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MAJOR ARTICLE

High-Sensitivity Troponins and Subclinical Coronary Atherosclerosis Evaluated by Coronary Calcium Score Among Older Asians Living With Well-Controlled Human Immunodeficiency Virus

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Background. Elevated levels of high-sensitivity cardiac troponin (hs-cTn) are suggestive of myocardial cell injury and coronary artery disease. We explored the association between hs-cTn and subclinical arteriosclerosis using coronary artery calcification (CAC) scoring among 337 virally suppressed patients with human immunodeficiency virus (HIV) who were ≥50 years old and without evidence of known coronary artery disease.

Methods. Noncontrast cardiac computed tomography and blood sampling for hs-cTn, both subunit I (hs-cTnI) and subunit T (hs-cTnT), were performed. The relationship between CAC (Agatston score) and serum hs-cTn levels was analyzed using Spearman correlation and logistic regression models.

Results. The patients, of whom 62% were male, had a median age of 54 years and had been on antiretroviral therapy for a median of 16 years; the CAC score was >0 in 50% of patients and ≥100 in 16%. Both hs-cTn concentrations were positively correlated with the Agatston score, with correlation coefficients of 0.28 and 0.27 ($P < .001$) for hs-cTnI and hs-cTnT, respectively. hs-cTnI and hs-cTnT concentrations of ≥4 and ≥5.3 pg/mL, respectively, provided the best performance for discriminating patients with Agatston scores ≥100, with a sensitivity and specificity of 76% and 60%, respectively, for hs-cTnI and 70% and 50% for hs-cTnT. In multivariable logistic regression analysis, each log unit increase in hs-cTnI level was independently associated with increased odds of having an Agatston score ≥100 (odds ratio, 2.83 [95% confidence interval, 1.69–4.75]; $P < .001$). Although not an independent predictor, hs-cTnT was also associated with an increased odds of having an Agatston score ≥100 (odds ratio, 1.58 [95% confidence interval, .92–2.73]; $P = .10$).

Conclusions. Among Asians aged ≥50 years with well-controlled HIV infection and without established cardiovascular disease, 50% had subclinical arteriosclerosis. Increasing hs-cTnI and hs-cTnT concentrations were associated with an increased risk of severe subclinical arteriosclerosis, and hs-cTn may be a potential biomarker to detect severe subclinical arteriosclerosis.

Keywords. PLWH; coronary artery calcification; high-sensitivity cardiac troponin; subclinical atherosclerosis.

With improvements in effective antiretroviral therapy (ART) and accessibility to treatment, people living with human immunodeficiency virus (HIV) (PLWH) are living longer with better quality of life. However, as PLWH age, the major causes of disease and death have shifted from those related to HIV toward comorbid conditions including atherosclerosis and cardiovascular disease (CVD) [1–3]. Several recent studies have demonstrated that HIV infection accelerates the process of atherosclerosis, by mechanisms including HIV-related immune dysregulation and inflammation, HIV therapies, host factors, and conventional CVD risk factors [4–7].

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Several studies have assessed the prevalence of subclinical coronary atherosclerosis using different modalities [8]. Coronary artery calcification (CAC) detected with noncontrast cardiac computed tomography (CT) can predict future cardiovascular events and all-cause mortality rates in both PLWH and HIV-negative populations [4, 9–11]. Despite this, CAC screening in asymptomatic patients is still limited owing to accessibility, concerns about radiation exposure, and price [12]. Therefore, having an alternative technique for predicting CVD is desirable. Potential methods include the detection of high-sensitivity cardiac troponin (hs-cTn), both subunit I (hs-cTnI) and subunit T (hs-cTnT). hs-cTn has an important diagnostic role in acute cardiac care and provides prognostic value in predicting long-term cardiovascular events in asymptomatic, at-risk populations [13–15]. Several recent studies conducted in healthy volunteers without known CVDs showed that hs-cTn was associated with subclinical coronary atherosclerosis detected based on CAC [16–18]. However, its ability to predict subclinical coronary atherosclerosis in virologically suppressed, older PLWH has yet to be validated. We therefore sought to investigate the correlation between hs-cTn and subclinical atherosclerosis among Asian PLWH with well-controlled HIV infection and without established CVD, who had received ART for a median of 16 years.

