CANDIDATE LOCUS FOR FAMILIAL ABDOMINAL AORTIC ANEURYSMS BY GENOME-WIDE DNA LINKAGE ANALYSIS

Hidenori Shibamura, Wayne State Univ Sch of Medicine, Detroit, MI; Sarah Buxbaum, Jane M Olson, Case Western Reserve Univ, Cleveland, OH; Gerard Tromp, Magdalena Skunca, Wayne State Univ Sch of Medicine, Detroit, MI; Claudette Arthur, Dalhousie Univ, Hal

Background - Abdominal aortic aneurysms (AAAs) are frequently familial. Interviews and ultrasonography screening studies among relatives of AAA patients have shown the increased prevalence of AAA among first-degree relatives with up to 18% of brothers and 5% of sisters having AAA. Population-based ultrasonography screening studies have also emphasized family history as an important risk factor for AAA. Formal segregation studies have demonstrated that AAAs are likely to be a genetic disease with autosomal, either dominant or recessive, inheritance pattern. Methods - We identified 229 families with at least two individuals diagnosed with AAA. Blood samples from altogether 186 affected relative pairs (ARPs) and their unaffected relatives, if available, were collected for DNA isolation. We carried out a whole genome scan on 65 ARPs and followed up with 121 ARPs and used additional markers in the region with the highest logarithm of odds (lod) score. Results and Conclusions - There were 633 aneurysm patients in these families with an average of 2.8 cases per family. More than half of the families were small with only two affected individuals. There were, however, six families with six, three with seven and one with eight affected individuals. The majority of the probands (82%) and the affected relatives (76%) were males and the most common relationship to the proband was brother. In the whole genome scan with 65 ARPs, five chromosomal regions exceeded our exploratory threshold lod score of 0.8. One region had a lod score of 4.4 with covariate analyses and was selected for further study. The region remained significant with a lod score of 3.6 with two different markers in a larger sample. In conclusion, our study identified at least one candidate locus for familial AAAs.