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FULL PAPER

Utility of routine non-gated CT chest in detection of subclinical atherosclerotic calcifications of coronary arteries in hospitalised HIV patients

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Objectives: To evaluate coronary artery calcification (CAC) on routine CT chest in hospitalised HIV patients and to assess individual risk factors.
Methods: Routine CT chests, May 2010–November 2015, of 143 hospitalised HIV-positive patients were reviewed for qualitative assessment of calcification in major coronary arteries by two radiologists. Presence, location and burden of calcification were evaluated on 3 mm axial images of CT chest. Cardiovascular risk factors and HIV lab parameters such as CD4 count, viral load and duration, and status of antiretroviral treatment were collected. Statistical analysis including multivariate logistic regression was performed.
Results: Forty-one patients (28.7%) showed CAC, left anterior descending (n = 38, 92.7%), circumflex (n = 18, 43.9%) and Right Coronary Artery (n = 13, 31.7%); mostly mild CAC burden and mostly proximal left coronary arteries with excellent interobserver and intraobserver agreements (K = 0.9, and 1). Age of CAC+ group (53.9 years) was significantly higher than CAC− group (43.4, p < 0.001, minimum age of CAC+, 27 years). No significant difference between two groups in sex, ethnicity and risk factors and HAART status. CAC+ group showed significantly longer HIV duration (12.3 years *vs* 8.6, p < 0.0344) and higher CD4 cell counts (mean = 355.9 *vs* 175.3, p = 0.0053) and significantly lower viral load (76 *vs* 414K, p = 0.02) than CAC− group. On multivariate logistic regression, age, HIV duration and CD4 were significantly associated with CAC+ (p-values < .05).
Conclusions: One-third of hospitalised HIV patients showed subclinical CAC on CT chest. HIV duration and age of patients were independent risk factors for developing CAC. Higher CD4 cell count was strongly associated with CAC+.
Advances in knowledge: Routine CT chest with or without contrast performed for non-cardiac indications is helpful in identification of subclinical CAC in HIV patients and radiologists should be encouraged to report CAC.
CAC is seen in younger age group in HIV, and awareness of this finding on routine CT chest would help guiding clinicians to assess risk stratification for primary prevention of ischemic heart disease in this population at an earlier stage when compared to normal population.
Duration of HIV infection and age of patients were independent risk factors for developing CAC in our study and CD4 count was strongly associated with presence of CAC.

INTRODUCTION

The introduction of highly active antiretroviral therapy (HAART) provides a longer life expectancy in patients with human immunodeficiency virus (HIV).[1] Recent studies have shown increased rates of atherosclerosis, coronary artery disease and myocardial infarction (MI)[2–4] in HIV patients and ischaemic heart disease is a leading cause of morbidity and mortality in this population.[5] Accelerated immune senescence secondary to the exhaustion of immunological resources, drug toxicity of HAART, positive response to HAART with increased CD4 cell count, or metabolic abnormalities related to HIV have been suggested as possible reasons for increased cardiovascular (CV) events in HIV-infected patients.[6–9] In previous

studies, HIV patients showed higher rates of coronary artery calcification (CAC) or systemic arterial calcification than non-infected controls.[3,9–12] However, the relation between increased CAC and HIV status remains controversial and the mechanism is not completely understood.[3,9,11] Most of these studies were looked at quantitative assessment of coronary artery atherosclerosis on ECG-gated CT chest using the Agatston score method in non-hospitalised and stable HIV outpatients.

CAC is an established imaging marker of subclinical atherosclerosis and quantification of calcium score had been validated with CT.[13] The prognostic value of CAC score for CV events and morality was shown on various studies.[14–18] The CAC scoring is conventionally performed using the Agatston method on an EKG-gated non-contrast cardiac CT. However, there was good correlation of visual calcium scoring with traditional Agatston score[19–21] and recently visual scoring of CAC on non-EKG-gated low-dose screening CT for lung cancer proved to be useful in predicting future CV mortality.[22]

Our aim is to retrospectively evaluate subclinical CAC in hospitalised HIV patients undergoing routine non-EKG-gated chest CT for non-cardiac indications and to assess prevalence and risk factors.

METHODS AND MATERIALS

This study was approved by the institutional review board. The acquisition of informed consent was waived due to the retrospective study design.

