



Prognostic value of coronary computed tomographic angiography findings in asymptomatic individuals: a 6-year follow-up from the prospective multicentre international CONFIRM study

Iksung Cho^{1,2,3}, Subhi J. Al'Aref¹, Adam Berger⁴, Bríain Ó Hartaigh¹, Heidi Gransar⁵, Valentina Valenti¹, Fay Y. Lin¹, Stephan Achenbach⁵, Daniel S. Berman⁶, Matthew J. Budoff⁷, Tracy Q. Callister⁸, Mouaz H. Al-Mallah⁹, Filippo Cademartiri¹⁰, Kavitha Chinnaiyan¹¹, Benjamin J.W. Chow¹², Augustin DeLago¹³, Todd C. Villines¹⁴, Martin Hadamitzky¹⁵, Joerg Hausleiter¹⁶, Jonathon Leipsic¹⁷, Leslee J. Shaw⁴, Philipp A. Kaufmann¹⁸, Gudrun Feuchtner¹⁹, Yong-Jin Kim²⁰, Erica Maffei¹⁰, Gilbert Raff¹¹, Gianluca Pontone²¹, Daniele Andreini²¹, Hugo Marques²², Ronen Rubinshtein²³, Hyuk-Jae Chang², and James K. Min^{1*}

¹Department of Radiology, Dalio Institute of Cardiovascular Imaging, NewYork-Presbyterian Hospital, Weill Cornell Medical College, 413 East 69th Street, Suite 108, New York, NY 10021, USA; ²Division of Cardiology, Severance Cardiovascular Hospital, Severance Biomedical Science Institute, Yonsei University College of Medicine, Yonsei University Health System, Seoul, South Korea; ³Division of Cardiology, Department of Internal Medicine, Chung-Ang University Hospital, Chung-Ang University, Seoul, South Korea; ⁴Division of Cardiology, Emory University School of Medicine, Atlanta, GA, USA; ⁵Department of Imaging, Cedars Sinai Medical Center, Los Angeles, CA, USA; ⁶Department of Medicine, University of Erlangen, Erlangen, Germany; ⁷Department of Medicine, Harbor UCLA Medical Center, Los Angeles, CA, USA; ⁸Tennessee Heart and Vascular Institute, Hendersonville, TN, USA; ⁹King Saud bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, King AbdulAziz Cardiac Center, Ministry of National Guard, Health Affairs, Riyadh, Saudi Arabia; ¹⁰Department of Radiology, Montreal Heart Institute, Montreal, Quebec, Canada; ¹¹William Beaumont Hospital, Royal Oaks, MI, USA; ¹²Department of Medicine and Radiology, University of Ottawa, Ottawa, Ontario, Canada; ¹³Capitol Cardiology Associates, Albany, NY, USA; ¹⁴Department of Medicine, Walter Reed Medical Center, Washington, DC, USA; ¹⁵Division of Cardiology, Deutsches Herzzentrum Munchen, Munich, Germany; ¹⁶Medizinische Klinik I der Ludwig-Maximilians-Universität München, Munich, Germany; ¹⁷Department of Medicine and Radiology, University of British Columbia, Vancouver, British Columbia, Canada; ¹⁸University Hospital, Zurich, Switzerland; ¹⁹Department of Radiology, Medical University of Innsbruck, Innsbruck, Austria; ²⁰Seoul National University Hospital, Seoul, South Korea; ²¹Department of Clinical Sciences and Community Health, University of Milan, Centro Cardiologico Monzino, IRCCS Milan, Milan, Italy; ²²UNICA, Cardiac CT and MRI Unit, Hospital da Luz, Lisbon, Portugal; and ²³Department of Cardiology at the Lady Davis Carmel Medical Center, The Ruth and Bruce Rappaport School of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Received 15 November 2016; revised 14 September 2017; editorial decision 14 December 2017; accepted 18 December 2017; online publish-ahead-of-print 20 January 2018

See page 942 for the editorial comment on this article (doi: 10.1093/eurheartj/ehx801)

Aim

The long-term prognostic benefit of coronary computed tomographic angiography (CCTA) findings of coronary artery disease (CAD) in asymptomatic populations is unknown.

