Gender-related disparities in the treatment and outcomes in patients with non-ST-segment elevation myocardial infarction: results from the Polish Registry of Acute Coronary Syndromes (PL-ACS) in the years 2012–2014

Łukasz Piątek1,2, Krzysztof Wilczek2, Jacek Kurzawski2, Marek Gierlotka4, Mariusz Gąsior4, Lech Poloński3, Marcin Sadowski1,5

Abstract

Introduction: Gender-related differences in the treatment of patients with non-ST elevation myocardial infarction (NSTEMI) have been reported in many previous studies despite the fact that an equal approach is recommended in all current guidelines. The aim of the study was to investigate whether gender-related discrepancies in the management of NSTEMI patients have changed.

Material and methods: Between 2012 and 2014 a total of 66,667 patients (38.3% of whom were women) with the final diagnosis of NSTEMI were included into the retrospective analysis of the Polish Registry of Acute Coronary Syndromes (PL-ACS). Differences in clinical profile, treatment, and outcomes were analysed.

Results: Women were older than men and more often had comorbidities. They were less likely to undergo coronary angiography (88.4% vs. 92.1%, \( p < 0.05 \)) as well as percutaneous coronary intervention (59.6% vs. 71.9%, \( p < 0.05 \)). In the general population women had also significantly worse in-hospital prognosis as well as in 12-month follow-up. After the age adjustment the outcomes in women were at least as good as in men. In multivariate analysis females had the same risk as men in-hospital RR = 1.02 (95% CI: 0.97–1.08, \( p = 0.45 \)) and lower in 12-month observation RR = 0.94 (95% CI: 0.92–0.97, \( p < 0.0001 \)).

Conclusions: In comparison with previous reports on NSTEMI patients, gender-related disparities in the treatment and outcomes were radically reduced. Unadjusted mortality rates were still higher in women as a consequence of their older age. After the age adjustment, mortality ratios were similar in both genders. The long-term prognosis seems to be even better in women.

Key words: women, elderly, mortality, NSTEMI, invasive treatment.
Introduction

In many previous studies on non-ST-segment elevation myocardial infarction (NSTEMI) patients, gender-related differences in the management and outcomes have been reported. Despite the fact that the guidelines recommend the same therapy for both men and women, significant disparities between genders are still observed in many countries. The differences are particularly notable in acute coronary syndromes without ST-segment elevation due to a variable clinical manifestation as well as different comorbidities. Older patients and women are often excluded from the clinical trials, and thus the results of prior reports were sometimes contradictory. The final impact of sex category on prognosis remains unclear. We sought to investigate whether the gender-related differences in the management and prognosis in NSTEMI patients still persist.

Material and methods

We conducted a retrospective cohort study analysis of the Polish Registry of Acute Coronary Syndromes (PL-ACS). The basic principles of our registry have been published elsewhere [1, 2]. Briefly, a total of 463 hospitals providing care for patients with myocardial infarction contributed to the registry. This analysis covers three years, from 2012 to 2014. Data on 66,667 patients were collected in that period. Contribution to the study was voluntary; nevertheless, it comprises more than a half of all NSTEMI cases in Poland in that time. The inclusion criterion was a diagnosis of NSTEMI as a basic clinical condition according to the guidelines of European Society of Cardiology released in 2011. Cases with myocardial ischaemia secondary to other critical conditions were excluded. The study complies with the Declaration of Helsinki and was approved by the PL-ACS Registry committee.

Data were collected from the PL-ACS Registry questionnaires that include variables on demographic factors (gender, age), risk factors (smoking, hypertension, hypercholesterolaemia, diabetes, and obesity), previous cardiovascular history and procedures (myocardial infarction – MI, percutaneous coronary intervention – PCI, coronary artery by-pass grafting – CABG), clinical presentation on admission (Killip class, heart rate, systolic blood pressure, electrocardiographic abnormalities, left ventricular ejection fraction in echocardiography ejection fraction [EF]), in-hospital management (coronary angiography, percutaneous coronary intervention, medical treatment), and medication on discharge. In-hospital, 30-day, six-month, and 12-month follow-up mortality rates were estimated. Kaplan-Meier survival curves and the log-rank test were used to compare the survival between groups.

Statistical analysis

The gender groups were analysed separately and afterward compared to each other. To investigate the age impact on outcomes additional analyses were conducted in age groups (below 55, between 55 and 64, between 65 and 74, and over 75 years) as well as in consecutive decades of life.