Subjects

Using electronic medical records, we retrospectively identified consecutive male and female inpatients with known history of HIV but without a documented CV events who underwent routine CT chest during their hospital admission, from 2010 May to 2015 November. A total of 145 HIV positive patients were identified as having undergone a thoracic CT during their hospitalisation. All these patients were under internal medicine and/or infectious disease division, mostly admitted from ED. Two patients were treated for CV events: one underwent coronary artery bypass graft (CABG) surgery and the other underwent a pacemaker insertion, thus were excluded from analysis. Finally, a total of 143 patients (M:F = 119:24; mean age, 46.4) were enrolled in this study.

CV risk factors

We obtained clinical information about traditional CV risk factors including lipid profile (total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides), systolic blood pressure (BP), antihypertensive medication, smoking status, number of pack years of smoking, fasting blood sugar and body mass index (BMI). Smoking status was categorised as non-smoker, ex-smoker and current smoker.

HIV status parameters

We collected clinical and laboratory parameters reflecting the status of HIV infection, including CD4 count, viral load, duration since HIV diagnosis, status of antiretroviral treatment including any prior use of antiretrovirals. Laboratory parameters including CD4 count and viral load were used for analysis only in patients for whom the result of CD4 count was obtained less than 6 months before or after the date of CT chest study (n = 82). Viral load was also used for analysis in cases where the test was performed less than 6 months around the date of CT exam (n = 81). Status of antiretroviral treatment was categorised into never, prior and currently on treatment.

IMAGING AND READING OF THE IMAGES

Fifty-eight patients underwent chest CT without contrast while 85 patients underwent chest CT with contrast. All CT examinations were performed in the department of radiological sciences of UC medical centre. Thoracic CT was performed at 120 kVp and 150–200 effective mA based on body habitus with use of multidetector row CT scanner (Siemens Sensation 64 and Philips 256 iCT). The CT scan was obtained from the lung apices to the bases in a single breath hold at maximum inspiration. All CT images were transferred to picture archiving and communicating system and readers reviewed only 3 mm axial images of non-contrast CT or contrast CT chest to identify CAC. The reader interpreted images by using standard mediastinal settings (width, 350 HU; level, 50 HU) with smooth kernel on non-contrast CT. Readers adjusted contrast CT images from standard mediastinal settings to bone window settings (width 2000 HU; level, 500 HU) for better identification CAC.

VISUAL ASSESSMENT FOR CORONARY ARTERY CALCIUM

Two cardiothoracic radiologists of more than 15 years of experience (EJC and MK) reviewed all the images of CT chest scans and performed visual identification of CAC, and one radiologist (MK) reviewed the studies for two times with two weeks apart between the first and second readings. Each of the four main coronary arteries was identified (left main (LM), left anterior descending (LAD), circumflex (LCX), and right (RCA)). Calcification in each artery was categorised as absent-0, mild-1, moderate-2 or severe-3 by the radiologist. Calcification was classified as mild when less than one-third of the length of the entire artery showed calcification; moderate when one-third to two-thirds of the artery showed calcification; and severe when more than two-thirds of the artery showed calcification. Locations of calcification were noted as the proximal-1, mid-to-distal-2 or both-3. In LAD, the proximal and distal portions were divided where the first diagonal branch takes off. In LCX, the proximal and distal portions were divided where the first obtuse marginal branch originates. In Right Coronary Artery (RCA), they were divided where the first acute marginal artery arises. Given the non-ECG-gated CT scans of our study, we neither did conventional scoring of coronary artery calcium with Agatston method nor directly compared our qualitative results of CAC in HIV patients to quantitative Agatston calcium scoring on ECG-gated coronary CT in normal population or MESA.

STATISTICAL ANALYSES

To determine the independent risk factors associated with positive CAC, we divided the 143 subjects into two groups: the CAC negative group (CAC–, category I) and the CAC positive

group (CAC+, category II). The demographic and clinical characteristics of the two groups were summarised by means, standard deviations, percentages and compared by Student's t-tests for continuous, normally distributed variables and χ^2 or Fisher exact tests for categorical variables. Subsequently, the variables that were found to be significantly associated with CAC+ were included in the multivariate logistic regression analysis to determine any independent risk factors for coronary calcium by stepwise selection method. An odds ratio (OR) >1.00 indicated a greater likelihood of CAC+. Statistical analysis was performed using statistical software SAS (V.9.4, SAS Institute Inc., Cary, NC, USA). A p-value < 0.05 was considered statistically significant. κ statistics was performed to assess interobserver and intraobserver agreements among readers.

