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Short Communication

Under-utilization of statins among people with HIV who were aged 40 years or older



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Abstract From June 2022 to April 2023, 1629 HIV-positive participants were assessed for the risk of atherosclerotic cardiovascular disease (ASCVD). The 10-year ASCVD risk of <5 %, 5 % to <7.5 %, ≥7.5 % to <20 % and ≥20 % were 59.9 %, 14.4 %, 20.7 % and 5.0 %, respectively; 440 (27.0 %) participants met the criteria for statin therapy, but only 171 (38.8 %) were prescribed statins.

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Introduction

The prevalence of non-communicable diseases, such as atherosclerotic cardiovascular disease (ASCVD), hypertension, dyslipidemia, and diabetes mellitus (DM), are higher among people with HIV (PWH) than among the general population.¹ PWH have a 1.5- to 2-fold higher risk for ASCVD when compared with people without HIV, particularly in those aged ≥ 45 years.² Furthermore, HIV infection is independently associated with an increased risk of ASCVD due to chronic inflammation, activation and dysfunction of the immune system, and immunosenescence.^{2,3}

Other than being the treatment of choice for dyslipidemia, statins have been shown to slow the progression of coronary plaque and exert anti-inflammatory and immunomodulatory effects.³ A systematic review and meta-analysis showed that statin use was associated with a 33 % reduction in all-cause mortality.⁴ However, statins are under-utilized among PWH who are eligible according to the ACC/AHA guidelines.^{5,6} In a cohort study of 16,409 PWH in the US, 7386 (45 %) (median age 53 years and 7 % with DM) met eligibility criteria for statin use per the guidelines (2001–2017); however, only 25%–32 % initiated statins in 2014–2017.⁷ The statin under-utilization was significantly higher in smokers and PWH without ASCVD or with low-density lipoprotein-cholesterol (LDL-C) ≥ 190 mg/dl.⁸ In this study, we aimed to assess the risk of ASCVD and status of statin use among PLWH aged ≥ 40 years who met the eligibility for initiating statins by the 2019 ACC/AHA guidelines.⁹

Methods

This cross-sectional study enrolled PWH aged 40–75 years who had been receiving HIV care at the outpatient clinics of the National Taiwan University Hospital between January to December 2022. Face-to-face questionnaire interview was conducted from June 2022 to April 2023. Exclusion criteria included PWH who were lost to follow-up, death, and stranded abroad due to COVID-19, and had missing data to estimate ASCVD risk. The rates of statin prescription were calculated based on documentation of statin prescription from June 2022 to April 2023. The study was approved by the Research Ethics Committee of the hospital (registration number, 202205071RIND) and written informed consent was obtained from all of the participants.

Clinical information was collected from the electronic medical records of the participants. The baseline data collected included demographics, smoking status, viral hepatitis co-infection, comorbidities (eg, DM, hypertension and hyperlipidemia), concurrent medications, updated plasma HIV RNA load, CD4 count, and lipid profile, body-mass index (BMI), systolic blood pressure, diastolic blood pressure, and statin therapy.

Ten-year ASCVD risk score was calculated with the use of ACC/AHA Risk Estimator Plus.¹⁰ According to the ACC/AHA guidelines, statins are recommended to be prescribed as (1) secondary prevention for people with clinical ASCVD; (2) primary prevention for people with LDL-C levels of ≥ 190 mg/dl; (3) primary prevention for people with DM who are aged 40–75 years and have LDL-C levels of 70–189 mg/dl; and (4) primary prevention for people aged 40–75 years

without DM or ASCVD who have an estimated 10-year ASCVD risk score ≥ 7.5 %.

