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Title

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ABSTRACT

Introduction: Lipoprotein(a) [Lp(a)] is a predominantly genetically determined risk factor for atherosclerotic cardiovascular disease (ASCVD); however, menopause is one of the few conditions that can lead to an increase in Lp(a). We aimed to investigate whether menopause status modifies the association between Lp(a) and ASCVD risk.

Methods: A total of 153,890 pre- and post-menopausal women free of prior ASCVD were studied using data from the UK Biobank. Menopause status was based on self-report while ASCVD was a composite outcome based on ICD10-coded myocardial infarction, stroke or cardiovascular death. Multivariable Cox proportional hazards models evaluated the association between Lp(a) and incident ASCVD events stratified by menopause status.

Results: The median age was 56.1 years, with 60% of women post-menopausal. Median Lp(a) was 22.5 [10.1, 62.1] nmol/L, 21% had Lp(a) $\geq$ 75 nmol/L, and 12% had Lp(a) $\geq$ 125 nmol/L. There were 5,160 (3.4%) incident ASCVD events during a median follow up of 13.7 years. Standard deviation increases in Lp(a) were associated with higher risk of ASCVD events among pre-menopausal (HR 1.06, 95% CI 1.00-1.12, p = 0.041) and post-menopausal women (HR 1.06, 95% CI 1.03 - 1.09, p <0.001). Among post-menopausal women, Lp(a) between 75-125 nmol/L (HR 1.13, 95% CI 1.01, 1.25, p = 0.03) and $\geq$ 125 nmol/L (HR 1.15, 95% CI 1.05, 1.26, p = 0.003) were associated with increased ASCVD risk when compared to Lp(a) < 75 nmol/L. The association between Lp(a) and ASCVD risk did not vary with menopause status (p-interactions >0.05).

Conclusion: Lp(a) is an independent risk factor for ASCVD events for both pre- and post-menopausal women.