RESULTS

Among 143 HIV patients, 41 patients (28.7%) showed calcifications in one or more coronary arteries. Characteristics of subjects according to the presence of CAC were shown in Table 1. Age of CAC+ group (53.9 years) was significantly higher than that (43.4 years) of CAC− group ($p < 0.001$). Minimum age of patient in CAC+ was noted at 27 years. There was no significant difference between the two groups in sex, ethnicity and traditional CV risk factors including hypertension, systolic BP, smoking status, pack years of smoking, diabetes and BMI,. Duration of HIV infection in CAC+ group (12.3 years) was significantly higher than that (8.6 years) in CAC− group ($p < 0.0344$). With undetected viral load assigned to a value of 0, mean viral load was significantly lower value in CAC+ group compared to that in CAC− group based on parametric t-test (mean = 76 *vs* 414K, t-test $p = 0.0251$,). In terms of CD4 cell count, CAC+ group showed significantly higher cell counts than CAC− group (mean = 355.9 *vs* 175.3, $p = 0.0053$). There was no significant difference in HAART status between the two groups (current HAART receivers 84.4 *vs* 85.7%, $p = 0.539$).

Results of CAC in 41 patients of CAC+ group is shown in Table 2. LAD ($n = 38$, 92.7%) was most commonly affected, followed by LCX ($n = 18$, 43.9%) and RCA ($n = 13$, 31.7%). CAC deposited at the proximal portion in LAD and LCX (76.3% and 77.7%, respectively) while at the mid-to-distal portion in RCA (61.5%). Mild degree of CAC is seen in almost 83% of patients. Interobserver and intraobserver agreements were excellent to identify CAC and burden of calcium on non-gated CT chest, with κ coefficient > 0.9 as shown in Table 2. Since age and HIV duration were both significantly associated with CAC+ while these two variables are also correlated with each other, we performed two separate multivariate logistic regression analyses, one with each of these variables as the main independent in the regression model. In addition, we included viral load and CD4 as the independent variables in the models as these variables were found significantly associated with CAC+ in the bivariate analyses. In the multivariate logistic regression analysis with age as the main independent variable, we found that age and CD4 were significantly associated with CAC+ while viral load was no longer related significantly with coronary calcium. Similarly, in the multivariate logistic regression analysis with duration of HIV infection as the main independent variable, we found that HIV duration and CD4 were significantly associated with CAC+, but not the viral load. Both age and HIV duration are independent predictors for positive coronary artery calcium in patients with HIV infection. The OR for age being an independent factor for positive CAC is 1.92 (CI 1.16–3.17, $p = 0.0113$, estimate 0.6499). The OR for HIV duration being an independent factor for positive CAC is 1.06 (CI 1.00–1.12, $p = 0.0408$, estimate 0.0598). The rate of CAC+ among patients who were 45+ years old was significantly higher than those who were 44 years old (41.2% *vs* 12.5%, $p < .0001$), and the OR was 5.0 (CI = 2.1–11.9, $p = 0.0003$, and coefficient = 1.6136). The OR for CD4 count being significantly associated with presence of CAC is 1.003 (CI 1.001–1.005, $p = 0.0136$, estimate 0.00270).

DISCUSSION

Our results showed that nearly one-third of the hospitalised HIV patients showed subclinical coronary artery calcium on routine CT chest. Radiologists were able to identify CAC on both CT chest with or without contrast that were performed without ECG gating technique (Figures 1–3). Calcified plaques were most commonly depicted in LAD, followed by LCX and RCA as seen in general population. HIV patients in our study showed most commonly proximal distribution of calcification in LAD and LCX as in general population but isolated proximal location of CAC in RCA was not common in our cohort when compared to normal population. The age of onset of detectable CAC was third decade in HIV-infected patients. In comparison with age-specific curves of CAC scores appropriate for sex and ethnicity based on the Multiethnic Study of Atherosclerosis (MESA),[23] CAC was positive as early as third decade in our study thus resulting in premature subclinical atherosclerosis of coronary arteries in our cohort of hospitalised HIV patients. This finding is almost consistent with previous studies but were performed in the outpatient setting, which demonstrated that HIV patients have more CAC in young age.[3,9–11] A study compared CAC in Hawaii ageing with HIV CV study (HAHCS) and MESA cohorts showed that HIV patients were more likely to have CAC with increased likelihood of occurrence between 45 and 50 years of age;[11] however, the age of onset of CAC was not different on these studies, unlike the results of our study which showed onset as early as third decade. In MESA and other studies,[11,23] CAC typically noted during fifth decade of age in general population, that is why calcium scoring CT maybe performed in asymptomatic patients with age above 45 years who are at high risk for future IHD. However, we noticed in our small but slightly larger sample size than HAHCS study[11] that the onset of CAC in HIV patients was as early as 27 years of age, at an earlier age than general population. A different study showed that Framingham score underestimated the presence of subclinical atherosclerosis in young HIV-infected patients[24] and this finding suggests that we need alternative tools such as CT scan to directly visualise coronary calcium in order to better stratify the risk of CV events in this young HIV patients. Another study showed that the presence of CAC was associated with a significantly higher all-cause mortality rate in HIV patients when compared to those patients without CAC.[12] Age is an independent risk factor in our study for atherosclerosis in coronary arteries, with more prevalence of subclinical coronary atherosclerosis in HIV patients with age above 40 years although the CAC was noted in this cohort as early as third decade of age.

