Substantial gender differences in longitudinal arterial stiffness in children on ART

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Background

- Accelerated atherosclerotic vascular disease (AVD) is common determinant of morbidity and survival in HIV+ adults on ART
- Women affected less severely than men
- AVD originates in childhood and whether this gender difference is present before puberty is unknown
- AVD progression is reflected in pulse wave velocity (PWV), a direct measure of arterial stiffness [1]

Methods

- Prospective PWV z-score for height and gender (PWVz) over 2 years in HIV+ children on ART = Cape Town participants exiting CHER trial [2,3] n=87, Initiated ZDV + 3TC + LPV/r at median 9 (7, 12) weeks of age
- Existing control group [4] of HIV-exposed (HEU) and -unexposed (HUU) children from the same communities
- Likely risk factors were modeled using forward stepwise addition and backward elimination in linear regression modelling
- Starting variables: age, gender, serum cotinine (measures tobacco smoke exposure), fasted total cholesterol, HDL, LDL, triglycerides, glucose, blood pressure, extensive anthropometrics
- Linear mixed effects model compared longitudinal change in PWV in HIV+ and HIV- boys and girls

Results

- PWV abnormally elevated in HIV+ children compared with HIV-unexposed (median 3.9 versus 3.4, p=0.02)
- In HIV+, PWVz was predicted by fasting glucose (p<0.0001), waist circumference (p<0.0001) and gender (p<0.0001), but not by lipids
- In HIV+, PWVz was higher in boys than girls at baseline (median 4.0 versus 3.3, p=0.006), but both slowly improved with accumulating time on suppressive ART (Figure 1)
- PWVz improved more quickly in boys than girls (mean improvement -0.53 per year in boys versus -0.27 in girls, p<0.0001) but remained higher than girls after 2 years (Figure 1)
- No change in arterial stiffness was seen in HIV-uninfected over time in either gender

Demographics and clinical characteristics presented as median (interquartile range)	HIV+ n = 87	HIV- n = 53	Unadjusted p-value (2-tailed)
Age at study visit (years)	7.7 (7.6, 7.8)	8.5 (7.8, 8.7)	<0.0001
Gender (male/female)	46% / 54%	60% / 40%	0.10
Nadir CD4%	21% (16%, 26%)	---	---
Cumulative months with low CD4 or CD4% §	3 (0, 14)	---	---
Nadir CD4 (cells/mm^3)	694 (521, 871)	---	---
Maximum WHO clinical stage (1 or 2 / 3 / 4)	10% / 42% / 48%	---	---
Nadir weight-for-age Z-score	-1.7 (-2.5, -0.8)	-0.8 (-1.5, +0.1)	0.0007
Nadir height-for-age Z-score	-1.9 (-2.6, -1.5)	-1.5 (-2.2, -0.9)	0.11
Nadir weight-for-height Z-score	-0.8 (-2.0, 0.0)	-0.5 (-1.4, +0.4)	0.06
Cumulative time on ART (years)	7.1 (6.7, 7.5)	---	---
% with undetectable HIV RNA PCR (<150 c/ml)	91%	---	---
Cumulative time with undetectable VL (years)	5.2 (2.4, 5.6)	---	---
Serum cotinine (tobacco smoke exposure) (µg/L)	1.3 (0.5, 1.9)	1.3 (0.5, 2.1)	0.63
Current weight-for-age Z-score	-0.4 (-1.0, +0.3)	-0.2 (-1.0, +1.1)	0.13
Current height-for-age Z-score	-0.8 (-1.3, +0.1)	-0.4 (-1.1, +0.3)	0.12
Current body mass index-for-age Z-score	+0.1 (-0.5, +0.7)	0.0 (-0.5, +1.2)	0.26
Waist circumference to height ratio	0.5 (0.4, 0.5)	0.5 (0.4, 0.5)	0.48
Systolic blood pressure (mmHg)	96 (90, 100)	96 (92, 105)	0.10
Current CD4 (cells/mm^3)	1115 (861, 1434)	---	---
Total cholesterol (mmol/L)	4.2 (3.7, 4.8)	3.5 (3.0, 4.0)	<0.0001
Triglycerides (mmol/L)	0.8 (0.7, 1.2)	0.6 (0.4, 0.7)	<0.0001
Triglyceride to HDL cholesterol ratio	0.7 (0.5, 1.0)	0.4 (0.3, 0.7)	<0.0001
LDL cholesterol (mmol/L)	2.5 (2.0, 2.9)	1.9 (1.5, 2.4)	<0.0001
Glycosylated hemoglobin (%)	5.4% (5.2%, 5.7%)	5.8% (5.5%, 6.0%)	0.11