MATERIALS AND METHODS

Study Design and Population

PLWH aged ≥50 years were consecutively recruited from the prospective HIV-NAT 006 long-term cohort (clinicaltrials.gov NCT00411983) from March 2016 to May 2017 at the HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand. Thorough medical history and HIV and non–HIV-related parameters were extracted from HIV-NAT's electronic health database. For the present study, the following were recorded on the same day noncontrast cardiac CT was performed: clinical examination findings, weight, height, waist circumference, body mass index (BMI), blood pressure, other medical conditions, including traditional cardiovascular risk factors, and fasting blood samples for lipid profile, glucose, and hs-cTn. The 10-year cardiovascular morbidity and mortality risks were calculated using the atherosclerotic CVD (ASCVD) risk score, with risk categorized as low (<7.5%), intermediate (7.5 to <20%), or high (≥20%) [19]. The exclusion criteria were established CVD and estimated glomerular filtration rate <50 mL/min/1.73 m^2, calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation; the latter can affect hs-cTn levels [20]. All eligible participants underwent transthoracic echocardiography to exclude those with abnormal structural heart conditions that could increase hs-cTn levels—in particular, aortic stenosis, left or right ventricular systolic dysfunction, severe pulmonary hypertension, and severe ventricular hypertrophy [21].

Patient Consent Statement

The protocol was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. All participants gave their written informed consent.

Multisection CT Study of CAC

A multisection CT scanner (Somatom Sensation 64; Siemens Medical Systems) was used to quantify the coronary calcium using the Agatston score, which was calculated by multiplying the weighted density score by the pixel area of the calcification speck [22, 23]. After the initial scout images were acquired, the field of scan was placed on the chest area, covering the whole heart. The standard scan parameters included a 3-mm section thickness, 1.2 × 24-mm collimation, 0.37-second rotation, and spiral mode with 120 kVp at 80 mAs. The reconstruction was performed at 60% of the R-R interval. The Agatston scores were analyzed and confirmed by a single experienced observer who was blinded to the participant's medical history and biomarker levels.

Biochemical Analyses

Peripheral venous blood samples were taken on the same day as cardiac CT, processed, and stored at −80°C until analysis. The hs-cTnI levels were measured with the STAT high-sensitive cardiac troponin-I immunoassay on an Architect analyzer (Abbott Diagnostics), with a lower limit of detection (LLD) of 1.9 pg/mL. The 99th percentile reference limit for the overall population is 26.2 pg/mL, with a 4% intra-assay coefficient of variation. The hs-cTnT levels were quantified with the Cobas analyzer (Roche Diagnostics), with an LLD of 3 pg/mL and intra-assay coefficients of variation of 5% at 10 and 1% at 100 pg/mL.

Statistical Analysis

Categorical variables were expressed as frequencies and percentages, and continuous variables were summarized as mean (standard deviation) for normally distributed data and median (interquartile range [IQR]) for nonnormally distributed data. The hs-cTnT and hs-cTnI concentrations below the LLD were imputed as the LLD. The hs-cTnI and hs-cTnT levels were log-transformed to linearize their relationship with the logit function. The Agatston score was categorized into 4 groups—0, 1–99, 100–399, and ≥400—and the distribution of hs-cTn levels were assessed across the quartiles. A linear trend test was used to formally assess hs-cTn concentrations across ordered categories of Agatston score, and the relationship between hs-cTn and Agatston score as continuous variables were assessed using Spearman rank correlation coefficients.

Multivariable logistic regression analysis was used to assess the association between CAC scores ≥100 and hs-cTn. Potential confounders included sex, age, waist circumference,

hypertension, dyslipidemia, diabetes mellitus, absolute CD4 cell count, weight, smoking status, and hepatitis C virus infection. These were adjusted for in the multivariable model if the univariable *P* value was <.2. We assessed the relationship between log-transformed hs-cTnI and hs-cTnT levels and these confounders in multivariable linear regression models. Receiver operator characteristic (ROC) curves were constructed to assess the ability of hs-cTn to predict the Agatston score ≥100, for both hs-cTn alone and after adding it to the ASCVD score. Nested models were compared using the Aikake information criterion (AIC), and a likelihood ratio test was used compare the model fit. Differences were considered statistically significant at $P < .05$. Analyses were performed using Stata/SE software, version 15.0.