We showed that presence of coronary artery calcium was significantly associated with duration of HIV since the time of diagnosis

Table 1. Comparison of Demographic and Clinical Variables between CAC- and CAC+ HIV Patients

Demographic and Clinical Characteristics	CAC- (Category I) N = 102	CAC+ (Category II) N = 41	P-value
Age*, mean (SD)	43.4 (11.0)	53.9 (10.9)	<.0001
Sex, n (%)			0.3520
Male	83 (81.4%)	36 (87.8%)	
Female	19 (18.6%)	5 (12.2%)	
Ethnicity, n (%)			0.625
Caucasian	72 (70.6%)	32 (78.0%)	
African American	9 (8.8%)	1 (2.4%)	
Asian	8 (7.8%)	4 (9.8%)	
Others	13 (12.7%)	4 (9.8%)	
Smoking status, n (%)			0.2704
Non-smoker	55 (53.9%)	21 (51.2%)	
Ex-smoker	12 (11.8%)	9 (22.0%)	
Current smoker	35 (34.3%)	11 (26.8%)	
Systolic BP, mean (SD)	122.6 (17.8)	123.8 (21.2)	0.7459
Fasting blood sugar, mean (SD)	109.2 (40.9), N = 94	123.4 (71.0), N = 36	0.2662
Diabetes, n (%)			0.0865
Absent	89 (87.3%)	31 (75.6%)	
Present	13 (12.7%)	10 (24.4%)	
Hypertension diagnosis			0.0530
No	92 (90.2%)	32 (78.0%)	
Yes	10 (9.8%)	9 (22.0%)	
Body mass index, mean (SD)	263.9 (5.8), N = 99	23.6 (4.7), N = 40	0.7752
Total cholesterol, mean (SD)	152.7 (66.1), N = 40	151.8 (59.3), N = 20	0.9746
LDL, mean (SD)	98.5 (47.0), N = 40	89.6 (38.3), N = 20	0.6592
HDL, mean (SD)	36.3 (21.8), N = 40	40.8 (26.3), N = 20	0.7003
Triglyceride, mean (SD)	157.3 (85.4), N = 40	179.9 (173.6), N = 20	0.7399
Duration of HIV*, mean (SD)	8.5 (7.5), N = 97	11.8 (8.8), N = 37	0.0357
Viral load*, mean (SD)	414,413 (1,294,071), N = 80	75,971 (175,817), N = 28	0.0251
CD4 count*, mean (SD)	175.3 (198.8), N = 94	355.9 (347.9), N = 36	0.0053
HAART status, n (%)	N = 77	N = 32	0.4125
Never	3 (3.9%)	0 (0.0%)	
Ever, but not current	8 (10.4%)	5 (15.6%)	
Current	66 (85.7%)	27 (84.4%)	

*P <0.05 denotes statistically significant association with positiveCAC on univariate analysis.

and it may be an independent risk factor for positive CAC in HIV patients. Various hypotheses suggested for accelerated coronary atherosclerosis in HIV patients that includes chronic inflammatory state, smoking in HIV patients or metabolic dysfunction from HAART.[5–9] Supporting those hypotheses, CD4 cell count, HAART and duration of HIV have been shown in the literature as predictors for CAC, but studies were not consistent in terms of causative factors for CAC in HIV patients. Lower CD4 count was associated with increased CV risk in some studies,[10,25,26] while increase in CD4 count in response to HAART was the predictor of increased vascular ageing in a different study.[3] Our study indeed showed a statistically significant higher value of CD4 count in CAC+ group compared to CAC– group. The HAHCS study[11] did not show any significant association between CD4 cell count and

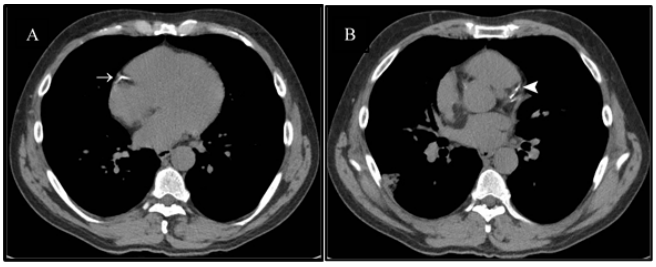
Table 2. Qualitative Assessment of Coronary Artery Calcium in HIV Patients on CT Chest

