 75 years of age were included in the trial [18]. It should be mentioned that the patients ≥ 65 years of age had a significantly higher absolute and relative reduction in 6-month mortality or MI risk compared to younger age groups, a result that persisted over a 2 years of follow-up [19]. Interestingly, the subgroup analysis of the TACTICS-TIMI 18 (Treat Angina With Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy — Thrombolysis in Myocardial Infarction) trial found that over 6 months of follow-up, the patients who benefited the most from an invasive strategy were those ≥ 75 years of age [20]. The absolute reduction in the 6-month mortality or MI risk in this age group was 10.8%, whilst the relative reduction compared to the conservative strategy was as high as 56%. Furthermore, advanced age was associated with greater benefit from invasive treatment. Also, the cost effectiveness of the invasive therapy increased with age. Nevertheless, a threefold higher incidence of major bleedings was observed in the oldest age group (≥ 75). It should be mentioned that no significant differences in mortality, reinfarction or rehospitalization due to unstable angina in the year following the NSTEMI-ACS were observed for the patients in latest ICTUS (Invasive versus Conservative Treatment in Unstable Coronary Syndromes) trial, including those aged ≥ 65 [21]. To sum up randomized trials, it seems that the subgroup analyses, despite their limitations, demonstrate the benefits of invasive treatment in elderly patients with NSTEMI-ACS, which is consistent with the results of our analysis.

Registry studies also show the superiority of invasive treatments over conservative treatment in elderly NSTEMI-ACS patients [22, 23]. In a 2002 Italian registry, the patients ≥ 75 years of age received treatment consistent with the guidelines less frequently; in the multifactorial analysis, conservative treatment significantly worsened the 30-days prognosis [22]. The analysis of the GRACE (The Global Registry of Acute Coronary Syndromes) registry clearly shows that the patients ≥ 80 years of age, who made up 16% of the population, received treatment consistent with the guidelines less frequently. This result applied to both invasive treatment and pharmacotherapy, which was used half as frequently in those ≥ 80 years of age than in younger age groups [23]. In the multifactorial analysis, invasive treatment significantly lowered the 6-month

mortality in patients ≥ 80 years of age (odds ratio 0.68, 95% CI 0.49–0.95), a finding which is similar to our analysis PL-ACS registry. However, the latest analysis of the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of ACC/AHA Guidelines) registry did not find decreased in-hospital mortality in invasively treated patients ≥ 75 years of age [24]. It is worth mentioning that Li et al. [25] have shown that invasive treatment for ACS significantly improves quality of life, with the greatest improvement in patients ≥ 80 years of age.

In our analysis, we observed an increasing trend in the frequency of using pharmacological and invasive treatment in elderly patients, which was reflected in improved in-hospital and 12-month prognoses. We know from the CRUSADE registry that the frequency of using drugs recommended by the treatment guidelines (mainly antiplatelet agents, anticoagulants and beta-blockers) and the frequency of invasive treatment is lower in older patients, especially in the elderly [26]. This finding was confirmed by an analysis of the GRACE registry in which the percentage of patients ≥ 85 years of age treated by invasive strategy was only 20%, as compared to over 50% in younger age groups [27]. A trend towards more aggressive treatment of older patients has been observed by Schiele et al. [28] using a French registry that compared the year 2000–2001 to the year 2005–2006. The increased frequency of using the recommended pharmacotherapy and invasive treatments decreased the 35-day mortality only in the STEMI patients; mortality remained stable in NSTEMI patients, and the incidence of major bleeding increased. However, the number of patients in the analysis was not large ($n = 868$), which undoubtedly affected the statistical power. An analysis of the trends in a 1996–2006 Canadian study of patients ≥ 80 years of age showed a significant increase in the frequency of using pharmacotherapy and invasive treatments recommended by the guidelines, which resulted in a reduction in the 12-month mortality [29].

Limitations of the study

There are several limitations of our analysis. The PL-ACS registry is a prospective observational study and not all hospitals treating ACS in Poland participated in data collection. Consequently, the reported significant trend in reduction of mortality in NSTEMI should be interpreted with caution. Additionally, the retrospective nature of our analysis is a potential weakness. Even after data

adjustment, the results could be biased by potentially important parameters that are not available in the registry thus, despite using the propensity score method and the multivariable analysis, the conclusions require confirmation by a randomized trial. Finally, as it is a single-country study, it may be not applicable to populations of the other countries.

Conclusions

Elderly patients with NSTEMI benefit significantly from invasive strategies and modern pharmacotherapy recommended by treatment guidelines. Nevertheless, this approach is associated with an increased incidence of major bleeding. The lack of randomized clinical trials that include a representative group of elderly patients is evident. Hence, the conclusions of this analysis should be confirmed by an appropriately designed randomized trial.

