Supplementary Results

Subgroup analysis of genotype–phenotype correlations for the *RNF213* R4810K variant upon age at onset

Among 248 adult MMD patients, 189 were heterozygous and none were homozygotes (Supplementary Table 2 and Supplementary Figure 3B). Heterozygotes had a family history of MMD (19% vs. 3%; $P<0.001$), underwent more revascularization surgeries (19% vs. 5%; $P=0.01$), and were more susceptible to posterior cerebral artery (PCA) involvement than were those with the wild type (22% vs. 9%; $P=0.02$). Cerebral hemorrhage as an initial clinical manifestation was significantly more common in heterozygotes than in those with the wild type (11% vs. 2%; $P=0.026$). The AA, GA, and GG genotypes did not differ significantly in other clinical presentations.

Among 63 pediatric MMD patients, 49 were heterozygous and 5 were homozygous (Supplementary Table 3 and Supplementary Figure 3C). Homozygotes were more susceptible to PCA involvement than were heterozygotes (80% vs. 14%; $P<0.001$). The AA, GA, and GG genotypes did not differ significantly in other clinical presentations.

The clinical characteristics were compared between pediatric and adult MMD patients among heterozygotes (Supplementary Table 4). Compared to adult MMD heterozygotes, pediatric MMD heterozygotes more frequently presented with TIA and underwent more revascularization surgeries. Moreover, pediatric MMD heterozygotes had a higher proportion of bilateral vasculopathy than did adult MMD heterozygotes. The AA, GA, and GG genotypes did not differ significantly in terms of Suzuki grades.

Supplementary References

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