

In-Hospital Mortality of Patients with Acute Myocardial Infarction before and after Introduction of PCI in Split University Hospital Center, Croatia

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ABSTRACT

Aim of the study was to estimate the in-hospital mortality and death rate in patients with AMI according to gender and location of infarction during 5 years before and after the introduction of percutaneous coronary intervention (PCI) procedures in Split University Hospital Center, Croatia. The hospitalized patients were divided in two groups, from 2000 to 2004 and from 2005 to 2009. The analysis included total mortality and mortality according to gender and location of AMI. The location of infarction was detected toward typical ECG changes. The analysis included the model of death in patients with AMI and in-hospital mortality of patients undergoing the PCI procedures. The patients in the first group were treated with the standard medication therapy, and the patients in the second group were treated with PCI. The number of hospitalized patients with AMI, in ten years, increased from 475 to 652. A total of 5339 patients with AMI were hospitalized, and included 67.5% males and 32.5% females. The first group included 2336 patients (68% males and 32% females). The second group included 2973 patients (67% males and 33% females). Male patients in average were 5 years younger than female patients. A total in-hospital mortality was significantly higher in the first group (13.5 vs. 7.6%). The mortality in the first group was significantly higher in females (22.7 vs. 12%) and in males (9 vs. 5.5%) comparing with second group. In-hospital mortality in the patients with STEMI was significantly higher in the first group (16.6 vs. 9%). Among the patients with NSTEMI there were no significant differences in the in-hospital mortality (4 vs. 2.5%). The most frequent trigger of death in males were ventricular fibrillation in both groups such as heart failure in females. Cx occlusion is more often among the male patients treated with PCI. In-hospital mortality in patients with STEMI treated with PCI was 5.7%. A in-hospital mortality in the patients with AIM after PCI was almost halved. Females had two times higher in-hospital mortality before and after PCI introduction.

Keywords: mortality, acute myocardial infarction, percutaneous coronary intervention

Introduction

Myocardial infarction is probably the most important manifestation of atherosclerosis. It occurs as a consequence of long term development of atherosclerotic changes in coronary vessels caused by various risk factors as hypertension, hypercholesterolemia, smoking diabetes, stress, obesity, heredity and elderly¹⁻⁴. The pathological basis of acute myocardial infarction with ST elevation (STEMI) is usually based on rupture of unstable atherosclerotic plaque and the following thrombotic occlusion of coronary vessel with consequential necrosis of heart muscle followed by increase of corresponding enzyme values. Rupture of unstable plaque and thrombotic occlusion in myocardial infarction without ST elevation (NSTEMI) is followed by delayed recanalization of coronary vessel. Delay of recanalization also causes necrosis of myocardial muscle and increase of enzymes. Early recog-

rosclerotic plaque and the following thrombotic occlusion of coronary vessel with consequential necrosis of heart muscle followed by increase of corresponding enzyme values. Rupture of unstable plaque and thrombotic occlusion in myocardial infarction without ST elevation (NSTEMI) is followed by delayed recanalization of coronary vessel. Delay of recanalization also causes necrosis of myocardial muscle and increase of enzymes. Early recog-

nition of acute myocardial infarction and urgent transport to coronary care unit reduce damage of heart muscle and rate of death⁵⁻⁷.

More than 50% of total mortality in developed countries, as well as in Croatia, belong to cardiovascular disease, and 50% of deaths are because of coronary diseases. According to that, every fourth or fifth patient die because of myocardial infarction⁸.

In the last 30 years, in-hospital mortality because of acute myocardial infarction (AMI), decreased from 25–30% to 7–10% in North America and West Europe. This decreasing in mortality is due to introduction of Coronary Care Units, new medications such as beta-blockers and fibrinolytics, and introduction of percutaneous coronary interventions (PCI)⁹.

In Croatian capital Zagreb mortality of AMI was 50% from 1979 to 2001, and 31% of the AMI patients die out of hospital¹⁰. In Split, the second biggest city in Croatia, in 2002 diagnosis of AMI was established in 1022 patients, among them only 450 (44%) were hospitalized. A total 30-day mortality of AMI was 30–50%, and half of the AMI patients died in the first two hours^{11,12}. PCI was introduced in University Hospital Split (UHS) in 2005, with 24-hour intervention team available for invasive treatment of AMI. The goal of this study was to analyze a total in-hospital mortality of patients with AMI, according to infarction location and gender, 5 years before and after PCI introduction.