Methods and results

From the prospective multicentre international CONFIRM long-term study, we evaluated asymptomatic subjects without known CAD who underwent both coronary artery calcium scoring (CACS) and CCTA ($n = 1226$). Coronary computed tomographic angiography findings included the severity of coronary artery stenosis, plaque composition, and coronary segment location. Using the C-statistic and likelihood ratio tests, we evaluated the incremental prognostic utility of CCTA findings over a base model that included a panel of traditional risk factors (RFs) as well as CACS to predict long-term all-cause mortality. During a mean follow-up of 5.9 ± 1.2 years,

* Corresponding author. Tel: +1 646 962 6192, Fax: +1 646 962 0129, Email: jkm2001@med.cornell.edu

Published by Oxford University Press on behalf of the European Society of Cardiology 2018. This work is written by US Government employees and is in the public domain in the US.

78 deaths occurred. Compared with the traditional RF alone (C-statistic 0.64), CCTA findings including coronary stenosis severity, plaque composition, and coronary segment location demonstrated improved incremental prognostic utility beyond traditional RF alone (C-statistics range 0.71–0.73, all $P < 0.05$; incremental χ^2 range 20.7–25.5, all $P < 0.001$). However, no added prognostic benefit was offered by CCTA findings when added to a base model containing both traditional RF and CACS (C-statistics $P > 0.05$, for all).

Conclusions

Coronary computed tomographic angiography improved prognostication of 6-year all-cause mortality beyond a set of conventional RF alone, although, no further incremental value was offered by CCTA when CCTA findings were added to a model incorporating RF and CACS.

Keywords

Coronary artery calcium scoring • Coronary CT angiography • Prognosis • Coronary artery disease
• Computed tomography • Atherosclerosis

Introduction

In asymptomatic individuals, coronary athero-phenotyping using imaging modalities such as coronary artery calcium scoring (CACS) has been widely used and numerous studies have documented that CACS provides powerful prognostic information across various age groups, gender, baseline risk factors (RFs), and ethnicities.^{1–3}

Considering coronary computed tomographic angiography (CCTA) could provide more detailed coronary atherosclerotic information [i.e. degree of luminal stenosis, plaque composition, and location of coronary segment location including non-calcified plaques (NCPs)], it has been proposed that CCTA might afford additional prognostic benefit over CACS, as well as traditional risk stratification system in asymptomatic populations. Despite this, recent data from a large multicentre international registry revealed that CCTA has negligible benefit for cardiovascular risk stratification in asymptomatic populations.⁴ Yet, given the relatively short-term follow-up duration of the latter study, along with the lack of CCTA information such as plaque composition and plaque location, it remains to be clarified whether CCTA adds further prognostic value beyond CACS and traditional RFs, especially when considering more sophisticated plaque and degree of stenosis information across a more long-term follow-up study.

In light of the preceding discussion, we sought to evaluate whether comprehensive assessment of coronary atherosclerosis by CCTA that included degree of stenosis, plaque composition, and coronary segment location, would stratify future risk of all-cause mortality of asymptomatic individuals, and second, whether the addition of the aforementioned CCTA measures augmented prognostication of all-cause death beyond a set of traditional RF and CACS.

Methods

Design overview, setting, and participants

We previously described the initial study design and rationale of the initial CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry elsewhere.⁵ In brief, the CONFIRM registry was designed to assess the capability of CCTA findings to predict all-cause mortality in patients referred for CCTA. Foremost, study follow-up has been extended and the CONFIRM long term follow-up registry completed, which included study sites that prolonged their follow-up duration of more than 3 years. Thus, overall, 17 181 patients

who underwent CCTA at 17 centres in nine countries (e.g. Austria, Canada, Germany, Israel, Italy, Portugal, South Korea, Switzerland, and USA) were enrolled between February 2003 and May 2011 as part of the long-term follow-up registry. Inclusion criteria were age 18 years or older, an evaluation by CCTA scanner with 64-detector rows or greater, and the presence of interpretable CCTA. For the current study, we excluded patients according to the following exclusion criteria: the presence of chest pain or dyspnoea ($n = 13\,590$), the absence of CACS data ($n = 2133$) or CCTA stenosis information ($n = 6$), the absence of age or gender information ($n = 1$), or individuals with revascularization within index period from CCTA (< 90 days) or prior history of CAD ($n = 225$). Eleven patients with missing baseline Framingham risk scores (FRS) were analysed for baseline characteristics but not included in the predictive analysis. Hence, the analytic sample comprised 1226 subjects. All study participants provided written informed consent and each of the study sites' institutional review boards approved the study protocol.