Features	LM	LAD	LCX	RCA	κ[d] for inter and intraobserver agreements
1. Calcified plaques	8[c]	38[c]	18[c]	13[c]	K = .92(inter), K = 1(intra)
2. CAC Burden[a]					K = .92, K = 1
Mild	8[c]	27[c]	17[c]	12[c]	
Moderate	0[c]	8[c]	1[c]	1[c]	
Severe	0[c]	3[c]	0[c]	0[c]	
3. CAC location[b]					K = .90, K = 1
Proximal segment of the vessel	N/A	29[c]	14[c]	3[c]	
Distal segment of the vessel	N/A	0[c]	1[c]	2[c]	
Both proximal and distal segment of the vessel	N/A	9[c]	3[c]	8[c]	

[a]CAC burden percentages were 83.1% mild, 13% moderate and 3.9% severe.
[b]CAC location for LM coronary artery was not divided as proximal anddistal segments.
[c]Number of patients demonstrating positive features.
[d]Kappa values reflect excellent interobserver and intraobserveragreements of readers.

presence of CAC in HIV patients. Duration since diagnosis of HIV was attributed as a risk factor of CAC, owing to increased duration of inflammatory state from HIV infection[24,27] and our results also showed a statistically significant association between duration of HIV and positive CAC. However, in contrary to literature on CT calcium score in HIV patients,[11] our study showed length of HIV infection was an independent predictor of CAC in addition to age of patients. Chronic oxidative stress and inflammatory process may support the increased risk of CV disease in this patients.[24] Our results did not find any direct association between the status of HAART and CAC. There was no significant difference between CAC+ and CAC– groups in terms of HAART treatment status. Previous studies have also been controversial in attributing HAART as a direct cause for CAC as some studies suggested that HAART reduces inflammation and consequently decreased CHD risk,[8,28] while other studies showed that some antiretroviral drugs may be related to increased CAC or CHD risk.[6,7]

Figure 1. Subclinical atherosclerosis of coronary arteries in a 52-year-old male with 12 years of HIV who underwent CT chest for fever, shortness of breath and cough. (A) 3 mm axial image of a routine CT chest without contrast shows a focal mild atherosclerotic calcified plaque (white arrow) in the right coronary artery. Note mild motion artefact given the non-gated study. (B) 3 mm axial image of the same patient at a different location demonstrates mild calcification of proximal left anterior descending and diagonal coronary arteries (arrowhead)



We performed qualitative assessment of extent and severity CAC, rather than Agatston scoring, on routine CT chests, which were originally obtained for detection of various pulmonary problems. Callaway et al showed that incidental CAC can be easily detected on standard thoracic CT scans but areas of mild calcification could be missed when compared to electron-beam CT.[29]Visual scoring of CAC on non-EKG-gated low-dose CT scans (LDCT) of the chest performed for lung cancer screening has been demonstrated to be predictive of death from CV disease.[22,30] Hughes-Austin et al showed CAC scores on standard 6 mm chest CTs are strongly correlated with 3 mm EKG-gated CTs and predict similarly

Figure 2. 49-year-old male, known HIV patient on HAART, presented with a history of cough for 1 month that had grown worse over the past 2 days and was associated with fever and underwent a routine CT scan. Axial image of a non-gated CT chest without contrast demonstrates severe subclinical atherosclerotic calcified plaques in left main stem and proximal LAD (white arrow). Subtle calcification also noted in left circumflex coronary arteries. His CD4 count and viral load were 168 and 1650, respectively.

