ORIGINAL ARTICLE

Pharmacological approach to patients with non-ST segment elevation myocardial infarction: does sex make a difference?

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KEY WORDS

sex, myocardial infarction, pharmacotherapy

ABSTRACT

INTRODUCTION A number of the recently published papers have suggested that high mortality among women with acute coronary syndromes might be related to suboptimal pharmacological treatment, namely to the lower rate of administration of antiplatelet agents, statins, β-blockers, and angiotensin-converting enzyme inhibitors (ACEIs).

OBJECTIVES The aim of the study was to compare pharmacotherapy between women and men with non-ST-segment elevation myocardial infarction (NSTEMI) treated in cardiology and general internal medicine wards.

PATIENTS AND METHODS A total of 682 consecutive patients (43.4% of women) with NSTEMI were hospitalized in a reference cardiology ward and several internal medicine wards between June 1, 2005 and May 31, 2006 in the Świętokrzyskie region of Poland (over 1 million inhabitants). Data were obtained from the Polish Acute Coronary Syndrome Registry. In-hospital and discharge pharmacotherapy in men and women were compared.

RESULTS Ticlopidine, clopidogrel, and unfractionated heparin were administered in the cardiology ward significantly more frequently than elsewhere. Acetylsalicylic acid was used with similar frequency in all wards. There were no significant differences in pharmacotherapy between male and female patients admitted to cardiology and other wards. Acetylsalicylic acid, clopidogrel, ACEIs, statins, and β-blockers were prescribed significantly less frequently at discharge from internal medicine wards than from the cardiology ward. The proportion of patients receiving specific drugs was similar among women and men.

CONCLUSIONS We did not observe significant differences in pharmacotherapy between women and men within a particular facility. Patients discharged from internal medicine wards were prescribed β-blockers, statins, and ACEI significantly less frequently.

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INTRODUCTION For many years, both coronary artery disease (CAD) and acute coronary syndromes (ACS) were regarded as typically male diseases.[1] It appears to be an underestimated health problem among women. Only within the last 10 years, investigators have noticed that CAD is the most frequent cause of death also in women.[2,3] In 2004, 55% of women and 43% of men died from cardiovascular disease in Europe.[4] Diagnostic difficulties and misconception about the small risk of developing heart disease in women may contribute to inadequate medical treatment in women with acute coronary syndrome.[1] Available evidence and data registries indicate that coronary revascularization and new antiplatelet drugs are significantly less

TABLE 1 In-hospital pharmacotherapy

	Świętokrzyskie Cardiology Center			Internal medicine wards			Statistical significance between the groups	
	women, % n = 177 39.5%	men, % n = 271 60.5%	*P*	women, % n = 119 50.9%	men, % n = 115 49.1%	*P*	women, *P*	men, *P*
ASA	92.7	95.2	0.26	95	94.8	0.95	0.43	0.86
ticlopidine	40.1	42.1	0.68	25.2	30.4	0.37	0.0080	0.032
clopidogrel	34.5	42.8	0.077	12.6	11.3	0.76	<0.0001	<0.0001
UFH	34.5	39.9	0.25	21.8	16.5	0.30	0.019	<0.0001
LMWH	54.8	51.3	0.47	58.8	68.7	0.12	0.49	0.0016
β-blockers	82.5	77.9	0.23	84	73.9	0.057	0.73	0.40
statins	72.3	77.1	0.25	68.9	69.6	0.91	0.53	0.12
ACEIs	88.7	89.3	0.84	82.4	75.7	0.21	0.12	0.0006
nitrates	67.2	62	0.26	80.7	72.2	0.13	0.011	0.056

Abbreviations: ACEIs – angiotensin-converting enzyme inhibitors, ASA – acetylsalicylic acid, LMWH – low-molecular-weight heparin, UFH – unfractionated heparin

frequently used in female patients.[5-9] In the recent decade, the European Society of Cardiology, including the Polish Cardiac Society as a member, has published 3 versions of its recommendations regarding treatment of non-ST-segment elevation myocardial infarction (NSTEMI)[5,10,11] and, additionally, recommendations regarding percutaneous revascularization, partly referring to NSTEMI.[12] In patients with NSTEMI, appropriate pharmacotherapy is of major importance. First of all, it maintains the favorable outcome of invasive treatment, but it has also been shown to prevent the development of new episodes, thus improving survival. In the acute phase, it is recommended to use antianginal, anticoagulant, and a combination of 2 antiplatelet drugs. Furthermore, each hospitalized patient without contraindications should receive β-adrenolytics, nitrates, heparin, or bivalirudine.[5] The cornerstone of long-term management are lifestyle changes, while fundamental pharmacotherapy includes 2 antiplatelet drugs, a β-adrenolytic agent and a statin. Moreover, subjects with type 2 diabetes, heart failure, and chronic renal insufficiency require angiotensin-converting enzyme inhibitors (ACEIs) and, if not tolerated, angiotensin-2 receptor blockers.[4]

