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Management and risk factor control of coronary artery disease in elderly versus nonelderly: a multicenter registry

Arintaya Phrommintikul[1], Rungroj Krittayaphong[2], Wanwarang Wongcharoen[1], Smonporn Boonyaratavej[3], Chaiyasith Wongvipaporn[4], Woraporn Tiyanon[5], Pakaphan Dinchuthai[6], Rapeephon Kunjara-Na-Ayudhya[7], Pyatat Tatsanavivat[4], Piyamitr Sritara[8], the CORE investigators

[1]*Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*
[2]*Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand*
[3]*Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok,Thailand*
[4]*Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*
[5]*Department of Medicine, Phramongkutklao College of Medicine, Bangkok, Thailand*
[6]*Faculty of Medicine, Burapha University, Chonburi, Thailand*
[7]*Vichaiyut Hospital and Medical Center, Bangkok, Thailand*
[8]*Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

Abstract

Background Coronary artery disease (CAD) is a leading cause of death in elderly because aging is the important non-modifiable risk factors of atherosclerosis and also a predictor of poor outcomes. Underuse of guideline directed therapy may contribute to suboptimal risk factor control and worse outcomes in the elderly**.** We aimed to explore the management of CAD, risk factors control as well as goal attainment in elderly compared to nonelderly CAD patients. **Methods** The CORE-Thailand is an ongoing multicenter, prospective, observational registry of patients with high atherosclerotic risk in Thailand. The data of 4120 CAD patients enrolled in this cohort was analyzed comparing between the elderly (age ≥ 65 years) *vs.* nonelderly (age < 65 years). **Results** There were 2172 elderly and 1948 nonelderly patients. The elderly CAD patients had higher prevalence of hypertension, dyslipidemia, atrial fibrillation and chronic kidney disease. The proportion of patients who received coronary revascularization was not different between the elderly and nonelderly CAD patients. Antiplatelets were prescribed less in the elderly while statin was prescribed in the similar proportion. Goal attainments of risk factor control of glycemic control, low density lipoprotein cholesterol, and smoking cessation except the blood pressure goal were higher in the elderly CAD patients. **Conclusions** The CORE-Thailand registry showed the equity in the treatment of CAD between elderly and non-elderly. Elderly CAD patients had higher rate of goal attainment in risk factor control except blood pressure goal. The effects of goal attainment on cardiovascular outcomes will be demonstrated from ongoing cohort.

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Keywords: Aging; Coronary artery disease; Goal attainment; Inequity; The elderly

1 Introduction

The aging population has become an important health issue globally due to the increased life expectancy of the population. Coronary artery disease (CAD) is a leading cause of death in this population[1] because aging is the crucial non-modifiable risk factor of atherosclerosis and also a predictor of poor outcomes.[2,3]

The management of CAD medically and invasively have been shown to be beneficial in elderly in the same way as nonelderly.[4,5–7] Moreover, due to the higher risk for adverse outcomes, several treatments such as statin showed the greater magnitude of benefits in elderly.[8,9] However, those treatments may be underused in elderly. Several cohorts of acute coronary syndrome (ACS) have demonstrated the lower rate of evidence-based therapy and higher rate of adverse outcomes in elderly population.[10–13] Elderly patients undergoing percutaneous coronary intervention (PCI) also received lower rate of drug-eluting stent used.[14]

Correspondence to: Rungroj Krittayaphong, MD, Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand. E-mail: rungroj.kri@mahidol.ac.th
Telephone: +6681-805-9992 **Fax:** +662-412-7412
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There are several factors affecting decision making on treatments including the different pharmacological effect of medications in elderly, co-morbidities, and the higher incidence of complications of interventions. In order to improve outcomes in the elderly, the current clinical practice in management of CAD as well as risk factor control should be explored. However, the information regarding management of stable CAD in the elderly is still limited. Therefore, we analyzed the data of CAD patients enrolled in prospective cohort study of high atherosclerotic risk population in Thailand (CORE-Thailand). We aimed to study the management of CAD, risk factors control as well as goal attainment in elderly CAD patients compared to nonelderly CAD patients.

