

# Long-Term Outcomes in Women and Men Population Participating In Program of Managed Care after Acute Myocardial Infarction (MC-AMI): A 12-Months Follow-Up from a Single Cardiology Care Centre

Katarzyna Wilkosz<sup>1\*</sup>,  
Krystian Wita<sup>1</sup>,  
Maciej T. Wybraniec<sup>1</sup>,  
Marcin Wita<sup>1</sup>,  
Joanna Fluder<sup>1</sup>,  
Monika Malta<sup>1</sup>,  
Jarosław Chmurawa<sup>2</sup> and  
Andrzej Kubicjus<sup>2</sup>

## Abstract

**Background:** The number of studies confirming the importance of Cardiac Rehabilitation (CR) towards the reduction of mortality and morbidity has increased. On the basis of scientific evidence, we developed a care program in Poland for patients with myocardial infarction I (MC-AMI (in Polish KOS-zawał)). There is a lack of data on possible improvement in long-term prognosis among women after acute myocardial infarctions (AMI), who were also involved with CR.

**Aim:** The aim of the study is to compare the male and female population who participate in MC-AMI, regarding major cardiovascular events (MACE), defined as a composite of death, recurrent myocardial infarction, and hospitalization for heart failure in a one-year follow-up.

**Methods:** This is a prospective research study from a single cardiology care centre. The study compares two groups: women and men who have agreed to participate in the MC-AMI program.

**Results:** As such, 529 patients were included in the study: 167 women and 362 men. In the 12-month follow-up, the incidence of MACE events was not statistically significantly, as observed in the study groups (11.38% vs. 11.33%;  $P=0.98$ ). Cox multivariate regression analysis of the surveyed population also revealed that coronary heart disease, diabetes mellitus type II, and previous percutaneous coronary intervention was significantly related to the primary endpoint.

**Conclusion:** Women who participate in the MC-AMI program do not exhibit a worse prognosis following MACE, compared to men in 12-month follow-up. Given the benefits of the program, the percentage of women participating in the program should definitely improve.

**Keywords:** MC-AMI; Cardiac rehabilitation; MACE; Sex differences

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## Introduction

In Poland, about 85-90 thousand people suffer from acute Myocardial Infarction (AMI) every year. Women constitute 48% of patients with AMI. Despite a well-functioning network of interventional cardiology departments and a large percentage of patients treated invasively Percutaneous Coronary Intervention (PCI) (59% vs. Coronary Artery Bypass Graft (CABG) 1.9% vs.

thrombolysis 1%), mortality at 1-year follow-up remains high (total, 19.4%; in-hospital mortality, 10.5%; and mortality after discharge, 8.9%). However, women after AMI continue to have a worse prognosis than men [1].

According to the AMI-PL register, only 22% of patients participate in cardiac rehabilitation (CR) in the first 12 months after a MI [2]. Early cardiac rehabilitation is an important component of

- 1 Department of Cardiology, School of Medicine, Medical University of Silesia, Katowice, Poland
- 2 Department of Cardiology in Cieszyn, Upper Silesian Medical Center, Cieszyn, Poland

### \*Corresponding author:

Katarzyna Wilkosz

✉ katarzyna.wilkosz@gmail.com

Department of Cardiology, School of Medicine, Medical University of Silesia, Katowice, Poland.

**Tel:** +48722398297; +48323598890

**Fax:** +48322523032

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the therapeutic process after myocardial infarction. Multiple meta analyses have reported that cardiac rehabilitation reduces overall mortality in patients With Coronary Artery Disease (CAD) [3-6]. Considering scientific reports and the results of national registers Polish Cardiac Society, the National Health Foundation and Ministry of Health of Poland have created a program of coordinated care for patients with MI (MC-AMI, in polish KOS-zawal) [7]. The program includes treatment of the acute phase of myocardial infarction, early cardiac rehabilitation, ambulatory care in the first year after the MI, qualification and possible implantation of Cardiac Implantable Electronic Devices (CEID).

There is still a lack of data on possible improvement in long-term prognosis among women after AMI who were involved in early cardiac rehabilitation.

The aim of this study is to compare the male and female population participating in the MC-AMI program regarding Major Cardiovascular Events (MACE), defined as a composite of death, recurrent myocardial infarction, and hospitalization for heart failure during a 1-year follow-up period.

