AID-2021-0141-ver9-Bonjoch_1P
Type: research-article
FULL MANUSCRIPT

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 00, Number 00, 2022

DOI: 10.1089/aid.2021.0141

Open camera or QR reader and scan code to access this article and other resources online.

Ultrasound-Based Assessment of Preperitoneal Fat as a Surrogate Marker of Cardiovascular Risk: Comparative Study Between People Living with HIV and Controls

AU1 ▶ Anna Bonjoch,[1,*,i] Francisco de Cabo,[2,3,*] Jordi Puig,[1] Núria Perez-Alvarez,[1,4] Patricia Echeverria,[1] Bonaventura Clotet,[1,5,6] Guillem Cuatrecasas,[3,7] and Eugènia Negredo[1,5]

AU5 ▶ AU4 ▶ **Abstract**

Optimal management of cardiovascular disease should start with the identification of subjects at subclinical stages. However, available tools are not always accurate or affordable. We assess the usefulness of ultrasound-guided measurement of abdominal fat layers as a surrogate marker of cardiovascular risk. We performed a cross-sectional, case–control, exploratory, pilot study in 10 people living with HIV (PLWH) and 10 HIV-uninfected subjects (control group) matched for age, sex, and body mass index. All participants were men 45–60 years of age, with no active disease or previous abdominal surgery; the PLWH group had been virologically suppressed for ≥2 years under stable antiretroviral therapy. The thickness of abdominal superficial and deep subcutaneous fat, preperitoneal fat, omental (periaortic) fat, and retroperitoneal (perirenal) fat was compared between both groups. Correlations between fat layers and traditional markers of cardiovascular risk were assessed. The thickness of most layers was always higher among PLWH. The differences were statistically significant for the preperitoneal fat layer ($p = .04$). The presence of atherosclerotic plaque was correlated with the preperitoneal fat layer in the PLWH group (odds ratio = 1.49, $p = .02$), and metabolic syndrome was correlated with superficial subcutaneous fat, although this was low (odds ratio = 0.54, $p = .02$). In the control group, several associations were found between carotid intima media thickness and abdominal fat layers. All abdominal fat layers were thicker in the PLWH group, especially preperitoneal fat, and several associations were found between specific fat layers and traditional cardiovascular risk markers. Our results suggest that the thickness of abdominal fat layers, assessed by ultrasound, could be a marker of cardiovascular risk. However, further studies with larger populations are required to confirm these findings.

Keywords: cardiovascular risk, abdominal fat layers, preperitoneal fat layer, marker of cardiovascular risk, ultrasound, PLWH, HIV

AU3 ▶ AU2 ▶ [1]Lluita Contra la SIDA Foundation, Germans Trias i Pujol Research Institute-IGTP, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona, Badalona, Catalonia, Spain.
[2]Instituts Guirado, Barcelona, Spain.
[3]Endocrinology Department, Clínica Sagrada Familia, Barcelona, Spain.
[4]Statistics and Operational Research Department, Technical University of Catalonia, Barcelona, Catalonia, Spain.
[5]Infectious Diseases and Immunity, Centre for Health and Social Care Research (CESS), School of Medicine, University of Vic-Central University of Catalonia (UVic-UCC), Catalonia, Spain.
[6]AIDS Research Institute-IrsiCaixa, Germans Trias i Pujol Research Institute-IGTP, Hospital Universitari Germans Trias i Pujol, Barcelona, Catalonia, Spain.
[7]School of Health Sciences, Universitat Oberta Catalunya, Barcelona, Spain.
*Both authors contributed equally.
[i]ORCID ID (https://orcid.org/0000-0002-5343-2881).

