

Triglyceride glucose index and smoking are linked to new coronary artery calcification after normal baseline scan

Received: 5 November 2025

Accepted: 13 April 2026

Published online: 21 April 2026

Cite this article as: Won K., Choi S., Chun E.J. *et al.* Triglyceride glucose index and smoking are linked to new coronary artery calcification after normal baseline scan. *Sci Rep* (2026). <https://doi.org/10.1038/s41598-026-49265-w>

Ki-Bum Won, Su-Yeon Choi, Eun Ju Chun, Sung Hak Park, Jidong Sung, Hae Ok Jung & Hyuk-Jae Chang

We are providing an unedited version of this manuscript to give early access to its findings. Before final publication, the manuscript will undergo further editing. Please note there may be errors present which affect the content, and all legal disclaimers apply.

If this paper is publishing under a Transparent Peer Review model then Peer Review reports will publish with the final article.

Triglyceride glucose index and smoking are linked to new coronary artery calcification after normal baseline scan

Running title: Risk factors for new onset of CAC and its severity

Authors:

Ki-Bum Won¹, Su-Yeon Choi², Eun Ju Chun³, Sung Hak Park⁴, Jidong Sung⁵, Hae Ok Jung⁶, Hyuk-Jae Chang^{7*}

Affiliations:

¹Division of Cardiology, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Gwangmyeong, South Korea

²Division of Cardiology, Healthcare System Gangnam Center, Seoul National University Hospital, Seoul, South Korea

³Division of Radiology, Seoul National University Bundang Hospital, Seongnam, South Korea

⁴Division of Radiology, Gangnam Heartscan Clinic, Seoul, South Korea

⁵Division of Cardiology, Samsung Medical Center, Seoul, South Korea

⁶Division of Cardiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, South Korea

⁷Division of Cardiology, Yonsei University College of Medicine, Seoul, South Korea

E-mail:

Ki-Bum Won, E-mail: kbwon99@naver.com

Su-Yeon Choi, E-mail: sychoi9@gmail.com

Eun Ju Chun, E-mail: drejchun@hanmail.net

Sung Hak Park, E-mail: shparkmdmax@gmail.com

Jidong Sung, E-mail: jidong.sung@gmail.com

Hae Ok Jung, E-mail: hojheart@catholic.ac.kr

Hyuk-Jae Chang, E-mail: hjchang@yuhs.ac

Address for correspondence:

Hyuk-Jae Chang, MD, PhD

Division of Cardiology, Severance Cardiovascular Hospital

Yonsei University College of Medicine

50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, South Korea

Tel.: +82(0)2 22288460; Fax: +82(0)2 3932041

E-mail: hjchang@yuhs.ac

Abstract

This study evaluated the incidence and severity of the new onset of coronary artery calcification (CAC) related to clinical factors assessed at follow-up CAC scan among 6993 asymptomatic Korean adults (48.4 ± 7.2 years; 79.8% men) without underlying baseline CAC. During a median follow-up of 3.3 years, the risk of (a) the new onset of CAC (defined as coronary artery calcium score [CACS] >0 at follow-up), (b) difference of ≥ 2.5 between baseline and follow-up square root ($\sqrt{\cdot}$) transformed CACS ($\Delta\sqrt{\text{transformed CACS}}$), and (c) CACS >100 at follow-up was evaluated. The incidence of the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 was 19.3%, 13.0%, and 1.0%, respectively. After adjusting for traditional risk factors identified at initial CT scan and interscan period, the levels of systolic blood pressure, triglyceride glucose (TyG) index, hemoglobin A1C (HbA1C), and low-density lipoprotein cholesterol and current smoking were positively associated with the risk of the new onset of CAC and $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, respectively. TyG index, HbA1C, and current smoking were associated with the risk of CACS >100 (all $P < 0.05$). An age-based subgroup analysis revealed that TyG index and current smoking were significantly associated with the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 among participants aged <55 years. In conclusion, both TyG index and smoking were independently associated with the new onset of CAC and its severity, especially in adults aged <55 years without baseline CAC.

Keywords: Triglyceride glucose index, Smoking, Atherosclerosis, Coronary artery calcification

ARTICLE IN PRESS

Introduction

Coronary atherosclerosis develops subclinically and progresses over time. The degree of coronary artery calcification (CAC) is positively associated with the total plaque burden of coronary arteries [1]. The coronary artery calcium score (CACS), measured using computed tomography (CT), is effective in detecting asymptomatic individuals at risk of adverse clinical events beyond traditional cardiovascular (CV) risk factors [2,3]. CACS measurement using CT offers the advantages of low cost, high reproducibility, low inter- and intra-observer variability, and easy acquisition of images. Furthermore, CACS has been widely used to stratify CV risk in the asymptomatic adult population regardless of sex and ethnicity.