Methods of Analysis

This was a prospective study of patients hospitalized with AMI in UHS, from January 2000 to December 2009. The following data were collected from the patients' charts: date of hospital admission, age, gender, location of AMI, therapy administered in the hospital (ASK, beta-blockers, ACE inhibitors, fibrinolytics and PCI after it had been introduced), in-hospital patient outcome (survived/died), mechanism of death (according to ECG changes and clinical evaluation) and mortality according to

age and gender in AMI patients undergoing PCI treatment. For comparison of in-hospital mortality, patients were divided into two groups – patients treated before PCI was introduced (January 2000 – December 2004) and patients treated after the PCI introduction (January 2005 – December 2009).

Inclusion criteria were clinical signs and symptoms of myocardial infarction, ECG changes and enzyme values in blood analysis.

Location of myocardial infarction was determined according to ECG changes.

ST elevation more than 1 mm from V1 to V4 and growing troponin were denoted as anteroseptal ST-segment elevation myocardial infarction (STEMI), ST elevation in II, III and aVF as inferior STEMI, and ST elevation in I, aVL, V5 and V6 as lateral STEMI. ST denivelation more than 1 mm and T wave inversion with growing value of troponin were denoted as non-ST-segment elevation myocardial infarction (NSTEMI) infarction.

The patient data were anonymized and recorded in electronic charts. Categorical data were presented as frequencies and percents. The statistical analysis of data was performed with statistical package GrapPad Prism (GraphPad Inc, San Diego, CA, USA) using chi-squared (χ^2) test. Statistical significance level was set as $p < 0.05$. Continuous variables were expressed as means and standard deviation ($\bar{X} \pm SD$).

Results

In the period from 2000 to 2009, 5339 patients with AMI were hospitalized in UHS – 3600 (67%) men aged 61.1 ± 9.7 and 1739 (33%) women aged 66.3 ± 10.4 years. Before PCI introduction (years 2000 to 2004), 2366 AMI patients were treated, 1608 (68%) men aged 61.2 ± 9.6 years and 758 (32%) women aged 66.4 ± 10.5 years. After the PCI introduction (years 2005 to 2009), 2973 patients were included, 1992 (67%) men aged 61.0 ± 9.4 years and 981 (33%) women aged 66.2 ± 10.2 years. These results demonstrate that the average age of men and women in

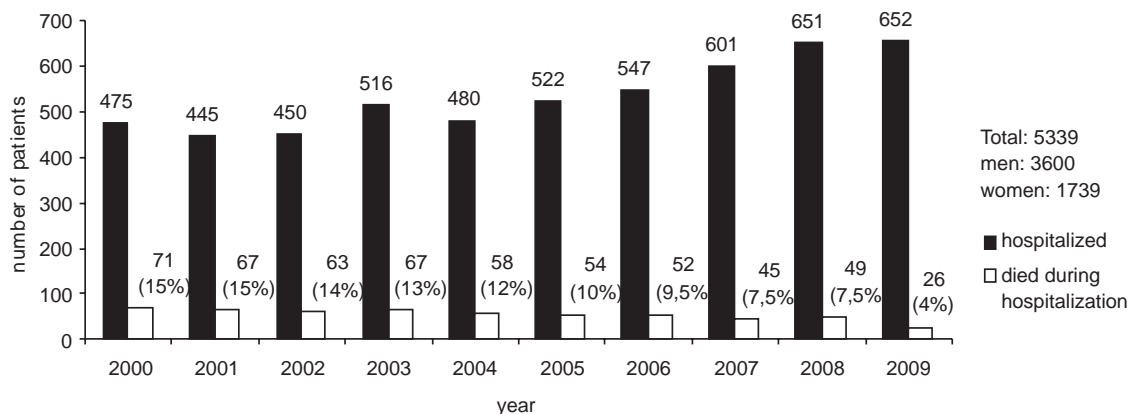


Fig. 1. Number of hospitalized patients with myocardial infarction and in-hospital mortality in University Hospital Split according to years from 2000 to 2009.

the both periods remained unchanged, with women being on average 5 years older. The number of patients hospitalized for AMI in UHS grew from 475 in 2000 to 652 in 2009.