2 Methods

The CORE-Thailand is an ongoing multicenter, prospective, observational registry of patients with high atherosclerotic risk in Thailand. The patients aged 45 years or older with established CAD, cerebrovascular disease (CVD) or peripheral arterial disease (PAD), or with ≥ 3 atherothrombotic risk factors (diabetes mellitus or impaired fasting glucose, hypertension, dyslipidemia, chronic kidney disease, current smoking, men aged 55 years or older, or women aged 65 years or older and family history of premature atherosclerosis) were enrolled during April 2011 to March 2014. Patients with following conditions were excluded from the cohort; patients who had acute atherosclerotic event within 3 months, had large aortic aneurysm indicated for surgery, participated in a blinded clinical trial, had limited life expectancy from non-cardiovascular condition such as cancer or documented human immunodeficiency virus (HIV) infection, or those who might have difficulty returning for a follow-up visit. Physical examination and laboratory data were recorded from medical record at enrollment. Available information was used to determined goal attainment.

Data were collected locally using a standardized case report form and forwarded to the data management group of Medical Research Network of the Consortium of Thai Medical Schools (MedResNet). The data management group and statistician performed quality data checks before data analysis. The annual site monitoring was performed randomly.

2.1 Definitions

The criteria for documented CAD consisted of 1 or more of the following criteria: stable angina with evidence of CAD by noninvasive study or coronary angiogram, history of unstable angina with evidence of CAD by noninvasive study or coronary angiogram, history of myocardial infarction (MI), history of PCI, or history of coronary artery bypass graft surgery (CABG). Polyvascular disease was defined as co-existing between CAD and CVD or PAD.

Patients with CAD were enrolled in this analysis. Patients aged 65 years or older at study enrollment were classified as elderly.

Goal attainment of risk factors was considered individually as following; systolic blood pressure (SBP) < 140 mmHg and diastolic blood pressure (DBP) < 90 mmHg, HbA1C < 7 %, low density lipoprotein cholesterol (LDL-C) < 70 mg/dL, and no current smoking. Good risk factor control was defined if 3 from 4 risk factors attained goal.

2.2 Statistical analysis

Continuous variables are expressed as mean ± SD and compared between groups by the Student-*t* test or one-way analysis of variance (one-way ANOVA) where appropriate. Categorical variables are expressed as frequencies and percentages, and compared between groups by the Pearson χ^2 test. Statistical significance was considered as a 2-tailed probability of less than 0.05. Statistical analysis was performed using SPSS version 19.

3 Results

3.1 Clinical characteristics of CAD and atherosclerotic risk factors

From 9390 patients in the CORE-Thailand cohort, 4120 patients had established CAD. Among these, 2172 patients were 65 years or older. Mean age of elderly CAD and nonelderly CAD patients were 73.2 ± 5.9 and 57.1 ± 5.1 years (Table 1). The elderly CAD group had lower proportion of men compared to nonelderly CAD (61.7% *vs.* 74.4%, $P < 0.001$).

The elderly CAD patients had higher prevalence of stable angina (31.2% *vs.* 26.6%, $P = 0.001$) and less prevalence of prior myocardial infarction (56.6% *vs.* 63.1%, $P < 0.001$) at enrollment. The median time from the latest events was 3.00 (range 1.00–6.00) years. The prevalence of poly-vascular disease were higher in elderly CAD (8.8% *vs.* 6.4%, $P = 0.003$).

Hypertension and dyslipidemia were more prevalent in elderly CAD patients than non-elderly patients (79.4% *vs.* 67.6% and 80.9% *vs.* 75.7%, $P < 0.001$ for both comparisons) while the prevalence of dysglycemia was similar (42.2% *vs.* 42.6%, $P = 0.085$). The elderly CAD patients had lower body mass index (BMI) and waist circumference than non-elderly CAD (86.8 ± 11.6 *vs.* 89.0 ± 11.1 and 24.3 ± 8.6 *vs.* 25.8 ± 7.8, $P < 0.001$ for both comparisons). Eld-

Table 1. Clinical characteristic and risk factors of CAD patients.

