Prevalence of vertebral artery origin stenosis and occlusion in outpatient extracranial ultrasonography

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Abstract

Background and purpose—Most data on the prevalence of vertebral artery origin (VAo) disease is derived from hospital-based studies of patients with posterior circulation strokes and TIA. The prevalence of VAo disease in patients without posterior circulation symptoms or asymptomatic patients is poorly characterized. Our objective was to examine the prevalence of VAo stenosis and occlusion in consecutive patients, presenting for extracranial ultrasonography to an outpatient laboratory.

Methods—We retrospectively identified 2490 consecutive extracranial duplex studies performed in an ambulatory neurovascular ultrasound laboratory. All studies were reviewed for the presence of >50% VAo stenosis, defined as a PSV > 114 cm/s, and VA occlusion. We also reviewed the prevalence of >50% carotid stenosis, defined as a PSV > 120 cm/s, in the same population, to draw comparisons with VAo stenosis prevalence.

Results—We identified right VAo stenosis in 52/1955 (2.7%) and occlusion in 74/1955 (3.9%) and left-sided VAo stenosis in 45/1973 (2.5%) and occlusion in 64/1973 (3.6%). The prevalence of having any (either right or left) VAo stenosis or occlusion was 8.2% and 1.4% had bilateral VAo stenosis or occlusion. Right carotid stenosis and occlusion was found in 236/2399 (9.8%) and 53/2399 (2.2%) and left carotid stenosis and occlusion in 236/2397 (9.8%) and 45/2397 (1.9%), respectively. Any carotid disease, either right or left, was present in 18.9% and 4.7% had bilateral carotid disease.

Conclusion—Although less prevalent than cervical carotid disease, we found that approximately 8% of patients who presented to an ambulatory ultrasound laboratory had >50% VAo disease.

Introduction

Approximately a quarter of strokes occur in the vertebrobasilar circulation with atherosclerosis of the vertebral artery being an important cause [1–4] Extracranially vertebral artery stenosis typically occurs at the origin (VAo) and is the direct cause of 9% of posterior circulation ischemic strokes and TIA [5]. Despite being a significant cause of stroke and TIA, the prevalence of VAo stenosis in asymptomatic populations is not well established. Endovascular interventions and operative procedures are used in clinical practice in carefully selected patients with symptomatic VAo disease, which increases the need to understand both the symptomatic and asymptomatic prevalence of this vascular lesion.

The proximal vertebral artery is technically difficult to insonate which has contributed to the lack of studies pertaining to atherosclerotic disease in that segment. Only a few studies have been done on the prevalence of VAo disease and these have been in patients with posterior circulation stroke/TIA. Little is known about its prevalence in asymptomatic populations. Ultrasonography remains the most widely used test in the clinical evaluation of patients with cerebrovascular disease and has been used in population-based research of carotid stenosis prevalence. We therefore undertook the present study to determine the prevalence of VAo stenosis and occlusion in patients referred for outpatient extracranial ultrasonography, a population which is largely free of posterior circulation symptoms.

Methods

After approval from our local institutional review board, we retrospectively reviewed all extracranial duplex stud-

ies performed in an outpatient neurosonlogy laboratory affiliated with an academic medical center. The serves as the referral vascular laboratory for the and is accredited by the Intersocietal Accreditation Commission (IAC). No inpatient studies were included. All studies performed between 2002 and 2010 were reviewed for VAo stenosis. Studies were initially done with a General Electric Logiq 700, which was subsequently replaced by a Logiq S6. All studies were done using a standard 8–12 MHz probe by one of two experienced ultrasonographers.

Studies were performed according to a standard insonation protocol. The vertebral arteries were initially located in a longitudinal axis by color-coded duplex in the intraforaminal segment, identified by the acoustic shadow of the vertebral bodies. This segment is commonly referred to as V2. The vertebral artery is then insonated in the prevertebral segment and its course followed proximally as far as technically feasible, to the origin from the subclavian artery. The prevertebral segment is commonly referred to as V1. Because of technical difficulties the VAo can often not be visualized. The angle-corrected ultrasonographic peak systolic (PSV) and end diastolic velocity (EDV) were obtained at the VAo, V1, and V2 segments. Origin stenosis was diagnosed if the PSV at the VAo exceeded 114 cm/s. We had previously correlated this criterion with catheter angiography and found this criterion to have the highest diagnostic accuracy when compared to several other criteria [6]. If no color flow imaging, B-flow image, or Doppler flow signal was obtained from the proximal or intraforaminal segment, the artery was assumed to be occluded.