Statistical analysis

Demographic and clinical characteristics are presented in average and standard deviation (SD) for continuous variables and in frequencies for categorical variables. Categorical variables were compared using χ^2 or Fisher's exact test whereas non-categorical variables were compared using the Student's *t* test. Kruskal–Wallis H-test analysis was used for multi-group comparisons. Only variables with a two-sided *p* value < 0.05 were considered statistically significant. Significant variables in univariate analysis were entered into a multiple logistic regression. SAS software version 9.4 (SAS Institute, Cary, NC) was used for statistical analysis.

Results

During the 10-month study period, 1629 (89.3 %) participants had complete data for ASCVD risk assessment (Fig. 1A). There were no significant differences in the demographic and clinical characteristics (age, sex, BMI, smoker, lipid levels and comorbidities) between the PWH enrolled and those not enrolled (data not shown). The characteristics of the participants with complete data for assessment of ASCVD score are shown in Supplementary Table 1. The participants were predominantly male (94.5 %) with a mean age of 50.4 years; and the mean plasma HIV RNA load was 1.36 log₁₀ copies/ml and CD4 count 670 cells/mm³ when the survey was conducted. The mean BMI was 25.0 kg/m², total cholesterol 178 mg/dl, LDL-C 107 mg/dl, and high-density lipoprotein cholesterol 49 mg/dl. Nearly one third (31.9 %) of the participants were current smokers and 16.9 % past smokers. The most common comorbidities of the participants were hyperlipidemia (35.3 %), followed by hypertension (21.4 %), DM (10.9 %), and chronic hepatitis B coinfection (14.2 %); and 11.2 % and 5.1 % had two and three or more comorbidities, respectively. A total of 516 (31.7 %) participants had been prescribed statins before this survey (Supplementary Table 1).

Of all participants, the ASCVD risks of < 5 %, 5 % to < 7.5 %, ≥ 7.5 % to < 20 % and ≥ 20 % were present in 976 (59.9 %), 235 (14.4 %), 337 (20.7 %) and 81 (5.0 %), respectively (Supplementary Table 2). Participants with ASCVD risk score ≥ 20 % were older with a mean age of 65.8 years; 59.3 % of them had DM, 63.0 % hypertension, 53.1 % hyperlipidemia; and 42.0 % received statins (Supplementary Table 2).

Overall, 440 participants (27.0 %) met criteria for statin therapy, including 40 (9.1 %) with ASCVD before the study, 127 (28.9 %) aged ≥ 45 years with DM and LDL-C of 70–189 mg/dl, 15 (3.4 %) with LDL-C ≥ 190 mg/dl, and 272 (61.8 %) with 10-year ASCVD risk ≥ 7.5 % (no DM or ASCVD) (Fig. 1B); and 14 (3.2 %) met two criteria for statin therapy. After excluding the 40 participants with ASCVD before the study (Table 1), we found that only 146 (36.5 %) participants who met the criteria for statins were prescribed statins. The participants who were prescribed statins had a higher BMI (mean, 26.2 vs 25.0 kg/m², *p* = 0.01), fasting glucose (109 vs 100 mg/dl, *p* < 0.001) and HbA1c levels

