Associations of changes in patient characteristics and management with decrease in mortality rates of men and women with ST-elevation myocardial infarction – a propensity score-matched analysis

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Abstract

Introduction: The aim of this study is to estimate how much of the recent decrease in mortality among patients with myocardial infarction with ST-segment elevation (STEMI) can be attributed to improved treatment strategies, and how much it is related to changes in baseline clinical characteristics, and to compare these findings for men and women.

Material and methods: This was a retrospective analysis of 32,790 patients with STEMI from the Polish Registry of Acute Coronary Syndromes PL-ACS hospitalised in 2005 and 2011. Changes in treatment strategies including pharmacotherapy were analysed. Observed in-hospital and 12-month mortality rates were compared with the outcomes in the groups matched on the propensity scores.

Results: There was a substantial improvement in STEMI patient management between 2005 and 2011 in Poland. It included greater use of percutaneous coronary interventions and other guideline-based adjunctive therapies, and it was associated with a significant decline in in-hospital mortality. Relative 12-month mortality reduction rates were less pronounced and more related to changes in patients’ clinical characteristics. Higher mortality risk reductions were observed in women and were driven by relatively more positive changes in their baseline risk profiles when compared to men.

Conclusions: The progress in the treatment strategies has helped to achieve better survival rates in STEMI patients. However, the ongoing changes in clinical characteristics of patients also played an important role, especially in women. Clinicians should focus on modifiable risk factors and post-discharge management to possibly prolong the positive aspects of in-hospital efforts.

Key words: women, registry, all-cause mortality, in-hospital mortality, ST-elevation myocardial infarction, propensity score, clinical characteristics, gender-related matters, management and treatment.
Introduction

The management of myocardial infarction with ST-segment elevation (STEMI) has undergone major changes in recent decades. Although many recent studies have confirmed a reduction of crude mortality rates in STEMI patients [1–5], there is some uncertainty about the determinants of this decline. In fact, studies investigating reasons for the mortality decline in STEMI are limited [4, 6, 7]. Early reperfusion is the most important predictor of favourable outcome in STEMI patients, with primary percutaneous coronary intervention (PCI) being the preferred strategy [8]. The widespread use of PCI, the implementation of recent advances in angioplasty devices, and pharmacologic therapy have unquestionably contributed to better acute survival rates as well as long-term prognosis in STEMI patients [9]. In view of the results of randomised, controlled trials in STEMI, it is often presumed that new treatments should be the main reason for mortality reduction. Although there is no doubt that changes in patient management are among the most important aspects related to decreased mortality in STEMI, the outcomes are also influenced by patients’ risk profiles at presentation. It is known that STEMI patients’ clinical characteristics at admission have markedly changed over the last decades and should be considered as an important prognostic factor to control for when analysing reasons for survival improvement [5].

In Poland, between 2005 and 2011 we witnessed significant progress in the interventional approach to STEMI treatment, which made Poland a model example of rapid progress in STEMI management, achieving one of the highest levels of utilisation of primary PCI in Europe [10]. In 2005 in Poland around half of all STEMI patients were treated with PCI. Due to the rapidly increasing number of catheterisation labs this number rose to over 90% in 2011 [5, 11]. Concurrently, a significant decline in crude mortality rates among STEMI patients in Poland has also been observed [5, 12]. It is possible that other European countries could experience similar progress because large variations in reperfusion treatment are still present across Europe [10]. This is why we believe it is important to analyse and present details and outcomes of this evolution [13].

In this population-based study we aim to estimate how much of the observed decrease in in-hospital and 12-month mortality in STEMI patients could be attributed to improved treatment strategies, and how much it was related to changes in baseline clinical characteristics, and compare these findings for men and women.