Clinical data collection

Prior to scanning procedures, we prospectively collected information regarding the presence of traditional cardiac RFs in each study participant. We employed standardized data collection methods in each participating study site.⁶ Systemic arterial hypertension was defined as a documented history of high blood pressure or treatment with anti-hypertensive medications. Diabetes mellitus was defined as known untreated diabetes and/or use of insulin or oral hypoglycaemic agents. We defined dyslipidaemia as known but untreated dyslipidaemia or current treatment with lipid-lowering medications. A positive current smoking history was defined as current smoking or cessation of smoking within 3 months of investigation. Family history of coronary artery disease (CAD) was determined by patient query. Symptom presentation was classified into asymptomatic and symptomatic and symptomatic individuals were further classified into typical chest pain, atypical chest pain, non-cardiac pain, or dyspnoea. From these data, we calculated FRS based on the calculation method by National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NCEP ATP III).⁷

Image acquisition and analysis

Coronary computed tomographic angiography and CACS measures were uniformly acquired using multi-detector row computed tomography (CT) scanners consisting of 64-rows or greater. Coronary artery calcium scoring were measured using the scoring system (in units) developed by Agatston *et al.*,⁸ and participants were categorized in 0, 1–100, 101–400, and >400 . In the analysis, the absolute CACS was

incorporated on top of traditional RFs utilized in the calculation of the FRS category, in order to be consistent with previously developed predictive models that use absolute clinical variables values in a model that already incorporates age and gender as separate variables.

For CCTA, we examined all identified coronary lesions by maximum-intensity-projection and multiplanar reconstruction methods along multiple longitudinal axes and in the transverse plane. We utilized a modified American Heart Association (AHA) 16-segment coronary artery model for analyses.⁹ We defined the coronary plaque as any tissue structures larger than 1 mm², which were identified in two more planes and located either within the lumen of the coronary artery or adjacent to the coronary artery lumen that were able to be distinguished from adjacent epicardial fat, pericardial tissue, or the artery lumen. In each coronary artery segment, we visually classified plaques as non-calcified, mixed, or calcified. The presence of coronary calcification was determined visually in the contrast-enhanced dataset and calcified plaque was defined as a coronary plaque only containing calcification. Non-calcified plaque was defined as a coronary plaque with a density below the contrast-enhanced blood pool without calcification component. Coronary plaques showing both calcified areas of any extent and NCP were classified as mixed plaques. Further classification of NCP into lipid-rich or fibrous tissue was not undertaken due to limited accuracy and reproducibility of such a measurement with the generation of CT scans used during the enrolment period and the dependability of such a measurement on technical aspects such as the concentration of intraluminal contrast.

We defined coronary artery luminal stenosis as the presence of any plaque resulting in diameter reduction. We categorized coronary artery luminal stenosis: non-obstructive stenosis was defined as coronary artery segments displaying plaque with a luminal diameter stenosis 1–49%. Obstructive stenosis was defined as coronary artery plaques imparting luminal diameter stenosis $\geq 50\%$. We defined coronary segment location according to Society of Cardiovascular Computed Tomography (SCCT) guidelines.¹⁰ The total mean dose length product for CCTA and coronary artery calcium scans was 598 ± 324 mGy \times cm.

Statistical analysis

Continuous and categorical variables are expressed as mean \pm standard deviation and absolute counts with percentages, respectively. Differences between continuous and categorical variables were analysed by the Student's *t*-test and the χ^2 test, or the Fisher's exact test, as appropriate. The primary endpoint of this study was all-cause mortality. Cumulative event rates as a function of time and CACS or CCTA parameters were calculated by use of the Kaplan–Meier survival estimates and compared using the log-rank test. Hazard ratios (HR) with 95% confidence intervals (CI) for the association of CACS and the various measures of CCTA with all-cause mortality were calculated by use of unadjusted and adjusted Cox proportional hazard regression models. In this study, the adjusted model controlled for covariates employed for the FRS.