Introduction

Observational cohort studies have demonstrated a higher prevalence of cardiovascular events in people living with HIV (PLWH) than in the general population. The relative risk is ~1.5- to 2-fold[1–6] and persists even when traditional cardiovascular risk factors are controlled for and in patients on suppressive antiretroviral therapy.[7,8] The risk is related to multiple factors, including the higher prevalence of smoking habit or the use of recreational drugs among PLWH with respect to the general population.[9,10] The inflammatory and prothrombotic state associated with HIV infection are other causes, as well as endothelial dysfunction, and/or changes in body composition previously associated with antiretroviral drugs, such as loss of subcutaneous fat and/or accumulation of visceral fat, which leads to an increased prevalence of metabolic disorders.[11]

Optimal management of cardiovascular disease in PLWH should start with the appropriate identification of subjects at high cardiovascular risk to identify those in subclinical stages. However, cardiovascular risk prediction functions developed for the general population are inaccurate for PLWH, whose risk may therefore be underestimated.[12] Carotid artery intima media thickness (IMT) is a well-recognized surrogate marker of atherosclerosis, but it is not always available, and other measurements such as computed tomography (CT) and functional imaging (positron emission tomography-CT) are expensive. Visceral fat (assessed using dual-energy X-ray absorptiometry and CT) has traditionally been considered a predictor of fatty liver, with increased cardiovascular risk,[13,14] although these techniques do not allow us to discriminate in detail between the various layers of adipose tissue.

Structured ultrasound imaging of abdominal adipose tissue is a recently described, noninvasive, easily reproducible tool used to assess both subcutaneous and intra-abdominal fat layers.[15] Subcutaneous adipose tissue is divided into two layers, superficial and deep, each of which has different physiological roles.[16] Ultrasound also makes it possible to easily examine deeper intra-abdominal layers such as preperitoneal fat, omental (periaortic) fat, and perirenal fat (as a marker of retroperitoneal fat).[17–19] Despite anatomical and physiological differences, all these layers were traditionally included under the global concept of visceral adiposity. Both omental and perirenal depots are linked to metabolic syndrome and cardiovascular risk at certain cutoff values. Perirenal fat has been associated with IMT.[20]

The aim of our study was to assess the usefulness of measuring different abdominal fat layers by ultrasound as a possible surrogate marker of cardiovascular risk in chronically infected PLWH.

Materials and Methods

Study design and population

We performed an observational, cross-sectional, comparative, case–control, exploratory pilot study, including the first 10 PLWH with long-standing infection consecutively attended in our HIV unit, who fulfilled the selection criteria and agreed to participate in the study. We also included 10 non-HIV-infected controls selected from among hospital workers and relatives and matched (1:1) by sex, age, and body mass index (BMI), who fulfilled the selection criteria and agreed to participate.

The analyses were repeated, including a further 10 PLWH with the same inclusion criteria to increase the sample size (i.e., 20 PLWH). However, the respective matched controls for the second group of 10 PLWH were not finally included because of difficulties with recruitment during the COVID-19 pandemic.

The PLWH group comprised patients with long-standing infection (at least 10 years of infection), 45–60 years of age, who had been virologically suppressed for at least 2 years under a stable antiretroviral regimen (at least 6 months) with elvitegravir/cobicistat/TAF/FTC, darunavir/cobicistat or ritonavir, or dolutegravir or raltegravir plus TAF/FTC, TDF/FTC, or abacavir/lamivudine. Those with acute diseases (previous 6 months) and active chronic diseases (e.g., neoplasms, infections, and hepatitis), as well as those who had undergone abdominal surgery, were excluded from the study.

All participants who agreed to participate in the study signed the informed consent.

Internal review board approval

The study protocol was approved by the local ethics committee (REF. CEI 18–245).

Study variables and standardized ultrasound protocol

The variables were measured using a General Electric Logiq E ultrasound device with a linear 12-MHz probe and a convex 5-MHz probe as follows: (1) superficial and deep abdominal subcutaneous fat, preperitoneal fat, omental (periaortic) fat, and retroperitoneal (perirenal) fat on both the left and the right sides; (2) common carotid posterior IMT (abnormal value: ≥0.9 mm); and (3) hepatic steatosis.