RESULTS

Population Characteristics

A total of 337 PLWH were included, and their characteristics are shown in Table 1. Their median age (IQR) was 54 (52–59) years, and 210 (62%) were male. Nearly one-third had hypertension (n = 107 [32%]), and 60 (18%) had diabetes mellitus. Fourteen percent were current smokers. The median systolic blood pressure was 128 mm Hg, and the median diastolic blood pressure, 77 mm Hg. The median BMI (calculated as weight in kilograms divided by height in meters squared) was 23 kg/m^2, and 11 participants (3%) had a BMI >30. The median waist circumference was 84 cm, and 34% of male and 58% of female participants had waist circumferences >90 and >80 cm, respectively. One-third of participants (33%) were on a statin regimen at the time of the study.

The median (IQR) serum total cholesterol, low-density lipoprotein cholesterol, triglyceride and high-density lipoprotein cholesterol levels were 203 (179–236) mg/dL, 123 (99–147) mg/dL, 160 (103–221) mg/L, and 46 (39–57) mg/L, respectively. All participants were on ART, with a median duration (IQR) of 16 (13–19) years, and 98% had HIV-1 RNA levels <50 copies/mL. The median and nadir CD4 cell counts (IQR) were 614/μL (483–803/μL) and 176/μL (88–256/μL), respectively. Based on the 10-year ASCVD risk score, 56.8%, 31.7%, and 11.5% of participants were classified as low, moderate, and high risk, respectively.

A total of 316 participants (94%) had hs-cTnI concentrations above the limit of detection (1.9 pg/mL); the median (IQR) was 3.7 (2.7–5.2) pg/mL. The overall 99th percentile for hs-cTnI was 39.7 pg/mL. Ten (3%) participants had hs-cTnI levels elevated to >26 pg/mL. A total of 288 participants (85%) had hs-cTnT concentrations above the limit of detection (3 pg/mL), with a median (IQR) of 5.5 (3.8–8.7) pg/mL. The 99th percentile for hs-cTnT was 38.3 pg/mL.

Half of the participants had an Agatston score of 0, 34% had a score of 1–99, and 16% had an score of ≥100 (31 [9%] 100–399 and 23 [7%] ≥400; Table 1). In adjusted linear regression models, older age, higher serum creatinine levels, hypertension, and diabetes were associated with higher log hs-cTnT levels; older age, higher serum creatinine, and hypertension, with higher log hs-cTnI levels. Female sex was associated with lower levels of both troponin isoforms (Supplementary Table 1).

Table 1. Demographics and Clinical Characteristics in Study Participants

Baseline Characteristic	Participants, No. (%)[a] (N = 337)
Male sex	210 (62)
Age, median (IQR), y	54 (52–59)
Hypertension	107 (32)
Diabetes mellitus	60 (18)
BMI, median (IQR)[b]	23 (21–25)
Waist circumference, median (IQR), cm	84 (78–90)
Current smoker	48 (14)
Blood pressure, median (IQR), mm Hg	
Systolic	128 (118–137)
Diastolic	77 (71–84)
Current statin therapy	111 (33)
Laboratory values, median (IQR),	
Total cholesterol, mg/dL	203 (179–236)
Triglycerides, mg/dL	160 (103–221)
LDL cholesterol, mg/dL	123 (99 -147)
HDL cholesterol, mg/dL	46 (39–57)
Absolute CD4 cell count, cells/μL	614 (483–803)
Viral load <50 copies/mL	330 (98)
ART duration, median (IQR), y	16 (13–19)
NNRTI-based ART regimen	301 (89)
NRTI	197 (58)
PI	129 (38)
INSTI	9 (2.7)
Other	1 (0.3)
HCV infection	30 (8.9)
hs-cTnI, median (IQR), pg/mL	3.7 (2.7–5.2)
hs-cTnI above LLD	316 (94)
hs-cTnT, median (IQR), pg/mL	5.5 (3.8–8.7)
hs-cTnT above LLD	288 (85)
CAC (Agatston) score	
0	170 (50)
1–99	113 (34)
100–399	31 (9)
≥400	23 (7)
ASCVD risk	
Low risk (<7.5%)	191 (57)
Intermediate risk (≥7.5 to <20%)	107 (32)
High risk (≥20%)	39 (11)

