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Clinical Impact and Cost-Effectiveness of Coronary Computed Tomography Angiography or Exercise Electrocardiogram in Individuals Without Known Cardiovascular Disease

Gyung-Min Park, MD, Seon Ha Kim, PhD, Min-Woo Jo, MD, Sung Ho Her, MD, Seungbong Han, PhD, Jung-Min Ahn, MD, Duk-Woo Park, MD, Soo-Jin Kang, MD, Seung-Whan Lee, MD, Young-Hak Kim, MD, Cheol Whan Lee, MD, Beom-Jun Kim, MD, Jung-Min Koh, MD, Hong-Kyu Kim, MD, Jaewon Choe, MD, Seong-Wook Park, MD, and Seung-Jung Park, MD

Abstract: It is not clear whether screening by coronary computed tomographic angiography (CCTA) and/or exercise electrocardiogram (ECG) can improve clinical outcomes and reduce costs in individuals without known cardiovascular disease (CVD).

In total, 71,811 consecutive individuals without known CVD who underwent general health examinations were enrolled. Using propensity-score matching according to screening tests, 1-year clinical outcomes and 6-month total and coronary artery disease–related medical costs were analyzed in separate groups: group 1 (CCTA [n = 2578] vs no screening [n = 5146]), group 2 (exercise ECG [n = 2898] vs no screening [n = 5796]), and group 3 (CCTA and exercise ECG [n = 2003] vs no screening [n = 4006]).

There were no significant differences in the composite outcome of death, myocardial infarction, and stroke in each matched group: group 1 (0.35% vs 0.45%, $P = 0.501$), group 2 (0.14% vs 0.28%, $P = 0.157$), and group 3 (0.25% vs 0.27%, $P = 0.858$). However, revascularization was more frequent in the CCTA screening groups: group 1 (2.02% vs 0.45%, $P < 0.001$) and group 3 (1.40% vs 0.45%, $P < 0.001$). Matched screening groups had higher 6-month total and coronary artery disease–related medical costs: group 1 ($777 vs $603, $P < 0.001$ and $177 vs $39, $P < 0.001$), group 2 ($544 vs $492, $P = 0.045$ and $12 vs $15, $P = 0.611$), and group 3 ($705 vs $627, $P = 0.090$ and $135 vs $35, $P < 0.001$).

In individuals without known CVD, CCTA screening with or without exercise ECG led to more frequent revascularization at the expense of higher medical costs, but did not decrease the 1-year risk of death, myocardial infarction, and stroke.

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Abbreviations: CABG = coronary artery bypass graft, CAD = coronary artery disease, CCTA = coronary computed tomographic angiography, CHF = congestive heart failure, CVD = cardiovascular disease, ECG = electrocardiogram, HIRA = Health Insurance Review & Assessment Service, ICD-10 = International Classification of Diseases, 10th Revision, ICER = incremental cost-effectiveness ratio, MI = myocardial infarction, NCEP = National Cholesterol Education Program, NHI = National Health Insurance, PCI = percutaneous coronary intervention.

INTRODUCTION

Coronary artery disease (CAD) is a major cause of death and disability globally.[1] Although CAD mortality rates have declined over the past decades, it still remains the leading cause of death in adults.[2] Moreover, the first clinical manifestation is often asymptomatic until the onset of sudden cardiac death or myocardial infarction (MI). Therefore, there has been substantial interest in early detection and treatment for subclinical stages of CAD.[3]

Coronary computed tomography angiography (CCTA) and exercise electrocardiogram (ECG) have been widely used in the evaluation and prognostic assessment of patients with known or suspected CAD.[4,5] Despite the lack of evidence, CCTA and exercise ECG have been used as a screening tool for CAD evaluation.[6–8] However, there are limited data on whether screening for CAD using CCTA or exercise ECG can improve clinical outcomes in individuals without known cardiovascular disease (CVD). Moreover, little is known on whether CAD screening is cost-effective in a country with a relatively low health care expenditure such as South Korea.[9]

To evaluate the impact of CAD screening (CCTA and/or exercise ECG) in individuals without known CVD, we compared the clinical outcomes and costs in matched groups (screening vs no screening).

