

Sex-related differences in treatment and outcome in patients with ACS

Dragana Radovanovic, MD¹ • Marc Auer, MD² • Paul Erne, MD²

In Western countries, acute coronary syndrome (ACS) accounts for most cases of cardiovascular morbidity and mortality in both sexes. ACS encompasses a spectrum of clinical conditions. These include acute myocardial infarction (MI), which encompasses both ST-segment elevation MI (STEMI) and non-STEMI (NSTEMI), and unstable angina pectoris. The differences in presentation, awareness, diagnosis, treatment, and outcome between men and women with ACS have been widely investigated.¹⁻⁵ Some studies have found that although reperfusion therapy benefits all patients with ACS and has become standard practice, not all women who experience acute MI receive this treatment.

We investigated sex-related differences in management and in-hospital outcomes in a large, randomly selected population of patients (N = 26,452) admitted to hospitals in Switzerland for ACS between 1997 and 2007. We also assessed whether women with ACS are at a disadvantage compared with men regarding treatment and outcomes, something previous studies do not address.

Subjects and methods

In January 1997, the Steering Committee, consisting of members of the Swiss Societies of Cardiology, Intensive Care, and Internal Medicine, initiated the AMIS (Acute Myocardial Infarction in Switzerland) Plus project, a prospective cohort study of ACS patients admitted to academic and nonacademic hospitals in Switzerland. The project was approved by the Over-Regional Ethics Committee for Clinical Studies and the Swiss Board for Data Security.

Centers participated voluntarily, with coordinators at each institution providing deidentified data for patients using a standardized questionnaire administered electronically or on paper. All data were checked for plausibility and consistency, and incomplete questionnaires were returned to their respective enrollment centers for completion. Patients were included in the study if they met the following criteria for specific ACS con-

TIME-SAVER

The AMIS (Acute Myocardial Infarction in Switzerland) Plus prospective cohort study compared treatment and in-hospital outcomes between men and women with acute coronary syndrome (N = 26,452) admitted to Swiss hospitals between 1997 and 2007. The study reached several important conclusions: women had different baseline characteristics than men at admission, were treated with different drug regimens, and were significantly less likely to undergo percutaneous coronary intervention. After adjusting for these differences, researchers found no significant difference in the rates of in-hospital mortality between men and women, except for women aged 51 to 60 years, who were more likely to die in-hospital.

Disclosure The AMIS Plus registry is funded by unrestricted grants from the Swiss Heart Foundation and from Abbott, AstraZeneca, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol-Myers Squibb, Essex/MSD, GlaxoSmithKline, Guidant, INVATEC, Johnson & Johnson-Cordis Division, A Menarini, Medtronic, Mepha Pharma, Merck Sharp & Dohme-Chibret, Novartis, Pfizer, Sanofi-Aventis, Schering, Servier, SPSS, St. Jude Medical, and Takeda Pharma, all in Switzerland. The supporting institutions did not play any role in the design of the registry; in data collection, analysis, or interpretation; or in the preparation of the manuscript.

From the ¹AMIS Plus Data Center, Institute of Social & Preventive Medicine, University of Zurich, ²department of cardiology, Canton Hospital Lucerne, Switzerland.

ditions: STEMI, defined as ST-segment elevation or new left bundle branch block on initial electrocardiogram (ECG) and elevated cardiac enzymes (levels of total creatinine kinase [CK; normal, <2.8 μ kat/L] or CK-MB fractions [normal, <5 μ g/L] at least twice the upper limits of normal); NSTEMI, defined as symptoms and/or ECG changes compatible with ACS and elevated cardiac enzymes not meeting the criteria for STEMI; and unstable angina pectoris, defined as symptoms and/or ECG changes compatible with ACS and normal cardiac enzymes.