Categorical data are summarised as frequency and percentage while continuous data as median or arithmetic mean ± standard deviation (SD). Differences in categorical variables were tested by \( \chi^2 \) test with Pearson modification whereas in continuous variables with Student’s \( t \)-test. A two-sided \( p \) value ≤ 0.05 was considered significant. A logistic regression was used to identify variables that independently contributed to mortality. The relative risk (RR) and 95% confidence intervals (CI) were calculated.

Results

Women constituted 25,542 (38.3%) of the study population. They were older than men, and they predominated in the over 70 age group (Figures 1 and 2). They more often had a history of arterial hypertension, diabetes, and obesity. On the contrary, they less often were smokers and had histo-

![Figure 1](image1.png)  
**Figure 1.** Age histogram of patients with non-ST elevation myocardial infarction in 2012–2014

![Figure 2](image2.png)  
**Figure 2.** The elderly contribution in patients with non-ST elevation myocardial infarction in 2012–2014
Gender-related disparities in the treatment and outcomes in patients with non-ST-segment elevation myocardial infarction: results from the Polish Registry of Acute Coronary Syndromes (PL-ACS) in the years 2012–2014

Mild gender disparities in medical therapy were observed. Men more often were administered aspirin, clopidogrel, and statin while women received more calcium channel blockers (CCB). There were no differences in administration of β-blockers, angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), and nitrates (Table II).

Women less frequently underwent coronary angiography (88.4% vs. 92.1% in men; \(p < 0.0001\)) and PCI (59.6% vs. 66.1% in men; \(p < 0.0001\)). The ratio of patients managed invasively to those treated medically was age-dependent and was the lowest in patients over 75 years old. Interestingly, the differences in PCI utilisation were especially noticeable among patients under 55 years old (59.6% vs. 71.9% in men; \(p < 0.0001\)) (Table III).

In women the risk of stroke (0.3% vs. 0.2% in men; \(p < 0.05\)), bleeding complications (1.5% vs. 1.0% in men; \(p < 0.05\)), as well as cardiovascular death (3.1% vs. 2.3% in men; \(p < 0.05\)) was higher than in men.

The unadjusted in-hospital and 12-month mortality rates remained far higher in women – in

| Table I. Clinical characteristics of patients with non-ST elevation myocardial infarction in 2012–2014 |
|------------------|------------------|------------------|------------------|
| Factor          | Women n (%)      | Men n (%)        | \(P\)-value      |
| Hypertension    | 20,568 (80.5)    | 31,219 (75.9)    | < 0.05           |
| Diabetes        | 9623 (37.3)      | 11,999 (29.2)    | < 0.05           |
| Hypercholesterolaemia | 11,262 (44.1)  | 18,067 (43.9)    | 0.67             |
| Smoking         | 3340 (13.1)      | 10,989 (26.7)    | < 0.05           |
| Obesity         | 6391 (25.0)      | 7807 (19.0)      | < 0.05           |
| Previous MI     | 5681 (22.2)      | 10,728 (26.1)    | < 0.05           |
| Previous PCI    | 4301 (16.8)      | 8534 (20.8)      | < 0.05           |
| Previous CABG   | 1092 (4.3)       | 2755 (6.7)       | < 0.05           |

MI – myocardial infarction, PCI – percutaneous coronary intervention, CABG – coronary artery by-pass grafting.

| Table II. Medication on discharge |
|------------------|------------------|------------------|------------------|
| Factor           | Women n (%)      | Men n (%)        | \(P\)-value      |
| Aspirin          | 21,898 (88.7)    | 35,904 (89.5)    | < 0.05           |
| Clopidogrel      | 18,893 (76.5)    | 31,072 (77.5)    | < 0.05           |
| β-blocker        | 16,593 (76.6)    | 24,079 (76.4)    | 0.42             |
| ACEI/ARB         | 18,779 (76.1)    | 30,767 (76.7)    | 0.05             |
| Statin           | 17,340 (85.0)    | 25,702 (85.6)    | < 0.05           |
| Nitrate          | 2577 (10.4)      | 4151 (10.4)      | 0.73             |
| CCB              | 3675 (14.9)      | 5112 (12.7)      | < 0.05           |

ACEI – angiotensin-converting enzyme inhibitors, ARB – angiotensin receptor blockers, CCB – calcium channel blockers.