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From the Department of Cardiology (G-MP, SHH), Daejeon St Mary's Hospital, The Catholic University of Korea, Daejeon, Korea; Department of Nursing (SHK), College of Medicine, Dankook University, Cheonan; Departments of Cardiology (J-MA, D-WP, S-JK, S-WL, Y-HK, CWL, S-WP, S-JP), Preventive Medicine (M-WC), Endocrinology (B-JK, J-MK), and the Health Screening and Promotion Center (H-KK, JC), Asan Medical Center, University of Ulsan College of Medicine, Seoul; and Department of Applied Statistics (SH), Gachon University, Seongnam, Korea.
Correspondence: Young-Hak Kim, Department of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, 388–1 Poongnap-dong, Songpa-gu, Seoul, 138–736, Korea (e-mail: mdyhkim@amc.seoul.kr).
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METHODS

Data Sources

A total of 105,710 consecutive individuals aged 18 years and older were enrolled in this study between January 2007 and June 2011. All individuals had undergone self-referral medical checkups in the Health Screening and Promotion Center at the Asan Medical Center, a tertiary treatment referral hospital located in Seoul. Of these, 79,813 (75.5%) agreed to participate in the study. Subjects were excluded if, before the index day, the Health Insurance Review & Assessment Service (HIRA) database indicated they had a history of CVD (codes I00–99 in the *International Classification of Diseases*, *10th Revision*) or if their data were not available in the HIRA database. The HIRA is a quasi-governmental organization that systematically reviews medical fees to minimize the risk of redundant and unnecessary medical services. South Korea has a National Health Insurance (NHI) system. It is mandatory that all health care providers join this system on a fee-for-service basis. Consequently, all NHI claims are reviewed by the HIRA.[10] In the current study, the HIRA database was used until December 2011. This study was conducted with the permission of the National Strategic Coordinating Center of Clinical Research and the HIRA in Korea. Subjects with angina, MI, structural heart disease, percutaneous coronary intervention (PCI), previous cardiac procedures, or open-heart surgery before the index day were excluded. Finally, 71,811 subjects were enrolled (Figure 1). This study was approved by the local Institutional Review Board. All enrolled subjects provided written informed consent.

The basic demographic data of the subjects were acquired from a database that is maintained by the Health Screening and Promotion Center at the Asan Medical Center. Any medical history, family history of CAD, smoking status, physical activity, education status, and annual salary were collected from a systemized questionnaire prior to general health examination. Diabetes mellitus was defined as a fasting plasma glucose concentration $\geq$126 mg/dL or a self-reported history of diabetes and/or treatment by dietary modification, or use of antidiabetic medication. Hypertension was defined as blood pressure $\geq$140/90 mm Hg or a self-reported history of hypertension and/or use of antihypertensive medication. Hyperlipidemia was defined as total cholesterol $\geq$200 mg/dL or use of an antihyperlipidemic treatment. A family history of CAD was defined as CAD occurring in a first-degree relative of any age. Physical activity was classified according to exercise frequency (>5 days, 3–5 days, <3 days, and none). Education status was classified into 4 levels (>college or university graduate, college or university graduate, high school graduate, and $\leq$middle school graduate). In this study, cost was calculated on the basis of an exchange rate of the Korean Won 1108 = US $1 in 2011. Annual salary was also categorized (>$75,000, $55,000–75,000, $35,000–55,000, and <$35,000). In the general health examination, height, body weight, body mass index, waist circumference, and blood pressure were measured. Moreover, fasting plasma glucose, glycated hemoglobin, blood urea nitrogen, creatinine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride were measured on the day of the examination after a fast of $\geq$12 hours. Aspirin or statin medication history was obtained from the HIRA database. All subjects were assigned to low, intermediate, or high-risk groups according to the National Cholesterol Education Program (NCEP) guideline.[11]

Study Outcomes

The primary study outcome was defined as a composite of all-cause death, MI, and stroke in 1 year after the index test. We also examined coronary revascularization and CAD and congestive heart failure (CHF)–related hospitalizations in 1 year following the index test. To evaluate the subsequent flow of patient care related to the results of the screening tests, subsequent use of cardiac tests, total medical costs, and CAD-related medical costs were investigated within 6 months of the index test. The incremental cost-effectiveness ratio (ICER) was calculated for each strategy relative to the no screening for the primary study outcome and detection of significant CAD (diameter stenosis $\geq$50%) on invasive coronary angiography.

In subjects with multiple primary events, the first event was considered to be the component of the composite outcome. All deaths up until December 31, 2011, were confirmed by matching the information to the death records from the National Statistical Office.[12] MI and stroke were defined by using the hospital discharge databases of the HIRA (ICD-10 codes I21–22 and I60–69). In the procedure codes of the HIRA database, we identified coronary angiogram (HA670), PCI (M6551, M6552, M6561–4, M6571, and M6572), and coronary artery bypass graft (CABG) surgery (O1641, O1642, O1647, OA641, OA642, and OA647). CAD- and CHF-related hospitalizations were also defined by using the hospital discharge databases of the HIRA with ICD-10 codes of I20–25 and I50. Additional noninvasive diagnostic tests for CAD, such as exercise ECG (E6543), myocardial perfusion image (HC292, HC297, and HC298), and CCTA (HA474), were tracked after the index test if these tests were performed before any subsequent coronary angiogram, revascularization, MI, or hospitalization for CAD or CHF in the HIRA database.