Our evaluation of abdominal fat layers started from the deeper layers and advanced to the most superficial ones. Using a convex probe, perirenal fat was measured with the patient lying on the left side. Then, with the patient face up, the abdominal aorta was localized, and the probe was moved down as far as the iliac bifurcation, where omental fat can be measured by minimizing the pressure over the abdomen. In the same external abdominal area (this can be drawn on the skin), the technician must switch to the linear probe and consecutively measure the preperitoneal, deep, and superficial subcutaneous fat layers. The correlation coefficient of the mean ultrasound distance assessed by two technicians at baseline was 0.94 ($p < .001$), with a mean difference 0.40 cm (SD 0.90) and a coefficient of variation of 5.40%, indicating good reproducibility of the measurements.

We also collected the following data: National Cholesterol Education Panel/Adult Treatment Panel III (NCEP/ATP III) criteria for metabolic syndrome,[21] BMI, and the homeostatic model assessment of insulin resistance (HOMA-IR) value (fasting insulin [mU/mL] × fasting glucose [mg/dL]/405) as a biomarker of insulin resistance.[22] The medical records were consulted to collect epidemiological and clinical data (time with HIV infection, viral load, CD4 T cell count, nadir CD4 T cell count, current antiretroviral therapy, history of cardiovascular events, and traditional cardiovascular risk factors: high blood pressure, smoking, high cholesterol, diabetes, overweight, and family history of cardiovascular disease). Cardiovascular events were defined as follows: diagnosis of ischemic heart disease, peripheral arterial disease, stroke, or transient ischemic attack.

Study objectives and endpoints

To assess the usefulness of measuring the different abdominal fat layers as a possible surrogate marker of cardiovascular risk in PLWH with long-standing infection, we first compared the thickness of abdominal fat layers (mm) in each region (defined previously in ''Study variables'') between PLWH and noninfected controls and then established correlations between abdominal fat layers and the following traditional cardiovascular risk markers: (1) carotid IMT, (2) presence of atherosclerotic plaques, (3) presence of the NCEP/ATP III criteria for metabolic syndrome, (4) HOMA-IR, and (5) presence of hepatic steatosis.

Statistical analysis

We performed a general descriptive analysis of all study variables, both overall and separately by groups with respect to clinical and demographic characteristics. Values were expressed as mean, standard deviation, median, interquartile range, and minimum and maximum for quantitative variables and absolute and relative frequencies of each category for categorical variables.

The endpoints were assessed using linear or logistic regression to compare fat measurements and inflammatory markers between patients with high and low cardiovascular risk.

The statistical significance of differences between the groups was assessed using the *t*-test, Mann-Whitney test, if the variable tested follows the normal distribution or not. For the categorical variables, the chi-squared was used when the cell's observed values in the contingency table are 5 or larger, otherwise Fisher exact tests were used. The Pearson and Spearman correlations were calculated to evaluate the linear association between pairs of variables depending on their characteristics.

The significance level was set at 5% for hypothesis testing. The statistical analysis was performed using SPSS 25.

Results

A total of 20 PLWH and 10 controls were included. The subjects' characteristics are summarized in Table 1. Briefly, ◀T1 all subjects were male, and median (IQR) age was 52.5 years (47–56.75). Five (25%) subjects in the PLWH group presented dyslipidemia, 4 (20%) presented arterial hypertension, and 1 (5%) presented diabetes mellitus. Fourteen PLWH (70%) were receiving an integrase inhibitor-based antiretroviral regimen, and 6 (30%) were receiving treatment based on the protease inhibitor darunavir. Regarding the control group, three subjects (30%) had dyslipidemia, one (10%) had arterial hypertension, and none (0%) had diabetes mellitus.

All analyses were performed considering the 10 PLWH and the 10 matched controls; the results are set out below. However, the analyses were repeated by comparing the overall group of PLWH (20 subjects) with the 10 controls; these results are reported only in the case of differences with respect to results from the matched subjects.

