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Eveningness is associated with coronary artery calcification in a middle-aged Swedish population

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ABSTRACT

Coronary artery calcification (CAC) is an established imaging biomarker of subclinical atherosclerosis, but its relationship to diurnal preference is not well studied. We investigated the association between chronotype and CAC in the Swedish CardioPulmonary BioImage Study (SCAPIS) pilot cohort. Participants aged 50–64 years were randomly recruited and underwent extensive examination including imaging and accelerometry-assessed physical activity. 771 participants (47.3 % male, 57.6 ± 4.4 years) were included in this cross-sectional analysis. CAC was assessed by non-contrast computed tomography, and a CAC score > 10 was considered significant calcification. Self-assessed chronotype was classified as extreme morning, moderate morning, intermediate, moderate evening, or extreme evening. 10-year risk of first-onset cardiovascular disease was estimated by the Systemic Coronary Risk Evaluation 2 (SCORE2). Significant CAC was present in 29 % of the cohort. CAC prevalence increased from extreme morning to extreme evening type (22 %, 28 %, 29 %, 27 %, 41 % respectively, p = 0.018). In a multivariate logistic regression model controlling for confounders, extreme evening chronotype was independently associated with increased CAC prevalence compared to extreme morning type (OR 1.90, [95%CI 1.04–3.46], p = 0.037). When stratified by SCORE2 risk category (low: <5 %; moderate: 5 to <10 %; high: ≥10 %), significant CAC was most prevalent among extreme evening chronotypes in the low and moderate-risk groups, while chronotype seemed less important in the high-risk group (p = 0.011, p = 0.023, p = 0.86, respectively). Our findings suggest circadian factors may play an important role in atherosclerosis and should be considered in early cardiovascular prevention.

1. Introduction

Cardiovascular disease (CVD) is a major cause of morbidity and mortality worldwide. Approximately 49 million people in the European Union live with CVD, which accounts for 37 % of all deaths in the region [1]. Atherosclerosis is the most common cause of CVDs such as myocardial infarction and stroke. Coronary artery calcification (CAC) assessed by coronary artery calcium score (CACS) is a widely used and reliable imaging biomarker of atherosclerotic burden, especially in asymptomatic individuals [2]. High CACS has been associated with coronary artery disease and other atherosclerotic CVD events as well as all-cause mortality [3,4]. CACS has also been used successfully in risk stratification in conjunction with other risk prediction models [5,6], and considered useful in clinical decision-making [7–9].

Chronotype is the individual’s propensity to time sleep and other activities throughout the day. It is a descriptive, multifactorial trait influenced by the circadian system, environment, and behavior [10]. Evening chronotypes, or the “night owls” tend to have more energy later on.
in the day, go to bed later, and wake up later, whereas the opposite is true of morning chronotypes, or the “morning larks” or “early birds.” The circadian system dictates the temporal organization of nearly all physiological processes including cardiovascular function. This can be observed in instance diurnal variations in physiological conditions such as heart rate, blood pressure, coagulation, and vascular function [11]. It is proposed that evening chronotype represents a form of circadian desynchrony between biology, environment, and behavior, resulting in observed increases in cardiovascular (CV) risk, morbidity, and mortality [12–15]. Others have reported that morning type is associated with cardiometabolic risk [16]. More studies are thus needed to clarify the link between chronotype and cardiovascular function.

In a recent study, extreme evening chronotype was found to be associated with increased 10-year risk of first-onset CVD assessed by the European “Systemic Coronary Risk Evaluation 2” (SCORE2) algorithm [15,17]. The association between chronotype and imaging biomarkers (e.g., CACS), however, has not been explored. In the current study, we investigated the relationship between atherosclerotic burden and chronotype in a middle-aged Swedish population [18,19]. We hypothesized that evening chronotype is associated with the presence of significant CAC, independent of other CV risk factors. Furthermore, we applied chronotype information as an add-on to SCORE2 to assess the prevalence of significant CAC.