	Nonelderly (< 65 years) (*n* = 1948)	Elderly (≥ 65 years) (*n* = 2172)	*P*-value
Age, yrs	57.1 ± 5.1	73.2 ± 5.9	< 0.001
Female	505 (25.9%)	834 (38.4%)	< 0.001
Chronic stable angina	518 (26.6%)	678 (31.2%)	0.001
Previous history of myocardial infarction	1230 (63.1%)	1229 (56.6%)	< 0.001
Previous history of unstable angina	252 (12.9%)	299 (13.8%)	0.436
Polyvascular disease	124 (6.4%)	192 (8.8%)	0.003
Diabetes or received glucose lowering agents	829 (42.6%)	917 (42.2%)	0.850
Hypertension	1317 (67.6%)	1724 (79.4%)	< 0.001
Dyslipidemia	1474 (75.7%)	1758 (80.9%)	< 0.001
Family history of premature atherothrombosis	173 (8.9%)	137 (6.3%)	0.002
Chronic kidney disease	241 (12.4%)	489 (22.5%)	< 0.001
eGFR	71.6 ± 24.2	56.5 ± 20.8	< 0.001
Atrial fibrillation or atrial flutter	51 (2.9%)	125 (6.3%)	< 0.001
Waist circumference	89.0 ± 11.1	86.8 ± 11.6	< 0.001
BMI	25.8 ± 7.8	24.3 ± 8.6	< 0.001

Data were presented as mean ± SD or *n* (%). BMI: body mass index; CAD: coronary artery disease; eGFR: Estimated glomerular filtration rate.

erly CAD patients had more atrial fibrillation (6.3% *vs.* 2.9%, $P < 0.001$) and chronic kidney disease (22.5% *vs.* 12.4%, $P < 0.001$).

3.2 Management of CAD

Regarding pharmacological therapy, elderly patients received less anti-platelet therapy including aspirin (89.5% *vs.* 93.1%, $P = 0.001$), clopidogrel (42.7% *vs.* 45.8% $P = 0.048$) as well as dual anti-platelets (37.0% *vs.* 42.7%, $P < 0.001$) (Table 2). Warfarin was prescribed in similar proportion in elderly and non-elderly CAD patients (4.5% *vs.* 3.4%, $P = 0.079$). Statin was prescribed in 94% of both groups. Ezetimibe and combination of stain and ezetimibe were prescribed similarly in elderly and non-elderly CAD patients (5.0% *vs.* 5.2%, $P = 0.832$ and 4.7% *vs.* 5.0%, $P = 0.717$ respectively). Glucose lowering agents were prescribed in a similar proportion for both groups except biguanide which was more common in non-elderly patients (24.3% *vs.* 19.8%, $P < 0.001$). The elderly patients received less angiotensin converting enzyme inhibitor (ACEI) but higher angiotensin receptor blocker (ARB) than nonelderly CAD patients (35.5% *vs.* 42.2%, $P < 0.001$ and 32.1% *vs.* 22.9%, $P < 0.001$ respectively). Elderly CAD patients

Table 2. Management of CAD.

	Nonelderly (< 65 years) (*n* = 1948)	Elderly (≥ 65 years) (*n* = 2172)	*P*-value
Percutaneous coronary intervention	1252 (64.3%)	1292 (59.5%)	0.002
Coronary artery bypass grafting	195 (10.0%)	291 (13.4%)	0.001
Medical treatment only	534 (27.4%)	638 (29.4%)	0.167
Aspirin	1813 (93.1%)	1944 (89.5%)	< 0.001
P2Y12 inhibitor	903 (46.4%)	938 (43.2%)	0.041
Dual antiplatelet (aspirin and P2Y12 inhibitors)	831 (42.7%)	804 (37.0%)	< 0.001
Warfarin	66 (3.4%)	97 (4.5%)	0.079
Statins	1833 (94.1%)	2044 (94.1%)	1.000
Ezetimibe	101 (5.2%)	109 (5.0%)	0.832
Statins and ezetimibe	98 (5.0%)	103 (4.7%)	0.717
Angiotensin converting enzyme inhibitor	821 (42.2%)	772 (35.5%)	< 0.001
ARB	484 (24.9%)	697 (32.1%)	< 0.001
ACEI or ARB	1278 (65.6%)	1442 (66.4%)	0.598
Beta blocker	1623 (83.3%)	1731 (79.7%)	0.003
Nitrate	726 (37.3%)	921 (42.4%)	0.001
Calcium channel blocker	458 (23.5%)	768 (35.4%)	< 0.001
Antidiabetic agents	639 (32.8%)	687 (31.6%)	0.423
Insulin	126 (6.5%)	126 (5.8%)	0.397
Sulfonylurea	368 (18.9%)	374 (17.2%)	0.168
Metformin	474 (24.3%)	430 (19.8%)	< 0.001
Thiazolidinedione	68 (3.5%)	59 (2.7%)	0.176
DDP4-inhibitor	50 (2.6%)	62 (2.9%)	0.632
Others	31 (1.6%)	29 (1.3%)	0.517

Data were presented as *n* (%). ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker; CAD: coronary artery disease; DPP4: dipeptidyl peptidase-4.

received beta-blocker in lower proportion than nonelderly (80.1% *vs.* 84.3%, $P = 0.001$) while received calcium channel blocker (CCB) and nitrate in higher proportion (35.4% *vs.* 23.5% $P < 0.001$ and 42.4% *vs.* 37.3%, $P < 0.001$ respectively).