The absence of underlying CAC indicates a very low short-term risk of major CV events or mortality [4-6]. However, numerous studies have revealed that CAC progression is common, especially in adults who have experienced major CV events [7,8]. Identifying the conversion from the absence of CAC to any measurable CAC and its determinants is particularly important because the risk of CV increases parallelly even at a very low CAC burden [3,6]. Data on whether repeated CAC scans for assessing changes in CACS help predict the prognosis of asymptomatic adults are limited. Recently, the Heinz Nixdorf Recall (HNR) study showed the significance of early detection of the presence of CAC and its progression in asymptomatic adults [9]. According to the HNR study, CAC progression assessed using repeated CAC scans could readjust CV risk in clinical

condition without heavy CAC at baseline. The management of CV risk factors has a substantial impact on the progression of subclinical arteriosclerosis. Despite the possible changes in the degree of managing CV risk factors after CT-based evaluation [10], the determinants of the new onset of CAC have been evaluated in asymptomatic adults without underlying baseline CAC using only clinical factors measured at the time of initial CT scan [11]. In the present study conducted among asymptomatic Korean adults who had no underlying CAC at baseline, we focused on assessing (a) the incidence of the new onset of CAC according to the presence of traditional risk factors at initial CAC scan and (b) the association of numerous clinical factors assessed at follow-up CAC scan with the new onset of CAC and its severity.

Methods

Study design and participants

The present study analyzed data from the Korea Initiatives on Coronary Artery Calcification (KOICA) registry, which was designed to identify the effectiveness of CACS for primary prevention in asymptomatic Korean adults. Data were gathered from six healthcare centers in South Korea (Severance Cardiovascular Hospital, Seoul National University Hospital, Seoul National University Bundang Hospital, Seoul St. Mary's Hospital, Samsung Medical Centre, and Gangnam Heartscan Clinic). In the present study, 6993 individuals who had undergone at least two CAC screening scans from December 2003 to August 2017 and had no CAC at

the initial CAC scan were enrolled. A flowchart of the inclusion and exclusion criteria of the present study is shown in **Supplementary Fig. S1**.

At each visit for CAC screening, participants completed a self-reported medical questionnaire on their medical history. Participants' height and weight were measured while they were wearing light clothing and no shoes, and their body mass index (BMI) was calculated. Participants' blood pressure was measured using an automatic manometer on the right arm after letting them rest for at least 5 min. The value of blood pressure after single measurement was used if it was in the normal range, and the mean value of blood pressure was used after two measurements if it was in the abnormal range. For all blood tests, blood was drawn after participants fasted for at least 8 h. The triglyceride glucose (TyG) index was calculated following the formula of $\ln(\text{triglyceride [mg/dL]} \times \text{glucose [mg/dL]} / 2)$ [12]. Traditional CV risk factors were assessed at the time of initial CAC scan. Hypertension was defined as systolic blood pressure (SBP) of more than 140 mmHg, diastolic blood pressure of more than 90 mmHg, or the use of antihypertensive medication with a previous diagnosis of hypertension based on the Korean Hypertension Society Guidelines. Diabetes mellitus was defined as a fasting glucose level of more than 126 mg/dL, hemoglobin A1C (HbA1C) of more than 6.5%, or the use of antidiabetic medication with a prior diagnosis of diabetes. Hyperlipidemia was defined as the total cholesterol level of more than 240 mg/dL or the use of antihyperlipidemic medication. Obesity was classified as a BMI of

more than 25.0 kg/m² based on cutoffs for the Korean population [13]. Current smoking was defined as either currently smoking at the time of the CT examination or having quit less than 1 month prior.

Measurement of CAC

We determined CACS using CT scans captured with the following scanners exhibiting ≥ 16 -slice multidetectors: Siemens 16-slice Sensation (Siemens, Forchheim, Germany), Philips Brilliance 256 iCT (Philips Healthcare, Cleveland, OH), Philips Brilliance 40-channel multidetector CT (Philips Healthcare, Cleveland, OH), and GE 64-slice Lightspeed (GE Healthcare, Milwaukee, WI, USA). An electrocardiogram (ECG)-triggered scan protocol was used for all CT scans. CACS was determined by experienced CV radiologists, and the results were reported in participants' electronic health records. The new onset of CAC was defined as CACS > 0 at the follow-up CT scan. Both (a) CAC progression defined as a difference of ≥ 2.5 between baseline and follow-up square root ($\sqrt{}$) transformed CACS ($\Delta\sqrt{\text{transformed CACS}}$) using the SQRT method [14,15] and (b) CACS > 100 at follow-up were assessed together. Informed consent for CT examination was obtained from each participant. All methods were performed in accordance with the relevant guidelines and regulations. The study protocol was approved by the Institutional Review Board of Severance Cardiovascular Hospital (IRB no: 4-2014-0309). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies. The funders were not

involved in the design, conduct, reporting, or dissemination of the study.

