

Comparison of outcomes in young versus nonyoung patients with ST elevation myocardial infarction treated by primary angioplasty

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Objectives We sought to determine in-hospital and intermediate-term outcomes of primary percutaneous coronary intervention (PCI) for ST elevation myocardial infarction (STEMI) in young adults.

Methods We reviewed 2424 consecutive patients treated with primary angioplasty for acute MI; 465 were aged 45 or less (young group) and 1959 were 46–74 years of age (nonyoung group). Clinical characteristics, in-hospital and intermediate-term outcomes of primary PCI were analyzed.

Results Compared with nonyoung patients, the young patients had significantly lower in-hospital and intermediate-term mortality (for in-hospital mortality: 5.4 vs. 1.2%, $P < 0.001$; for intermediate-term mortality: 5 vs. 1.3%, $P < 0.001$). By multivariate Cox regression analysis in all 2424 patients; cardiogenic shock, diabetes mellitus, anterior MI and unsuccessful procedure were independent predictors of both in-hospital and intermediate-term mortality whereas age [odds ratio (OR): 1.07, $P < 0.001$], female sex (OR: 1.88, $P = 0.04$), MI history (OR: 3.05, $P = 0.001$) and multivessel disease (OR: 2.15, $P = 0.01$) were independent predictors of only intermediate-term mortality.

Introduction

It is well recognized that old age is one of the important predictors of untoward clinical outcomes after acute myocardial infarction (AMI) with and without reperfusion therapy [1]. Although thrombolytic therapy has been shown to improve survival in elderly AMI patients when compared with placebo [2], many studies have shown lower mortality rates when these patients are treated with primary percutaneous coronary intervention (PCI) for AMI [3]. Therefore, direct PCI for AMI is now widely accepted as standard therapy for elderly patients. However, elderly patients (> 75 years) treated by primary PCI have a higher mortality in comparison with those below 75 years [4]. In contrast to this well-known impact of advanced age on clinical outcomes of primary PCI for AMI, the efficacy and outcomes of primary PCI in young adults have not been fully investigated.

The young group had lower unsuccessful procedure rates of primary PCI for STEMI (4.9 vs. 10.1%, $P = 0.001$).

Conclusion These results suggest that young adults who underwent primary PCI have favorable in-hospital and intermediate-term outcomes. Moreover, primary PCI for young adults with STEMI is safer, more feasible and effective than for a relatively older population. *Coron Artery Dis* 21:72–77 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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There have been many studies investigating AMI patients in different age groups [5–7]. However, these studies either included all patients of AMI or some have not the design of focusing on primary angioplasty [6–8]. There are also many reports indicating efficacy and clinical outcomes of primary angioplasty for AMI in different age groups but, in these reports, study populations are divided as patients below and above 75 years of age [4,9]. In contrast, there are young patients below 45 years old suffering from AMI with a percentage of 2–10% of all AMIs [10]. Taking into account the worse long-term prognosis in these young patients [11], early complete revascularization, which can salvage myocardium at risk and improve survival, has the highest importance. However, on the basis of the difference in etiology of AMI according to age [5,10], there is a possibility that the clinical effectiveness of PCI for young adults with AMI might be different from that of older patients.

With regard to the importance and lack of information in young patients undergoing primary PCI, our aim in this study was to compare the outcomes of primary PCI in young and nonyoung patients under the age of 75 years.

Methods

Patient populations

In a retrospective study, 2644 consecutive patients with ST elevation myocardial infarction (STEMI) presenting at the institution of Siyami Ersek Thoracic and Cardiovascular Surgery Center, Training and Research Hospital between October 2003 and March 2008 were included. The study inclusion criteria were as follows: ECG revealing STEMI, defined as more than 30 min of continuous typical chest pain and ST-segment elevation of at least 2 mm in two contiguous electrocardiography leads within 12 h of symptom onset or up to 18 h if there was evidence continuing ischemia or hemodynamic instability. A total of 220 patients above 74 years age were excluded in an attempt to overcome, as far as possible, the influence of increased age on the in-hospital and intermediate-term outcomes and to compose a specific study population without elderly patients. Therefore, the final study population consisted of 2424 patients. Patients were classified by age as young (≤ 45 years of age) and nonyoung (46–74 years of age) groups. The study protocol was approved by the Siyami Ersek Thoracic and Cardiovascular Surgery Center, Training and Research Hospital's Ethics Committee.