Material and methods

We analysed data on 32,790 patients with STEMI from the Polish Registry of Acute Coronary Syndromes PL-ACS. The patients were admitted to hospitals in Poland in 2005 (12,180 men and 6422 women) and in 2011 (9141 men, 5047 women). All patients registered in the PL-ACS registry in 2005 or 2011 with a confirmed diagnosis of STEMI were included in the current study. For the patients who presented more than once during the study period, only the first hospitalisation was analysed. The methodology of the PL-ACS Registry was described previously [14]. In brief, the PL-ACS Registry is an ongoing, nationwide, multicentre, prospective, observational study of consecutively hospitalised patients, representing 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. All admitted patients with suspected ACS were screened for their eligibility to enter the registry, but they were not enrolled until ACS was confirmed. STEMI was defined as the presence of ST-segment elevation of ≥ 2 mm in the contiguous chest leads and/or ST-segment elevation of ≥ 1 mm in two or more standard leads or new left bundle branch block, together with positive cardiac necrosis markers. All-cause mortality data were obtained from the official mortality records of the National Health Fund. Study endpoints were in-hospital, and 12-month all-cause death. The vital statuses at discharge and after 12 months were available for all of the included patients.

In order to reduce the bias of confounding when using observational data to estimate effects of changes in treatment on STEMI patients’ outcomes, a propensity score (PS) matching technique was applied. Methods based on PS were proposed in the early 1980s by Rosenbaum and Rubin [15] and were dedicated to estimate causal relationships based on large non-randomised datasets. Recently, there has been increasing interest in these methods, and they have been developed and widely used also in medical and cardiological research [16].

All available baseline characteristics were incorporated into a regression model to estimate a PS for each individual. The overlap and the region of common support between the groups were checked by a visual inspection of the density distribution of the propensity scores in the 2005 and 2011 groups. Patients from 2005 and 2011 were matched one-to-one on their PS to same-sex individuals within a pre-defined PS limit of 60% of standard error. Greedy nearest neighbour matching algorithm without replacement was used. Out of a total of 32,790 patients 14,160 men (7080 from 2005 and 7080 from 2011) and...
Table I. Balance of initial clinical characteristics covariates after propensity score matching