CD4 preserved

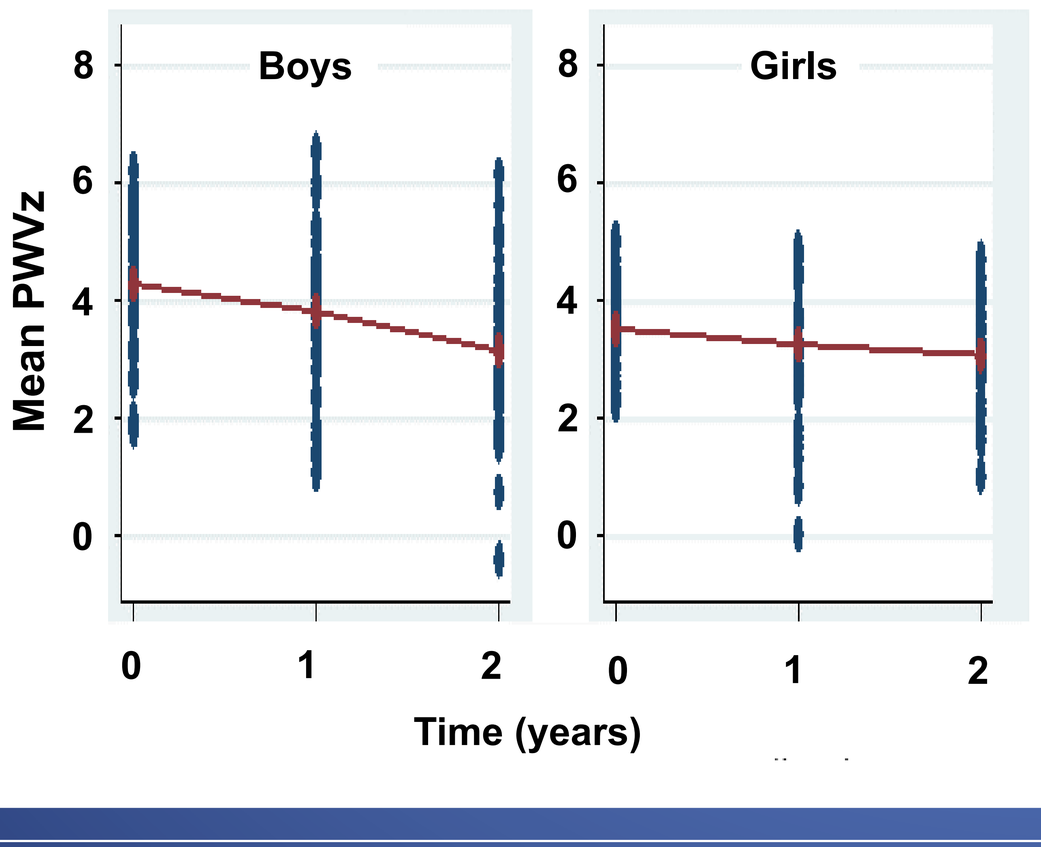
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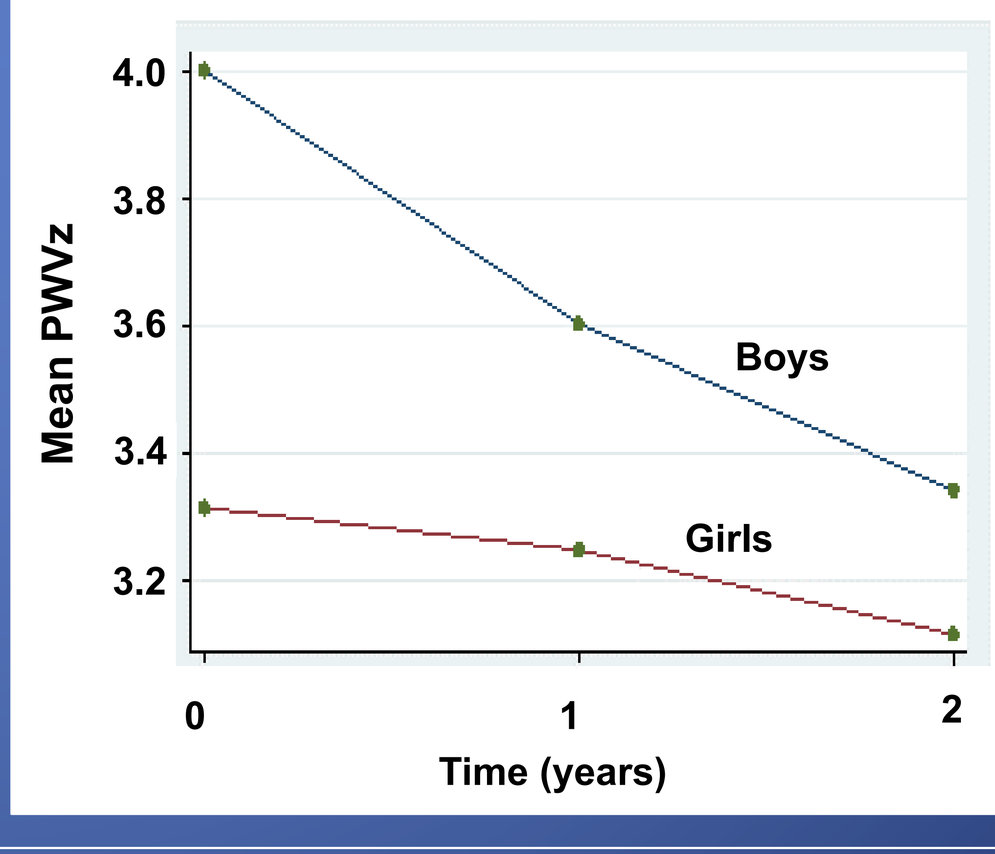
Well grown

Elevated lipids

§ Low CD4 or CD4% was defined as CD4<1000 or CD4%<25% for <12 months of age; CD4<750 or CD4%<20% for 12-35 months of age; and CD4<500 or CD4%<20% for >36months of age. ZDV = zidovudine; 3TC = lamivudine; LPVr = lopinavir/ritonavir

Figure 1: Prospective pulse-wave velocity z-scores (PWVz) in HIV+ children by gender





Conclusions

In prepubertal HIV+ children on suppressive ART, arterial stiffness is abnormally elevated in both genders, with boys more severely affected. Over 2 years, boys improved more quickly than girls but remain more severely affected

References

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