Prevalence of cardiovascular disease (CVD) and Comparison of risk category predictions of Systemic Coronary Risk Evaluation Score-2 (SCORE2) and four other CVD risk calculators among people living with HIV(PLWH) in Türkiye

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Objective

CVD is a major cause of mortality among PLWH[1,2]. Data on the agreement between the commonly used risk estimation equations in Türkiye are limited. We aimed to determine prevalence of CVD risk and compare the degree of agreement between Atherosclerotic Cardiovascular Disease (ASCVD), Framingham (FRS-CVD), Modified Framingham (Mod-FRS), Data Collection on Adverse events of Anti-HIV Drugs (DAD) and SCORE-2 in a multicenter cohort. SCORE2 predicts 10-year risk of first-onset CVD in European populations. European countries were grouped into four risk regions (low, moderate, high, and very high) according to the WHO report on the risk of CVD mortalities[3]. CVD risk determination in the PLWH group with SCORE2 has not been previously studied in Türkiye.

Methods

This retrospective cross-sectional study included adult PLWH with a follow up visit between October 2019-2021 in 20 tertiary centers. Inclusion criteria were age 40-75 years, receiving antiretrovirals (ARVs) for at least six months. Exclusion criteria were: PLWH who have used ART for less than six months and who have never had a follow-up visit in the prior two years. Individuals aged < 40 or >75 years were also excluded, as most CVD risk prediction models do not include those people. All necessary information to calculate risk scores were collected during follow up visits with a standardized form.

Web-based tools for each score were used for calculations in the subgroup with no known CVD and not using lipid-lowering treatments. The individuals were considered at higher risk if their 10-year CVD risk was >20% for FRS-CVD and Mod-FRS, >20% for ASCVD, 5-year risk >5% for DAD and high/very high risk for SCORE2 for high-risk countries. Based on the interpretation of CVD risk, the individuals were categorized as high/very high and non-high risk. Agreement between the scores was assessed by Cohen's kappa (κ) statistics. The level of agreement was considered poor if κ <0.20, fair if κ = 0.21-0.40, moderate if κ = 0.41-0.60, substantial if κ = 0.61-0.80, and very good if κ >0.80.

The 2021 European Society of Cardiology[4] and 2019 American College of Cardiology/American Heart Association[5] guidelines were used to determine statin eligibility for participants.

Results

A total of 1425 PLWH were included into this study. Baseline characteristics of PLWH are shown in Table 1. Of 1425 PLWH (82.7% male), 151 had a confirmed CVD (10.6%). Median (IQR) age was 51 (45-58) years. Prevalence of CVD risk factors were: 45.7% current smoking, 34.9% hyperlipidemia, 29.5% hypertension, 18.3% obesity, 17% diabetes mellitus and 7.2% family history of early-onset CVD. Of 1425 PLWH, 1132 were eligible to assess CVD risk-scores. Risk strata distributions are displayed in the Table 2. According to the 2021 European[4] and American[5] guidelines, 75.3% and 47.1% of PLWH would be eligible for lipid-lowering agents, respectively. The FRS-CVD, Mod-FRS, DAD-reduced and SCORE2 had an overall agreement of 82%, 94%, 91% and 36% compared with ASCVD (κ=0.42, 0.64, 0.55 and 0.06) respectively and agreement was higher for lower scores (Table 3). In the multivariate logistic regression analysis, besides several traditional risk factors, low CD4 cell count in DAD, housing, and education in ASCVD and DAD were positively associated with CVD. Hovever, no HIV specific parameter was associated with a higher SCORE2 CVD risk (Table 4).

