Effects of Posture on Right-to-Left Shunt Detection by Contrast Transcranial Doppler

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Background and Purpose—There is controversy about the optimal patient position for the detection of right-to-left shunt (RLS). The study was performed to investigate which patient position best detects RLS during contrast-enhanced transcranial Doppler.

Methods—We prospectively evaluated consecutive patients with ischemic stroke or TIA referred to our Noninvasive Cerebrovascular Laboratory for suspected paradoxical embolism. The standard protocol for RLS detection recommended by the International Consensus Criteria was followed. Each patient was examined at rest and after Valsalva maneuver in 4 positions: supine, right lateral decubitus, right lateral leaning, and upright sitting, in random order. RLS was graded 0 (no microbubbles [mB] detected), 1 (1–10 mB), 2 (>10 mB but no curtain), and 3 (curtain, shower of mB). Blood pressure, heart rate, and neurological symptoms were monitored. Data were analyzed using SPSS version 17.

Results—RLS was detected in at least 1 position in 89 of 240 patients (37.1%; 95% CI, 33.1%–43.3%). The detection of at least 1 mB with normal breathing was lowest in supine position and highest in right lateral decubitus. With Valsalva maneuver, this was highest in upright sitting (20.4% versus 8.3%; P<0.0002). If mB were undetected on upright sitting position, then they may still be detected in other positions. Changes in the position of the body and the injection of agitated saline were well-tolerated.

Conclusions—RLS is best detected in the upright sitting position with Valsalva maneuver. If negative, then other positions may be used. Validation of our findings by other centers may be helpful. (Stroke. 2011;42:2201-2205.)

Key Words: paradoxical embolism ■ right-to-left shunt ■ transcranial Doppler ■ ultrasound

Right-to-left shunting (RLS) is encountered in a number of medical situations. These include cryptogenic ischemic stroke, migraine headaches (especially those with aura), cerebral white matter changes detected by MRI, Alzheimer disease, sleep apnea, neurosurgery in a patient in a sitting position, and diving.1–7 Although there is still controversy about the role of shunt closure for ischemic stroke in reducing recurrence,8,9 it may reduce the frequency of migraine headaches.10 An accurate diagnosis of RLS is important. Contrast transesophageal echocardiography remains the clinical gold standard for the detection of RLS.11 However, the procedure is uncomfortable for the patient, requires skill to perform, and is usually conducted in the setting of a specialized cardiology laboratory. Contrast-enhanced transcranial Doppler (cTCD) has been found to be comparable or complementary to transesophageal echocardiogram in detecting clinically significant RLS.12–14 It is rapid, safe, well-tolerated, and can be performed at the patient’s bedside.

Four previous cTCD studies have provided contradictory evidence of the impact of posture change on the detection of RLS. In the earliest published study, patients were preselected by having a cTCD study with Valsalva maneuver (VM) in the supine position showing “pertinent” RLS. The sitting posture produced a lower signal count compared to the supine posture.15 In the second study of patients with transesophageal echocardiogram-proven patent foramen ovale (PFO), no significant difference was found in the number of microbubbles (mB) detected by cTCD in the sitting or supine posture, although for each individual 1 of the 2 positions was more sensitive.16 In the third study, among subjects with RLS already detected on transthoracic echocardiography, cTCD detected an increase in bubble load on standing versus recumbent in some subjects, but no change or even reduced load in other subjects.17 All 3 studies investigated cTCD among subjects with RLS already diagnosed. Whereas these studies do yield valuable information, they describe an
unlikely scenario in clinical practice because patients are more likely to be referred to the neurologist for the diagnosis of RLS rather than for a confirmation of RLS already diagnosed by another technique. The fourth cTCD study involving subjects suspected to have paradoxical embolism showed that if the supine study were negative for RLS, then it remained negative in all other positions; however, if mB was detected in supine position, then the count increased in other positions, especially in the upright sitting position.18 However, because the sequence of these positions was not randomly assigned, it is possible that the buoyant gaseous mB from the preceding injection were carried forward.17 The authors also called for a validation of their findings by other laboratories. Our study was conducted to investigate the effects of posture on detection of RLS using cTCD in patients with cerebrovascular disease referred for assessment of suspected paradoxical embolism.