Abdominal fat layers measured by ultrasound

Considering only the matched subjects (10 PLWH and 10 controls), the thickness of most of the layers was always higher among the PLWH (Table 2). However, differences ◀T2 between the groups were only statistically significant for the

Table 1. Demographic, Anthropometric, and Clinical Characteristics of Participants

	Control group (n = *10*)	*Matched PLWH* (n = *10*)	*All HIV* (n = *20*)	p *value between controls and 10 matched PLWH*	p *value between controls and 20 PLWH*
Male sex (%)	10 (100)	10 (100)	20 (100)	1	1
Age (years) (median [IQR])	52 (47–56.8)	54 (48–58.3)	53 (49.3–57.8)	.91	.71
BMI (kg/m^2)	25.2 (24.3–28.2)	26.1 (24.8–30.1)	26.3 (24.6–29.5)	.40	.39
Waist (cm)	98.5 (90.3–104)	100.6 (90.9–110.4)	98.7 (90.2–104.7)	.80	.81
Hip (cm)	99.5 (95.3–108)	100.2 (97.42–105.4)	98 (96–105)	.66	.98
AU14▶ Systolic arterial tension (mmHg)	116 (110–122.8)	127 (121.5–137.5)	136 (124.25–139.8)	.09	**<.01**
Diastolic arterial tension (mmHg)	74.5 (73.3–79.3)	78 (71.5–80.5)	82 (78–8.8)	.98	.12
Smokers, *n* (%)	3 (10%)	3 (10%)	6 (10%)	1	1
Dyslipidemia, *n* (%)	3 (30)	2 (20)	5 (25)	.61	.77
Arterial hypertension, *n* (%)	1 (10)	2 (20)	2 (10)	.53	.64
Diabetes mellitus, *n* (%)	0	1 (10)	1 (5)	1	1
Nadir CD4+ T-cell count, *n*	—	226 (22.25–399.75)	108.5 (33.50–387.25)	—	—
Current CD4+ T cell count, *n*	—	608 (331.25–940.5)	615 (394–833)		
Time since diagnosis of HIV infection (months)	—	271 (172.5–335.75)	268.1 (218–337.25)	—	—
Undetectable HIV viral load, *n* (%)	—	10 (100%)	20 (100%)	—	—

Values are expressed as median (IQR), except when otherwise specified.
BMI, body mass index; PLWH, people living with HIV.

Table 2. Abdominal Fat Layers of People Living with HIV and Controls Measured by Ultrasound

	Control group (n = 10)	*PLWH (n = 10)*	*PLWH (n = 20)*	p *value between controls and 10 matched PLWH*	p *value between controls and 20 PLWH*
Total subcutaneous	18 (15.5–5.3)	19.5 (13.8–29.5)	17.5 (11.5–24.5)	.74	.73
Superficial subcutaneous	6.5 (4.8–8.3)	5 (3.75–9.5)	5 (3.3–8.5)	.58	.59
Deep subcutaneous	12 (9.8–15)	13 (9.8–19.5)	10.5 (7.5–17.5)	.52	.51
Preperitoneal	7.5 (4–9.25)	9 (7.8–12.8)	9.5 (9–12)	**.04**	**.04**
Right renal	19 (13.8–24.3)	22.5 (16.8–26.35)	20.5 (16.3–26.8)	.82	.84
Left renal	19 (13.8–24.3)	22 (17–27.5)	22 (12.5–27.5)	.40	.44
Omental	47 (40.3–63)	66.5 (45.8–82.8)	58 (44–82)	.23	.25

Values are expressed as median (IQR). Abdominal fat layers were expressed in mm.

preperitoneal fat layer: median (IQR) of 9 (7.75–12.75) mm in the PLWH group versus 7.5 (4–9.25) mm in the control group ($p = .04$) (Table 2).

Markers of cardiovascular risk

All these results are summarized in Table 3. Briefly, carotid IMT measurements were higher in the 10 PLWH than in the control group, although differences were not statistically significant. The median (IQR) carotid IMT was 0.71 (0.57–0.75) mm in the PLWH group versus 0.68 (0.62–0.80) mm in the control group for the right side ($p = .73$) and 0.75 (0.65–0.84) versus 0.65 (0.55–0.76), respectively, for the left side ($p = .15$).