AMIS Plus enrolled a cumulative 26,698 patients admitted to 74 Swiss hospitals between 1997 and 2007. The study included only those patients for whom valid data on their initial ECG and reperfusion therapy had been provided. Baseline characteristics between men and women were compared using *t*-test and chi-square tests (Table 1). Independent predictors of in-hospital mortality were calculated using logistic regression models that considered all variables available at hospital admission (Table 1): per year increase in age; history of coronary heart disease; presence of arterial hypertension, dyslipidemia, or diabetes; current smoking; delay >6 hours between symptom onset and hospital admission; left bundle branch block, ST-segment elevation, ST-segment depression, and Q-waves on initial ECG; Killip class, body mass index, heart rate, and systolic blood pressure at admission; and whether the patient underwent percutaneous coronary intervention (PCI). Variables significant at the 0.05 level were included in the stepwise logistic regression analysis using the backwards method. Statistical analyses were performed using SPSS software (Chicago, Illinois; Version 14.0).

Results

The 26,452 ACS patients included in the analysis comprise 7341 women and 19,111 men. The mean age of women in the study was

Table 1. Baseline characteristics of patients with ACS and treatment received, according to sex.

Characteristics	Men (n = 19,111)	Women (n = 7341)	P value
Demographics			
Age (years), mean (SD)	63.4 (12.9)	71.2 (12.3)	<.001
BMI (kg/m ²), mean (SD)	26.9 (3.9)	26.3 (5.0)	<.001
Delay from symptom onset to admission (hours), median (interquartile range)	3:50 (1:53, 11:30)	4:43 (2:35, 13:30)	.008
Cardiovascular risk factors, %			
Coronary artery disease	39.6	37.7	.011
Diabetes	18.6	23.6	<.001
Hypertension	53.3	66.4	<.001
Dyslipidemia	58.2	54.6	<.001
Current smoker	42.8	25.1	<.001
Overweight (BMI >25 kg/m ²)	67.0	55.3	<.001
ECG characteristics, %			
ST-segment evaluation	55.8	52.7	<.001
Q-waves	20.2	18.2	<.001
ST-segment depression	24.7	26.6	.001
T-wave changes	24.7	26.7	.001
Left bundle branch block	5.0	6.1	<.001
Heart rhythm, %			
Sinus rhythm	91.9	89.2	.132
Atrial fibrillation	4.6	7.0	<.001
Presenting characteristics			
Pain	84.5	81.6	<.001
Dyspnea	23.8	32.6	<.001
Heart rate (beats/min), mean (SD)	78 (20)	81 (22)	<.001
Systolic blood pressure (mm Hg), mean (SD)	136 (27)	138 (30)	<.001
Diastolic blood pressure (mm Hg), mean (SD)	80 (18)	78 (18)	<.001
Killip class I	79.4	70.7	<.001
Killip class II	14.3	20.6	<.001
Killip class III	3.8	6.3	<.001
Killip class IV	2.5	2.4	.989
Pharmacologic therapies administered			
Aspirin	94.7	92.7	<.001
Clopidogrel	53.3	43.9	<.001
Glycoprotein IIb/IIIa antagonist	36.0	25.9	<.001
Beta-blockers	72.6	66.8	<.001
Nitrate	64.6	64.6	.943
Lipid-lowering drugs	75.3	65.8	<.001
Procedures performed			
Thrombolysis	14.8	11.9	<.001
PCI	43.8	33.3	<.001

ACS indicates acute coronary syndrome; BMI, body mass index; ECG, electrocardiogram; PCI, percutaneous coronary intervention; SD, standard deviation.

Table 2. Sex as an independent predictor of in-hospital mortality in various age groups (N = 26,452).

Age group (years)	Men (reference)	OR (95% CI for OR)	
		Women, unadjusted	Women, adjusted ^a
≤50 (n = 3871)	1	2.31 (1.36-3.92)	1.27 (0.54-2.95)
51-60 (n = 5570)	1	1.52 (1.02-2.27)	1.67 (1.03-2.72)
61-70 (n = 6481)	1	1.34 (1.03-1.76)	1.28 (0.92-1.79)
71-80 (n = 6979)	1	1.02 (0.86-1.20)	1.06 (0.87-1.29)
>80 (n = 3551)	1	1.03 (0.87-1.22)	0.94 (0.76-1.17)

^aAdjusted for Killip class; history of diabetes, hypertension, or dyslipidemia; ST-elevation on initial electrocardiogram; and percutaneous coronary intervention. CI indicates confidence interval; OR, odds ratio.