Subjects and Methods

We prospectively evaluated consecutive patients with ischemic stroke or TIA referred to our noninvasive cerebrovascular laboratory for suspected paradoxical embolism. We used a transcranial Doppler machine (Nicolet EME Companion III; Viasonyx) with 2-MHz Doppler probes. The middle cerebral arteries were monitored bilaterally at a depth of 40 to 60 mm over the transtemporal windows using the Spencer head frame. In patients with absent temporal windows, the basilar artery was insonated through the foramen magnum, failing which the extracranial internal carotid artery through the submandibular approach was insonated. One single window was used for each patient, and the same window was used throughout that procedure.

The cTCD procedure recommended by the International Consensus Criteria was adopted.19 Briefly, an 18-gauge needle was inserted into the antecubital vein. Contrast agent was formed using 9 mL isotonic saline solution and 1 mL of air that was rapidly and vigorously agitated between two 10-mL syringes via a 3-way stopcock. After 10 mixes, the contrast was injected as a rapid bolus. Testing was performed at both normal breathing and subsequently with VM. Contrast agent was injected 5 seconds before the start of VM. The patient started the VM on the examiner’s command and held it for 10 seconds. The strength of the VM was considered sufficient when the middle cerebral artery flow velocity amplitude decreased by 25%. TCD monitoring commenced 30 seconds before contrast injection and continued for 1 minute after end of VM. The procedure was repeated after an interval of 5 minutes. Each patient was examined in 4 positions: supine, right lateral decubitus, right lateral leaning, and upright sitting. The order of positions was randomly assigned. Two injections were administered in each position. Those performing the TCD examination were experienced physicians preparing and injecting the contrast was the same for each position.

The grading system proposed by the International Consensus Criteria was adopted to detect and quantify RLS: grade 0, no mB; grade 1, 1 to 10 mB; grade 2, >10 mB but no curtain; and grade III, curtain (shower of mB). Interpretation was performed offline by a single investigator blinded to the identity and position of the patient (S.J.U.A.). Detection of mB on cTCD would mean a functional RLS.

All subjects or their legally acceptable representative provided written informed consent before any study-related procedures were performed. The study was approved by the institutional Ethics Committee.

### Table 1. Right-to-Left Shunt Grade in Different Body Positions (n=240)

<table>
<thead>
<tr>
<th></th>
<th>Grade 0 (No mB)</th>
<th>Grade 1, 1–10 mB</th>
<th>Grade 2, &gt;10 mB</th>
<th>Grade 3, Curtain/ Shower</th>
<th>≥1 mB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine</td>
<td>Normal breathing: 220</td>
<td>18</td>
<td>1</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Valsalva:        207</td>
<td>29</td>
<td>3</td>
<td>1</td>
<td>33</td>
</tr>
<tr>
<td>Lateral decubitus</td>
<td>Normal breathing: 206</td>
<td>29</td>
<td>5</td>
<td>0</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>Valsalva:        205</td>
<td>29</td>
<td>4</td>
<td>2</td>
<td>35</td>
</tr>
<tr>
<td>Sitting leaning to the right</td>
<td>Normal breathing: 209</td>
<td>28</td>
<td>3</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Valsalva:        205</td>
<td>29</td>
<td>5</td>
<td>1</td>
<td>35</td>
</tr>
<tr>
<td>Upright sitting</td>
<td>Normal breathing: 208</td>
<td>28</td>
<td>3</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Valsalva:        191</td>
<td>41</td>
<td>7</td>
<td>1</td>
<td>49</td>
</tr>
</tbody>
</table>

mB indicates microbubble.