Next, we assessed the incremental benefit of CACS and CCTA for improving prognostic utility by evaluating the statistical significance of the contribution of each added variable by use of the likelihood ratio test¹¹ and model discrimination with calculation of C-statistics.^{12,13} Initially, a base model according to traditional RF only was employed, and included categories of the published FRS: low (<10%), intermediate (10–20%), and high (>20%). Subsequently, CACS, expressed as four categories (e.g. 0, 1–100, 101–400, >400), was added to determine its predictive value beyond the traditional RF. Last, we added the following CCTA diagnosed parameters to the model that included traditional RF model and both CACS and FRS model: (i) coronary luminal stenosis severity assessment models including number of segments with any stenosis (e.g. none, one, and \geq two segments), number of segments with obstructive ($\geq 50\%$)

stenosis (e.g. none, one, and \geq two segments), number of obstructive ($\geq 50\%$ stenosis) vessel disease [e.g. none, non-obstructive, obstructive one-vessel disease (VD), obstructive two-VD, and obstructive three-VD or left main disease]; (ii) coronary plaque composition assessment models including number of segments with non-calcified or mixed plaques (e.g. none, one, and \geq two segments), number of segments with calcified plaques (e.g. none, one, and \geq two segments); and (iii) coronary luminal stenosis location assessment models including number of proximal segments with any stenosis (e.g. none, one, and \geq two segments), number of proximal segments with obstructive stenosis (e.g. none, one, and \geq two segments). All analyses were performed using STATA version 12.0 (StataCorp LP, College Station, TX, USA), and a statistical value of *P*-value <0.05 was considered significant.

Results

Baseline characteristics

Overall, the study population consisted of 1226 asymptomatic subjects: mean age was 58 ± 12 years and 66% were male. As reported in Table 1, among the study population, 639 (52%) subjects had coronary artery luminal stenosis and 587 (48%) subjects had no coronary atherosclerosis by CCTA. Patients with any coronary atherosclerosis tended to be older, male, and had a higher prevalence of hypertension, diabetes, current smokers, dyslipidaemia, and a higher body mass index (all *P* < 0.01).

Clinical outcomes and risk prediction models of FRS and coronary artery calcium scoring

During a mean follow-up of 5.9 ± 1.2 years, 78 deaths occurred. In Cox regression analysis, compared with individuals with low risk (FRS <10%), individuals with intermediate risk (FRS 10–20%) had an increased risk of all-cause death (HR 2.05, 95% CI 1.19–3.51; *P* = 0.009). As described in Table 2, individuals with high risk (FRS >20%) had a more pronounced risk of all-cause death (HR 3.87, 95% CI 2.21–6.78; *P* < 0.001). Increasing categories of CACS was also associated with a higher risk of mortality. That is, when compared with individuals with CACS 0, those with CACS 1–100 (HR 3.68, 95% CI 1.92–7.05; *P* < 0.001), CACS 101–400 (HR 3.04, 95% CI 1.45–6.40; *P* < 0.003), and CACS >400 (HR 7.88, 95% CI 4.19–14.83; *P* < 0.001) had a higher risk of death.

Risk prediction models of coronary computed tomographic angiography

The risk of death was classified using the degree and extent of luminal stenosis by CCTA with unadjusted and adjusted for traditional RF (Figure 1). Individuals with any stenosis in one segment had a 3.9-fold (95% CI 1.84–8.28; *P* < 0.001) higher risk of death, and those with stenosis in \geq two segments had 4.1-fold (95% CI 2.14–7.76; *P* < 0.001) higher risk of death than those without luminal stenosis after adjustment of traditional RF. In addition, the number of segments with obstructive luminal stenosis strongly predicted risk of death. Notably, individuals with one segment and more than two segments with obstructive stenosis experienced a 2.6-fold (95% CI 1.39–4.87; *P* = 0.003) and 3.5-fold (95% CI 1.95–6.32; *P* < 0.001) higher risk of death, respectively. Further, compared with individuals without

Table 1 Baseline characteristics according to presence or absence of coronary artery luminal stenosis by coronary computed tomographic angiography

Variables	Total (n = 1226)	No stenosis (n = 587)	Any stenosis (n = 639)	P-value
Age (years)	58.0 ± 12.4	53.1 ± 12.0	62.6 ± 10.8	<0.001
Gender (male)	813 (66.3)	339 (57.8)	474 (74.2)	<0.001
Hypertension	709 (58.3)	276 (47.4)	433 (68.3)	<0.001
Diabetes	123 (10.1)	42 (7.2)	81 (12.8)	0.001
Current smoking	196 (16.1)	78 (13.4)	118 (18.6)	0.010
BMI (kg/m ²)	26.8 ± 4.6	26.4 ± 4.5	27.3 ± 4.6	<0.001
Dyslipidaemia	674 (55.3)	240 (41.2)	434 (68.1)	<0.001
Aspirin use (%)	344 (31.7)	101 (19.8)	243 (42.3)	<0.001
Beta-blocker use (%)	290 (26.8)	143 (28.1)	147 (25.6)	0.357
Statin use (%)	376 (34.4)	94 (18.3)	282 (48.6)	<0.001

Continuous values are mean + SD and categorical values are number and percentage (%).
BMI, body mass index.

