Racial Associations with Hemorrhagic Presentation in Cerebral Arteriovenous Malformations

Wuyang Yang, Justin M. Caplan, Xiaobu Ye, Joanna Y. Wang, Maria Braileanu, Daniele Rigamonti, Geoffrey P. Colby, Alexander L. Coon, Rafael J. Tamargo, Judy Huang

■ BACKGROUND: **Studies focusing on hemorrhagic presentation of brain arteriovenous malformations (AVMs) have largely limited their analysis to angiographic features. We report the importance of race/ethnicity as a clinical factor associated with hemorrhagic AVM presentation in addition to previously reported angiographic features.**

■ METHODS: **Data were prospectively and retrospectively collected on patients ($N = 194$) during the period 1993–2010 who presented with a single intracranial AVM, and baseline characteristics were compared for hemorrhagic presentation versus nonhemorrhagic presentation. Features that were statistically significant in univariate analysis or clinically significant were included in a multivariate analysis.**

■ RESULTS: **The median age at presentation was 32 years; 37.2% of patients were male. Spetzler-Martin grades were I in 17.5%, II in 37.1%, III in 28.9%, IV in 14.9%, and V in 1.5%. Baseline characteristics that differed significantly between patients presenting with hemorrhage compared with patients without hemorrhage were the following: race ($P < 0.01$), AVM size ($P < 0.01$), <3 feeding arteries ($P = 0.01$), absence of middle cerebral artery supply to AVM ($P < 0.01$), and AVM location ($P < 0.01$). Multivariate analysis revealed nonwhite race (odds ratio [OR] = 3.09 [95% confidence interval (CI) = 1.52, 6.44], $P < 0.01$); smaller AVM size (OR = 0.65 [95% CI = 0.19, 0.86], $P < 0.01$); and nonfrontal lobar (OR = 2.61 [95% CI = 1.2, 5.59], $P = 0.02$), basal ganglia (OR = 6.20 [95% CI = 1.52, 26.26], $P = 0.01$), or brainstem locations (OR = 4.41 [95% CI = 1.38, 14.92], $P = 0.01$) as factors associated with hemorrhagic presentation of brain AVMs.**

■ CONCLUSIONS: **To our knowledge, this is the first study demonstrating that race/ethnicity is significantly associated with hemorrhagic presentation of AVMs. We also confirmed previous observations that AVM size and location are associated with hemorrhagic presentation.**

INTRODUCTION

Brain arteriovenous malformations (AVMs) are a rare cerebrovascular disease with a prevalence of 0.1%–0.5% in United States (14, 45). Patients with AVMs generally present at a young age with symptomatic complications such as intracranial hemorrhage (ICH), seizures, or headaches. ICH is responsible for most of the morbidity and mortality associated with AVMs (5, 9, 13, 45). The proportion of patients with AVMs presenting with ICH in the literature is 30%–82% (14, 25, 29, 43), with an annual incidence of hemorrhages of 1.9%–4.61% (5, 11, 14, 24, 29, 45).

Longitudinal studies examining the overall incidence of ICH from all causes (including AVMs) demonstrated several factors to be associated with a higher risk of hemorrhage, including age, male sex, alcohol intake, hypertension, and black race (1, 4, 12, 27, 31, 49). In contrast, studies that examined factors associated with hemorrhagic presentations of AVMs mainly focused on angiographic features. To our knowledge, hypertension is the only clinical feature that has been shown to be associated with AVM hemorrhage at time of presentation (25). Data regarding the role of race/ethnicity in the risk of AVM hemorrhage are limited. One

Key words
- Arteriovenous malformation
- Hemorrhagic presentation
- Intracranial hemorrhage
- Race

Abbreviations and Acronyms
AVM: Arteriovenous malformation
CI: Confidence interval
ICH: Intracranial hemorrhage
OR: Odds ratio
VIF: Variance inflation factor

Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

To whom correspondence should be addressed: Judy Huang, M.D. [E-mail: jhuang24@jhmi.edu]

Citation: World Neurosurg. (2015) 84, 2:461-469.
http://dx.doi.org/10.1016/j.wneu.2015.03.050

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

longitudinal study from Kim et al. (21) suggested that race/ethnicity is important in determining the natural history of AVMs. In this study, we examined the association of patient demographics and angiographic features with hemorrhagic presentation of AVMs in a multivariate regression model to find model-adjusted factors that are associated with hemorrhagic presentation of AVMs.