| Factor                              | Women    | Men       | S. diff. | Women    | Men       | S. diff. |
|-------------------------------------|----------|-----------|----------|----------|-----------|----------|
|                                     | 2005 n = 3950 | 2011 n = 3950 | S. diff. | 2005 n = 7080 | 2011 n = 7080 | S. diff. |
| Age [years]                         | 69.2 ±11.9 | 69.7 ±12.5 | 0.06     | 61.6 ±11.7 | 61.6 ±11.6 | 0.00     |
| Hypertension                        | 69.9%     | 68.5%     | −0.03    | 58.2%     | 59.5%     | 0.03     |
| Diabetes                            | 30.6%     | 29.1%     | −0.03    | 17.3%     | 18.2%     | 0.02     |
| Hypercholesterolaemia               | 37.1%     | 38.3%     | 0.03     | 37%       | 37.4%     | 0.01     |
| Current smoking                     | 30%       | 29.7%     | −0.01    | 64.8%     | 64.9%     | 0.00     |
| Obesity                             | 24.9%     | 23.7%     | −0.03    | 14.2%     | 15.1%     | 0.03     |
| Prior MI                            | 7.7%      | 7.9%      | 0.01     | 9.8%      | 9.4%      | −0.01    |
| Prior PCI                           | 1.3%      | 2.6%      | 0.03     | 1.6%      | 1.6%      | 0.00     |
| Prior CABG                          | 1.2%      | 1%        | −0.02    | 1.6%      | 1.6%      | 0.00     |
| Systolic BP on admission:           |          |           |          |          |           |          |
| < 100 mm Hg                         | 9.5%      | 10.3%     | 0.03     | 7.8%      | 8%        | 0.01     |
| 100–160 mm Hg                       | 68.1%     | 68.6%     | 0.01     | 73.5%     | 71.9%     | −0.04    |
| > 160 mm Hg                         | 22.4%     | 21.1%     | −0.03    | 18.7%     | 20.1%     | 0.04     |
| ECG on admission (rhythm):          |          |           |          |          |           |          |
| Sinus rhythm                        | 91.3%     | 89.9%     | −0.05    | 93.4%     | 92.9%     | −0.02    |
| Atrial fibrillation                 | 6.8%      | 7.1%      | 0.01     | 4.1%      | 4.6%      | 0.03     |
| Pacing                              | 0.1%      | 0.3%      | 0.05     | 0.2%      | 0.2%      | 0.00     |
| Other                               | 1.8%      | 2.2%      | 0.03     | 2.3%      | 2.3%      | 0.00     |
| HR > 100/min                        | 9.5%      | 10.3%     | 0.03     | 7.4%      | 8%        | 0.02     |
| ECG on admission (intraventricular conduction): |          |           |          |          |           |          |
| Normal                              | 86.7%     | 85.9%     | −0.02    | 87%       | 86.5%     | −0.02    |
| LBBB                                | 2.2%      | 2.8%      | 0.04     | 1.9%      | 1.8%      | −0.01    |
| RBBB                                | 2.7%      | 2.9%      | 0.01     | 3.3%      | 3.4%      | 0.01     |
| Other                               | 8.4%      | 8.4%      | 0.00     | 7.7%      | 8.3%      | 0.02     |
| Infarct location:                   |          |           |          |          |           |          |
| Anterior                            | 42%       | 42.4%     | 0.01     | 39.8%     | 39.5%     | −0.01    |
| Inferior                            | 46.8%     | 47.6%     | 0.02     | 51.2%     | 50.3%     | −0.02    |
| Other                               | 11.1%     | 10%       | −0.04    | 9%        | 10.2%     | 0.04     |
| Time from symptom-onset to admission: |          |           |          |          |           |          |
| 0–2 h                               | 25.9%     | 25.3%     | −0.01    | 28.6%     | 28.9%     | 0.01     |
| 2–12 h                              | 52%       | 52.3%     | 0.01     | 51.8%     | 51.5%     | −0.01    |
| > 12 h                              | 22.2%     | 22.4%     | 0.01     | 19.6%     | 19.7%     | 0.00     |
| Prehospital cardiac arrest          | 1.9%      | 2.3%      | 0.03     | 3%        | 2.5%      | −0.03    |
| Killip class on admission:          |          |           |          |          |           |          |
| IV                                  | 6.3%      | 6.2%      | 0.00     | 5.5%      | 5.7%      | 0.01     |
| III                                 | 3.2%      | 3.6%      | 0.02     | 2%        | 2.1%      | 0.01     |
| II                                  | 17.6%     | 16.2%     | −0.04    | 12.7%     | 13.1%     | 0.01     |
| I                                   | 72.9%     | 74%       | 0.03     | 79.8%     | 79.1%     | −0.02    |
| Left ventricular ejection fraction: |          |           |          |          |           |          |
| > 50%                               | 48.2%     | 45.3%     | −0.06    | 48.7%     | 47.6%     | −0.02    |
| 30–50%                              | 46.7%     | 48.6%     | 0.04     | 45.7%     | 47.4%     | 0.03     |
| < 30%                               | 5.1%      | 6.1%      | 0.04     | 5.6%      | 4.9%      | −0.03    |

S. diff – standardised difference, MI – myocardial infarction, PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting, BP – blood pressure, HR – heart rate, LBBB – left bundle branch block, RBBB – right bundle branch block.
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Table II. In-hospital management of ST-segment elevation patients admitted in 2005 and 2011 matched on the propensity scores

| In-hospital management    | Women | Men        |
|---------------------------|-------|------------|
|                           | 2005  | 2011       | 2005  | 2011       |
|                           | n = 3950 | n = 3950 | n = 7080 | n = 7080 |
| Conservative treatment    | 45.7% | 8.1%       | < 0.01 | 37% | 5.1%       | < 0.01 |
| Thrombolysis              | 8.6% | 0.6%       | < 0.01 | 8.5% | 0.3%       | < 0.01 |
| Invasive treatment – PCI  | 49.8% | 91.3%      | < 0.01 | 58.8% | 94.4%      | < 0.01 |