Studies were also analyzed for the prevalence of internal carotid artery stenosis and occlusion to allow a comparison of internal carotid and vertebral origin stenosis. Internal carotid artery stenosis was defined according to our laboratory's validated criteria as a focal increase of Doppler PSV >120 cm/s (with the internal to common carotid ratio exceeding 1.5) at the site of the plaque. The internal carotid artery was assumed to be occluded if no flow was detected by color flow imaging, B-flow imaging or Doppler.

In a subset of 470 patients, evaluated most recently, an intake questionnaire was completed, inquiring about demographics, past medical history, vascular risk factors, and indications for the study. This data was analyzed with the intention to describe the study population, assess risk factors for VAo stenosis, and examine referral patterns to the laboratory. In patients with more than

Table 1. Prevalence of vertebral artery origin stenosis, *n* (%).

| | Vertebral artery origin | |
	Right (*n* = 2393)	Left (*n* = 2390)
Not visualized	438 (18.3)	597 (25.0)
Normal	1829 (76.4)	1684 (70.5)
Stenosis	52 (2.2)	45 (1.9)
Occluded	74 (3.1)	64 (2.7)

one study, only the first study was included. We excluded patients with ultrasonographic subclavian steal.

Statistics

Statistical analyses include summary statistics presented as mean and standard deviation (SD) for continuous variables and frequency and percentages for categorical variables. Between groups comparisons were made with Student's *t* test with significance set as $p \leq 0.05$. Categorical variables were compared by means of a chi-square test or Fisher exact test as appropriate. Using a logistic regression model the relationship between patient demographics, vascular risk factors and VAo stenosis or occlusion was analyzed. Variables were included in the model if found to be significant in univariate analysis. Analysis was performed with Statistical Package for Social Sciences (SPSS Version 18, Chicago, IL).

Results

A total of 2490 studies were available for analysis. The right and left vertebral artery could not be insonated in 18% and 25% of patients, respectively. The prevalence of right and left vertebral artery stenosis and occlusion is shown in Table 1.

Including only those patients from whom the VAo was insonated, the prevalence of right-sided stenosis was 52/1955 (2.7%) and occlusion 74/1955 (3.9%) and left-sided stenosis was 45/1973 (2.5%) and occlusion 64/1973 (3.6%). Either right or left VAo stenosis/occlusion was found in 8.2% patients and 1.4% patients had bilateral VAo stenosis/occlusion.

Table 2 shows the mean flow velocities in those patients with and without stenosis at the three vertebral segments insonated. As expected, the differences in flow velocities were largest at the VAo, but were also found in the more distal vertebral segments. We also evaluated the prevalence of >50% internal carotid stenosis to allow a standard of references for the prevalence of VAo stenosis in this study population. In 236/2399 (9.8%), right internal carotid stenosis >50% was found and occlusion was present in 53/2399 (2.2%). Left internal carotid

Table 2. Comparison of mean velocities at Vo, V1 and V2 in patients with and without vertebral origin stenosis.

	Right		Left	
	Normal (*n* = 1829)	Stenosis (*n* = 52)	Normal (*n* = 1684)	Stenosis (*n* = 45)
Vo	54.2±18.9	149.0±57.8*	53.5±17.5	143.9±31.4*
V1	40.8±23.0	59.4±48.7*	39.4±22.2	55.9±35.3*
V2	42.4±16.9	62.7±27.4*	40.6±16.2	59.2±20.5*

*p< 0.0001

Table 3. Comparison of patients with and without VAo stenosis/occlusion.

