Loss of Y Chromosome and Major Cardiovascular Events in a Prospective Study of Older Men

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Abstract

Background: Loss of the Y chromosome (LOY) from a percentage of circulating leukocytes is common in older men, and associated with cardiovascular risk. However, most studies have involved men with pre-existing disease, not healthy men followed prospectively. The aim of this study was to investigate association between LOY and risk of incident major adverse cardiovascular events (MACE), including myocardial infarction (MI) and ischemic stroke.

Methods: This study includes 5,131 men aged ≥65 from the ASPirin in Reducing Events in the Elderly (ASPREE) trial with no prior cardiovascular disease at baseline. LOY percentage was measured in peripheral blood using microarrays and the Log-R-Ratio method. MACE, including myocardial infarction (MI) and ischemic stroke, were collected during the trial and subsequent observational follow-up. Cox regression assessed associations of LOY as a continuous (per SD) and categorical (decile-based) variable. D1-D6 (reference) represented no LOY, D7-D9 moderate, and D10 substantial.

Results: Over median 8.4 years follow-up, 9.8% (n=505) men experienced MACE, with 5% (n=256) MI and 4% (n=207) ischemic stroke. In the fully-adjusted model, each SD increase in LOY was associated with 14% higher MI risk (HR per SD:1.14; 95% CI: 1.02-1.28). Men with substantial LOY (D10) had 68% higher MI risk versus men without LOY (HR:1.68; 95% CI: 1.16-2.54). No associations were observed for ischemic stroke. Results were robust to sensitivity analyses. In 191,340 men aged 40-70 years from the UK Biobank, LOY was also associated with MI (HR per SD:1.03; 95% CI: 1.01-1.06).

Conclusion: LOY is associated with increased MI risk, but not stroke, in older men.