Transcranial Doppler ultrasonography of the basilar artery in patients with retrograde vertebral artery flow

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Objective: **Reversal of flow in the extracranial vertebral artery secondary to a proximal subclavian/innominate artery stenosis or occlusion is a frequent finding during carotid duplex ultrasonography. The characteristics of basilar artery flow are not well defined in these patients. The objective of this study is to evaluate basilar artery flow in patients with retrograde vertebral artery flow.**

Methods: **From a transforaminal vice transforamen approach with the patient seated, pulsed Doppler scan spectral waveforms were obtained from the distal segment of each vertebral artery (depths of 66 mm and 70 mm) and throughout the basilar artery (depths of 80 mm up to 116 mm). The direction of flow and the peak flow velocity were recorded at each location. In the subset of patients with antegrade flow, we initiated a 5-minute period of arm ischemia (produced by brachial blood pressure cuff inflated to a suprasystolic pressure) and compared flow direction to baseline.**

Results: **Twenty-five patients with retrograde vertebral artery flow on carotid duplex ultrasonography underwent transcranial Doppler (TCD) ultrasonography scan of the distal vertebral arteries and the basilar artery. There were 10 males (58-85-years-old; mean 70.7 years) and 15 females (47-85-years-old; mean 66.0 years). An additional 11 patients who had normal vertebral flow underwent TCD and served as a control group. Nineteen patients (76%) demonstrated antegrade basilar artery flow at rest. Six patients (24%) demonstrated abnormal basilar artery flow at rest. Five had complete reversal of flow; one had intermittent flow reversal which became retrograde throughout the cardiac cycle following a period of arm ischemia ipsilateral to the patient's retrograde vertebral artery flow. No patient with retrograde vertebral artery flow and antegrade basilar artery flow at rest demonstrated a change in basilar artery peak velocity or direction of flow following arm ischemia.**

Conclusion: **Less than 25% of patients with retrograde vertebral artery flow on carotid duplex ultrasonography scan demonstrated a corresponding reversal of flow in the basilar artery. The vast majority of patients do not develop flow reversal in the basilar artery. Provocative maneuvers to increase collateral flow to the arm ipsilateral to retrograde vertebral artery flow did not appear to alter basilar artery flow velocity or direction of flow. Transcranial Doppler ultrasonography is indicated in patients with retrograde vertebral artery flow to document basilar artery flow, especially prior to intervention in patients with symptoms suggestive of posterior cerebral circulation insufficiency. (J Vasc Surg 2008;48:859-64.)**

Reversal of flow in the vertebral artery distal to a subclavian stenosis (commonly referred to as "subclavian steal") has been recognized for more than 40 years.[1] Although various definitions and interpretations have been proposed, for the purposes of this article, subclavian steal is defined as the reversal of blood flow in the vertebral artery ipsilateral to a proximal occlusion or high-grade stenosis of the subclavian artery.[2]

Although historically thought to represent flow contribution from the cerebral circulation, a general consensus on the direction of blood flow through the basilar artery has yet to be achieved. Likewise, no uniform set of clinical symptoms consistently associated with subclavian steal has been found. Patients may exhibit reversal of flow in the vertebral artery with no clinical manifestations, or may have severe vertebro-basilar insufficiency symptoms due to reversal of basilar artery flow. This study seeks to evaluate the direction of basilar artery blood flow in subclavian steal using transcranial Doppler ultrasonography (TCD) and to propose the use of a diagnostic ratio which would help to identify patients at risk for reversal of basilar flow and, in the proper clinical setting, deserve further evaluation.

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Competition of interest: none.