| Table III. Invasive treatment |
|------------------|------------------|------------------|------------------|
| Age groups       | Coronary angiography | Percutaneous coronary intervention |
|                  | Women n (%)      | Men n (%)        | \(P\)-value      | Women n (%)      | Men n (%)        | \(P\)-value      |
| < 55 years       | 1542 (93.6)      | 5195 (95.0)      | < 0.05           | 980 (59.5)       | 3929 (71.9)      | < 0.05           |
| 55–64 years      | 4717 (94.0)      | 12189 (94.4)     | 0.38             | 3270 (65.2)      | 8958 (69.3)      | < 0.05           |
| 65–74 years      | 6233 (91.9)      | 10366 (92.8)     | < 0.05           | 4170 (61.5)      | 7305 (65.4)      | < 0.05           |
| ≥ 75 years       | 10097 (83.5)     | 10124 (87.5)     | < 0.05           | 6808 (56.3)      | 7006 (60.5)      | < 0.05           |
the years 2012–2014 the in-hospital mortality rate was 3.3% in women vs. 2.5% in men; \( p < 0.0001 \), while the 12-month mortality rate was 15.1% in women vs. 12.8% in men; \( p < 0.0001 \), respectively.

When analysing the mortality according to age there were no differences in the in-hospital mortality between genders (Figure 3). Women had even better long-term prognosis. In the seventh, eighth, and ninth decades of life their 12-month mortality rates were lower than in men (Figure 4).

Mortality analysis adjusted to age groups is presented in Figure 5. When analysing only patients who underwent PCI there were no differences between genders in the short-term prognosis whereas women had lower mortality rates in the age group of 65 to 74 years. Mortality analysis adjusted to strategy of treatment is presented in Figure 6. Multivariable analysis was performed, and there were no differences between gender in in-hospital observation (RR = 1.02, 95% CI: 0.97–1.08,
Gender-related disparities in the treatment and outcomes in patients with non-ST-segment elevation myocardial infarction: results from the Polish Registry of Acute Coronary Syndromes (PL-ACS) in the years 2012–2014

On the other hand, female sex was one of the independent factors that improved 12-month prognosis (RR = 0.94, 95% CI: 0.92–0.97, p < 0.0001) (Table V). These results were in accordance with our previous observation in the age groups. One of the most important variables that has a substantial impact on mortality rates is the age of the patients. With each decade of life the relative risk of death increases rapidly; in short-term prognosis RR = 1.63 (95% CI: 1.59–1.68, p < 0.0001).

### Table IV. Multivariate analysis of factors influencing in-hospital mortality

| Factor                                           | RR (95% CI)       | P-value |
|--------------------------------------------------|-------------------|---------|
| Invasive treatment                               | 0.31 (0.29–0.33)  | < 0.0001|
| Hypercholesterolaemia                            | 0.73 (0.69–0.77)  | < 0.0001|
| Hypertension                                     | 0.73 (0.69–0.78)  | < 0.0001|
| Previous PCI                                     | 0.80 (0.73–0.88)  | < 0.0001|
| Previous CABG                                    | 0.80 (0.71–0.91)  | 0.0006  |
| Current smokers                                  | 1.02 (0.94–1.10)  | 0.6776  |
| Female (vs. male)                                | 1.02 (0.97–1.08)  | 0.4485  |
| Previous MI                                      | 1.07 (1.01–1.14)  | 0.0255  |
| Diabetes                                         | 1.09 (1.03–1.15)  | 0.0021  |
| Time to admission > 12 hours                     | 1.09 (1.03–1.16)  | 0.0030  |
| EF = 35–50%                                      | 1.10 (1.01–1.20)  | 0.0240  |
| ST-T abnormalities on ECG                       | 1.16 (1.07–1.27)  | 0.0007  |
| Obesity                                          | 1.18 (1.10–1.26)  | < 0.0001|
| Other than sinus rhythm on ECG                   | 1.19 (1.12–1.27)  | < 0.0001|
| Age (on each decade)                             | 1.63 (1.59–1.68)  | < 0.0001|
| EF < 35%                                         | 2.31 (2.11–2.53)  | < 0.0001|
| Prehospital cardiac arrest                       | 2.37 (2.09–2.69)  | < 0.0001|
| Killip 3 class                                   | 3.67 (3.41–3.94)  | < 0.0001|
| IABP                                             | 3.89 (3.23–4.69)  | < 0.0001|
| Killip 4 class                                   | 13.2 (12.0–14.4)  | < 0.0001|

*EF – ejection fraction, ECG – electrocardiogram, IABP – intra aortic balloon pomp. Other abbreviations as in Table I.*
1.59–1.68, p < 0.0001), whereas in long-term prognosis RR = 1.57 (95% CI: 1.55–1.59, p < 0.0001).

