Platelet Derived Soluble Glycoprotein VI Decreases Prior to Coronary Event in HIV Positive Patients

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Disclosures

- The authors have no conflicts of interest relevant to this work to declare

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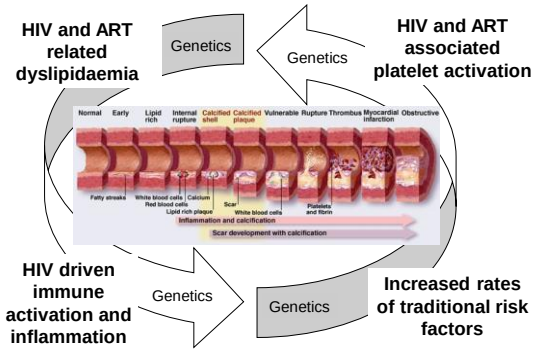
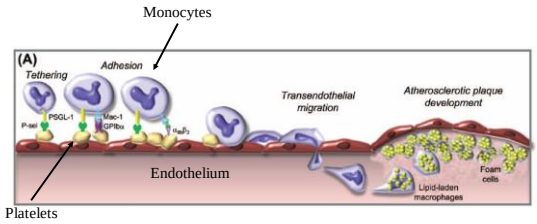
HIV+ individuals are at increased risk for cardiovascular disease



Role of platelets in atherosclerosis



Adapted from: Kaplan et al. 2011 *Haematology*

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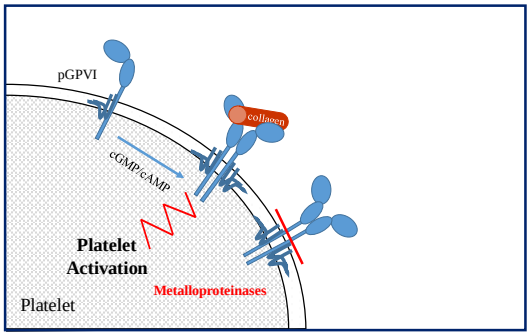
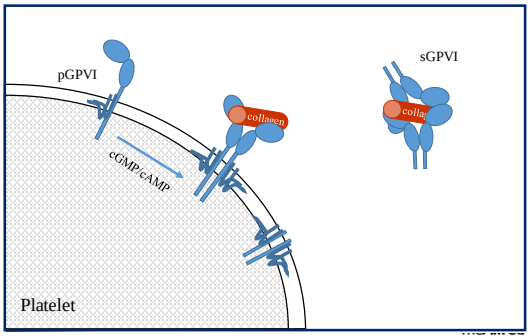
Platelet receptor function is a key component of the pathogenesis of atherosclerosis



Soluble glycoprotein VI may be an important negative feedback mechansim



Aims

- To determine if sGPVI levels were different in HIV positive individuals compared with HIV negative controls
- To determine if sGPVI levels were predictive of a diagnosis of coronary artery disease in people living with HIV

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Methods

- Retrospective case-control study of HIV positive individuals seen at the Alfred Hospital, Melbourne
- January 1996 – December 2009
- Cases were HIV positive individuals with a first diagnosis of coronary artery disease (CAD)
- Defined as:
  - Acute myocardial infarction
  - Positive coronary Angiogram
  - Clinical diagnosis (angina with consistent ECG)

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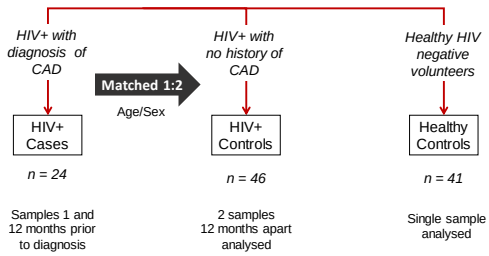
Methods



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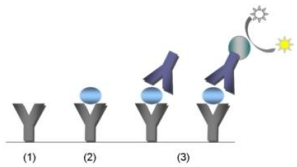
Platelet function assessment

