Coffee consumption and coronary artery calcium in young and middle-aged asymptomatic adults

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ABSTRACT

Objective To investigate the association between regular coffee consumption and the prevalence of coronary artery calcium (CAC) in a large sample of young and middle-aged asymptomatic men and women.

Methods This cross-sectional study included 25 138 men and women (mean age 41.3 years) without clinically evident cardiovascular disease who underwent a health screening examination that included a validated food frequency questionnaire and a multidetector CT to determine CAC scores. We used robust Tobit regression analyses to estimate the CAC score ratios associated with different levels of coffee consumption compared with no coffee consumption and adjusted for potential confounders.

Results The prevalence of detectable CAC (CAC score >0) was 13.4% (n=3364), including 11.3% prevalence for CAC scores 1–100 (n=2832), and 2.1% prevalence for CAC scores >100 (n=532). The mean ±SD consumption of coffee was 1.8±1.5 cups/day. The multivariate-adjusted CAC score ratios (95% CIs) comparing coffee drinkers of <1, 1–<3, 3–<5, and ≥5 cups/day to non-coffee drinkers were 0.77 (0.49 to 1.19), 0.66 (0.43 to 1.02), 0.59 (0.38 to 0.93), and 0.81 (0.46 to 1.43), respectively (p for quadratic trend=0.02). The association was similar in subgroups defined by age, sex, smoking status, alcohol consumption, status of obesity, diabetes, hypertension, and hypercholesterolaemia.

Conclusions In this large sample of men and women apparently free of clinically evident cardiovascular disease, moderate coffee consumption was associated with a lower prevalence of subclinical coronary atherosclerosis.

INTRODUCTION

The effect of coffee consumption on cardiovascular health has remained controversial.1 In spite of earlier concerns about a potential increase in cardiovascular disease (CVD) risk associated with coffee consumption, a recent meta-analysis of 36 prospective studies showed that moderate coffee consumption was associated with a decreased risk of CVD, with the strongest reduction at 3–5 cups/day.2 Coffee consumption has been associated with improved insulin sensitivity,3–5 reduced low density lipoprotein cholesterol (LDL-C) oxidation,6,7 and reduced risk of type 2 diabetes.8,9 However, coffee consumption has also been associated with increased cholesterol concentrations10,11 and acute pressor effects, although the relationship of coffee consumption to the risk of hypertension is still unclear.1

Coronary artery calcium (CAC) detected by cardiac CT is a subclinical marker of coronary atherosclerosis that predicts future coronary heart disease (CHD)12 in a wide range of ages, including asymptomatic young adults.13 CAC provides information on underlying pathologic changes in coronary arteries and thus allows for a detailed assessment of the early stages of CVD, which is distinct from the occurrence of plaque rupture and thrombosis in clinical events.14 Only two studies have examined the relationship between coffee consumption and CAC, with inconsistent results.15,16 We therefore examined the association between coffee consumption and the presence of CAC in a large sample of asymptomatic men and women attending a health screening examination.

METHODS

Study population

The Kangbuk Samsung Health Study is a cohort study of Korean men and women who underwent comprehensive annual or biennial examinations at the Kangbuk Samsung Hospital Total Healthcare Centers in Seoul or Suwon, South Korea.17 The population for this cross-sectional analysis included all participants (n=30 485) who completed a food frequency questionnaire (FFQ) and who underwent a comprehensive health screening examination including cardiac CT for CAC scoring between March 2011 and April 2013. Annual or biennial health screening examinations are widely performed in Korea, as health examinations are mandatory for all workers under the Industrial Safety and Health Law. CAC scoring has become a common CVD screening test in Korea.17 After participants had completed self-administered questionnaires, all examinations including CT scan for CAC scoring were performed.

We excluded 437 participants with a history of CVD, 474 participants who had implausible estimated energy consumption levels (beyond 3 SDs from the loge-transformed mean energy consumption), 1824 participants with missing information on coffee consumption, and 3371 participants with missing information on smoking status. The final sample size for the analysis was 25 138 participants (figure 1).