## Methodology

We present prospective research from a single cardiology care centre, where the MCAMI program was included as a care standard. The study groups included all AMI patients from November 1, 2017 to August 31, 2018 who agreed to participate in MC-AMI. The study compares two groups: female population (group 1, n=167) and male population (group 0, n=362). All patients were at least 18 years old and agreed to participate in the MC-AMI program.

The MC-AMI program consists of four integrated modules. Treatment of acute coronary syndrome according to ESC guidelines (module I), early cardiac rehabilitation in outpatient or stationary conditions (module II), qualification for CEID implantation (module III), and 12 months of observation in a cardiology outpatient clinic (module IV).

The program included those patients with Non-ST-Elevation Myocardial Infarction (NSTEMI) and ST-Elevation Myocardial Infarction (STEMI), who agreed to participate in MC-AMI. Treatment was based on guidelines. Each patient began cardiac rehabilitation within 14 days, which was preceded by a coordinating visit. During the screening visits, basic laboratory parameters (CRP, creatinine, electrolytes and morphology) were monitored.

Patients were qualified for outpatient cardiac rehabilitation or in-hospital cardiac rehabilitation based on peri-infarction and comorbidities. After completion of the CR, the patients were monitored at outpatient clinics for the next 12 months. Control visits were scheduled every 3-4 months. During the visit, each patient was evaluated for the indication for implantable cardioverter-defibrillator (ICD) and Cardiac Resynchronization Therapy (CRT) implantation. In a research we compare the male and female population participating in the MC-AMI program regarding Major Cardiovascular Events (MACE), defined as a composite of death, recurrent myocardial infarction, and hospitalization for heart failure during a 1-year follow-up period.

The study protocol was approved by the Ethics Committee of the Medical University of Silesia in Katowice.

For statistical analysis, we used SPSS v.25.0 software (IBM Corp, Armonk, NY, USA). Quantitative variables were described as mean and Standard Deviation (SD) or median and 25-75 percentiles limits, while qualitative parameters were defined as number and percentage. The variable distribution type was confirmed using the Shapiro-Wilk test. All continuous variables were not normally distributed; the Mann-Whitney double-sided U test was a Pearson chi-square test. Relative Risk Ratios (RR) was calculated with 95% Confidence Intervals (95% CI). All variables with  $P < 0.1$  in the univariate model were included in the Cox proportional hazard model using Wald's step-backward approach. Kaplan-Meier survival curves for females (group 1) and males (group 0) were determined, and log-rank tests were calculated. A p-value below 0.05 was considered statistically significant.

## Results

Five-hundred-twenty-nine patients were included in the study; women constituted 31.6% of the examined population (167 women vs. 362 men). Arterial hypertension (AH) (80.2%), hyperlipidemia (73.9%), Coronary Heart Disease (CHD) (51.0%), and Diabetes Mellitus (DM) (31.8%) were frequently observed in the study group, and less than half of the respondents had a history of nicotine use (40.6%). There were no differences in the study groups in terms of age and comorbidities (**Table 1**). No differences were observed in the AMI treatment method in the study groups (**Table 2**). A comparable percentage of women and men participated in outpatient CR (46.71% vs. 40.06%  $P=0.15$ ). Around half (51.2%) of the women and 58.29% of men qualified for in-hospital CR ( $P=0.13$ ).

Over the year, in the study population (n=529), total mortality was 3.6% (4.19% women vs. 3.31% men), 5.1% of the patients were re-hospitalized because of HF exacerbation (4.19% women vs. 5.52% of men), and 4.0% again experienced AMI (4.79% women vs. 3.39%). In the 12-month follow-up, the incidence of MACE events was not significantly different in any of the study groups (11.38% vs. 11.33%;  $P=0.98$ ) (**Figure 1**). Differences in the incidence of recurrent AMI (4.79% vs. 3.59%;  $P=0.51$ ) (**Figure 2**) and mortality from any cause (4.19% vs. 3.31%;  $P=0.61$ ) (**Figure 3**) showed only the trend against female disadvantage in research groups.

Cox multivariate regression analysis of the surveyed population participating in the program MC-AMI has also revealed that CHD, DM type II, and previous PCI are significantly related to the primary endpoint (**Table 3**). In the Cox multivariate analysis, female gender was associated with a better prognosis in terms of MACE, but this did not reach statistical significance (HR 0.71, 95% CI 0.49-1.03,  $P=0.07$ ).