Regarding coronary revascularization, both groups received revascularization comparably. However, the elderly CAD patients had history of CABG in the higher proportion than the non-elderly patients while they underwent PCI in the less proportion than the non-elderly patients. (13.4% *vs.* 10.0%, $P = 0.001$ and 60.7% *vs.* 65.9%, $P = 0.002$ respectively).

3.3 Goal attainment of risk factor control

From available data, goal attainment of risk factor control was evaluated individually as well as combined. Lower

Table 3. Goal attainment of risk factor control.

Risk factors	Nonelderly (< 65 years) (*n* = 1948) (Reference)	Elderly (≥ 65 years) (*n* = 2172)	OR (95% CI)	*P*-value	Adjusted OR* (95% CI)	*P*-value
SBP < 140 and DBP < 90 mmHg	1387/1948 (71.2%)	1394/2172 (64.2%)	0.73 (0.64–0.83)	< 0.001	0.69 (0.59–0.80)	< 0.001
LDL-C < 70 mg/dL	223/1095 (20.4%)	297/1169 (25.4%)	1.33 (1.09–1.62)	0.004	1.27 (1.02–1.57)	0.033
Sugar control (HbA1C < 7% or FBS < 140 mg/dL)	834/1195 (69.8%)	1005/1329 (75.6%)	1.34 (1.13–1.60)	0.001	1.57 (1.29–1.90)	< 0.001
No current smoking	1780/1,948 (91.4%)	2082/2172 (95.9%)	2.18 (1.68–2.84)	< 0.001	1.77 (1.32–2.36)	< 0.001
≥ 3 of 4 risk factors	630/1369 (45.1%)	751/1505 (49.9%)	1.22 (1.05–1.41)	0.009	1.23 (1.05–1.44)	0.012
All 4 risk factors	100/1388 (7.2%)	128/1505 (8.5%)	1.21 (0.92–1.59)	0.175	1.14 (0.85–1.53)	0.371

*adjusted OR was adjusted by potential confounders including, gender, type of coronary artery disease, concurrent risk factors, body mass index, waist circumference, estimated glomerular filtration rate, medications. Data were presented as *n* (%). DBP: diastolic blood pressure; FBS: fasting blood sugar; LDL-C: low density lipoprotein cholesterol; SBP: systolic blood pressure.

proportion of elderly CAD patients attained blood pressure compared to the nonelderly patients OR 0.73 (95% CI 0.64–0.83), $P \leq 0.001$ (Table 3). In contrast, Higher proportion of elderly CAD patients attained LDL-C goal, HbA1c goal, and stop smoking goal compared to the nonelderly CAD patients [OR (95% CI): 1.33 (1.09–1.62), 1.34 (1.13–1.60), 2.18 (1.68–2.84), all $P < 0.01$)]. Elderly patients had significantly higher "good controlled" patients than nonelderly CAD patients [OR (95% CI): 1.22 (1.05–1.41); $P = 0.009$). Only small proportion of patients attained goal of all 4 risk factors and this was not significantly different between elderly and nonelderly groups [8.5% *vs.* 7.2%, OR (95% CI): 1.21 (0.92–1.59); $P = 0.175$). The differences in goal attainment were significant after the adjustment for potential confounders including age, gender, type of coronary artery disease, concurrent risk factors, body mass index, waist circumference, estimated glomerular filtration rate, medications.

Due to the nature of observational study in real life practice, laboratory investigation was performed according to physicians' practice. Therefore we compared the clinical characteristics of patients with and without complete laboratory data. Patients with complete data had more prevalent of comorbidities including hypertension (76.6% *vs.* 67.1%), diabetes (51.2% *vs.* 21.3%), dyslipidemia (83.8% *vs.* 67.4%), chronic kidney disease (19.7% *vs.* 13.1%); all $P < 0.01$.

4 Discussion

Cardiovascular disease is the important health problem in elderly causing limited quality of life as well as economic burden. Optimal management of CAD and risk factor control has been shown to improve outcomes in elderly and non-elderly population and should be emphasized. Prior registries have demonstrated the negative impact of age on guidelines-recommended care leading to the poorer outcomes in elderly patients with ACS.[13]

Our analysis of the CAD patients from the CORE- Thailand registry pointed out the high prevalence of conventional atherosclerotic risk factors in both elderly and non-elderly CAD patients. Elderly patients received less antiplatelets but received statin in similar rate to non-elderly. Both groups received coronary revascularization (either PCI or CABG) in the similar proportion. The elderly CAD patients achieved higher rate of goal attainments of risk factor control compared to non-elderly patients except blood pressure control.

Management of CAD has been shown to improve prognosis and symptoms. Medical therapy that reduce cardiovascular events in stable CAD are antiplatelet, statin, beta blocker during 3 years after ACS in normal left ventricular ejection fraction (LVEF) or life-long in patients with impaired LVEF, and renin-angiotensin aldosterone system blockage with ACEI or ARB.[15,16] The CAD patients in this cohort received antiplatelet therapy in high proportion compared to previous registry,[17] even though the elderly CAD patients received less antiplatelet than nonelderly. The concurrent atrial fibrillation or atrial flutter indicating warfarin use may contribute to reduction of antiplatelet use in stable CAD.

There are several potential factors associated with lower rate of blood pressure goal attainment in elderly including vascular aging, co-morbidities as well as adverse effects of medication. Due to vascular change in aging, the increased arterial stiffness causing high systolic blood pressure accompanied with lower diastolic blood pressure which is a coronary perfusion pressure. Although the benefit of aggressive blood pressure lowering has been demonstrated in elderly patients, the proportion of stable in CAD in these

studies was small.[18,19] Furthermore, the J-curve relationship between diastolic blood pressure in CAD[20] patients raised the concerns of physicians in clinical practice. Some co-morbidities such as chronic kidney disease which present more often in the elderly including our study may contribute to suboptimal blood pressure control.[21,22] In addition, elderly population experienced more adverse effects from antihypertensive agents such as orthostatic hypotension.[23]

In contrast to blood pressure control, the goal attainment of LDL-C and sugar control significantly higher in our elderly CAD patients. Even though the goal attainment rate of LDL-C in elderly was higher than nonelderly, both groups had low rate of LDL-C goal attainment. Almost all of the patients received statin but very small proportion (5%) received ezetimibe. The potency of statin was not identified in this cohort but previous cohorts in Thailand showed that two-third of the ACS patients received simvastatin.[24,25] Low rate of high potency statin and non-statin use may contribute to low goal attainment rate. However, the long term outcomes of the LDL-C goal attainment on cardiovascular events in out cohort will be studied in ongoing cohort. Because the post-hoc analysis of RCT[26] and recent cohort[27] showed no benefit of lowering LDL-C less than 70 mg/dL, long term follow up data from our cohort population should be useful in guideline implementation.

Age has been shown to be associated with glycemic control, however the association did not persist when other factors including diabetes duration, baseline HbA1C were considered.[28] In addition our elderly population had lower BMI, waist circumference which may have contributed to better glycemic control. Although glycemic goal attainment achieved in about 68%–75% of patients, tight glycemic control has not been shown to reduce cardiovascular events in high risk patients.[29] Furthermore, tight glycemic control increases hypoglycemic risk especially in elderly, therefore the HbA1C should be individualized considered according to the health status.[30]

To the best of our knowledge, this is the largest cohort focusing management and risk factor control in elderly CAD patients. Even though goal attainments of risk factor control in elderly were higher than nonelderly, the attainment rates were still low especially LDL-C goal. The barriers of goal attainment should be addressed to achieve the better outcomes.

There are some limitations in our study, the factor associated with goal attainment such as patients' compliance or adverse effects of treatment were not studied. The goal attainment was collected from available data in routine clinical practice and some patients did not have available information. However, patients with co-morbidities were likely to have available laboratory data. In addition, goal attainment analysis adjusting according to co-morbidities consistently showed the higher goal attainment rate in the elderly CAD.

In conclusions, the CORE-Thailand registry showed the equity in treatment of CAD between elderly and non-elderly. Elderly CAD patients had higher rate of goal attainment in risk factor control except blood pressure goal. The effects of goal attainment on cardiovascular outcomes will be demonstrated from ongoing cohort.

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