Poster No. WEPEB0503

D:A:D

IAS 2017

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Cardiovascular Disease (CVD) and Chronic Kidney Disease (CKD) Event Rates in HIV-positive Persons at high Predicted CVD and CKD Risk: Results from the D:A:D Study

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BACKGROUND

- Combination drug therapy has transformed the lives of people living with HIV (PLH)
- PLH appear to experience greater and earlier onset of comorbidities compared with their HIV-negative peers
- Chronic kidney disease (CKD: 2 eGFRs <60 ml/min/ 1.72m^2 at least 3 months apart) is an independent risk factor for cardio-vascular disease (CVD: myocardial infarction, stroke, invasive proceedure, sudden cardiac death); CVD in turn is associated with CKD
- The data collection on adverse events of anti-HIV drugs (D:A:D) study has developed predictive risk-scores for CVD[1] and CKD[2] events in PLH

We hypothesised that D:A:D participants at high (>5%) CVD and CKD predicted risk would be at multiplicative risk for CVD and CKD event outcomes.

METHODS

- We included individuals for whom a complete set of risk covariate data was available as required by both the D:A:D CVD[1] and CKD[2] risk equations. All those included had a baseline eGFR >60 ml/min/1.72m^2 and ≥2 eGFRs thereafter to calculate the CVD and CKD scores
- We calculated CVD and CKD event rates by predicted 5-year CVD and CKD risk strata (≤1%, 1-5% and >5%)
- We fitted Poisson models to assess whether CKD and CVD risk strata effects are additive or multiplicative

RESULTS

Of the 49,717 individuals enrolled in D:A:D, 27,215 (55%) individuals were included in the analysis and contributed 202,034 person years of follow-up (py) (Table 1).

Table 1. Participant baseline characteristics

	N	%		Median	(IQR)
Overall	27,215	(100%)	Age (years)	42	(36, 49)
Male	20,206	(74.3%)	eGFR ml/min/1.72m²	100	(86, 117)
IDU exposure to HIV	3,673	(13.5%)	Total cholesterol mmol/L	4.8	(4.1, 5.7)
Current smoker	13,466	(49.5%)	HDL cholesterol mmol/L	1.2	(0.9, 1.5)
Ex-smoker	5,466	(20.1%)	CD4 µmol/L	464	(319, 650)
Diabetes	1,031	(3.8%)	Systolic BP mm/Hg	120	(113, 130)
Family History of CVD	2,257	(8.3%)	Diastolic BP mm/Hg	80	(70, 82)
HCV positive	5,276	(19.4%)	Cumulative PI years	0.9	(0, 4.0)
			Cumulative Nucleoside years	3.9	(0.5, 7.7)
HBV positive	1,462	(5.4%)	5-year predicted CKD risk	1.1%	(0.55%, 3.7%)
On ABC	4,551	(16.7%)	5-year predicted CVD risk	1.6%	(0.77%, 3.3%)
On TDF	8,212	(30.2%)	Year of baseline	2005	(2004, 2008)
On AZV	2,336	(8.6%)			
On IDV	559	(2.1%)			
On LPV	4,522	(16.6%)			
On RTV	8,295	(30.5%)			

Table 2. Combined effect on CKD and CVD risk groups in predicting CKD and CVD events

CKD and CVD risk groups	IRR	95% CI	p-value	Interaction p-value*
Predicting CKD events				
CKD ≤1%	1.0			
CKD 1-5%	3.46	(2.79, 4.30)	<0.001	
CKD >5 %	13.81	(1122, 17.01)	<0.001	
CVD ≤1%	1.0			
CVD 1-5%	2.70	(2.16, 3.38)	<0.001	
CVD >5 %	5.63	(4.47, 7.09)	<0.001	0.291
Predicting CVD events				
CVD ≤1%	1.0			
CVD 1-5%	8.43	(5.91, 12.03)	<0.001	
CVD >5 %	26.97	(18.68, 38.95)	<0.001	0.329
CKD ≤1%	1.0			
CKD 1-5%	1.19	(1.01, 1.44)	0.041	
CKD >5 %	1.31	(1.09, 1.56)	0.005	

*Test for interaction is likelihood ratio test global p-value for non-additive effect (4 degrees of freedom)