Statistical analysis

Continuous variables are presented as means and standard deviations, whereas categorical variables are presented as frequencies and percentages. A logistic regression model adjusted for interscan periods was used to evaluate the associations of traditional risk factors assessed at the initial CT scan and clinical factors assessed at the follow-up CT scan with the risk of newly developed CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and $\text{CACS} > 100$. To identify the independent association of clinical factors assessed at the follow-up CAC scan with CAC changes, baseline traditional risk factors were adjusted together in the regression model using the forced entry method. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 19.0 (IBM Corp., Armonk, NY) and SAS version 9.1.3 (SAS Institute Inc., Cary, NC). A P-value of < 0.05 was considered statistically significant for all analyses.

Results

Clinical characteristics

The clinical characteristics of participants are presented in **Table 1**. Their mean age was 48.4 ± 7.2 years, and 5583 participants (79.8%) were men. At the initial CT scan, the proportions of participants with an advanced age (≥ 55 years), hypertension, diabetes mellitus, hyperlipidemia, obesity, and a smoking history were 18.0%, 23.5%, 7.9%, 22.5%, 38.1%,

and 14.4%, respectively. At the follow-up CT scan, the proportions of participants with an SBP <120 mmHg, low-density lipoprotein cholesterol (LDL-C) <130 mg/dL, and current smoking were 53.9%, 60.7%, and 22.0%, respectively; the levels of TyG index and HbA1C were 8.6 ± 0.6 units and $5.7\% \pm 0.6\%$, respectively. Clinical factors (continuous variables) at the initial CT scan are described in **Supplementary Table S1**.

Changes in CAC during follow-up

During a median follow-up period of 3.3 years, the incidence of the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 was 19.3%, 13.0%, and 1.0%, respectively (**Table 2**). The incidence of the new onset of CAC was significantly higher in participants with traditional risk factors than in those without traditional risk factors at the initial CT scan (**Fig. 1**). The risk of the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 related to traditional risk factors identified at the time of initial CT scan is presented in **Table 3**.

Association of clinical factors with newly developed CAC and its severity

In the multivariate logistic regression analysis, both SBP <120 mmHg and LDL-C <130 mg/dL were associated with a lower risk of the new onset of CAC and $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$. The TyG index, HbA1C level, and current smoking were associated with a higher risk of the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 (**Table 4**). In a subgroup

analysis of participants aged <55 and ≥ 55 years, the TyG index and current smoking were independently associated with the new onset of CAC, $\Delta\sqrt{\text{transformed CACS}} \geq 2.5$, and CACS >100 only in participants aged <55 years (**Table 5**). P-values for interactions of the TyG index, HbA1C, and current smoking in participants aged <55 and ≥ 55 years are presented in **Supplementary Table S2**.

Discussion

To the best of our knowledge, this longitudinal study analyzed data of the largest number of asymptomatic adults without underlying baseline CAC. Considering the predominant effect of baseline coronary plaque burden on the rapid progression of coronary atherosclerosis [16], it is important to identify determinants for the early development and progression of CAC in asymptomatic adults. The greatest strength of our study is that the CAC change was examined using clinical factors measured at follow-up CT scan in asymptomatic adults without baseline CAC.

In the Cardiovascular Risk in Young Finns Study [17], elevated levels of LDL-C and SBP were both independent predictors of CAC in adulthood. This cross-sectional study indicated that risk factors in adolescence may play important roles in the pathogenesis of coronary atherosclerosis. In contrast, recent data revealed that the prediction of CAC progression using clinical risk factors or biomarkers might be difficult in the elderly or in adults with moderate-to-severe CAC at baseline [18–20]. These findings

emphasized on the early detection of the presence and progression of CAC to prevent advanced coronary artery disease or major adverse CV events among asymptomatic adults.

The HNR study showed that clinical factors such as age, LDL-C, blood pressure, and current smoking were strongly associated with CAC development in a cohort of 4184 middle-aged-to-older adults who had no CAC at baseline during a mean follow-up of 5.1 years [11]; however, all clinical factors in the HNR study were examined at the initial CAC scan. In the cross-sectional study of Progression of Early Subclinical Atherosclerosis, the LDL-C levels were closely associated with early systemic atherosclerosis in 1779 participants without traditional risk factors [21]. Similarly, in a cohort of 1250 asymptomatic adults who were considered healthy according to conventional guidelines, the optimal LDL-C level for predicting subclinical coronary atherosclerosis was determined as 127.5 mg/dL [22]. Regarding the definition of hypertension, the guidelines of the American College of Cardiology/American Heart Association on the management of blood pressure have lowered the blood pressure thresholds for the diagnosis of hypertension [23]. However, the 2024 European Society of Cardiology guidelines for the management of hypertension retained the traditional definition of hypertension [24]. Considering the lack of consensus on the optimal targets of LDL-C or blood pressure in asymptomatic adults who are at low-to-intermediate CV risk, the use of CACS to individualize therapeutic targets of clinical risk factors has been suggested for this population [25–28]. In the present study,