Average in-hospital mortality before PCI introduction was 13.5%, and after the PCI introduction it decreased to 7.6% ($\chi^2=49.71$; $p<0.01$) (Figure 1). The in-hospital mortality rates were reduced after introduction of PCI both in men (9.0 vs. 5.5%; $\chi^2=37.1$; $p<0.01$), and in women (23 vs. 12%; $\chi^2=24.5$; $p<0.01$).

During the two observed periods, the number of patients with STEMI of anterior and inferior location was almost equal (26–29%), representation of STEMI of lateral location was significantly lower (14–15%), and the percentages of NSTEMI infarction was higher (21–23%) ($p<0.05$). The myocardial infarction without clear location included 6–8% patients (usually patients with left bundle branch block and idioventricular rhythm in terminal stage).

In-hospital mortality before PCI introduction was higher in patients with STEMI of antero-septal location (20%), compared with period after PCI introduction (11%). Patients with STEMI of inferior and lateral location, in the same period, had lower in-hospital mortality (15%), compared with period after PCI introduction (8%). The lowest in-hospital mortality was recorded in the group of patients with NSTEMI 4%.

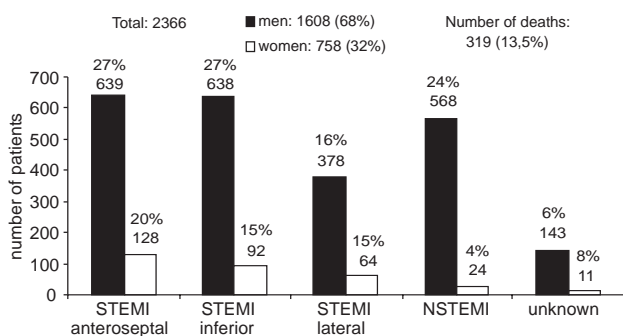


Fig. 2. Representation of location of myocardial infarction and in-hospital mortality in University Hospital Split from 2000 to 2004.

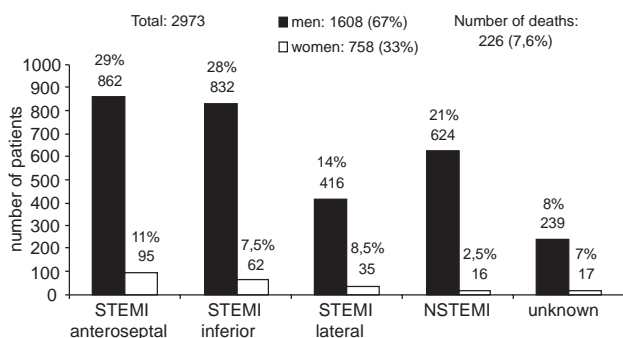


Fig. 3. Representation of location of myocardial infarction and in-hospital mortality in University Hospital Split from 2005 to 2009.

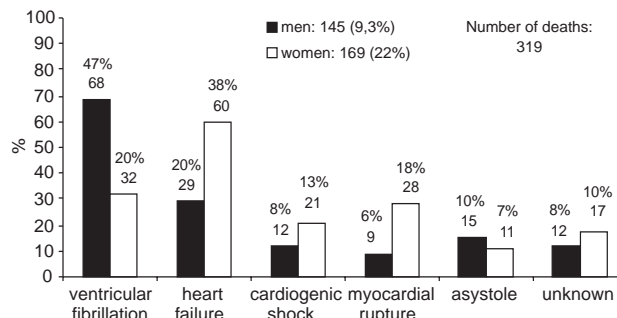


Fig. 4. Mechanism of dying in patients with myocardial infarction in males and females in Split University Hospital Center from 2000 to 2004.

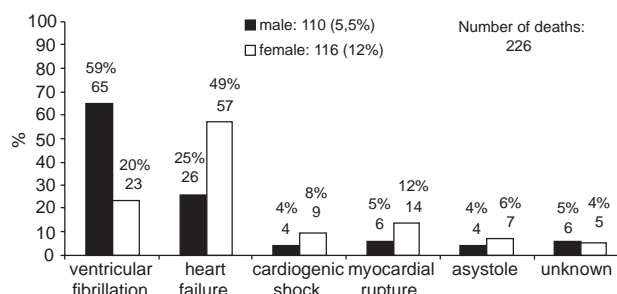


Fig. 5. Mechanism of dying in patients with myocardial infarction in males and females in Split University Hospital Center from 2005 to 2009.

