Editorial

Large-Scale Pooled Data and Beyond

Hirohito Metoki

Department of Community Medical Supports, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan

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There is little evidence of the association between serum uric acid and cardiovascular mortality for non-white population. A recent study from a single Japanese cohort with 3487 subjects reported that there is a significant association between high uric acid at baseline and all-cause and cardiovascular mortalities in women; however, linearity is not mentioned¹⁾. The authors of this study tried to evaluate the association between serum uric acid levels and cardiovascular mortality with a 10-year follow-up of 36,313 subjects from 13 integrated existing cohorts regarding cardiovascular mortality in Japan and suggested that there is a J- or U-shaped association between uric acid levels and cardiovascular mortality²⁾.

Although a U-shaped association between uric acid and cardiovascular mortality was revealed, the reason for such a U-shaped association is unclear. There may be a reverse causal bias in this study. A previous study tried to examine the causal effect of uric acid levels on cardiovascular events using Mendelian randomization and revealed a linear association between uric acid and cardiovascular events among 3315 subjects³⁾. After trying to exclude reverse causal bias in several ways including censoring deaths in the first several years, the observed association still remained. As previously reported⁴⁾, pooled data of huge number of participants enabled us to analyze in detail with large number of endpoints.

In a previous report, U-shaped association of uric

acid with loss of kidney function was observed^{4, 5)}. The same pathway may be acting between cardiovascular mortality and loss of kidney function. Although hypouricemic patients may be rare, genetic polymorphism or variants are reported to cause hypouricemia^{6, 7)}. In near future, the role of genetic differences among participants for the U-shaped association may be revealed. In addition, the combination of genetic background and environmental factors may cause each linear association to appear as a U-shaped association.

There are some sex-based differences in uric acid metabolism. In addition, subtype-specific cause is also unclear. Here we can know reveal this U-shaped association and sex heterogeneity; therefore, our next step is to reveal the reason why there are U-shaped association between serum uric acid and cardiovascular mortality with fine classified endpoints and with fine classified background.

Conflicts of Interest

None.

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Address for correspondence: Hirohito Metoki, Division of Public Health, Hygiene and Epidemiology, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai, 981-8558, Japan

E-mail: hmetoki@tohoku-mpu.ac.jp

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