MATERIALS AND METHODS

Patient Population and Data Collection

Information on patients presenting to Johns Hopkins Hospital with AVMs from January 2010 was prospectively collected and compiled into an institutional review board–approved AVM database. Additional patients were identified retrospectively from the Johns Hopkins Hospital billing department data system with an International Classification of Diseases, Ninth Revision, diagnosis of 747.81 (congenital anomalies of cerebrovascular system), and the diagnosis of AVM was confirmed with the medical record. Patient information was entered into a large-scale database, which includes patients seen at Johns Hopkins Hospital during the years 1990–2011. Inclusion criteria were applied to patients during the period 1993–2010 with a confirmed diagnosis of AVM. The following patients were excluded: patients for whom data were unavailable, patients with multiple AVMs, patients with cavernous malformations, and patients with extracranial AVMs or associated syndromes (i.e., patients with hereditary hemorrhagic telangiectasia). Billing data from Johns Hopkins Hospital revealed 378 patients with diagnosis 747.81 (anomalies of cerebrovascular system) in International Classification of Diseases, Ninth Revision, from the years 1993–2010. Digital subtraction angiography was performed to confirm the AVM diagnosis in 243 patients. Among these 243 patients, clinical data were unobtainable in 47 patients (19.3%), and 2 additional patients had either extracranial AVMs or multiple AVMs (0.8%). After the application of inclusion and exclusion criteria, there were 194 patients included in this study.

Variables of Interest

Clinical and angiographic variables were collected for each patient and included age, sex, race, family history of stroke, hypertension, AVM size, AVM location, side of AVM, venous drainage pattern, number of feeding arteries, number of draining veins, Spetzler-Martin grade, location of feeding arteries, presence of intranidal aneurysms, and presence of venous stenosis or varix or both. Racial information was documented by providers at the time of patient registration or admission and was available in our electronic medical record on the first patient encounter. Radiographic studies of the AVMs were reported by diagnostic and interventional neuroradiologists as part of the clinical care of the patients, without regard to the collection of data for this study. Important angiographic features related to this study were readily available and extracted from radiology reports.

Race was categorized into 5 distinct groups (White, Black, Asian, Hispanic, Other races) based on category. Family history of stroke was defined in our database as any family member of the patient who experienced a stroke event in their medical history. Hypertension was defined as a patient with a confirmed diagnosis of hypertension at initial consultation. All angiographic parameters were evaluated and confirmed on digital subtraction angiography (DSA) with supplementation of information by radiology reports or other imaging studies such as magnetic resonance imaging. AVM size was primarily assessed as a continuous variable and was defined by the maximum length of the AVM in centimeters on digital subtraction angiography. Size was categorized into 2 groups (<3 cm vs. ≥ 3 cm). Feeding arteries were defined as any arterial contribution to the nidus, instead of exclusive feeding arteries. The number of feeding arteries (<3 vs. ≥ 3) and number of draining veins (<2 vs. ≥ 2) were evaluated as categorical variables. Cutoff points for these variables were arbitrarily selected to maximize balance between statistical needs and clinical significance.

For univariate analysis, age was regrouped into 3 categories (≤ 18 years, 19–45 years, and ≥ 46 years). Race was recategorized as white or others based on previous literature that suggests a lower risk of hemorrhagic events in the white population (1, 19, 21, 48). AVM location (frontal, nonfrontal lobar, basal ganglia, brainstem, and cerebellum) was classified into 4 categories to reduce overstratification of the data.

Statistical Analysis

The primary clinical outcome variable in this study was defined as hemorrhagic presentation in this patient population at the time of initial presentation. Baseline characteristics were summarized using descriptive statistics. χ^2 test was used for categorical variables, and Student t test was used for comparison of continuous variables between the 2 groups. Variables of clinical interest or with P value < 0.1 in the baseline description were included in the univariate analysis.

Univariate logistic regression analysis was used to assess an association between an individual factor and the primary outcome variable. The variables were selected for the multivariate logistic regression analysis if they were perceived as clinically important or the significant level of individual association was < 0.1 ($P < 0.1$). The multivariate logistic regression model was used to estimate the odds ratio (OR) of hemorrhagic AVM presentation or not with forward and backward techniques. The technique was based on the Akaike Information Criterion method with the addition of clinical significance variables to generate the final model. Collinearity was checked for the final model using variance inflation factor (VIF) analysis; a test result of VIF <10 is tolerated as nonsignificant collinearity exists between variables in the multivariate model. Statistical significance is defined as $P < 0.05$. All P values were reported as 2-sided, and all statistical analyses were performed using R version 3.0.1 (R Project for Statistical Computing, Vienna, Austria).

RESULTS

Baseline Characteristics

The median age of all patients was 32 years (range, 0–74 years), and 37.0% were male ($n = 72$). Spetzler-Martin grades were I in 17.5%, II in 37.1%, III in 28.9%, IV in 14.9%, and V in 1.5%. Of the 194 patients in the study, 66 (34.0%) presented with hemorrhage. Of the 62 nonwhite patients, 32 (51.6%) presented with a hemorrhage in contrast to 34 of 132 (24.6%) white patients ($P = 0.01$). More specifically, of 39 black patients, 21 (53.8%) presented with hemorrhage, which was significantly increased compared with the white population ($P < 0.01$). Summaries of all patient demographics are presented in Table 1 and Figure 1.