7 years greater than the mean age of the men. Women were more likely to have preexisting hypertension and diabetes, but less likely to have dyslipidemia, be overweight, or smoke. On average, women arrived at the hospital 1 additional hour after symptom onset compared with men.

At admission, more women than men were ranked Killip class II or III, and presented with dyspnea, ST-segment depression, left bundle branch block, or atrial fibrillation. Women were less likely to receive aspirin, clopidogrel (Plavix, Iscover, Clopilet), glycoprotein IIb/IIIa antagonists, beta-blockers, and lipid-lowering drugs. Women were also less likely to undergo PCI than men, and even after adjusting for covariables, being of the female sex remained an independent factor that decreased a patient's likelihood of undergoing PCI (odds ratio [OR], 0.83; 95% confidence interval [CI], 0.78-0.89; $P < .001$).

Crude in-hospital mortality was higher overall for women than

men (9.8% vs 5.9%, respectively; $P < .001$). In-hospital mortality was also higher for more women than men with STEMI (12.0% vs 6.7%, respectively; $P < .001$) and NSTEMI (6.8% vs 4.7%, respectively; $P < .001$) and for women who underwent PCI (4.2% vs 3.1%; $P = .009$). After adjusting for covariables, it was determined that sex is not an independent predictor of in-hospital mortality for ACS patients (adjusted OR for men vs women, 1.07; 95% CI, 0.94-1.22). **Table 2** provides unadjusted and adjusted ORs for in-hospital patient mortality for women, allocated by age group. For the most part, direct comparisons between men and women of the same age ranges indicate no significant differences between the sexes in the in-hospital mortality rates for ACS patients. However, the in-hospital mortality rate for women aged 51 to 60 years is statistically greater ($P = .038$) than the mortality rate for men of this age range, even after adjustment.

Discussion

Some studies have shown that even when women with ACS present with greater risk factors and have a higher in-hospital mortality risk than men, they receive less aggressive treatment.⁶ Data from AMIS Plus show that in addition to differences in baseline characteristics between men and women admitted for ACS between 1997 and 2007, their conditions were treated differently from the outset. For example, women in our study were less likely to receive certain drug treatments and reperfusion therapy. This finding supports other studies that have concluded women and men do not receive identical interventional treatment and women are less likely to receive PCI, although they have comparable or better outcomes than men following the procedure.^{4,7}

Routine PCI appears to be a safe revascularization procedure. It is associated with a low rate of clinical complications in patients with STEMI, NSTEMI, or unstable angina pectoris and has become the preferred treatment in Switzerland for patients with ACS. It is unclear why the women with ACS in our study underwent PCI less frequently than the men, and this should be investigated further.

The TACTICS-TIMI (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy—Thrombolysis in Myocardial Infarction)—18 trial found that employing an early invasive approach

CME In the Heart of Women

in ACS patients with non-ST-segment elevation benefitted both men and women.⁸ In contrast, the FRISC II (Fragmin and Fast Revascularization During Instability in Coronary Artery Disease) and RITA 3 (Third Randomized Intervention Trial of Unstable Angina) trials found that these women did not benefit from an early invasive approach.^{9,10}

Some studies have documented a higher mortality rate in women following interventional treatment,¹¹ which was attributed to differences in body size between men and women, anatomical differences, basic biological differences,^{12,13} and/or the differing pathophysiology of ACS conditions dependent on patient age.¹⁴ On the whole, however, our study found similar rates of in-hospital mortality for men

and women with ACS after adjustment for covariables, despite the less frequent use of interventional procedures in women.