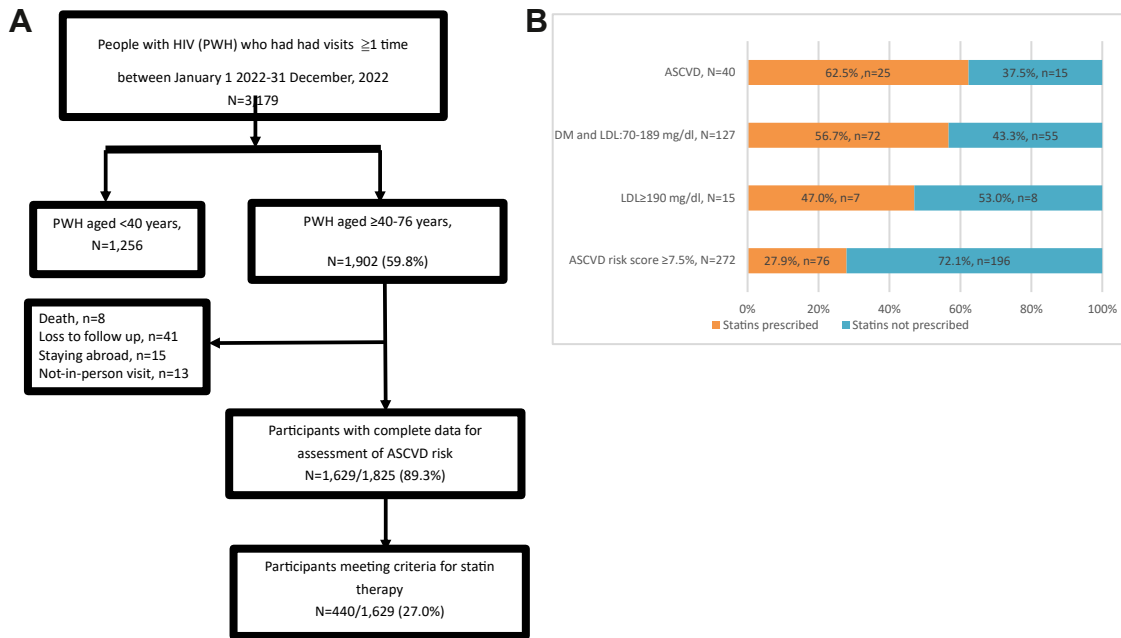


Figure 1. A. Study flow. B. Utilization of statins in participants who met eligibility for initiation of statins. ASCVD, atherosclerotic cardiovascular disease diagnosed before the study; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol.

(6.4 % vs 5.9 %, $p < 0.001$) and higher prevalence of DM (45.2 % vs 20.5 %, $p < 0.001$) (Table 1).

In multivariable analysis, we found that HCV seropositivity (AOR, 5.835; 95 % CI, 2.091–16.286) and a higher LDL-C level (AOR, 1.015; 95 % CI, 1.003–1.028) were associated with statin under-utilization (Supplementary Table 3).

Discussion

In this cross-sectional study among PWH aged 40–75 years who sought HIV care at a university hospital, only 38.8 % of PWH who met the criteria for statin therapy were prescribed statin therapy. Statins were less likely to be prescribed to PWH who were HCV-seropositive and those who had higher LDL-C levels.

The percentage of the participants meeting the 2019 ACC/AHA guidelines on statin therapy who were prescribed statin therapy ranged from 38.5 % to 71.8 % in the published studies.^{5,6,8} The differences in terms of statin prescription among the studies could be related to the study populations. For example, compared with the study by Cottino et al.,⁸ in which 71.8 % were prescribed statins, our study population consisted predominantly of male participants (94.5 % vs. 53.0 %), had a lower mean BMI (25.0 vs. 29.1 kg/m²), and lower percentages of comorbidities such as hypertension (21.4 % vs. 52.1 %) and chronic kidney disease (1.8 % vs. 21.3 %).

We found that HCV seropositivity and a higher LDL-C level were associated with statin under-utilization. While the explanation for the association between HCV seropositivity and statin under-utilization remains unclear, the paradoxical correlation between higher LDL-C levels and statin under-utilization could be because fasting lipid data in our study were collected cross-sectionally between 2022

and 2023, when PWH who had received statins had lower LDL-C while those who had not received statins had higher LDL-C levels.

Smoking has been identified as a predictor of statin under-utilization in published reports.^{5,8} The finding of a higher rate of smoking among PLWH not having received statins might imply that the lack of awareness among HIV health-care providers of smoking as a modifiable risk factor for CVD. Other possible reasons could be that physicians prioritized smoking cessation over statin prescription; or that current smokers were more likely to have additional medical conditions (eg. mental health disorders and pain) or competing priorities (eg. insurance issues) that needed to be addressed.