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MATERIALS AND METHODS

All patients seen in the Providence Surgical Care Group Vascular Laboratory between May 1, 2005 and June 30, 2007 who met the criteria for subclavian steal (ie, reversal of flow in a vertebral artery) were eligible for participation in this study. Patients signed informed consent documents authorizing the use of the data collected. In addition to patients with subclavian steal, an additional group of patients without vertebral flow reversal and with transcranial

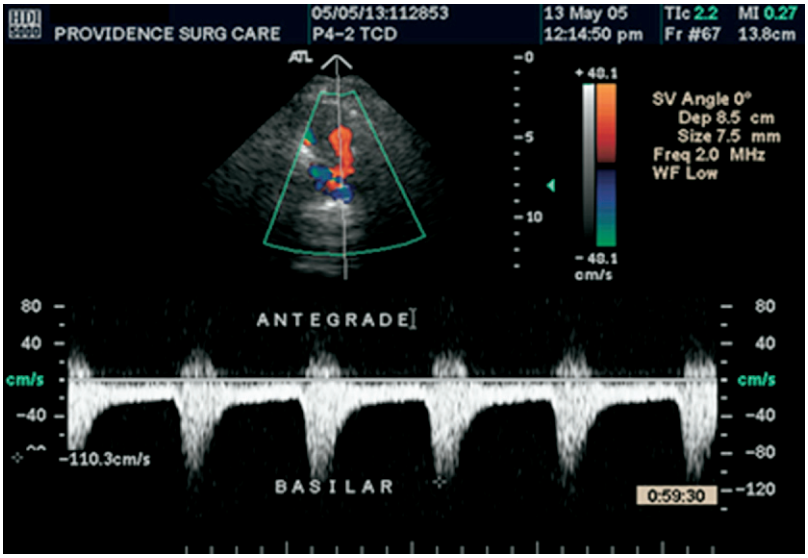

Fig 1. Doppler waveform of the basilar artery in a patient with normal antegrade flow. Velocity is represented as a negative value (downward deflection of the waveform) due to the fact that flow is directed away from the probe.

Doppler scan studies for other indications were identified as a control group.

Carotid duplex ultrasonography scan technique. Extracranial carotid duplex ultrasonography scan (ECDU) studies were performed in a single laboratory accredited by the Intersocietal Commission for the Accreditation of Vascular Laboratories (ICAVL) in Extracranial Cerebrovascular Testing. Ultrasonography was performed using a GE Logiq 9 (GE, Milwaukee, Wis), ATL HDI-5000 (ATL Ultrasound, Bothell, Wash), or Philips Sonos 5500 (Phillips Ultrasound, Bothell, Wash) ultrasound scan system with a 7.5 MHz – 10.0 MHz linear array transducer. B-mode imaging, color Doppler scan imaging, and Doppler scan spectral analysis of the common carotid, internal carotid, external carotid, and midcervical vertebral arteries were performed in accord with standard protocols.[3] All spectral Doppler scan measurements were obtained at an angle of insonation of 60 degrees or less. Vertebral artery spectral waveforms were obtained from the midcervical segment of the vertebral artery. The vertebral artery peak velocity and the direction of flow were noted in all patients.

Posterior circulation transcranial Doppler ultrasonography scan technique. Posterior circulation transcranial Doppler (pTCD) scan examinations were performed with the patient in a sitting position and the chin tucked slightly downward according to standardized criteria.[4] Recordings were obtained at the base of the neck through the foramen magnum. All TCD studies were performed using a Philips Sonos 5500 (Phillips Ultrasound, Bothell, Wash) imaging system with a 2.0 MHz phased array probe by a registered vascular technologist (RVT) experienced in transcranial Doppler scan techniques. The distal vertebral artery and the basilar artery are identified by depth and by direction of flow. General reference values for the vertebral artery using the transforamenal window are 60-70 mm deep and an average peak velocity of 36 cm/second while the basilar is generally found at a depth of 80-120 mm with an average peak velocity of 39 cm/second.[4] Unlike carotid duplex ultrasonography, the angle of insonation with TCD techniques is assumed to be zero degrees. Pulsed Doppler scan spectral waveforms are obtained from the distal segment of each vertebral artery at depths of 66 mm and 70 mm. Basilar artery waveforms (Fig 1) are obtained at a depth of 80 mm, and in increasing increments of 4-6 mm to a maximum depth of 120 mm. Increasing the insonation depth allows the vertebral arteries to be traced to their confluence with the basilar artery. At each location, the direction of flow and peak flow velocity through the vessels is recorded.

