A Reanalysis of Predictors for the Risk of Hemorrhage in Brain Arteriovenous Malformation

Zheng Huang, PhD, MD,* Kang Peng, MD,* Changqing Chen, PhD, MD,† Feiyue Zeng, PhD, MD,† Junyu Wang, PhD, MD,* and Fenghua Chen, PhD, MD*

Background: Brain arteriovenous malformation (BAVM) is a congenital cerebral vascular disease that characterized with intracranial hemorrhage and epilepsy. It has some risk in current treatments including microsurgery, endovascular, and radiation therapy. Some patients with bAVMs may keep unruptured in their whole life. Whether it should be treated depends on the evaluation of the hemorrhage risk of bAVM. Although previous studies gave many significant predictors, we tried to find some new and more significant predictors in 173 patients with bAVMS by retrospective analysis. *Methods:* Except for previous predictors reported such as age, gender, epilepsy, location, aneurysm related with bAVM, volume of nidus, types of venous drainage, and the number of draining veins, we also collected time to peak (TTP) and sum of cross-sectional area of the feeding arteries and sum of cross-sectional area of the draining veins (∑SA/∑SV) data to proceed univariate and multivariate statistical analysis in 173 patients with bAVM. *Results:* The results of the statistical analysis show that gender, the location of bAVM nidus, and TTP are significant predictors of hemorrhage risk, but age, size, the number of draining veins, and types of venous drainage do not appear so significant. The value of predictors of bleeding risk including TTP was assessed by receiver operating characteristic curve and area under curve to be stronger. *Conclusions:* When TTP and ∑SA/∑SV data were added, some previous important indicators such as age, size, the number of draining veins, and types of venous drainage appear less significant in predicting the hemorrhage risk of bAVM in statistics, but TTP, gender, and the location of bAVM nidus are significant; moreover, TTP is a predictor that needs to be emphasized. **Key Words:** Arterivenous malformation—hemorrhage risk—angiography—regression analysis—ROC—AUC.

From the *Department of Neurosurgery; and †Department of Radiology, Xiangya Hospital, Central South University, Changsha, China.Received November 11, 2017; revision received January 3, 2018; accepted March 8, 2018.

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Data Sharing:

N/A

Address correspondence to Fenghua Chen, PhD, MD, Department of Neurosurgery, Xiangya Hospital, Central South University, Xiangya Road 87#, Kaifu District, Changsha 410008, China. E-mail: xyswcfh@csu.edu.cn.

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Introduction

Two major clinical features in patients with brain arteriovenous malformations (bAVMs) are epilepsy and hemorrhage.[1,2] Hemorrhage is a dangerous complication that can possibly lead to neurological dysfunction even death. However, current treatments including microsurgery, endovascular, and radiation therapy are not perfect for all bAVMs.[3] The outcomes of some bAVMs are even very sad. In natural history, some bAVMs kept stable and unrupture in patients' whole life.[2,4] So whether a patient with bAVM should be treated depends on evaluating the hemorrhage risk. Previous studies have suggested that some predictors such as size, location, and deep draining veins are associated with the hemorrhage risk of bAVM, but there are still some conflicting viewpoints on them.[5,6]

In this paper, a retrospective analysis of bAVM was performed. In addition to previous predictors reported,[5,7-9] 2 new predictors namely the ratio of sum of cross-sectional area of the feeding arteries and sum of cross-sectional area of the draining veins (∑SA/∑SV) and time to peak (TTP) of bAVM in digital subtracted angiography (DSA) were added into multivariate statistical analysis. The significance of TTP in predicting the hemorrhage risk was evaluated, and the "high flow resistance and high pressure" and "low flow resistance and low pressure" types of bAVM hemodynamic models based on TTP were posed.

Methods

Study Design

The study protocol was approved by the Institutional Review Board of our institution. A retrospective study on consecutive patients with bAVMs who were admitted to the department of neurosurgery in Xiangya hospital between January 2014 and April 2017 was performed. bAVM was diagnosed by DSA or histology. The patients who were not included are as follows: (1) patients with dural arteriovenous fistulae, caroticocavernous fistulae, and vein of Galen malformations; (2) patients who underwent surgical, endovascular, and radiosurgical treatment; and (3) patients with incomplete clinical data.

Baseline Assessment

Clinical data including age, sex, clinical presentation, intervals between intracranial hemorrhage, and DSA were collected. A bAVM was considered ruptured before admission if there were signs of bleeding on a computed tomography (CT) scan or magnetic resonance imaging or lumbar puncture. Two experienced neuroradiologists (CQ Chen and FY Zeng) blinded to clinical data, evaluated angiographic, magnetic resonance and CT images separately and resolved disagreement by consensus. Variables included bAVM's location, nidus volume, diameters of feeding arteries and draining veins, types of venous drainage, feeding arterial aneurysms, hematoma volume, and TTP.

Radiological Assessment

Location of bAVM was classified into superficial (frontal, temporal, parietal, and occipital lobes), deep (basal ganglia, thalamus paracallosal, and intraventricular), and infratentorial (brain stem and cerebellum). Venous drainage was classified as cortical, deep, and mixed. The number of draining veins was counted and classified as single and multiple. Feeding arterial aneurysm was defined as an aneurysm located on the wall of feeding arteries of AVM and related to blood flow to the AVM, which was confirmed by DSA. The length, width, and height of AVM nidus were measured on the DSA, and the volume was calculated by the following formula: V = length*width*height/2. The volume of hematoma was estimated by the first CT image after hemorrhage, and calculated by the following formula: V = length*width*height/2. The diameters of the identified feeding arteries and draining veins were measured in DSA, and ∑SA/∑SV was calculated by the following formula: ∑SA/∑SV = sum of cross-sectional areas of all feeding arteries/Sum of cross-sectional areas of all draining veins; the cross-sectional area of an artery = πr^2.

All patients underwent DSA (AlluraXper; Philips Healthcare, Eindhoven, The Netherlands). Dynamic images rate in the machine parameters was 4 frames per second, the contrast injection rate was 6 ml/s and the injection time (IT) was 1.5 seconds in carotid artery angiography, the contrast injection rate was 3 ml/s, and the IT was 2 seconds in vertebral artery angiography. The postprocess software (Dongruan Company, Hangzhou, China) connected with central image database was applied for finding TTP. First, the region of interest (ROI) was drawn along the border of bAVM's nidus in the software, then the software will tell us which frame is the deepest color image of the ROI gray value (Fig 1). The number of frames (NOF) was counted between the first visualization and the mostly obvious visualization of bAVM nidus. TTP was calculated by the following formula in angiography: TTP = NOF*.25/IT (IT, injection time; .25 second: 4 fps).

Statistics Analysis

Statistics analysis was performed using SPSS 18.0 (SPSS Inc., Chicago, IL) and statistical significance was set at $P < .05$. Fisher's exact test or Pearson $\chi 2$ test was used for comparison of categorical variables, and continuous variables were compared using independent samples *t*-test. Factors associated with TTP were analyzed with linear regression analysis. Predictors for rupture of bAVM were analyzed using logistic regression analysis. To assess the value of those predictors, we used receiver operating characteristic curve (ROC) and area under curve (AUC).