

# Vertebral Artery Blood Flow Velocity Changes Associated with Cervical Spine Rotation: A Meta-Analysis of the Evidence with Implications for Professional Practice

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**T**he clinical importance and relevance of changes in vertebral artery (VA) blood flow associated with cervical spine rotation, as used by manual therapists in the treatment of patients, have been the focus of considerable research over the past 50 years. The findings of early cadaver studies<sup>1-5</sup>, suggesting a significant decrease of VA blood flow on the side contralateral to the direction of cervical spine rotation, led to *in vivo* measurements of VA blood flow using flowmetry, angiography, magnetic resonance imaging<sup>6-13</sup> and, most commonly, Dop-

pler insonation<sup>10,14-45</sup>. Despite the many studies published to date, the findings remain controversial, and the evidence base for clinical practice is not strongly convincing.

The majority of these studies report compromised contralateral VA blood flow<sup>15,16,19,22,25,27-29,39,42,43</sup>. However, some authors found no associated change in VA blood flow<sup>10,18,21,32,35,38,41</sup>, while a few reports indicated an increase, in some cases, in contralateral<sup>15,30,40,44</sup> and in ipsilateral<sup>25</sup> blood flow. These contradictory findings are most likely because of differ-

ences in methodology and procedures for measuring VA blood flow changes across the various studies. For instance, healthy persons<sup>10,16,18,19,22,24,25,29,39-43</sup> as well as patients<sup>15,23,30-32,35,38</sup>, some exhibiting signs and symptoms of vertebrobasilar insufficiency or ischemia (VBI)<sup>21,23,29-32,38</sup>, were used as subjects. The individuals were variously positioned in sitting<sup>16,22,30,43,44,46</sup>, supine lying<sup>25,29,40,42</sup>, or prone lying<sup>39</sup>. Different instrumentation was used by the researchers for Doppler insonation of the VA, including continuous wave<sup>18,23,30,31</sup> and pulsed-wave<sup>10,15,16,19,21,22,25,26,28,29,32,35,38-44,46</sup> Doppler, with and without color flow imaging. Lastly, different parts of the VA were studied, such as the pre-vertebral (VA1)<sup>10,25,26,32,38</sup>, cervical (VA2)<sup>15,18,19,21,23,24,29-31,35-37,40-42</sup>, suboccipital (VA3)<sup>44,45</sup>, or intracranial (VA4)<sup>16,22,28,39,43</sup> parts (Figure 1). All of these differences are possible sources of bias and, ideally, should be standardized in future research projects.

It has been suggested in the literature that the part of the VA insonated is an important factor in measurements of blood flow changes associated with cervical spine rotation<sup>47,48</sup>. This view relates to the belief that the most vulnerable part of the VA to distortion is that part between the axis and atlas vertebrae, where most cervical spine rotation takes place<sup>15,29,35,40-42,49-52</sup>. However, it has been proposed also that the natural tortuosity

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**ABSTRACT:** Many studies of vertebral artery (VA) blood flow changes related to cervical spine rotation have been published, but the findings are controversial and the evidence unconvincing. Recent Doppler measurements suggest that contralateral VA blood flow is compromised on full rotation in both healthy subjects and patients. More rigorous research is needed, and it was the aim of this study to conduct a meta-analysis of published data to inform professional practice. A systematic literature search, including only Doppler studies of VA blood flow velocity associated with cervical spine rotation in adults, yielded nine reports with published data. Using weighted means of the pooled data, the magnitude of the effect size (Cohen's *d*) was calculated for differences between patients and subjects, sitting or lying supine for testing, the parts of the VA insonated, and the changes recorded after cervical spine rotation. From this meta-analysis, VA blood flow velocity was found to be compromised more in patients than healthy individuals, on contralateral rotation, with the subject sitting, and more in the intracranial compared to the cervical part of the VA. Possible reasons for these findings are suggested, and it is advised that sustained end-of-range rotation and quick-thrust rotational manipulations be avoided until there is a stronger evidence base for clinical practice.

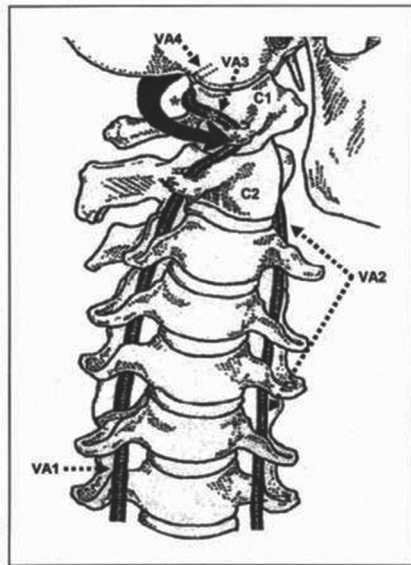
**KEYWORDS:** Blood Flow, Cervical Spine Rotation, Physical Therapy, Vertebral Artery

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**FIGURE 1.** Anterior view of the cervical spine and vertebral arteries. The head is fully rotated to the left. The right vertebral artery, divided into its four parts (VA1-4), is illustrated. Note the possible torsion, during cervical spine rotation, on VA3, as it passes through the transverse foramen, along the posterior arch, or around the lateral mass of the atlas vertebra (C1) (marked with \*). **Key:** C1 = atlas, C2 = axis

of the VA between the first and second vertebrae should prevent much of this apparent distortion of the vessel<sup>35,51,53</sup>. In addition, mechanical compression and/or stretching of the VA is more likely to occur to its suboccipital part, on full-range cervical spine rotation, as it passes through the transverse foramen and along the posterior arch<sup>47,48,54-60</sup>, or around the bony lateral mass of the atlas vertebra<sup>39,43,48,49,51,59-63</sup>, where it is bound down by connective tissue<sup>16,22,35,39,43,59,64</sup> (Figure 1).

