29th Annual Canadian Conference on HIV / AIDS Research

29e Congrés annuel canadien de recherche sure le VIH/sida

Microbial Translocation of Fungal β-D-Glucan is Associated with Cardiovascular Risk in People Living with HIV

Brandon Fombuena, B.Sc.

Research Institute of the McGill University Health Centre, Montréal, QC, Canada
Team Dr. Jean-Pierre Routy
brandon.fombuena@mail.mcgill.ca

Conflict of Disclosure: I have no conflicts of disclosure

Centre universitaire de santé McGill
Institut de recherche

McGill University Health Centre
Research Institute

Background and Methods

Background

- **Microbial translocation** from the gut to circulation contributes to **immune activation** during HIV infection and is usually assessed by measuring plasma levels of bacterial lipopolysaccharide (LPS).

- Gut fungal colonization increases during HIV infection and **elevated systemic levels** of the **fungal polysaccharide β-D-Glucan (βDG)** have been reported in people living with HIV (PLWH). βDG represents one of the most abundant components of fungal cell walls and serves as a potent pathogen-associated molecular pattern in triggering antifungal immunity

- Despite antiretroviral therapy (ART), PLWH have an **increased risk of inflammatory comorbidities**. Gut damage and translocation of bacterial LPS and fungal βDG drive inflammation in ART-treated PLWH.

Herein, we investigated whether markers of gut damage and bacterial and fungal translocation are associated with cardiovascular risk in ART-treated PLWH.