Provocative ischemia testing. Ischemia is induced in the arm ipsilateral to the site of subclavian steal by the inflation of a brachial blood pressure cuff to supra-systolic pressure for a 5-minute period. After the 5-minute period, the cuff is deflated while the basilar artery peak systolic velocity waveform is monitored for 30 seconds following deflation to document any changes in peak velocity or direction of flow compared to baseline. With increased flow across a hemodynamically significant lesion, upon release of the blood pressure cuff, reversal of antegrade baseline basilar flow is expected if this is a significant collateral vessel.

Statistical analysis. The distribution (histogram) of each variable was examined. Since the sample size of the variables is small, and in some cases did not fit the profile of a normal distribution, nonparametric analysis was performed. The outcome variables (vertebral artery flow velocity, basilar artery flow velocity, and systolic blood pressure) as well as patient-specific information (such as severity of carotid stenosis) were compared between the three patient

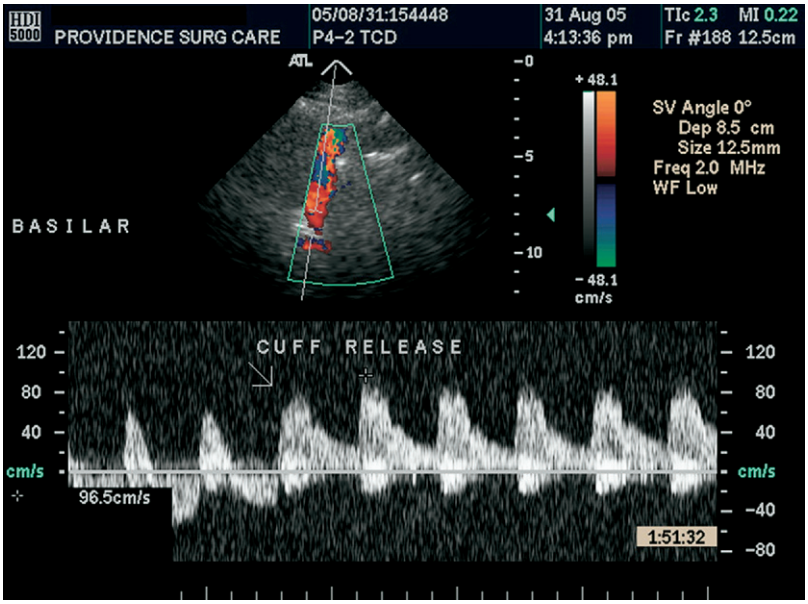

Fig 2. Doppler waveform of a patient with bidirectional basilar flow (note sinusoidal pattern prior to cuff release) which converted to retrograde flow upon release of blood pressure cuff following provocative ischemic challenge. Note the waveform is upright indicating blood flow directed toward the probe (retrograde flow) after cuff release.

groups: controls, subclavian steal with antegrade basilar artery flow, and subclavian steal with retrograde vertebral artery flow. A nonparametric Kruskal-Wallis test was applied to compare the distribution of the continuous outcome variables between groups.

The ratio of the brachial systolic blood pressure ipsilateral to retrograde vertebral artery flow to the brachial systolic pressure contralateral to the retrograde vertebral artery flow was calculated. The ratio was compared between patients with antegrade basilar artery flow and those with retrograde basilar artery flow. Based on the distribution of the ratios, a threshold of 0.66 was selected. Fisher's exact *t* test was used to analyze the distribution of ratios between the two groups based on a threshold ratio of 0.66. A receiver operating characteristic (ROC) curve would be ideal to achieve a more precise threshold, but this requires a greater population size than the one used in this study.

RESULTS

Extracranial carotid duplex ultrasonography, bilateral brachial systolic blood pressures, and blood flow in the vertebral arteries was assessed in 1681 patients. Of the 57 patients with reversal of flow in a vertebral artery on ECDU, 10 males (aged 58-85 years; mean 70.7) and 15 females (aged 47-85 years; mean 66) agreed to assessment of the posterior cerebral circulation via transcranial Doppler ultrasonography scan (pTCD). There was no difference in ECDU between patients agreeing to participate and those refusing, with refusal based primarily upon unwillingness to undergo further testing. In those patients who exhibited retrograde vertebral flow with antegrade basilar flow at rest, a provocative test was performed on the arm ipsilateral to the subclavian steal in order to assess the possibility of reversal of flow in response to induced arm ischemia. Five of the 25 patients presented with symptoms suggestive of posterior circulation ischemia (vertigo, diplopia, lightheadedness, dizziness, and near syncope); the remaining 20 did not exhibit symptoms of posterior circulation ischemia. There was no correlation between presence of symptoms and basilar artery flow. An additional 11 patients (6 males, 5 females, aged 34-91 years, mean 68.9), with normal (antegrade) vertebral flow were studied with pTCD at the request of referring physicians for neurologic symptoms. This group is included as a control population. All 11 control patients presented with symptoms suggesting posterior circulation insufficiency.