PCI – percutaneous coronary intervention.
Table III. In-hospital pharmacotherapy in ST-segment elevation patients admitted in 2005 and 2011 matched on the propensity scores

| In-hospital pharmacotherapy                  | Women       | Men         | P-value | Women       | Men         | P-value |
|---------------------------------------------|-------------|-------------|---------|-------------|-------------|---------|
|                                             | 2005 n = 3950 | 2011 n = 3950 |         | 2005 n = 7080 | 2011 n = 7080 |         |
| Acetylsalicylic acid                        | 93.8%       | 88.9%       | < 0.01  | 94.8%       | 90%         | < 0.01  |
| Any thienopyridine                         | 62.5%       | 98.1%       | < 0.01  | 70.8%       | 98.4%       | < 0.01  |
| Clopidogrel                                 | 49.2%       | 97.9%       | < 0.01  | 57%         | 98.3%       | < 0.01  |
| GP IIb/IIIa blocker                         | 12.4%       | 28.1%       | < 0.01  | 17.3%       | 33.7%       | < 0.01  |
| β-Adrenolytic                               | 70.2%       | 68.5%       | 0.1      | 72.6%       | 73.6%       | 0.2     |
| Statin                                      | 71%         | 73.4%       | 0.02     | 76%         | 78.7%       | 0.01    |
| ACE inhibitor or ARB                        | 67.8%       | 62.9%       | < 0.01  | 68.7%       | 67.7%       | 0.22    |
| Calcium channel blocker                     | 4.4%        | 8.3%        | < 0.01  | 3.2%        | 6.9%        | < 0.01  |
| Nitrate                                     | 44.3%       | 14.3%       | < 0.01  | 40.3%       | 12.7%       | < 0.01  |
| Diuretic                                    | 30.2%       | 23.2%       | < 0.01  | 21.2%       | 16.8%       | < 0.01  |

GP – glycoprotein, ACE – angiotensin converting enzyme, ARB – angiotensin receptor blocker.

Table IV. Pharmacotherapy at discharge in ST-segment elevation patients admitted in 2005 and 2011 matched on the propensity scores

| Pharmacotherapy at discharge             | Women       | Men         | P-value | Women       | Men         | P-value |
|------------------------------------------|-------------|-------------|---------|-------------|-------------|---------|
|                                            | 2005 n = 3523 | 2011 n = 3614 |         | 2005 n = 6634 | 2011 n = 6754 |         |
| Acetylsalicylic acid                     | 83%         | 93.6%       | < 0.01  | 84.1%       | 94.2%       | < 0.01  |
| Any thienopyridine                       | 58.1%       | 90.6%       | < 0.01  | 65.9%       | 91.3%       | < 0.01  |
| Clopidogrel                               | 25.1%       | 89.7%       | < 0.01  | 29.2%       | 90.6%       | < 0.01  |
| β-Adrenolytic                            | 73.5%       | 85.4%       | < 0.01  | 75.0%       | 85.3%       | < 0.01  |
| Statin                                   | 79.5%       | 90.5%       | < 0.01  | 81.4%       | 90.3%       | < 0.01  |
| ACE inhibitor or ARB                      | 70.4%       | 79.8%       | < 0.01  | 70.6%       | 81.4%       | < 0.01  |
| Calcium channel blocker                   | 4.6%        | 8.5%        | < 0.01  | 3.4%        | 7.5%        | < 0.01  |
| Nitrate                                  | 31.4%       | 11.7%       | < 0.01  | 27.3%       | 10.8%       | < 0.01  |
| Diuretic                                 | 25.2%       | 26.9%       | 0.1      | 17.4%       | 18.5%       | 0.09    |

ACE – angiotensin converting enzyme, ARB – angiotensin receptor blocker.

Table V. Mortality of ST-segment elevation patients admitted in 2005 and 2011 – relative risk reductions in crude observed mortality rates and in mortality rates in patients matched on the propensity scores

| Mortality rates | In-hospital | 12-month | 12-month if discharged |
|-----------------|-------------|----------|------------------------|
|                 | 2005 | 2011 | RRR | 2005 | 2011 | RRR | 2005 | 2011 | RRR |
| Women:          |      |      |     |      |      |     |      |      |     |
| Observed        | 12.3%| 7.7% | 37% | 23.1%| 17.7%| 23% | 12.3%| 10.8%| 12% |
| After PSM       | 10.8%| 8.5% | 21% | 20.9%| 18.8%| 10% | 11.3%| 11.3%| 0%  |
| Men:            |      |      |     |      |      |     |      |      |     |
| Observed        | 7.1% | 4.6% | 35% | 15.1%| 12.7%| 16% | 8.6% | 8.4% | 2%  |
| After PSM       | 6.3% | 4.6% | 27% | 13.8%| 12.2%| 11% | 8.0% | 8.0% | 0%  |