2. Methods

2.1. Study population

The Swedish CardioPulmonary BioImage Study (SCAPIS), which has previously been described in detail [20], was initiated to further understand CVD, chronic obstructive pulmonary disease, and associated metabolic disease. A pilot study was conducted in Gothenburg, Sweden in 2012 to assess the feasibility of the SCAPIS design and to estimate the frequency of pathological findings amongst participants [21]. In this pilot study, 2243 individuals aged between 50 and 64 years were randomly selected. They were stratified by socioeconomic status (SES), which due to socioeconomic segregation in the city, was based on residential neighborhood. The inability to understand spoken and written Swedish was the sole exclusion criteria, due to purposes of informed consent. The 1111 individuals who were included in the pilot study underwent extensive examination with imaging and functional testing, blood sampling, objective assessment of physical activity, anthropometric measurements, and questionnaires assessing health and lifestyle.

SCAPIS was approved by the ethics committee at Umeå University (Dnr 2010-228-31 M) as a multicenter study. The current cross-sectional analysis was approved by the Regional Ethical Review Board in Gothenburg (Dnr 638-16). Written informed consent was obtained from all study participants. Data was collected at the SCAPIS center, Sahlgrenska University Hospital, Gothenburg, Sweden and data analysis was performed at the Center for Sleep and Vigilance Disorders, University of Gothenburg, Sweden.

2.2. Sleep and circadian variables

Chronotype was assessed by a multiple-choice question: “Try to specify to what extent you consider yourself a morning or evening type.” The possible answers were (1) I am a distinct morning person (extreme morning type); (2) I am a morning person to a certain degree (moderate morning type); (3) I am neither a morning nor evening person (intermediate type); (4) I am an evening person to a certain degree (moderate evening type); (5) I am a distinct evening person (extreme evening type); (6) I do not know. Participants who did not answer or indicated “I do not know” were excluded from the analysis. Subjective sleep quality was assessed by Pittsburg Sleep Quality Index (PSQI) [22]. Participants with PSQI score > 5 were considered to have poor sleep quality. Habitual sleep duration was derived from a multiple-choice question with seven options: (1) 4 h or less; (2) 5 h; (3) 6 h; (4) 7 h; (5) 8 h; (6) 9 h; (7) 10 h or more, and sleep duration < 6 h was considered short [23].

2.3. Coronary artery calcification

CAC was assessed with computed tomography (CT) using a dual source CT system with Stellar detector (Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany) with a high-pitch or sequential electrocardiogram-gated protocol depending on patient weight and heart rate. The protocol has previously been described in detail [24]. CACS was then calculated using the Agatston method, a standardized weighted score of coronary artery calcium volume and density and a widely used imaging biomarker [25]. CACS 0–10 was defined as non-significant CAC, and CACS > 10 was defined as significant CAC. This cut-off has been shown to reduce the false positive rate and is associated with increased CV mortality [4,26].

2.4. Anthropometric and basic health variables

Height, weight, and waist circumference were measured during a clinical visit to the SCAPIS center at Sahlgrenska University Hospital [20]. Office blood pressure was measured twice in each arm in the supine position with an automatic device (Omron M10-IT, Omron Health Care Co., Kyoto, Japan) and reported as the average of the two systolic blood pressures (SBP) registered in the arm with the highest mean SBP [27]. Blood lipids, glucose, and HbA1c were analyzed in a fasting venous blood sample.

2.5. Social and lifestyle variables

Physical activity was measured using a triaxial accelerometer (ActiGraph GT3X and GT3X+, ActiGraph, LCC, Pensacola, FL, USA) worn during waking hours on the right hip for seven days. Time spent sedentary (SED) and in moderate to vigorous intensity physical activity (MVPA) were classified according to measured vector counts per minute (cpm). SED was defined as 0–199cpm and MVPA as ≥ 2690cpm, based on 60 s epochs. This has previously been described in detail [15].

Other social and lifestyle factors were derived from questionnaire data. Income-related work (yes/no) was used to determine employment status. Education level was reported as “no secondary school/secondary school education/university education”. Smoking status was reported as “never smoker/occasional smoker/former smoker/current smoker”. Alcohol consumption was assessed using the Alcohol Use Disorders Identification Test for consumption (AUDIT-C) where a total score of 5 or higher in men and 4 or higher in women was classified as unhealthy drinking [28,29].