Analysis of patient data

The patients' demographic information, cardiovascular history and risk factors [smoking, hypercholesterolemia, hypertension, and diabetes mellitus (DM)] were obtained from medical records. Reperfusion time and door-to-balloon time were also determined.

Blood values, which were determined at hospital admission and on a daily basis during patient stay in hospital, were recorded from medical reports. A 12-lead ECG was recorded in each patient just after hospital admission, and also the MI type was recorded from ECGs.

Global left ventricular ejection fraction (EF) was measured by transthoracic echocardiography that was performed using a system V (GE Vingmed Ultrasound, Horton, Norway) with a 2.5 MHz phased-array transducer. The left ventricular EF was measured using modified Simpson's rule [12].

Coronary angiography, primary angioplasty, and stenting

All patients received chewable 300 mg aspirin, and clopidogrel (300 mg loading dose) before coronary angiography. Angiographic data of the patients were evaluated from catheter laboratory records. Emergency coronary angiography and angioplasty were performed by the

percutaneous femoral approach. Heparin (10 000 IU) was administered when arterial access was secured. After visualizing the left and right coronary arteries, 2.5 mg of nitrate was selectively injected into the infarct-related artery (IRA) to rule out possible coronary spasm. Angiographic assessments were made at the treating hospital by visual assessment. IRA was graded according to thrombolysis in MI classification [13]. Primary angioplasty including balloon angioplasty and/or stent implantation were performed only for IRA according to lesion type. For each procedure, interventional success at the acute phase is defined as reducing to less than 50% of stenosis for balloon angioplasty and less than 10–20% reduction of stenosis for stenting of the IRA with thrombolysis in myocardial infarction 2 or 3 flow just after primary angioplasty. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/h of intravenous heparin or 1 mg/kg/day of subcutaneous low molecular weight heparin were given; 100 mg aspirin and 75 mg clopidogrel were continued in all patients. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the operator. Concomitant medical treatment with β -blockers, angiotensin-converting enzyme inhibitors, and statins were prescribed according to American College of Cardiology/American Heart Association guidelines.

Definition

Time to reperfusion was measured as the time from symptom onset to the coronary reperfusion obtained with balloon inflation. Door-to-balloon time was defined as the time between hospital admission and balloon inflation. Cardiogenic shock was defined as prolonged hypotension (systolic blood pressure < 85 mmHg), with evidence of decreased organ perfusion caused by severe left ventricular dysfunction, right ventricular infarction, or mechanical complications of infarction. Patients were also evaluated according to Killip clinical examination classification [14]. Multivessel disease was defined as a presence of more than 50% lesion in at least two major epicardial coronary arteries or left main coronary artery lesion. Advanced heart failure was defined as New York Heart Association classification of at least 3. Renal failure was defined as a glomerular filtration rate less than $60 \text{ ml/min/1.73 m}^2$, which was estimated by the simplified modification of diet in renal disease equation [15]. Patient with DM was defined as the patient with documented DM using either oral hypoglycemic agents or insulin treatment at admission. Hypercholesterolemia was defined as total cholesterol of at least 200 mg/dl or use of cholesterol-lowering agents.

Cardiovascular death was defined as unexplained sudden death, death as a result of AMI, heart failure, and arrhythmia. Repeat target vessel revascularization (TVR) was defined as need for PCI or coronary surgery because of restenosis or reocclusion of the IRA. Reinfarction was defined as an increase in creatine kinase (CK) more than

twice the last value associated with CK-MB at least 10% of the total CK and ST segment reelevations. Cerebral vascular accident was defined as a permanent loss of neurological function caused by an ischemic vascular event.