Most of the data regarding management of acute coronary syndrome were gathered from cardiology wards. The Polish Acute Coronary Syndrome Registry (PL-ACS) also included patients admitted to internal medicine wards, so it is possible to evaluate treatment offered in these wards as well. The present study was undertaken to compare pharmacotherapy in women treated for NSTEMI in internal medicine wards and a reference cardiology ward in the Świętokrzyskie region of Poland.

PATIENTS AND METHODS The records of 682 consecutive patients with NSTEMI admitted to hospitals in the Świętokrzyskie region between June 1, 2005 and May 31, 2006 were reviewed. There were 296 women (43.4%) and 386 men (56.6%). We analyzed in-hospital treatment and drugs prescribed at discharge. Permission was obtained to retrieve the data from PL-ACS. The study was approved by the Ethics Committee in the regional Chamber of Physicians (Świętokrzyska Izba Lekarska; No. 8/2007).

Statistical analysis Continuous variables were expressed as arithmetic mean ± standard deviation. Depending on data distribution, the Student *t* test or Mann-Whitney test was performed to test for statistical significance between the means of variables. The χ^2 test was used to analyze statistical significance of qualitative variables.

RESULTS Of all patients, 448 (65.7%) were admitted to the Świętokrzyskie Cardiology Center (Świętokrzyskie Centrum Kardiologii – ŚCK) in Kielce, and the remaining 234 (34.3%) to internal medicine wards in regional hospitals. During hospital stay, patients received ticlopidine, clopidogrel, and unfractionated heparin significantly more frequently in the ŚCK than elsewhere; however, acetylsalicylic acid (ASA) was used with similar frequency in all wards. The administration rate of low-molecular-weight heparin was higher in men in internal wards. The administration rate of thienopiridine derivatives and unfractionated heparin during the initial treatment in patients hospitalized in internal medicine wards was significantly lower than in those admitted to the reference center. A significantly lower administration rate of ACEIs in men and higher administration rate of nitrates in both sexes was observed in internal medicine wards. There were no significant

TABLE 2 Pharmacotherapy at discharge

	Świętokrzyskie Cardiology Center			Internal medicine wards			Statistical significance between the groups	
	women, % n = 166 39.5%	men, % n = 254 60.5%	*P*	women, % n = 113 50.5%	men, % n = 111 49.5%	*P*	women, *P*	men, *P*
ASA	89.2	94.1	0.066	76.1	76.6	0.93	0.0036	<0.0001
ticlopidine	22.9	24.4	0.72	17.7	26.1	0.13	0.29	0.73
clopidogrel	16.9	28.7	0.0054	5.3	3.6	0.75	0.0038	<0.0001
β-blockers	81.9	77.6	0.28	71.7	69.4	0.70	0.043	0.096
statins	78.9	85.8	0.065	54.9	64	0.17	<0.0001	<0.0001
ACEIs	90.4	90.9%	0.84	67.3	61.3	0.35	<0.0001	<0.0001
nitrates	54.8	49.2%	0.26	61.9	60.4	0.81	0.24	0.05

Abbreviations: see TABLE 1

differences in the administration of other agents between male and female patients admitted to cardiology and other wards (TABLE 1). Women and men discharged from internal medicine wards were prescribed ASA, clopidogrel, ACEIs, and statins (women additionally β-adrenolytics) significantly less frequently than those from the reference center. The proportion of patients receiving specific drugs was similar among women and men in general; however, in the reference center with percutaneous coronary intervention (PCI) available, women were prescribed clopidogrel as a secondary prevention less frequently than men (TABLE 2).