- sGPVI levels were determined by ELISA from platelet-poor plasma using standard techniques



Al-Tamimi et al. Platelets 2009;20(3):143-149

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Statistical Methods

- Results are summarized by group, using Fisher's exact or chi-squared tests for categorical variables and the Mann-Whitney U-Test for continuous data.
- Correlations were determined using Spearman's correlation co-efficient
- Multiple linear regression was performed to adjust for possible confounders
- Statistical significance defined as $p<0.05$
- Stata 11.0/IC (College Station, Texas)

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Ethics approval

- This project was approved by the Alfred Hospital Ethics Committee (Project Number: 205/09)
- All participants provided written consent to have their plasma stored and used for future research

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Participant Characteristics

n (%)	HIV cases (A)	HIV controls (B)	Healthy controls (C)	p value		
				A v's B	A v's C	B v's C
Participants	24	46	41			
Male	21 (87.5)	42 (91.3)	37 (90.2)	0.620	0.735	0.866
Age, years	52.5 (42-62)	52.0 (42-59)	49.0 (42-56)	0.368	0.174	0.628
Current Smokers	12 (50.0)	19 (41.3)	3 (7.32)	0.490	**<0.001**	**<0.001**
Diabetes	4 (16.6)	3 (6.5)	0 (0)	0.184	**0.007**	0.098
Hypertension	13 (54.1)	5 (10.8)	7 (17.0)	**<0.001**	**0.001**	0.405
Antiplatelet treatment	10 (41.6)	1 (2.1)	0 (0.0)	**<0.001**	**<0.001**	0.345
Framingham Risk score, %	10 (8-14.5)	7 (3.5-14.5)	5.9 (3.8-10.1)	**0.057**	**0.008**	0.679

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Cholesterol levels

median (IQR), mmol/L	HIV cases (A)	HIV controls (B)	Healthy controls (C)	p value		
				A v's B	A v's C	B v's C
Total cholesterol	5.0 (4.7-6.3)	5.2 (4.5-5.6)	5.5 (5.1-6.2)	0.706	0.260	**0.044**
LDL-cholesterol	2.9 (2.4-3.5)	2.8 (2.2-3.2)	3.6 (3.1-4.1)	0.803	**0.020**	**0.004**
HDL-cholesterol	1.0 (0.9-1.2)	1.0 (0.9-1.6)	1.4 (1.1-1.8)	0.459	**<0.001**	0.08
Triglycerides	2.0 (1.5-3.2)	1.8 (1.3-2.7)	0.8 (0.7-1.5)	0.199	**<0.001**	**<0.001**

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HIV specific characteristics

n (%) or median (IQR)	HIV cases (A)	HIV controls (B)	p value
Duration of HIV infection, years	13.6 (9.3-17.3)	10.8 (5.0-15.5)	0.103
Receiving ART	24 (100)	41 (89.1)	0.113
ARV regimen			
Protease inhibitor	16 (66.6)	24 (52.1)	0.251
NNRTI	6 (25.0)	19 (41.3)	0.181
Integrase Inhibitor	2 (8.3)	0 (0.0)	0.047
CD4+ cell nadir, cells/μL	129 (70-225)	113 (20-240)	0.421
CD4+ T-cell count, cells/μL	485.5 (335-699)	411 (287-546)	**0.044**
CD8+ T-cell count, cells/μL	1076 (885-1293)	888 (584-1615)	0.404
Detectable HIV VL‡	11 (45.8)	10 (22.7)	0.059

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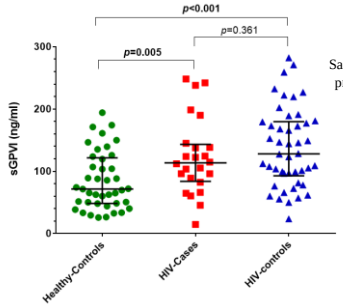
sGPVI levels are higher in HIV positive individuals