Abbreviations: ART, antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CAC, coronary artery calcification; HCV, hepatitis C virus; HDL, high-density lipoprotein; hs-cTnI, high-sensitivity troponin I; hs-cTnT, high-sensitivity troponin T; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; LDL, low-density lipoprotein; LLD, lower limit of detection; NNRTI, nonnucleoside reverse-transcriptase inhibitor; NRTI, nucleoside reverse-transcriptase inhibitor; PI, protease inhibitor.

[a]Data represent no. (%) of participants unless otherwise specified.

[b]BMI calculated as weight in kilograms divided by height in meters squared.

hs-cTn and Coronary Artery Calcium

Across quartiles of hs-cTnI and hs-cTnT values, there were increasing proportions of participants with higher Agatston

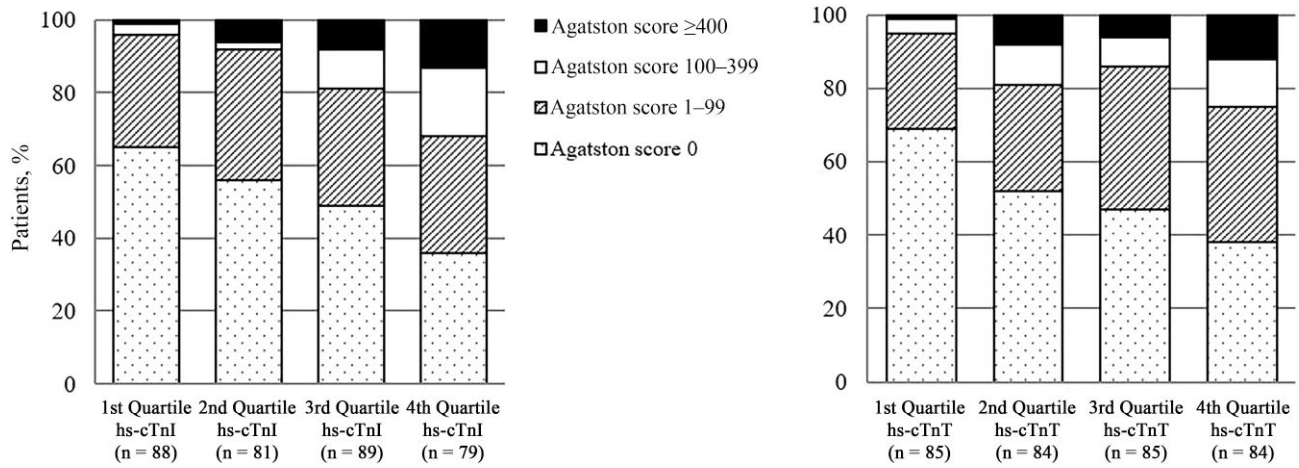

Figure 1. Distribution of Agatston score expressed as percentages across high-sensitivity cardiac troponin (hs-cTn) quartiles, for hs-cTn subunit I (hs-cTnI) (*left*) and subunit T (hs-cTnT) (*right*).

scores, particularly in the third and fourth quartiles ($P < .001$; Figure 1). Box-and-whisker plots (Figure 2) demonstrate increasing hs-cTn levels with increasing Agatston scores ($P < .001$ for both hs-cTnI and hs-cTnT). These levels differentiated clearly between participants with Agatston scores <100 and those with scores ≥100 ($P < .001$ for both subunits). The hs-cTn levels were slightly correlated with CAC, with Spearman correlation coefficients of 0.28 for hs-cTnI and 0.27 for hs-cTnT (both $P < .001$).