2.6. Comorbidities

Hypertension (yes/no) was defined as self-reported treatment of hypertension and/or systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mmHg. Diabetes mellitus (yes/no) was defined as fasting venous blood glucose ≥7 mmol/L, HbA1c ≥ 48 mmol/L, or self-reported treatment of diabetes. History of myocardial infarction (yes/no) was based on the question, “have you ever been hospitalized for a certain myocardial infarction?”. Obstructive sleep apnea diagnosis was based on self-report. Depression symptoms (yes/no) was based on the question, “During the past 12 months, have you experienced a period of two weeks or more of feeling sad, downhearted or depressed?”. Feelings of chronic stress (yes/no) was based on a multiple-choice question with the response “constant stress in the past year” or “constant stress during the past five years”.

2.7. SCORE2: estimation of the 10-year risk of first-onset CVD

SCORE2 was calculated using gender, age, smoking status, systolic
blood pressure, and non-high density lipoprotein (non-HDL) cholesterol based on the European Society of Cardiology’s region-specific chart [17]. SCORE2 was reported as a percentage as a continuous variable, as well as divided into three risk categories (low risk: <5 %; moderate risk: 5 to <10 %; high risk: ≥10 % in this cohort) [17].

2.8. Statistics

Statistical analyses were performed using SPSS 28.0.1.1 (IBM, Armonk, NY, USA). Data are shown as percentage, mean ± standard deviation (SD) or 95 % confidence interval (CI). Chi-square tests and independent samples t-tests were applied for categorical and continuous variables respectively for between-groups comparisons.

The association between chronotype and CACS was analyzed using a binary generalized linear regression model (GLM), adjusting for SCORE2, body mass index, waist circumference, SES, education level, work status, unhealthy drinking, short sleep duration, MVPA, depression symptoms, chronic stress, obstructive sleep apnea, and diabetes mellitus. In a secondary analysis, low and moderate SCORE2 risk categories were stratified by extreme evening chronotype. The association between the resulting 5 risk categories (low SCORE2 risk & non-extreme-evening chronotype; low SCORE2 risk & extreme evening chronotype; moderate SCORE2 risk & non-extreme-evening chronotype; moderate SCORE2 risk & extreme evening chronotype; high SCORE2 risk & all chronotypes) and CACS was analyzed using a GLM. A sensitivity analysis was conducted adjusting for the individual factors previously included in SCORE2 (age, gender, smoking pack-years, hypertension, and non-HDL cholesterol). A p-value less than 0.05 (two-tailed) was considered statistically significant.

Fig. 1. Study flow chart
Participants with missing data on chronotype, CACS, and covariates, including actigraphy data were excluded. Those with a history of hospitalization for myocardial infarction were not sure, or with missing data were also excluded.
3. Results

771 participants (47.3% male, 57.6 ± 4.4 years) were included in the final analysis after excluding participants with missing chronotype, CAC, covariate, and actimetry data as well as those who had previously been hospitalized for myocardial infarction (Fig. 1). Compared to excluded participants, the analyzed cohort was female to a higher degree, had a healthier lifestyle and less morbidity. Chronotype, however, did not differ between the two groups (Table S1). In our cohort, compared to those with CACS 0–10, participants with significant CAC (CACS > 10) were generally older, more often male, had lower socioeconomic factors, unhealthier lifestyles, and increased morbidity (Table 1).

3.1. Chronotype and CAC

The proportion of participants with significant CAC was lowest among extreme morning types (22.2%) and highest among extreme evening types (40.6%; p = 0.018; Fig. 2). Compared to extreme morning types, extreme evening types had 90% higher odds of significant CAC after controlling for SCORE2, BMI, waist circumference, SES, education level, income-related work, alcohol consumption, sleep duration, time spent in MVPA, depression symptoms, chronic stress, obstructive sleep apnea, and diabetes mellitus (p = 0.037; Table 2). In a sensitivity analysis in which the SCORE2 components were analyzed separately, extreme evening type remained at higher risk of significant CAC (OR = 1.93, 95%CI [1.03–3.60], p = 0.039; Table S2).