Basilar artery flow. Nineteen of 25 (76%) patients with retrograde vertebral artery flow demonstrated antegrade basilar artery flow at rest. Reversal of basilar artery flow was present in the remaining 6 patients (24%). Five demonstrated complete flow reversal at rest; one demonstrated bidirectional flow at rest which became retrograde throughout the cardiac cycle following the provocative ischemia test (Fig 2).

Basilar artery peak velocity was significantly decreased in patients with retrograde basilar artery flow at rest compared to patients with subclavian steal and antegrade basilar artery flow. The basilar artery peak velocity was 92 +/− 22 cm/second in patients with antegrade basilar artery flow compared to 47 +/− 20 cm/second in patients with retrograde basilar flow at rest ($P = .033$).

In the 19 patients with antegrade basilar artery flow at rest, no patient developed retrograde flow following the provocative ischemia test. There was no significant change

Table I. Comparison of peak systolic velocities in the vertebral and basilar arteries among the three groups. Retrograde vertebral artery velocities are significantly decreased compared to antegrade in both subclavian steal groups

	n	*Antegrade VA PSV*	*Retrograde VA PSV*	*BA PSV @ rest*	*BA PSV post-provocative*
Antegrade B A Flow	19	92 +/− 32	71 +/− 36*	92 +/− 22	81 +/− 23***
Retrograde B A Flow	5	93 +/− 30	55 +/− 11**	47 +/− 20	N/A
Control	11	(R) 44 +/− 11	(L) 48 +/− 16	68 +/− 23	N/A

VA, vertebral artery; *BA*, basilar artery; *PSV*, peak systolic velocity (cm/sec); *(R)*, right; *(L)*, left.
*$P = .023$.
**$P = .042$.
***$P = .238$.

in basilar artery peak velocity following provocative testing (baseline: 92 +/− 22 cm/second; after provocative testing: 81 +/− 23 cm/second; $P = .238$). In addition, there was no significant difference in basilar artery peak velocity between the control patients (68 +/− 23 cm/second) and subclavian steal patients with antegrade basilar artery flow at rest ($P = .35$) (Table I).

Vertebral artery flow. There was a significant increase in vertebral artery peak velocity in the antegrade vertebral artery compared to the retrograde vertebral artery, regardless of the direction of flow in the basilar artery. In patients with antegrade basilar artery flow, the peak velocity in the antegrade vertebral artery was 92 +/− 32 cm/second compared to 71 +/− 36 cm/second in the retrograde vertebral artery ($P = .023$). In patients with retrograde basilar artery flow, the peak velocity in the antegrade vertebral artery was 93 +/− 40 cm/second compared to 55 +/− 11 cm/second in the retrograde vertebral artery ($P = .042$). There was no difference between the right (44 +/− 11 cm/second) and left (48 +/− 16 cm/second) vertebral artery flow velocity in the control group ($P = .365$) (Table I).

Association of retrograde basilar flow with carotid stenosis. One of 11 (9%) control patients demonstrated a unilateral carotid stenosis of more than 50%. Six of 19 (32%) of subclavian steal patients with antegrade basilar artery flow had a greater than 50% carotid stenosis. Three of the 6 (50%) patients with retrograde basilar artery flow also demonstrated greater than 50% carotid stenosis; 2 had bilateral carotid artery stenosis.