maintaining both LDL-C of <130 mg/dL and SBP of <120 mmHg were associated with a lower risk of the new onset of CAC and CAC progression defined using the SQR method; however, these factors were not significantly associated with the risk of CACS >100 . Further randomized studies with larger samples are necessary to confirm the optimal targets of LDL-C or blood pressure for minimizing the development and progression of CAC.

Data on the changes of CAC related to insulin resistance (IR) among adults without underlying baseline CAC are limited. The TyG index has been suggested as a simple and reliable biomarker of IR [29,30]. In the Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging study, the TyG index was closely associated with the risk of rapid progression of coronary atherosclerosis [31]. In addition, HbA1C was closely related to the rapid plaque progression of major epicardial coronary arteries, even in conditions without baseline coronary plaques [32]. These results showed a substantial role of both IR and glycemic control in the progression of coronary atherosclerosis. In the present study, TyG index, HbA1C, and current smoking were significantly associated with the new onset of CAC and its severity in 6993 participants without underlying CAC at baseline. Notably, these clinical factors showed independent associations with the risk of the new onset of CAC, Δ transformed CACS ≥ 2.5 , and CACS >100 in participants aged <55 years. Similar to observations of previous studies [17,33], these results suggest that the efforts to reduce IR, achieve optimal

glycemic control, and quit smoking should be further emphasized for young or middle-aged adults in the field of primary prevention.

The present study had some limitations. First, all participants voluntarily visited healthcare centers for general health examinations. Therefore, a selection bias might be present due to the differences of participants in health concerns. Second, the use of pharmacological agents was not controlled owing to the observational nature of the KOICA registry. Third, we did not perform a variability analysis in the present study. However, previous studies confirmed both high reproducibility and low variability in the measurement of CACS [34,35]; according to the data from the Multi-Ethnic Study of Atherosclerosis registry, inter- and intra-observer agreements were very high, with kappa values of 0.90 and 0.93, respectively. Based on this firm evidence, the CACS has been widely used for general health examinations in recent clinical practice. In the present study, the initial and follow-up CAC scans for each participant were performed using the same CT scanner with an ECG-triggering method. Fourth, we did not consider environmental risk factors and the potential roles of diet or exercise in this study. Fifth, information on other significant confounders and detailed smoking status was limited in the present study. Finally, 79.8% of participants in the present study were male, potentially limiting the generalizability of the results.

In summary, both TyG index and current smoking are strongly associated with the new onset of CAC and its severity, especially among adults aged <55 years without underlying CAC at baseline. Further

prospective and randomized studies are necessary to determine the target level of the TyG index for preventing subclinical atherosclerosis and major CV events in the primary prevention.

ARTICLE IN PRESS

References

1. Greenland, P. et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. *J. Am. Coll. Cardiol.* 49, 378–402. <https://doi.org/10.1016/j.jacc.2006.10.001> (2007).
2. Polonsky, T.S. et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. *JAMA* 303, 1610–1616. <https://doi.org/10.1001/jama.2010.461> (2010).
3. Erbel, R. et al. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. *J. Am. Coll. Cardiol.* 56, 1397–1406. <https://doi.org/10.1016/j.jacc.2010.06.030> (2010).
4. Kondos, G.T. et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. *Circulation* 107, 2571–2576. <https://doi.org/10.1161/01.CIR.0000068341.61180.55>

(2003).

5. Taylor, A.J. et al. Coronary calcium independently predicts incident premature coronary heart disease over measured cardio-vascular risk factors: mean three-year outcomes in the prospective army coronary calcium (PACC) project. *J. Am. Coll. Cardiol.* 46, 807–814.
<https://doi.org/10.1016/j.jacc.2005.05.049> (2005).
6. Erbel, R., Budoff, M. Improvement of cardiovascular risk prediction using coronary imaging: subclinical atherosclerosis: the memory of lifetime risk factor exposure. *Eur. Heart J.* 33, 1201–1213.
<https://doi.org/10.1093/eurheartj/ehs076> (2012).
7. Raggi, P., Callister, T.Q., Shaw, L.J. Progression of coronary artery calcium and risk of first myocardial infarction in patients receiving cholesterol-lowering therapy. *Arterioscler. Thromb. Vasc. Biol.* 24, 1272–1277. <https://doi.org/10.1161/01.ATV.0000127024.40516.ef> (2004).
8. Budoff, M.J. et al. Progression of coronary calcium and incident coronary heart disease events: MESA (Multi-Ethnic Study of Atherosclerosis). *J. Am. Coll. Cardiol.* 61, 1231–1239.
<https://doi.org/10.1016/j.jacc.2012.12.035> (2013).
9. Lehmann, N. et al. Value of Progression of Coronary Artery Calcification for Risk Prediction of Coronary and Cardiovascular Events: Result of the HNR Study (Heinz Nixdorf Recall). *Circulation* 137, 665–679.
<https://doi.org/10.1161/CIRCULATIONAHA.116.027034> (2018).