After the PCI was introduced (from 2005 to 2009), total in-hospital mortality was 50% lower, as well as mortality according to AMI location, comparing to pre-PCI period (Figure 3).

The main cause of death in men was ventricular fibrillation in both analyzed periods, but the frequency of ventricular fibrillation increased from 47% before PCI to 59% after the PCI introduction. Heart failure was the most common cause of death in women both before (38%) and after (49%) the PCI introduction (Figures 4 and 5). Ventricular fibrillation was significantly more common cause of death in men comparing to women both before the PCI (47 vs. 20%; $\chi^2=26.7$, $p<0.001$) and after the PCI introduction (59 vs. 20%; $\chi^2=38$, $p<0.001$). Heart failure was significantly more frequent cause of death in women comparing to men before PCI (38 vs. 20%; $\chi^2=13.4$, $p<0.001$) and after PCI introduction (49% vs. 25%; $\chi^2=14.62$, $p<0.001$). In both periods cardiogenic shock and myocardial rupture as causes of death were more frequently observed in women than in men, and after introduction of PCI frequency of both these causes of death was reduced in women and men (Figures 4 and 5).

In-hospital mortality among the patients with STEMI was 17% before PCI introduction and 9% after the PCI introduction ($\chi^2=37.9$; $p<0.01$). Among patients with NSTEMI there were no significantly differences in the in-hospital mortality in the period before and after PCI (4 vs. 2.5%; $\chi^2=2.1$; $p=0.15$).

Analysis of patients with STEMI undergoing PCI procedures in the period from 2005 to 2009, demonstrated that men were mostly in the age group between 40 to 60 years, and women between 60 and 90 years. Analysis of coronary artery occlusion in patients treated with PCI showed that occlusion of circumflex artery was significantly more frequent in men than in women (20 vs. 10%; $\chi^2=7.2$; $p<0.01$).

Among 638 AMI patients who had died in-hospital during 2005–2009 period, there were 481 (76%) men and 156 (24%) women. In-hospital mortality of women with STEMI who were treated with PCI was almost 2.5 times higher comparing to men (10% vs. 4.2%; $\chi^2=7.82$, $p<0.01$).

Discussion and Conclusion

After the introduction of percutaneous coronary intervention, the in-hospital mortality of patients with acute myocardial infarction at Split University Hospital Center was decreased by 44%. In the analyzed ten-year period (2000–2009), the annual in-hospital mortality was reduced from 14% in 2000 to 4% in year 2009. At the same time, the number of patients hospitalized due to AMI at UHS increased by 28% in the year 2009, comparing to year 2000.

The incidence of myocardial infarction in Croatia in the last decade slowly decreased, whereas number of hospitalisation because of AMI (in both gender) increased¹².

In the last century (analysed period from 1970 to 1990), coronary artery disease (CAD) mortality rate in Croatia, was lower than in the developed countries. The developed European countries work on successful preventive measures and treatments and this is a cause of decreased CHD mortality to 100 deaths on 100000 inhabitants.

In Croatia, in 1991, 150 deaths (because of CHD) on 100000 inhabitants were recorded, what is higher than in developed countries, but lower than in Eastern European countries, where mortality rate of CHD was 200–270 on 100000 inhabitants¹³. The same trend was observed in year 2000¹⁴.

In our study, distribution of myocardial infarction according to location was almost equal in the analyzed periods before and after introduction of PCI.

Distribution of myocardial infarction toward location was in accordance to frequency of atherosclerotic lesions on coronary arteries. According to the available data from the literature, the most frequent atherosclerotic changes was on left anterior descending coronary artery – 43.4%, than right coronary artery – 28.4% and circumflex artery – 23.7%. This changes are in accordance to haemodynamic load¹⁵.

Anteroseptal myocardial infarction developed after occlusion of left anterior descending coronary artery, and inferior infarction after occlusion of right or dominate circumflex coronary artery, whereas lateral myocardial infarction developed after occlusion of circumflex coronary artery¹⁶.

Before introduction of PCI (period from 2000 to 2004), a total in-hospital mortality of AMI patients was 13.5%. The highest mortality was seen in patients with antero-septal location of STEMI (20%). In-hospital mortality of patients with STEMI of inferior and lateral location was significantly lower (15%), as well as in the patients with NSTEMI (4%). Mortality was often in correlation to size of irrigation domain of coronary artery occlusion.