This study was approved by the Institutional Review Board of the Kangbuk Samsung Hospital. The requirement of informed consent was waived because we used non-identified retrospective data routinely collected during the health screening process.
Assessment of coffee consumption
Usual dietary consumption was assessed using a 103-item self-administered FFQ designed for use in Korea. The reproducibility and validity of the nutrient information provided by this FFQ have been evaluated among 124 Korean subjects aged 40--70 years. Participants were asked how often, on average, they consumed each type of food or beverage during the past year. The FFQ had three predefined categories of portion size, ranging from small to large, and nine predefined categories of frequency, ranging from never or seldom to ≥ three times per day for foods, and from never or seldom to ≥ five times per day for beverages. Participants were also asked to report the consumption period (ie, 3, 6, 9, or 12 months) for seasonal consumption of fruits. The FFQ asked about total coffee consumption without differentiating between caffeinated and decaffeinated coffee. However, decaffeinated coffee is not yet widely popular in Korea. A recipe, portion size, and nutrient database was constructed with a food composition table from the Korean Nutrition Society.

Measurement of CAC
All CT scans were obtained with a Lightspeed VCT XTe 64 slice multidetector CT (MDCT) scanner (GE Healthcare, Tokyo, Japan) with a standard scanning protocol using 2.5 mm thickness, 400 ms rotation time, 120 kV tube voltage, and a 124 mAS (310 mA×0.4 s) tube current under ECG-gated dose modulation. Quantitative CAC scores were calculated using the method proposed by Agatston et al. The interobserver and intraobserver reliability values of CAC scores were both excellent, with intraclass correlation coefficients of 0.99. If more than one CAC measurement was available for a participant during the study period, the initial measurement was used.

Assessment of other variables
Data on medical history, medication use, family history, physical activity, alcohol consumption, smoking habits, and sociodemographic characteristics were collected through a self-administered questionnaire, whereas the anthropometric parameters and blood pressure were measured by trained staff during the health examinations. Physical activity levels were assessed by the Korean-validated version of the International Physical Activity Questionnaire (IPAQ); participants were classified as inactive, minimally active, and health enhancing physically active (HEPA).

Statistical analysis
Habitual coffee consumption was categorised as none, <1, 1--<3, 3--<5, and ≥5 cups/day. For the primary analyses, we modelled logₑ(CAC score+1) using robust Tobit regression model with the Huber-White estimation of SEs. We logₑ-transformed the CAC scores since their distribution was skewed to the right and used Tobit models because the CAC scores were left-censored at 0 Agatston units (non-detectable CAC scores). Tobit models were used to estimate CAC score ratios and their 95% CIs for each category of coffee consumption. CAC score ratios represent the ratio of the geometric means of CAC scores comparing each category of coffee consumption to the group with no coffee consumption. In a secondary analyses, we categorised CAC scores as a dichotomous variable (CAC score >0 compared with CAC score 0) and used logistic regression to estimate the ORs for detectable CAC according to the categories of coffee consumption.

Statistical models were initially adjusted for age, sex, centre, and year of screening examination (model 1) and then further adjusted for potential confounding factors determined a priori, including education level (high school graduate or less, community college or university graduate, graduate school or higher, and unknown), physical activity level (inactive,
minimally active, HEPA, and unknown), smoking status (never, former, and current), BMI (body mass index, kg/m²), parental history of CHD (yes vs no), alcohol consumption (none, <5, 5–<20, ≥20 g/day, and unknown), total energy consumption (kcal/day), and consumption of fruits, vegetables, and red and processed meats (quartiles, g/day) (model 2). Further adjusting for tea consumption (including black, green tea, and any other teas) did not materially change the results. We additionally adjusted for potential intermediate variables, including SBP, fasting serum glucose, total cholesterol, triglycerides, and HDL-C (model 3).

We conducted quadratic trend tests by including linear and quadratic terms of the median coffee consumption within each coffee consumption category as continuous variables in the regression models, and statistical significance was evaluated using Wald tests.

We conducted subgroup analyses by age (<40 vs ≥40 years), sex (men vs women), smoking (non-current vs current smoker), BMI (<25 vs ≥25 kg/m²), alcohol drinking (non-drinker vs drinker), diabetes (yes vs no), hypertension (yes vs no), and hypercholesterolaemia (yes vs no). We tested for statistical interactions by using Wald tests for the product term of coffee consumption categories with the stratification variable.

In sensitivity analyses, we repeated the multivariate analyses after excluding those who did not consume coffee because of the possibility that they could represent individuals with unfavourable health conditions, and each category was compared with the reference category of coffee drinkers of <1 cup/day. All analyses were conducted using STATA V12.1 (Stata Corp, College Station, Texas, USA). Statistical tests were a two-sided test, and p<0.05 was considered statistically significant.

