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Original Article

Clinical characteristics and prognosis of very elderly patients with coronary artery disease

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Abstract: *Background*: Elderly patients with coronary heart disease (CHD), especially the super-elderly, have been significantly increasing in number and are being referred for percutaneous coronary intervention. *Methods*: The present study is a retrospective analysis conducted in Anzhen Hospital from January 2007 to December 2015. The very elderly group, composed of 443 CHD patients aged ≥80 years, were compared with a control group consisting of 400 matching patients aged ≤65 years. Comparisons conducted between the 2 groups included the medical history, clinical characteristics, features of coronary artery lesions, and clinical events. *Results*: There were higher rates of old myocardial infarction, revascularization, and most complications (both cardiogenic and non-cardiogenic) in the elderly group than in the control group. Meanwhile, the levels of low-density lipoprotein-cholesterol and hemoglobin, and the left ventricular ejection fraction in the elderly group were lower than that in the control group (all $P<0.05$). Furthermore, fasting glucose and serum creatinine in the elderly group were higher than those in the control group ($P<0.05$). The very elderly patients had more multivessel lesions, left main involvement, and chronic total occlusions than the control group (all $P<0.05$). The rates of in-hospital bleeding and death were not different between the 2 groups, but at 1 year, the rates of cardiovascular re-hospitalization, all-cause mortality, and cardiovascular mortality in the very elderly group were higher than that in the control group (all $P<0.05$). *Conclusion*: Very elderly CHD patients had more risk factors, more complex coronary artery lesions, worse prognosis, and more complications than younger patients.

Keywords: Elderly, coronary artery disease, coronary angiography, clinical characteristic, prognosis

Introduction

During the recent four decades, the morbidity of patients with coronary heart disease (CHD) has significantly risen, with the rapid development of economy and the accelerated build-up of adverse lifestyle. In contrast, the mortality of CHD has prominently decreased, which is primarily attributed to the tremendous advancement of theory and technology in the cardiovascular fields, especially in interventional diagnosis and treatment. As the main suffering population, the number of elderly CHD patients, particularly the very elderly, has been significantly increasing; this population has been receiving great attention in China since the country has rapidly entered the aged society [1]. Moreover, elderly patients make up a large portion of those referred for percutaneous coronary intervention (PCI) [2, 3]. Based on these, the present study was designed to retrospectively elucidate the clinical characteristics of very elderly CHD patients, with ages more than 80 years, which may provide evidence for clinical decision making in this population.

Materials and methods

Study population

The present study retrospectively included 443 CHD patients aged ≥80 years (very elderly group) and 400 patients aged ≤65 years (control group), who underwent coronary imaging evaluation with coronary angiography (CAG) from January 2007 to December 2015 in Anzhen Hospital. The diagnostic criteria for CHD were based on related guidelines [4, 5]: transient or persistent chest pain or discomfort while laboring or resting; dynamic changes in the ST-T segment on electrocardiogram; reversible changes in myocardial biomarkers in

patients with acute myocardial infarction (AMI); and/or evidence of myocardial infarction (acute or chronic) on echocardiography or nuclear imaging. Coronary stenosis was defined as a decrease of more than 50% in luminal diameter of a major coronary artery on angiography. Inclusion criteria were as follows: (1) age ≥80 years for the very elderly group, or age ≤65 years for the control group; (2) patients diagnosed with CHD based on the abovementioned criteria; (3) patients with CAG indicating at least 1 major coronary artery with a diameter stenosis ≥50%; and (4) those with complete medical records. Excluded patients were: (1) those with myocardial ischemia derived from non-atherosclerotic coronary artery malformations, such as Kawasaki Disease or Takayasu's arteritis; (2) those with other coexisting disease requiring cardiac surgery; (3) those suffering from severe infection; (4) those suffering from malignant tumors; (5) those who did not undergo CAG; and (6) those with incomplete medical records. The study protocol was approved by the Institutional Review Board at Anzhen Hospital, and informed consent was obtained, as patient privacy must always be observed. This work was carried out in accordance with The Code of Ethics of the World Medical Association for experiments involving human subjects and was approved by the Anzhen Hospital Ethics Board.

