Determinants of De-novo High-Risk Carotid Ultrasound Features in Middle-Aged People Living with HIV

839

Napon Hiranburana[1,2], Waratchaya Walailaksanaporn[3], Aurauma Chutinet[3], Tanakorn Apornpong[1], Stephen J. Kerr[1,4,5], Porntep Amornritvanich[6], Anchalee Avihingsanon[1,2]

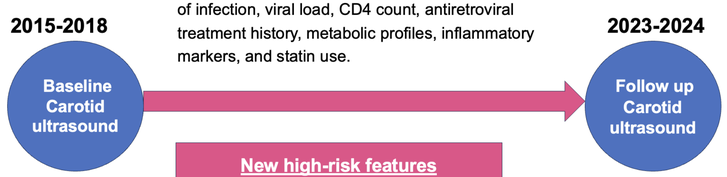
1 HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand, 2 Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, 3 Chulalongkorn Stroke Center of Excellence, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, 4. Biostatistics Excellence Centre, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, 5. The Kirby Institute, University of New South Wales, Sydney, Australia, 6. Cardiovascular unit, Department of internal medicine, Police general hospital.

BACKGROUND

- People living with HIV (PLWH) have a higher risk of cardiovascular and cerebrovascular events.
- Identifying factors driving the progression of high-risk carotid ultrasound features, indicative of subclinical atherosclerosis, is essential for improving preventive strategies and outcomes in this population.

METHODS

- PLWH aged ≥50 years at HIV-NAT, Bangkok
- Baseline data modelled included 10-year ASCVD risk, and HIV-related parameters including duration of infection, viral load, CD4 count, antiretroviral treatment history, metabolic profiles, inflammatory markers, and statin use.



New high-risk features
- Carotid intimal-medial thickness
- (CIMT) >0.9 mm
- thick (>4 mm.) or echolucent plaques.

Analysis method: Logistic regression was used to identify the factors associated with progression to high-risk carotid features

- Baseline intermediate-to-high 10-year ASCVD risk, protease inhibitor use, and CAC score ≥100 independently predicted the development of new high-risk carotid ultrasound features in middle-aged Thai PLWH.
- Early identification and intervention are crucial to mitigate cardiovascular risk.

RESULTS

Table 1: Demographic Characteristics by Presence of High-Risk Carotid Features on Follow-Up

Characteristic	Stable carotid ultrasound features (n=142)	New high risk carotid ultrasound features (n=87)	p-value
Age (years), median (IQR)	53.9 (51.4 - 56.6)	55.6 (52.3 - 61.3)	**0.002**
Baseline 10 yr-ASCVD (%)	4.94 (2.54 - 8.57)	7.78 (4.8 - 16.4)	**<0.001**
Male	78 (54.9%)	53 (60.9%)	0.41
BMI (kg/m^2)	23.1 (21.1 - 25.4)	23.0 (20.5-24.7)	0.53
Smoking status			0.37
Never smoke, n (%)	101 (71.1%)	55 (63.2%)	
Smoking history, n (%)	24 (16.9%)	21 (24.1%)	
Current smoking, n (%)	17 (12.0%)	11 (12.6%)	
Alcohol use, n (%)	27 (19.0%)	14 (16.1%)	0.60
Diabetes, n (%)	32 (22.5%)	33 (37.9%)	**0.016**
Hypertension, n (%)	41 (28.9%)	43 (49.4%)	**0.002**
Total cholesterol (mg/dL), median (IQR)	204 (178 - 230)	205 (187 - 232)	0.39
HDL(mg/dL), median (IQR)	48.0 (41.0 - 55.0)	45.5 (39.0 - 54.5)	0.41
LDL(mg/dL), median (IQR)	123.3 (102.2-146.9)	124.0 (101.8-152.6)	0.74
Triglyceride (mg/dL), median (IQR)	151 (101 - 200)	149 (99 - 230)	0.52
Triglyceride-glucose index	8.8 (8.5 - 9.2)	8.9 (8.4 - 9.4)	0.29
CKD-EPI <60 , n (%)	7 (5.0%)	7 (8.0%)	0.40
Duration on ART (years) median (IQR)	15.9 (11.4 -18.5)	16.4 (13.7 -19.3)	**0.08**
Current CD4+ T-cell count(cell/mm^3), median (IQR)	620.5 (467.0 - 797.0)	635.5 (513.0 - 808.0)	0.27
Nadir CD4+ T-cell count (cell/mm^3), median (IQR)	171.0 (92.0 - 240.0)	201.0 (111.0 - 279.0)	0.13

229 participants were analyzed, over a median follow-up period of 6.9 (IQR 6.6-7.4) years