	Right		Left	
	Yes (*n* = 20)	No (*n*=291)	Yes *n*=(17)	No (*n*=239)
Age	66.2±9.2	62.6±14.5	69.4±10.3	62.4±14.8
Men	13 (65)	144 (49)	7 (41)	126 (52)*
Hypertension	14 (70)	159 (55)	14 (82)	125 (52)*
Dyslipidemia	13 (65)	130 (45)*	11 (65)	109 (46)*
Diabetes mellitus	9 (45)	70 (24)*	7 (41)	49 (21)*
Cigarette smoking	1 (5)	19 (7)	2 (12)	15 (6)
BMI	28.2 ±4.6	26.7±4.5	26.5±4.2	26.9±4.8

*P<0.05; BMI= body-mass index

stenosis >50% and occlusion was noted in 236/2397 (9.8%) and 45/2397 (1.9%), respectively. The prevalence of either right or left internal carotid artery occlusion or stenosis was 18.9% and 4.7% had bilateral internal carotid stenosis/occlusion.

In 470 consecutive patients, self-reported demographic information was available. The mean age of this population was 65.4 ± 13.9 years and 49% were men. Hypertension was the most common risk factor, present in 58% of cases, followed by dyslipidemia (49%) and diabetes mellitus (26%). The most common reason for ultrasonography was history of stroke/TIA (42%), history of carotid stenosis (27%), carotid bruit (4%), and other reasons (27%).

In an analysis of risk factors for VAo stenosis, we compared demographic characteristics in patients with and without origin stenosis in Table 3. A trend toward a higher vascular risk factor burden was found in patients with VAo stenosis. In univariate analysis, diabetes mellitus and hypertension was associated with VAo stenosis. In a multivariate analysis of patients, who had at least one VAo insonated, age, hypertension, and diabetes were not independently associated with stenosis.

Discussion

We found the prevalence of right and left VAo stenosis and occlusion to be 5.6% and 6.1%, respectively, in an outpatient vascular ultrasound laboratory. In the same population and serving as comparison, the prevalence of right and left carotid stenosis and occlusion was 12% and 11.7%, respectively. There was a suggestion that hypertension and diabetes are risk factors for VAo stenosis in univariate, but not multivariate analysis.

The prevalence of carotid artery stenosis has been well described in general populations and varies from 2%–18%, depending on the age of the population screened. In the Cardiovascular Health Study of asymptomatic subjects >65 years, the prevalence of >50% carotid stenosis was 7% in men and 5% of women [7]. In the Bruneck Ischemic Heart Disease and Stroke Prevention Study, >50% carotid stenosis was present in 11% in 60- to 79-year-old men and 6% in 60- to 79-year-old women [8]. The prevalence of carotid stenosis increases in the presence of multiple vascular risk factors and maybe be as low as 2% with no risk factors and as high as 16% with three risk factors [9].

The prevalence of proximal vertebral artery disease has been less well studied and most of the data is in patients with posterior circulation stroke. In the New England Posterior Circulation Stroke Registry, 131/407 (25%) of all posterior circulation stroke/TIA patients had VAo stenosis. This was virtually identical to the prevalence of intracranial vertebral artery disease, reported in 132/407 (25%) [5]. A lower prevalence was found in the Oxford Vascular Study, which showed that 16/141 (11%) patients with posterior circulation stroke and TIA, who underwent contrast enhanced MRA, had proximal extracranial vertebral stenosis [10].

Little is known about the prevalence of vertebral artery origin stenosis in patients who do not have posterior circulation symptoms. In the Second Manifestations of ARTerial disease (SMART) study, a subgroup of 3717 patients with arterial atherosclerotic disease (excluding those with posterior circulation stroke) underwent ultrasonographic examination of the extracranial carotid and vertebral arteries. A PSV >100 cm/s was used as a diag-

