啓明醫大學術誌 第28券 2號
Keimyung Med J
Vol. 28, No. 2, December, 2009

Three-year Clinical Outcomes of Elective Percutaneous Coronary Interventions in Elderly Patients

Hong Won Shin, M.D., Chang Wook Nam, M.D., Ji Hyun Son, M.D.,
Yun Kyeong Cho, M.D., Hyoung Seob Park, M.D., Hyuck Jun Yoon, M.D.,
Hyung Seop Kim, M.D., Seung Ho Hur, M.D., Yoon Nyun Kim, M.D., Kwon Bae Kim, M.D.

Division of Cardiology, Department of Internal Medicine, Keimyung University School of Medicine, Daegu, Korea

Abstract : Background: Because of co-morbidities, shorter life expectancy, higher risk for complications, and poor clinical outcomes of percutaneous coronary intervention (PCI), the treatment strategy for the elderly is often conservative. The aim of this study was to evaluate long-term clinical outcomes of elective PCI in selected elderly patients with coronary artery disease and compare with young patients in real world scenario.

Methods: The present study enrolled 1895 consecutive patients who underwent elective PCI from March 2003 to October 2007. The definition of elderly patient in this study was ≥ 75 year-old. Selected elderly patients (198 patients) who had more than 70 in Karnofsky score underwent elective PCI during study period. The outcomes of elderly group were compared to those of younger group (1697 patients) in the same period. The primary outcome is a composite of major adverse cardiac events (MACE) including cardiac death, myocardial infarction, and target vessel revascularization, 3 years after the index procedure.

Results: The elderly group (77.9 ± 2.8 year-old) had more female gender (52.0% vs. 33.2%, $p < 0.01$), lesser smoker (19.7% vs. 37.2%, $p < 0.01$), and more acute coronary syndrome (67.9% vs. 59.4%, $P = 0.04$), than the young group (60.3 ± 9.3 year-old). However, there was no significant difference in MACE (6.5% in elderly vs. 7.1% in younger group, $p = 0.81$) 3 years after index procedure.

Conclusions: Three-year clinical outcomes of elective PCI in selected elderly patients were acceptable, comparable to those of young patients.

Key Words : age, outcome, percutaneous coronary intervention

Corresponding Author: Chang Wook Nam, M.D., Ph.D., Division of Cardiology, Department of Internal Medicine, Keimyung University School of Medicine, 216, Dalseongno, Jung-gu, Daegu, 700-712 KOREA
Tel: +82-53-250-8040 E-mail: ncwcv@dsmc.or.kr

Introduction

The increase in the elderly population is associated with an increase in diseases, especially cardiovascular diseases. Cardiovascular disease is now one of the most common causes of death in older persons in a long-term health care facility [1]. Mortality and complications of percutaneous coronary interventions (PCI) are increased in elderly patients with chronic coronary artery disease (CAD) as compared to those in younger patients [2-5]. Because of co-morbidities, shorter life expectancy, higher risk for complications, and poor clinical outcomes of PCI, the treatment strategy for the elderly is often conservative [6]. There are limited data on the extent of procedural success, complications and long-term outcome in the elderly group. Most of the data come from national registries. However, recent studies have demonstrated good clinical outcomes in the selected older patients with ischemic heart disease by the managements with not only conservatively medication, but also invasively by means of invasive coronary revascularization [7-9]. The aim of this study was to evaluate three-year clinical outcomes of elective PCI in selected older patients with coronary artery disease and compare it with young patients in real world scenario.

