#1187 REAL-WORLD, OBSERVATIONAL STUDY OF ELEVATED Lp(a) AND CARDIOVASCULAR EVENTS

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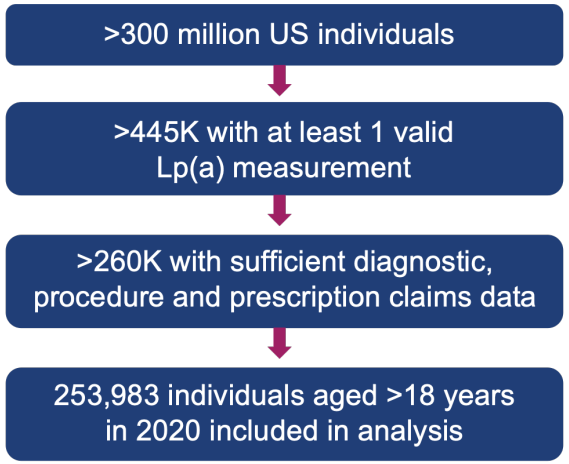
Background and Aims

Lipoprotein(a) [Lp(a)] is rarely measured and the impact of inherited elevation on cardiovascular disease (CVD) is incompletely understood. This study aims to characterize Lp(a) levels and cardiovascular events in a large US dataset.

Methods

The Family Heart Database includes more than 300 million people in the US with diagnostic, laboratory, procedure and prescription claims from 2012-2020. A cohort of 253,983 >/=18 years (**Figure 1)** with an Lp(a) level and sufficient claims data were included in this observational cohort study.

Figure 1: Family Heart Database



Methods (cont.)

Most (93%) Lp(a) levels were reported in nmol/L. Major CVD events were tracked from time of first Lp(a) measurement to determine annual CVD event rate.

Individuals having low versus high Lp(a) level were compared across 6 groups with or without Atherosclerotic Cardiovascular Disease (ASCVD) and/or diagnosed or probable Familial Hypercholesterolemia (FH) using case-controlled propensity score matching. Probable FH was determined using a validated machine learning model.

Results

Individuals were female (55%); over 60 years (58%); Black (8%), Hispanic (7%) and White (56%). Mean Lp(a) levels were 119, 81 and 87 nmol/L across Black, Hispanic and White individuals, respectively. Individuals with low (<16 nmol/L; <20th percentile) versus high (>/= 165 nmol/L; >/=80th percentile) Lp(a) (**Table 1**) were tracked for 911+/-690 and 878+/-761 days, respectively. In several risk groups, individuals with high Lp(a) levels had significantly greater annual CVD event rates (**Table 2**). Although Blacks had higher mean Lp(a) levels, Blacks and Whites with elevated Lp(a) had similar annual CVD event rates (both 2.8%, p-value=0.88).

Table 1: Lp(a) Level in Individuals at High (≧80th) and Low (<20th) Percentile

Percentile of Individuals with Lp(a) Below Threshold	Lp(a) Threshold nmol/L	Classification
0%	0.3	Low
5%	5.0	Low
10%	10.0	Low
15%	13.0	Low
20%	16.0	Normal
80%	165.0	High
85%	191.0	High
90%	227.0	High
95%	299.0	High

Table 2: Annual CVD Event Rate

Risk Group	High Lp(a) (n)	Low Lp(a) (n)	Absolute Difference [95% CI]	p-value	% Diff.
No ASCVD or FH	0.9% (28,977)	0.8% (28,977)	0.18 [0.08, 0.27]	<0.001	22.7%
ASCVD only	4.4% (10,049)	3.9% (10,049)	0.49 [0.13, 0.87]	0.004	13.0%
Probable FH + ASCVD	3.9% (410)	2.8% (410)	1.1	0.09	40.2%
Probable FH only	1.2% (687)	0.6% (687)	0.64 [0.03, 0.13]	0.02	114.3%
Diagnosed FH + ASCVD	4.7% (35)	2.5% (35)			
Diagnosed FH only	1.2% (64)	0% (65)			

Discussion

- In this very large US database, Lp(a) ≧80th percentile versus <20th percentile predicted incident ASCVD events in primary and secondary prevention as well as in individuals with probable FH.
- Notably, the 80th percentile for Lp(a) (165 nmol/L) in this database is higher than reported previously for White and Black Americans (100 and 148 nmol/L, respectively). [1] It is possible that the 253,983 individuals who had an Lp(a) measurement from the database of over 300 million were at high CV risk and thus may not represent the general population. Alternatively, the small sample size of 2,929 Whites and 1899 Blacks in the previous report might also be a factor.[1]
- Our data agrees with previous studies which have found higher Lp(a) levels in Blacks versus Whites. As noted in the UK Biobank participants – Lp(a) levels drive risk.[2] Following propensity score matching on race, Black and White individuals with elevated Lp(a) levels had similar ASCVD risk.[2]

Conclusion

Within a large real-world dataset, individuals with high versus low Lp(a) levels experience an increased rate of CVD events, regardless of race, during an observational follow-up period. Lp(a) levels, rather than race, drive the risk.

1 Marcovina SM, Albers JJ, Wijsman E, et al. Differences in Lp(a) concentrations and apo(a) polymorphs between black and white Americans. J. of Lipid Res. 1996. 37:2569-2585.
2 Patel AP, Wang M, Pirruccello JP, Ellinor et al. Lp(a) (Lipoprotein[a]) Concentrations and Incident Atherosclerosis Cardiovascular Disease: New Insights From a Large National Biobank. Arterioscler Thromb Vasc Biol. 2021. 41:465-474.

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