Table 2 Risk of all-cause mortality according to Framingham risk score and coronary artery calcium score categories

Model	No. of deaths/ subjects	HR (95% CI)	P-value
Framingham risk score			
Low (<10%)	26/681	1.00	NA
Intermediate (10–20%)	27/363	2.05 (1.19–3.51)	0.009
High (>20%)	25/171	3.87 (2.21–6.78)	<0.001
CACs			
0	15/602	1.00	NA
1–100	23/276	3.68 (1.92–7.05)	<0.001
101–400	13/188	3.04 (1.45–6.40)	0.003
>400	27/160	7.88 (4.19–14.83)	<0.001

CACS, coronary artery calcium scoring; CI, confidence interval; HR, hazard ratio; NA, not applicable.

luminal stenosis, the adjusted hazards for all-cause death increased proportionally on the background of CAD extent for any non-obstructive (1–49% stenosis) stenosis (HR 3.16; 95% CI 1.64–6.12; $P < 0.001$), obstructive ($\geq 50\%$ stenosis) one-vessel stenosis (HR 5.78, 95% CI 2.73–12.23; $P < 0.001$), obstructive two-vessel stenosis (HR 6.65, 95% CI 2.31–19.16; $P < 0.001$), and obstructive three-vessel stenosis or left main stenosis (HR 8.48, 95% CI 3.28–21.92; $P < 0.001$).

Moreover, coronary plaque composition assessment models including the presence of non-calcified or mixed plaque, as well as calcified plaque, heightened the risk of all-cause death in both unadjusted and adjusted models. For instance, the presence of non-calcified or mixed plaque in a single segment (HR 2.34, 95% CI 1.23–4.48; $P = 0.010$) and multi-segments (HR 2.50, 95% CI 1.48–4.21; $P = 0.001$) were shown to increase the risk of all-cause death as compared with individuals without any plaque, even after adjustment of traditional RF. Further, the presence of calcified plaque in multiple

segments increased risk of death after adjustment of baseline RFs (HR 2.21, 95% CI 1.32–3.69; $P = 0.003$).

Incremental value of coronary computed tomographic angiography for prediction of all-cause death

As reported in Table 3, adding CACS over a traditional risk stratification model that used FRS significantly improved prediction of all-cause mortality (e.g. incremental χ^2 20.4, $P < 0.001$). Inclusion of CCTA information including the degree of luminal stenosis and plaque composition also improved prediction of all-cause death beyond the traditional RF model (all, P for incremental $\chi^2 < 0.001$). However, compared with the model that included both traditional RF and CACS, addition of CCTA information did not lead to a significant increase in prediction for all-cause mortality (all $P > 0.05$), with the exception of number of vessels with stenosis $\geq 50\%$ (χ^2 9.69, $P = 0.046$), which provided only a modest significant increase.

The incremental benefit of CCTA was also evaluated using the C-statistic as described in Table 4. The added benefit of CCTA information including degree of luminal stenosis and plaque composition was significant when compared with the traditional RF model. However, no incremental benefit of any of the CCTA variables over traditional RFs and CACS (all $P > 0.05$) for prognostication was observed.

