Published in final edited form as:
Am J Med. 2008 February ; 121(2): e17–e19. doi:10.1016/j.amjmed.2007.10.008.

Lipoprotein(a) and Venous Thromboembolism

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Keywords

Lp(a); venous thrombosis; pulmonary embolus; risk factors; prospective study; epidemiology

October 3, 2007

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Editor-in-Chief

The American Journal of Medicine

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To the Editor:

Sofi et al. recently reported a meta-analysis of six case-control studies suggesting that high lipoprotein(a) [Lp(a)] levels (>300 mg/L compared with <300 mg/L) were associated in a random effects model with a 1.77 fold (95% CI, 1.14–2.75) increased risk of venous thromboembolism.[1] That report overlooked a cohort study, our Longitudinal Investigation of Thromboembolism Etiology (LITE),[2] which found no such association over eight years. Our study may have been overlooked because the units were mislabeled mg/dL rather than mg/L, and values were 1/3 of conventional values because they reflected only the protein part of Lp (a).[2] For comparison with the meta-analysis, we report here LITE findings for four more years of follow-up using conventional Lp(a) units.

The LITE investigators pooled the Atherosclerosis Risk in Communities (ARIC) Study and Cardiovascular Health Study (CHS).[3] Participants were whites and African Americans ≥ 45 years from six US communities at baseline in the late 1980s. Lp(a) was measured at baseline as previously described,[2] and dichotomized for this analysis at 300 mg/L. Venous thromboembolism events were identified through 2001 and validated via physician review of hospital records. Because of the large difference in Lp(a) distributions between whites and African Americans, race-specific Cox proportional hazards regressions were run.

The LITE sample included 19,921 participants who at baseline had no venous thromboembolism history, were not taking warfarin, and had Lp(a) measured. The percentage of Lp(a) values >300 mg/L was 2.7% in whites and 11.5% in African Americans. 327 venous

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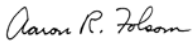
thromboembolism events occurred over 187,044 person-years of follow-up in whites, and 83 events in 57,246 person-years in African Americans. The age and sex-adjusted hazard ratio (95% CI) for Lp(a) >300 mg/L versus ≤300 mg/L was 1.12 (0.55–2.27) for whites and 1.31 (0.69–2.47) for African Americans. These were little changed after further adjustment for body mass index, diabetes, and factor $VIII_c$. When pooled and adjusted also for race, the hazard ratio was 1.21 (0.75–1.94).

We found a much smaller hazard ratio of venous thromboembolism in relation to elevated Lp (a) than the pooled odds ratio estimate of Sofi et al.[1] Sofi et al. identified statistically significant heterogeneity among studies; two of the six prior case-control studies had odds ratios similar to our estimates.[1] Although Lp(a) in our study was measured well before most venous thromboembolism events, this should not bias our results because the Lp(a) level is quite stable within individuals. Thus, based on all current evidence, any association between elevated Lp (a) and venous thromboembolism is likely modest, at best.

Sincerely,



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for the LITE Investigators

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References

1. Sofi F, Marcucci R, Abbate R, Gensini GF, Prisco D. Lipoprotein(a) and venous thromboembolism in adults: A meta-analysis. Am J Med 2007;120:728–733. [PubMed: 17679133]
2. Tsai AW, Cushman M, Rosamond WD, Heckbert SR, Polak JF, Folsom AR. Cardiovascular risk factors and venous thromboembolism incidence: The Longitudinal Investigation of Thromboembolism Etiology Study. Arch Intern Med 2002;162:1182–1189. [PubMed: 12020191]
3. Cushman M, Tsai AW, White RH, Heckbert SR, Rosamond WD, Enright P, Folsom AR. Deep vein thrombosis and pulmonary embolism in two cohorts: The Longitudinal Investigation of Thromboembolism Etiology. Am J Med 2004;117:19–25. [PubMed: 15210384]