Follow-up

Follow-up data were obtained from hospital records or by interviewing with (directly or by telephone) patients, their families, or their personal physicians. Major adverse cardiac events (MACE) were defined as cardiovascular death, reinfarction, repeat TVR (percutaneous or surgical). Only cardiovascular mortality was recorded. Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), atrioventricular block, transient pace intervention, intraaortic balloon usage, atrial fibrillation, major bleeding requiring at least 2 units blood transfusion were also recorded during the in-hospital period.

Statistical analysis

Quantitative variables were expressed as mean value \pm SD, and qualitative variables were expressed as percent (%). Comparison of parametric values between two groups was performed by means of two-tailed Student's *t*-test. Categorical variables were compared by the likelihood-ratio χ^2 test or Fisher's exact test. Backward stepwise multivariate Cox regression analysis, which included variables with *P* value less than 0.1, was performed to identify independent predictors of in-hospital and intermediate-term cardiovascular mortality.

Sex, age, DM, smoking habit, hypertension, renal failure (glomerular filtration rate < 60 ml/min/1.73 m²), MI history, PCI history, multivessel disease, unsuccessful procedure, anterior MI, cardiogenic shock, time-to-reperfusion more than 6 h were entered into the model. The cumulative survival curves for cardiovascular mortality were constructed using the Kaplan–Meier method with differences assessed with the log-rank test. A *P* value less than 0.05 was considered statistically significant. All statistical studies were carried out with SPSS program (version 15.0, SPSS, Chicago, Illinois, USA).

Results

Patient characteristics

The clinical characteristics and risk factors in the young and nonyoung groups' patients are summarized in Table 1. Among the 2424 patients treated with primary angioplasty (mean age 54.7 ± 10.2 years), 465 patients (19.1%) were classified as the young group; and 1959 patients (80.9%) were in the nonyoung group. Young patients remarkably consisted of male and more commonly had family history, anterior MI, hypercholesterolemia and were current smoker. Hypertension, DM, PCI and MI history, renal failure, advanced Killip class and cardiogenic shock at admission were significantly less prevalent in the young group.

Table 1 Patient characteristics

	Young (n=465)	Non-young (n=1959)	<i>P</i> value
Range, years	26–45	46–74	
Age, years (SD)	40.3 (4.2)	58.1 (8)	<0.001
Male, <i>n</i> (%)	433 (93.1)	1626 (83)	<0.001
Diabetes mellitus, <i>n</i> (%)	71 (15.2)	521 (26.5)	<0.001
Hypertension, <i>n</i> (%)	102 (21.9)	790 (40.3)	<0.001
Hypercholesterolemia, <i>n</i> (%)	195 (41.9)	644 (32.8)	<0.001
Current smoker, <i>n</i> (%)	349 (75)	1092 (55.7)	<0.001
Family history, <i>n</i> (%)	123 (26.4)	282 (14.3)	<0.001
PCI history, <i>n</i> (%)	24 (5.1)	171 (8.7)	0.01
MI history, <i>n</i> (%)	30 (6.6)	232 (11.8)	0.001
Anterior MI, <i>n</i> (%)	255 (54.8)	925 (47.2)	0.003
Admission cardiogenic shock, <i>n</i> (%)	9 (1.9)	88 (4.5)	0.01
Killip >1, <i>n</i> (%)	20 (4.4)	147 (7.5)	0.01
Reperfusion time, hours (SD)	3 (2.3)	3.3 (2.4)	NS
Door-to-balloon time, minutes (SD)	34 (20)	32 (25)	NS
GFR (MDRD) < 60 ml/min/1.73 m ² , <i>n</i> (%)	11 (2.4)	231 (11.8)	<0.001
Multivessel disease	188 (40.5)	1180 (60.5)	<0.001
Stent <i>n</i> (%)	392 (84.3)	1591 (81.2)	NS
Stent length, mm (SD)	18.9 (6.1)	19.4 (6.9)	NS
Stent diameter, mm (SD)	3.1 (0.4)	3.1 (0.3)	NS
LVEF, (%) (SD)	49.2 (9.9)	47.3 (11.4)	0.03
Glycoprotein IIb/IIIa inhibitors use, <i>n</i> (%)	222 (47.7)	949 (48.4)	NS
Infarct related artery			
Left main (%)	2 (0.4)	2 (0.1)	NS
Left anterior descending, <i>n</i> (%)	257 (55.2)	930 (47.4)	0.004
Left Circumflex, <i>n</i> (%)	63 (13.5)	260 (13.2)	NS
Right, <i>n</i> (%)	138 (29.6)	750 (38.2)	NS
By-pass graft, <i>n</i> (%)	3 (0.6)	15 (0.7)	NS
Intermediary artery, <i>n</i> (%)	2 (0.4)	2 (0.1)	NS

GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; MDRD, modification of diet in renal disease; MI, myocardial infarction; NS, not significant; PCI, percutaneous coronary intervention; SD, standard deviation.

Angiographic and procedural characteristics are also depicted in Table 1. Mean left ventricular EF was less in nonyoung patients ($P=0.03$). Patients in the young group were more likely to have single-vessel disease (59 vs. 39%, $P < 0.001$), whereas the nonyoung group more often had multivessel disease ($P < 0.001$). Left anterior descending coronary artery as a culprit lesion was more common in younger patients ($P=0.004$). In patients of the nonyoung group, postprocedural epicardial flow and procedural success were worse than young the group ($P < 0.001$). Number of stent use, stent length (18.9 ± 6.1 vs. 19.4 ± 6.9) and diameter (3.1 ± 0.4 vs. 3.1 ± 0.3) were similar in the two groups.

In-hospital outcomes

Table 2 presents the in-hospital adverse outcomes after primary angioplasty. In-hospital mortality rate was four-fold higher in patients of the nonyoung group than the young group (5.4 vs. 1.2%, $P < 0.001$). In-hospital mortality was also analyzed for cardiogenic shock in the whole study population, and was found to be at a rate of 54.7%. MACE were more frequent (9 vs. 5.3%, $P=0.009$) in patients of the nonyoung group than the young group. Compared with young group, patients in the nonyoung group had higher incidence of advanced heart failure, serious ventricular arrhythmia, and higher percentage of cardiopulmonary resuscitation, intra-aortic balloon pump use, need for transient pacemaker and blood transfusion.

Table 2 In-hospital and intermediate-term cardiac events

In-hospital cardiac events and complications	Young (n = 465)	Nonyoung (n = 1959)	P value
In-hospital mortality, n (%)	6 (1.2)	106 (5.4)	<0.001
Reinfarction, n (%)	13 (2.7)	32 (1.6)	NS
Target vessel revascularization, n (%)	19 (4)	82 (4.1)	NS
MACE, n (%)	25 (5.3)	178 (9)	0.009
Unsuccessful procedure, n (%)	23 (4.9)	196 (10.1)	0.001
Advanced heart failure, n (%)	26 (5.5)	282 (14.3)	<0.001
Time of hospital stay, days (SD)	6.3 (2.8)	7.2 (4.5)	<0.001
Cardiopulmonary resuscitation, n (%)	8 (1.7)	122 (6.2)	<0.001
Stroke, n (%)	2 (0.4)	12 (0.6)	NS
Serious ventricular arrhythmia, n (%)	14 (3.0)	144 (7.3)	0.01
New atrial fibrillation, n (%)	4 (0.8)	30 (1.5)	NS
Intra-aortic balloon pump, n (%)	8 (1.7)	120 (6.1)	<0.001
Renal failure requiring dialysis, n (%)	2 (0.4)	13 (0.6)	NS
Acute stent thrombosis, n (%)	7 (1.5)	15 (0.7)	NS
Major bleeding requiring BT	6 (1.2)	77 (3.9)	0.005
Complete AVB requiring PM, n (%)	7 (1.5)	83 (4.2)	0.005
Intermediate-term cardiac events	Young	Nonyoung	P value
Mortality, n (%)	^(a) n = 450 6 (1.3)	^(b) n = 1822 92 (5)	0.001
Reinfarction, n (%)	31 (6.8)	157 (8.6)	NS
Target-vessel revascularization, n (%)	57 (12.6)	318 (17.4)	0.02
MACE, n (%)	69 (15.3)	425 (23.3)	<0.001
Advanced heart failure, n (%)	14 (3.1)	138 (7.5)	0.001

AVB, atrioventricular block; BT, blood transfusion; MACE, major adverse cardiac events (cardiovascular death, reinfarction, target vessel revascularization); NS, not significant; PM, pace maker; SD, standard deviation.