Subjects and Methods

Patient population and study design

The patient population consisted of 1895 consecutive patients who successfully underwent elective PCI between March 2003 and October 2007 in a real world population at Keimyung University Dongsan Medical Center. Inclusion criteria included patients with a history of stable angina or acute coronary syndrome, and signs of myocardial ischemia. Patient should be able to selfcare (≥ 70% in Karnofsky score) [10]. Patients were not eligible for enrollment if they had undergone intervention in the setting of 1) cardiogenic shock, 2) emergency or primary PCI, and they had 3) intolerance or a contraindication to aspirin or clopidogrel, 4) a major life-threatening illness. This registry designed to record data pertaining to all PCI and to perform clinical follow-up at 30 days after index procedures, 12 months, 24 months and 36 months. Briefly, demographic, clinical, angiographic and procedural information of consecutive patients undergoing PCI were gathered on case report forms using standardized definitions for all fields. The definition of elderly patient in this study was ≥ 75 year-old. The patients were separated into two groups according to age. Selected 198 elderly patients underwent elective PCI, and 1697 younger patients, aged below 75 years, during this study.

Procedural details

Intracoronary stenting was performed with standard interventional techniques. Before the index procedure, all patients received oral aspirin (a loading dose of 200 mg) and clopidogrel (a loading dose of 300-600 mg before the procedure). Oral antiplatelet therapy during the study period followed guidelines recommending a combination of aspirin and clopidogrel for a minimum of 1 month for BMS and between 6 to 12 months

for DES. Intravenous boluses of heparin (100 U/kg) were administered before intervention and the dose adjusted to maintain an activated clotting time exceeding 250 seconds during the procedure. Peri-procedural use of glycoprotein IIb/IIIa inhibitors was left to operator's discretion.

Quantitative angiographic analysis

Coronary angiography was performed in multiple views after the intracoronary injection of nitroglycerin to control for vasomotor tone. All coronary angiograms were analyzed using standard definitions and measurements. Quantitative coronary angiography (Quantcor QCA, version 4.0, Pie Medical Imaging, Maastricht, Netherlands) was performed by a single experienced technician who was blinded to the type of stent deployed. Minimal luminal diameter (MLD), percent stenosis, and reference vessel diameter were measured. MLD was measured during diastole at the tightest lumen narrowing site pre-intervention and post-intervention from multiple projections.

Definitions and study outcomes

Lesions were also qualitatively classified by use of the modified American College of Cardiology/American Heart Association grading system. The primary outcome is a composite of major adverse cardiac events (MACE) three years after the index procedure. MACE in this study was defined as cardiac death, myocardial infarction (MI), and target lesion revascularization (TVR). The diagnosis of MI was based on either the development of new pathological Q waves in $\geq$ 2 contiguous electrocardiogram leads and/or elevation of CK-MB isoenzyme level > 2 times the upper limit of normal value. TVR included target lesion revascularization and bypass surgery of pertinent lesion. TVR was only based on the presence of clinical symptoms and/or signs of ischemia by cardiac stress test during the follow-up period. Revascularization of other coronary arteries was not evaluated.

Statistical analyses

Data are expressed as mean $\pm$ standard deviation (SD) for continuous variables and as percentages for discrete variables. Continuous variables were compared using Student's unpaired t-test. Categorical variables were compared using chi-square tests as appropriate. All calculated p-values were two-sided and differences were considered to be statistically significant when the respective p-values were < 0.05. We estimated cumulative incidence of primary outcome curve according to the Kaplan-Meier method and used the log-rank test to evaluate differences between groups. All statistical analyses were performed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Baseline Clinical and Angiographic Characteristics

The results of baseline characteristics are shown in Table 1. Mean age of the elderly group was 77.9 $\pm$ 2.8 year-old, and mean

average age of the younger group was aged 60.3 ± 9.3 year-old. Female was more frequently observed in the elderly group as compared to the younger group (52.0% vs. 33.2%, p < 0.01). Smoking was less frequently diagnosed in the elderly group (19.7% vs. 37.2%, p <0.01). But, the incidence of previous myocardial infarction or coronary intervention history and frequency of other coronary risk factors such as diabetes, hypertension, and dyslipidemia were not significantly different between two groups. Body mass index (BMI) was significantly lower in elderly group than in younger group (23.5 ± 3.2 kg/m^2 vs. 24.5 ± 3.3 kg/m^2, p < 0.05). Acute coronary syndrome was more frequently occurred in elderly group than in younger group (67.9% versus 59.4%, p < 0.05). Procedural and angiographic characteristics are shown in

Table 1. Comparison of Baseline Characteristics

	Elderly group (n=198)	Younger group (n=1697)	*P*-value
Age, yrs	77.9 ± 2.8	60.3 ± 9.3	< 0.01
Gender			
Male : female, %	48.0:52.0	66.8:33.2	< 0.01
Past history			
prior MI	15(7.3%)	141(8.3%)	0.29
prior PCI	17(11.0%)	151(11.4%)	0.87
prior CABG	4(2.6%)	20(1.5%)	0.32
Risk factor			
Diabetes mellitus	51(25.8%)	563(33.2%)	0.79
Hypertension	97(49%)	784(46.3%)	0.97
Dyslipidemia	27(13.6%)	282(16.7%)	0.28
Smoking	39(19.7%)	630(37.2%)	< 0.01
LVEF, %	54 ± 13	55 ± 13	0.42
Creatinine, mg/dl	1.3 ± 1.3	1.3 ± 1.3	0.92
BMI, kg/m^2	23.5 ± 3.2	24.5 ± 3.3	< 0.01
Clinical Diagnosis			
Stable angina	52(32.1%)	566(40.6%)	0.04
Acute coronary syndrome	110(67.9%)	827(59.4%)	

MI: Myocardial Infarction, PCI: Percutaneous Coronary Intervention, CABG: Coronary Artery Bypass Graft, LVEF: Left Ventricle Ejection Fraction, BMI: Body Mass Index, NSTEMI: Non ST-segment Elevation Myocardial Infarction, STEMI: ST-segment Elevation Myocardial Infarction.

Table 2. Comparison of Procedural and Angiographic Characteristics

	Elderly group (n=198)	Younger group (n=1697)	*P*-value
Number of diseased vessel			
SVD/MVD, %	51.6/48.4	35.0/65.0	< 0.01
Lesion Length, mm	26.9 ± 14.9	26.0 ± 15.1	0.45
preDS, %	85.1 ± 9.2	84.4 ± 9.5	0.32
preMLD, mm	0.4 ± 0.3	0.5 ± 0.3	0.08
pre reference VD, mm	3.2 ± 0.4	3.2 ± 0.4	0.24
postDS, %	9.2 ± 3.7	8.8 ± 3.7	0.17
postMLD, mm	2.9 ± 0.4	3.0 ± 0.4	0.18
Deployed stent			
BMS/DES, %	28.2/71.8	30.7/69.3	0.53
Post PCI medication			
Beta-blocker, %	74.2	81.8	0.03
ACE inhibitor, %	46.3	48.1	0.62
Statin, %	57.8	55.7	0.67

SVD: Single Vessel Disease, MVD: Multiple Vessel Disease, DS: Diameter Stenosis, MLD: Minimal Luminal Diameter, VD: Vessel Diameter, BMD: Bare Metal Stent, DES: Drug Eluting Stent.

Table 2. In the extent of coronary disease, multi-vessel disease was more frequently in elderly group (2.0 ± 0.8 vs. 1.7 ± 0.8, $p < 0.05$). Other angiographic findings were not significantly different between the two groups.

Clinical outcomes

Cumulative adverse cardiac event rates at 30 days, 12, 24 and 36 months are summarized in Tables 3. At 30-day follow-up, there were no significant differences in overall major adverse cardiac event rates (1.5% in elderly group vs. 1.1% in younger group, $p = 0.96$). Thirteen cases of cardiac death were observed. Likewise, at 12-month follow-up, there were no significant differences in major adverse cardiac event rate (4.3% in elderly group vs. 4.4% in younger group, $p = 0.95$), and in all cause of death (3.3% in elderly group vs. 2.0% in younger group, $p = 0.27$). And there were no significant differences in major adverse cardiac events at the end of 24 months follow-up, irrespective of the age (5.2 % in elderly group, 5.6 % in younger group, $p = 0.83$). No differences emerged with regard to cardiac death, myocardial infarction, and TVR. Incidence of MACE after PCI at 36 months was 9 in elderly group and 93 patients in younger group (6.5% vs. 7.1%, p=0.808).