Discussion

In this international multi-centre study with long-term follow-up duration, we set out to determine whether comprehensive CAD assessment by CCTA improved risk prediction for future mortality over a traditional RF model and also when CACS was considered in asymptomatic population. The principle finding was that the incremental risk-predictive benefit of comprehensive CAD information by CCTA, including degree and extent of plaque, coronary segment location, and plaque composition, over traditional RFs and CACS model was negligible in asymptomatic population across a long-term follow-up. Such a finding is in agreement with the 2013 European

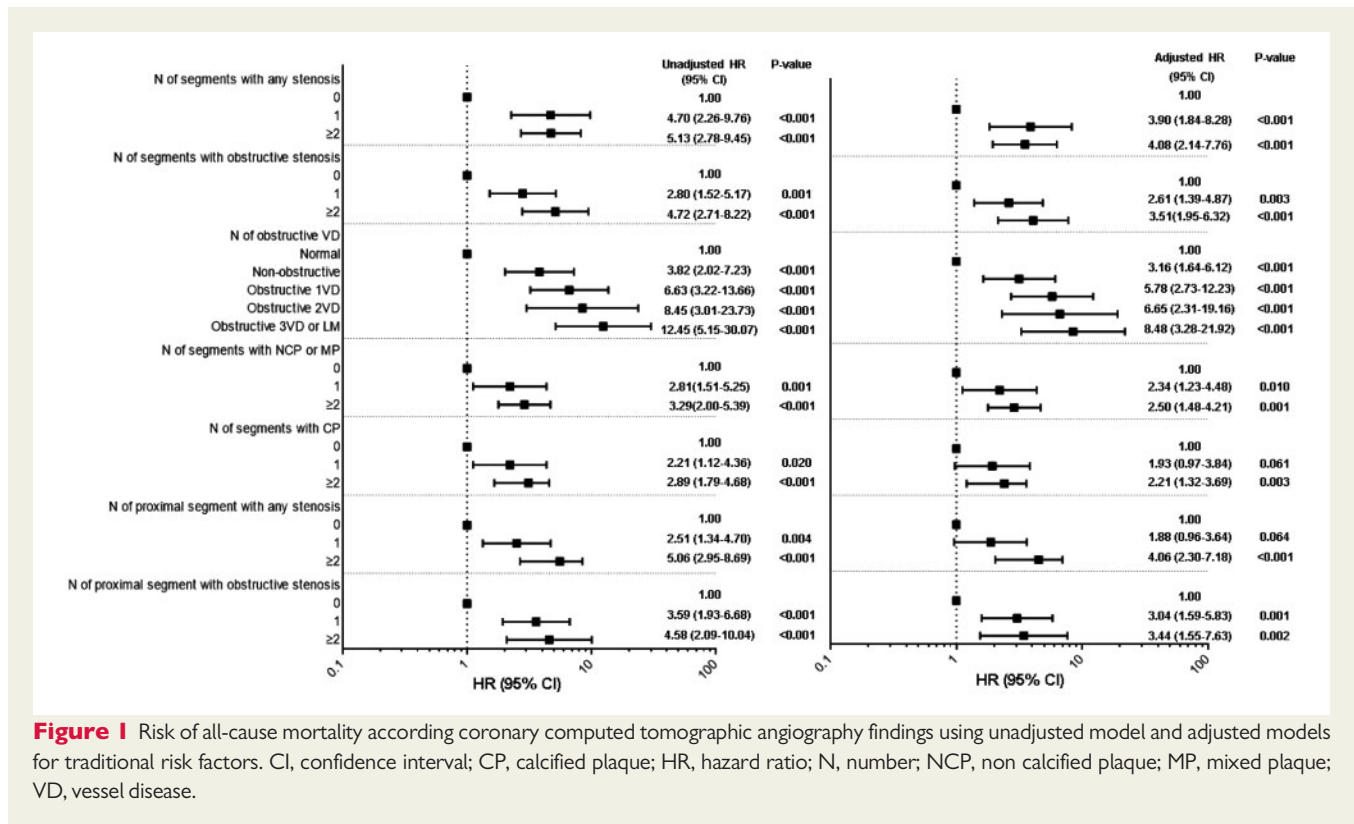


Figure 1 Risk of all-cause mortality according coronary computed tomographic angiography findings using unadjusted model and adjusted models for traditional risk factors. CI, confidence interval; CP, calcified plaque; HR, hazard ratio; N, number; NCP, non calcified plaque; MP, mixed plaque; VD, vessel disease.