ROC Curves to Detect Agatston Score ≥100

Figure 3 demonstrates that the 10-year ASCVD risk score and hs-cTn concentrations had similar abilities to discriminate Agatston scores ≥100. The area under the ROC curve (AUROC) was 0.757 (95% confidence interval [CI], .692–.822) for ASCVD risk score, 0.733 .659–.808) for hs-cTnI, and 0.672 (.594–.750) for hs-cTnT. The AIC for ASCVD risk score alone was 271.8436. Combining hs-cTn concentrations with the 10-year ASCVD risk resulted in an increase in AUROC after adding hs-cTnI (0.797 [95% CI, .734–.860]). The AIC for the combined model decreased to 257.2909 (likelihood ratio χ^2 $P < .001$).

After adding hs-cTnT to the ASCVD risk score, there was a small increase in median AUROC to 0.760 (95% CI, .696–.826). The AIC of the combined model decreased to 266.2953 (likelihood ratio χ^2 $P = .006$). A hs-cTnI concentrations ≥4 pg/mL was the cutoff that maximized the sensitivity and specificity for an end point of Agatston score ≥100, with a sensitivity and specificity of 76% and 60%, respectively. For hs-cTnT, a cutoff value of ≥5.3 pg/mL provided the best performance to discriminating patients with Agatston scores ≥100, with a sensitivity and specificity of 70% and 50%, respectively.

Multivariable Logistic Regression Evaluating Factors Associated With Agatston Scores ≥100

The results from the logistic regression are presented in Table 2. In the univariable model, both subunits of hs-cTn were significantly associated with Agatston score ≥100 (odds ratio [OR] per log unit increase [95% CI], 3.92 [95% CI 2.46–6.24] for hs-cTnI and 2.75 (1.74–4.33 for hs-cTnT; both $P < .001$) After adjustment for potential CVD risk factors in the multivariable model, hs-cTnI continued to be significantly associated with Agatston scores ≥100. Each log unit increase in hs-cTnI concentration increased the odds of Agatston scores ≥100 by 2.83 times (OR, 2.83 [95% CI, 1.69–4.75]; $P < .001$). In the multivariable model for hs-cTnT, male sex (OR, 2.44; $P = .048$), diabetes (2.34; $P = .03$), hypertension (2.27; $P = .02$), and waist circumference (1.04; $P = .02$) were also independently associated with Agatston scores ≥100. The AUROC was 0.830 (95% CI, .774–.885), and the AIC for this model was 243.6867, representing a significant improvement over the AUROC for hs-cTnI combined with ASCVD risk score (likelihood ratio χ^2 $P < .001$).

In the multivariable hs-cTnT model, hs-cTnT was no longer an independent predictor, but the 95% CI remained consistent with an increased risk (OR, 1.58, [95% CI, .92–2.73]; $P = .10$). The AUROC for this model was 0.802 (95% CI, .745–.859), and the AIC was 257.429, representing a significant improvement over the AUROC for hs-cTnT combined with the ASCVD risk score (likelihood ratio χ^2 $P = .002$). Other potential confounders in the model had ORs and 95% CIs that were consistent in magnitude and precision with the multivariable model for hs-cTnI (Table 2). The multivariable models for both hs-cTnI and hs-cTnT showed adequate calibration (Hosmer and Lemeshow χ^2 $P = .58$ and $P = .50$, respectively).