Table 1. Baseline characteristics of PLWH at enrollment

Participant Characteristics	Median (IQR) or proportion (n=1425)
Age, y, median (IQR)	51 (45-58)
Male, Sex	1178 (82.7)
Smoking (current smoker)	651 (45.7)
Alcohol use (1-7 or >7 drinks/week)	411 (28.9)
IV non-prescription drug use	35 (2.5)
Exercise & physical activity	248 (17.4)
Body mass index	
Obese (≥30 kg/m²)	258 (18.3)
Diabetes mellitus	242 (17)
Hypertension	420 (29.5)
Hypercholesterolemia	498 (34.9)
Family history of premature cardiovascular disease	102 (7.2)
Family history of CAD (In parents)	310 (21.1)
Years since HIV diagnosis, median (IQR)	5.0 (2.0-9.0)
Cumulative months of ART use, median (IQR)	
Protease Inhibitor	218 (15.3)
Nucleoside Reverse Transcriptase Inhibitor	1390 (97.5)
Others	1325 (93)
Nadir CD4+ cell count, cells/µL, median (IQR)	318 (168-480)
Nadir CD4<200 cells/µL	424 (29.8)
Current CD4+ cell count, cells/µL, median (IQR)	696 (479-920)
Viral load, <200 copies/mL	1345 (94.4)

Table 2. CVD risk prediction strata according to different CVD risk prediction models

(n=1132)				
ASCVD	Low risk(<5%) n (%)	Borderline risk (≥5% to <7.5%) n (%)	Intermediate risk (≥7.5% to <20%) n (%)	High risk(20%) n (%)
	459 (40.5)	189 (16.7)	378 (33.4)	106 (9.4)
FRS-CVD 10 year	Low risk(<10%) n (%) 464 (41)		Moderate risk (10% - <20%) n (%) 372 (32.9)	High risk (≥ 20%) n (%) 296 (26.1)
Modified Framingham	728 (64.3)		304 (26.9)	100 (8.8)
	<1% n (%)	1-5% n (%)	5-10% n (%)	>10% n (%)
DAD-reduced 5 year	62 (5.5)	651 (57.5)	276 (24.4)	143 (12.6)
DAD-reduced 10 year	8 (0.7)	319 (28.2)	375 (33.1)	430 (38.0)
Score2/ Score2-OP for high risk countries	Low-moderate n (%) 320 (28.3)		High risk n (%) 615 (54.3)	Very high risk n (%) 197 (17.4)

Table 3. Agreement between selected CVD risk scores

	ASCVD Non-high Risk	High Risk	Observed Agreement	Agreement for higher scores	Agreement for lower scores	Kappa
Framingham						
Non-high Risk	831	5	0.82 (0.77-0.88)	0.50 (0.46-0.54)	0.89 (0.84-0.95)	0.42 (0.39-0.46)
High Risk	195	101				
Modified Framingham						
Non-high Risk	995	37	0.94 (0.88-0.99)	0.67 (0.62-0.72)	0.97 (0.91-1.0)	0.64 (0.59-0.69)
High Risk	31	69				
DAD 5 year						
≤10	957	32	0.91 (0.86-0.97)	0.59 (0.55-0.64)	0.95 (0.89-1.0)	0.55 (0.51-0.59)
>10	69	74				
Score 2						
Non-high Risk	313	7	0.36 (0.33-0.40)	0.22 (0.19-0.25)	0.46 (0.42-0.50)	0.06 (0.05-0.08)
High Risk	713	99				

Table 4. Logistic regression analysis of three CVD risk scores for higher risk status