When the matched participants were compared, atherosclerotic plaque was present in three PLWH (30%) and no controls (0%) ($p = .21$). When we compared the total PLWH ($n = 20$) with the 10 controls, the differences were statistically significant: 40% of the PLWH group versus 0% of controls had atherosclerotic plaques ($p = .03$).

Metabolic syndrome was present in 2 out of 10 PLWH (20%) and in 1 control (10%) ($p = .64$). With regard to the HOMA-IR value, abnormal values were recorded for 8 PLWH (80%) and 4 controls (40%) ($p = .06$).

Hepatic steatosis was present in three subjects (30%) in both groups ($p = 1$).

Associations between abdominal fat layers and markers of cardiovascular risk

Among the 10 PLWH, a weak association ($r < 0.500$) was observed between fat layers and carotid IMT. Regarding the control group, an association was detected between higher right carotid IMT and the following layers: preperitoneal ($r = 0.595$), renal right side ($r = 0.880$), renal left side ($r = 0.714$), and omental ($r = 0.696$); an association was also detected between the left IMT and the preperitoneal layer ($r = 0.643$).

With regard to the associations between atherosclerotic plaque and fat layers, the presence of plaque in PLWH was correlated with the preperitoneal fat layer (odds ratio = 1.49, $p = .02$). No case of atheroma was detected in the control group.

Metabolic syndrome was associated with the superficial subcutaneous fat layer, although the correlation was poor when only PLWH were assessed (odds ratio = 0.54, $p = .02$). This was also the case when we included the 10 matched PLWH and 10 controls (odds ratio = 0.47, $p = .02$), as well as the 20 PLWH and 10 controls (odds ratio = 0.57, $p = .01$).

Abnormal HOMA values were associated with a thicker right renal fat layer in the control group (odds ratio = 0.73, $p = .03$) and when both groups were included in the analysis (odds ratio = 0.85, $p = .05$).

No association was observed between abdominal fat layers and the presence of steatosis.

Similar results were observed when the previous analyses were repeated, considering the overall sample (20 PLWH and 10 controls), except for the cases specified above.

Discussion

All abdominal fat layers, except for the subcutaneous fat layer, were thicker among PLWH from this exploratory study compared to the age-, sex-, and BMI-matched controls. Our findings showed increased thickness of abdominal fat layers and may suggest associations between specific abdominal fat layers and carotid IMT and the presence of atherosclerotic plaques.

An easily applied, accessible, and inexpensive tool is necessary to better assess cardiovascular risk and identify

Table 3. Cardiovascular Risk Factors of People Living with HIV and Controls

	Control group (n = 10)	*PLWH (n = 10)*	*PLWH (n = 20)*	p *value between controls and 10 matched PLWH*	p *value between controls and 20 PLWH*
Right carotid IMT (mm)	0.68 (0.62–0.80)	0.71 (0.57–0.75)	0.72 (0.59–0.79)	.73	.72
Left carotid IMT (mm)	0.65 (0.55–0.76)	0.75 (0.65–0.84)	0.74 (0.62–0.88)	.15	.13
Atherosclerotic plaque	0	3 (30)	8 (40)	.21	**.03**
Hepatic steatosis (%)	3 (30)	3 (30)	9 (45)	1	.69
HOMA	1.2 (0.9–3.7)	2 (1.5–5.1)	1.7 (1.2–4.2)	.51	.83

IMT, intima-media thickness; HOMA, homeostatic model assessment.

persons at subclinical stages, especially in high-risk populations such as PLWH. Routine ultrasound to assess abdominal fat could provide useful cardiovascular data earlier in these persons.