The only exception was women aged 51 to 60 years, who demonstrated a marginally higher rate of in-hospital mortality than men of the same age. This corresponds with results from the USIC (Unité de Soins Intensifs Coronaires) French nationwide registries, which showed that women (30-67 years) had higher mortality following acute MI compared with men regardless of the patient's clinical characteristics or treatment received.¹⁵

Conclusion

The AMIS Plus data show that among patients admitted to hospitals for ACS, women are less likely

than men to receive specific drug treatments and PCI. Despite this, the men and women in our study had similar rates of in-hospital mortality overall, after adjustments were made to account for differences in their baseline characteristics and management.

We concluded that sex is not an independent predictor of in-hospital mortality, and simply being a woman does not increase the risk of dying in-hospital due to ACS. The only exception was observed in women aged 51 to 60 years, who had a higher rate of in-hospital mortality compared with men of the same age. Further investigation is needed to determine why this is the case and why women with ACS are less likely than men to receive interventional treatment, including PCI. •

References

1. Rosengren A, Wallentin L, Gitt AK, et al. Sex, age, and clinical presentation of acute coronary syndromes. *Eur Heart J*. 2004;25(8):663-670.
2. Nau DP, Ellis JJ, Kline-Rogers EM, et al. Gender and perceived severity of cardiac disease: evidence that women are "tougher." *Am J Med*. 2005;118(11):1256-1261.
3. Schulman KA, Berlin JA, Harless W, et al. The effect of race and sex on physicians' recommendations for cardiac catheterization. *N Engl J Med*. 1999;340(8):618-626.
4. 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(6):832-837.
5. Lansky AJ, Pietras C, Costa RA, et al. Gender differences in outcomes after primary angioplasty versus primary stenting with and without abciximab for acute myocardial infarction: results of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. *Circulation*. 2005;111(13):1611-1618.
6. Bhatt DL, Roe MT, Peterson ED, et al; CRUSADE Investigators. Utilization of early invasive management strategies for high-risk patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE Quality Improvement Initiative. *JAMA*. 2004;292(17):2096-2104.
7. Mehilli J, Ndrepepa G, Kastrati A, et al. Gender and myocardial salvage after reperfusion treatment in acute myocardial infarction. *J Am Coll Cardiol*. 2005;45(6):828-831.
8. Cannon CP, Weintraub WS, Demopoulos LA, et al; TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)—Thrombolysis in Myocardial Infarction 18 Investigators. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. *N Engl J Med*. 2001;344(25):1879-1887.
9. Clayton TC, Pocock SJ, Henderson RA, et al. Do men benefit more than women from an interventional strategy in patients with unstable angina or non-ST-elevation myocardial infarction? The impact of gender in the RITA 3 trial. *Eur Heart J*. 2004;25(18):1641-1650.
10. Lagerqvist B, Safstrom K, Stahle E, et al; FRISC II Study Group Investigators.

(Continued on page 26)

In the Heart of Women

Is early invasive treatment of unstable coronary artery disease equally effective for both women and men? FRISC II Study Group Investigators. *J Am Coll Cardiol*. 2001;38(1):41-48.

11. Hannan EL, Racz MJ, Arani DT, et al. Short- and long-term mortality for patients undergoing primary angioplasty for acute myocardial infarction. *J Am Coll Cardiol*. 2000;36(4):1194-1201.
12. Vakili BA, Kaplan RC, Brown DL. Sex-based differences in early mortality of patients undergoing primary angioplasty for first acute myocardial infarction. *Circulation*. 2001; 104(25):3034-3038.
13. Alter DA, Naylor CD, Austin PC, et al. Biology or bias: practice patterns and long-term outcomes for men and women with acute myocardial infarction. *J Am Coll Cardiol*. 2002;39(12): 1909-1916.
14. 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(7):789-795.
15. Simon T, Mary-Krause M, Cambou JP, et al; USIC Investigators. Impact of age and gender on in-hospital and late

mortality after acute myocardial infarction: increased early risk in younger women: results from the French nation-wide USIC registries. *Eur Heart J*. 2006;27(11):1282-1288.

A more detailed discussion of this topic can be found in Radovanovic D, Erne P, Urban P, et al; AMIS Plus Investigators. 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(11):1369-1375. Tables are original to this report.