RESULTS

The average ±SD age of study participants was 41.3±7.5 years, and 83.7% of participants were male. The prevalence of CAC scores ≥0 was 13.4% (n=3364), including 11.3% prevalence for CAC scores 1–100 (n=2832), and 2.1% prevalence for CAC scores >100 (n=532). The mean ±SD consumption of coffee was 1.8±1.5 cups/day. Compared with non-coffee drinkers, individuals in the highest categories of coffee consumption were more likely to be older, men, and current smokers and to have higher education, less frequent vigorous-intensity physical activity, obesity, and hypercholesterolaemia, and to have a lower proportion of hypertension (table 1). Compared to non-coffee drinkers, those with high coffee consumption also had higher concentrations of fasting serum glucose, HbA1c, total cholesterol, triglycerides, and LDL-C, and lower HDL-C and SBP and they had a higher consumption of total energy, red and processed meats, alcohol, and a lower consumption of fruits and vegetables.

### Table 1. Characteristics of study participants by categories of coffee consumption

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>None (n=1381)</th>
<th>&lt;1 cup (n=6666)</th>
<th>1–&lt;3 cups (n=9849)</th>
<th>3–&lt;5 cups (n=6084)</th>
<th>≥5 cups (n=1158)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.1 (8.8)</td>
<td>40.6 (8.0)</td>
<td>41.4 (7.4)</td>
<td>42 (6.7)</td>
<td>42.1 (6.7)</td>
</tr>
<tr>
<td>Males (%)</td>
<td>73.8</td>
<td>82.2</td>
<td>82.6</td>
<td>88.5</td>
<td>87.9</td>
</tr>
<tr>
<td>College graduation or higher (%)</td>
<td>77.7</td>
<td>81.3</td>
<td>83.3</td>
<td>83.3</td>
<td>83.2</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>13.8</td>
<td>23.6</td>
<td>28.7</td>
<td>40</td>
<td>48.9</td>
</tr>
<tr>
<td>HEPA (%)</td>
<td>9.6</td>
<td>7.4</td>
<td>8</td>
<td>7.1</td>
<td>7.2</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>31.9</td>
<td>37.2</td>
<td>38.2</td>
<td>43.2</td>
<td>46.9</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6.4</td>
<td>6.2</td>
<td>5.8</td>
<td>5.8</td>
<td>7.2</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>19</td>
<td>16.4</td>
<td>16.6</td>
<td>16.6</td>
<td>15.5</td>
</tr>
<tr>
<td>Hypercholesterolaemia (%)</td>
<td>21.8</td>
<td>24.6</td>
<td>25.8</td>
<td>27.7</td>
<td>29.1</td>
</tr>
<tr>
<td>Parental history of CHD (%)</td>
<td>7.9</td>
<td>7.1</td>
<td>7.5</td>
<td>8.1</td>
<td>7.3</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>115.0 (13.5)</td>
<td>115.6 (13.2)</td>
<td>114.9 (13.2)</td>
<td>114.9 (12.6)</td>
<td>114.6 (12.4)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>73.7 (10.3)</td>
<td>74.0 (10.4)</td>
<td>73.7 (10.5)</td>
<td>73.9 (10.1)</td>
<td>73.5 (9.9)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.4 (0.81)</td>
<td>5.5 (0.9)</td>
<td>5.5 (0.9)</td>
<td>5.5 (0.9)</td>
<td>5.5 (0.9)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.67 (0.45)</td>
<td>5.69 (0.53)</td>
<td>5.69 (0.52)</td>
<td>5.71 (0.55)</td>
<td>5.72 (0.53)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.1</td>
<td>5.2 (0.9)</td>
<td>5.2 (0.9)</td>
<td>5.3 (0.9)</td>
<td>5.4 (0.9)</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.2 (0.8–1.7)</td>
<td>1.3 (0.9–1.9)</td>
<td>1.3 (0.9–1.9)</td>
<td>1.3 (0.9–1.9)</td>
<td>1.4 (1.0–2.0)</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.3)</td>
<td>1.4 (0.3)</td>
<td>1.3 (0.3)</td>
<td>1.3 (0.3)</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>3.2 (0.8)</td>
<td>3.3 (0.8)</td>
<td>3.3 (0.8)</td>
<td>3.4 (0.8)</td>
<td>3.5 (0.8)</td>
</tr>
<tr>
<td>hsCRP (mg/L)</td>
<td>0.5 (0.3–0.9)</td>
<td>0.5 (0.3–1.0)</td>
<td>0.5 (0.3–1.0)</td>
<td>0.5 (0.3–1.1)</td>
<td>0.5 (0.3–1.1)</td>
</tr>
<tr>
<td>Daily dietary consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total energy (Kcal/day)</td>
<td>1570.8 (728.4)</td>
<td>1519.7 (653.7)</td>
<td>1604.4 (636.7)</td>
<td>1720.4 (676.1)</td>
<td>1840.9 (722.6)</td>
</tr>
<tr>
<td>Vegetables (g/day)</td>
<td>96.6 (112.9)</td>
<td>80.2 (76.7)</td>
<td>86.0 (84.1)</td>
<td>85.4 (78.5)</td>
<td>91.1 (94.6)</td>
</tr>
<tr>
<td>Fruits (g/day)</td>
<td>220.0 (343.1)</td>
<td>185.0 (213.4)</td>
<td>195.6 (205.8)</td>
<td>197.0 (207.1)</td>
<td>210.6 (259.1)</td>
</tr>
<tr>
<td>Red and processed meat (g/day)</td>
<td>55.6 (52.9)</td>
<td>60.8 (57.1)</td>
<td>61.1 (54.5)</td>
<td>67.5 (59.7)</td>
<td>74.7 (72.4)</td>
</tr>
<tr>
<td>Alcohol (g/day)</td>
<td>3.9 (0.6–16.9)</td>
<td>6.0 (1.8–19.2)</td>
<td>7.0 (2.3–20.8)</td>
<td>7.9 (2.7–22.6)</td>
<td>8.6 (2.8–24.3)</td>
</tr>
<tr>
<td>Tea drinker, 0 &gt;cup/day (%)*</td>
<td>54.0</td>
<td>72.1</td>
<td>67.2</td>
<td>65.3</td>
<td>59.4</td>
</tr>
</tbody>
</table>

