Vertebral Artery Occlusive Disease: Data from the Angiographically Confirmed Vertebral Artery Disease Registry

Adnan I. Qureshi, MD,* Sehar Babar, MD,† Omar Saeed, MD,* Muhammad A. Saleem, MD,*,† and Shawn S. Wallery, MD‡

Background: We performed this study to identify demographic, clinical, and angiographic characteristics of adult patients with angiographically confirmed vertebral artery occlusive disease (VAOD) and associated risk factors. *Methods:* The demographic and clinical characteristics, and angiographic features were ascertained using predefined criteria. Controls were selected from the National Health and Nutrition Examination Surveys matched according to age, sex, and ethnicity. A stepwise logistic regression for odds ratio (OR) was performed to identify the effects of risk factors on occurrence of VAOD. *Results:* Of 56 patients with VAOD (mean age ± standard deviation [SD]; 65.4 ± 11.7 years, 44.6% women), 37.5% were classified as suffering from moderate stenosis (50%-69%), 16.1% from severe stenosis (70%-99%), and 46.4% from occlusion of at least 1 vertebral artery. There was a significantly higher severity of stenosis (percentage with SD; 88.1 ± 16.5 versus 75.4 ± 20.8, $P = .02$) and frequency of bilateral vertebral artery disease in patients with ischemic symptoms (40.9% versus 8.8%, $P = .004$). In the multivariate analysis, hypertension (OR 3.0; 95% confidence interval [CI], 1.4-6.5), diabetes mellitus (OR 2.5; 95% CI, 1.4-4.6), coronary artery disease (OR 3.2; 95% CI, 1.7-6.0), and active cigarette smoking (OR 3.1; 95% CI, 1.5-6.3) were significantly associated with vertebral artery disease. *Conclusions:* Severity of stenosis and bilateral involvement were associated with symptomatic VAOD. Hypertension, diabetes mellitus, coronary artery disease, and active cigarette smoking were associated with occurrence of VAOD.

Key Words: Vertebral artery disease—posterior circulation disease—angiography—risk factors—vertebral artery occlusive disease.

Introduction

Extracranial vertebral artery occlusive disease (VAOD) occurs in 10%-20% of patients with ischemic events in the vertebral and basilar arterial distribution.[1-4] Asymptomatic VAOD is also relatively common in patients with ischemic stroke[2] or those with symptomatic internal carotid artery (ICA) stenosis.[5] In a hospital-based cohort of 3717 patients with atherosclerotic arterial disease enrolled in the Second Manifestations of Arterial disease study, 282 patients (7.6%) had asymptomatic extracranial vertebral artery stenosis greater than 50% as diagnosed with duplex ultrasound.[6]

The prevalence of extracranial VAOD is higher than ICA stenosis in unselected patients, those with ischemic events in respective territories, and asymptomatic patients.[6,7] The prevalence of stenosis of the proximal vertebral artery, distal vertebral/basilar artery, and ICA was 12.9%, 5.5%, and 7.2%, respectively, in 935 patients who underwent high-resolution contrast-enhanced magnetic resonance (MR) angiography in a regional general hospital.[7] In the Oxford Vascular Study,[8] 26.2% of patients with ischemic events in vertebrobasilar arterial distribution had greater than or equal to 50% vertebral and basilar stenosis compared with 11.5% of patients with carotid artery distribution

From the *Zeenat Qureshi Stroke Institute, St. Cloud, Minnesota; †Marcyhealth Janesville, Janesville, Wisconsin; and ‡Marcyhealth Rockford, Rockford, Illinois.

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Address correspondence to Adnan I. Qureshi, MD, Zeenat Qureshi Stroke Institute, 925 Delaware St SE, Suite 300B, Minneapolis, MN 55414. E-mail: aqureshi@hotmail.com

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ischemic events who had greater than or equal to 50% ipsilateral ICA stenosis.

VAOD remains understudied despite a high prevalence. Almost all studies are based on identification of VAOD using MR angiography or Doppler ultrasound, which limit the accuracy of diagnoses due to false positive cases.[9-12] There are limited data regarding the risk factors for VAOD. The multisocietal guidelines on management of patients with extracranial carotid and vertebral artery disease[13] recognized the large gaps in knowledge of VAOD and recommended well-designed registries to study various aspects of VAOD. To address the gaps in our understanding of risk factors and clinical and angiographic characteristics of VAOD, we initiated a prospective registry that included all consecutive patients with angiographically confirmed vertebral artery stenosis measuring 50% or greater in severity.