Characteristic	Stable carotid ultrasound features (n=142)	New high risk carotid ultrasound carotid features (n=87)	p-value
HIV viral load < 50 copies/mL, n (%)	140 (98.6%)	84 (97.7%)	0.63
Baseline ART regimen , n (%) and cumulative exposure until follow up study, year (IQR)			
PIs, n (%), year (IQR)	43 (30.3%), 8.2(0.1-14.1)	40 (46.0%), 11.7 (1.4-15.9)	**0.02, 0.031**
NNRTIs, n (%) , year (IQR)	96 (67.6%), 11.6 (6.2-17.2)	46 (52.9%), 9.9 (3.8-17.6)	**0.04, 0.48**
INSTIs, n (%) , year (IQR)	3 (2.1%), 1.0 (0.3-1.9)	6 (6.9%), 1.4 (0.6-2.3)	0.09, 0.13
ABC exposed n (%), year (IQR)	14 (9.9%), 0.0 (0.0-3.8)	11 (12.6%), 0.0 (0.0-3.7)	0.52, 0.65
Inflammatory markers			
hs-CRP(mg/L), median (IQR)	1.0 (0.5 - 2.3)	1.3 (0.6 - 2.6)	0.12
IL-6 (pg/dL), median (IQR)	5.3 (3.8 - 7.2)	6.1 (4.4 - 7.8)	0.21
CIMT			
CIMT measurements (right carotid artery), mm., median (IQR)	0.6 (0.5 - 0.7)	0.6 (0.6 - 0.8)	**0.019**
CIMT measurements (left carotid artery), mm., median (IQR)	0.6 (0.5-0.7)	0.7 (0.6 - 0.8)	**<0.001**
CAC score			**<0.001**
0	90 (64.7%)	38 (44.2%)	
0-99	42 (30.2%)	32 (37.2%)	
100-400	2 (1.4%)	10 (11.6%)	
≥400	5 (3.6%)	6 (7.0%)	
On statin at baseline, n (%)	40 (28.2%)	31 (35.6%)	0.24
Statin use during follow-up			0.31
Remain statin Naïve, n (%)	69 (48.6%)	35 (40.2%)	
Start statin after follow up, n (%)	33 (23.2%)	21 (24.1%)	
Quit statin after follow up, n (%)	19 (13.4%)	10 (11.5%)	
Continue statin	21 (14.8%)	21 (24.1%)	
Duration between follow up CIMT (years), median (IQR)	6.9 (6.6 - 7.3)	7.0 (6.6 - 7.4)	0.24

CONCLUSIONS

- Baseline intermediate to high 10-year ASCVD risk, use of protease inhibitors, and a CAC score ≥100 were associated with the progression of high-risk carotid features, suggesting PLWH with these factors are particularly vulnerable to future high-risk atherosclerosis and cerebrovascular events.
- Early identification and intensive targeted interventions are essential to mitigate further cardiovascular complications in this population.

Figure: Adjusted Odds ratios (95%CI) for development of high-risk carotid features

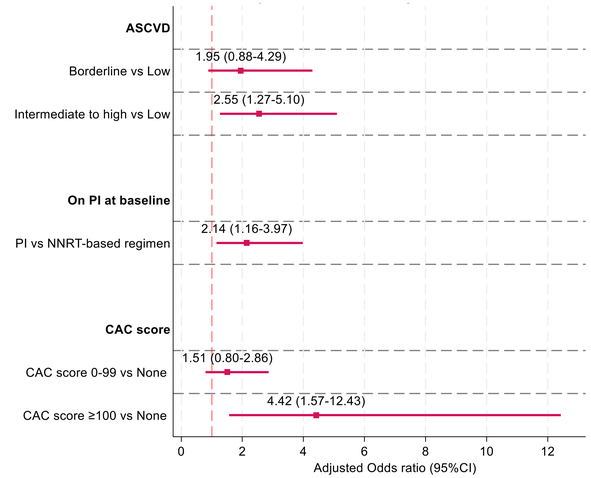


Table 2: Associations with development of high-risk carotid features, adjusted by age, sex, smoking, DM, HT, nadir CD4 and statin use

Baseline characteristics	Univariable			Multivariable		
	OR	95%CI	p-value	OR	95%CI	p-value
ASCVD risk						
Low	Ref			Ref		
Borderline	2.05	0.97 - 4.32	0.06	1.95	0.88 - 4.29	0.10
Intermediate to high	3.21	1.7 - 6.06	<0.001	**2.55**	**1.27 - 5.10**	**0.008**
Nadir CD4+ T-cell count (per 100 cell increase)	1.16	0.93 - 1.43	0.18	1.25	0.98 - 1.60	0.08
On PI at baseline	1.96	1.13 - 3.41	0.02	**2.14**	**1.16 - 3.97**	**0.02**
Cumulative year exposed on PI>10 year	1.99	1.16-3.43	0.013	**2.27**	**1.24-4.17**	**0.008**
Statin during follow-up						
Remained statin naive	Ref			Ref		
Initiated during follow-up	1.25	0.63 - 2.48	0.51	1.03	0.48 - 2.21	0.94
Ceased during follow up	1.04	0.44 - 2.47	0.93	0.91	0.36 - 2.34	0.85
Continued statin	1.97	0.95 - 4.09	0.07	1.23	0.54 - 2.81	0.62
CAC_score						
0	Ref			Ref		
0-99	1.80	0.99 - 3.28	0.05	1.51	0.8 - 2.86	0.21
≥100	5.41	2.06 - 14.2	0.001	**4.42**	**1.57 - 12.4**	**0.005**
hs-CRP >2 mg/L	1.01	0.57 - 1.78	0.97			
IL-6 > 6 pg/dL	1.53	0.9 - 2.62	0.20			
ABC exposure	1.32	0.57 - 3.06	0.51			

Acknowledgements: We gratefully thank all study participants and HIV-NAT study team.

Author Contact Information: napon.hir@gmail.com