Association of retrograde basilar flow with systolic blood pressure. In patients with subclavian steal and antegrade basilar artery flow, the average difference in brachial systolic pressure was 35 +/− 14 mm Hg. In patients with subclavian steal and retrograde basilar artery flow, the average difference in brachial systolic pressure was 53 +/− 17 mm Hg. This difference was not statistically significant. A ratio of the pressure in the affected arm compared to the pressure in the unaffected arm was also calculated (arm/arm index [AAI]) to discount inter-patient variability. The average ratio was 0.75 in patients with antegrade basilar artery flow and 0.62 in patients with retrograde basilar artery flow. The difference in the brachial systolic pressure ratio was significant between the two groups with a threshold of 0.66 ($P = .015$) (Fig 3).

DISCUSSION

Subclavian steal syndrome was originally reported in 1960 but was first formally described in the United States by Fisher in 1961.[5] This syndrome was defined in hemodynamic terms as reversal of blood flow in the vertebral artery due to proximal stenosis of the ipsilateral subclavian artery, most commonly occurring on the left side.[6,7] There was no mention of clinical symptoms associated with subclavian steal, however, they hypothesized that vertebrobasilar ischemia was due to abnormal blood flow in the cerebral vasculature.

The potential contribution of basilar artery blood flow to retrograde vertebral artery flow is important. Were blood to be siphoned from the Circle of Willis through the basilar artery, patients could potentially be at risk for ischemic stroke or hypoperfusion symptoms. The first published study by Patel et al[8] to investigate this question concluded that blood was indeed being siphoned from the basilar artery using aortic arch angiography in order to visualize the vertebral and subclavian arteries.

Our study demonstrates that intracranial circulation is an infrequent contributor to collateral arm circulation in patients with subclavian steal. Even in those patients with retrograde basilar flow, basilar velocities were substantially lower than both patients with antegrade flow at rest and controls, suggesting a minor contribution to collateral flow, with the majority coming from the unaffected vertebral artery.

Case reports of symptomatic patients investigated with TCD demonstrate flow reversal in the basilar artery, but larger series have reported variable results.[9,10] Budigen et al[11] found some abnormality in basilar flow in most patients, but they were unable to insonate the basilar artery in 40% of the patients they studied. Bornstein et al[12] found normal basilar flow at rest in all 33 patients studied with severe subclavian steal and unilateral vertebral flow reversal, and suggested that "subclavian steal is little more than a harmless hemodynamic phenomenon".

Studies utilizing provocative testing, either with exercise of the affected arm or induced ischemia, have also returned disparate results. In six patients with symptomatic subclavian steal, Webster et al[13] found a decrease in regional blood flow of 13% to 90% after arm exercise, using xenon-computed tomography cerebral flow mapping.