Adipose tissue is found throughout the body, and its distribution determines its function. The superficial subcutaneous layer acts as a protective barrier against infection, and mesenteric fat surrounding the intestine may act as a supporting architectural structure, although adipose cells also act as an energy deposit. The ability of adipose tissue to secrete specific adipose hormones (adipokines, i.e., leptin, adiponectin, tumor necrosis factor, and interleukin) makes it the most extended endocrine system in the body, with the ability to control almost all homeostatic processes, including hunger, glucose balance, blood pressure, and lipolysis, thus affecting future cardiovascular risk events. The differences in the action of some adipose tissue layers, particularly in the abdominal cavity, can be explained by differences in adipokine secretion: preperitoneal and visceral fat are associated with increased cardiovascular risk, whereas a thicker subcutaneous layer plays a protective role.[23]

Few data have been published on ultrasound as a key diagnostic tool for assessment of metabolic syndrome-associated cardiovascular risk. Preliminary data suggest that omental and perirenal fat are the main depots associated with type 2 diabetes, HDL cholesterol, and abdominal perimeter, and cutoffs have been defined (54 mm for omental fat and 22.5 mm for perirenal fat, in men).[15] In our study, subcutaneous fat was thinner in PLWH than in controls, and, as we mentioned above, a thicker subcutaneous layer has a protective role.

In the same sense, the remaining abdominal fat layers were thicker among PLWH, and these findings could be clinically relevant in terms of cardiovascular risk. Strikingly, only preperitoneal fat was significantly thicker among PLWH, and a positive correlation was observed with the presence of atherosclerotic plaques, consistent with the increased cardiovascular risk associated with PLWH. However, the exploratory nature of this study avoid to confirming differences between PLWH and matched controls. The outbreak of the COVID-19 pandemic necessarily reduced the control group and, consequently, the power of the analysis.

Information about the role of preperitoneal fat remains scarce. This layer is located between subcutaneous and omental fat, immediately below the rectus abdominalis (Fig. 1), and may act as an intermediate ''buffer'' between the two main depots. When patients lose visceral fat, the thickness of the preperitoneal layer increases. If weight loss is maintained, then the preperitoneal layer thickens, transferring fat into the ''protective'' subcutaneous layer. This intimate relationship with visceral fat may also explain its association with hepatic steatosis[24] (not observed in the present study). In addition, the pattern of adipokine secretion in the preperitoneal layer is very similar to that observed in omental fat, suggesting an association with insulin resistance and increased cardiovascular risk.[25]

Our results seem to show an association between abdominal fat layers and IMT in controls. However, this is the first time that a relationship between fat layers and the presence of atherosclerotic plaque has been observed in individuals prone to atherosclerosis, such as PLWH, even when the low number of subjects included in the study is taken into account. Consequently, fat layers could be a potential marker of cardiovascular risk.

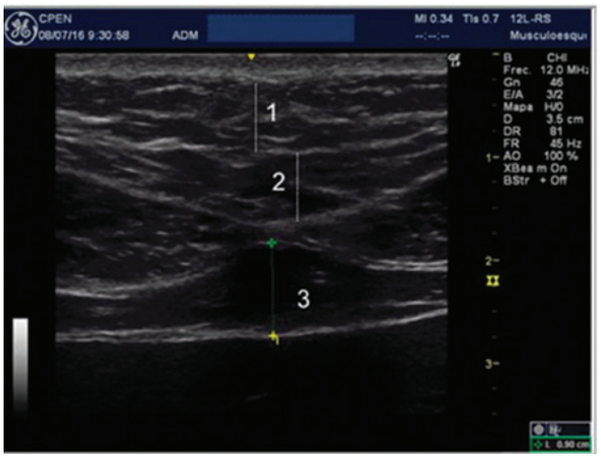

FIG. 1. Echographic superficial, deep subcutaneous fat and preperitoneal fat. Subcutaneous fat is divided by the *fascia superficialis* (*strong white line*) and preperitoneal fat (between the *linea alba* and the peritoneum) (1) superficial subcutaneous fat, (2) deep subcutaneous fat and (3) preperitoneal fat.

Conclusion

In summary, our preliminary findings suggest that abdominal fat layers, especially subcutaneous and preperitoneal fat, differ between PLWH and controls and are probably clinically relevant in terms of cardiovascular risk. Ultrasound is an inexpensive, noninvasive tool that enables us to measure abdominal fat layers as easily detectable markers and thus identify early persons at high risk of cardiovascular disease.