nostic criterion and detected VAo stenosis/occlusion in 7.6%. In the same population, the prevalence of >50% carotid stenosis was 10.3% [11]. We are not aware of any other studies that have assessed the prevalence of VAo stenosis outside of hospital-based stroke registries. Several features allow for a comparison between the SMART study and our study. Both studies assessed subjects with a high burden of vascular disease, but largely free of posterior circulation strokes, used similar, ultrasonographically based, diagnostic criteria and showed a similar prevalence of VAo stenosis. In both instances, the prevalence of VAo stenosis was less than that of carotid stenosis. This confirms the early reports that have also suggested a lower prevalence of VAo stenosis compared with extracranial carotid stenosis. The Joint Study of Extracranial Arterial Occlusion conducted in 4748 patients with stroke/TIA who underwent catheter angiography, showed a prevalence of VAo stenosis/occlusion of approximately 25%, whereas that of carotid stenosis was about 40%. Interestingly in a more recent study 379 patients undergoing coronary angiography proximal vertebral artery stenosis >50% was present in 13.7% vertebral and 9.5% carotid arteries. Vertebral artery stenosis was associated with coronary artery disease severity ($p = 0.002$), creatinine level, male gender, claudication, and low HDL cholesterol level [12].

The proximal vertebral artery is often not insonated during routine clinical ultrasonography. Several reasons may account for the understudy of this segment. There are technical challenges with insonation, given the artery's deep location in the proximal neck and thoracic outlet. Even in experienced hands the origin may not be visualized in a quarter of cases, as in our study. The lack of well-established surgical treatment and generally assumed low recurrence rates may also be factors contributing to the failure to fully assess the proximal segments. It has been our experience that ultrasonographers are often not adequately trained to examine the VAo. We hope that by contributing to the existing data on VAo prevalence in a previously unstudied population, we continue to raise awareness of this condition.

A limitation of studies assessing VAo stenosis is the difficulty in reliably evaluating this segment noninvasively. In the only prospective study comparing three noninvasive diagnostic techniques, contrast enhanced MRA had the highest sensitivity and specificity. Although the specificity of all three imaging modalities is excellent, exceeding 90%, the sensitivity is lower at approximately 80% for CTA, 85% for unenhanced MRA, and 70% for duplex. A reduced sensitivity will lead to underestimation of the true prevalence of VAo stenosis. We had pre-viously validated our diagnostic criteria and found that a PSV >114 cm/s maximized sensitivity and specificity, but with a sensitivity of only 70% [6]. Duplex criteria for VAo stenosis are not well established and a variety of criteria have been proposed. PSV criteria yielding optimal sensitivity and specificity compared with catheter angiography have included PSV >108 cm/s (sensitivity 88%, specificity 71%) and PSV >140 cm/s (sensitivity 96%, specificity 96%) [13,14]. A PSV ratio criteria >2.2, between the PSV at the stenosis and PSV distal to the stenosis, has been proposed to have improved diagnostic accuracy than PSV alone [13]. Others, however, have found such ratio criteria less useful than PSV [6,14]. These uncertainties highlight the need for each laboratory to develop independent diagnostic criteria.

Our study was not population based and included patients with established cardiovascular disease, as 42% had a history of stroke and TIA and 27% a history of carotid stenosis. We were not able to ascertain the exact location of strokes/TIA but it is likely that patients with posterior circulation symptoms were included. As 70%–80% of strokes occur in the anterior circulation we estimate that only a small proportion, approximately 10%–15% of the overall study population, had posterior circulation symptoms. The high burden of disease in this population likely overestimates the true prevalence of vertebral stenosis in the general populations. Our patient population was also race-ethnically diverse and included a large Hispanic population. In symptomatic patients, extracranial vertebral disease has been associated with whites [5,15]. Whether this is also true for asymptomatic populations is uncertain, but may yield different prevalence rates depending on the race-ethnic background of the population screened. We were also only able to assess risk factors for VAo stenosis in a smaller subset of patients, and not the whole population. This may have led to reduced power to find statistical associations with other risk factors for VAo stenosis.

In summary, we report the prevalence of VAo stenosis >50% to be around 8% in a patients presenting to an ambulatory ultrasound laboratory. The prevalence of internal carotid stenosis and occlusion was higher than that of VAo disease in the same population. We feel that our findings contribute to the understanding of proximal vertebral artery disease prevalence in patients largely free of posterior circulation strokes and TIA.

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