Table 3 Comparison of performance of coronary computed tomographic angiography over traditional risk factors alone and traditional risk factor plus coronary artery calcium scoring in predicting long-term risk of all-cause mortality using likelihood ratio tests

Models	LR incremental χ^2		LR incremental χ^2	
	Compared with traditional RF alone	P-value	Compared with CACS + traditional RF	P-value
Baseline models				
Traditional RF	NA	NA	NA	NA
Traditional RF + CACS	20.40	<0.001	NA	NA
Adding degree of stenosis Information by CCTA				
No. of segments with any stenosis	26.05	<0.001	5.65	0.059
No. of segments with stenosis $\geq 50\%$	25.43	<0.001	5.03	0.080
No. of vessels with stenosis $\geq 50\%$	30.09	<0.001	9.69	0.046
Adding plaque characterization Information by CCTA				
No. of segments with calcified plaques	20.70	<0.001	0.30	0.860
No. of segments with NCP or mixed plaque	23.26	<0.001	2.86	0.240
Adding plaque location information by CCTA				
No. of proximal segment with any stenosis	25.52	<0.001	5.12	0.080
No. of proximal segment with stenosis $\geq 50\%$	25.50	<0.001	5.10	0.080

CACS, coronary artery calcium scoring; CCTA, coronary CT angiography; LR, likelihood ratio; NCP, non-calcified plaque; NA, not applicable; RF, risk factors (covariates in the Framingham risk score such as age, gender, smoking status, total cholesterol, high-density lipoprotein cholesterol, blood pressure and treatment for hypertension).

Table 4 C-Statistics for evaluation of added benefit of coronary computed tomographic angiography findings over traditional risk factors alone and combined model of traditional risk factors plus coronary artery calcium scoring in predicting long-term all-cause mortality

Model	C-statistics	P compared with traditional RF	P compared with traditional RF + CACS
Baseline models			
Traditional RF	0.641	NA	NA
Traditional RF + CACS	0.711	0.030	NA
Adding degree of stenosis Information by CCTA			
No. of segments with any stenosis	0.723	0.009	0.305
No. of segments with stenosis $\geq 50\%$	0.728	0.013	0.075
No. of vessels with stenosis $\geq 50\%$	0.734	0.008	0.117
Adding plaque characterization Information by CCTA			
No. of segments with calcified plaques	0.709	0.033	0.597
n of segments with NCP or mixed plaque	0.721	0.013	0.286
Adding plaque location information by CCTA			
No. of proximal segment with any stenosis	0.727	0.012	0.071
No. of proximal segment with stenosis $\geq 50\%$	0.724	0.015	0.117

CACS, coronary artery calcium scoring; CCTA, coronary CT angiography; NCP, non-calcified plaque; NA, not applicable; RF, risk factors (detailed in footnote of Table 3).

guidelines on the management of stable CAD and the 2016 European guidelines on Cardiovascular Disease Prevention in Clinical Practice, which give CACS a Class IIb label (level of evidence B) for use as a risk modifier in the assessment of cardiovascular risk and a Class III label (level of evidence C) for CCTA for use as a screening test in asymptomatic individuals.^{14,15}

We previously demonstrated that CCTA afforded little to no benefit for prediction of fatal outcomes over a traditional RF and CACS model in an asymptomatic population across a short-term follow-up duration.⁴ Since, several studies have analysed the prognostic benefit of CCTA in other asymptomatic populations.^{16,17} Rodriguez *et al.*¹⁸ demonstrated that diabetes, cholesterol level, and systolic blood pressure were related to NCP burden by CCTA, which cannot be distinguished by CACS, in an asymptomatic population at low-to-moderate risk. Lee *et al.*¹⁶ also reported that CCTA offered added prognostic benefit over exercise testing in another asymptomatic population. More recently, Plank *et al.*¹⁷ reported that high prevalence of CAD in a high-risk asymptomatic population and CACS = 0 did not exclude significant non-calcified coronary atherosclerosis. However, none of these studied observed that CCTA provided incremental benefit above and beyond traditional RF and CACS in an asymptomatic population. Further, a recent prospective randomized trial reinforced the lack of evidence of CAD screening by CCTA in asymptomatic populations.¹⁹ In that trial, although the study sample represented an asymptomatic diabetic population considered being at high risk, a CAD screening strategy by CCTA failed to lower fatal and non-fatal outcomes.

The chief cause why CCTA appeared to lack additional prognostic utility over the base model that included CACS, most likely owes to the contention that CACS is a robust marker of global coronary atherosclerotic burden. Although recent studies using CCTA demonstrated that patients with high-risk features such as NCP or positive remodelling experienced higher incidence of acute coronary syndrome, the total atherosclerotic plaque burden was not accounted

for as a confounder.²⁰ Further, these studies enrolled symptomatic cohorts while there has been no evidence to suggest that high-risk plaque features were prognostically important in asymptomatic population. The current study suggests that the added benefit of assessing plaque composition and location over total atherosclerotic burden detected by CACS was not clinically beneficial in asymptomatic individuals.