Patients

A prospective registry, Angiographically Confirmed Vertebral Artery Disease, was maintained that collected data on all adult patients who underwent cerebral angiography at a single institution and were diagnosed with either symptomatic or asymptomatic extra- or intracranial vertebral artery stenosis greater than or equal to 50% or occlusion between May 2016 and November 2017. Asymptomatic VAOD was identified in patients who underwent cerebral angiogram for other indications such as evaluation of carotid artery stenosis or intracranial aneurysms. The protocol for data collection was approved by local institutional review board and informed consent was waivered. All cerebral angiographic procedures were performed by 1 operator (AIQ).

Data Collection

The following demographic and clinical data were collected for each patient: (1) age, gender, ethnicity; (2) blood pressure measurements (systolic and diastolic measurement in mmHg) at admission; (3) hypertension, diabetes mellitus, cigarette smoking status (current or past), hyperlipidemia, and coronary artery disease; (4) medication use, whether patient is on antihypertensive medication, oral hypoglycemic agents, insulin therapy, or statin use; (5) body mass index and weight; and (6) total cholesterol concentration. We further ascertained whether patient had transient ischemic attack or ischemic stroke in the distribution of vertebrobasilar distribution.

We collected the following data from angiographic images: (1) the severity of stenosis; (2) side of stenosis (right or left); (3) location (intracranial that included dural location and extracranial disease); (4) characteristics of lesion (regular or irregular); and (5) presence of collaterals (retrograde filling from contralateral side, or anterograde filling from anastomoses by ipsilateral ascending cervical artery or occipital artery). The severity of intracranial stenosis was measured using the Warfarin-Aspirin Symptomatic Intracranial Disease criteria,[14] and extracranial stenosis was measured using a previously described method.[15,16]

A total of 747 control subjects (50:1 to maximize number of matched controls) were selected who were matched for age, sex, and race/ethnicity from a nationally representative cohort of adults who participated in the National Health and Nutrition Examination Survey (NHANES) 2015-2016. None of the control population had any history of stroke. The survey is conducted by National Center for Health Statistics and Centers for Disease Control and Prevention. The details have been published previously.[17] In 2015-2016, 15,327 persons were selected for NHANES from 30 different survey locations. Of those selected, 9971 completed the interview and 9544 were examined.

Age in years, at the time of the screening interview, is reported for survey participants between the ages of 18 and 79 years. All participants aged 80 years and older are coded as "80." Reporting of age in single years for adults aged 80 years or older was considered a disclosure risk. For this reason, all patients aged 80 years or older in our registry were similarly coded as "80." The race-ethnicity variable included in the NHANES file was derived from responses to the survey questions on race and Hispanic origin. All non-Hispanic participants are categorized as: non-Hispanic white, non-Hispanic black, non-Hispanic Asian coded, and other non-Hispanic races including non-Hispanic multiracial. Since there were Hispanic ethnicity patients in our registry, we included all Hispanics/Mexican-Americans as 1 variable. Blood pressure readings were measured in seated position for 3 consecutive readings. We utilized the initial reading for our analysis.

Statistical Analysis

All statistical analysis was performed using IBM SPSS statistics version 23 of 64-bit edition property to IBM Corporation. We used chi-squared and ANOVA for categorical and continuous variables, respectively. Case control matching function was utilized to exactly match age, sex and ethnicity variables with controls at a ratio of 50:1. Tolerance was kept zero to match variables for demander (cases) and supplier (controls) cases as exact equal. A stepwise logistic regression analysis was performed to identify the effects of hypertension, diabetes, mellitus, hyperlipidemia, coronary artery disease and cigarette smoking on occurrence of VAOD. A $P < .05$ was considered significant for entry into the model.

Results

A total of 56 patients with VAOD confirmed by cerebral angiography were identified. The mean patient age was 65.4 ± standard deviation 11.7 years; 55.4% were men.