Samples 12 months prior to diagnosis

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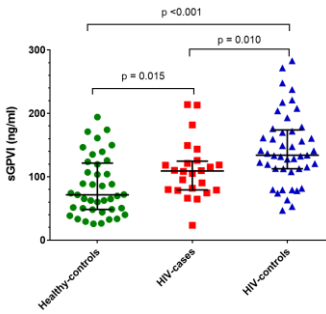
sGPVI levels are lower immediately prior to CAD diagnosis in HIV Positive Patients



Samples 1 month prior to diagnosis

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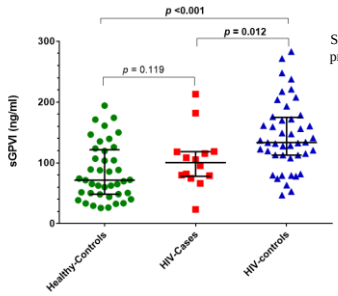
Changes remained when those taking antiplatelets were excluded



Samples 1 month prior to diagnosis

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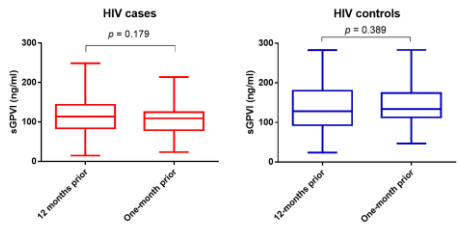
No significant change in sGPVI across time points for HIV cases or controls



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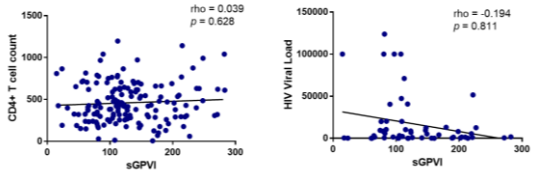
No correlation between sGPVI and HIV measured factors



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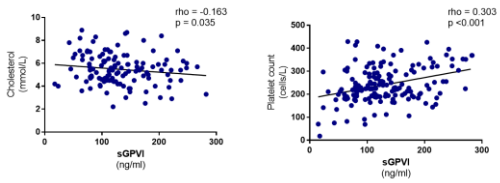
Weak correlation between sGPVI and cholesterol levels and platelet count



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Difference remained significant following adjustment

- Following adjustment for:
  - Smoking status
  - Total and LDL cholesterol
  - Antiplatelet use
  - Platelet count
  - Systolic blood pressure
- Healthy controls continued to have lover sGPVI than HIV positive individuals ($p < 0.001$)
- At one month prior to event HIV-cases continued to have lower sGPVI compared with HIV-controls ($p = 0.033$)

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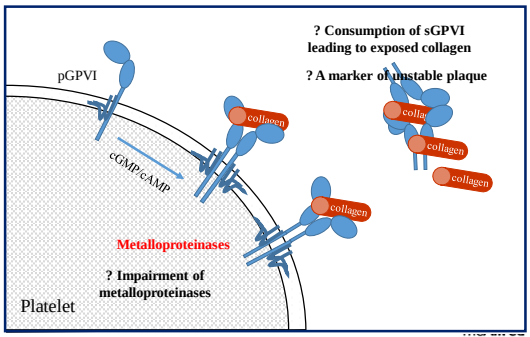
Is lower sGPVI a pathological process directly contributing to CVD in HIV?



Limitations

- Small sample size
- Homogeneous patient population
- Single centre
- Retrospective design
- Use of stored samples

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Conclusion

- HIV infection is associated with increased sGPVI levels
- Lower sGPVI levels are seen prior to diagnosis of coronary artery disease in HIV positive individuals
- This may reflect a loss of negative-feedback mechanisms and be an important pathological step in the development of symptomatic coronary artery disease

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ACBD

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