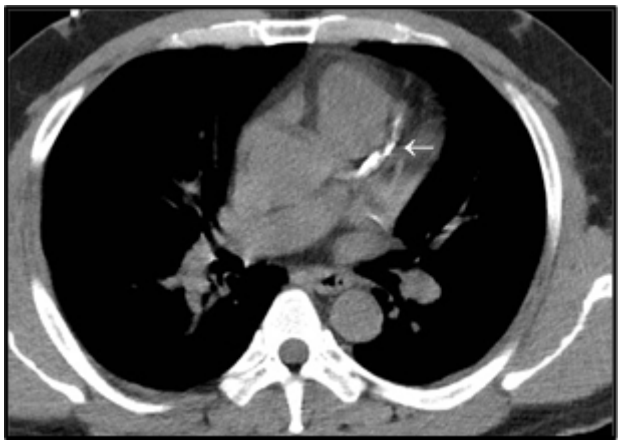
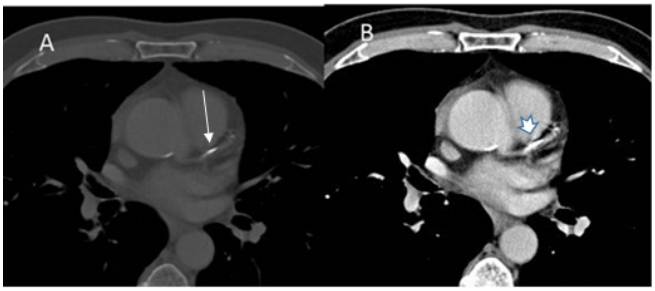


Figure 3. A 61-year-old hospitalised male with a history of HIV infection and cough underwent a diagnostic CT chest with contrast. (A) 3 mm axial image on bone window settings (width 2000 HU; level, 500 HU) shows a moderate calcified plaque in proximal LAD. (B)Corresponding soft tissue window image clearly shows presence of atherosclerotic calcification in LAD but with more blooming artefact.



mortality.[31] Visual scoring and Agatston score showed good correlation even with coronary CT angiography in spite of intravenous contrast given.[32] We analysed both routine non-contrast and contrast CT chests, and readers were able to visualise calcified plaque on contrast CT in bone window settings in spite of the presence of iodinated contrast enhancement in the triple vessel coronary arteries. However, future studies warranted to compare ECG-gated non-contrast CT chest scan with non-ECG-gated contrast scan of chest CT. Our study is unique from other studies as hospitalised patients represents a different and sicker population than the multicentre Acquired Immunodeficiency Syndrome (AIDS) cohort[33] and other recent publications such as the Swiss study.[34] Our patients were sicker because they were admitted through emergency room for pulmonary conditions and non-cardiac/non-coronary causes. These hospitalised HIV patients from emergency room have higher probability of undergoing CT chest than non-hospitalised HIV population. Therefore, identification of incidental subclinical CAC on routine CT chest in these hospitalised HIV patients, who were originally asymptomatic for IHD, would help in risk stratification for IHD in HIV cohort. In addition, while assessment of coronary calcifications on non-contrast chest CT was previously done, the use of post-contrast CT chest for the same purpose was not evaluated and probably underappreciated.

Retrospective study design is one of the limitations of our study. Although evaluation of coronary artery calcium in contrast CT may be considered as a technical limitation but the use of contrast CT images in bony window setting for visual assessment of CAC was underappreciated in literature as our results showed there was an excellent inter-readers' and intra-reader's agreement for qualitative CAC assessment. However, inter-reader or intrareader agreement does not provide reliable information about the accuracy of technique itself in detecting CAC, and there still could be a systematic bias. We did not directly compare the presence of CAC in HIV patients with healthy normal subjects as there is already abundance of evidence from MESA; however, we showed that hospitalised HIV patients had CAC, particularly in younger population. There is selection bias because only known patients with HIV, who were hospitalised in the selected time frame and who had CT chest were included, so the true prevalence of CAC in HIV patients may be underestimated because of our study excluded hospitalised HIV patients who did not have CT chest during their stay from ER, the above systematic bias that a subtle calcification could have been missed in contrast CTs as the coronary lumen was opacified with iodinated contrast and non-evaluation of other plaque types such as non-calcified plaque. Despite no significant difference between HAART receivers and non-receivers, lack of data collection on duration of HAART as a variable maybe a limitation, which can be addressed in future prospective studies.

In conclusion, almost one-third of hospitalised HIV patients showed subclinical coronary artery atherosclerosis, which was identified on routine non-gated CT chest, both with and without contrast. Duration of HIV disease and age of patients were independent predictors of atherosclerotic coronary artery disease in our cohort and CD4 count was significantly associated with the presence of CAC.