After the introduction of PCI (from 2005 to 2009), in-hospital mortality of AMI patients was almost halved (to 7.6%) as well as in-hospital mortality according to location of myocardial infarction. This was the most important reason that in-hospital mortality of AMI in University Hospital Split in year 2009 became almost equal to the results of developed European countries¹⁴.

The analysis of in-hospital mortality according to gender before PCI introduction established that mortality of women was almost 2.5 higher than in the men (22.7 vs. 9%). After the PCI intervention mortality in both women and men decreased about 50%, but the mortality of women was still more than twice higher than in men (12 vs. 5.5%). The higher mortality of AIM in women and female gender as a independent predictor of AIM mortality, were proven in many studies^{17,18}. In patients with AIM, in-hospital mortality of women (after adjusting to age and risk factors) was twice higher then mortality in men^{19,20}.

On the other hand, lot of authors, fortified that (after adjusting to age), higher mortality in females become equal to mortality in males^{21–23}.

In our study, women with AIM were on average 5 years older than men, but after adjusting to other factors, in-hospital mortality of women was higher than in males.

We found that men with AMI most commonly die because of ventricular fibrillation, and women because of heart failure, cardiogenic shock and myocardial rupture. After the introduction of PCI, the percent of men and women dying from ventricular fibrillation and heart failure, respectively, increased, while mortality due to cardiogenic shock and myocardial rupture decreased²⁴.

It has already been described that women with AIM at hospital admission, present more often with lung rales, lung edemas and cardiogenic shock. Values of creatin kinase and incidence of anterior location of AMI, in both gender, had no statistically differences²⁶. The authors concluded that higher percentage of heart failure in AMI of equal size, suggested that females in non-infarction myocardial regions had lower compensatory reserve, which makes congestion a more frequent problem in women than in men^{26,27}. Men are able to increase heart volume with increasing of ejection fraction, and women with increasing of end-diastolic volume. Echocardiography investigation established that myocardial mass is about 30% lower in women than in men, and explanation for this could be effect of androgens^{25–27}.

Authors, in different investigations, suggested that men with AIM are more often dying because of malig-

nant arrhythmias, and women because of refractory decompensation, cardiogenic shock and myocardial rupture^{21–23}.

This differences in cause of death between men and women, could have explanation in gender differences, in sensibility on ischaemic and reperfusion lesions, electrophysiology specificity and differences in autonomic regulations^{28,29}. Activity of autonomic system have significant role in prognosis of patients with acute coronary syndrome. Hyperactivity of sympatic system could be trigger of malignant arrhythmias, on the other side, activity of vagus could have antifibrillation effect²⁹. Men more often die in acute phases of myocardial infarction, with higher sympatico-tonus and higher values of adrenaline (in relation to pain and fear)^{21–23}.

During two-minute occlusion of coronary arteries with balloon in women, high vagus activity is associated with bradycardia, decrease of blood pressure, and lower heart ectopic activity. This vagus activity protects women of malignant arrhythmias^{29,30}.

This could be explanation of higher mortality in men before hospitalization and higher in-hospital mortality in acute myocardial infarction phases, while mortality in women is significantly higher in subacute phases with mechanical heart failure because of lower mass and power of myocardium in females^{26,27}.

Analysis of patients who underwent PCI interventions according to gender demonstrated that the most common age of treated men was between 40 and 60 years, while women were mostly between 60 and 90 years. Among patients with STEMI treated with PCI, the most frequent coronary occlusions were detected at left anterior descending coronary artery and right coronary artery, in both genders. PCI procedures on circumflex arteries were two time higher in men than in women. This could be due to the higher hemodynamic burden of circumflex artery and stronger heart muscle in men, which is in relation with higher risk of atherosclerotic lesions.

In-hospital mortality of patients with STEMI was 16% before and 9% after the introduction of STEMI. We

did not detect significant differences of in-hospital mortality in patients with NSTEMI before and after introduction of PCI procedures. NSTEMI patients were initially treated with standard treatment, and afterwards they may have been treated with PCI procedures with stent implantation in subacute phases of myocardial infarction because of re-infarction prevention.

Analysis of in-hospital mortality of patients with myocardial infarction treated with PCI demonstrated that total mortality was 5.7%; mortality of women was 2.5 times higher than in men (10 vs 4.2%)³¹.