Total medical costs were defined as the sum of 3 direct medical costs: inpatient care, outpatient care, and prescription drugs. When it comes to medical costs, we assessed medical costs for the 6 months regardless of events. For the measurement of CAD-related medical costs, we obtained CAD-related claim costs from the HIRA databases (ICD-10 codes I20–25). To measure total and CAD-related medical costs, the baseline costs of CCTA and exercise ECG ($227 and $42) were excluded to ensure that differences in baseline test costs did not obscure any significant differences in downstream health care costs.[13] However, in the measurement of ICER, the baseline test cost was included.

Statistical Methods

Categorical data are compared using χ^2 statistics or Fisher exact test, as appropriate. Continuous variables are compared using 1-way parametric or nonparametric (Kruskal–Wallis test) analyses of variance. To reduce the effect of initial screening test-selection bias and potential confounding factors in this observational study, we performed an adjustment for significant differences in the 17 baseline clinical characteristics of patients with the use of propensity-score matching (age, gender, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, diabetes mellitus, hypertension, hyperlipidemia, current smoking, family history of CAD, family history of stroke, physical activity, educational level, annual salary, and medication history of aspirin and statin).[14] Analyses were performed by 1:2 propensity-score matching in separate subgroups: group 1 (CCTA [n = 2578] vs no screening [n = 5146]), group 2 (exercise ECG [n = 2898] vs no screening [n = 5796]), and group 3 (CCTA and exercise ECG [n = 2003]