10. Won, K.B. et al. Longitudinal quantitative assessment of coronary plaque progression related to body mass index using serial coronary computed tomography angiography. *Eur. Heart J. Cardiovasc. Imaging*. 20, 591–599. <https://doi.org/10.1093/ehjci/je192> (2019).
11. Lehmann, N. et al. Effect of smoking and other traditional risk factors on the onset of coronary artery calcification: results of the Heinz Nixdorf recall study. *Atherosclerosis* 232, 339–345. <https://doi.org/10.1016/j.atherosclerosis.2013.11.045> (2014).
12. Simental-Mendía, L.E., Rodríguez-Morán, M., Guerrero-Romero, F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab. Syndr. Relat. Disord.* 6, 299–304. <https://doi.org/10.1089/met.2008.0034> (2008).
13. Kim, K.K. et al. Evaluation and Treatment of Obesity and Its Comorbidities: 2022 Update of Clinical Practice Guidelines for Obesity by the Korean Society for the Study of Obesity. *J. Obes. Metab. Syndr.* 32, 1–24. <https://doi.org/10.7570/jomes23016> (2023).
14. Hokanson, J.E. et al. Evaluating changes in coronary artery calcium: an analytical approach that accounts for interscan variability. *AJR Am. J. Roentgenol.* 182, 1327–1332. <https://doi.org/10.2214/ajr.182.5.1821327> (2004).
15. Budoff, M.J. et al. Progression of coronary artery calcium predicts all-cause mortality. *JACC Cardiovasc. Imaging*. 3, 1229–1236. <https://doi.org/10.1016/j.jcmg.2010.08.018> (2010).

16. Han, D. et al. Machine learning framework to identify individuals at risk of rapid progression of coronary atherosclerosis: from the paradigm registry. *J. Am. Heart Assoc.* 9, e013958. <https://doi.org/10.1161/JAHA.119.013958> (2020).
17. Hartiala, O. et al. Adolescence risk factors are predictive of coronary artery calcification at middle age: the cardiovascular risk in young Finns study. *J. Am. Coll. Cardiol.* 60, 1364–1370. <https://doi.org/10.1016/j.jacc.2012.05.045> (2012).
18. Won, K.B. et al. Different associations of atherogenic index of plasma, triglyceride glucose index, and hemoglobin A1C levels with the risk of coronary artery calcification progression according to established diabetes. *Cardiovasc. Diabetol.* 23, 418. <https://doi.org/10.1186/s12933-024-02508-4> (2024).
19. Won, K.B. et al. Triglyceride glucose index is an independent predictor for the progression of coronary artery calcification in the absence of heavy coronary artery calcification at baseline. *Cardiovasc. Diabetol.* 19, 34. <https://doi.org/10.1186/s12933-020-01008-5> (2020).
20. Won, K.B. et al. Atherogenic index of plasma and coronary artery calcification progression beyond traditional risk factors according to baseline coronary artery calcium score. *Sci. Rep.* 10, 21324. <https://doi.org/10.1038/s41598-020-78350-x> (2020).
21. Fernández-Friera, L. et al. Normal LDL-cholesterol levels are associated with subclinical atherosclerosis in the absence of risk

- factors. *J. Am. Coll. Cardiol.* 70, 2979–2991.
<https://doi.org/10.1016/j.jacc.2017.10.024> (2017).
22. Won, K.B. et al. Independent role of low-density lipoprotein cholesterol in subclinical coronary atherosclerosis in the absence of traditional cardiovascular risk factors. *Eur. Heart J. Cardiovasc. Imaging.* 20, 866–872. <https://doi.org/10.1093/ehjci/jez091> (2019).
23. Whelton, P.K. et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 71, e13–e115. <https://doi.org/10.1161/HYP.0000000000000065> (2018).
24. McEvoy, J.W. et al. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur. Heart J.* 45, 3912–4018. <https://doi.org/10.1093/eurheartj/ehae178> (2024).
25. McEvoy, J.W. et al. Coronary artery calcium to guide a personalized risk-based approach to initiation and intensification of antihypertensive therapy. *Circulation* 135, 153–165. <https://doi.org/10.1161/CIRCULATIONAHA.116.025471> (2017).
26. Uddin, S.M.I. et al. Role of coronary artery calcium for stratifying cardiovascular risk in adults with hypertension. *Hypertension* 73, 983–989. <https://doi.org/10.1161/HYPERTENSIONAHA.118.12266> (2019).
27. Hong, J.C. et al. Implications of coronary artery calcium testing for