3.2. Chronotype, SCORE2, and CAC

A significant interaction between extreme evening chronotype and SCORE2 was found in a GLM (p = 0.030). SCORE2 risk categories were therefore stratified by chronotype. In this explorative analysis, extreme evening chronotypes had an increased risk of significant CAC compared to other chronotypes in the low and moderate CV risk groups (p = 0.011 and 0.023, respectively; Fig. 3). Prevalence of significant CAC did not differ between chronotypes within the "high" CV risk group (p = 0.86). We further divided the cohort into five categories. Characteristics of these risk categories are shown in Table S3. A GLM comparing distribution of significant CAC in these categories revealed a significant dose-

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the participants with and without significant coronary artery calcification.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n=771)</td>
</tr>
<tr>
<td>Male gender</td>
<td>365 (47.3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.6 ± 4.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.0 ± 4.3</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.3 ± 12.3</td>
</tr>
<tr>
<td>Low SES neighborhood</td>
<td>340 (44.1)</td>
</tr>
<tr>
<td>Education Level</td>
<td>No Secondary school</td>
</tr>
<tr>
<td>Smoking Status</td>
<td>Never smoker</td>
</tr>
<tr>
<td></td>
<td>Occasional smoker</td>
</tr>
<tr>
<td></td>
<td>Former smoker</td>
</tr>
<tr>
<td></td>
<td>Current smoker</td>
</tr>
<tr>
<td>Income-related work</td>
<td>612 (79.4)</td>
</tr>
<tr>
<td>Unhealthy alcohol consumption</td>
<td>215 (27.9)</td>
</tr>
<tr>
<td>Chronotype</td>
<td>Extreme morning</td>
</tr>
<tr>
<td></td>
<td>Moderate morning</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
</tr>
<tr>
<td></td>
<td>Moderate evening</td>
</tr>
<tr>
<td></td>
<td>Extreme evening</td>
</tr>
<tr>
<td>Self-reported sleep duration &lt; 6 hours</td>
<td>81 (10.5)</td>
</tr>
<tr>
<td>% Sleep quality PSQI &gt; 5 (n=689)</td>
<td>327 (47.5)</td>
</tr>
<tr>
<td>% Time spent in MVPA/day [%]</td>
<td>5.9 ± 3.1</td>
</tr>
<tr>
<td>% Time spent in SED/day [%]</td>
<td>53.1 ± 9.9</td>
</tr>
<tr>
<td>Hypertension</td>
<td>235 (30.5)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.8 ± 1.0</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.8 ± 0.9</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.7 ± 0.5</td>
</tr>
<tr>
<td>Triglycerides (mmol/L) (n=770)</td>
<td>1.3 ± 0.8</td>
</tr>
<tr>
<td>10-year risk of first-onset CVD (SCORE2) [%]</td>
<td>5.4 ± 2.8</td>
</tr>
<tr>
<td>Depression symptoms in the past 12 months</td>
<td>194 (25.2)</td>
</tr>
<tr>
<td>Self-reported chronic stress</td>
<td>157 (20.4)</td>
</tr>
<tr>
<td>Self-reported diagnosis of OSA</td>
<td>35 (4.5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>44 (5.7)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: BMI = body mass index; SES = socioeconomic status; MVPA = moderate to vigorous intensity physical activity; SED = sedentary; LDL = low-density lipoprotein; HDL = high-density lipoprotein; OSA = obstructive sleep apnea.

Data are expressed as mean ± SD or n(%).

p-values reflect chi-square tests for categorical variables and independent sample T-tests for continuous variables.
notypes have a markedly higher risk of significant CAC than extreme dependent increases in risk of CAC in all risk categories compared to the group with low SCORE2 risk & non-extreme evening chronotypes (OR = 2.46, [1.14–5.35], p = 0.023; OR = 4.02, [2.47–6.53], p < 0.001; OR = 8.01, [4.06–15.78], p < 0.001; OR = 15.20, [7.75–29.82], p < 0.001; Table 3).