Method

The analyzed clinical characteristics include the following: age, gender, body mass index (BMI), smoking history, family history of CHD, history of angina, primary hypertension, type 2 diabetes, typical chest pain, and other concomitant cardiogenic or non-cardiogenic diseases.

Blood tests were performed on the second morning of admission. The indices included in the final statistical analyses were the following: total cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), serum creatinine (SCr), hemoglobin, fasting glucose, and plasma fibrinogen.

Left ventricular end diastolic diameter (LVDD) and left ventricular ejection fraction (LVEF) were evaluated by ultrasonic cardiogram (Philips, Amsterdam, The Netherlands).

Every patient underwent CAG after admission into the hospital. The procedure was as follows: CAG was performed by insertion of a multifunctional catheter through the radial artery or by the Judkins method through the femoral artery. The evaluation was performed by 2 experienced chief physicians using visual measurement. The coronary artery system was divided into 3 main arteries: the left anterior descending artery (LAD), the left circumflex artery (LCX), and the right coronary artery (RCA). Lesions in the branches, such as the diagonal or the marginal branches, were ascribed to the main artery to which they belong. Stenosis was defined as decrease in luminal diameter of ≥50%. A left main coronary artery (LM) lesion was defined similarly. According to the number of affected arteries and branches, the lesions were divided into single-vessel, double-vessel, or multi-vessel (three or more vessels) lesions. Both the interventional strategy and stent selection were left to the discretion of the operator in all procedures. At our institution, the majority of procedures are performed by either the femoral or the radial routes. Clopidogrel was given as indicated by contemporary guidelines (loading dose of 300 or 600 mg, maintenance dose of 75 mg/day for 6 weeks to 12 months, depending on stent type and clinical indication. Angiographic success was defined as <20% residual stenosis in the target vessel. Multi-vessel disease was defined as the presence of a 70% lesion in 2 major coronary arteries. Renal insufficiency pre-procedurally was defined as a creatinine clearance of <60 ml/min.

Every subject received a 12-month follow-up by telephone or outpatient visit after release from the hospital. To ensure accurate assessment of clinical outcomes, additional information was obtained from visits or telephone/mail contacts with patients or their family members, from their local physicians, and from medical records obtained from other hospitals, as necessary. All-cause death, cardiovascular death, and cardiovascular re-hospitalization were recorded.

Statistics

Measurement data were described as mean ± standard deviation and t-test was used for comparisons between the 2 groups. Frequencies were used for categorical variables. Categorical data were compared using Chi-square test. A value of $P<0.05$ was considered to be statistically significant. Logistic regression analysis

Table 1. The demographic characteristics of the 2 groups of patients

	Super-elderly group n=443 (%)	Control group n=400 (%)	P	χ^2/t
Sex (F/M)	155/288	170/230	0.030	4.69
Age (yrs)	81.5±2.1	53.6±11.2	0.000	51.44
BMI (kg/m^2)	25.0±3.1	27.4±2.1	0.000	-13.02
Smoking	155 (35.0)	220 (55)	0.000	33.30
Angina pectoris	287 (64.8)	308 (77.0)	0.000	14.52
OMI	153 (34.5)	79 (19.8)	0.000	22.31
Previous PCI	128 (28.9)	84 (21.0)	0.011	6.55
Previous CABG	41 (9.3)	21 (5.3)	0.036	4.38
NYHA III-IV	68 (15.3)	25 (6.3)	0.000	16.82
Hypertension	310 (70.0)	220 (55.5)	0.000	19.56
Diabetes mellitus	157 (35.4)	92 (23.0)	0.000	15.04
Stroke history	164 (37.0)	56 (14.0)	0.000	56.57
Renal insufficiency	62 (14.0)	21 (5.3)	0.000	17.14
Chronic Hepatopathy	12 (2.7)	4 (1.0)	0.118	2.44
Anemia	59 (13.3)	17 (4.3)	0.000	19.98
COPD	24 (5.4)	9 (2.3)	0.029	4.80
Malignant tumor	12 (2.7)	5 (1.3)	0.208	1.59

BMI, body mass index; OMI, old myocardial infarction; PCI, Percutaneous coronary intervention; CABG, coronary artery bypass grafting; NYHA, New York Heart Association (classification); COPD, chronic obstructive pulmonary disease.

Table 2. The clinical characteristics of the 2 groups of patients

	Super-elderly group n=443	Control group n=400	P	t
LDL-C (mmol/L)	2.4±1.3	2.9±1.5	0.000	-5.18
HDL-C (mmol/L)	1.0±0.3	1.0±0.4	1.0	0
LVEDd (mm)	48±10	46±8	0.001	3.18
LVEF (%)	54±11	58±14	0.000	-4.63
Fasting glucose (mmol/L)	6.7±3.1	6.1±2.9	0.004	2.89
SCr (μmol/L)	142±57	102±35	0.000	12.12
Hemoglobin (g/L)	10.1±1.9	11.5±2.0	0.000	-10.42

LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; LVEDd, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; SCr, serum creatinine.

was performed to identify independent predictors of 12-month mortality by entering all variables. All data recordings and statistical analyses were performed using SPSS 22.0 software (IBM Corporation, New York, USA).

Results

Clinical characteristic

Between January 2007 and December 2015, the clinical, angiographic, procedural, and outcome variables of 843 consecutive patients who underwent a PCI procedure at Anzhen Hospital were entered into a retrospective analysis database. Baseline demographics, and clinical and angiographic data for patients are shown in **Tables 1**-**3**, respectively. As shown in **Table 1**, the very elderly group, was composed of 288 males and 155 females, with a mean age of 81.5±2.1 years. Compared with the younger cohort, very elderly patients had a greater burden of comorbidities, including previous myocardial infarction (MI), hypertension, diabetes mellitus, stroke, renal insufficiency, left ventricular (LV) systolic dysfunction, and pulmonary disease. The gender, age, BMI, history, and concomitant disease proportion between the 2 groups were statistically significant (P<0.05), except in terms of chronic hepatopathy and malignancy (P>0.05).

The echocardiography showed that, in comparison to the control group, the elderly group had a significantly lower LVEF and higher LVDD (P<0.05). The levels of fasting glucose and SCr in the elderly group were higher than in the control group, while the levels of low-density lipoprotein-cholesterol and hemoglobin were lower (P<0.01) (**Table 2**).

Coronary artery lesion

Very elderly patients had significantly more complex disease than the younger patients, reflected in a greater number of left mainstem involvement (n=70, 15.8%), chronic total occlusions (n=125, 28.2%), and multi-vessel disease (n=231, 52.1%). Comparing with the control group, the elderly group had fewer single-ves-

Table 3. Coronary artery lesions in the 2 groups of patients

	Super-elderly group n=443 (%)	Control group n=400 (%)	P	X^2
Single-vessel lesion	66 (14.9)	155 (38.8)	0.000	60.60
Double-vessel lesion	146 (33.0)	140 (35.0)	0.580	0.31
Multi-vessel lesion	231 (52.1)	98 (24.5)	0.000	66.35
LM lesion	70 (15.8)	32 (8.0)	0.001	11.31
CTO	125 (28.2)	82 (20.5)	0.012	6.35

LM, left main coronary artery; CTO, chronic total occlusion.

sel and double-vessel lesions, as shown in **Table 3**.

In-hospital outcomes

The in-hospital bleeding rate for very elderly patients was 1.1%, while for the control, it was 0.3%. The in-hospital mortality rate for very elderly patients was 4%, while there were no mortalities for the control group. No significant difference was seen between the 2 groups (P>0.05).

Prognosis

In the very elderly group, there was an incremental increase in 12-month all-cause mortality (n=60, 13.5%) and cardiovascular death (n=18, 4.1%) compared with the control group (both P<0.05). Furthermore, the rate of re-hospitalization due to cardiovascular disease in the very elderly group was also higher than in the control group (P<0.05), as shown in **Table 4**. Multivariate logistic regression analysis was performed to evaluate the effect of age and other variables on 12-month cardiovascular death in **Table 5**. After adjustment, very old age was predictive of 12-month mortality (OR, 4.19; CI, 1.41-12.50, P=0.010), However, its effect was several-fold lower than that of other variables. The presence of severe LV systolic dysfunction (New York Heart Association or NYHA functional class III-IV) was the single strongest predictor of 12-month mortality (OR, 16.44; CI, 6.69-40.39, P<0.0001). Pre-existing renal insufficiency, myocardial infarction, and previous PCI or coronary artery bypass grafting (CABG) predicted higher mortality, as did markers of disease complexity (left mainstem stenosis).

Discussion

CHD is a multifactorial disease; possible risk factors include hypertension, diabetes, dyslipidemia, smoking, obesity, lack of exercise, and family history of cardiovascular disease, among others. Elderly patients represent an increasing proportion of those referred for PCI, and yet, they are routinely excluded in randomized clinical trials of cardiovascular disease and its management [6]. Several large registries have examined outcomes following intervention in very elderly patients aged over 80 years [7-9], but few studies focused on the Chinese population. Very elderly patients formed a small, but not insignificant, proportion of patients undergoing PCI. A study showed that among 152,373 patients who received PCI, 64.64% were <70 years, 23.83% were 70-79 years, 7.85% were 80-84 years, 3.09% were 85-89 years, and 0.58% were >90 years, indicating that the proportion of elderly patient who receive PCI has increased [10].

The present study provides useful insights into outcomes following PCI in the very elderly population, a group in whom data are limited. Very elderly patients have more extensive baseline cardiovascular disease, more complex coronary lesions, increased cardiovascular mortality, and higher re-hospitalization rates compared to patients younger than 65 years. This study showed that smoking history, BMI, and angina history in the elderly group were lower than in the control group, but that the rate of accompanying diseases, both cardiogenic and non-cardiogenic, was higher. These findings are consistent with previous studies on elderly patients [10]. This result indicates that with age, patients tend to develop multiple diseases, which is probably related to the worse prognosis of elderly patients. In our study, the proportion of females in the elderly group was lower than in the control group. This phenomenon is different from large-scale surveys in our country [1], maybe because the sample size is relatively small. The baseline information showed that LDL-C, glucose, and SCr in the elderly group were higher than in the control group, and cardiac function was worse. This result indicates that the elderly group had more CHD-associated risk factors, which is a similar finding to that of a previous study [10].

The technology of PCI has been advancing continuously and the proportion of CHD patients

Table 4. Prognosis of the 2 groups of patients

	Super-elderly group n=443 (%)	Control group n=400 (%)	P	χ^2
In-hospital bleeding	5 (1.1)	1 (0.3)	0.27	1.22
In-hospital death	4 (0.9)	0 (0)	0.16	1.97
12-month follow-up	377 (85.1)	348 (87.0)		
All-cause death	60 (15.9)	13 (3.7)	0.000	26.87
Cardiovascular death	18 (4.8)	4 (1.1)	0.010	6.60
Cardiovascular re-hospitalization	69 (18.3)	20 (5.7)	0.000	23.79

Table 5. Multivariate correlates of 12-month cardiovascular mortality

Variable	Odds Ratio	95% CI	P
Female	0.24	0.07-0.83	0.024
Age >80	4.19	1.41-12.50	0.010
Smoking	1.56	0.67-3.66	0.305
Angina pectoris	1.90	0.64-5.68	0.249
OMI	3.28	1.40-7.70	0.006
Previous PCI	2.55	1.09-6.0	0.031
Previous CABG	3.08	1.01-9.39	0.048
NYHA III-IV	16.44	6.69-40.39	0.000
Hypertension	0.70	0.30-1.64	0.410
Diabetes mellitus	1.38	0.57-3.32	0.474
Stroke history	0.28	0.06-1.19	0.095
Renal insufficiency	12.68	5.29-30.37	0.000
Anemia	2.3	0.76-7.02	0.142
Multi-vessel lesion	1.91	0.81-4.47	0.138
LM lesion	8.02	3.38-19.03	0.000
CTO	1.16	0.45-2.99	0.759

MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NYHA, New York Heart Association (classification); LM, left main coronary artery; CTO, chronic total occlusion.

who are treated with PCI has been steadily rising, which allows us to know more about the coronary lesion features of elderly patients. Although randomized controlled trials have, for the most part, excluded very elderly patients, PCI in this age group has been validated for the relief of chronic stable angina [11], in the setting of both acute coronary syndromes [12] and primary PCI [13, 14]. Kasanuki et al. [15] analyzed 3,021 AMI patients from 17 health centers in Japan, beginning in 1999 to 2001. In the report, 851 (28.2%) were >76 years, and 1,755 (58.1%) were treated with PCI. The CADILLAC trial also demonstrated that 13.1% of patients were >75, and the success rate of PCI was similar in the elderly and in younger patients. Elderly patients can thus significantly benefit from stent implantation [16]. The CAG results in our study showed that, the lesions in the elderly group were mostly multi-vessel and CTO lesions, and that LM lesions were more common in the elderly than in the control group. This result explains that features of coronary lesions can predict the rate of major adverse coronary events (MACE).

The TIME study [11] included 301 CHD patients, with a baseline age of 80±4 years. They were randomly divided into an invasive therapy group (n=153) and an optimal medical therapy group (n=148). The study demonstrated that the survival rate of the 2 groups were 91.5% vs. 95.9% in 6 months, 89.5% vs. 93.9% in 1 year, 70.6% vs. 73.0% in 4.1 years (P>0.05). The mortality was significantly higher in patients who were ≥80, those with previous heart failure, LVEF ≤45%, ≥2 complications, and those who didn't receive revascularization during the first year. Revascularization within 1 year can obviously improve the mortality rate of each group. Both of the therapies can improve the anginal symptoms and quality of life, but the invasive therapy group had a higher event-free survival rate. In conclusion, the long-term survival rate was not significantly different between the 2 groups, but the non-fatal event rate in the optimal medical therapy group was higher than in the invasive therapy group. Although our study didn't make a sub-group analysis based on treatment in the elderly group, the overall prognostic analysis demonstrated that the 1-year cardiovascular mortality in the elderly group was higher than the control group. The difference in prognosis was in accordance with the differences in clinical information between the 2 groups. The presence of significant comorbidities (renal insufficiency, severe LV dysfunction or high NYHA class) was more predictive of cardiovascular mortality than age.

Although patient selection impacts PCI outcomes in general, this appears to be even more critical in very elderly patients. Our logistic regression analysis suggested that clinical characteristics, such as a history of previous PCI/CABG, renal insufficiency, severe LV dysfunction, and age more than 80 years, were more predictive of adverse outcomes than procedural factors, including the presence of CTO or multi-vessel disease, and traditional factors, such as hypertension, diabetes mellitus and anemia. It was noticeable that the presence of left mainstem disease was a strong predictor of cardiovascular mortality. Thus, the absolute benefit of PCI in these very elderly patients at high risk may be considerable. The relatively higher adverse event rate must be considered when considering revascularization in very elderly patients.

In conclusion, the present study preliminarily showed that, although there are many clinical studies and assessment systems about indications and contraindications of CHD revascularization, targeted studies and point-scoring systems in elderly patients are relatively absent. However, our country and international community are facing aging of the population, associated with increased morbidity and absolute number of elderly CHD patients. Thus it is necessary to enhance our knowledge about this aspect, in order to subsequently provide targeted assessment systems for elderly CHD patients. Limitations of this study include lack of a sub-group analysis focused on treatment options in the elderly group, and a short follow-up time, which should be completed and analyzed further.

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Disclosure of conflict of interest

None.

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