**Discussion**

In many previous studies gender-related disparities in the treatment and outcomes of acute coronary syndromes have been reported. There are concerns that women less frequently receive optimal therapy according to the contemporary guidelines [3]. In particular, invasive procedures have been underutilised in the past [4–9]. In the French Registry FAST-MI 2005 the likelihood of having an invasive strategy was 34% lower in women compared to men. Five years later, in FAST 2010, the disproportion between genders was less indicated but still observed (OR = 0.84). Additionally, in many studies an adverse prognosis in women was pronounced [8, 10, 11].

A significant body of evidence indicates that several differences in the demographic and clinical profile among men and women with NSTEMI exist. Women are older and predominate in older groups. Almost half of them are over 75 years old while a quarter are over 80 years old. They more frequently have a history of hypertension, diabetes and renal failure. Moreover, atypical symptoms that delay the diagnosis are more often encountered in women. This implies analyses adjusted for age [12, 13].

The majority of former studies have revealed significant inequalities in the application of recommended medical and invasive therapies. In the report by Blomkalns et al. the likelihood of coronary angiography and subsequent invasive treatment in women was up to 30% lower than in men [7]. In our study the differences were diminished substantially, and in the medical treatment they are just minimal.

A similar trend in the application of invasive procedures has been observed. That means that previously reported gender discrimination in that matter is no longer apparent [14–16]. Similarly, the percutaneous coronary intervention (PCI) rate in women was far greater than was reported in previous studies. However, women still tend to have less PCI that their male counterparts. We speculate that non-obstructive coronary artery

---

| Parameter                        | OR (95% CI)    | P-value |
|----------------------------------|----------------|---------|
| Invasive treatment               | 0.51 (0.49–0.52) | < 0.0001 |
| Hypercholesterolaemia            | 0.81 (0.79–0.83) | < 0.0001 |
| Previous CABG                    | 0.84 (0.80–0.88) | < 0.0001 |
| Hypertension                     | 0.85 (0.83–0.88) | < 0.0001 |
| Previous PCI                     | 0.90 (0.87–0.94) | < 0.0001 |
| Female (vs. male)                | 0.94 (0.92–0.97) | < 0.0001 |
| Obesity                          | 0.99 (0.96–1.02) | 0.37     |
| Time to admission > 12 hours     | 1.03 (1.00–1.06) | 0.022    |
| Current smokers                  | 1.06 (1.03–1.10) | 0.0005   |
| Previous MI                      | 1.12 (1.09–1.15) | < 0.0001 |
| ST-T abnormalities on ECG        | 1.15 (1.11–1.19) | < 0.0001 |
| Other than sinus rhythm on ECG   | 1.14 (1.11–1.18) | < 0.0001 |
| Diabetes                         | 1.29 (1.26–1.32) | < 0.0001 |
| EF = 35–50%                      | 1.52 (1.47–1.57) | < 0.0001 |
| Age (each decade)                | 1.57 (1.55–1.59) | < 0.0001 |
| Prehospital cardiac arrest       | 1.74 (1.63–1.85) | < 0.0001 |
| Killip 3 class                   | 1.98 (1.91–2.06) | < 0.0001 |
| IABP                             | 2.17 (1.99–2.38) | < 0.0001 |
| EF < 35%                         | 2.67 (2.57–2.78) | < 0.0001 |
| Killip 4 class                   | 4.48 (4.26–4.71) | < 0.0001 |

Abbreviations as in Table I and IV.
Gender-related disparities in the treatment and outcomes in patients with non-ST-segment elevation myocardial infarction: results from the Polish Registry of Acute Coronary Syndromes (PL-ACS) in the years 2012–2014

In conclusion, our study provides additional data contributing to the ongoing debate on gender-related differences in the management and prognosis in NSTEMI patients. We clearly demonstrated that women, when treated with appropriate access to interventional treatment and modern pharmacotherapy, still have worse short- and long-term prognosis, but this is ascribed mostly to their advanced age. After adjustment for age, those discrepancies no longer exist. Moreover, in some age groups the interventional treatment may be more beneficial in women.

Conflict of interest

The authors declare no conflict of interest.