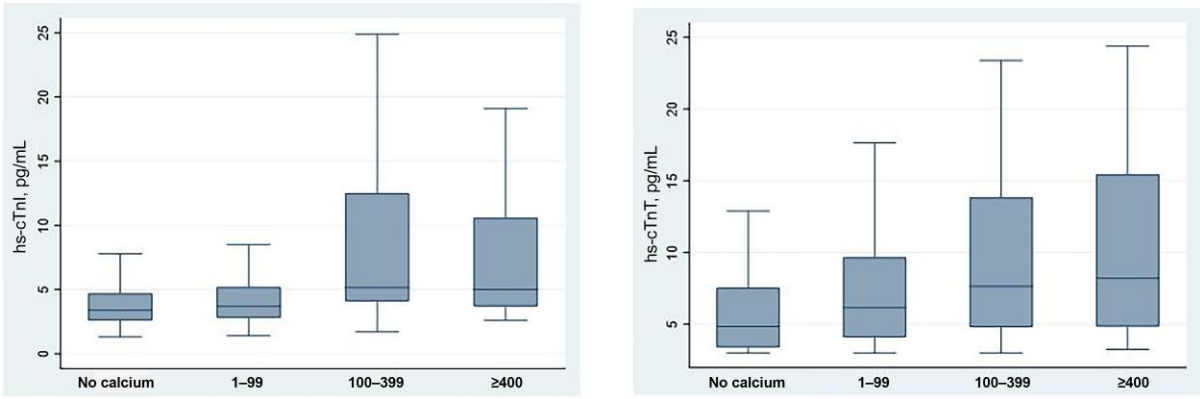

Figure 2. Box-and-whisker plots for high-sensitivity cardiac troponin subunit I (hs-cTnI) (*left*) and subunit T (hs-cTnT) (*right*) concentrations by Agatston score category. Lower edges of boxes represent the 25th percentile; upper edges, the 75th percentile; line within boxes, median values; whiskers, range of data, including outliers. $P < .001$ for both hs-cTnI and hs-cTnT, across score categories.

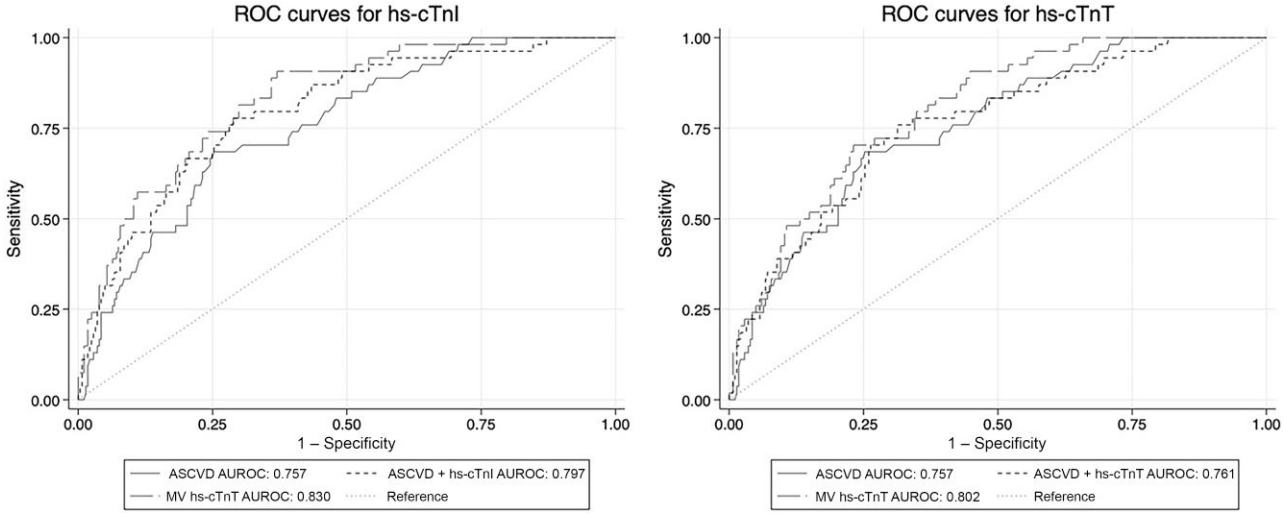

Figure 3. Receiver operating characteristic (ROC) curves to detect the presence of Agatston score ≥100 and atherosclerotic cardiovascular disease (ASCVD) risk score only or ASCVD risk score combined with high-sensitivity cardiac troponin subunit I (hs-cTnI) or subunit T (hs-cTnT) levels and multivariable (MV) models for hs-cTnI or hs-cTnT. Abbreviation: AUROC, area under the ROC curve.