*Data are presented as proportions, means (SD), or medians (IQR).

Data were missing in 1.9% of participants.

CHD, coronary heart disease; DBP, diastolic blood pressure; HbA1c, haemoglobin A1c; HDL-C, high density lipoprotein cholesterol; HEPA, health enhancing physical activity; hsCRP, high sensitivity C reactive protein; LDL-C, low density lipoprotein cholesterol; SBP, systolic blood pressure.
Coronary artery disease

In a model that adjusted for age, sex, centre, and year of screening examination (table 2; model 1), the CAC ratios (95% CI) comparing coffee drinkers of <1, 1–<3, 3–<5, and ≥5 cups/day to non-coffee drinkers were 0.86 (0.55 to 1.34), 0.82 (0.53 to 1.34), 0.82 (0.53 to 1.26), 0.78 (0.50 to 1.22), and 1.77 (0.66 to 2.06), respectively (p for quadratic trend=0.20). Further adjusting for potential confounders strengthened the inverse association between coffee consumption and CAC, most likely due to smoking status. In multivariable adjusted models (model 2), the corresponding estimates were 0.77 (0.49 to 1.19), 0.66 (0.43 to 1.02), 0.59 (0.38 to 0.93), and 0.81 (0.46 to 1.43), respectively (p for quadratic trend=0.02). The findings were similar after adjustment for SBP, fasting serum glucose, total cholesterol, triglycerides, and HDL-C (model 3).

The results from logistic regression models using categories of CAC scores were consistent with the Tobit models. The multivariable adjusted ORs (95% CIs) for CAC score >0 comparing coffee drinkers of <1, 1–<3, 3–<5, and ≥5 cups/day to non-coffee drinkers were 0.90 (0.74 to 1.10), 0.85 (0.71 to 1.03), 0.80 (0.66 to 0.97), and 0.94 (0.73 to 1.20), respectively (p for quadratic trend=0.02) (table 3, model 2), with little change after adjustment for potential intermediate variables. The significant quadratic trend between coffee consumption and detectable CAC scores was also evident after adjusting for potential confounders (figure 2).

The association was consistent in subgroup analyses, and there were no statistically significant interactions (data not shown; p for interaction>0.05). In sensitivity analyses where we excluded non-coffee drinkers, the multivariable adjusted CAC score ratios (95% CIs) comparing coffee drinkers of 1–<3, 3–<5, and ≥5 cups/day to coffee drinkers of ≤1 cup/day were 0.86 (0.68 to 1.09), 0.77 (0.59 to 1.00), and 1.04 (0.67 to 1.62), respectively (model 2).

DISCUSSION

In this large sample of Korean men and women apparently free of clinically evident CVD, coffee consumption was associated with a lower prevalence of CAC, a marker of subclinical coronary atherosclerosis. The association was U-shaped, with participants drinking 3–<5 cups/day having the lowest prevalence of subclinical coronary atherosclerosis. The association was similar after adjustment for cardiovascular risk factors or potential mediators. Our findings are consistent with a recent body of literature showing that moderate coffee consumption may be inversely associated with cardiovascular events.