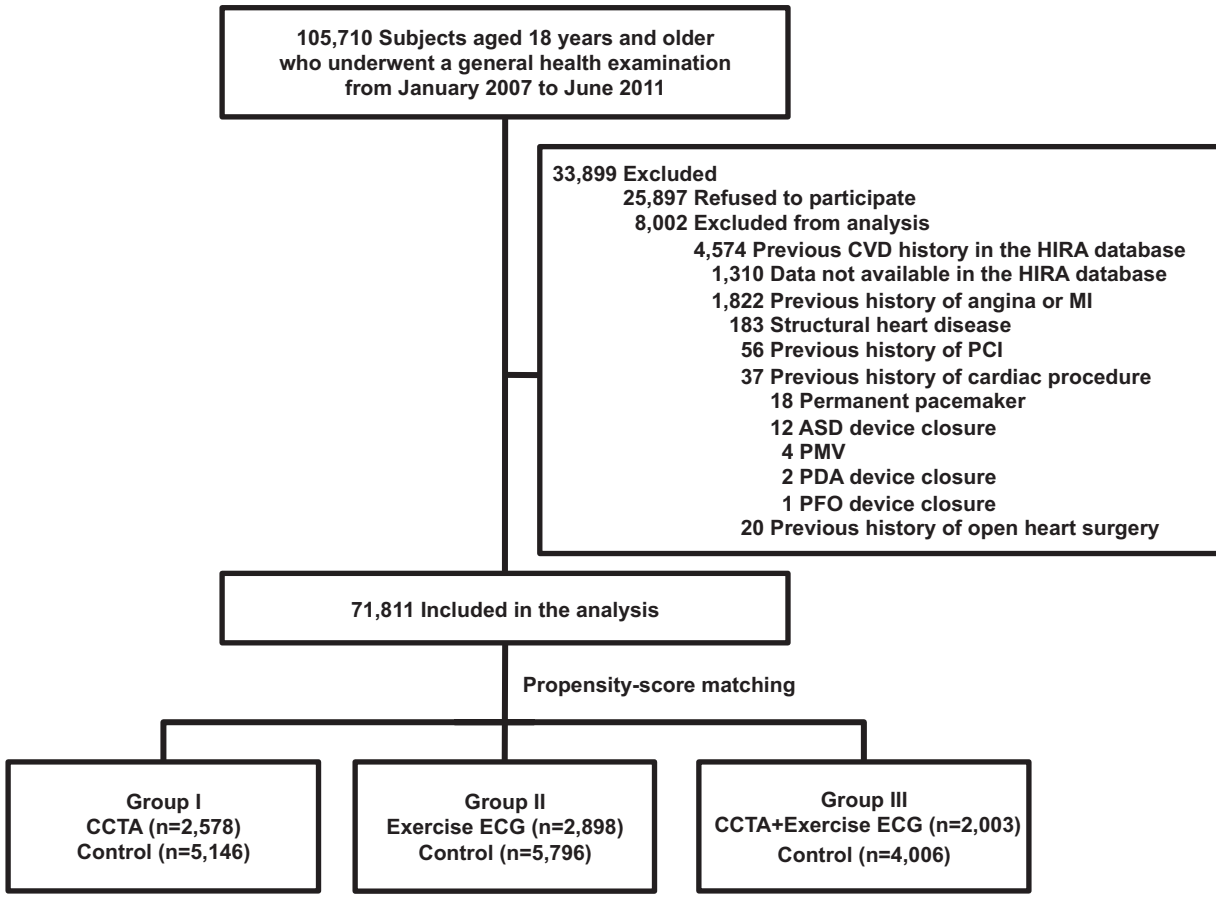

FIGURE 1. Overview of the study population. ASD = atrial septal defect, CVD = cardiovascular disease, HIRA = Health Insurance Review & Assessment Service, MI = myocardial infarction, PCI = percutaneous coronary intervention, PDA = patent ductus arteriosus, PFO = patent foramen ovale, PMV = percutaneous mitral valvuloplasty.

vs no screening [n = 4006]), respectively. In the propensity-score matched pairs, the risks of each outcome were compared by logistic regression using generalized estimating equations for categorical variables or by the linear mixed model for continuous variables that accounted for the clustering of matched pairs.[15,16] Subgroup analyses were also conducted in individuals with low-, intermediate-, and high-risk according to the NCEP guideline and diabetes mellitus. All reported P values were 2-sided, and values of $P < 0.05$ were considered to be statistically significant. Data manipulation and statistical analyses were conducted using SAS Version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Population Characteristics

Table 1 summarizes the baseline characteristics of the study participants according to each CAD screening test. The mean age of the study population was 47.4 ± 10.6 years, 41,228 (57.4%) individuals were male. Diabetes mellitus, hypertension, hyperlipidemia, and current smoking were observed in 6012 (8.4%), 15,360 (21.4%), 30,968 (43.1%), and 17,302 (24.1%) participants, respectively. Individuals undergoing CCTA were older, with greater comorbidity, and a higher annual salary than those in the control and exercise ECG groups.

Comparisons in Propensity-Matched Pairs

CCTA Versus No Screening

Compared with the matched no screening group, the CCTA group was associated with higher rates of subsequent cardiac tests (9.19% vs 2.74%, $P < 0.001$), detection of significant CAD (2.52% vs 0.33%, $P < 0.001$), coronary revascularization (2.02% vs 0.45%, $P < 0.001$), and CAD-related hospitalization (3.84% vs 0.97%, $P < 0.001$). Consequently, the CCTA group had a higher 6-month total and CAD-related medical costs than the no screening group ($777 vs $603, $P < 0.001$ and $177 vs $39, $P < 0.001$). However, the primary composite outcome of death, MI, and stroke was not statistically different between the CCTA and no screening groups (Table 2).

Exercise ECG Versus No Screening

The exercise ECG group underwent further cardiac tests than the matched no screening group (3.90% vs 2.43%, $P < 0.001$). However, despite detecting more significant CAD, coronary revascularizations were less frequently performed in the exercise ECG group (0.03% vs 0.21%, $P < 0.001$) and the primary composite clinical outcome was not statistically different between the 2 groups (0.14% vs 0.28%, $P = 0.157$). Total medical costs were higher in the exercise ECG group ($544 vs $492, $P = 0.045$), but CAD-

TABLE 1. Baseline Characteristics of the Study Population According to Each Screening Test

	No Screening (n = 64,331)	CCTA (n = 2578)	Exercise ECG (n = 2898)	Exercise ECG and CCTA (n = 2004)	*P* Value
Clinical characteristics					
Age, y, mean (SD)	46.8 (10.8)	53.8 (8.5)	50.4 (9.4)	53.3 (7.7)	<0.001
Male, no. (%)	36,067 (56.1)	1829 (70.9)	1851 (63.9)	1481 (73.9)	<0.001
Body mass index, kg/m^2, mean (SD)	23.6 (3.1)	24.6 (3.0)	24.0 (3.0)	24.6 (2.8)	<0.001
Waist circumference, cm, mean (SD)	81.4 (9.1)	85.8 (8.6)	83.6 (8.6)	85.9 (8.2)	<0.001
Systolic blood pressure, mm Hg, mean (SD)	116.9 (14.3)	118.2 (13.2)	119.3 (13.2)	120.8 (12.4)	<0.001
Diastolic blood pressure, mm Hg, mean (SD)	73.0 (10.2)	75.1 (10.5)	76.5 (10.7)	77.5 (10.1)	<0.001
Diabetes mellitus, no. (%)	4945 (7.7)	408 (15.8)	332 (11.5)	327 (16.3)	<0.001
Hypertension, no. (%)	12,951 (20.1)	909 (35.3)	792 (27.3)	708 (35.3)	<0.001
Hyperlipidemia, no. (%)	26,863 (41.8)	1449 (56.2)	1511 (52.1)	1145 (57.1)	<0.001
Current smoker, no. (%)	15,470 (25.6)	628 (25.8)	718 (26.3)	486 (25.6)	<0.001
Family history of coronary artery disease,* no. (%)	6096 (9.5)	393 (15.2)	364 (12.6)	322 (16.1)	<0.001
Family history of stroke, no. (%)	7012 (10.9)	383 (14.9)	391 (13.5)	326 (16.3)	<0.001
Physical activity, exercise average frequency per week, no. (%)					<0.001
>5 d	6098 (9.7)	362 (14.4)	253 (8.9)	215 (11.0)	
3–5 d	17,501 (27.8)	823 (32.7)	809 (28.6)	670 (34.3)	
<3 d	19,932 (31.6)	866 (34.5)	968 (34.2)	667 (34.1)	
None	19,465 (30.9)	463 (18.4)	802 (28.3)	403 (20.6)	
Educational level, no. (%)					<0.001
>College or university graduate	9238 (14.5)	432 (16.9)	426 (14.9)	360 (18.1)	
College or university graduate	30,873 (48.4)	1219 (47.8)	1210 (42.2)	847 (42.5)	
High school graduate	16,814 (26.4)	619 (24.3)	815 (28.4)	563 (28.3)	
≤Middle school graduate	6852 (10.7)	280 (11.0)	416 (14.5)	222 (11.1)	
Annual salary, no. (%)					<0.001
>$75,000	14,112 (25.3)	1347 (57.7)	905 (35.3)	1033 (55.5)	
$55,000–75,000	12,078 (21.7)	359 (15.4)	503 (19.6)	347 (18.7)	
$35,000–55,000	14,289 (25.6)	330 (14.1)	554 (21.6)	285 (15.3)	
<$35,000	15,305 (27.4)	298 (12.8)	602 (23.5)	196 (10.5)	
Medical treatment					
Aspirin	2259 (3.5)	289 (11.2)	227 (7.8)	244 (12.2)	<0.001
Statin	4146 (6.4)	497 (19.3)	387 (13.4)	453 (22.6)	<0.001

CCTA = coronary computed tomographic angiography, ECG = electrocardiogram, SD = standard deviation.
* Coronary artery disease in a first-degree relative of any age.

related costs were not different between the 2 groups ($12 vs $15, $P = 0.611$) for 6 months. However, considering the baseline cost of an exercise ECG ($42), the exercise ECG group had higher 6-month CAD-related medical costs ($P < 0.001$) (Table 2).

CCTA and Exercise ECG Versus No Screening

The combined CCTA and exercise ECG group was given more cardiac tests (6.29% vs 3.47%, $P < 0.001$), had a higher detection rate of significant CAD (1.70% vs 0.25%, $P < 0.001$), and subsequently received more coronary revascularization (1.40% vs 0.45%, $P < 0.001$), and CAD-related hospitalization (2.75% vs 1.02%, $P < 0.001$) than the matched no screening group. Therefore, the screening group had higher 6-month CAD-related medical costs ($135 vs $35, $P < 0.001$). Although there were no significant differences in the 6-month total medical costs between the 2 groups ($705 vs $627, $P = 0.090$), when taking the baseline costs ($268) into account, the screening group was also associated with higher 6-month total medical costs ($P < 0.001$). The rate of primary composite outcome of death, MI, and stroke was not statistically different between the 2 groups (Table 2).

ICER for the Clinical Outcome and Detection of Significant Coronary Artery Disease

In the overall study population, the unadjusted rate of the primary study outcome was not significantly different among the 4 groups (0.21% [138/64,331] in the no screening group, 0.35% [9/2578] in the CCTA group, 0.14% [4/2898] in the exercise ECG group, and 0.25% [5/2004] in the CCTA and exercise group; $P = 0.388$). Because of the absence of differences in the rate of primary outcomes, we did not calculate the ICER for the hard clinical event of death, MI, and stroke. In overall cohort, for another outcome of detection of significant CAD on invasive coronary angiography, the ICER was $16,116 in the CCTA

