

## Circulating Annexin V1 and Annexin A1 plasma levels correlate with cardiovascular outcomes in HIV subjects

Ucciferri Claudio<sup>1,3</sup>; Auricchio Antonio<sup>3</sup>; Vignale Francesca<sup>1</sup>, Costantini Erica<sup>1</sup>, D'Angelo Chiara<sup>1</sup>, Reale Marcella<sup>1</sup>, Vecchiet Jacopo<sup>1</sup>, Falasca Katia<sup>1</sup>.



1Clinic of Infectious Diseases, Department of Medicine and Science of Aging, University "G. d'Annunzio" Chieti-Pescara, Italy

2Unit of Immunodiagnostic and Molecular Pathology, Department of Medical, Oral and Biotechnological Sciences, University "G. d'Annunzio", Chieti- Pescara, Italy 3University of Molise Department of Medicine and Health Sciences Campobasso Italy.

### Background

The vascular endothelium plays a pivotal role in the pathogenesis of atherosclerosis and its clinical manifestations of the cardiovascular disease (CVD), myocardial infarction, heart failure, stroke, and peripheral artery disease. Experimental and clinical studies in general population suggest that endothelial dysfunction as an independent predictor of adverse events in CVD patients (1) can be assessed quantitatively by measurement of CD31+/annexin (Anx)V plasma levels (2). Also the AnxA1 has consistently been found to play an inhibitory role in innate forms of inappropriate inflammation. HIV-1 disease progression is paradoxically characterized by systemic chronic immune activation and gut mucosal immune dysfunction, which is not fully defined. AnxA1, an inflammation modulator, is a potential link between systemic inflammation and immune dysfunction during the simian immunodeficiency virus (SIV) infection (3). The aim of this study was evaluated to correlation between AnxV and AnxA1 plasma levels and cardiovascular risk scores in patients with HIV infection and viro-immunological stable.

### Materials and methods

We enrolled 74 HIV-positive patients in cART at the Infectious Diseases Clinics of Chieti. Demographic and anamnestic data were collected, blood and immunological parameters were measured in addition to the Cystatin C, PCR, microalbuminuria, AnxA1 and V1 were analyzed. Different CVD Risk scores by Framingham, ASCVD, DAD and PROCAM risk scores were calculated.

Population	MEAN	SD (+/-)
Età (y)	49,18	10,738
BMI	26,66	4,33
CD4(cells/ul)	640,74	333,46
CD56 (cells/ul)	341,74	220,73
CD45/19 (cells/ul)	272,70	255,20
CD4/CD8 (cells/ul)	6,36	34,87
Cystatin C (mg/L)	1,03	0,22
Microalbuminuria (mg/L)	3,06	4,55
HOMA IR	2,45	2,30
Total Cholesterol (mg/dl)	185,31	34,34
LDL (mg/dl)	107,84	29,90
HDL (mg/dl)	45,72	17,51
Triglycerides (mg/dl)	158,26	96,39
FRAMINGHAM %	8,37	6,62
ASCVD score %	8,56	6,50
DAD score%	3,40	3,12
PROCAM %	8,07	7,06

### Results

We found levels of AnxA1 (15.04+/-12.16 ng/ml) and AnxV with levels of 2.80+/-2.00 ng/ml. We had a negative association between AnxV1 level and Framingham score ( $r=-0.22$  e  $p=0.05$ ), ASCVD ( $r=-0.23$  e  $p=0.04$ ), DAD score ( $r=-0.24$  e  $p=0.03$ ), and PROCAM score ( $r=-0.30$  e  $p=0.008$ ). Also the anxA1 was associated to cardiovascular risk score, in fact we found a negative correlation between AnxA1 and Framingham score ( $r=-0.40$  e  $p=0.001$ ), ASCVD ( $r=-0.48$  e  $p=0.001$ ), DAD score ( $r=-0.39$  e  $p=0.001$ ), and PROCAM score ( $r=-0.49$  e  $p=0.001$ ). Therefore an association between AnxV and microalbuminuria ( $r=-0.26$  and  $p=0.02$ ), between AnxA1 and cystatin C ( $r=-0.41$  and  $p=0.001$ ) and microalbuminuria ( $r=-0.55$  and  $p=0.001$ ) was found.

### Conclusions

Our work shows that exists a correlation between the inflammatory annexins and the results obtained from the HIV cardiovascular risk scores. Indeed low levels annexins were significantly correlated with high CVD risk, highlighting how the inflammatory process participates in the pathogenesis of cardiovascular damage in the HIV-positive population.

### References

1. Heitzer T, Schlinzig T, Krohn K, Meinertz T, Munzel T. Endothelial dysfunction, oxidative stress, and risk of cardiovascular events in patients with coronary artery disease. *Circulation* 2001;104:2673.
2. Werner N, Wassmann S, Ahlers P, Kosiol S, Nickenig G. Circulating CD31+/annexin V+ apoptotic microparticles correlate with coronary endothelial function in patients with coronary artery disease. *Arterioscler Thromb Vasc Biol* 2006;26:112–116.
3. Jan-Malte Sinning, Jan Losch, Katrin Walenta, Michael Boßhm, Georg Nickenig, and Nikos Werner. Circulating CD311/Annexin V1 microparticles correlate with cardiovascular outcomes. *European Heart*