The relationship between coffee consumption and CVD has been extensively investigated with conflicting results. However, several large prospective studies and reviews have concluded that habitual coffee consumption is associated with decreased risk of cardiovascular events, and this

### Table 3 OR* (95% CIs) for the presence of coronary artery calcium (CAC) score by categories of coffee consumption

<table>
<thead>
<tr>
<th>Daily coffee consumption</th>
<th>CAC score &gt;0 vs 0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P for quadratic trend†</td>
</tr>
<tr>
<td></td>
<td>No. of cases</td>
</tr>
<tr>
<td>Model 1†</td>
<td></td>
</tr>
<tr>
<td>1.00</td>
<td>181</td>
</tr>
<tr>
<td>Model 2§</td>
<td></td>
</tr>
<tr>
<td>1.00</td>
<td>844</td>
</tr>
<tr>
<td>Model 3¶</td>
<td></td>
</tr>
<tr>
<td>1.00</td>
<td>1300</td>
</tr>
</tbody>
</table>

*Derived from logistic regression models using dichotomous CAC score as outcome variable (CAC score >0 compared to CAC score 0).
†Derived from the quadratic trend tests by including a linear and quadratic term of the median coffee consumption value within each group in the regression models.
§Model 2: Model 1 with additional adjustments for education level (high school graduate or less, community college or university graduate, graduate school or higher, and unknown), physical activity (inactive, minimally active, health enhancing physical activity, and unknown), smoking (never, former, and current smoker), body mass index (kg/m2), parental history of coronary heart disease (yes vs no), alcohol consumption (none, ≤5, <20, ≥20 g/day, and unknown), total energy consumption (kcal/day), consumption of fruits, vegetables, and red and processed meats (quartiles, g/day).
¶Model 3: Model 2 with additional adjustments for potential intermediate variables, including systolic blood pressure, fasting serum glucose, total cholesterol, triglyceride, and high density lipoprotein cholesterol.
Caféa asociada a un menor riesgo de enfermedad cardiovascular (EVC). En el estudio Rotterdam (n=1570),15 una tasa moderada de cafés consumida se asoció con un riesgo disminuido de EVC. Se observó una correlación inversa asociada con marcadores de inflamación28 y disfunción endotelial.29 En el otro lado, el café, especialmente el no filtrado, ha mostrado un efecto elevado de los colesterol.30

La asociación entre consumo de café moderado y riesgo cardiovascular es considerada un efecto potencial beneficioso. Aunque no se encontró una asociación clara entre el consumo diario de café y la presencia de CAC, varios mecanismos han sido propuestos para explicar la asociación entre el consumo moderado de café y el riesgo cardiovascular. El consumo crónico de café puede tener un efecto beneficioso en la presión arterial y la sensibilidad a la insulina, con la mayor reducción asociada con la ingesta moderada de café.31

En conclusión, se encontró que el consumo moderado diario de café puede asociarse con un menor riesgo de enfermedad cardiovascular. Aunque no se encontró una asociación clara entre el consumo de café y la presencia de CAC, varios mecanismos han sido propuestos para explicar la asociación entre el consumo moderado de café y el riesgo cardiovascular. El consumo crónico de café puede tener un efecto beneficioso en la presión arterial y la sensibilidad a la insulina, con la mayor reducción asociada con la ingesta moderada de café.31
Coronary artery disease

Key messages

What is already known on this subject?
The relationship between coffee consumption and cardiovascular disease is controversial. Several large prospective studies and reviews have concluded that habitual coffee consumption may be associated with decreased risk of cardiovascular events, and this association was most evident for moderate coffee consumption levels.

What might this study add?
In this large sample of Korean men and women free of clinically evident cardiovascular disease, coffee consumption was associated with a lower prevalence of coronary artery calcium, a marker of subclinical coronary atherosclerosis. The association was U-shaped, with participants drinking 3–5 cups/day having the lowest prevalence of subclinical coronary atherosclerosis.

How might this impact on clinical practice?
Moderate daily coffee consumption was inversely associated with subclinical coronary atherosclerosis. Large scale and randomised controlled studies are needed to prove causation.

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Contributors All authors were involved in the preparation of the manuscript, have read the manuscript, agree with the analyses of the data and the conclusions reached in the manuscript, and are accountable for all aspects of the work.

Competing interests None.

Patient consent Requirement for informed consent was waived because the study used non-identified retrospective data routinely collected during health screening process.

Ethics approval Ethics approval was provided by the Institutional Review Board of the Kangbuk Samsung Hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES