Lipoprotein(a) Trajectories in Aging PLWH on Long-Term Suppressive ART: A Seven-Year Follow-Up Study

654

Napon Hiranburana[1,2], Tanakorn Apornpong[1], Stephen J. Kerr[1,3,4], Sasiwimol Ubolyam[1,2], Sarawut Siwamogsatham[5], Pairoj Chattranukulchai[5], Weerapan Khovidhunkit[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 The Kirby Institute, University of New South Wales, Sydney, Australia, 4.Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand,
5.Division of Cardiovascular Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.,
6. Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

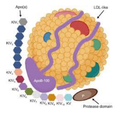
BACKGROUND

- Lipoprotein(a) [Lp(a)] is a genetically determined lipoprotein associated with atherosclerotic cardiovascular disease (ASCVD).
- Current guidelines recommend a once-in-a-lifetime measurement, assuming stability over time.
- Chronic inflammation in people living with HIV (PLWH) may influence Lp(a) trajectories.
- Data on long-term Lp(a) stability in aging PLWH on suppressive ART remain limited.

METHODS

We analyzed PLWH with viral suppression from the HIV-NAT 006 cohort, aged ≥50 years, with stored serum at baseline (2016–2017) and follow-up (2023–2024).

Lp(a) was measured by isoform-dependent immunoturbidometric assay and classified by baseline quartiles and increased cardiovascular risk-cutpoint (>30 and >50 mg/dL).



1. **Longitudinal changes in Lp(a) stratified by baseline Lp(a) cardiovascular risk-cutpoint (>30 and >50 mg/dL)**
2. **Quartile persistence and reclassification rates were assessed by Stuart-Maxwell test.**
   - **Subgroup analyses compared participants with elevated baseline interleukin-6 (IL-6 >6 ng/dL) versus normal IL-6**
3. **Agreement of log[Lp(a)] across two time points was assessed using Bland-Altman plots.**

Over 7 years, Lp(a) levels were stable in aging PLWH on suppressive ART, suggesting repeat testing is unnecessary within this interval except in those with elevated IL-6 or borderline values.

RESULTS

Table 1: Baseline and follow-up lipoprotein(a) [Lp(a)] levels

Variable	N=176
Male	94 (53.4%)
Female	82 (46.6%)
Age at first Lp(a) measurement, years	54.5 (51.7- 59.5)
Interval between baseline and follow-up Lp(a), years	7.3 (7.1-7.7)
IL6, pg/ml	6.0 (4.4-7.8)
IL6<6 pg/ml	87 (49.7%)
IL6≥6 pg/ml	88 (50.3%)
Baseline Lp(a)	N (%)
Median (IQR)	14.06 (4.91-26.69)
Lp(a)>30 mg/dL	40 (22.73%)
Lp(a)>50 mg/dL	19 (10.80%)
Log10(Lp(a) mg/dL	1.15 (0.69-1.43)
Follow-up Lp(a)	N (%)
Median (IQR)	13.23 (6.12-31.45)
Lp(a)>30 mg/dL	46 (26.14%)
Lp(a)>50 mg/dL	19 (10.80%)
Log10(Lp(a) mg/dL	1.12 (0.79 -1.50)
Change from baseline	
Median difference (IQR)	0.92 (-2.16 to 4.77) p-value (*Wilcoxon signed-rank test)=0.019
Percent Difference change from baseline	N (%)
<20%	64 (36.36)
≥ 20%	112 (63.64)

Quartile analyses indicated strong persistence in highest quartiles (89% remained Q4:>26.7 mg/dL), with greater reclassification in others ; (p=0.011)

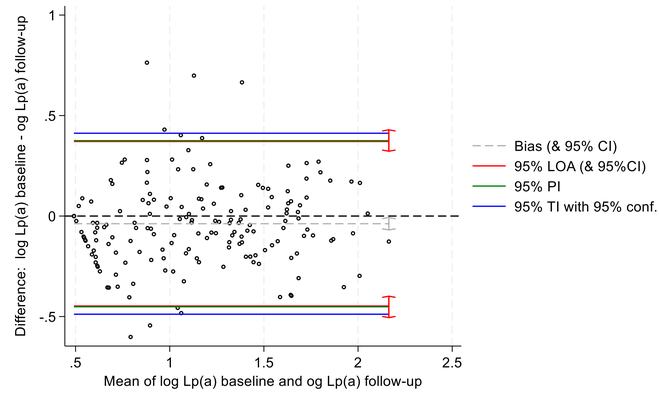
Table 3: Agreement between baseline and follow-up Lp(a) quartiles