Table 3. Comparison of Cumulative Clinical Outcomes

	Elderly group (n=196)	Younger group (n=1697)	*P*-value
One Month			
Death			
All cause of	2(1.0%)	15(0.9%)	0.85
Cardiac	1(0.5%)	12(0.7%)	0.75
Myocardial infarction	1(0.5%)	6(0.4%)	0.73
TVR	1(0.5%)	6(0.4%)	0.73
MACE	3(1.5%)	18(1.1%)	0.96
One Year			
Death			
All cause of	6(3.3%)	33(2.0%)	0.27
Cardiac	1(0.5%)	15(0.9%)	0.61
Myocardial infarction	2(1.1%)	12(0.7%)	0.60
TVR	6(3.3%)	56(3.4%)	0.91
MACE	8(4.3%)	73(4.4%)	0.95
Two Year			
Death			
All cause of	9(5.2%)	48(3.1%)	0.15
Cardiac	2(1.1%)	19(1.2%)	0.93
Myocadial infarction	2(1.1%)	18(1.2%)	0.98
TVR	6(3.4%)	66 (4.3%)	0.61
MACE	9(5.2%)	86(5.6%)	0.83
Three Year			
Death			
All cause of	10(7.2%)	53(4.0%)	0.08
Cardiac	2(1.5%)	20(1.5%)	0.95
Myocardial infarction	2(1.5%)	19(1.4%)	0.99
TVR	6(4.4%)	72(5.5%)	0.59
MACE	9(6.5%)	93(7.1%)	0.81

MACE: Major Cardiac Adverse Events, TVR : Target Vessel Revascularization.

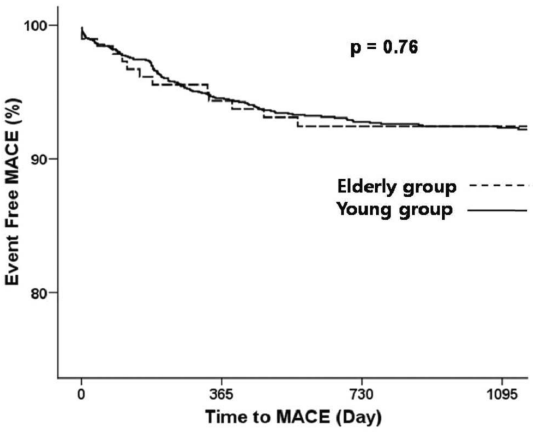

Fig. 1. Kaplan-Meier estimates of cumulative freedom from composite MACE including death, MI, and TVR at three-year follow-up in patients who underwent elective percutaneous coronary intervention, compared elderly patients (dotted line) with younger patients (solid line).

There were no differences between two groups, as well. Kaplan-Meier estimates of cumulative freedom from MACE during the three-year follow-up are shown in Fig. 1.

Discussion

The major findings in the current study are 1) elective PCI in patients with documented ischemic heart disease was associated with excellent three-year clinical outcomes, and 2) there were no significant differences in long-term clinical outcomes of PCI between elderly and younger patients, if PCI is performed in selected cases. Although the elderly group had an increased tendency of all cause of death, cardiac death was not different.