TABLE 2. Clinical Outcomes and Medical Costs in Each Propensity-Matched Group

	Group 1			Group 2			Group 3		
	No Screening (n = 5146)	CCTA (n = 2578)	*P* Value	No Screening (n = 5796)	Exercise ECG (n = 2898)	*P* Value	No Screening (n = 4006)	CCTA and Exercise ECG (n = 2003)	*P* Value
Additional CAD diagnostic tests, no. (%)									
Exercise ECG	45 (0.87)	62 (2.40)	<0.001	54 (0.93)	9 (0.31)	<0.001	45 (1.12)	17 (0.85)	0.297
Myocardial perfusion image	55 (1.07)	89 (3.45)	<0.001	56 (0.97)	26 (0.90)	0.749	59 (1.47)	49 (2.45)	0.013
CCTA	14 (0.27)	1 (0.04)	0.005	14 (0.24)	66 (2.28)	<0.001	11 (0.27)	6 (0.30)	0.866
Coronary angiogram	27 (0.52)	85 (3.30)	<0.001	17 (0.29)	12 (0.41)	0.385	24 (0.60)	54 (2.70)	<0.001
Significant CAD on CAG, no. (%)	17 (0.33)	65 (2.52)	<0.001	10 (0.17)	8 (0.28)	0.355	10 (0.25)	34 (1.70)	<0.001
Clinical outcomes within 1 y, no. (%)									
All-cause death	11 (0.21)	3 (0.12)	0.292	10 (0.17)	1 (0.03)	0.033	5 (0.12)	2 (0.10)	0.790
Myocardial infarction	5 (0.10)	2 (0.08)	0.776	0 (0)	0 (0)	0.999	4 (0.10)	0 (0)	0.998
Stroke	8 (0.16)	5 (0.19)	0.713	6 (0.10)	3 (0.10)	0.999	2 (0.05)	4 (0.20)	0.157
Coronary revascularization									
Percutaneous coronary intervention	20 (0.39)	48 (1.86)	<0.001	10 (0.17)	1 (0.03)	0.046	17 (0.42)	26 (1.30)	0.002
Coronary artery bypass graft surgery	3 (0.06)	4 (0.16)	0.254	2 (0.03)	0 (0)	0.999	1 (0.02)	2 (0.10)	0.317
CAD-related hospitalization	50 (0.97)	99 (3.84)	<0.001	31 (0.53)	20 (0.69)	0.397	41 (1.02)	55 (2.75)	<0.001
CHF-related hospitalization	1 (0.02)	2 (0.08)	0.319	2 (0.03)	1 (0.03)	0.999	2 (0.05)	1 (0.05)	0.999
All-cause death/MI/stroke	23 (0.45)	9 (0.35)	0.501	16 (0.28)	4 (0.14)	0.157	11 (0.27)	5 (0.25)	0.858
Medical cost, per person, mean (SD)									
Total cost within 6 mo, $	603 (1613)	777 (1678)	<0.001	492 (1138)	544 (1115)	0.045	627 (1716)	705 (1625)	0.090
CAD-related cost within 6 mo, $	39 (626)	177 (1179)	<0.001	15 (293)	12 (183)	0.611	35 (524)	135 (1043)	<0.001

CAD = coronary artery disease, CAG = coronary angiogram, CCTA = coronary computed tomographic angiography, CHF = congestive heart failure, ECG = electrocardiogram, MI = myocardial infarction, SD = standard deviation.

group, $22,778 in the exercise ECG group, and $24,375 in the CCTA and exercise ECG group, respectively. In each propensity-matched group, the ICER for the detection of significant CAD was $16,621 in the CCTA group, $35,455 in the exercise ECG group, and $25,379 in the CCTA and exercise ECG group (Table 3).

TABLE 3. ICER for Significant Coronary Artery Disease Detection in the Overall Cohort and Each Matched Group

	Number	Number of Significant CAD Detection	Total Average Cost per Person ($)	Cost per Significant CAD Detection ($)	Significant CAD Detection Rate (%)	ICER (vs Control) ($)
Overall cohort						
No screening	64,331	67	13	12,482	0.10	—
CCTA	2578	65	403	15,984	2.52	16,116
Exercise ECG	2898	8	54	19,562	0.28	22,778
CCTA and exercise ECG	2004	34	403	23,753	1.70	24,375
No screening versus CCTA						
No screening	5146	17	39	11,806	0.33	—
CCTA	2578	65	403	15,984	2.52	16,621
No screening versus Exercise ECG						
No screening	5796	10	15	8694	0.17	—
CCTA	2898	8	54	19,562	0.28	35,455
No screening versus CCTA and Exercise ECG						
No screening	4006	10	35	14,021	0.25	—
CCTA and exercise ECG	2003	34	403	23,741	1.70	25,379

CAD = coronary artery disease, CCTA = computed tomographic angiography, ECG = electrocardiogram, ICER = incremental cost-effectiveness ratio.