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References

1. Cardiovascular Diseases in Europe. Euro Heart Survey 2006. Edited by Wilma Scholte et al. <http://www.escardio.org/guidelines-surveys/ehs/Documents/EHS-CVD-report-2006.pdf>.
2. Główny Urząd Statystyczny. <http://demografia.stat.gov.pl/Baza-Demografia/Tables.aspx>.
3. Główny Urząd Statystyczny. http://www.stat.gov.pl/cps/rde/xbcr/gus/PUBL_L_progniza_ludnosci_P1_2008-2035.pdf.
4. Gąsior M, Zembala M, Poloński L. Chorzy starsi z ostrym zespołem wieńcowym: Narastający problem w praktyce klinicznej. *Kardiologia Polska*, 2006; 64: 1154–1157.
5. Alexander KP, Newby LK, Cannon CP et al. American Heart Association Council on Clinical Cardiology; Society of Geriatric Cardiology. Acute coronary care in the elderly, part I: Non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology; in collaboration with the Society of Geriatric Cardiology. *Circulation*, 2007; 115: 2549–2569.
6. Bassand JP, Hamm CW, Ardissino D et al. for the Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. *Eur Heart J*, 2007; 28: 1598–1660.
7. Wijns W, Kolh P, Danchin N et al. for The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Guidelines on myocardial revascularization. *Eur Heart J*, 2010; 31: 2501–2555.
8. Ciszewski A, Karcz M, Kepka C et al. Primary angioplasty in patients > or = 75 years old with ST-elevation myocardial infarction: One-year follow-up results. *Kardiologia Polska*, 2008; 66: 828–833.
9. Polewczyk A, Janion M, Gąsior M, Gierlotka M, Poloński L. Benefits from revascularisation therapy in the elderly with acute myocardial infarction. Comparative analysis of patients hospitalised in 1992–1996 and in 2005–2006. *Kardiologia Polska*, 2010; 68: 873–881.
10. Poloński L, Gąsior M, Gierlotka M et al. A comparison of ST elevation versus non-ST elevation myocardial infarction outcomes in a large registry database: Are non-ST myocardial infarctions associated with worse long-term prognoses? *Int J Cardiol*, 2011; 152: 70–77.
11. Kashima K, Ikeda D, Tanaka H et al. Mid-term mortality of very elderly patients with acute myocardial infarction with or without coronary intervention. *J Cardiol*, 2010; 55: 397–403.
12. Poloński L, Gąsior M, Gierlotka M et al. Polish Registry of Acute Coronary Syndromes (PL-ACS). Characteristics treatments and outcomes of patients with acute coronary syndromes in Poland. *Kardiologia Polska*, 2007; 65: 861–872.

13. Flynn MR, Barrett C, Cosio FG et al. The Cardiology Audit and Registration Data Standards (CARDS), European data standards for clinical cardiology practice. *Eur Heart J*, 2005; 26: 308–313.
14. Topol EJ, Califf RM, Van de Werf F et al. Perspectives on large-scale cardiovascular clinical trials for the new millennium: The Virtual Coordinating Center for Global Collaborative Cardiovascular Research (VIGOUR) Group. *Circulation*, 1997; 95: 1072–1082.
15. Kandzari DE, Roe MT, Chen AY et al. Influence of clinical trial enrollment on the quality of care and outcomes for patients with non-ST-segment elevation acute coronary syndromes. *Am Heart J*, 2005; 149: 474–481.
16. The TIMI IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: Results from the TIMI IIIB Trial. *Circulation*, 1994; 89: 1545–1556.
17. Anderson HV, Cannon CP, Stone PH et al. One-year results of the Thrombolysis In Myocardial Infarction (TIMI) IIIB clinical trial: a randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q-wave myocardial infarction. *J Am Coll Cardiol*, 1995; 26: 1643–1650.
18. FRagmin and Fast Revascularization during InStability in Coronary artery disease (FRISC II) Investigators. Long-term low-molecular-mass heparin in unstable coronary artery disease: FRISC II prospective randomised multicentre study. *Lancet*, 1999; 354: 701–707.
19. Lagerqvist B, Husted S, Kontny F et al. for the Fast Revascularization during In Stability in Coronary artery disease-II Investigators. A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease: Two-year follow-up of the FRISC-II invasive study. *J Am Coll Cardiol*, 2002; 40: 1902–1914.
20. Bach RG, Cannon CP, Weintraub WS et al. The effect of routine, early invasive management on outcome for elderly patients with non-ST-segment elevation acute coronary syndromes. *Ann Intern Med*, 2004; 141: 186–195.
21. de Winter RJ, Windhausen F, Cornel JH et al. for the Invasive versus Conservative Treatment in Unstable Coronary Syndromes (ICTUS) Investigators. Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med*, 2005; 353: 1095–1104.
22. De Servi S, Cavallini C, Dellavalle A et al.; for the ROSAI-2 Investigators. Non-ST-elevation acute coronary syndrome in the elderly: Treatment strategies and 30-day outcome. *Am Heart J*, 2004; 147: 830–836.
23. Devlin G, Gore JM, Elliott J et al. for the GRACE Investigators. Management and 6-month outcomes in elderly and very elderly patients with high-risk non-ST-elevation acute coronary syndromes: The Global Registry of Acute Coronary Events. *Eur Heart J*, 2008; 29: 1275–1282.
24. Bhatt DL, Roe MT, Peterson ED, et al. for the CRUSADE Investigators. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes: Results from the CRUSADE Quality Improvement Initiative. *JAMA*, 2004; 292: 2096–2104.
25. Li R, Yan BP, Dong M et al. Quality of life after percutaneous coronary intervention in the elderly with acute coronary syndrome. *Int J Cardiol*, 2010; 155: 90–96.
26. Alexander KP, Roe MT, Chen AY et al. for the CRUSADE Investigators. Evolution in cardiovascular care for elderly patients with non-ST-segment elevation acute coronary syndromes: Results from the CRUSADE National Quality Improvement Initiative. *J Am Coll Cardiol*, 2005; 46: 1479–1487.
27. Avezum A, Makdisse M, Spencer F et al. for the GRACE Investigators. Impact of age on management and outcome of acute coronary syndrome: Observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*, 2005; 149: 67–73.
28. Schiele F, Meneveau N, Seronde MF et al. Changes in management of elderly patients with myocardial infarction. *Eur Heart J*, 2009; 30: 987–994.
29. Pagé M, Doucet M, Eisenberg MJ, Behlouli H, Pilote L. Temporal trends in revascularization and outcomes after acute myocardial infarction among the very elderly. *CMAJ*, 2010; 182: 1415–1420.