There were several different major cardiovascular risk factors in this study, such as gender, history of smoking, and clinical presentations. With increasing age, the gender composition of patients with ischemic heart disease was changed. Whereas in middle-aged patients, men were dominant, in patients aged 75 and over, the definite predominance of women revealed. Female predominance among the elderly is the result of their longer lifespan in comparison to men [11]. Because of female usually had lower smoking rate than men, elderly group was lower smoking rate than young age group in Korea. Elderly patients are also more likely to have silent or unrecognized MIs compared to younger patients. These facts often result in delays in MI diagnosis in the elderly. Therefore elderly patients had more frequently acute coronary syndrome and multi-vessel disease. However, after controlling for these different characteristics using a multivariate regression model, age could not prove their adverse effect on three-year clinical outcomes.

The population older than 75 years is the fastest growing segment in Korea [9]. There is a high prevalence of coronary artery disease in this group with an increased need of PCI and an increasing gradient of mortality [11,13]. All cause of mortality was slightly higher in elderly without statistical significance in current study, However, if we excluded noncardiac death related to co-morbidities, cardiac death was similar between two groups. There was no difference between two groups in short term outcomes and long term outcomes. In previous studies [11,14,15], mortality rates were not affected by treatment strategy, either medication or revascularization, but the latter gave more relief of angina symptoms in elderly [11,14,15]. In a health economic study before the drug-eluting stent (DES) era,

reported Clark, the repeat revascularization rate was 16.9% in nearly 10,000 patients older than 65 years [13], In comparison, the revascularization rate in our trial is remarkably low, and the TVR rate for elderly patients in this study was nearly similar to the data of randomized DES trials [17-19]. The emphasis of aging as poor cardiovascular risk factor is strongly related with co-morbidities and historical data about high rate of restenosis and revascularization before the DES era. The penetration rate of DES was more than two thirds of all studied patients. The high rate of DES usage in this study may partially explain the similar outcomes between two age-different groups. The other important factors, which can affect current result, are selection guidelines of PCI for elderly patients. Elderly patients who could care for themselves were included in this study. Biologic activities can be different from their presented age. Emergency or primary PCI were also excluded and only elective PCI was enrolled in this study. These factors can also affect good long-term clinical outcomes, especially in the elderly.

As expected, elderly patients undergoing PCI are at higher risk than the younger population, showing an increased mortality probably due to the lower life expectancy and the substantially greater burden of co-morbidities. The MACE after 3 years in this selected population showed no difference to younger patients, providing strong evidence that elective PCI in the elderly is feasible and associated with a low rate of repeat TVR, as comparable to younger patients, and should be recommended to avoid the procedural risk of repeat revascularization. This study demonstrated that, if feasible, old age is not always a contraindication of PCI. There are important limitations to the findings of this study because of its retrospective nature; the fact that the study population was included consecutively according to the study protocol might help mitigate biases. Several different characteristics existed between the two groups. However, after controlling for these differences using a multivariate regression model, aging could not prove their adverse effect on three-year clinical outcome. Second, according to inclusion criteria, we did not include elderly patients with coronary artery disease who did not undergo PCI. This study can have an inherent selection bias. The authors would like to emphasize the value of PCI in selected elderly patients.

Conclusion

Three-year clinical outcomes of elective percutaneous coronary intervention in selected elderly patients were excellent, comparable to those of younger patients.

Acknowledge

This work was supported by the Korea Institute of Medicine grant.

References

1. Aronow WS. Clinical causes of death of 2372 older persons in a nursing home during 15-year follow-up. *J Am Med Dir Assoc* 2000;**1**:95-6.
2. Nasser TK, Fry ETA, Annan K, Khatib Y, Peters TF, VanTassel J, *et al*. Comparison of six-month outcome

of coronary artery stenting in patients <65, 65-75, and >75 years of age. *Am J Cardiol* 1997;**80**:998-1001.