TABLE 4. Outcomes in Each Propensity-Matched Group for Individuals With Low-, Intermediate-, and High-Risk and Diabetes Mellitus

	No Screening	CCTA	*P* Value	No Screening	Exercise ECG	*P* Value	No Screening	CCTA and Exercise ECG	*P* Value
Low-risk individuals									
Number	2446	1223		2718	1359		1822	911	
Significant CAD on CAG, no. (%)	1 (0.04)	11 (0.90)	0.002	2 (0.07)	1 (0.07)	0.999	2 (0.11)	11 (1.21)	0.002
Clinical outcomes within 1 y, no. (%)									
Coronary revascularization									
Percutaneous coronary intervention	3 (0.12)	7 (0.57)	0.048	2 (0.07)	0 (0)	0.973	3 (0.16)	7 (0.77)	0.034
Coronary artery bypass graft surgery	0 (0)	0 (0)	0.999	0 (0)	0 (0)	0.999	0 (0)	0 (0)	0.999
All-cause death/MI/stroke	2 (0.08)	1 (0.08)	0.999	3 (0.11)	3 (0.22)	0.439	4 (0.22)	1 (0.11)	0.535
ICER (vs no screening), $		30,930			—			30,455	
Intermediate-risk individuals									
Number	1828	914		1656	828		1492	746	
Significant CAD on CAG, no. (%)	4 (0.22)	30 (3.28)	<0.001	2 (0.12)	4 (0.48)	0.157	6 (0.40)	13 (1.74)	0.001
Clinical outcomes within 1 y, no. (%)									
Coronary revascularization									
Percutaneous coronary intervention	8 (0.44)	24 (2.63)	<0.001	2 (0.12)	1 (0.12)	0.999	9 (0.60)	9 (1.21)	0.180
Coronary artery bypass graft surgery	1 (0.05)	1 (0.11)	0.655	1 (0.06)	0 (0)	0.971	1 (0.07)	1 (0.13)	0.655
All-cause death/MI/stroke	9 (0.49)	3 (0.33)	0.543	7 (0.42)	0 (0)	0.967	9 (0.60)	1 (0.13)	0.052
ICER (vs no screening), $		14,248			12,778			26,940	
High-risk individuals									
Number	798	399		674	337		640	320	
Significant CAD on CAG, no. (%)	5 (0.63)	22 (5.51)	<0.001	4 (0.59)	3 (0.89)	0.617	3 (0.47)	9 (2.81)	0.016
Clinical outcomes within 1 y, no. (%)									
Coronary revascularization									
Percutaneous coronary intervention	7 (0.88)	16 (4.01)	0.003	3 (0.45)	0 (0)	0.978	6 (0.94)	8 (2.50)	0.105
Coronary artery bypass graft surgery	0 (0)	3 (0.75)	0.977	1 (0.15)	0 (0)	0.981	1 (0.16)	1 (0.31)	0.655
All-cause death/MI/stroke	7 (0.88)	5 (1.25)	0.564	7 (1.04)	1 (0.30)	0.132	3 (0.47)	3 (0.94)	0.439
ICER (vs no screening), $		11,578			Dominated			17,094	
Diabetic individuals									
Number	794	407		663	332		624	327	
Significant CAD on CAG, no. (%)	6 (0.76)	21 (5.16)	<0.001	3 (0.45)	2 (0.60)	0.766	3 (0.48)	9 (2.75)	0.022
Clinical outcomes within 1 y, no. (%)									
Coronary revascularization									
Percutaneous coronary intervention	8 (1.01)	16 (3.93)	0.006	2 (0.30)	0 (0)	0.982	5 (0.80)	8 (2.45)	0.102
Coronary artery bypass graft surgery	2 (0.25)	2 (0.49)	0.567	1 (0.15)	0 (0)	0.981	0 (0)	1 (0.31)	0.979
All-cause death/MI/stroke	4 (0.50)	5 (1.23)	0.253	4 (0.60)	1 (0.30)	0.477	5 (0.80)	3 (0.92)	0.963
ICER (vs no screening), $		11,591			3333			20,704	

CAD = coronary artery disease, CAG = coronary angiogram, CCTA = coronary computed tomographic angiography, ECG = electrocardiogram, ICER = incremental cost-effectiveness ratio, MI = myocardial infarction.

Subgroup Analysis

In subgroups of low, intermediate, and high risk according to the NCEP guideline and diabetes mellitus, unadjusted rates of the primary study outcome did not differ in overall and propensity-matched cohorts. A tendency of higher detection rate of significant CAD and improved ICER according to risk category was observed with the screening of CCTA compared with no screening group. Individuals undergoing CCTA experienced more coronary revascularizations compared with no screening group, irrespective of risk category (Table 4).