Our findings underscore the importance of establishing a standard of care for HIV health-care providers and urging infectious-disease specialists to keep up with the latest guidelines on statin therapy. In addition to addressing smoking cessation, limited time for providers to address cardiovascular complications and discuss statin use, lower rates of consecutive annual visits,⁵ and less attention to primary prevention than to secondary prevention^{5,8} might have all contributed to statin under-utilization in our already-strained health care system during the COVID-19 pandemic.

There are several limitations to this survey. This was a single-center study and the generalizability of the results may be limited. We did not identify the medications that had been prescribed by outside health-care providers and might have underestimated the rate of statin use. The cross-sectional study design precludes us from establishing causal relationship between the statistically significant variables identified and under-utilization of statins.

Our study highlights the space for improvement in that the rate of statin prescription among PWH who are eligible

Table 1 Comparison of clinical characteristics between the 146 participants who met the criteria to initiate statins and were prescribed statins and the 254 participants who met the criteria to initiate statins but were not prescribed after the exclusion of the 40 patients who had been diagnosed with ASCVD before the study.

	On statin N = 146	Not on statin N = 254	All N = 400	P value
Male gender, n (%)	131 (89.7)	247 (97.2)	378 (94.5)	0.0024
Age, mean (SD), years	57.7 (9.3)	57.0 (7.7)	57.3 (8.3)	0.4751
Body-mass index, mean (SD), kg/m ²	26.2 (4.4)	25.0 (4.2)	25.4 (4.3)	0.0103
BW, mean (SD), kg	74.1 (14.3)	71.4 (13.6)	72.4 (13.9)	0.0645
ASCVD score, mean (SD)	13.0 (9.0)	13.6 (7.8)	13.4 (8.2)	0.5638
ASCVD score \geq 7.5 %	120 (82.2)	238 (93.7)	358 (89.5)	0.0006
Current smoker, n (%)	47 (32.2)	137 (53.9)	184 (46.0)	<0.0001
Diabetes mellitus, n (%)	66 (45.2)	52 (20.5)	118 (29.5)	<0.0001
Hypertension, n (%)	58 (39.7)	94 (37.0)	152 (38.0)	0.5945
CKD, n (%)	3 (2.1)	5 (2.0)	8 (2.0)	0.9527
Positive HBsAg, n (%)	21 (14.4)	42 (16.5)	63 (15.8)	0.6692
Positive anti-HCV, n (%)	7 (4.79)	47 (18.50)	54 (13.5)	<0.0001
CD4, mean (SD), cells/mm ³	702 (297)	648 (285)	668 (290)	0.0748
Plasma HIV RNA load, mean (SD), log ₁₀ copies/ml	1.3 (0.1)	1.4 (0.3)	1.4 (0.3)	0.0590
Systolic blood pressure, mean (SD), mm Hg	135 (17)	135 (20)	135 (19)	0.8867
Diastolic blood pressure, mean (SD), mm Hg	82 (13)	82 (13)	82 (13)	0.7929
TG, mean (SD), mg/dl	188 (159)	195 (148)	192 (152)	0.6464
T-cholesterol, mean (SD), mg/dl	175 (42)	189 (35)	184 (39)	0.0011
HDL-C, mean (SD), mg/dl	48 (12)	45 (11)	46 (11)	0.0013
LDL-C, mean (SD), mg/dl	102 (37)	118 (32)	112 (35)	<0.0001
Fasting glucose, mean (SD), mg/dl	109 (25)	100 (21)	104 (23)	0.0005
HbA1c, mean (SD), %	6.4 (1.2)	5.9 (0.8)	6.1 (1.0)	<0.0001

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; BMI, body-mass index; BW, body weight; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; TG, triglyceride.

for statins is low in the modern ART era. More information, education and communication on timely prescription of statins to PWH should be provided to HIV health-care providers, given that fact that PWH have a higher risk for ASCVD and are living longer after early diagnosis of HIV infection and ART initiation with sustained viral suppression.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jmii.2024.01.003>.