In the Heart of Women

CASE REPORT

■ Feature 21
■ Commentary 27

Successful PCI in an elderly woman

A 75-year-old woman who experienced chest discomfort that caused her to awaken and persisted as retrosternal pain was admitted to the emergency department. Her medical history included arterial hypertension, diabetes, hypercholesterolemia, and a 50-pack-year history of cigarette smoking, but she had no history of major medical events. Her drug regimen consisted of a once-daily dose of aspirin (100 mg), metoprolol (50 mg), felodipine (5 mg), and simvastatin (20 mg), and a twice-daily dose of glimepiride (40 mg).

On physical examination, she

had dyspnea and appeared uncomfortable. Her respiratory rate was 25 breaths per minute, her oxygen saturation was 88% on room air, and her blood pressure was 170/90 mm Hg. Auscultation of her chest revealed crackles in the lungs and a regular rhythm with an S₄ gallop. Cardiomegaly and bilateral edema were documented by a chest radiograph. An electrocardiogram showed a left bundle branch block, and blood tests indicated elevated levels of total creatinine kinase and troponin T. Echocardiography documented a markedly reduced ejection fraction of 0.40, based on an anterolateral hypokinesia with

dilated left ventricle.

In the emergency department, the patient received furosemide, nitroglycerin, clopidogrel, and low-molecular-weight heparin. Subsequent coronary angiography demonstrated 3-vessel disease. Approximately 5 hours after her symptoms started, the patient underwent percutaneous coronary intervention (PCI). During the procedure, 2 bare metal stents were deployed in the left anterior descending artery and 1 drug-eluting stent was deployed in the right coronary artery. The patient was discharged from the hospital with a 12-month prescription for clopidogrel 75 mg daily. •

Differences in treatment and outcomes in women with ACS

More than 1 million percutaneous coronary interventions (PCIs) are performed annually in the United States.¹ Although more women than men die from cardiovascular disease in this country every year, and the benefits of PCI in reducing fatal and nonfatal ischemic complications in patients with acute myocardial infarction (MI) and high-risk acute coronary syndromes (ACS) are well-established, less than one-third of PCIs annually are performed in women.¹⁻³ Significant sex-related disparities exist in time to intervention, referral to diagnostic catheterization, and use of evidence-based medicine.³⁻⁷ While some of these disparities have been explained by women's older age at presentation, greater risk profile, and increased risk for an adverse procedural outcome; differences in symptoms and in pain perception between men and women, and a lower predictive accuracy of noninvasive testing in women; data from numerous studies suggest sex bias in treatment.⁴⁻⁷

The AMIS (Acute Myocardial Infarction in Switzerland) Plus prospective cohort study (page 21) compared treatment and in-hospital outcomes between men and women with ACS admitted to Swiss hospitals between 1997 and 2007. This study provides a unique opportunity to explore sex differences in care and clinical outcomes in a large, nationally representative cohort of men and women. In total, 7341 women and 19,111 men (N = 26,452)

were randomly selected for the analysis. Patients were included in the study if they met the following criteria: ST-segment elevation MI (STEMI), defined as ST-segment elevation or new left bundle branch block on initial electrocardiogram (ECG) and elevated cardiac enzymes (levels of total creatinine kinase [CK; normal, <2.8 μ kat/L] or CK-MB fractions [normal, <5 μ g/L] at least twice the upper limits of normal; non-ST-segment elevation MI (NSTEMI), defined as symptoms and/or ECG changes compatible with ACS and elevated cardiac enzymes not meeting the criteria for STEMI; and unstable angina pectoris, defined as symptoms and/or ECG changes compatible with ACS and normal cardiac enzymes.