References

1. Poloński L, Gasior 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. Kardiol Pol 2007; 65: 861-72.
2. Gierlotka M, Gasior M, Wilczek K, et al. Temporal trends in the treatment and outcomes of patients With non-ST-segment elevation myocardial infarction in Poland from 2004-2010 (from the Polish Registry of Acute Coronary Syndromes). Am J Cardiol 2012; 109: 779-86.
3. Hamm CW, Bassand JP, Agewall S, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2011; (32): 2999-3054.
4. Donatello MP, Puymirat E, Parapid B, et al. In-hospital outcomes and long-term mortality according to sex and management strategy in acute myocardial infarction. Insights from the French ST-elevation and non-ST-elevation Myocardial Infarction (FAST-MI) 2005 Registry. Int J Cardiol 2015; 201: 265-70.
5. Simon T, Puymirat E, Lucci V, et al. Acute myocardial infarction in women. Initial characteristics, management and early outcome. The FAST-MI registry. Ann Cardiol Angeiol (Paris) 2013; 62: 221-6.
6. Isorni MA, Blanchard D, Teixeira N, et al. Impact of gender on use of revascularization in acute coronary syndromes: the national observational study of diagnostic and interventional cardiac catheterization (ONACI). Catheter Cardiovasc Interv 2015; 86: 58-65.
7. Blomkalns AL, Chen AV, Hochman JS, et al. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE. J Am Coll Cardiol 2005; 45: 832-7.
8. Bugiardini R, Yan AF, Yan RT, et al. Factors influencing underutilization of evidence-based therapies in women. Eur Heart J 2011; 32: 1337-44.
9. Radovanovic D, Erne P, Urban P, et al. Gender differences in management and outcomes in patients with acute coronary syndromes: results on 20,290 patients from the AMIS Plus Registry. Heart 2007; 93: 1369-75.
10. Kołodziej M, Kurzawski J, Janion-Sadowska A, et al. Mortality of women with ST-segment elevation myocardial infarction and cardiogenic shock – results from the...
PL-ACS registry. Medical Studies/Studia Medyczne 2016; 32: 157-63.

11. Poon S, Goodman SG, Yan RT, et al. Bridging the gender gap: Insights from a contemporary analysis of sex-related differences in the treatment and outcomes of patients with acute coronary syndromes. Am Heart J 2012; 163: 66-73.

12. Schmidt M, Jacobsen JB, Lash TL, Bøtker HE, Sørensen HT. 25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. BMJ 2012; 344.

13. Malkin CJ, Prakash R, Chew DP. The impact of increased age on outcome from a strategy of early invasive management and revascularisation in patients with acute coronary syndromes: retrospective analysis study from the ACACIA registry. BMJ Open 2012; 2.

14. Jortveit J, Govatsmark RE, Langørgen J, et al. Gender differences in the assessment and treatment of myocardial infarction. Tidsskr Nor Laegeforen 2016; 136: 1215-22.

15. Sielski J, Janion-Sadowska A, Sadowski M, et al. Differences in presentation, treatment, and prognosis in elderly patients with non-ST-segment elevation myocardial infarction. Pol Arch Med Wewn 2012; 122: 253-61.

16. Redfors B, Angerås O, Råmunddal T, et al. Trends in gender differences in cardiac care and outcome after acute myocardial infarction in western Sweden: a report from the Swedish Web System for Enhancement of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). J Am Heart Assoc 2015; 4.

17. Alfredsson J, Lindbäck J, Wallentin L, Swahn E. Similar outcome with an invasive strategy in men and women with non-ST-elevation acute coronary syndromes: from the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). Eur Heart J 2011; 32: 3128-36.

18. Darling CE, Fisher KA, McManus DD, et al. Survival after hospital discharge for ST-segment elevation and non-ST-segment elevation acute myocardial infarction: a population-based study. Clin Epidemiol 2013; 5: 229-36.

19. Bucholz EM, Butala NM, Rathore SS, Dreyer RP Lanský AL, Krumholz HM. Sex differences in long-term mortality after myocardial infarction: a systematic review. Circulation 2014; 130: 757-67.

20. Heer T, Gitt AK, Juenger C, et al. Gender differences in acute non-ST-segment elevation myocardial infarction. Heart 2007; 93: 1327-8.

21. Bradshaw PJ, Thompson PL. Sex in the CCU: women with non-ST-segment elevation acute coronary syndrome may do no worse despite less intervention. Am J Cardiol 2006; 98: 160-6.

22. Alfredsson J, Stenestrand U, Wallentin L, Swahn E. Gender differences in management and outcome in non-ST-elevation acute coronary syndrome. Heart 2007; 93: 1357-62.