DISCUSSION Sex-related discrepancies in the treatment of NSTEMI patients were widely researched in a large-scale observation from the CRUSADE Initiative by Blomkalns et al.[3] The main conclusion of this study is that the management of women with NSTEMI is far from ideal. However, the available evidence[13-15] shows a significant improvement in the mode of treatment of NSTEMI patients. Nevertheless, it appears that medical treatment of most European and American patients is suboptimal. The administration rate of the most popular agent, ASA, varies from 88%[3,16] to 98%[8,14] of patients and is similar in men and women.[3,8,16] In the present study, an initial ASA treatment rate was high regardless of the type of a facility; however, some significant differences between men and women appeared at discharge. Thienopyridine derivatives are most frequently administered in patients qualifying for percutaneous revascularization as a second antiplatelet drug preventing acute thrombosis. Thienopyridines are used less often, namely in 50% to 70% of men and in 33% to 50% of women.[3,13-16] They were used in 74.6% of women on admission to our reference center, which exceeds the rates reported elsewhere and appears to be satisfactory, but it is still much less than in men (84.9%). Initial treatment rate in internal wards was poor (about 36%–42%). One of the possible reasons for this discrepancy is that almost all high-risk patients were transferred to the PCI facility for invasive treatment, and those who remained in internal wards were treated medically with a very low rate of thienopyridine administration for secondary prevention. The reasons for doing so are not clear. The most probable explanation is very poor adherence to the guidelines despite of their wide dissemination.[3] β-adrenolytics are given in 76% to 96%[3,14,16] of patients with a slight predominance of men.[16] These results were similar in our region. Surprisingly, contrary to previous reports, women in our study received β-blockers more frequently both on admission and at discharge, but the difference was not significant. Statins are used in 50% to 80% of patients, usually more frequently in men.[3,13,14,16] In our group, the initial rate of statin administration was even better than in other observational studies. We suppose that a wide recommendation of β-block were more commonly used when a medical treatment was the method of choice.

Registries indicate that drugs prescribed at discharge are similar to those used during hospitalization with a general tendency towards reduced amounts of ASA in favor of the remaining medications.[3,16] In the Świętokrzyskie region, the use of specific medications does not differ much from the quoted proportions. However, some sex- and facility-related discrepancies, sometimes statistically significant, may be identified and call for an effort to improve the quality of care. Patients in the cardiology ward received thienopyridines more frequently, which was probably due to the fact that they were referred for coronary angiography. Contrary to the previous studies, a smaller percentage of patients received the recommended medications at discharge (i.e., antiplatelet agents), which might be associated with contraindications identified during hospitalization, such as bleeding complications (i.e., intracranial and gastrointestinal bleeding),[17] thrombocytopenia, ticlopidine intolerance, or referral for

a surgical treatment directly after coronary angiography. The numbers are especially small in internal medicine wards (TABLE 2), which may be the result of a different patient distribution with predominantly elderly people having more contraindications to aggressive therapy. Although only some patients with acute coronary syndrome are optimally treated, progress is being made.[13,14] Improvement in the quality of patient care is possible due to monitoring by means of patient registries and observational studies.[13-15] Special programs making physicians adhere to the guidelines are also valuable.[18]

Study limitations The retrospective nature of our analysis and the lack of possibility to modify the type of the collected data limited our assessment of certain issues. This pertains mainly to the lack of reasons for not administering some of the agents and to the lack of subanalyses of clinical characteristics of patients presenting at different facilities. That was the main reason why we did not assess the effect of pharmacotherapy on mortality.

Conclusions The present findings suggest that there are no significant differences in pharmacotherapy between women and men with NSTEMI within a particular facility. In-hospital treatment in the reference center favored the use of anitiplatelet agents and unfractionated heparin in both sexes. The biggest concern is the reduced proportion of β-blockers, statins, and ACEIs prescribed in patients discharged from internal medicine wards.

REFERENCES

1 Elsaesser A, Hamm CW. Acute coronary syndrome: the risk of being female. Circulation. 2004; 109: 565-567.

2 Glaser R, Herrmann HC, Murphy SA, et al. Benefit of an early invasive management strategy in women with acute coronary syndromes. JAMA. 2002; 288: 3124-3129.

3 Blomkalns AL, Chen AY, Hochman JS, et al; CRUSADE Investigators. Gender disparities in the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: large-scale observations from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) National Quality Improvement Initiative. J Am Coll Cardiol. 2005; 45: 832-837.

4 Janion M. [Epidemiology of cardiovascular diseases]. In: Świątecka G, Kornacewicz-Jach Z, eds. [Heart diseases in pregnant women]. Gdańsk, Poland: Via Medica, 2007: 87-98. Polish.

5 Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology, Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Eur Heart J. 2007; 28: 1598-1660.

6 Kornacewicz-Jach Z, Podolec P, Kopeć G, et al. [Polish Forum for Prevention Guidelines on Cardiovascular Diseases Prevention in Women]. Kardiol Pol. 2007; 65: 334-337.

7 Janion M. [Myocardial infarction in pregnant women]. In: Świątecka G, Kornacewicz-Jach Z, eds. [Heart diseases in pregnant women]. Gdańsk, Poland: Via Medica, 2006: 41-70. Polish.