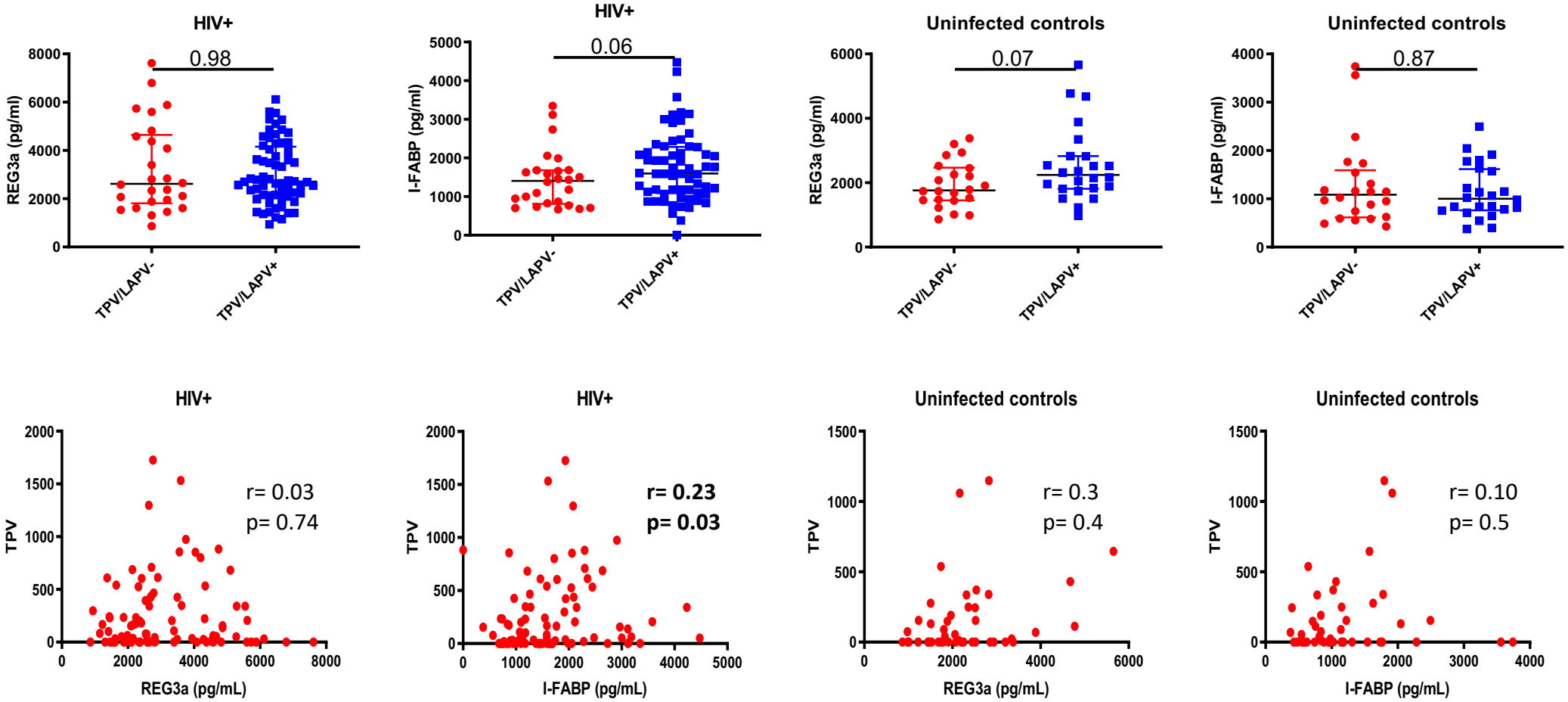
Methods

As part of the Canadian HIV and Aging Cohort (CHAC), we analyzed plasma from 147 participants > 40 y.o., 95 ART-treated PLWH with viral load <50 copies/ml, and 52 uninfected controls. Participants were free of clinical cardiovascular disease at baseline and underwent a cardiac computed tomography. Total coronary plaque volume (TPV) and low-attenuation coronary plaque volume (LAPV) were measured. Plasma levels of REG3α, I-FABP and LPS were measured by ELISA. Plasma BDG levels were analyzed using the Fungitell® assay.