DISCUSSION

This present study evaluated the association between hs-cTn and subclinical atherosclerosis in Asian PLWH ≥50 years old with well-controlled HIV infection and without documented coronary artery disease. We used CAC as determined by Agatston score as a surrogate for subclinical atherosclerosis burden because it has been shown to be superior to carotid intima-media thickness in predicting future cardiovascular events [8]. The overall prevalence of detectable CAC (score >0) in our cohort was 50%, which was close to the findings reported in a previous study conducted in PLWH without known CVDs in the Multicenter AIDS Cohort Study [24]. We found that both hs-cTn concentrations were associated with Agatston score ≥100. Multivariable analysis revealed that hs-cTnI concentration could discriminate well for PLWH with Agatston scores ≥100 or <100.

In the present study, 94% and 85% of our participants had detectable hs-cTnI and hs-cTnT concentrations, respectively. Although hs-cTn can be detected in 74%–94% of the general population, hs-cTnI and hs-cTnT are detected at very low levels [15, 25, 26]. Korosoglou et al [27] suggested that repetitive microrupture of atherosclerotic plaques could result in embolization of the coronary microcirculation, which possibly accounts for microleakage of hs-cTnI and hs-cTnT into the bloodstream. Thus, elevated hs-cTnI and hs-cTnT levels could indirectly indicate an increased atherosclerotic burden [27].

Table 2. Univariable and Multivariable Logistic Regression Models for High-Sensitivity Troponin Subunits and Agatston Scores ≥100

	Univariable Model		Multivariable Model for hs-cTnI[a,b]		Adjusted Model for hs-cTnT[a,c]	
Variable	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Log_e hs-cTnI	3.92 (2.46–6.24)	<.001[d]	2.83 (1.69–4.75)	<.001[d]	…	…
Log_e hs-cTnT	2.75 (1.74–4.33)	<.001[d]	…	…	1.58 (.92–2.73)	.10
Male sex	3.58 (1.68–7.60)	.001[d]	2.44 (1.01–5.92)	.048[d]	2.68 (1.14–6.31)	.02[d]
Age	1.09 (1.04–1.14)	<.001[d]	1.05 (.99–1.11)	.08	1.06 (1.001–1.19)	.04[d]
Hypertension	4.03 (2.21–7.38)	<.001[d]	2.27 (1.14–4.52)	.02[d]	2.36 (1.20–4.63)	.01[d]
Diabetes	4.11 (2.11–8.01)	<.001[d]	2.34 (1.07–5.10)	.03[d]	2.15 (1.004–4.60)	.049[d]
Dyslipidemia	1.34 (.48–3.74)	.57	…	…	…	…
Waist circumference	1.07 (1.04–1.11)	<.001[d]	1.04 (1.01–1.08)	.02[d]	1.04 (1.01–1.08)	.01[d]
Current smoker	1.25 (0.57–2.76)	.58	…	…	…	…
Absolute CD4 cell count	1.00 (0.99–1.00)	.39	…	…	…	…
Serum creatinine	2.73 (1.00–7.45)	.05	0.44 (.11–1.72)	.24	0.48 (.13–1.82)	.28
HCV infection	1.34 (.43–4.18)	.62	…	…	…	…

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; hs-cTnI, high-sensitivity troponin, subunit I; hs-cTnT, high-sensitivity troponin, subunit T; log_e, natural logarithm transformed; OR, odds ratio.

[a]Adjusted for variables with $P < .1$ in univariable models.

[b]For the multivariable model for hs-cTnI, the Aikake information criterion (AIC) was 243.6867, and the area under the receiver operating curve (AUROC) was 0.8298.

[c]For the adjusted model for hs-cTnT, the AIC was 257.4729, and the AUROC, 0.8020.

[d]Significant at $P < .05$.