Overall population	Follow-up Lp(a) quartile				
Baseline Lp(a) quartile	Q1	Q2	Q3	Q4	Total
Q1 <4.91	27 (61.36)	16 (36.36)	1 (2.27)	0 (0)	44 (100)
Q2 (4.91-14.05)	4 (9.09)	30 (68.18)	10 (22.73)	0 (0)	44 (100)
Q3 (14.06-26.69)	1 (2.27)	11 (25)	19 (43.18)	13 (29.55)	44 (100)
Q4 (>26.69)	0 (0)	2 (4.55)	3 (6.82)	39 (88.64)	44 (100)
p-value*= 0.011					
*Stuart-Maxwell test					
Participants with IL-6 <6 pg/mL	Follow-up Lp(a) quartile				
Baseline Lp(a) quartile	Q1	Q2	Q3	Q4	Total
Q1 <4.91	11 (68.75)	5 (31.25)	0 (0)	0 (0)	16 (100)
Q2 (4.91-14.05)	3 (11.54)	15 (57.69)	8 (30.77)	0 (0)	26 (100)
Q3 (14.06-26.69)	0 (0)	6 (28.57)	8 (38.1)	7 (33.33)	21 (100)
Q4 (>26.69)	0 (0)	0 (0)	1 (4.17)	23 (95.83)	24 (100)
p-value*= 0.152					
*Stuart-Maxwell test					
Participants with IL-6 ≥6 pg/mL	Follow-up Lp(a) quartile				
Baseline Lp(a) quartile	Q1	Q2	Q3	Q4	Total
Q1 <4.91	15 (55.56)	11 (40.74)	1 (3.7)	0 (0)	27 (100)
Q2 (4.91-14.05)	1 (5.56)	15 (83.33)	2 (11.11)	0 (0)	18 (100)
Q3 (14.06-26.69)	1 (4.35)	5 (21.74)	11 (47.83)	6 (26.09)	23 (100)
Q4 (>26.69)	0 (0)	2 (10)	2 (10)	16 (80)	20 (100)
p-value*= 0.007					
*Stuart-Maxwell test					

Table 2: Longitudinal changes in lipoprotein(a) [Lp(a)] stratified by baseline Lp(a) thresholds and IL-6 status

Subgroup analysis	Lp(a) baseline ≤30 mg/dL	Lp(a) baseline >30 mg/dL	p-value (between group)
n	136	40	
Lp(a) baseline, median (IQR)	8.84 (3.91, 18.02)	49.42 (38.88, 69.09)	
Lp(a) follow-up, median (IQR)	9.28 (5.28, 18.10)	46.51 (39.44, 66.66)	
Difference, median (IQR)	1.03 (-0.67, 4.19)	-3.32 (-17.58, 12.26)	0.032
p-value within group	<0.001	0.450	
Subgroup analysis	Lp(a) baseline ≤ 50 mg/dL	Lp(a) baseline >50	p-value (between group)
n	157	19	
Lp(a) baseline, median (IQR)	10.97 (4.21, 21.76)	72.22 (56.91,87.19)	
Lp(a) follow-up, median (IQR)	11.82 (5.6, 24.22)	64.37 (45.16, 103.74)	
Difference, median (IQR)	0.97 (-1.31, 4.40)	-11.35 (-32.88, 19.56)	0.076
p-value within group	<0.001	0.459	
Subgroup analysis	IL6<6 pg/ml	IL6≥6 pg/ml	p-value (between group)
n	87	88	
Lp(a) baseline, median (IQR)	14.41 (7.12,33.87)	12.69 (4.18, 25.86)	
Lp(a) follow-up, median (IQR)	15.97 (6.91, 35.7)	12.35 (6.12, 27.04)	
Difference, median (IQR)	1.05 (-3.3, 5.48)	0.88 (-1.69, 4.37)	0.950
p-value within group	0.138	0.064	
Note: Within-group p-values were calculated using the Wilcoxon signed-rank test comparing baseline and follow-up Lp(a) levels.			

Figure: Bland-Altman plot to assess the agreement between **baseline log[Lp(a)] and follow up log[Lp(a)]**



Bland-Altman analysis showed minimal bias overall and narrow limits of agreement between log(baseline Lp(a)) and log(follow-up Lp(a)), indicating **stability of Lp(a) levels over time.**

CONCLUSIONS

- **In aging PLWH on long-term ART, Lp(a) levels remain stable over 7 years, with strongest persistence in extreme quartiles and those with Lp(a) below guideline cut points (<30 or <50 mg/dL).**
- **However, significant variability was observed in intermediate quartiles and among participants with higher baseline IL-6.**

Author Contact Information: napon.hir@gmail.com