Considering these anatomical factors and the hemodynamics of normal blood flow in medium-sized muscular vessels such as the VA<sup>65</sup>, some researchers have put forward the idea that VA blood flow changes associated with rotation would be more accurately measured down-stream from or distal to the possible point of distortion, that is, in the suboccipital or intracranial parts of the artery<sup>41,47,48</sup>. According to Bernoulli's Principle<sup>65</sup>, there is an increase in blood flow velocity at and/or immediately beyond the point of constriction of a vessel, because of either compression or stretching. At this point, there is a reduction in the diameter of the vessel, which causes an increase in flow velocity (Poiseuille's Law: Flow is proportional to the fourth power of the radius of the vessel)<sup>65</sup>. This may manifest as a "spurting" of blood at this point or turbulence of

flow in the artery immediately downstream from the region of distortion. This results in a decrease in blood flow velocity a short distance distal to this point in the artery, and blood flow usually returns to normal laminar flow in the more distal parts of the vessel<sup>65</sup>. Therefore, it seems logical to measure blood flow in that part of the VA distal to these regions of disturbed hemodynamics as it is likely that the part of the VA measured for changes in blood flow associated with cervical spine rotation may affect the outcomes.

Most blood flow studies conducted have measured changes in blood flow velocity associated with cervical spine rotation. Although blood flow volume is the main parameter affecting brain perfusion<sup>65</sup>, relative changes in velocity may be used to reflect changes in volume<sup>47,66,67</sup>. These assumptions are based on the low pulsatility index of the VA and the fact that its internal diameter (and mean cross-sectional area) does not change during normal laminar blood flow. It may be expected, therefore, that blood flow velocity (cm/s, i.e., speed of blood flow) and blood flow volume (cm<sup>3</sup>/s, i.e., taking the speed of flow and the cross-sectional area of the vessel into account) will vary proportionally<sup>66,67</sup>. Thus, a measure of changes in blood flow velocity, associated with movements of the cervical spine, can be considered a good

indicator of related changes in blood flow volume.

Several narrative or descriptive critical reviews of available reports have been conducted<sup>47,48,59,68</sup>, and all concluded that more controlled research is needed. However, to the best knowledge of this author, an analysis of the data of these studies has not been done. In this context, a quantitative analysis, such as a meta-analysis of published data, may be of value. A meta-analysis is an accepted method of quantitatively comparing and summarizing the results of previous research across a range of studies. It does not depend on sample size as do traditional statistical tests such as the *t*- and *F*-tests, and it uses an estimate of the measure of the magnitude of the effect of an intervention. The most common estimate of effect size in current meta-analyses is Cohen's *d*, which is calculated as the standardized difference between two means, that is, by dividing the difference of the means by the pooled standard deviations for the pre- and post-intervention data reported in the studies.

As no meta-analyses of VA blood flow data have been published to date, it was the aim of this study to critically review the current literature and quantitatively analyze the reported findings of VA blood flow velocity changes related to cervical spine rotation. From this

analysis, unreliable and invalid findings can be disregarded, and key messages based on stronger evidence can be put forward to inform professional practice.

### Methods

A systematic literature search was conducted of all available reports, related to VA blood flow changes associated with cervical spine rotation, in manual therapy, physical therapy, chiropractic, and allied medical journals over the past 50 years. The search engines AMED, CINAHL, Cochrane Library, Embase, Medline (PubMed), and Pedro were used, and previous searches<sup>47,48,68</sup> were refined to include only search terms such as *vertebral artery, vertebrobasilar insufficiency/ischemia, cervical spine movements/rotation/extension, blood flow volume/velocity/measurement, and Doppler/ultrasound/insonation*. Unpublished reports; papers written in foreign languages without English abstracts; human cadaver, animal, and *in vitro* studies; and single case studies were excluded. Reports of adult subjects and patients who may or may not have been exhibiting signs and symptoms of VBI, any or all parts of the VA measured, studies of multiple cases, descriptive studies, and controlled trials were included. The search was refined further by selecting only reports of Doppler insonation or measurement of VA blood flow velocity.

From this literature search, 40 articles were retrieved, of which 10 were reports of VA blood flow measurements in a neutral cervical spine position only, and 30 involved rotation of the cervical spine and pre- and post-rotational measurements of VA blood flow velocity. Of these 30 articles, nine were excluded initially in an effort to minimize the influence of confounding variables when comparing research findings across several studies. These either involved subjects under 18 years of age<sup>23</sup>; abnormal VA anatomical relationships such as hypoplasia or aplasia<sup>45</sup>; use of cervical spine traction<sup>18,24</sup>, spinal manipulation<sup>10,21,26</sup>, or extension<sup>28</sup> as opposed to normal, full-range rotation; and data on the internal carotid artery only re-

ported<sup>38</sup>. A further 12 articles were rejected finally: those reporting re-analysis of previously published data<sup>22,35</sup> and blood flow velocity data not given or able to be calculated from the documented measurements<sup>19,30-32,37,41,46,69-71</sup>.

Of the remaining nine reports, one article compared two groups of individuals: subjects not showing signs and symptoms of VBI on the standard test, and those positive for VBI on testing<sup>29</sup>, while eight studies involved pre- and post-rotational (-interventional) measurements of blood flow velocity, each subject acting as his or her own control<sup>15,16,25,39,40,42-44</sup> (Figure 2). None of these studies could be classified strictly as controlled trials, however.

In conducting a meta-analysis of the data given in these reports, the articles were reviewed according to the following factors:

- Type of Doppler used
- Patient or healthy subject measured
- Current signs and symptoms of VBI noted
- Measurement position of subject used
- Part of VA insonated
- Changes in VA blood flow recorded

To standardize the calculation of blood flow velocity across the studies that provided the required data, the following equation was used:  $BF_{vel} = [(PS - ED)/3] + ED$  where  $BF_{vel}$  = blood flow velocity, PS = peak systolic velocity, and ED = end diastolic velocity. This equation was derived from that used for mean arterial pressure, which equals a third of the pulse pressure (i.e., the difference between systolic and diastolic pressure) plus the diastolic pressure<sup>65</sup>. The standard *t*-test was used to test for statistical differences between the VA blood flow means across the various studies, using the weighted means and a significance level of  $p \leq 0.05$ . To compare the measured blood flow velocities and changes of VA blood flow associated with cervical spine rotation as a standardized mean across these studies, in order to calculate the magnitude of the effect of the intervention, the following equation was used:  $d = \text{mean}_1 - \text{mean}_2 /$

$\sqrt{[(sd_1^2 + sd_2^2) / 2]}$  where  $d$  = Cohen's  $d$ , the descriptive measure of effect size, and  $sd$  = standard deviation. Values for  $d$  of more than or equal to 0.8, 0.5, and 0.2 were taken to represent large, medium, and small effect sizes, respectively, with 0.0 indicating that there is a 50% overlap of the one mean value with the other mean value or that there is no difference in the distribution of scores between the two categories being compared (Table 1).

### Results

#### Doppler Method and Measurement Position

All nine studies reviewed and analyzed<sup>15,16,25,29,39,40,42-44</sup> used pulsed-wave Doppler and imaging of the vessel in insonating extracranial<sup>15,25,29,40,42,44</sup> and intracranial<sup>16,39,43</sup> VA blood flow changes (Table 2). Blood flow velocities were given or could be calculated from the peak systolic velocities in four studies<sup>15,29,40,42</sup>, and the remaining five reports<sup>16,25,39,43,44</sup> documented the data as blood flow velocities. Thus, it was possible to make comparisons of the blood flow data in this analysis.

With the exception of one study that did not record the patient's position<sup>15</sup>, and one that positioned the subjects in prone lying<sup>39</sup>, the measurements were carried out with the individuals in either sitting<sup>16,43,44</sup> or supine lying<sup>25,29,40,42</sup> (Table 2). On statistical analysis of the data, using the weighted means and the *t*-test, no significant difference between supine lying and sitting was found in any of the blood flow measurements recorded. However, again using the weighted means, when comparing the pooled blood flow data with the subjects sitting and lying supine, VA blood flow was found to be higher in supine lying for all measurements (Table 3). The effect size was large in the neutral cervical spine position ( $d = 1.45$  [total group],  $d = 1.39$  [subjects only]), with contralateral rotation ( $d = 0.90$  [total group],  $d = 1.01$  [subjects only]), and for the calculated mean change in blood flow across all studies ( $d = 4.03$  [total group],  $d = 3.27$  [subjects only]) (Table 4). On ana-

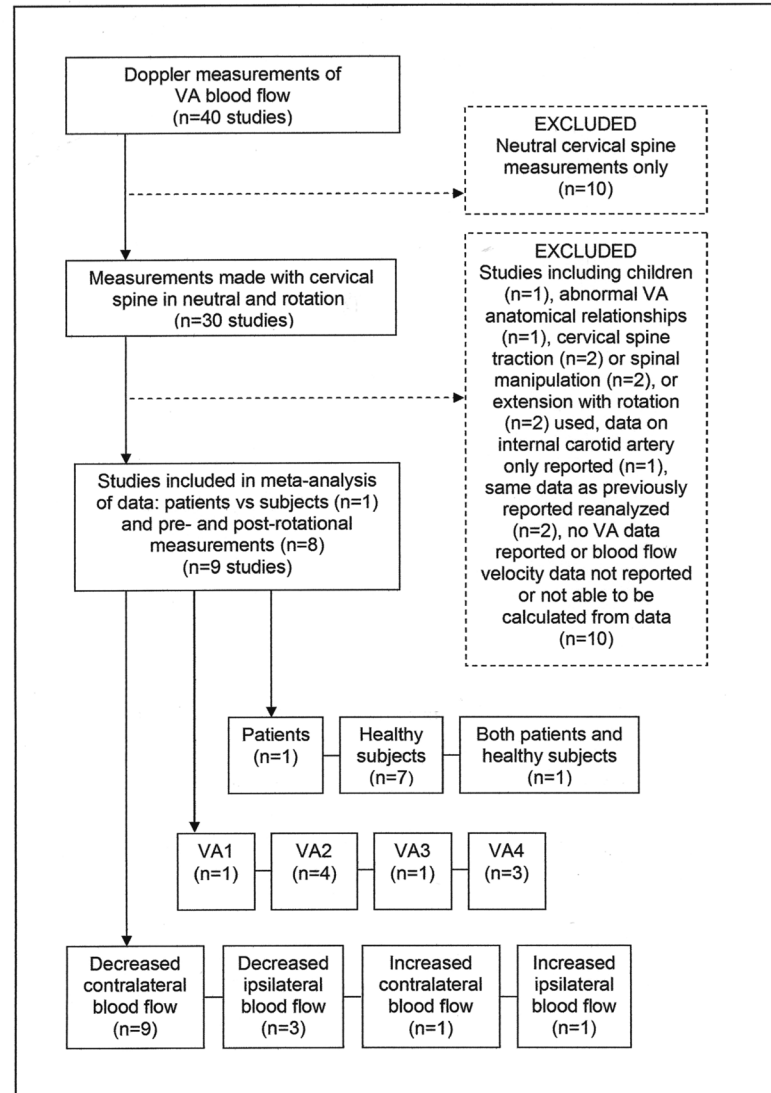


FIGURE 2. Flow chart illustrating the process of selection of research reports for the meta-analysis of published data.

lyzing the data across the few studies that provided ipsilateral blood flow measurements<sup>16,25,39,42,44</sup>, a small effect size ( $d = 0.10$ , [total group]) was found for changes with ipsilateral rotation.

### Subjects and VBI

One study<sup>15</sup> used patients only and did not report whether signs and symptoms of VBI were experienced during or as a result of the measurement procedure. A further report involved both healthy subjects and patients<sup>29</sup>, some of whom had a history of VBI. Healthy persons, with no manifestations of VBI, were the subjects in the remaining seven articles<sup>16,25,39,40,42-44</sup> (Table 2).

The mean VA blood flow values after pooling the data across all the studies indicated that patients had considerably lower blood flow velocities than healthy individuals, both in the neutral cervical spine position and with contralateral rotation (Table 3). Although this was the expected result, statistical analysis with the *t*-test and using the weighted means showed no significant differences between the two groups of subjects, either for VA1-4, or in VA2 alone, for the neutral position or with contralateral rotation. Values for ipsilateral rotation were not given for patients; hence, it was not possible to compare outcomes for this type of rotation in these two groups of individuals.

On further comparison of blood flow data between healthy subjects and patients, across all the studies, a large effect size was found for VA blood flow in the neutral cervical spine position ( $d = 1.64$ ), with contralateral rotation ( $d = 2.14$ ), and for the change in blood flow ( $d = 1.91$ ) for VA1-4, indicating a lower blood flow and a greater reduction in velocity in the patients in the pre- and post-intervention measurements (i.e., in the neutral and rotated cervical spine positions). On using data for VA2 only, a large effect size was found for contralateral rotation ( $d = 0.92$ ) only, and a larger change in blood flow ( $d = 4.04$ ) (Table 4). A comparison between healthy subjects and patients for VA4 blood flow

**TABLE 1.** Cohen's effect sizes and corresponding percentages

Effect size value <i>d</i>	Percentage of score distribution overlap	Effect size strength
0.0	50%	
0.1	54%	
0.2	58%	Small
0.3	62%	
0.4	66%	
0.5	69%	Moderate
0.6	73%	
0.7	76%	
0.8	79%	Large
0.9	82%	
1.0	84%	
1.2	88%	
1.4	92%	
1.6	95%	
1.8	96%	
≥ 2.0	98+%	

*d* = Cohen's *d* (measure of effect size)

could not be done as no data was provided for patients in the studies reviewed.

### *Changes in VA Blood Flow*

All nine studies reviewed described a change in VA blood flow velocity associated with cervical spine rotation (Tables 2 and 3). Overwhelmingly, this change was related to contralateral rotation regardless of whether healthy subjects or patients were measured.

Large effect sizes were calculated for VA1-4 (*d* = 1.31) and for VA2 (*d* = 1.35), comparing VA blood flow values in the neutral position with contralateral rotation of the cervical spine across the studies (Table 4). Interestingly, VA2 blood flow was not more effectively compromised in patients than healthy subjects (*d* = 0.8 and 0.9, respectively) (Table 4). The VA3 blood flow changes associated with cervical spine rotation only showed a small effect size (*d* = 0.16) (Table 4), and there was a similarly small effect size for ipsilateral rotation (*d* = 0.16).

### *Part of the VA Insonated*

In the nine articles reviewed, one reported measurement of blood flow in

the first or pre-cervical part of the artery (VA1)<sup>25</sup>, one in the suboccipital region (VA3)<sup>44</sup>, three in the intracranial area (VA4)<sup>16,39,43</sup>, and four in the mid- to upper cervical part of the artery (VA2)<sup>15,29,40,42</sup> (Tables 2 and 3). Further quantitative analysis comparing VA2, VA3, and VA4 blood flow velocities across the studies revealed that in the neutral cervical spine position, although the weighted means are similar, VA2 blood flow was effectively greater than that in VA3 (*d* = 0.60) but less than that in VA4 (*d* = 1.48) (Table 4). On contralateral rotation, VA blood flow was more effectively reduced in VA4 when compared to that in VA2 (*d* = 1.10) or VA3 (*d* = 0.87), while there was less of a reduction effect (*d* = 0.67) seen on comparing VA2 and VA3 blood flow.

## **Discussion**

### *Doppler Method and Measurement Position*

The method of insonation was not regarded as a differentiating factor for the purpose of this analysis as all nine studies reviewed used pulsed-wave Doppler and imaging to insonate the VA.

Both sitting and supine lying, as used in the reports analyzed, are the

common postures for the standard VBI test in clinical practice. Although prone lying may allow free access to VA3 and VA4, it is not the most comfortable position for many older individuals. Supine lying offers the most direct access to VA2 but does not enable unhindered insonation of VA3 or VA4, especially in the neutral position of the cervical spine. Although there was no significant difference shown between the measurements in the two positions in this analysis, the sitting position seems optimal for insonating all four parts of the VA.

However, the higher blood flow velocities recorded in supine lying and the larger effect sizes calculated on comparing the positions, for the neutral cervical spine position and contralateral rotation, indicate that the choice of the position used for measuring the subjects could effectively influence the outcome measures (i.e., VA blood flow). These differences are difficult to explain in terms of current hemodynamic theory, especially in the group of healthy, young adults. In the studies reviewed, different parts of the VA were measured in the two positions: VA4 in sitting and VA2 in supine lying. The position of the subject may have influenced the ease and accuracy of insonation and, hence, the blood flow measurements. The possibility of the various parts of the VA having different blood flow velocities is discussed further in the section below entitled Part of the VA Insonated.

### *Subjects and VBI*

This meta-analysis of data suggests that both the pre- and post-intervention blood flow values are greater in healthy subjects and effectively compromised by contralateral rotation more so in the patient group, particularly in VA2. This may be a result of a number of factors, including an inadequate collateral vertebral basilar circulation or vascular pathology (e.g., atherosclerosis) compromising VA blood flow in this patient group. This is partly supported by the fact that some of the patients manifested signs and symptoms of VBI. However, this was not discussed by any of the authors and remains a tentative suggestion

**VERTEBRAL ARTERY BLOOD FLOW VELOCITY CHANGES ASSOCIATED WITH CERVICAL SPINE ROTATION**

TABLE 2. Description of studies of vertebral artery blood flow measurements associated with cervical spine rotation

Authors	Subjects	VBI	Doppler			Mean blood flow measurements (cm/s)				
			method	VA	change	neutral	ipsi	difference	contra	difference
Arnold et al <sup>42</sup>	22s-supine	nil	PW+C	VA2	↓ contra	31.40	32.97	+1.57	27.17	-4.23
Licht et al <sup>25</sup>	20s-supine	nil	PW+C	VA1	↓ contra ↑ ipsi	68.00	72.00	+4.00	61.00	-7.00
Mitchell <sup>39</sup>	120s-prone	nil	TCD	VA4	↓ contra ↓ ipsi	36.78	33.56	-3.22	29.74	-7.04
Mitchell et al <sup>43</sup>	30s-sitting	nil	TCD	VA4	↓ contra ↓ ipsi	36.85	33.83	-3.02	33.53	-3.32
Mitchell & Krauschuster <sup>44</sup>	35s-sitting	nil	PW+C	VA3	↓ ipsi ↑ contra	24.93	24.67	-0.26	25.18	0.25
Rivett et al <sup>29</sup>	10p-supine 10c-supine	VBI nil	PW+C	VA2	↓ contra ↓ contra	30.78 27.70			24.33 21.17	-6.45 -6.53
Rivett et al <sup>40</sup>	20s-supine	nil	PW+C	VA2	↓ contra	21.25			20.05	-1.20
Rossitti et al <sup>16</sup>	30s-sitting	nil	TCD	VA4	↓ contra	34.00	29.00	-5.00	30.10	-3.90
Stevens <sup>15</sup>	7p	—	PW+C	VA2	↓ contra	14.83			8.33	-6.50

c = control group, C = Doppler with color flow imaging, change = VA blood flow change from neutral to rotated cervical spine position, contra = contralateral rotation/blood flow, difference = difference in blood flow measurements between the neutral and rotated positions, ipsi = ipsilateral rotation/blood flow, neutral = no cervical spine rotation, p = patients or subjects with VBI signs and symptoms, PW = pulsed-wave Doppler, s = healthy subjects with no VBI signs and symptoms, TCD = transcranial Doppler (PW+C), VA = vertebral artery (VA1-4 = parts 1, 2, 3, 4), VBI = vertebrobasilar insufficiency, ↓ = decreased blood flow, ↑ = increased blood flow

TABLE 3. Weighted mean vertebral artery blood flow velocity measurements (cm/s)

	VA1-4			VA2			VA3			VA4		
	neutral	contra	change	neutral	contra	change	neutral	contra	change	neutral	contra	change
<b>Blood flow velocity: pooled data</b>												
<b>Total group</b>	<b>n=10</b>			<b>n=5</b>			<b>n=1</b>			<b>n=3</b>		
mean	34.79	29.90	-4.89	27.43	23.45	-3.98	24.93	25.18	0.25	36.33	30.43	-5.90
sd	4.10	3.32	0.82	3.04	2.85	0.46	1.58	1.50	0.25	10.75	8.39	2.36
<b>Subjects</b>	<b>n=8</b>			<b>n=3</b>			<b>n=1</b>			<b>n=3</b>		
mean	35.42	30.62	-4.79	26.78	23.28	-3.51	24.93	25.18	0.25	36.33	30.43	-5.90
sd	4.59	3.66	0.96	4.03	3.71	0.67	1.58	1.50	0.25	10.75	8.39	2.36
<b>Patients</b>	<b>n=2</b>			<b>n=2</b>			<b>n=1</b>			<b>n=3</b>		
mean	24.21	17.74	-6.47	24.21	17.74	-6.47	24.93	25.18	0.25	36.33	30.43	-5.90
sd	8.49	7.70	0.79	8.49	7.70	0.79	1.58	1.50	0.25	10.75	8.39	2.36
<b>Supine-lying</b>												
<b>Total group</b>	<b>n=5</b>			<b>n=3</b>			<b>n=1</b>			<b>n=3</b>		
Mean	37.32	32.61	-4.72	26.78	23.28	-3.51	24.93	25.18	0.25	36.33	30.43	-5.90
sd	5.47	5.03	0.52	4.03	3.71	0.67	1.58	1.50	0.25	10.75	8.39	2.36
<b>Subjects</b>	<b>n=3</b>			<b>n=3</b>			<b>n=1</b>			<b>n=3</b>		
mean	38.23	33.75	-4.48	26.78	23.28	-3.51	24.93	25.18	0.25	36.33	30.43	-5.90
sd	6.66	6.08	0.68	4.03	3.71	0.67	1.58	1.50	0.25	10.75	8.39	2.36
<b>Patients</b>	<b>n=1</b>			<b>n=3</b>			<b>n=1</b>			<b>n=3</b>		
mean	30.78	24.33	-6.45	26.78	23.28	-3.51	24.93	25.18	0.25	36.33	30.43	-5.90
sd	6.66	6.08	0.68	4.03	3.71	0.67	1.58	1.50	0.25	10.75	8.39	2.36

(continued)

**VERTEBRAL ARTERY BLOOD FLOW VELOCITY CHANGES ASSOCIATED WITH CERVICAL SPINE ROTATION**

**TABLE 3.** Weighted mean vertebral artery blood flow velocity measurements (cm/s) (continued)

		VA1-4 neutral contra change	VA2 neutral contra change	VA3 neutral contra change	VA4 neutral contra change
<b>Sitting</b>					
<b>Total group</b>	<b>n=3</b>				
Mean		31.56	29.37	-2.19	
sd		1.24	0.70	0.72	
<b>Subjects</b>	<b>n=3</b>				
mean		31.56	29.37	-2.19	
sd		1.24	0.70	0.72	
<b>Patients</b>	<b>n=0</b>				

change = VA blood flow change from neutral to rotated cervical spine position, contra = contralateral rotation/blood flow. n = number of groups of subjects or patients/pooled measurements, neutral = no cervical spine rotation, VA = vertebral artery (VA1-4 = parts 1, 2, 3, 4).

**TABLE 4.** Effect size (Cohen's d) of comparable data

	VA1-4 neutral contra change	VA2 neutral contra change	VA3 neutral contra change	VA4 neutral contra change
<b>d (neutral / rotation)</b>				
total group	1.31	1.35		
subjects	1.16	0.90	0.16	0.61
patients	0.80	0.80		
<b>d (sitting / supine)</b>				
total group	1.45	0.90	4.03	
subjects	1.39	1.01	3.27	
patients				
<b>d (subjects / patients)</b>				
	1.64	2.14	1.91	
		0.39	0.92	4.04
<b>d (VA2 / VA3)</b>				
subjects		0.60	0.67	7.44
<b>d (VA2 / VA4)</b>				
subjects		1.18	1.10	1.38
<b>d (VA3 / VA4)</b>				
subjects			1.48	0.87
				3.66

change = VA blood flow change from neutral to rotated cervical spine position, contra = contralateral rotation/blood flow, d = Cohen's d (measure of effect size), neutral = no cervical spine rotation, VA = vertebral artery (VA1-4 = parts 1, 2, 3, 4).

as none of the studies reported evidence of turbulent blood flow, narrowing of vessels, or other reasons for compromised blood flow on insonation of the VAs.

### *Changes in VA Blood Flow*

This review indicates that it is contralateral rotation that is associated with VA blood flow velocity changes with cervical spine movements. An explanation for this may be that blood flow in the VA is likely to be reduced because of compression or stretching distortion forces by osteophytes in the cervical region<sup>46,72-78</sup>, between the atlas and axis vertebrae<sup>29,35,41,42,49-51</sup>, or along its course related to the atlas vertebra<sup>39,43,47-49,51,54-63</sup>. Where the VA was insonated is likely to be an influencing factor, therefore, and this is discussed in the following section.

In addition, Rivett et al<sup>40</sup> reported a decreased contralateral blood flow in the region of the second to third cervical vertebrae but an increased contralateral VA blood flow at the atlas-axis vertebral level. The authors gave no explanation for this difference in outcome. Similarly, the increase in VA2 blood flow found in 20% of cases on contralateral rotation by Stevens<sup>15</sup>, when 60% of subjects demonstrated decreased contralateral blood flow, may be a result of a number of confounding factors such as the small sample of seven patients used; a possible history or signs and symptoms of VBI, which were not discussed; the subject's position for blood flow measurement, which was not given; and the possibility of inaccurate insonation of the artery. On the other hand, Licht et al<sup>25</sup> reported an associated increase in blood flow on ipsilateral rotation in some subjects. However, these authors measured blood flow and documented average values only in VA1, which precludes further quantitative analysis of the data. Lastly, in a recent study of VA3<sup>44</sup>, a significant decrease in VA blood flow was found on ipsilateral rotation, possibly a result of compression of the vessel as discussed in the Introduction above, and a measurable but non-significant increase on contralateral rotation. Again, the part of

the VA measured may have influenced the outcome.

Despite these differences in the results in some of the studies, the overall evidence indicates significantly compromised VA blood flow on contralateral rotation of the cervical spine. The large effect sizes found for VA1-4 and for VA2, when comparing VA blood flow values in the neutral position with contralateral rotation of the cervical spine across the studies, support this (Table 4). Moreover, the lack of a more effectively compromised VA2 blood flow velocity in patients than in healthy subjects concurs with the findings of Rivett et al<sup>29</sup> of similar changes in VA2 blood flow in their patients and healthy subjects (Table 2). This suggests that the signs and symptoms of VBI on sustained cervical spine rotation reported by the patients in their study were more likely a result of an inadequate collateral vertebrobasilar circulation or of compromised blood flow because of vascular pathology, for example, in the more distal parts of the VA. No evidence was provided in that report to support this supposition, however, and it must be noted that false positive (and false negative) findings are possible in blood flow measurements. Nevertheless, the less effectively reduced blood flow in VA4, when compared with VA2, on contralateral rotation in the healthy subjects measured<sup>16,39,43</sup> may be a function of the part of the VA insonated, as discussed in the Introduction above and Part of the VA Insonated below.

The small effect size calculated in this analysis for VA3 blood flow changes associated with cervical spine rotation concurs with the previous finding of a non-significant change in VA3 blood flow with contralateral rotation<sup>44</sup>. However, the small effect size found for ipsilateral rotation is difficult to explain, considering the statistically significant change in blood flow velocities in healthy, young females<sup>44</sup>. It is likely that these results may have been confounded by the small sample size (n=30) in the earlier, single study<sup>44</sup>, and more evidence of such changes is necessary to establish the validity of the results.

### *Part of the VA Insonated*

The majority of all studies surveyed insonated VA2, which is the most easily accessible part of the vessel. However, neither VA2 nor VA1 fulfill the criteria for the optimal point for measurement of blood flow described in the Introduction, i.e., being upstream and often far removed from the region of cervical spine rotation. Although there is a lack of evidence for this, it seems logical that VA blood flow will vary below and above points of mechanical distortion associated with rotation of the cervical spine, with an increase in velocity because of the "spurting effect" at or immediately beyond the point of constriction of the artery<sup>65</sup>. Furthermore, the mean diameter of the artery changes along its course<sup>79,80</sup>, and because blood flow is a function of the cross-sectional area of a vessel<sup>65</sup>, the blood flow velocity would be expected to differ in the various parts of the VA, being greatest in the narrowest part (i.e., VA4). This is supported by the greater weighted mean blood flow values for VA4, compared to those for VA2 and VA3 (Table 3). In other words, the slower VA3 blood flow velocity to that of either VA2 or VA4, in the neutral cervical spine position, concurs with the hemodynamic theories related to blood flow velocities and size of vessels<sup>65</sup>.

However, on contralateral rotation, a greater reduction in VA4 blood flow velocity than in the more proximal VA2 and VA3 was found (Table 3). This is difficult to explain if one considers the hypothesis that rotation causes mechanical distortion of the VA at the suboccipital level and it would be expected that both VA3 and VA4 blood flow would be compromised. This was not shown in the recent study of VA3 blood flow<sup>44</sup>, when an insignificant reduction in contralateral but a significant increase in ipsilateral blood flow was reported. A possible explanation for the finding in the present analysis, shown as a small effect regardless of the direction of rotation, is that the compressive forces on VA3 associated with ipsilateral cervical spine rotation were as effective as any stretching of the vessel on contralateral rota-



tion, despite the blood flow being measurably more reduced in the former. It must be noted, however, that there is no proof of this to date. Nevertheless, the results of this quantitative meta-analysis support the suggestion that VA blood flow will vary according to the part insonated, and this should be taken into account in clinical practice.

### *Limitations of the Meta-Analysis*

Because these findings across all the studies reviewed apply to small groups of subjects and patients tested, they may be biased and the external validity or generalizability of the meta-analysis may be limited. Despite the claim that meta-analyses do not depend on sample sizes, there is always the possibility of both Type-I and Type-II errors occurring in individual studies such as these because of small sample sizes. Furthermore, the validity of a meta-analysis is dependent largely on the quality of the systematic review of reports. Ideally, both published and non-published studies should be analyzed, but in this analysis, only those reports published in English and with English abstracts were included. This means that some valuable data in unpublished or foreign reports may have been overlooked. Lastly, although an attempt was made to avoid some bias by using strict exclusion/inclusion criteria, the selection of studies to review may have confounded the findings in the meta-analysis of data. Such limitations should be taken into account in future analyses of this kind.

### **Conclusions and Implications for Professional Practice**

It is evident from this literature review that there is a paucity of rigorously controlled research trials to measure VA blood flow velocity changes associated with cervical spine rotation. More evidence of change in blood flow is needed, in larger homogeneous groups of both healthy persons (i.e., base-line values) and patients with a variety of neuromusculoskeletal conditions, across several discrete adult age groups, in males and in females. Therefore, it must be

emphasized that a stronger evidence base is necessary before any conclusions can be applied to the general patient population.

From the review of the literature, it is suggested that pulsed-wave Doppler insonation with color flow imaging is preferable in investigating VA blood flow, as this method ensures accurate visualization of the VA, and any pathology or unusual flow patterns during measurement of blood flow. It is advisable to use the sitting position for the subject, which is optimal for access to all parts of the VA, and for control of cervical spine rotation during insonation of the artery.

Despite there being only a small number of published reports with well-documented VA blood flow velocity data associated with rotation of the cervical spine, it was concluded from this meta-analysis that VA blood flow is compromised, particularly in VA4, with full or sustained contralateral rotation, with the subject measured in sitting, and in patients more so than in healthy, young individuals. This finding is of particular concern in patients or older persons who are more likely to have vascular pathology, such as atherosclerosis.

Although sustained, full-range rotation of the cervical spine, as used in the pre-treatment VBI test, can indicate only the functional state of an individual's vertebrobasilar and collateral circulations, it will allow suspect cases of vascular pathology to be referred for further investigation of the vascular system. This test cannot claim to indicate the safety of high-velocity, low-amplitude manipulative therapy thrusts in all patients, however, and more evidence of the effect of such cervical spine movements on the VA and its blood flow is needed, despite the many difficulties in carrying out such research.

Based on this meta-analysis of available evidence, the following key messages may be of value to manual therapists in clinical and professional practice:

- A thorough and complete pre-treatment history, including full subjective and objective assessments, must be taken for each pa-

tient. Where abnormal anatomical vascular patterns or vascular pathology are suspected, Doppler insonation of vessels, preferably using pulsed-wave Doppler and color flow imaging to ensure accuracy of VA insonation, should be carried out.

- The same position of the individual should be adopted for both pre-manipulative tests, such as the VBI test, and the subsequent treatment of each patient, as the large effect size for the comparison of sitting and supine lying suggests that this may influence results. Cognizance should be taken of the fact that false positive and false negative results of these tests are possible, and repeated measurements are advisable.
- Patients may have reduced VA blood flow compared to healthy, young subjects, as shown by the large effect size on comparing the two groups, in the neutral position and with rotation of the cervical spine. This result is of particular importance in older persons, regardless of whether they exhibit signs and symptoms of VBI, because this group is more likely to have associated risk factors for neurovascular incidents post-manual therapy, such as previous micro-trauma of the VA, atherosclerosis, loss of elasticity, increase in collagen in arterial walls concomitant with normal aging, or osteoarthritis.
- The large effect size found on comparing VA blood flow in the neutral cervical spine position and with contralateral rotation strongly supports the results of most studies of a significant decrease in blood flow on contralateral rotation. The fact that this finding relates to sustained, full rotation of the cervical spine indicates that it would be judicious to avoid such movements, particularly full-range rotation held for a minute or longer. In addition, it has been suggested in the literature that there is a danger of repeated thrusting rotational cervical spine movements causing micro-trauma to vessels such as the

VA. Therefore, in the absence of strong evidence to support or refute this, it is strongly advised that such high-velocity manipulative thrusts at the end-of-range of rotation should be avoided in clinical practice.

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