Acknowledgment

We are grateful to Thomas O'Boyle for editorial assistance.

Authors' Contributions

A.B., F.C., G.C., and E.N. conceived the study, interpreted the data, and drafted the article; B.C. supervised study conduction; F.C. performed ultrasonography measurements; J.P. performed the blood test; A.B. and P.E. selected and attended the patients; and F.C. and N.P.-A. carried out the database, compiled the data, and performed the statistical analysis; all the authors revised and approved the final version.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

No funding was received for this article.

References

1. Currier JS, Taylor A, Boyd F, *et al.*: Coronary heart disease in HIV-infected individuals. J Acquir Immune Defic Syndr 2003;33:506–512.
2. Durand M, Sheehy O, Baril JG, Lelorier J, Tremblay CL: Association between HIV infection, antiretroviral therapy, and risk of acute myocardial infarction: A cohort and nested case-control study using Québec's Public Health Insurance database. J Acquir Immune Defic Syndr 2011;57: 245–253.
3. Klein D, Hurley LB, Quesenberry CP, Sidney S: Do protease inhibitors increase the risk for coronary heart disease in patients with HIV-1 infection? J Acquir Immune Defic Syndr 2002;30:471–477.
4. Lang S, Mary-Krause M, Cotte L, *et al.*: Increased risk of myocardial infarction in HIV-infected patients in France, relative to the general population. AIDS 2010;24:1228–1230.
5. Obel N, Thomsen HF, Kronborg G, *et al.*: Ischemic heart disease in HIV-infected and HIV-uninfected individuals: A population-based cohort study. Clin Infect Dis 2007;44: 1625–1631.
6. 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;92:2506–2512.
7. Freiberg MS, Chang C-CH, Kuller LH, *et al.*: HIV infection and the risk of acute myocardial infarction. JAMA Intern Med 2013;173:614–622.
8. Islam F, Wu J, Jansson J, Wilson D: Relative risk of cardiovascular disease among people living with HIV: A systematic review and meta-analysis. HIV Med 2012;13: 453–468.
9. Pereira B, Mazzitelli M, Milinkovic A, *et al.*: Predictive value of HIV-related versus traditional risk factors for coronary atherosclerosis in people aging with HIV. AIDS Res Hum Retroviruses. 2021. DOI: 10.1089/AID.2021. 0064.
10. Douglas PS, Umbleja T, Bloomfield GS, *et al.*: Cardiovascular risk and health among people with HIV eligible for primary prevention: Insights from the REPRIEVE trial. Clin Infect Dis 2021;73:2009–2022.
11. Blanco J-R, Negredo E, Bernal E, Blanco J: Impact of HIV infection on aging and immune status. Expert Rev Anti Infect Ther 2021;19:719–731.
12. Triant VA, Perez J, Regan S, *et al.*: Cardiovascular risk prediction functions underestimate risk in HIV infection. Circulation 2018;137:2203–2214.
13. Kral JG, Schaffner F, Pierson RN, Wang J: Body fat topography as an independent predictor of fatty liver. Metabolism 1993;42:548–551.
14. Ma RCW, Liu KH, Lam PM, *et al.*: Sonographic measurement of mesenteric fat predicts presence of fatty liver among subjects with polycystic ovary syndrome. J Clin Endocrinol Metab 2011;96:799–807.
15. Cuatrecasas G, Cabo F, Coves MJ, *et al.*: Ultrasound measures of abdominal fat layers correlate with metabolic syndrome features in patients with obesity. Obes Sci Pract 2020;6:660–667.
16. Shen W, Wang Z, Punyanita M, *et al.*: Adipose tissue quantification by imaging methods: A proposed classification. Obes Res 2003;11:5–16.
17. Rolfe EDL, Sleigh A, Finucane FM, *et al.*: Ultrasound measurements of visceral and subcutaneous abdominal thickness to predict abdominal adiposity among older men and women. Obesity 2010;18:625–631.
18. Stolk R, Wink O, Zelissen P, Meijer R, van Gils A, Grobbee D: Validity and reproducibility of ultrasonography for the measurement of intra-abdominal adipose tissue. Int J Obes 2001;25:1346–1351.
19. Kawasaki S, Aoki K, Hasegawa O, *et al.*: Sonographic evaluation of visceral fat by measuring para- and perirenal fat. J Clin Ultrasound 2008;36:129–133.
20. Shabestari AA, Bahrami-Motlagh H, Hosseinpanah F, Heidari K: Abdominal fat sonographic measurement compared to anthropometric indices for predicting the presence of coronary artery disease. J Ultrasound Med 2013;32: 1957–1965.
21. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C: ◀AU11 Definition of metabolic syndrome. Arterioscler Thromb Vasc Biol 2004;24.
22. Gayoso-Diz P, Otero-González A, Rodriguez-Alvarez MX, *et al.*: Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: Effect of gender and age: EPIRCE cross-sectional study. BMC Endocr Disord 2013;13:47.
23. Kim SK, Kim HJ, Hur KY, *et al.*: Visceral fat thickness measured by ultrasonography can estimate not only visceral obesity but also risks of cardiovascular and metabolic diseases. Am J Clin Nutr 2004;79:593–599.
24. Fukuda K, Seki Y, Ichihi M, *et al.*: Usefulness of ultrasonographic estimation of preperitoneal and subcutaneous fat thickness in the diagnosis of nonalcoholic fatty liver disease in diabetic patients. J Med Ultrason 2015;42:357–363.
25. Silva KR, Côrtes I, Liechocki S, *et al.*: Characterization of stromal vascular fraction and adipose stem cells from subcutaneous, preperitoneal and visceral morbidly obese human adipose tissue depots. PLoS One 2017;12: e0174115.