## Discussion

In recent years, the number of studies and a meta-analysis confirming the importance of CR in reducing mortality and morbidity has increased [8-10]. In fact, full use of the benefits

**Table 1** Baseline characteristics in study groups (n=529).

Characteristics	Men Mean ± SD	n (%)	Women Mean ± SD	n (%)	p-value
Age [ years]	65.69 ± 10.64		67.80 ± 10.17		
LVEF [%]	45.37 ± 10.53	45.24 ± 11.83	0.890		
	<b>n= 362</b>		<b>n= 167</b>		<b>p-value</b>
Previous CHD	186	51.38%	84	50.30%	0.817
Hypertension	288	79.56%	136	81.44%	0.615
DM II	107	29.56%	61	36.53%	0.11
DM I	2	0.55%	2	1.20%	0.579
Hyperlipidemia	262	72.38%	129	77.25%	0.236
PAD	43	11.88%	15	8.98%	0.322
Previous stroke	16	4.42%	10	5.99%	0.438
CKD	54	14.92%	38	22.75%	0.027
Smoking	149	41.16%	66	39.52%	0.721
Previous STEMI	58	16.02%	23	13.77%	0.504
Previous NSTEMI	65	17.96%	28	16.77%	0.738
Previous UA	50	13.81%	28	16.77%	0.373
Previous PCI	118	32.60%	50	29.94%	0.542
Previous CABG	42	11.60%	21	12.57%	0.748

CABG: Coronary Artery Bypass Grafting, CHD: Coronary Heart Disease, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, LVEF: Left Ventricular Ejection Fraction, NSTEMI: Non: ST Elevation Myocardial Infarction, PAD: Peripheral Arterial Disease, PCI: Percutaneous Coronary Intervention, SD: Standard Deviation, STEMI: ST: Elevation Myocardial Infarction, UA: Unstable Angina.

**Table 2** Method of treatment in study groups.

Characteristics	Total		Men		Women		p-value
	n=529	n (%)	n=362	n (%)	n=167	n (%)	
PCI- LAD/D	211	39.90%	153	42.27%	57	34.13%	0.076
PCI-RCA	162	30.60%	106	29.28%	56	33.53%	0.324
PCI-Cx/OM	120	22.70%	80	22.10%	40	23.95%	0.636
PCI bypass	13	2.50%	8	2.21%	5	2.99%	0.588
Failed PCI	3	0.60%	2	0.55%	1	0.60%	0.947
PCI-LM	3	0.60%	3	0.83%	0	0.00%	0.238
Application of eptifibatide	51	9.60%	38	10.50%	13	7.78%	0.326
Urgent CABG	51	9.60%	43	11.88%	8	4.79%	0.01

CABG: Coronary Artery Bypass Grafting, Cx: Left Circumflex Artery, D: Left Diagonal Branch Artery: LAD: Left Anterior Descending Artery, LM: Left Main Coronary Artery, OM: Left Obtuse Marginal Artery, PCI: Percutaneous Coronary Intervention, RCA: Right Coronary Artery

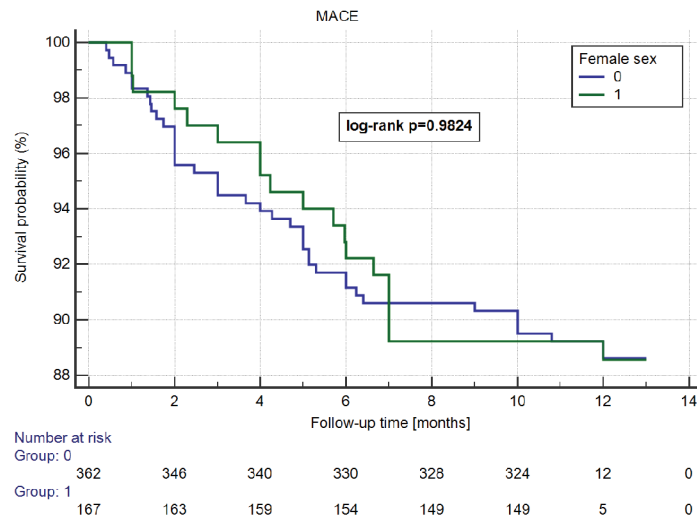
of early coronary revascularization is only possible with the subsequent support of patients in physiological and psychological rehabilitation. The MC-AMI program is a multistage, coordinated, and comprehensive AMI patient care program.