^an = 450 for younger group (there is no follow-up for nine patient and six patient died in hospital).

^bn = 1822 for older group (there is no follow-up for 31 patient and 106 patient died in hospital).

Table 3 Independent predictors of in-hospital and intermediate term cardiovascular mortality in all study patients

	Odds Ratio (%95 CI)	P value
In-hospital mortality		
Cardiogenic shock	17.78 (5.53–57.16)	<0.001
GFR <60 ml/min/1.73 m ²	9.8 (3.80–25.26)	<0.001
Diabetes mellitus	5.37 (2.08–13.87)	0.001
Unsuccessful procedure	5.35 (1.82–14.94)	0.001
Anterior MI	3.15 (1.95–14.70)	0.03
Intermediate term mortality		
Cardiogenic shock	5.96 (2.03–17.52)	0.001
Unsuccessful procedure	3.72 (1.86–7.4)	<0.001
MI history	3.05 (1.6–5.82)	0.001
Sex, female	1.88 (1.02–3.59)	0.04
Multivessel disease	2.15 (1.14–4.05)	0.01
Anterior MI	1.85 (1.06–3.24)	0.02
Diabetes mellitus	1.84 (1.04–3.25)	0.03
Age	1.07 (1.03–1.10)	<0.001

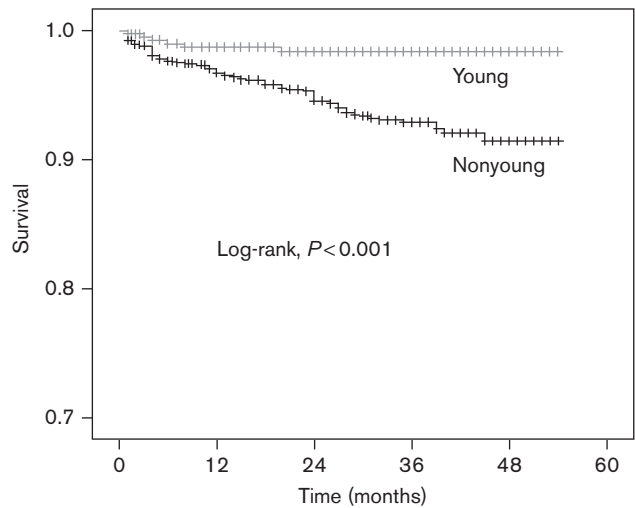
CI, confidence interval; GFR, glomerular filtration rate; MI, myocardial infarction.

Time of hospital stay was significantly lower in the young group. Independent predictors of in-hospital mortality are shown in Table 3.

Intermediate-term prognosis

The median follow-up time was 22 months for the young group and 21 months for the nonyoung group. Follow-up data after discharge were not obtained for nine patients in young group (1.9%) and 31 patients in the nonyoung group (1.5%). The Kaplan–Meier survival plot for

Fig. 1



Kaplan–Meier curve for intermediate-term survival according to young versus nonyoung patients.

cardiovascular death is presented in Fig. 1. The survival rate at the end of follow-up was 98.7% for young patients and 95% for nonyoung patients. Nonyoung patients had significantly higher incidence of intermediate-term cardiovascular mortality than younger patients (5 vs. 1.3%, *P* < 0.001). Intermediate-term mortality was also analyzed for cardiogenic shock in the whole study population, and found to be at a rate of 20.9%. TVR, advanced heart failure and MACE were significantly higher in patients of the nonyoung group (Table 2). Independent predictors of cardiovascular mortality were determined by Cox proportional hazard analysis in all study patients. These predictors of intermediate-term cardiovascular mortality are depicted in Table 3. Cardiogenic shock, unsuccessful procedure, multivessel disease, anterior MI, DM, and MI history, female sex and age were found to be independent predictors of intermediate-term cardiovascular mortality.