PSM – propensity score matching, RRR – relative risk reduction.
not exceed 6–7% [3, 17] and could be as low as 3.59%, as reported in men in a single-state American study [17]. However, some real-life data from Germany have shown surprisingly high in-hospital mortality rates and even a slight increase in STEMI in-hospital mortality from 11.2% in 2005 to 12.2% in 2009 [18]. Some sex-related disparities were also reported [1, 19]. In an Italian study, in-hospital mortality presented a small decrease from 7.6% in 2000 to 6.2% in 2010 in men, whereas it remained higher and substantially constant over time in women (16.6% in 2000, 15.5% in 2010) [1].

Most authors assume that new treatments should be the main reason for mortality reduction. Our study confirms that the progress in treatment contributed towards substantial reduction of mortality, and it could explain most of the in-hospital mortality decrease, especially in men. Two large American studies based on data from the NRMI (National Registry of Myocardial Infarction) estimated that in 1990–2006 relative reduction of hospital death in patients with STEMI after adjustment for baseline covariates was 24.2% [20]. Improved adherence to guideline therapies including the use of timely reperfusion accounted for 21% of the annual decline in the risk for hospital mortality among this population [7]. In our study the relative reduction in hospital mortality attributable to temporal improvements in hospital management has been estimated at similar levels: 27% for men and 21% for women, despite different region and time points for data collection. The sex-related difference is our specific finding. In men it constituted 77% of total observed RRR, whereas in women this fraction was considerably smaller (57%). Similarly, a French study estimated that a 74% reduction of absolute 30-day mortality between 1995 and 2010 could be attributed to the advances in treatment [4], but no sex-specific results were presented.

It has been reported that in recent years women experienced greater improvements in hospital mortality after MI than did men. Changes in comorbidity and clinical severity features at admission accounted for more than 90% of these mortality trends [21]. Our study supports similar findings in the Polish population. Relatively more positive changes in the baseline risk status (which might partly also be a consequence of pre-hospital management) definitely helped women to achieve substantial mortality rate reductions, despite the fact that men seemed to benefit more from the improved in-hospital treatment strategies. It may suggest that some sex-related disparities in STEMI treatment could still be present and should be explored further.

Besides improved frequencies of PCI reperfusion there was also the increased use of in-hospital novel antiplatelet agents (thienopyridines/clopidogrel and IIb/IIIa inhibitors). At the same time the use of aspirin decreased, which was clearly contrary to current guidelines. It might be explained by the increase in novel antiplatelet

Figure 1. 12-month mortality after ST-segment elevation among propensity score-matched subgroups of women from 2005 and 2011

Figure 2. 12-month mortality after ST-segment elevation among propensity score-matched subgroups of men from 2005 and 2011

Figure 3. Fractions of total observed mortality decline that could be attributed to changes in treatment (adjusted for baseline characteristics at admission)
agents usage and physicians being less insistent on dual-antiplatelet therapy in patients with even a minor intolerance to aspirin or an increased risk of bleeding. Single authors reported similar tendencies in aspirin usage in secondary prevention [22]. We did not observe significant changes in the hospital use of β-blockers and only a small increase in the use of statins. The routine administration of nitrates or diuretics in STEMI was not shown to be of value [23]. Although the proportions of patients according to Killip Class at admission were balanced (Table I), the lower in-hospital use of diuretics and nitrates could still be associated with a lower proportion of patients with signs or symptoms of congestion or acute cardiac failure during subsequent days of hospitalisation. It might also suggest lower rates of recurrent ischaemic pain, which required the use of nitrates; this was also true for discharge medications. The significant decrease in the in-hospital use of angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) in women was unexpected. Early ACE inhibition has been shown to reduce mortality as early as 30 days after STEMI, with most of the benefit observed in the first week [24]. The in-hospital use of ACE inhibitors or ARB remained relatively constant in men whereas it significantly decreased in women. It is not clear why this class of drugs was becoming less frequently used in women. AMIS-Plus (National Registry of Acute Myocardial Infarction in Switzerland) investigators from Switzerland also presented data that ACE inhibitors/ARB were less frequently used in women [2] despite the fact that earlier data from the same registry showed no differences in this field [25]. This finding could contribute towards the relatively small (compared to men) portion of the total observed in-hospital mortality decrease among women attributable to changes in hospital treatment.