Address correspondence to: ◀AU12
Anna Bonjoch ◀AU13
Lluita contra la SIDA Foundation
Germans Trias i Pujol Research Institute-IGTP
Hospital Universitari Germans Trias i Pujol
Universitat Autònoma de Barcelona
Badalona 08916
Spain

E-mail: abonjoch@flsida.org

AUTHOR QUERY FOR AID-2021-0141-VER9-BONJOCH_1P

AU0: The Publisher requests for readability that no paragraph exceeds 15 typeset lines. This paragraph contains 16 lines or more. Please divide where needed.
AU1: Please identify (highlight or circle) all authors' surnames for accurate indexing citations.
AU2: Please check the correctness of authors' affiliations.
AU3: Please provide the department in the affiliations 1, 2, and 5–7.
AU4: Include IRB approval or waiver statement in the Materials and Methods section. The Clinical Trial Registration number, if applicable, should be included at the end of the abstract.
AU5: As per journal style, structured headings from the abstract have been removed. Please confirm.
AU6: Please define ''TAF.''
AU7: Please define ''FTC.''
AU8: Please expand ''TDF.''
AU9: Please expand ''HDL.''
AU10: Kindly check the sentence for clarity, ''However, the exploratory nature of this study avoid to confirming differences between PLWH and matched controls.''
AU11: Please provide the page range for Ref. 21.
AU12: Please confirm the address of correspondence.
AU13: Please mention the degree abbreviation (e.g., MS, MD, and PhD) of the corresponding author.
AU14: Please mention the significance of bold value in Table 1 footnote.
AU15: Please provide the significance ''bold'' values in Table 2 footnote.
AU16: Please provide the significance ''bold'' value in Table 3.
AU17: Kindly check the sentence for clarity, ''Echographic superficial, deep subcutaneous fat and preperitoneal fat. Subcutaneous fat is divided by the *fascia superficialis* (*strong white line*) and preperitoneal fat (between the *linea alba* and the peritoneum) (1) superficial subcutaneous fat, (2) deep subcutaneous fat and (3) preperitoneal fat.''