Variable	ASCVD 10 year risk >10 % Crude OR (95%CI)	p	Adjusted OR (95%CI)	p	DAD 5 year risk >%5 Crude OR (95%CI)	p	Adjusted OR (95%CI)	p	Score 2 High+Very high risk Crude OR (95%CI)	p	Adjusted OR (95%CI)	p
Age, years	1.24 (1.21-1.27)	<0.002	1.40 (1.34-1.46)	<0.001	1.16 (1.14-1.18)	<0.001	1.29 (1.25-1.34)	<0.001	1.06 (1.04-1.08)	<0.001	1.27 (1.23-1.32)	<0.001
Current smoking	2.11 (1.63-2.73)	<0.001	43.7 (22.8-83.7)	<0.001	4.21 (3.26-5.45)	<0.001	69.1 (37.9-126.1)	<0.001	13.79 (9.32-20.40)	<0.001	19.6 (11.2-34.3)	<0.001
BMI kg/m²	1.05 (1.02-1.09)	<0.001	1.07 (1.01-1.13)	0.016	1.01 (0.97-1.1)	0.595			0.99 (0.96-1.03)	0.770		
HT	4.28 (3.21-5.70)	<0.001	7.03 (4.2-11.7)	<0.001	2.44 (1.85-3.22)	<0.001	2.55 (1.64-3.96)	<0.001	2.10 (1.49-2.95)	<0.001	4.23 (2.67-6.71)	<0.001
DM	9.36 (6.32-13.9)	<0.001	19.7 (10.3-37.7)	<0.001	7.22 (4.85-10.7)	<0.001	15.9 (8.57-29.7)	<0.001	1.38 (0.92-2.06)	0.116		
HL	1.53 (1.14-2.05)	0.004	2.21 (1.36-3.58)	<0.001	1.66 (1.25-2.21)	<0.001	2.3 (1.51-3.57)	<0.001	1.64 (1.17-2.29)	0.004	1.88 (1.17-3.0)	0.008
Years (yrs) since diagnosis	1.02 (0.99-1.05)	0.210			1.02 (0.99-1.05)	0.123			0.987 (0.96-1.02)	0.381		
Nadir CD4		0.748				0.047				0.411		
<200 vs 200-349	0.87 (0.62-1.23)	0.446			0.846 (0.62-1.17)	0.305			0.795 (0.563-1.12)	0.192		
<200 vs ≥350	0.94 (0.70-1.27)	0.713			0.702 (0.53-0.93)	0.014			0.930 (0.68-1.27)	0.647		
<200 vs ≥200	0.92 (0.70-1.21)	0.548			0.75 (0.58-0.97)	0.031	0.53 (0.35-0.79)	0.002	0.92 (0.66-1.28)	0.617		
Alcohol usage >7 drinks/w	0.50 (0.22-1.15)	0.102			1.11 (0.57-2.14)	0.767			1.49 (0.68-3.29)	0.322		
Income >10.000 TL	0.69 (0.43-1.13)	0.141			0.606 (0.38-0.96)	0.033	0.77 (0.36-1.64)	0.497	0.759 (0.49-1.18)	0.220		
Housing/ owner	1.39 (1.07-1.81)	0.013	1.28 (0.8-2.00)	0.112	1.43 (1.11-1.83)	0.005	1.58 (1.07-2.33)	0.022	1.04 (0.80-1.36)	0.761		
Education		0.009		0.025		0.002		0.019		0.111		
<5 yrs vs 5-8 yrs	1.15 (0.84-1.59)	0.385	1.35 (0.78-2.34)	0.279	1.21 (0.89-1.65)	0.229	1.66 (1.03-2.69)	0.037	0.872 (0.62-1.23)	0.433		
<5 yrs vs 8-11 yrs	0.89 (0.63-1.29)	0.560	2.23 (1.21-4.13)	0.010	1.05 (0.74-1.47)	0.793	2.28 (1.34-3.88)	0.002	1.03 (0.70-1.51)	0.882		
<5 yrs vs >11 yrs	0.59 (0.4-0.883)	0.010	2.38 (1.20-4.72)	0.013	0.595 (0.41-0.87)	0.007	1.79 (0.97-3.18)	0.062	0.665 (0.46-0.97)	0.033		

*Factors with p < 0.1 in the univariate analyses were included in multivariable regression. HT: Hypertension; DM: Diabetes Mellitus; HL: Hyperlipidemia; TL: Turkish Lira; OR: Odds ratio; CI: Confidence interval; ASCVD: Atherosclerotic Cardiovascular Disease Risk Score; DAD: Data Collection on Adverse events of Anti-HIV Drugs

Conclusions

We found moderate agreement among CVD risk prediction tools evaluated in this study, except for SCORE2 which attributed a considerably higher CVD risk in 71.7% of PLWH. Whether those scores accurately estimate risk at population level needs further evaluation. CVD risk among PLWH in Türkiye might be underestimated, therefore close-monitoring of CVD risk is warranted. Furthermore, the potential impact of ARVs on CVD risk factors and strategies to reduce clinical risk, such as initiation of lipid-lowering agents should be strongly considered.

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