Severe obesity is associated with novel single nucleotide polymorphisms of the ESR1 and PPARg locus in Han Chinese
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ABSTRACT
Background: A large number of potential obesity loci have been reported. At least 18 genes have been replicated in a minimum of 5 studies on obesity-related phenotypes. Fourteen additional genes have been associated with obesity in Asians.

Objectives: Our objectives were to examine how many common variants of these candidate genes are associated with severe obesity in Han Chinese and how they are combined to exert their effects. Design: In total, 304 severely obese patients [body mass index (BMI; in kg/m2) > 39] and 304 control subjects (BMI < 24) participated in a 2-staged association study. Subsequently, 220 additional severely obese patients (BMI ≥ 35) and 338 controls (BMI < 24) were recruited to replicate the results. All of the controls were age-, sex-, education- and residence-matched. Finally, a pooled analysis was carried out based on all 514 cases and 606 controls with complete information.

Results: The first-stage association analysis in 94 cases and 94 controls found 18 potentially associated single nucleotide polymorphisms (SNPs) (P = 0.01–0.1). The significance of 3 novel common SNPs, 1 on ESR1 and 2 on PPARc, were confirmed in the second stage and replicated further with odds ratios ranging from 1.89 to 2.24. The combined effect of these 3 genes was stronger (odds ratio: 5.27; 95% CI: 2.25, 12.32) than that from any individual gene.

Conclusions: Severe obesity in Han Chinese was associated with 3 novel common SNPs for ESR1 and PPARc. These 2 genes collectively result in a 5-fold risk of severe obesity. This information may contribute to the assessment of risk of severe obesity.