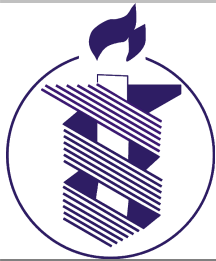


**Cerebral Aneurysm Renin Angiotensin System Study (CARAS): Renin-Angiotensin Polymorphisms in Pathophysiology of Aneurysmal Subarachnoid Hemorrhage**

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**Introduction**

Renin-angiotensin system (RAS) genetic polymorphisms are thought to play a role in cerebral aneurysm formation and rupture. The Cerebral Aneurysm Renin-Angiotensin System (CARAS) study prospectively evaluated common RAS polymorphisms and their relation to aneurysmal subarachnoid hemorrhage (aSAH).

**Methods**

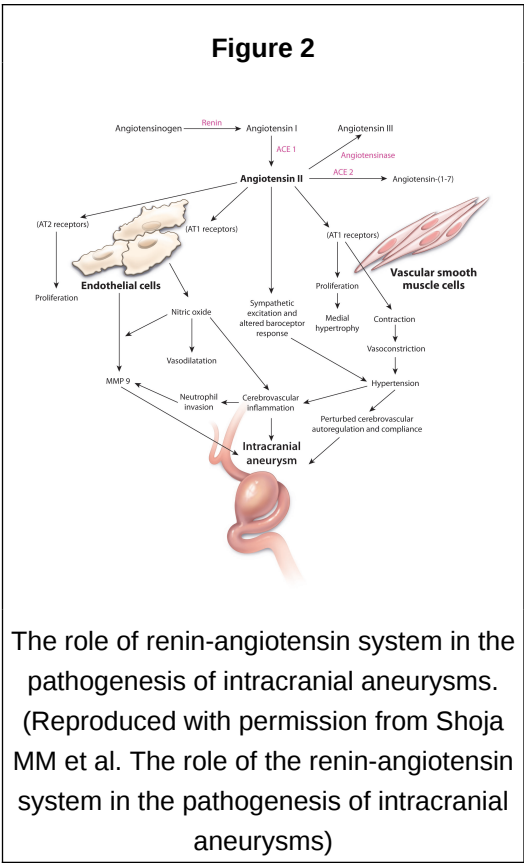
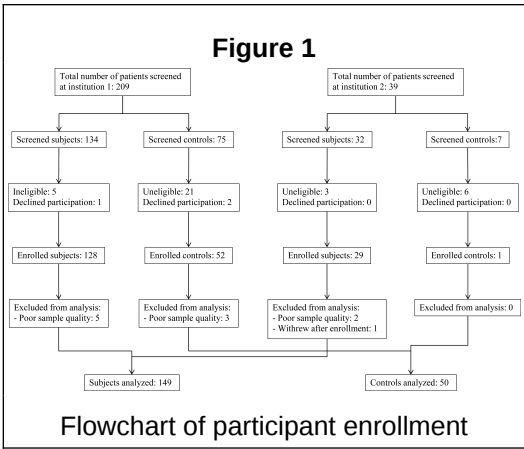
The CARAS study prospectively enrolled aSAH patients and controls at two academic centers in the United States. A blood sample was obtained from all patients for genetic evaluation and measurement of plasma ACE concentration. Common RAS polymorphisms were detected using 5’exonnuclase (Taqman) genotyping assays, and restriction fragment length polymorphism analysis.

**Results**

Two hundred and forty eight patients were screened. One hundred and forty nine aSAH patients and 50 controls were available for analysis. After controlling for race, there was a dominant effect of allele C of the angiotensin II receptor type 2 (AT2) A/C single nucleotide polymorphism (SNP) on aSAH in patients > 55 years of age (OR = 3.48, 95% CI = 1.23–9.84. p = 0.0192). In addition, in patients = 55 years and after controlling for race, there was a trend towards statistical significance for a recessive effect of allele C of the angiotensinogen (AGT) C/T SNP (OR = 3.06, 95% CI = 0.819–11.5, p = 0.0950), a recessive effect of allele D of the angiotensin converting enzyme (ACE) I/D polymorphism (OR = 2.64, 95% CI = 0.866–8.05, p = 0.0878), and a dominant effect of allele A of the AT2 A/C SNP (OR = 2.30, 95% CI = 0.0880–6.02, p = 0.0894). The ACE level was significantly lower in patients with II genotype ( $17.6 \pm 8.0$  U/L) as compared to ID ( $22.5 \pm 12.1$  U/L) and DD genotypes ( $26.6 \pm 14.2$  U/L) (p = 0.0195).

**Conclusions**

An age-dependent associations between the AT2 A/C, AGT C/T, and ACE I/D polymorphisms and aSAH were identified. Further studies are required to further elucidate the relevant pathophysiology and its potential implication in treatment of patients with aSAH.



The role of renin-angiotensin system in the pathogenesis of intracranial aneurysms. (Reproduced with permission from Shoja MM et al. The role of the renin-angiotensin system in the pathogenesis of intracranial aneurysms)