Women have lower possibility for myocardial infarction incident in fertility period because of estrogen role. In menopause, when protective role of estrogen decreases, frequency of myocardial infarction in women rises^{21–23}. We could conclude that women have lower incidence of myocardial infarction, but after the incident, mortality is significant higher.

According to our results, one third of patients with STEMI were treated with PCI in acute phases, and nearly 85% of patients with NSTEMI in subacute phases. In-hospital mortality of patients with AMI treated with standard therapy and PCI was 7.6%, mortality in patients with STEMI treated with PCI was 5.7%, and total mortality of patients with myocardial infarction was 4% in 2009.

These data are almost comparable with the most developed European countries, where 40% of patients with STEMI undergoing PCI procedures in clinical hospitals.

In conclusion, these data demonstrate that the introduction of PCI was beneficial for AMI patients in Split, Croatia. Even though the number of patients with AMI in the analyzed ten-year period had increased, their average in-hospital mortality was reduced by 44% after the introduction of PCI. As a result, treatment of acute myocardial infarction in Split University Hospital Center is now comparable to the most developed cardiology centres.

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BOLNIČKA SMRTNOST U BOLESNIKA S AKUTNIM INFARKTOM MIOKARDA PRIJE I NAKON UVOĐENJA PERKUTANE KORONARNE INTERVENCIJE U KBC SPLIT, HRVATSKA

S A Ž E T A K

Cilj rada je bio utvrditi bolnički mortalitet kod pacijenata s akutnim infarktom miokarda s obzirom na spol i lokalizaciju infarkta kroz 5 godina, prije i nakon uvođenja perkutane koronarne intervencije u Kliničkom bolničkom centru Split. Hospitalizirani bolesnici su podijeljeni u dvije skupine, prva obuhvaća pacijente s akutnim infarktom miokarda primljenih u bolnicu u razdoblju od 2000. do 2004. godine, a druga od 2005. do 2009. godine. Istraživanje uključuje ukupnu smrtnost i smrtnost s obzirom na spol i lokalizaciju infarkta miokarda. Lokalizacija je određivana na temelju tipičnih EKG promjena. U analizu je uključen i način umiranja pacijenata s akutnim infarktom miokarda i onih kod kojih je primijenjena perkutana koronarna intervencija. Pacijenti u prvoj skupini su liječeni standardnom terapijom, a oni u drugoj skupini, pored toga, i perkutanom koronarnom intervencijom. Ukupan godišnji broj hospitaliziranih bolesnika s akutnim infarktom miokarda, kroz period od 10 godina, povećao se od 475 na 652 bolesnika. Od ukupno 5339 hospitaliziranih bolesnika s akutnim infarktom miokarda 67,5% su bili muškarci, a 32,5% su bile žene. Prva grupa je uključivala 2336 bolesnika (68% muškaraca i 32% žena), a druga grupa je uključivala 2973 bolesnika (67% muškaraca i 33% žena). Muškarci su bili u prosjeku 5 godina mlađi od žena. Ukupni bolnički mortalitet je bio statistički značajno veći u prvoj skupini (13,5 prema 7,6%). Mortalitet u prvoj skupini je bio statistički značajno veći u žena (22,7 prema 12%) i u muškaraca (9 prema 5,5%) u odnosu na drugu skupinu. Bolnički mortalitet u bolesnika s STEMI je bio značajno veći u prvoj skupini (16,6 prema 9%). U bolesnika s NSTEMI nije bilo značajne razlike u bolničkom mortalitetu između skupina (4 prema 2,5%). Najčešći uzrok smrti kod muškaraca je bila ventrikularna fibrilacija u obje skupine dok je u žena to bilo popuštanje srca. Okluzija cirkumfleksne koronarne arterije je bila češća u muškaraca podvrgnutih perkutanoj koronarnoj intervenciji. Bolnički mortalitet u bolesnika s STEMI liječenih perkutanom koronarnom intervencijom je bio 5,7%. Bolnički mortalitet u bolesnika s akutnim infarktom miokarda nakon primjene perkutane koronarne intervencije je bio skoro dvostruko umanjen. Žene su imale dvostruko višu bolničku smrtnost u razdoblju prije i nakon uvođenja perkutane koronarne intervencije.