8 Sinkovic A, Marinsek M, Svensek F. Women and men with unstable angina and/or non-ST-elevation myocardial infarction. Wien Klin Wochenschr. 2006; 118 Suppl 2: 52-57.

9 Rosengren A, Wallentin L, Simoons M, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. Eur Heart J. 2006; 27: 789-795.

10 Bertrand ME, Simoons ML, Fox K, et al.; Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2002; 23: 1809-1840.

11 Bertrand ME, Simoons ML, Fox K, et al. Management of acute coronary syndromes: ACS without persistent ST segment elevation. Eur Heart J. 2000; 21: 1406-1432.

12 Silber S, Albertsson P, Avilès FF, et al.; The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Guidelines for percutaneous coronary interventions. Eur Heart J. 2005; 26: 804-847.

13 Fox KA, Steg PG, Eagle KA, et al; GRACE Investigators. Decline in rates of death and heart failure in acute coronary syndromes, 1999-2006. JAMA. 2007; 297: 1892-1900.

14 Mehta RH, Roe MT, Chen AY, et al. Recent trends in the care of patients with non-ST-segment elevation acute coronary syndromes: insights from the CRUSADE initiative. Arch Intern Med. 2006; 166: 2027-2034.

15 Carruthers KF, Dabbous OH, Flather MD, et al. GRACE Investigators. Contemporary management of acute coronary syndromes: does the practice match the evidence? The global registry of acute coronary events (GRACE). Heart. 2005; 91: 290-298.

16 Heer T, Gitt AK, Juenger C, et al.; ACOS Investigators. Gender differences in acute non-ST-segment elevation myocardial infarction. Am J Cardiol. 2006; 98: 160-166.

17 Imiela J, Opolski G, Rydzewska G, et al. Position paper of the working group of three Polish national consultants in internal medicine, gastroenterology, and cardiology on prevention of gastrointestinal complications during antiplatelet treatment. Pol Arch Med Wewn. 2009; 119: 347-348.

18 Elkoustaf RA, Boden WE. Is there a gender paradox in the early invasive strategy for non ST-segment elevation acute coronary syndromes? Eur Heart J. 2004; 25: 1559-1561.

ARTYKUŁ ORYGINALNY

Leczenie farmakologiczne chorych z zawałem serca bez uniesienia odcinka ST: czy płeć ma znaczenie?

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SŁOWA KLUCZOWE

farmakoterapia, płeć, zawał serca

STRESZCZENIE

WPROWADZENIE W literaturze pojawiły się ostatnio sugestie, że większa śmiertelność kobiet z ostrymi zespołami wieńcowymi jest związana z suboptymalnym leczeniem farmakologicznym polegającym na zbyt rzadkim stosowaniu leków przeciwpłytkowych, statyn, β-blokerów i inhibitorów konwertazy angiotensyny (*angiotensin-converting enzyme inhibitors* – ACEI).

CELE Celem pracy było porównanie farmakoterapii u kobiet i mężczyzn leczonych z powodu zawału serca bez uniesienia odcinka ST (*non-ST-segment elevation myocardial infarction* – NSTEMI) w oddziałach kardiologicznych i internistycznych.

PACJENCI I METODY Od 1 czerwca 2005 roku do 31 maja 2006 roku w referencyjnym ośrodku kardiologicznym i na oddziałach wewnętrznych w województwie świętokrzyskim (ponad milion mieszkańców) hospitalizowano z powodu NSTEMI 683 kolejnych pacjentów. Dane uzyskano z ogólnopolskiego rejestru ostrych zespołów wieńcowych PL-ACS. Analizie poddano farmakoterapię stosowaną u kobiet i u mężczyzn w okresie szpitalnym i zalecaną przy wypisie ze szpitala.

WYNIKI Tiklopidynę, klopidogrel i niefrakcjonowaną heparynę częściej stosowano na oddziale kardiologicznym niż na oddziałach wewnętrznych. Kwas acetylosalicylowy stosowano z podobną częstością na wszystkich oddziałach. Przy wypisie z oddziałów wewnętrznych rzadziej niż przy wypisie z oddziału kardiologicznego zalecano pacjentom kwas acetylosalicylowy, klopidogrel, ACEI, statyny i β-blokery. Proporcje kobiet i mężczyzn otrzymujących poszczególne leki były podobne.

WNIOSKI W badanej grupie nie obserwowano istotnych różnic w farmakoterapii kobiet i mężczyzn w obrębie jednego ośrodka. Pacjentom wypisywanym z oddziałów wewnętrznych istotnie rzadziej niż w ośrodku kardiologicznym zalecano β-blokery, statyny i ACEI.

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