A Bio-demographic Analysis of General, Independent, Joint, GxG and GxE Interaction Effects of FOXO Genotypes on Longevity

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Abstract:

We extend/apply the bio-demographic and statistical methods to genotypic/phenotypic data from 1,104 Han Chinese centenarians and 1,406 middle-age controls. Our estimates show that long-term survival probability from middle-age to age 100+ for female carriers of *FOXO1A-209* or *FOXO1A-213* are 29% (*P*=0.007) or 30% (*P*=0.015) lower than female non-carriers; the general negative impacts of *FOXO1A-213* in men is similar to that in women, but the male effect of *FOXO1A-209* is not significant. The general effects on long-term survival for those who carry one of the three minor alleles of *FOXO3A* are 61-73% (P=0.0002-0.005) higher in women and men. We present the independent, joint and interactive effects of *FOXO1A* and *FOXO3A* on long-term survival, taking into account presence or absence of another relevant genotype. We find that there are substantial gender differences in the independent effects of *FOXO1A* and *FOXO3A* on long-term survival. The positive effects of *FOXO3A* and negative effects of *FOXO1A* largely compensate each other if one carries both, although *FOXO3A* has a stronger impact. The 10-year-follow-up cohort analysis show that, adjusted for various confounders, the positive effects of *FOXO3A* on survival remain statistically significant at ages 92+, but the negative effects of *FOXO1A* disappear; GxG interactions between *FOXO1A-209* and *FOXO3A-310* or *FOXO3A-292* increase mortality risk by 32-36% (P<0.05); GxE interaction between *FOXO1A-209* and regular exercise reduces mortality risk by 31-32% (P<0.05). The first-hand findings concerning effects of *FOXO1A* and its interaction with regular exercise on longevity were generally replicated in Southern and Northern China Han women.

Key words:

Bio-demographic analysis; *FOXO* genes; GxG and GxE interactions; longevity; mortality