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Invited Commentary

Commentary on: A systematic review and meta-analysis of risk factors for unruptured intracranial aneurysm growth

Till date, risk factors that have been implicated for the growth of unruptured intracranial aneurysms (UIAs) are not completely understood. Therefore, the quest for identifying specific clinical and molecular players in the setting of UIA is paramount. Several reports have zeroed in on identifying specific hazard attributes to the disease; however, none have been able to establish a clearly defined set of risk factors that would pave the way for improved diagnosis and medical management of UIAs. Hence, the need for a holistic approach in identifying specific risk indicators for the disease is imperative.

In this study, the authors aptly portray a robust meta-analysis that is suggestive of aneurysm size and smoking status to be independent risk factors for the growth of intracranial aneurysm. Additionally, their data also reveal that prior subarachnoid hemorrhage (SAH) may have a negative effect on the growth of intracranial aneurysms [1]. However, too many limitations in the study as listed by the authors may demean its status in the scientific and medical intelligentsia, thereby obscuring its position in the existing knowledge of UIA in relation to public health.

Apart from environmental factors such as cigarette smoking responsible for UIA growth, several genetic and molecular determinants may essentially define the sequelae of UIA. Evidences have shown that variants on chromosomes 8q and 9p are tightly correlated with intracranial aneurysms (IAs) and the risk is greatly increased with cigarette smoking [2]. Genome-wide approaches such as DNA linkage and genetic association studies, as well as microarray-based mRNA expression studies, provide crucial functional insights on the identification of genetic risk factors and critical analyses of the molecular pathobiology of IAs [3]. Reports indicate that aberrations in the Matrix Metalloproteinase (MMP) genes, crucial for extracellular matrix (ECM) maintenance and arterial wall integrity, are a plausible underlying mechanism of intracranial aneurysm (IA) formation, growth and subsequent rupture. In context, data display a molecular perspective on the association between the functional MMP-2 rs243865 variant and IAs [4]. Therefore, it is quite surprising that in spite of an in-depth and well-reasoned study design, the authors of the current study failed to include crucial aspects of genetic risk indexes associated with UIAs in their meta-analysis work-up.

In conclusion, above all else, future studies on UIAs and SAH should primarily focus on the comparison of data on family sizes, sex ratios and age distributions for patients with familial and sporadic (defined as no first or second-degree family members with the same condition) disease. Genetic epidemiology studies should also try to adjust the results for the risk factor status in the study and control families because the accumulation of risk factors in families is likely to contribute to the risk of familial UIAs and SAH. In optimal circumstances, consanguinity between the family members should also be genetically confirmed in order to enable genetic variants associated with both UIAs and RIAs to be accounted for. Lastly, genetic studies should be designed with an aim to exclude for genetic associations that are caused by other familial and genetic conditions, such as hypertension [5].

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