Not surprisingly, the mean age of the women in the study was 7 years greater than the mean age of the men. Women were more likely to have hypertension and diabetes, but less likely to have dyslipidemia, be overweight, or smoke compared with men. On average, women arrived later after symptom onset, with higher Killip class, and more dyspnea, ST-segment depression, left bundle branch block, or atrial fibrillation compared with men. With respect to treatment strategies, women were less likely to receive aspirin, clopidogrel, glycoprotein IIb/IIIa antagonists, beta-blockers, and lipid-lowering drugs than men. Women were also less likely to undergo PCI than men. After robust adjustment, female sex remained an independ-



JoAnne M. Foody, MD, is associate professor, Harvard Medical School, director, Cardiovascular Wellness Center, Brigham and Women's Hospital, Boston, MA.

ent factor that decreased a patient's likelihood of undergoing PCI (odds ratio [OR], 0.83; 95% confidence interval [CI], 0.78-0.89; $P < .001$). While crude in-hospital mortality was higher overall for women than for men (9.8% vs 5.9%, respectively; $P < .001$) irrespective of NSTEMI, after adjusting for covariates, sex was no longer an independent predictor of in-hospital mortality (adjusted OR for men vs women, 1.07; 95% CI, 0.94-1.22). Consistent with other studies, young women (aged 51 to 60 years) had statistically greater mortality than men of the same age.

The AMIS PLUS study confirms findings from other large studies that women tend to have higher risk ACS presentations than men, which results from delays in seeking treatment and older patient age at presentation. Furthermore, women are less likely to receive evidence-based therapies, including PCI, when presenting with ACS. However, once these significant differences are accounted for,

mortality rates are similar between the sexes, except for young women presenting with ACS. This is consistent with clinical trial data from such studies as the TACTICS-TIMI (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy—Thrombolysis in Myocardial Infarction)—18 trial that found that employing an early invasive approach in ACS patients with non-ST-segment elevation benefitted both sexes, although this finding is contrary to the FRISC II (Fragmin and Fast Revascularization During Instability in Coronary Artery Disease II) and RITA 3 (Third Randomized Intervention Trial of Unstable Angina) trials, which found no benefit of an early invasive approach in women.

The AMIS PLUS study reached several important conclusions that provide further insight into the management of ACS in women. It is well-described that women have different baseline characteristics compared with men at admission,

are less likely to be treated with evidence-based therapies, and are significantly less likely to undergo PCI. After adjusting for these differences, there were no significant differences in the rates of in-hospital mortality between men and women, overall. These results provide important impetus for strategies to increase awareness in women and physicians alike regarding the signs and symptoms of ACS in order to promote earlier presentation and diagnosis, consistent application of evidence-based approaches irrespective of sex, and rapid referral of both men and women for PCI. The one exception is that younger women remain at higher risk of mortality when presenting with MI. The AMIS PLUS study is not unique in this regard. Ongoing studies, such as the VIRGO (Variation In Recovery: Role of Gender on Outcomes of Young AMI Patients; <http://www.virgostudy.com>) study may shed light on sex-disparities in young women with ACS. •

References

1. American Heart Association. Heart Disease and Stroke Statistics—2005 Update. Dallas, Tex: American Heart Association; 2005.
2. Mueller C, Neumann FJ, Roskamm H, et al. Women do have an improved long-term outcome after non-ST-elevation acute coronary syndromes treated very early and predominantly with percutaneous coronary intervention: a prospective study in 1450 consecutive patients. *J Am Coll Cardiol*. 2002;40(2):245-250.
3. Stone GW, Grines CL, Browne KE, et al. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. *Am J Cardiol*. 1995;75(15):987-992.
4. Glaser R, Herrmann HC, Murphy SA, et al. Benefit of an early invasive management strategy in women with acute coronary syndromes. *JAMA*. 2002;288(24):3124-3129.
5. Angeja BG, Gibson CM, Chin R; Participants in the National Registry of Myocardial Infarction 2-3. Predictors of door-to-balloon delay in primary angioplasty. *Am J Cardiol*. 2002; 89(10):1156-1161.
6. Ayanian JZ, Epstein AM. Differences in the use of procedures between women and men hospitalized for coronary heart disease. *N Engl J Med*. 1991; 325(4):221-225.
7. Shah R, Wang Y, Masoudi FA, et al. Sex and racial differences in outcomes and guideline-based management of troponin-only-positive acute myocardial infarction in older persons. *Am J Geriatr Cardiol*. 2007;16(2):97-105.