TPV/LAPV- → coronary plaque = 0

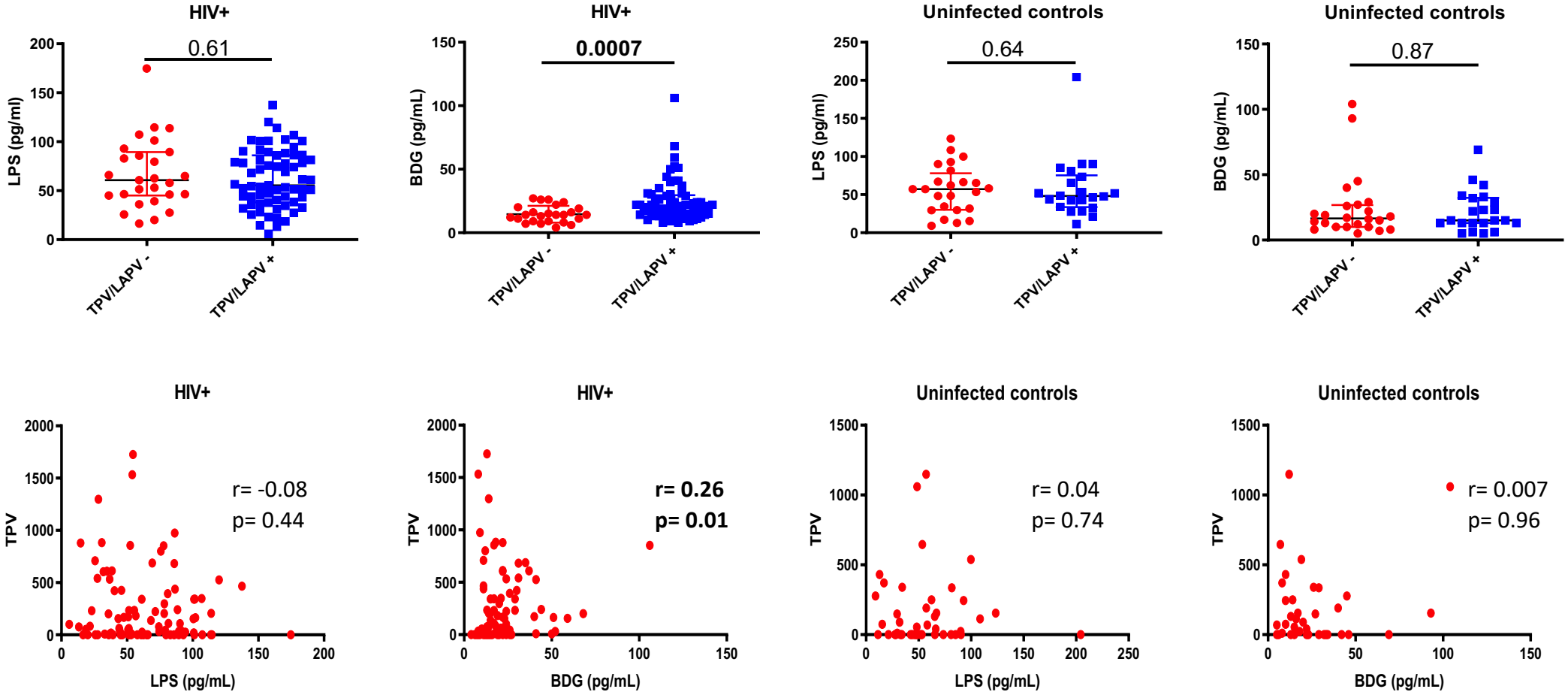
TPV/LAPV+ → coronary plaque volume >0

Gut Damage and Cardiovascular Risk



Plasma levels of I-FABP and Reg3α were slightly elevated although not significant in TPV/LAPV+ groups in comparison to TPV/LAPV- groups. Moreover, plasma levels of I-FABP and Reg3α correlated with TPV size in PLWH. In all participants (not depicted), TPV and LAPV correlated with gut damage markers REG3α (r=0.2, p=0.03 for both) and I-FABP (r=0.2, p=0.001 for both). In ART-treated PLWH, I-FABP but not REG3α levels correlated with TPV (r=0.23, p=0.03) and LAPV (r=0.27, p=0.01).

Microbial Translocation and Cardiovascular Risk



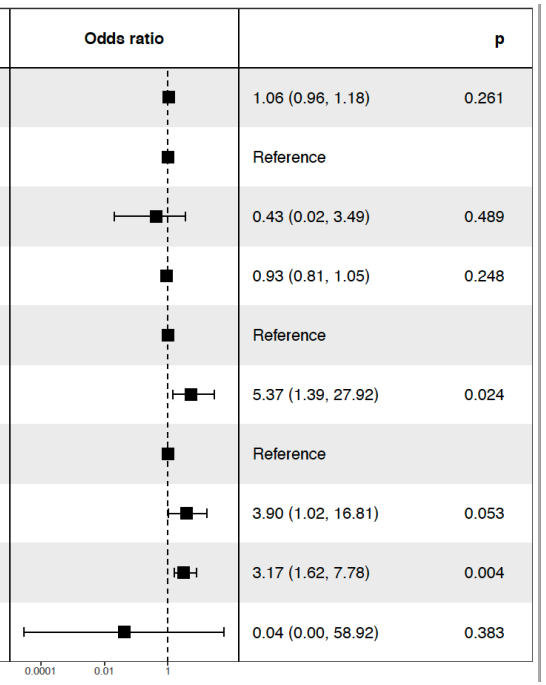
Plasma levels of BDG, but not LPS, were elevated in TPV/LAPV+ groups in comparison to TPV/LAPV- groups in PLWH. Moreover, Plasma levels of BDG, but not LPS, correlated with TPV size. In all participants (not depicted), BDG but not LPS levels correlated with TPV and LAPV (r=0.2, p=0.04 for both). In ART-treated PLWH, BDG but not LPS levels correlated with TPV (r=0.26, p=0.01) and LAPV (r=0.25, p=0.010).

Conclusion

Gut damage markers and translocation of fungal product BDG, but not bacterial LPS, were associated with the **burden of coronary atherosclerosis** in ART-treated PLWH.

Furthermore, following multivariate analysis, statin use and smoking habit (current or former) were also found to be associated with TPV in ART-treated PLWH (p=0.024 and p=0.053, respectively). However, **BDG proved to be a better marker** at predicting TPV risk (p=0.004). Per 10 units of BDG increase, there was shown to be a 3.17-fold increase in TPV risk.

Variable		N	Odds ratio	p
Age		84	1.06 (0.96, 1.18)	0.261
Sex	Female	7	Reference	
	Male	77	0.43 (0.02, 3.49)	0.489
BMI		84	0.93 (0.81, 1.05)	0.248
Statin use	No	54	Reference	
	Yes	30	5.37 (1.39, 27.92)	0.024
Smoking habit	Never	21	Reference	
	Current or former	63	3.90 (1.02, 16.81)	0.053
BDG		84	3.17 (1.62, 7.78)	0.004
(Intercept)			0.04 (0.00, 58.92)	0.383



More research is needed to appraise causality of the association; however, translocation of fungal products represents a potential therapeutic target to prevent cardiovascular disease in ART-treated PLWH.