3. De Gregorio J, Kobayashi Y, Albiero R, Reimers B, Di Mario C, Finci L, *et al*. Coronary artery stenting in the elderly: short-term outcome and long-term angiographic and clinical follow-up. *J Am Coll Cardiol* 1998;**32**:577-83.
4. Wennberg DE, Malenka DJ, Sengupta A, Lucas FL, Vaitkus PT, Quinton H, *et al*. Percutaneous transluminal angioplasty in the elderly: epidemiology, clinical risk factors, and in-hospital outcomes. *Am Heart J* 1999;**137**:639-45.
5. Batchelor WB, Anstrom KJ, Muhlbaier LH, Grosswald R, Weintraub WS, O'Neill WW, *et al*. Contemporary outcome trends in the elderly undergoing percutaneous coronary interventions: results in 7472 octogenarians. *J Am Coll Cardiol* 2000;**36**:723-30.
6. Wilbert SA. Treatment of unstable angina pectoris/non ST segment elevation myocardial infarction in elderly patients. *J Gerontol A Biol Sci Med Sci* 2003;**58**:927-33.
7. Nicolau JC, Lemos PA, Wajngarten M, Giraldez RR, Serrano CV Jr, Martinez EE, *et al*. The role of invasive therapies in elderly patients with acute myocardial infarction. *Clinics (Sao Paulo)* 2009;**64**:553-60.
8. Harpaz D, Rozenman Y, Behar S, Boyko V, Mandelzweig L, Gottlieb S. Coronary angiography in the elderly with acute myocardial infarction. *Int J Cardiol* 2007;**116**:249-56.
9. Jong Cheol P, Myung Ho J, Ju Han K, Sung Hee K, Jun Yoo K, Youl B, *et al*. Clinical Characteristics of Coronary Interventions in Old Aged Patients. *Korea Circ J* 1998:**28**:256-1.
10. Buccher G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution) enrolment criteria. *Eur J Cancer* 1996 Jun; **32A**(7):1135-41.
11. Kaiser C, Kuster GM, Erne P, Amann W, Naegeli B, Osswald S, *et al*. Risks and benefits of optimized medical and revascularisation therapy in elderly patients with angina-on-treatment analysis of the TIME trial. *Eur Heart J* 2004;**25**:1036-42.
12. Korean national statistical office. 2006 Oct; 1-37. 2006 Korean old age statistics.
13. Aronow WS, Ahn C, Gutstein H. Prevalence and incidence of cardiovascular disease in 1,160 older men and 2,464 older women in a long-term health care facility. *J Gerontol Med Sci* 2002;**57A**:45-6.
14. A. Gunal WRM, Aengevaeren HR, Gehlmann JE, Luijten JE, Bos JS, Verheugt FW. Outcome and quality of life one year after percutaneous coronary interventions in octogenarians. *Neth Heart J* 2008;**16**:117-22.
15. McKellar SH, Brown ML, Frye RL, Schaff HV, Sundt TM 3rd. Comparison of coronary revascularization procedures in octogenarians: a systematic review and meta-analysis. *Nat Clin Pract Cardiovasc Med* 2008 Nov;**5**(11):738-46.
16. Clark MA, Bakhai A, Lacey MJ, Pelletier EM, Cohen DJ. Clinical and economic outcomes of percutaneous coronary interventions in the elderly. *Circulation* 2004;**110**:259-64.
17. Holmes Jr DR, Leon MB, Moses JW, Popma JJ, Cutlip D, Fitzgerald PJ, *et al*. Analysis of 1-year clinical outcomes in the SIRIUS trial. A randomized trial of a sirolimus-eluting stent versus a standard stent in patients at high risk for coronary restenosis. *Circulation* 2004;**109**:634-40.
18. Schofer J, Schluter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, *et al*. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, andomised controlled trial (E-SIRIUS). *Lancet* 2003;**362**:1093-9.
19. Schampaert E, Cohen EA, Schluter M, Reeves F, Traboulsi M, Title LM, *et al.* The Canadian study of the sirolimus-eluting stent in the treatment of

patients with long de novo lesions in small native coronary arteries (C-SIRIUS). *J Am Coll Cardiol* 2004;**43**:1110-5.