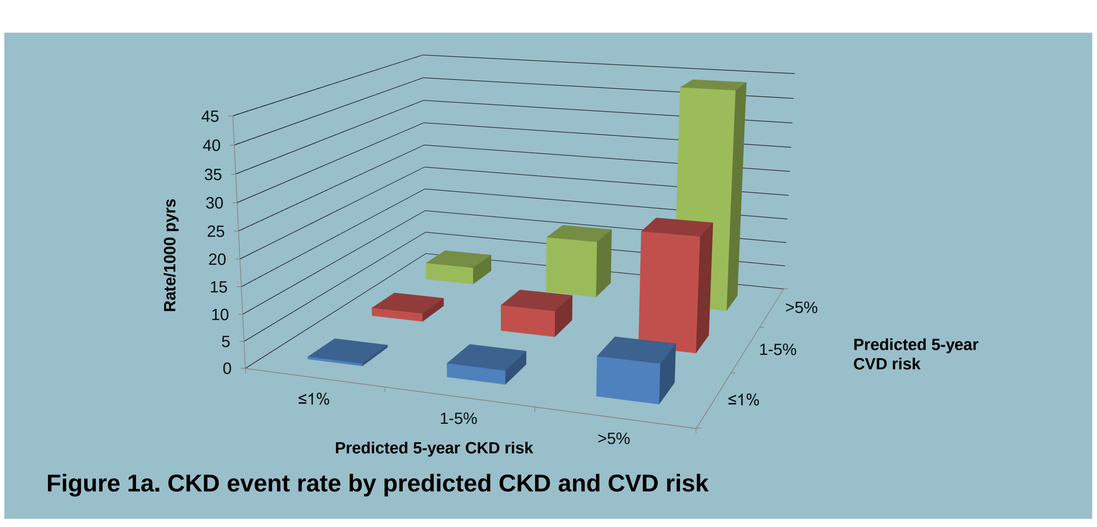

Figure 1a. CKD event rate by predicted CKD and CVD risk

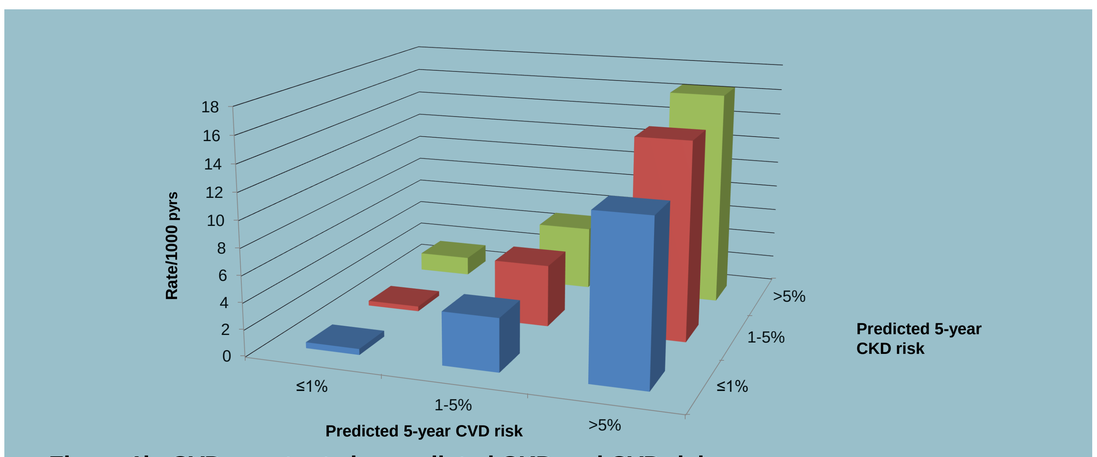

Figure 1b. CVD event rate by predicted CKD and CVD risk

CKD event rates according to CVD risk

- The overall rate of CKD events was 7.0 per 1000 py (95%CI 6.6 – 7.7 per 1000 py)
- Higher predicted CVD risk was associated with an increased rate of CKD events across all CKD risk strata (Fig. 1a)
- Poisson models confirmed that CKD and CVD predicted risk groups had a multiplicative effect on CKD events, with no statistical evidence of an interaction (Table 2)

CVD event rates according to CVD risk

- The rate of CVD events was 4.50 per 1000 py (95%CI 4.2 – 4.8 per 1000 py)
- Higher predicted CKD risk was also associated with an increased rate of CVD events, albeit more weakly (Fig. 1b)
- Poisson models confirmed multiplicative effects on CVD events, with no statistical evidence of an interaction (Table 2)

Investigating other covariates

- We found that after adjustment for predicted CKD risk group, total cholesterol (IRR 1.48, 95%CI 1.20, 1.83; p< 0.001), cumulative PI (IRR 1.11, 95%CI 1.06, 1.15; p<0.001) and N(t)RTI (IRR 1.05, 95%CI 1.03, 1.08; p<0.001) were associated with an increased risk and a higher current CD4+ cells/mm^3 count (IRR 0.90, 95%CI 0.86, 0.95; p <0.001) with a decreased risk of CKD events respectively
- After adjustment for CVD risk group, the nadir CD4+ count was associated with a decreased risk of CVD events (per 100 cells): (IRR 0.94, 95%CI 0.091,0.98, p = 0.002)

DISCUSSION

- HIV-positive people who have higher predicted CVD or CKD risk are at significant increased risk for future CVD or CKD
- The risks are multiplicative for those with greater degrees of risk, i.e. we observed a gradient from low to high risk for both CKD and CVD events

CONCLUSION

- Combining the CVD and CKD risk-scores improved prediction of CVD and CKD events, in particular CKD
- This suggests CVD and CKD risk in HIV-positive people should be assessed in tandem, and such risk factors treated

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REFERENCES

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