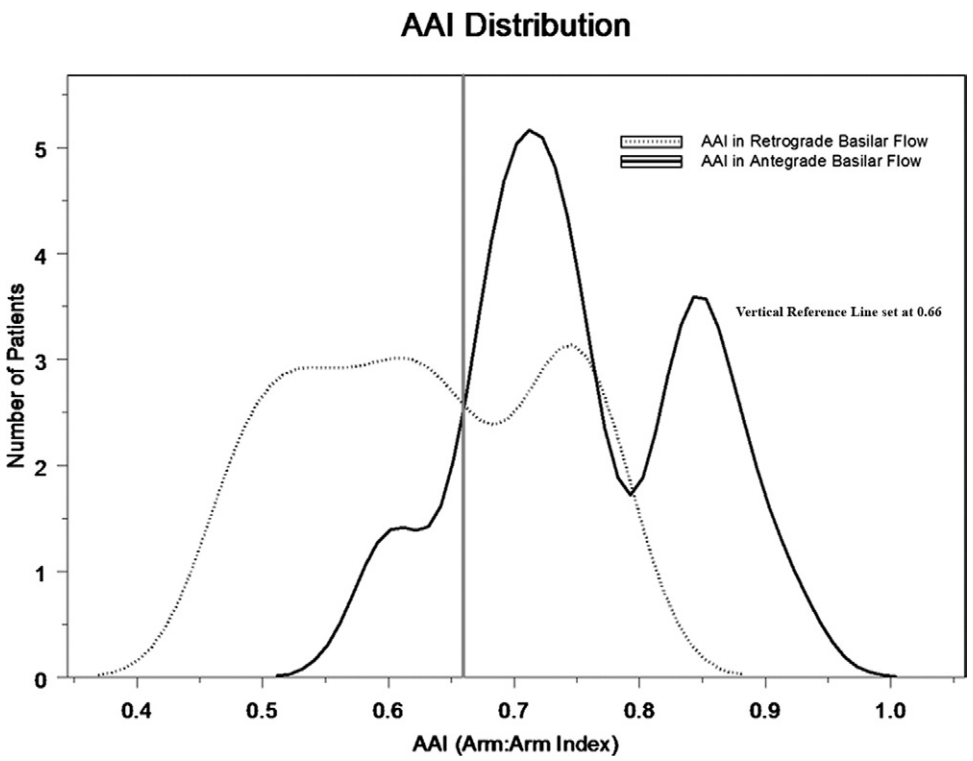

Fig 3. Distribution of arm:arm indices (AAI) in both antegrade and retrograde basilar flow groups. The retrograde basilar flow group clusters at a value below 0.66 indicated by the vertical line, while the antegrade basilar flow group clusters primarily above 0.66. We arbitrarily chose 0.66 as our threshold, values below which were found be predictive of retrograde basilar flow using Fisher's Exact *t* Test ($P = .015$).

Kaneko et al[14] evaluated 7 patients using single-photon emission computed tomography (SPECT) and found exercise induced a decrease in global regional cerebral blood flow only in the single patient with symptoms of vertebral basilar insufficiency, concluding that subclavian steal is a benign condition in asymptomatic patients. In a study similar to ours, de Bray et al[15] studied 54 patients with abnormal (reversed or to-and-fro) vertebral flow, and induced reactive hyperemia using a brief cuff occlusion (3 minutes) of the ipsilateral brachial artery. He noted only 1 patient with reversal of flow in the basilar artery at rest, with 7 additional patients having basilar flow abnormalities after reactive hyperemia. All were symptomatic.

The correlation of a low AAI with reversal of blood flow in the basilar artery is interesting, and may help direct the need for additional imaging studies in patients with non-specific symptoms of vertebro-basilar insufficiency when TCD is unavailable. Although our series correlated an increased incidence of basilar reversal of blood flow with AAI of <0.66, the series is too small to make an absolute recommendation for this as a cutoff.

There is increasing interest in percutaneous therapies for disease of the subclavian and vertebral arteries.[16] Both open surgical and percutaneous subclavian revascularization were reviewed by Palchik et al[17] from the University of Rochester, with generally satisfactory results, however only 18% of the patients had VBI symptoms, and hemodynamics of the intracranial circulation was not reported. The only randomized prospective clinical trial of vertebral artery angioplasty and stenting found no benefit to intervention over medical therapy, but the number of enrollees was small.[18]

Unfortunately, the symptoms of posterior circulation compromise are non-specific, including vertigo, diplopia, circumoral numbness, drop attacks, and dizziness. Similarly, subclavian steal hemodynamics are common, and generally thought to rarely cause reversible symptoms or presage posterior circulation stroke. Aggressive intervention for asymptomatic subclavian steal, or subclavian steal with non-specific symptoms, is not supported. Reversal of basilar artery blood flow, at rest or with stress, would support a hemodynamic etiology to presenting symptoms. Our study demonstrates the infrequent occurrence of basilar flow reversal with subclavian steal and suggests an increased role of TCD, or alternatively an AAI, in defining a population of patients that may warrant further investigation or therapy.

Our study does not address the true risk of basilar flow reversal for posterior circulation stroke, nor does it correlate true posterior circulation symptoms with basilar flow. It does, however, support the contention that collateral flow in subclavian steal syndrome is predominately from the

normal vertebral artery, and there is rarely a contribution from the cerebral circulation. The greater the disparity in arm pressures, as manifested by a low AAI, the greater the likelihood that basilar blood flow contributes to collateral support, and presumably the greater likelihood that symptoms of posterior circulatory insufficiency are due to the steal.

AUTHOR CONTRIBUTIONS

Conception and design: PC, RBP, AW
Analysis and interpretation: CH, RP, PC
Data collection: PC, RP, AW
Writing the article: CH, PC, RP
Critical revision of the article: RP, CH, PC
Final approval of the article: CH, RP, PC
Statistical analysis: CH
Obtained funding: Not applicable
Overall responsibility: CH, RP

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