12-month mortality

Data on sex-specific identification of reasons for longer term mortality decrease in STEMI are lacking. In our study, RRRs of crude 12-month mortality rates were considerably smaller when compared to RRRs of in-hospital mortality. They were also higher in women, but the changes in management had similar overall benefit to both sexes with 10–11% of RRRs being independent of patients’ clinical profiles. It suggests that women experienced greater overall 12-month mortality RRR, when compared to men, mostly due to changes in their initial risk-profiles. Relatively more positive changes in female patients’ characteristics at admission may epitomise the closing of the sex-gap reported in many previous studies [2, 7, 19, 26].

The long-term effects of the hospital survival improvements were still noticeable after 12 months. However, no added benefit of changes in post-hospital management was detected (Figure 3); the 12-month mortality reduction observed in crude real-life data among patients discharged from hospitals could be fully explained by changes in their clinical profiles at admission.

It is well known that patients after STEMI have a higher risk of death after leaving the hospital than the representatives of the general population, and secondary prevention therapies have been shown to improve their survival [23]. We observed an optimistic change in the guideline-recommended pharmacotherapy at discharge, with around a 10% absolute increase in the prescription of beta blockers, ACE inhibitors/ARB, and statins in both sexes. However, it did not help enough to detect any treatment-related advantage in 12-month mortality at the population level among the patients discharged from the hospital. There might be unsatisfactory patient adherence to discharge recommendations, subsequent suboptimal modification of the pharmacotherapy, lack of proper lifestyle modifications, or other non-pharmacological interventions.

There has been a report from a Polish population on secondary prevention therapies in coronary artery disease, including 2005–2006 and 2011–2013 time periods, suggesting room for further improvement in the prescription of guideline-recommended drugs, especially when post-hospital care is provided by primary care physicians [27]. There is also a potential concern that some patients survived the in-hospital period owing to improved treatment, but they remained at increased risk of death in the following months despite changes in the post-discharge care. These issues need to be explored further to possibly improve longer-term outcomes in STEMI patients.

A number of possible limitations of our study should be mentioned. First is the retrospective nature of the registry data. We believe that the propensity score matching technique is currently the most appropriate approach to eliminate the effects of confounding when using observational data and identifying causal relationships from a large non-randomised data set. However, some initial patients’ characteristics were not available (for example data on renal failure or anaemia), which might have affected the PS model quality. Participation in the PL-ACS Registry is voluntary, and the participating sites varied during the study period, so selection bias cannot be excluded. Finally, it is a single-country study, and generalising our findings on other populations with differing regions and time points for the data collection is tentative. Despite the listed limitations, we believe that our study allows a good view on recent
changes in STEMI management in a real-life setting and their actual relation to survival improvement, and it highlights the areas that require additional research and clinical attention.

In conclusion, there were substantial changes in STEMI patient management between 2005 and 2011 in Poland. Most of them followed current guideline recommendations and helped to achieve better survival rates in STEMI patients. Higher mortality risk reductions were observed in women, and they were driven by more positive changes in the females’ baseline risk profiles when compared to men. In contrast, men seemed to benefit relatively more from improvements in hospital treatment. Relative 12-month mortality reduction rates were less pronounced and could be fully explained by changes in patients’ initial characteristics and in-hospital mortality decline. The clinicians should pay attention to in-hospital use of aspirin in both sexes and ACE inhibitors/ARB in women and also focus on post-discharge management to possibly prolong the positive aspects of in-hospital efforts.

Conflict of interest

The authors declare no conflict of interest.

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