REFERENCES

1. Cihlar T, Fordyce M. Current status and prospects of HIV treatment. *Curr Opin Virol* 2016; **18**: 50–6. doi: https://doi.org/10.1016/j.coviro.2016.03.004
2. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab* 2007; **92**: 2506–12. doi: https://doi.org/10.1210/jc.2006-2190
3. Guaraldi G, Zona S, Alexopoulos N, Orlando G, Carli F, Ligabue G, et al. Coronary aging in HIV-infected patients. *Clin Infect Dis* 2009; **49**: 1756–62. doi: https://doi.org/10.1086/648080
4. Raggi P, Zona S, Scaglioni R, Stentarelli C, Ligabue G, Besutti G, et al. Epicardial adipose tissue and coronary artery calcium predict incident myocardial infarction and death in HIV-infected patients. *J Cardiovasc Comput Tomogr* 2015; **9**: 553–8. doi: https://doi.org/10.1016/j.jcct.2015.08.002
5. Carballo D, Delhumeau C, Carballo S, Bähler C, Radovanovic D, Hirschel B, et al. Increased mortality after a first myocardial infarction in human immunodeficiency virus-infected patients; a nested cohort study. *AIDS Res Ther* 2015; **12**: 4. doi: https://doi.org/10.1186/s12981-015-0045-z
6. Iloeje UH, Yuan Y, L'italien G, Mauskopf J, Holmberg SD, Moorman AC, et al. Protease inhibitor exposure and increased risk of cardiovascular disease in HIV-infected patients. *HIV Med* 2005; **6**: 37–44. doi: https://doi.org/10.1111/j.1468-1293.2005.00265.x
7. Friis-Møller N, Reiss P, Sabin CA, Weber R, Monforte Antonella d'Arminio, El-Sadr W, et al. Class of antiretroviral drugs and the risk of myocardial infarction. *N Engl J Med*