### Sample Size Calculation and Statistical Analysis

Sample size of 240 was calculated using matched proportions, estimating 11% discordant pairs, with 80% power, being 2-sided, and having alpha of 5%. Continuous parametric data are described as mean ±SD, whereas continuous nonparametric data are described as median and interquartile ranges. Noncontinuous data are described as percentages. Paired sample t test was used for comparison of normally distributed data such as heart rate and blood pressure in different positions; Wilcoxon matched pairs signed rank test was used for comparing nonparametric data and McNemar test was used for matched proportions. Friedman test was used for comparing mB counts at different body positions. Statistical significance was accepted if P < 0.05. Data were analyzed using the SPSS version 17 for Windows.

### Results

Of 280 eligible patients, 40 patients declined participation. Thus, 240 patients participated in this study; 73% were male, mean age was 54.0 ±11 years, 80.5% had stroke, and 19.5% had TIA. Vascular risk factors included hypertension (58%), hyperlipidemia (54%), cigarette smoking (32%), diabetes mellitus (25%), previous stroke (10%), previous TIA (3%), and heart disease (4%).

RLS was detected in at least 1 position, with normal breathing or VM, in 89 patients (37.1%; 95% CI, 33.1%–43.3%). In each position, subjects who had RLS with normal breathing also had RLS during VM, but not always vice versa. In 7 subjects, RLS was detected in all positions, both with normal breathing and VM. In 10 additional subjects, it was detected in all positions with VM only and not with normal breathing.

The grade of RLS in different positions is shown in Table 1. The presence of at least 1 mB with normal breathing was lowest in supine position and highest in right lateral decubitus. But when VM was used, the presence of at least 1 mB was highest in the upright sitting position (20.4% versus 8.3%; P < 0.0002; Figure). Among those with negative results on upright sitting, right lateral leaning added 8 more cases with at least 1 mB, right lateral decubitus added 7 more, and supine added 5 more. Three more cases that had negative results would be detected if the supine study were positive.
results on upright sitting had positive results on right lateral leaning and supine, 2 more had positive results supine and right lateral decubitus positions, and 1 more had positive results in right lateral decubitus and right lateral leaning positions; 1 more was positive in supine, right lateral decubitus, and right lateral leaning positions.

The number of mB detected in each position is shown in Table 2. The number was generally small but highest in right lateral leaning with VM. There was a statistically significant association between the body positions and mB count (P<0.001).

Changes in the position of the body and the injection of agitated saline were well-tolerated. Blood pressure and heart rate did not vary significantly with VM or posture change (Table 3). No subject had any symptoms during or after the procedure.

Discussion

Our study shows that body position affects the detection of RLS. The highest frequency of RLS was found in upright sitting position with VM and lowest in supine position with normal breathing. VM increased the detection of RLS in all positions. RLS may still be detected in other positions if upright sitting position with VM was negative for RLS, with additional pick-up in right lateral leaning, right lateral decubitus, and supine positions.

This is the largest study so far to our knowledge to investigate the effect of posture on frequency of RLS among patients with symptomatic cerebrovascular disease. Patients were not preselected on the basis of already having known RLS by echocardiography or by having ”pertinent” RLS already detected by supine position. An available acoustic window was used, with the transtemporal window preferred; those with no temporal windows were not excluded, as was performed in at least 1 previous study. Commercially available contrast such as Echovist was not used because of its high cost. Our study reflects real-world clinical practice in which patients with stroke or TIA are referred for detection of RLS without previous knowledge of the presence of RLS, are of unknown acoustic window status, and for whom cost limits the use of expensive contrast agents.

We tested 4 body positions instead of just 2. In our study, body positions were randomly assigned, as was performed in 2 other studies. This reduced any concern of a carry-over effect of mB from a previous injection. Standing position, used in 1 study, was not used in our study because
Our findings contradict those of Schwartze et al,15 who found not right lateral leaning) yielded more mB than did supine. In addition, the erect posture may allow buoyant mB to reach the superiorly located brain more easily than when in supine position, when the brain and heart are on a similar plane.16,18 In this position, when the brain and heart are on a similar plane.16,18 In the upright posture allows the buoyant mB to rise high into the right atrium close to the PFO and cross it, aided by an increase in the right-side pressures by VM. It is also possible that the upright posture allows gravity to stretch the PFO and this would further increase the opening of the shunt flap, thereby causing RLS to occur.17,18 In addition, the erect posture may allow buoyant mB to reach the superiorly located brain more easily than when in supine position, when the brain and heart are on a similar plane.16,18 Furthermore, VM may be naturally easier to perform in an upright sitting position than in any other position.16

