GDF-15 IS A MARKER OF HIGH-RISK CORONARY ATHEROSCLEROTIC PLAQUE IN PLWH

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BACKGROUND

Despite antiretroviral therapy (ART), people living with HIV (PLWH) experience a high burden of age-related non-AIDS comorbidities. Increased rates of cardiovascular diseases (CVD) and larger subclinical noncalcified coronary plaques at coronary CT angiography have been observed in ART-treated PLWH compared to HIV-uninfected people.

Growth differentiation factor-15 (GDF-15) is a transforming growth factor-β family cytokine/mitokine, emerging as one of the best markers for poor cardiovascular clinical outcomes in the general population**.**

METHODS

We cross-sectionally analyzed plasma of 89 PLWH on ART and 46 controls. We measured two mitochondrial stress-related cytokines/mitokines, GDF-15 and fibroblast growth factor 21 (FGF-21), and the comorbidity marker soluble urokinase plasminogen activator receptor (suPAR). HsCRP in plasma and HIV reservoir size (integrated HIV DNA) in CD4+ T cells were also quantified.

All 135 participants had no overt CVD and underwent coronary CT angiography with 3D reconstruction of coronary artery atherosclerotic plaques. Total plaque volume (TPV) and low attenuation plaque volume (LAPV, defined as density < 30 HU) were calculated (in mm^3).

Table 1

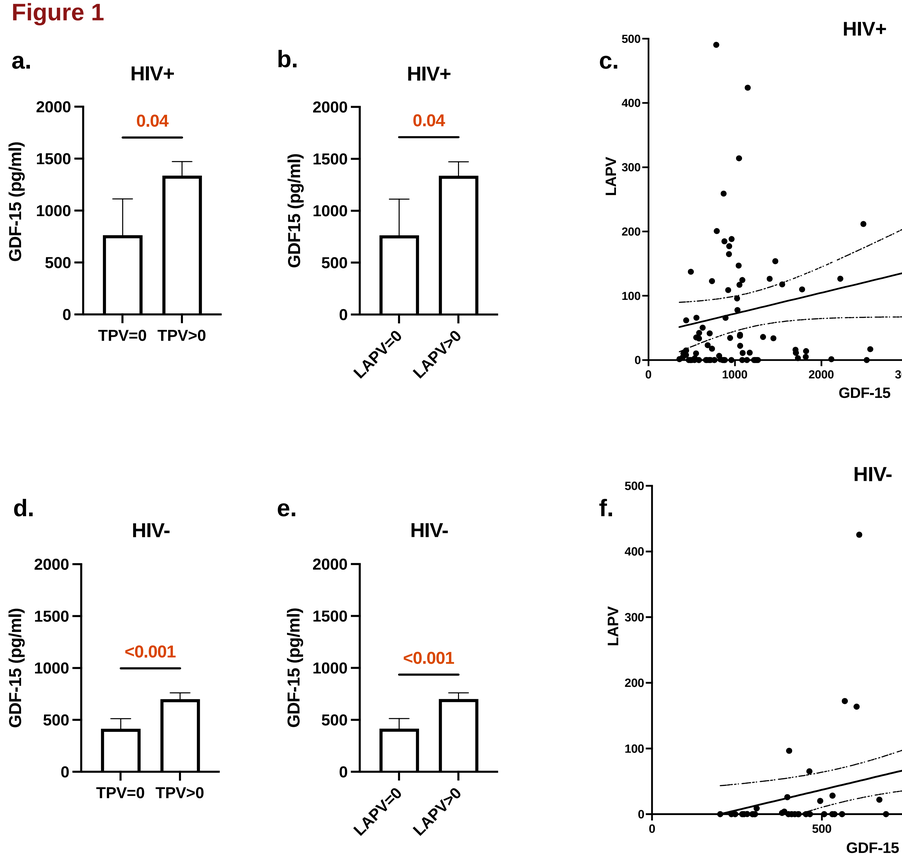
Characteristics	HIV+ (N=89)	HIV- (N=46)
Age, y		
Median (IQR)	55 (50-61)	50 (47-58)
Range	44-73	39-74
Sex, no. (%)		
Male	86 (90%)	40 (77%)
Female	9 (10%)	12 (23%)
Diabetes	9 (9%)	0 (0%)
Hypertension	33 (35%)	12 (23%)
Statin Use	32 (34%)	5 (10%)
Smoking Status		
Current smoker	24 (25%)	5 (10%)
Former smoker	43(45%)	19 (36%)
Never smoked	27 (29%)	28 (54%)
CD4 T-cells/µL		
Median (IQR)	594 (446-749)	N/A
Range	117-1840	N/A
CD4:CD8		
Median (IQR)	0.860 (0.546-1.138)	N/A
Range	(0.196-2.3)	N/A

GDF-15, a stress-induced cytokine, represents a new marker of high-risk coronary plaques in both PLWH and HIV-uninfected people.

RESULTS

- PLWH and controls had similar age (median 55 years) and were mostly males (91% and 80% of PLWH and controls, respectively, **Table 1**).
- GDF-15 levels were higher in PLWH than in HIV-uninfected controls (934pg/ml vs 480, *p*<0.001).
- In PLWH, GDF-15 levels were increased in participants with presence of coronary plaque vs without (total plaque: 1037pg/ml vs 764, *p*=0.04**, Figure 1a**, low-attenuation plaque: 1337pg/ml vs 905, *p*=0.04, **Figure 1b**), and correlated with TPV (r=0.27, *p*=0.009) and LAPV (r=0.28, *p*=0.008, **Figure 1c**).
- Similarly, among controls GDF-15 levels were higher in those with coronary plaque vs without (total and low-attenuation plaque: 640pg/ml vs 416, *p*<0.001, **Figure 1d/e**) and correlated with TPV (r=0.62, *p*<0.001) and LAPV (r=0.60, *p*<0.001, **Figure 1f**).
- Only in PLWH, TPV and LAPV also significantly correlated with HIV reservoir size and to hsCRP and suPAR, although to a lesser extent than GDF-15.
- Conversely, FGF-21 was not associated with TPV nor LAPV in both populations.

Figure 1



CONCLUSIONS

In PLWH, plasma GDF15 levels were higher than in HIV-uninfected controls. In both groups, increased GDF-15 levels were associated with the presence of coronary artery plaques, in particular low attenuation plaques, which were shown to predict future coronary events.

Altogether, GDF-15 represents a new marker of high-risk coronary plaques in PLWH.

ADDITIONAL KEY INFORMATION

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