The 99th percentile reference value of hs-cTnI in our cohort was 39.7 pg/mL, slightly higher than the 32.5 pg/mL found in a study using the same immunoassay in 4138 healthy individuals aged 55–64 years [15]. However, the overall distribution of hs-cTnI in the 2 cohorts was quite similar, with comparable median and IQR values. Accordingly, the difference in sample size between the studies could account for the difference in 99th percentile reference values. Because there is no established reference normal range of hs-cTnI specifically for the PLWH population, we were not able to compare our reference ranges with those in the prior study, conducted in an HIV-negative population. In our study, 3% of participants who were asymptomatic had hs-cTnI levels elevated above the recommended threshold for the diagnosis of acute myocardial infarction (26 pg/mL) [28]. Of these, 9 (90%) had detectable CAC. All of them had baseline characteristics similar to those in the whole HIV-NAT 006 cohort from which our study participants were drawn.

Consistent with findings of a previous study in people living without HIV, our study demonstrates a weak, although significant, correlation between both subunits of hs-cTn and CAC. Olson et al [17] found that hs-cTnI levels increase along with increasing Agatston scores in the general population, with a correlation coefficient of 0.23 ($P < .001$), which is comparable to our finding of a correlation coefficient of 0.28 ($P < .001$), Notably, about one-third (37% for hs-cTnI and 38% for hs-cTnT) of our PLWH in the highest hs-cTn quartile had CAC scores of 0. Similar findings have been observed in the general population, with CAC scores of 0 in 45% of participants in the highest hs-cTnI quartile [17]. This indicates that the coronary plaque calcification, a result of the healing process after silent rupture, is not the only pathogenetic mechanism that accounts for hs-cTn elevation.

Lee et al [29] reported that 7% of the plaques distributing along the coronary tree in healthy individuals are noncalcified. Several studies reported that asymptomatic PLWH had higher rates of noncalcified coronary plaque than persons without HIV [30, 31], Thus, if repetitive microrupture or erosion of such plaques occurred, it could be responsible for the elevation of hs-cTn in the absence of CAC. This has been highlighted in the study from Korosoglou et al [27], who reported a stronger correlation of hs-cTn with noncalcified plaques than with calcified plaques.

The current study has some limitations. First, it was conducted in PLWH aged ≥50 years, almost all of whom were virologically suppressed without ventricular dysfunction. These findings may not be generalizable to PLWH with different rates of virological suppression or in those with ventricular dysfunction, although rates of ventricular dysfunction in PLWH ≥50 years old at our center are low and comparable to those in age and sex-matched HIV-negative controls [21]. Second, apart from subclinical atherosclerosis, some non–coronary atherosclerosis–related conditions that potentially influence on hs-cTn level—such as occult chronic opportunistic infection, myocardial inflammation, or structural heart diseases—may exist [32, 33]. However, almost all of our participants had good immune status, and abnormal structural heart conditions were excluded by echocardiogram. Third, because we collected only a single baseline blood sample, possible intraindividual variation in levels of both hs-cTn subunits was not examined.

Fourth, in contrast to a previous study reporting that hs-cTnT concentrations were significantly associated with age

[34] we found significant associations with age, diabetes, sex, and creatinine levels, which could potentially bias our study results. Elevated hs-cTn levels have demonstrated prognostic value in patients with chronic kidney disease from the general population with suspected acute coronary syndrome [35], and our multivariable logistic models adjusted for these significant associations. Fifth, studies in the general population have shown that while hs-cTnT levels are significantly increased in patients with coronary artery disease, with or without myocardial ischemia, only those with coronary artery disease and ischemia showed higher levels of another biomarker [N-terminal pro B-type natriuretic peptide (NT-pro-BNP)] [36]. We did not measure other biomarkers in the current study, so whether this finding is also applicable to PLWH is uncertain but is an area for future research. Finally, owing to the nature of cross-sectional studies, it remains unclear whether hs-cTn elevation provides prognostic benefit for long-term adverse clinical outcomes in this population.

In conclusion, this study demonstrates a correlation between hs-cTn levels and subclinical atherosclerosis as indicated by CAC in Asians aged ≥50 years with well-controlled HIV-infection. hs-cTn could be a potential biomarker for early atherosclerotic risk stratification in this population. The clinical significance of elevated hs-cTnI levels and CAC score ≥100 with long-term adverse cardiovascular outcomes should be prospectively evaluated.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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