4. Discussion

This is the first study to demonstrate an association between chronotype and CAC. Our analysis indicates that extreme evening chronotypes have a markedly higher risk of significant CAC than extreme morning chronotypes, independent of confounding factors. We have also found that chronotype seems to play a particularly important role in CAC among those with low to moderate CV risk according to SCORE2. Our findings suggest that chronotype is not only associated with CV risk factors but may even play a role in the atherosclerotic process, represented by CAC. In addition, we argue that chronotype information can be relevant in early CV prevention.

Our results are congruent with early studies indicating that evening chronotypes have greater CV risk, morbidity, and mortality compared to morning chronotypes [12–15,30,31]. The mechanism behind these findings is not clear. Evening chronotype has been associated to unhealthy lifestyles, which could cause increased CV risk [15,32,33]. Circadian disruption among evening types is a possible mechanism for the direct relationship between chronotype and CV health [34–40]. Both external and internal desynchrony may be involved, and can result in impaired CV function [41]. Indeed, experiments utilizing forced desynchrony and simulated shift work have indicated increased blood pressure and decreased night-time blood pressure dipping, as well as decreased vagal tone and increased inflammatory markers [42,43]. This is coherent with observational studies of shift work, which represents a real-life condition of pronounced circadian desynchrony, indicating that it is associated with increased risk of coronary atherosclerosis and myocardial infarction [44–46]. Extreme evening chronotype may be another condition of circadian desynchrony, although the influence of other environmental factors such as light exposure and temperature cannot be excluded [10].

Our current findings indicate that extreme evening chronotype is not only associated with CV risk and CV health in general, but also more specifically with calcification in the coronary arteries and the atherosclerotic process. There are several potential mechanisms which may explain this association. First, there are peripheral clocks in endothelial cells and vascular smooth muscle cells, dictating the temporal organization of their functioning [47]. Dysfunction in these cells is involved in vascular senescence and are among the first stages of the atherosclerotic process [48–50]. Second, circadian dysfunction can lead to abnormal secretion of hormones such as melatonin, sex hormones, and the renin-angiotensin system, which are involved in vascular function, and oxidative stress [51]. Third, the circadian system may have direct impacts on vascular senescence through influence on telomerase activity as well as regulation of antioxidant enzymes and inflammatory factors [43,52]. Other physiological processes such as inflammation and autophagy...
Fig. 3. CAC, chronotype, and SCORE2
Extreme evening chronotypes have markedly higher risk of having significant coronary artery calcification with a CACS > 10 compared to the other chronotypes in the low and moderate risk groups as determined by SCORE2, but not in the high-risk group. (chi-square; p = 0.86).