Our study showed that women who participate in the MC-AMI program do not have a worse prognosis for the occurrence of MACE compared to men in the 12-month follow-up.

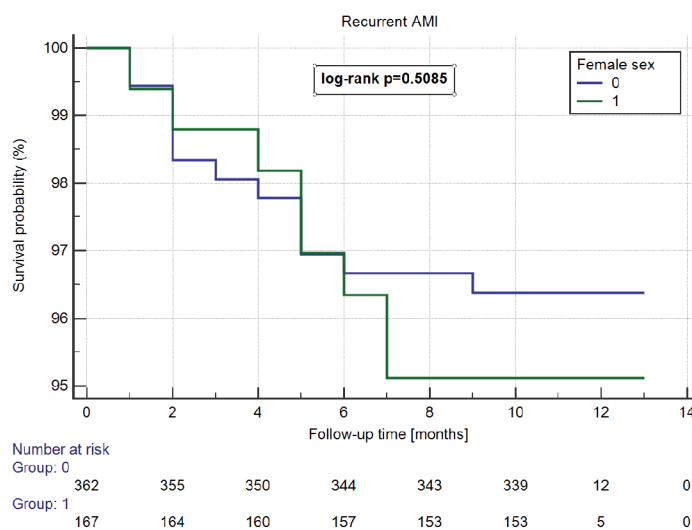
However, many studies have reported a worse long-term prognosis in women after AMI [11] and higher 30-day mortality than men [12-14]. According to the VIRGO analysis, women attribute symptoms occurring in MI to stress/anxiety more often than men do [15], which causes a delay with the first medical contact and diagnosis [16]. Zachura et al. reported that women with ST-segment elevation myocardial infarction (STEMI) are more likely to have associated diseases, such as AH, DM, and obesity. In long-term

follow-up, mortality in the female population after STEMI was significantly higher than in men. In addition, women were more often hospitalized for HF. In the above-mentioned study, as in our study, the female gender was not an independent risk factor for prognosis in long-term follow-up. The Zachura et al. study did not include participation in CR as a factor modifying mortality relative to gender [1]. Some studies report that despite a worse short-term prognosis, the long-term risk of mortality from Acute Coronary Syndrome (ACS) was similar in men and women [17,18]. Physical efficiency in women is lower than in men. Therefore, the benefits of CR might be greater for women [19].

The MC-AMI program is the first program of multi-stage, coordinated care after MI in Poland. As the results from the first work of our team show, participation in this program was associated with a 40% reduction in adverse cardiovascular and cerebrovascular (MACCE) events compared to the control group



**Figure 1** Kaplan Meier curves showing freedom from MACE.



**Figure 2** Kaplan Meier curves showing from recurrent AMI and mortality from any cause.

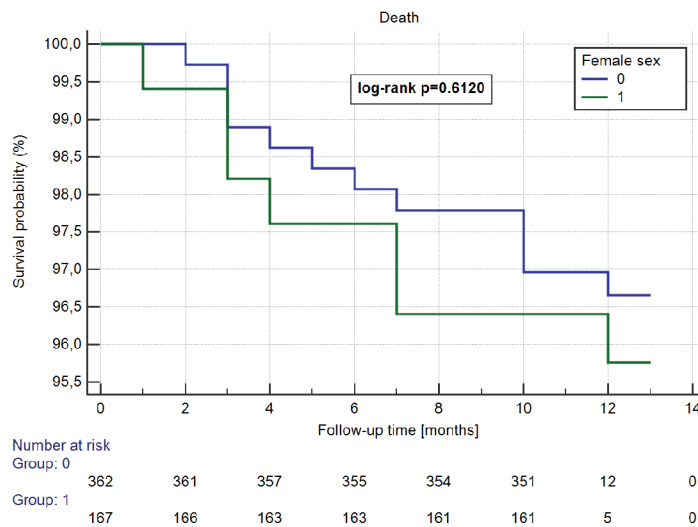
[20]. Patients participating in the program MC-AMI and was readmitted to hospital with HF at 5.1%, and due to AMI in 4.0% in the 12-month follow-up.

This is a much smaller percentage compared to published studies, where the frequency of re-hospitalization after MI due to HF ranges from around 9% [21] to 18% [22], and due to AMI from around 8% [21] to 12% [22].

In our study, multivariate analysis showed that CHD, DM type II, and previous PCI are significantly related to the primary endpoint. However, female gender was a non-independent risk factor in achieving the combined endpoint. The profile of patients after AMI has changed over the years; women were also older and more frequently had hypertension, diabetes, prior heart failure, and renal impairment than men [23]. In the FAST-MI study,

women are more obese, and usually smokers [24].

Both the first study and the study analysed here, in the groups of patients participating in the MC-AMI program, indicate that DM, hyperlipidemia, earlier Unstable Angina (UA) and PCI, low LVEF, and older age are associated with achieving primary endpoints. The data obtained are consistent with numerous publications. It was confirmed that high glucose blood level (< 7.52 mmol/L) was an independent predictor of high mortality MACE and no-reflow in patients with STEMI, undergoing PCI [25]. The rate of MACE was significantly higher in patients with reduced LVEF < 40% than in patients with LVEF ≥ 40% (26.8% vs. 11.4%) [26]. One of the latest meta-analyses calculated that each 1.0 mmol/L reduction of LDL-C resulted in a reduction in the annual incidence of MACCE, including death, myocardial infarction, need for re-revascularization, and stroke by about one-fifth [27]. According



**Figure 3** Kaplan Meier curves showing in women (Group 1) and men (Group 0) population-A 12 months follow up.

**Table 3** Multivariate analysis of independent predictors of MACE in both study groups.

Variables	HR	95% CI	p-value
Female sex	0.713	0.492-1.033	0.074
Hyperlipidemia	0.542	0.293-1.006	0.053
CHD	3,644	1.687- 7.873	0.001
CKD	0.462	0.201- 1.068	0.072
DM II	2,141	1.258- 3.642	0.005
eGFR	0.973	0.956- 0.990	0.002
LVEF	0.954	0.934- 0.975	<0.0001
Multivessel disease	2,086	1.208- 3.600	0.009
Previous CABG	0.469	0.215- 1.026	0.059
Smoking	0.547	0.304- 0.984	0.045
Previous PCI	0.429	0.219- 0.838	0.013
Previous UA	2,698	1.395- 5.217	0.003

CABG: Coronary Artery Bypass Grafting, CHD: Coronary Heart Disease, CKD: Chronic Kidney Disease, DM: Diabetes Mellitus, LVEF: Left Ventricular Ejection Fraction, PCI: Percutaneous Coronary Intervention, UA: Unstable Angina

to the KAMIR-NIH register, the risk of MACE after AMI increased with age: from 3.5% at <60 years, to 6.3% at 60-70 years old, 9.6% at 70-80 years old, and 17.6% at >80 years old, despite invasive treatment in all analysed groups [28].

According to the data, only 20-50% of patients participate in CR [29]. In Poland, the percentage of patients participating in cardiac rehabilitation after AMI is comparable with global data, and it is estimated at 22% according to the AMI-PL register. It is worrying that a much smaller percentage of women are recruited for CR compared to men. Based on the Cochrane review of the effectiveness of exercise-based cardiac rehabilitation compared to lack of exercise control for key outcomes, it showed that women accounted for less than 15% of patients enrolled in the study [30]. In our study, women made up only one-third of participants in the MC-AMI program. In a comparable percentage, they were qualified for outpatient CR and in-hospital CR (47.9% vs. 52.1%). Perhaps the introduction of innovative models of delivery, such

as home-based programs and telehealth interventions, has improved the number of patients participating in rehabilitation programs [31,32].

## Conclusion

The research presented above is a prospective study, but still a single-centre study. The main limitation of the analysis is limited number of analysed cases. A larger number of respondents and a longer observation period would allow for the collection of more accurate data. The MC-AMI program is a multi-stage, coordinated, and comprehensive AMI patient care program. Women who participate in the MC-AMI program do not have a worse prognosis for the occurrence of MACE compared to men in the 12-month follow-up. Due to the benefits of the program, the percentage of women participating in the program should be improved.



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