Indeed, CACS is well known to provide superior discrimination and reclassification beyond other useful markers, such as carotid intima-media thickness, brachial flow-mediated dilation, ankle-brachial index, or C-reactive protein.²¹ Further still, the prognostic benefit of CACS has been validated in numerous large-scale prospective multicentre studies utilizing several heterogeneous populations who were followed long-term.¹⁻³ Recently, a novel risk equation system for predicting 10-year CAD, which integrated traditional RFs and CACS, has been developed using data belonging to the Multi-Ethnic Study of Atherosclerosis (MESA) cohort.²² The purpose of this convenient scoring system is to facilitate the integrated use of CACS with traditional RF in clinical practice.

However, a major limitation of CACS is the lack of data for management or down-stream testing strategies according to CACS.²³ Although it is quite clear that a zero CACS warranted very good prognosis in a long-term follow-up duration,²⁴ there is no consensus of treatment or downstream screening strategies for patients with CACS >0. More recently, we established that CCTA might induce some benefit over traditional RFs and CACS, specifically in those with intermediate CACS (i.e. between 100 and 400).²⁵ Most correctly reclassified subjects by CCTA were those with a non-event (e.g. 0.70 vs. 0.05 for non-event vs. event, respectively). To this end, CCTA should perhaps be considered for downstream study, particularly in patients presenting with intermediate CACS, in order to reclassify those with low risk for the purpose of avoiding unnecessary treatment or clinical decisions. Though clearly, forthcoming studies

are needed to test this notion. Furthermore, plaque characterization and quantification on CCTA, beyond obtaining a CACS, may become useful for determination of plaque progression or regression, which could ultimately influence clinical decision.²⁶

This study had some limitations that bear mentioning. Our study sample were representative of a subgroup derived from the CONFIRM long-term follow-up registry who were referred for CCTA. As such, our patients do not truly reflect those in the general population, which might have led to potential selection bias. Though we may add, in order to minimize any potential for selection bias, we only employed experienced CCTA centres and prospectively used standardized data definitions. Although this study is considered to be the largest global multicentre CCTA registry to date, we cannot discount the possibility that the absence in incremental prognostic benefit associated with our CCTA measures might have been attributable to a small sample size, and consequently, low statistical power. Nevertheless, given the potential risk of radiation and intravenous contrast use, careful consideration of potential risks and benefits of the clinical investigation must be undertaken to perform prospective randomized studies to fully address these questions.

Inherent limitations of the CONFIRM study were such that baseline medication use was solely available without the recorded changes in medication intake after CCTA acquisition. Future studies investigating the impact of medication adjustment (e.g. aspirin, statin, and beta-blockers) on outcomes should be performed. Secondly, the FRS was used as the traditional RF assessment tool over contemporary and better-calibrated risk scores such as the ESC HEART SCORE, given the ability to compute such as score within the available clinical variables. Thirdly, the clinical endpoint examined was all-cause mortality, since major adverse cardiovascular events were not available for the entire cohort. Finally, there was no downstream functional testing performed in heavily calcified lesions when the degree of stenosis was questionable, which could have lead to misdiagnosis of luminal stenosis severity due to blooming and beam hardening artifacts. Previous studies have circumvented this issue through both anatomic and functional testing by integrating CT myocardial perfusion and fractional flow reserve -CT with CCTA.²⁷

Conclusion

While CCTA demonstrated improved prognostic utility for prediction of long-term mortality over traditional RF alone, CCTA findings did not augment prognostication beyond traditional RFs when CACS was also taken into consideration. Until further proven, the clinical utility of CCTA should not be considered for future cardiovascular risk stratification in asymptomatic individuals.

Funding

This work is supported by the National Heart, Lung and Blood Institute under award number (R01HL115150 and R01HL118019) and also in part by a generous gift from the Dalio Institute of Cardiovascular Imaging (New York, NY) and the Michael Wolk Foundation. This study was also funded by an unrestricted educational grant from GE Healthcare.

Conflict of interest: J.K.M. serves on the scientific advisory board of Arineta, has ownership in MDDX, and has a research agreement with GE healthcare. All other authors have no disclosures to report.

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