Table 3
Association between CAC, cardiovascular risk prediction categories based on SCORE2 and extreme evening chronotype, and confounders in a generalized linear regression model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>CAC</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>0.91</td>
<td>(0.84–0.99)</td>
<td>0.029</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>1.03</td>
<td>(1.00–1.06)</td>
<td>0.036</td>
</tr>
<tr>
<td>Low SES neighborhood</td>
<td>1.50</td>
<td>(1.01–2.20)</td>
<td>0.042</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Secondary school</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>0.82</td>
<td>(0.50–1.35)</td>
<td>0.442</td>
</tr>
<tr>
<td>University</td>
<td>0.82</td>
<td>(0.47–1.42)</td>
<td>0.486</td>
</tr>
<tr>
<td>Income-related work</td>
<td>1.19</td>
<td>(0.75–1.86)</td>
<td>0.463</td>
</tr>
<tr>
<td>Unhealthy alcohol consumption</td>
<td>1.18</td>
<td>(0.80–1.74)</td>
<td>0.398</td>
</tr>
<tr>
<td>Risk category based on chronotype &amp; SCORE2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCORE2 &lt;5% &amp; non-extreme evening</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCORE2 &lt;5% &amp; extreme evening</td>
<td>2.46</td>
<td>(1.14–5.35)</td>
<td>0.023</td>
</tr>
<tr>
<td>SCORE2 5 to &lt;10% &amp; non-extreme evening</td>
<td>4.02</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>SCORE2 5 to &lt;10% &amp; extreme evening</td>
<td>8.01</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>SCORE2 &gt;10% all chronotypes</td>
<td>15.20</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Self-reported sleep duration &lt;6 h</td>
<td>1.18</td>
<td>(0.66–2.10)</td>
<td>0.580</td>
</tr>
<tr>
<td>% Time spent in MVPA/day (%)</td>
<td>1.03</td>
<td>(0.97–1.09)</td>
<td>0.347</td>
</tr>
<tr>
<td>Depression symptoms in the past 12 months</td>
<td>1.09</td>
<td>(0.69–1.71)</td>
<td>0.708</td>
</tr>
<tr>
<td>Self-reported chronic stress</td>
<td>0.71</td>
<td>(0.43–1.16)</td>
<td>0.170</td>
</tr>
<tr>
<td>Self-reported diagnosis of OSA</td>
<td>2.18</td>
<td>(0.98–4.81)</td>
<td>0.055</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3.62</td>
<td>(1.81–7.26)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Definition of abbreviations: SCORE2 = 10-year risk of first-onset cardiovascular disease; BMI = body mass index; SES = socioeconomic status; MVPA = moderate to vigorous intensity physical activity; OSA = obstructive sleep apnea. Data are expressed as odds ratios (OR) with 95% confidence intervals (CI).
stages or potentially dangerous unstable plaque are not detected by CACS [61]. In addition to the inevitable limitations of CAC scoring, our study has several other possible limitations. First, we measure chronotype with a single multiple-choice question instead of with more established questionnaires [62,63]. This has, however, previously been associated with mid-sleep time in the SCAPIS pilot cohort [15], as well as to dim light melatonin onset [64]. Second, we did not have detailed information on certain social and environmental factors that may be influencing chronotype (e.g., shift work, social jetlag, light exposure). Third, depression and stress were characterized by self-reported symptoms rather than diagnostic tools. Fourth, study participants had a narrow age range and were generally healthier than the population as a whole [65], limiting the generalizability of our results. Finally, due to its cross-sectional design, we cannot determine causation. We hypothesize that circadian misalignment is a cause of CAC, but we cannot exclude the possibility that the relationship is reversed. Indeed, immune-mediated denervation of the pineal gland in CVD has been proposed as a mechanism for this type of relationship [66].

There is currently an unmet need for early CV prevention. Maintenance of a healthy lifestyle is a key component of preventive cardiology. Factors such as healthy diet, physical activity, and sufficient sleep are well-established lifestyle factors associated with CV health. It is important, however, to consider not only that these behaviors occur, but also that they are timed correctly with our physiology [41]. Our study suggests that the circadian system, as a fundamental regulator of behavioral and physiological timing, is also an integral component of CV health. Extreme evening chronotype, a potential marker of circadian disruption, may be useful in CV risk identification and health promotion.

5. Statement of Significance

Circadian rhythms, which dictate the temporal organization of our physiology and behavior, likely play a fundamental role in cardiovascular health. Evening chronotype has previously been associated with increased cardiovascular risk, morbidity, and mortality. However, the mechanisms behind these associations are not well understood. This is the first study that aims to clarify the link between chronotype and coronary artery calcification, a measure of subclinical atherosclerotic burden. In addition, it aims to fine-tune existing cardiovascular risk prediction models by integrating chronotype information, as early identification and prevention of cardiovascular disease is essential to reducing its burden.

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CRediT authorship contribution statement

Mio Kobayashi Frisk: Conceptualization, Methodology, Formal analysis, Writing – original draft, Visualization, Project administration. Erika Fagman: Conceptualization, Methodology, Investigation, Resources, Writing – review & editing. Daniel Arvidsson: Investigation, Methodology, Resources, Writing – review & editing. Orjan Ekblom: Investigation, Methodology, Resources, Writing – review & editing. Mats Börjesson: Investigation, Methodology, Resources, Writing – review & editing. Goran Bergström: Investigation, Methodology, Resources, Writing – review & editing. Ding Zou: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing – review & editing. Supervision.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2023.11.004.

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