- treatment decisions among statin candidates according to the ACC/AHA cholesterol management guidelines: a cost-effectiveness analysis. *JACC Cardiovasc. Imaging*. 10, 938–952.
<https://doi.org/10.1016/j.jcmg.2017.04.014> (2017).
28. Spahillari, A. et al. Cost-effectiveness of contemporary statin use guidelines with or without coronary artery calcium assessment in African American individuals. *JAMA Cardiol*. 5, 871–880.
<https://doi.org/10.1001/jamacardio.2020.1240> (2020).
29. Guerrero-Romero, F. et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J. Clin. Endocrinol. Metab*. 95, 3347–3351. <https://doi.org/10.1210/jc.2010-0288> (2010).
30. Vasques, A.C. et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. *Diabetes Res. Clin. Pract.* 93, e98–e100.
<https://doi.org/10.1016/j.diabres.2011.05.030> (2011).
31. Won, K.B. et al. Quantitative assessment of coronary plaque volume change related to triglyceride glucose index: The Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging (PARADIGM) registry. *Cardiovasc. Diabetol*. 19, 113. <https://doi.org/10.1186/s12933-020-01081-w> (2020).
32. Won, K.B. et al. Glycemic control is independently associated with rapid progression of coronary atherosclerosis in the absence of a baseline coronary plaque burden: a retrospective case-control study

from the PARADIGM registry. *Cardiovasc. Diabetol.* 21, 239.

<https://doi.org/10.1186/s12933-022-01656-9> (2022).

33. Ke, Z. et al. Long-term high level of insulin resistance is associated with an increased prevalence of coronary artery calcification: the CARDIA study. *J. Am. Heart Assoc.* 12, e028985.
<https://doi.org/10.1161/JAHA.122.028985> (2023).
34. Halliburton, S.S. et al. Potential clinical impact of variability in the measurement of coronary artery calcification with sequential MDCT. *AJR Am. J. Roentgenol.* 184, 643–648.
<https://doi.org/10.2214/ajr.184.2.01840643> (2005).
35. Budoff, M.J. et al. Reproducibility of coronary artery calcified plaque with cardiac 64-MDCT: the Multi-Ethnic Study of Atherosclerosis. *AJR Am. J. Roentgenol.* 192, 613–617.
<https://doi.org/10.2214/AJR.08.1242> (2009).

Acknowledgements

Author contributions

KBW conceived the study and interpreted the data. KBW, SYC, EJC, SHP, JS, HOJ, and HJC contributed to data acquisition. KBW and HJC performed statistical analyses. KBW drafted the manuscript. HJC revised the manuscript critically. All authors have read and approved the final manuscript. All authors have given final approval and agreed to be held accountable for all aspects of the work, ensuring its integrity and accuracy.

Data availability

The data underlying this manuscript cannot be shared publicly because of the lack of permission to share retrospective clinical data outside our institution without authorization as part of our Institutional Review Board approval. The authors had full access to all data in the study and were responsible for the integrity of the data and the accuracy of the data analysis. The datasets used and analyzed in this study are available from the corresponding author upon reasonable request.

Funding

This work was supported by the Institute of Information & Communications Technology Planning & Evaluation (IITP) grant funded by the Korean government (MSIT) (No.2022000972, Development of a flexible mobile healthcare software platform using 5G MEC).

Ethics approval and consent to participate

This study adhered to the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Severance Cardiovascular Hospital (IRB no: 4-2014-0309). Informed consent for procedures was obtained from all participants.

Competing interests

The authors declare no competing interests.

ARTICLE IN PRESS

Figure legend

Fig. 1. Incidence of newly developed CAC according to traditional risk factors assessed at initial CAC scan.

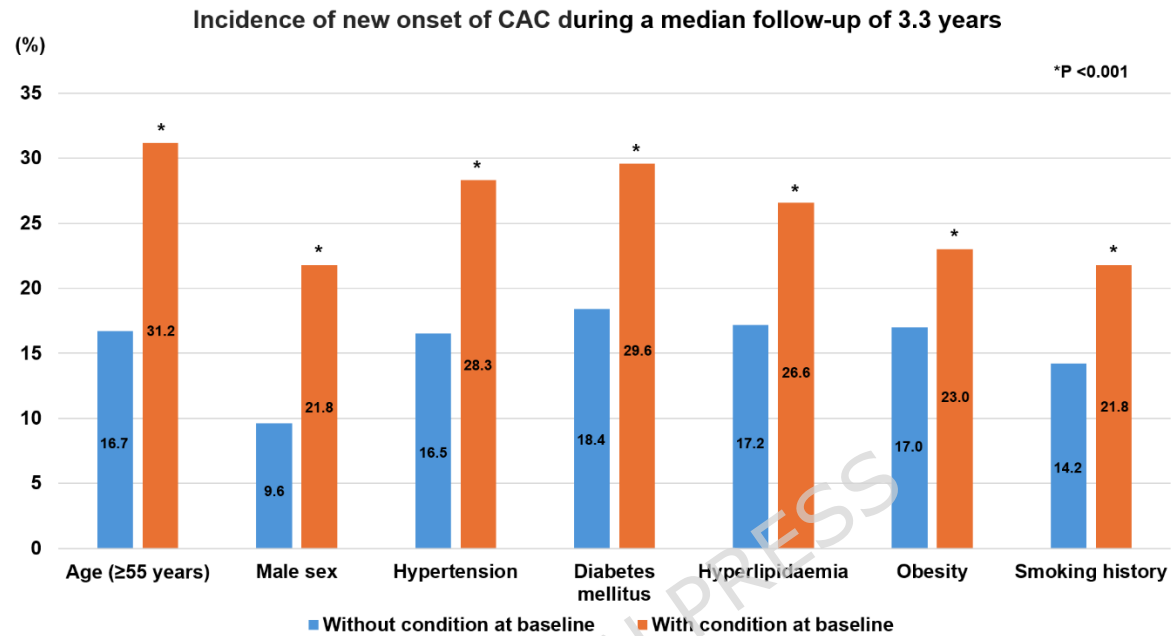


Table 1. Clinical characteristics

Characteristics	Overall participants (N = 6993)
At initial CT scan	
Age, years	48.4 ± 7.2
Age ≥55 years, n (%)	1261 (18.0)
Male, n (%)	5583 (79.8)
Hypertension, n (%)	1642 (23.5)
Diabetes mellitus, n (%)	554 (7.9)
Hyperlipidemia, n (%)	1575 (22.5)
Obesity, n (%)	2664 (38.1)
Smoking history/current smoking, n (%)	4170 (59.6)/1912 (27.3)
At follow-up CT scan	
SBP, mmHg	118.7 ± 14.3
SBP <120 mmHg, n (%)	3770 (53.9)
DBP, mmHg	75.2 ± 10.6
BMI, kg/m ²	24.3 ± 2.8
Total cholesterol, mg/dL	197.7 ± 34.6
Triglycerides, mg/dL	133.1 ± 84.2
HDL-C, mg/dL	54.2 ± 15.6
LDL-C, mg/dL	121.1 ± 32.2
LDL-C <130 mg/dL, n (%)	4243 (60.7)
Glucose, mg/dL	98.2 ± 18.1
TyG index, units	8.6 ± 0.6
HbA1C, %	5.7 ± 0.6
Creatinine, mg/dL	0.9 ± 0.2
Current smoking, n (%)	1541 (22.0)

Values are presented as mean ± standard deviation or number (%).

BMI body mass index; *CT* computed tomography; *DBP* diastolic blood pressure; *HbA1C* hemoglobin A1C; *HDL-C* high-density lipoprotein cholesterol; *LDL-C* low-density

lipoprotein cholesterol; *SBP* systolic blood pressure; *TyG* triglyceride glucose.

ARTICLE IN PRESS

Table 2. Follow-up CAC findings

Measures	Overall participants (N = 6993)
Newly developed CAC	1351 (19.3)
$\Delta \sqrt{\text{transformed CACS}} \geq 2.5$	908 (13.0)
Categorical CACS	
0	5642 (80.7)
1-10	605 (8.7)
>10 and ≤ 100	678 (9.7)
>100	68 (1.0)

Values are presented as number (%).

CAC coronary artery calcification; *CACS* coronary artery calcium score.

Table 3. CAC changes related to traditional risk factors assessed at the initial CT scan

	Newly developed CAC	P	Δ /transformed CACS ≥ 2.5	P	CACS >100	P
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Age	1.08 (1.07–1.09)	<0.001	1.08 (1.07–1.10)	<0.001	1.07 (1.03–1.10)	<0.001
Male	2.27 (1.87–2.76)	<0.001	2.47 (1.93–3.16)	<0.001	2.35 (0.94–5.89)	0.069
Hypertension	2.18 (1.90–2.51)	<0.001	2.15 (1.83–2.52)	<0.001	2.89 (1.78–4.70)	<0.001
Diabetes mellitus	1.86 (1.52–2.29)	<0.001	2.16 (1.72–2.71)	<0.001	4.13 (2.37–7.21)	<0.001
Hyperlipidemia	1.54 (1.34–1.77)	<0.001	1.43 (1.21–1.68)	<0.001	2.23 (1.37–3.63)	0.001
Obesity	1.39 (1.23–1.58)	<0.001	1.41 (1.21–1.64)	<0.001	1.84 (1.13–2.99)	0.014
Smoking history	1.46 (1.26–1.69)	<0.001	1.51 (1.27–1.80)	<0.001	1.25 (0.70–2.22)	0.457

CAC coronary artery calcification; CACS coronary artery calcium score; CI confidence

interval; *OR* odds ratio.

All analyses are adjusted for the interscan period.

ARTICLE IN PRESS

Table 4. CAC changes related to clinical factors assessed at the follow-up CT scan

	Newly developed CAC	P	$\Delta\sqrt{\text{transformed CACS}} \geq 2.5$	P	CACS >100	P
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
SBP, per 10-mmHg increase	1.06 (1.01–1.12)	0.019	1.08 (1.02–1.14)	0.013	1.06 (0.89–1.27)	0.506
SBP <120 mmHg	0.85 (0.73–0.98)	0.022	0.81 (0.69–0.96)	0.013	0.86 (0.51–1.47)	0.580
BMI, per 1-kg/m ² increase	1.02 (0.98–1.06)	0.259	1.01 (0.97–1.06)	0.613	1.11 (0.97–1.26)	0.136
TyG index, per 1-unit increase	1.21 (1.07–1.37)	0.003	1.27 (1.10–1.47)	0.001	1.61 (1.02–2.52)	0.039
HbA1C, per 1% increase	1.23 (1.09–1.39)	0.001	1.25 (1.09–1.43)	0.001	1.38 (1.02–1.87)	0.035
Current smoking	1.26 (1.06–1.51)	0.008	1.27 (1.04–1.56)	0.019	2.40 (1.29–4.49)	0.006
LDL-C, per 10-mg/dL increase	1.04 (1.02–1.06)	0.001	1.04 (1.02–1.07)	0.002	1.07 (0.98–1.16)	0.119
LDL-C <130 mg/dL	0.81 (0.70–0.93)	0.003	0.81 (0.69–0.96)	0.014	0.63 (0.37–1.09)	0.097
Creatinine, per 0.1-mg/dL increase	1.00 (0.95–1.05)	0.837	0.99 (0.93–1.04)	0.609	0.98 (0.81–1.18)	0.815

CAC coronary artery calcification; CACS coronary artery calcium score; CI confidence interval; HbA1C hemoglobin A1C; LDL-C low-density lipoprotein cholesterol; OR odds ratio; TyG triglyceride glucose.

All analyses are adjusted for (a) clinical conditions at the initial CT scan (age, sex, hypertension, diabetes mellitus, hyperlipidemia, obesity, and smoking history) and (b) the interscan period.

ARTICLE IN PRESS

Table 5. Age-based subgroup analysis for CAC changes related to TyG index, HbA1C, and current smoking

	Newly developed CAC	P	$\Delta\sqrt{\text{transformed CACS}} \geq 2.5$	P	CACS >100	P
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Age <55 years						
TyG index, per 1-unit increase	1.11 (1.08–1.40)	0.006	1.31 (1.11–1.54)	0.001	1.92 (1.14–3.23)	0.014
HbA1C, per 1% increase	1.31 (1.14–1.51)	<0.001	1.35 (1.16–1.58)	<0.001	1.40 (0.98–2.01)	0.066
Current smoking	1.29 (1.07–1.56)	0.008	1.29 (1.03–1.61)	0.026	2.56 (1.25–5.26)	0.010
Age $\geq$ 55 years						
TyG index, per 1-unit increase	1.16 (0.88–1.52)	0.286	1.14 (0.84–1.54)	0.400	0.88 (0.36–2.14)	0.778
HbA1C, per 1% increase	1.02 (0.78–1.33)	0.883	1.00 (0.75–1.33)	0.998	1.39 (0.79–2.46)	0.257
Current smoking	1.02 (0.64–1.63)	0.925	1.08 (0.65–1.79)	0.775	1.57 (0.38–6.45)	0.534

CAC coronary artery calcification; CACS coronary artery calcium score; CI confidence interval; HbA1C hemoglobin A1C; LDL-C low-density lipoprotein cholesterol; OR odds ratio; TyG triglyceride glucose.

All analyses were adjusted for (a) clinical conditions at the initial CT scan (age, sex, hypertension, diabetes mellitus, hyperlipidemia, obesity, and smoking history) and (b) the interscan period.