DISCUSSION

In this study with large individuals without known CVD who underwent health screening, the main findings were the following: screening with CCTA and/or exercise ECG detected significant CAD more frequently and was associated with higher subsequent cardiac tests and medical costs; coronary revascularization was more frequently performed with CCTA screening group; and CAD screening using either CCTA or exercise ECG did not decrease the 1-year risk of death, MI, or stroke.

The evaluation of CAD in individuals without known CVD has been a controversial issue. There is still a lack of evidence as to whether CAD screening is associated with an improvement in clinical outcomes at a reasonable price. Therefore, our study aimed to assess the clinical outcomes and cost-effectiveness of CAD screening tests, such as CCTA or exercise ECG, in a country where diagnostic costs are relatively inexpensive. Because of the relatively low coronary event rates in individuals without known CVD, our study included a large population who voluntarily received CAD screening tests for early detection of CAD. Well-controlled and reliable data from the National Statistical Office and HIRA database in Korea (ie, governmental and quasi-governmental organizations) enabled qualified analyses on clinical outcomes and costs after each screening strategy.

CCTA has shown the prognostic potential for predicting cardiac events in patients with known or suspected CAD.[5] However, in individuals without known CVD, the prognostic role of CCTA is ill defined. In this study, matched CCTA group received more subsequent diagnostic tests, had higher detection rates of significant CAD, and underwent more coronary revascularization. Accordingly, the higher medical costs and CAD-related hospitalizations after CCTA were documented. Nevertheless, of importance is that performance of CCTA was not associated with the improvement in hard clinical events such as death, MI, or stroke in the 1 year following the initial screening test. Therefore, CCTA did not show a promising role in risk stratification for individuals without known CVD.

In this study, exercise ECG was also associated with higher medical costs, but did not improve clinical outcomes of death, MI, or stroke. Moreover, despite a higher detection of significant CAD, revascularization was less frequently performed in the exercise ECG group. This finding may indicate that exercise ECG screening does not improve clinical outcomes nor potentially lead to inappropriate medical care. In addition, when both CCTA and exercise ECG were performed, no incremental benefits on the clinical outcomes were observed. Based on these findings, rather than supplementing diagnostic tests, care of individuals without known CVD should be focused on a personalized modification of cardiovascular risk factors.

The cost-effectiveness of certain diagnostic tests is dependent on the health care expenditure of the country. There was a possibility that the relatively low costs of CCTA or exercise ECG could improve the cost-effectiveness of diagnostic tests in South Korea, which has a relatively low health care expenditure.[9] In our study, because of the failure to show an improvement in primary outcomes, cost-effectiveness analysis for the primary outcome of death, MI, and stroke was not performed, yet it was secondarily undertaken for the detection of significant CAD. The ICER of $16,621–35,455 for the detection of significant CAD in each matched cohort corresponded to 80% to 170% of the South Korean per capita income in 2011 ($20,870) and indicated a relatively high diagnostic cost to the community.[13,17] Therefore, even in a country with relatively low health care expenditure, CCTA and/or exercise ECG were shown to have unreasonably high medical costs in the detection of CAD without clinical improvements in the overall population.

We additionally analyzed the clinical outcomes and medical costs in the subgroups of low-, intermediate-, and high-risk groups according to the NCEP guideline and diabetes mellitus. No significant differences in primary clinical outcomes within 1 year were observed. However, in the CCTA group, a trend of higher detection rates of significant CAD and improved ICER was observed in the high-risk and diabetic subgroups compared with the low-risk group. Therefore, further studies are required to assess the differential role of CCTA screening for risk-stratified individuals.

Our study had several limitations. First, despite matching with 17 clinical baseline variables, there was still a potential bias due to unobserved variables. Second, our study could not assess the impact of CAD screening on clinical outcomes for more than 1 year, nor could it assess the behavioral changes of the physician and patient, such as medication use and lifestyle modification. Therefore, there was a possibility of overlooking long-term beneficial effects for identifying and treating CAD through screening tests. Third, because the detection of significant CAD was only possible in individuals undergoing invasive coronary angiogram, ICER analysis was conducted in limited angiographic subgroups. Fourth, we did not include CAD screening strategies other than CCTA and exercise ECG. However, considering the limited applicability and relatively high cost of other diagnostic tests, such as myocardial perfusion imaging, positive emission tomography scan, magnetic resonance imaging, or stress echocardiography, the results of our study may be applicable to general practice. Finally, although we used the database by governmental and quasi-governmental organizations, there was a possibility that these data could not have fully reflected outcomes.

In conclusion, for individuals without known CVD, screening with CCTA and/or exercise ECG incurred higher medical costs and did not improve cardiovascular outcomes such as death, MI, or stroke within 1 year. However, for high-risk individuals, CCTA screening could detect more CAD requiring revascularization with decreased ICER.

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