2007; **356**: 1723–35. doi: https://doi.org/10.1056/NEJMoa062744
8. Kingsley LA, Cuervo-Rojas J, Muñoz A, Palella FJ, Post W, Witt MD, et al. Subclinical coronary atherosclerosis, HIV infection and antiretroviral therapy: multicenter AIDS cohort study. *AIDS* 2008; **22**: 1589–99. doi: https://doi.org/10.1097/QAD.0b013e328306a6c5
9. Fitch KV, Lo J, Abbara S, Ghoshhajra B, Shturman L, Soni A, et al. Increased coronary artery calcium score and noncalcified plaque among HIV-infected men: relationship to metabolic syndrome and cardiac risk parameters. *J Acquir Immune Defic Syndr* 2010; **55**: 495–9. doi: https://doi.org/10.1097/QAI.0b013e3181edab0b
10. Post WS, Budoff M, Kingsley L, Palella FJ, Witt MD, Li X, et al. Associations between HIV infection and subclinical coronary atherosclerosis. *Ann Intern Med* 2014; **160**: 458–67. doi: https://doi.org/10.7326/M13-1754
11. Chow D, Young R, Valcour N, Kronmal RA, Lum CJ, Parikh NI, et al. Hiv and coronary artery calcium score: comparison of the Hawaii aging with HIV cardiovascular study and multi-ethnic study of atherosclerosis (MESA) cohorts. *HIV Clin Trials* 2015; **16**: 130–8. doi: https://doi.org/10.1179/1528433614Z.0000000016
12. Lange DC, Glidden D, Secemsky EA, Ordovas K, Deeks SG, Martin JN, et al. Mitral annular and coronary artery calcification are associated with mortality in HIV-infected individuals. *PLoS One* 2015; **10**: e0130592. doi: https://doi.org/10.1371/journal.pone.0130592
13. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. *Circulation* 1995; **92**: 2157–62. doi: https://doi.org/10.1161/01.cir.92.8.2157
14. Kondos GT, Hoff JA, Sevrukov A, Daviglus ML, Garside DB, Devries SS, 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* 2003; **107**: 2571–6. doi: https://doi.org/10.1161/01.CIR.0000068341.61180.55
15. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. *Radiology* 2003; **228**: 826–33. doi: https://doi.org/10.1148/radiol.2283021006
16. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* 2004; **291**: 210–5. doi: https://doi.org/10.1001/jama.291.2.210
17. Raggi P, Shaw LJ, Berman DS, Callister TQ. Prognostic value of coronary artery calcium screening in subjects with and without diabetes. *J Am Coll Cardiol* 2004; **43**: 1663–9. doi: https://doi.org/10.1016/j.jacc.2003.09.068
18. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008; **358**: 1336–45. doi: https://doi.org/10.1056/NEJMoa072100
19. Kirsch J, Buitrago I, Mohammed T-LH, Gao T, Asher CR, Novaro GM. Detection of coronary calcium during standard chest computed tomography correlates with multi-detector computed tomography coronary artery calcium score. *Int J Cardiovasc Imaging* 2012; **28**: 1249–56. doi: https://doi.org/10.1007/s10554-011-9928-9
20. Blair KJ, Allison MA, Morgan C, Wassel CL, Rifkin DE, Wright CM, et al. Comparison of ordinal versus Agatston coronary calcification scoring for cardiovascular disease mortality in community-living individuals. *Int J Cardiovasc Imaging* 2014; **30**: 813–8. doi: https://doi.org/10.1007/s10554-014-0392-1
21. Watts JR, Daniel JD, Fineberg N, Budoff M, Nath H. Correlation between measured and visual scoring of coronary artery calcification. *International Journal of Cardiovascular and Cerebrovascular Disease* 2014; **2**: 11–17.
22. Shemesh J, Henschke CI, Shaham D, Yip R, Farooqi AO, Cham MD, et al. Ordinal scoring of coronary artery calcifications on low-dose CT scans of the chest is predictive of death from cardiovascular disease. *Radiology* 2010; **257**: 541–8. doi: https://doi.org/10.1148/radiol.10100383
23. McClelland RL, Chung H, Detrano R, Post W, Kronmal RA. Distribution of coronary artery calcium by race, gender, and age: results from the multi-ethnic study of atherosclerosis (MESA. *Circulation* 2006; **113**: 30–7. doi: https://doi.org/10.1161/CIRCULATIONAHA.105.580696
24. Parra S, Coll B, Aragonés G, Marsillach J, Beltrán R, Rull A, et al. Nonconcordance between subclinical atherosclerosis and the calculated Framingham risk score in HIV-infected patients: relationships with serum markers of oxidation and inflammation. *HIV Med* 2010; **11**: 225–31. doi: https://doi.org/10.1111/j.1468-1293.2009.00766.x
25. Kaplan RC, Kingsley LA, Gange SJ, Benning L, Jacobson LP, Lazar J, et al. Low CD4+ T-cell count as a major atherosclerosis risk factor in HIV-infected women and men. *AIDS* 2008; **22**: 1615–24. doi: https://doi.org/10.1097/QAD.0b013e328300581d
26. Lichtenstein KA, Armon C, Buchacz K, Chmiel JS, Moorman AC, Wood KC, et al. Initiation of antiretroviral therapy at CD4 cell counts >/=350 cells/mm3 does not increase incidence or risk of peripheral neuropathy, anemia, or renal insufficiency. *J Acquir Immune Defic Syndr* 2008; **47**: 27–35. doi: https://doi.org/10.1097/QAI.0b013e31815acacc
27. Law MG, Friis-Møller N, El-Sadr WM, Weber R, Reiss P, D'Arminio Monforte A, et al. The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D Study. *HIV Med* 2006; **7**: 218–30. doi: https://doi.org/10.1111/j.1468-1293.2006.00362.x
28. El-Sadr WM G, Lundgren J, et al. Strategies for management of antiretroviral therapy Study.CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med* 2006; **355**: 2283–96.
29. Callaway MP, Richards P, Goddard P, Rees MR. The incidence of coronary artery calcification on standard thoracic CT scans Br. *J.Radiol* 1997; **70**: 572–4.
30. Watts JR, Sonavane SK, Snell-Bergeon J, Nath H. Visual scoring of coronary artery calcification in lung cancer screening computed tomography: association with all-cause and cardiovascular mortality risk. *Coron Artery Dis* 2015; **26**: 157–62. doi: https://doi.org/10.1097/MCA.0000000000000189
31. Hughes-Austin JM, Dominguez A, Allison MA, Wassel CL, Rifkin DE, Morgan CG, et al. Relationship of coronary calcium on standard chest CT scans with mortality. *JACC Cardiovasc Imaging* 2016; **9**: 152–9. doi: https://doi.org/10.1016/j.jcmg.2015.06.030
32. Mylonas I, Alam M, Amily N, Small G, Chen L, Yam Y, et al. Quantifying coronary artery calcification from a contrast-enhanced cardiac computed tomography angiography study. *Eur Heart J Cardiovasc Imaging* 2014; **15**: 210–5. doi: https://doi.org/10.1093/ehjci/jet144
33. Chandra D, Gupta A, Leader JK, Fitzpatrick M, Kingsley LA, Kleerup E, et al. Assessment of coronary artery calcium by chest CT compared with EKG-gated cardiac CT in the Multicenter AIDS cohort study. *PLoS One* 2017; **12**: e0176557. doi: https://doi.org/10.1371/journal.pone.0176557
34. Tarr PE, Ledergerber B, Calmy A, Doco-Lecompte T, Marzel A, Weber R, et al. Subclinical coronary artery disease in Swiss HIV-positive and HIV-negative persons. *Eur Heart J* 2018; **39**: 2147–54. doi: https://doi.org/10.1093/eurheartj/ehy163