Discussion

This study, the largest to date examining the efficacy of primary angioplasty in young adults, produced several striking clinical implications. First, the in-hospital and intermediate-term mortality were lower in the young adult patients than the nonyoung patients. An important finding in this study was that in-hospital and intermediate-term MACE rates were substantially lower in the young adult patients. Therefore, young adults with STEMI undergoing primary PCI had relatively favorable in-hospital and intermediate-term clinical outcomes. Second, this study also identified that unsuccessful procedure was independently predictive of cardiac mortality. Third, age and female sex emerged as independent predictors of

intermediate-term mortality. Finally, young patients appear more likely to have less post-STEMI complications after the procedure.

On the basis of our hypothesis there is a difference in etiology of AMI between young and older patients, therefore it is possible that either the clinical effectiveness or the prognosis for young adults with STEMI undergoing primary PCI differ from that of older patients. In an attempt to exclude, as far as possible, the influence of increased age on outcome we did not enroll patients aged over 74 years.

Although our study population was completely different, there are some study results that can be compared with ours. For instance Sakai *et al.* [9] compared 30-day outcomes in patients younger than 75 years of age versus elder than 75 years of age with AMI treated by primary PCI. They found that older patients had a significantly higher incidence of cardiac mortality than younger patients. In our nonyoung population, the in-hospital cardiac mortality rate was greater than four times that of our young patients (1.2 vs. 5.4%, $P < 0.001$). A pooled analysis of the primary angioplasty in MI trials indicated a higher in-hospital mortality in patients aged > 75 years [4]. Different from those two studies, intermediate-term mortality was also shown to be increased in our non-young population (1.3 vs. 5%, $P = 0.001$) (Fig. 1). One of the few reports investigating young patients undergoing primary PCI found 6-month mortality rates lower in young patients [16]. Although there is information regarding long-term prognosis of young patients having AMI [11], a paucity of data exists about the long-term outcome after primary PCI in the specific subset of young patients. In this regard, our data also provide useful information with the longest follow up period, which was a median of 22 months in the young population.

Increased unsuccessful procedure, which was also an independent predictor of mortality, was seen more in the nonyoung population ($P < 0.001$). With aging, coronary arteries undergo remodeling of the vascular wall, including luminal enlargement, intimal, and medial thickening increased vascular stiffness and endothelial dysfunction [17]. These pathophysiology changes and presence of cardiac and noncardiac comorbidities contribute to the lower procedural success rates, necessitate more complex coronary intervention, and predispose to more in-hospital and long-term complication and mortality after primary angioplasty in the older patients [18,19].

Vaccarino *et al.* [20] first demonstrated a significant interaction between sex and age on mortality after AMI. Later on, another study indicated an increased in-hospital mortality among female patients younger than 75 years of age undergoing primary PCI [21]. With regard to age, a similar population was investigated in our study. However, female sex was an independent predictor only

for intermediate term mortality ($P = 0.01$). The preponderance of males in our study population may be the reason for this difference. In previous studies [9], age had been found as an independent predictor of in-hospital mortality in patients greater than 75 years whereas in our study, age was found as an independent predictor of intermediate-term mortality, but not in-hospital mortality.

In our study population, young patients, at present, had less advanced coronary disease ($P < 0.001$) and better left ventricular systolic function ($P = 0.03$). In addition, the rate of complications such as need for intraaortic balloon pump, advanced heart failure, serious ventricular arrhythmia, and cardiopulmonary arrest were lower in young patients after primary PCI.

In brief, this study provides evidence that young adults who underwent primary PCI for STEMI have favorable in-hospital and intermediate-term outcomes. Moreover, primary PCI for young adults with STEMI is safer, more feasible and effective than for a relatively older population.

Study limitations

This study carries the well-known limitation of the retrospective design, and in retrospective studies, selection biases can become potential problems. There is no consensus in the definition of age groups. We accepted patients aged 45 or less as young and patients between 46 and 74 years of age as nonyoung patients. This definition may be controversial.

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