There is controversy about the safety of contrast ultrasound, because stroke and TIA have been reported in some,21 but not other,22 studies. We are able to support the safety of repeated injections of agitated saline–air contrast. None of the subjects in our study or in the other 4 studies experienced any adverse event.15–18 Similarly, blood pressure and heart rate did not change significantly in our study.

Our study has a number of important clinical implications. The upright sitting posture with VM may be the most sensitive method to detect mB and may increase the chance of detecting RLS. One may consider performing the test in this position at the outset in patients able to do so. However, if this is negative in this position, other positions then may be tested because there appears to be no “single best position” for all patients. There should be little concern about the order of testing—mB from the previous contrast injection should not affect testing in the next position if at least a 5-minute interval is used between injections. Training effect for VM or fatigue by the patient or tester (for the latter) is unlikely. Whereas this study was performed in patients with stroke or TIA, it is likely to be applicable in other settings such as migraine, neurosurgery in the sitting posture, and divers. Finally, repeated injections of contrast are safe.

A study found that degree of RLS as assessed with cTCD is a significant predictor of recurrence of stroke23,24 and of the ability to successfully perform transcatheter closure of a PFO.25 However, the optimal management of PFO is still debatable.12,13 Thus, quantifying the amount of shunt may not impact on current clinical practice.

### Table 2. Number of Microbubbles Detected in Different Body Positions

<table>
<thead>
<tr>
<th>Position</th>
<th>Median</th>
<th>Interquartile Range (Quartile 1–Quartile 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>2</td>
<td>1–6</td>
</tr>
<tr>
<td>Valsalva</td>
<td>2</td>
<td>1–4</td>
</tr>
<tr>
<td>Lateral decubitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>Valsalva</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>Sitting leaning to the right</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>2</td>
<td>1–7</td>
</tr>
<tr>
<td>Valsalva</td>
<td>7</td>
<td>2–12</td>
</tr>
<tr>
<td><strong>Upright sitting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>3</td>
<td>1–8</td>
</tr>
<tr>
<td>Valsalva</td>
<td>3</td>
<td>1–4</td>
</tr>
</tbody>
</table>

Quartile 1 indicates 25th percentile; quartile 3, 75th percentile. Friedman test = 31.223; degrees of freedom = 7; P < 0.001.

stroke patients, especially those with significant lower limb weakness or ataxia, cannot be reliably expected to be able to stand and cooperate with cTCD procedures.

We are able to support the findings of Caputi et al,17 who found an erect posture (standing), on average, elicited a higher mB count than recumbency, similar to the study results of Lao et al18 who found an erect posture (standing), on average, elicited a higher mB count than recumbency, similar to our study results (37.1%). They found upright sitting position yielded the highest number of mB compared to identically lower median mB counts in supine, right lateral decubitus, and right lateral leaning positions; we found the highest counts in right lateral leaning with Valsalva compared to supine. However, our small number of mB suggests caution in the interpretation. Rather than counting mB, a preferred measure may be the presence or absence of RLS, ie, ≤1 mB.

Heart. Nevertheless, we agree with Telman et al16 that some patients may have a “preferred” position for which RLS is demonstrable.

Our findings most closely resemble those of Lao et al.18 Their study involved 55 patients with ischemic stroke, with mean age of 56 years, and 64% were male (our study: mean age, 54 years; 75% male). They found RLS in 35%, which is similar to our study results (37.1%). They found upright sitting position yielded the highest number of mB compared to identically lower median mB counts in supine, right lateral decubitus, and right lateral leaning positions; we found the highest counts in right lateral leaning with Valsalva compared to supine. However, our small number of mB suggests caution in the interpretation. Rather than counting mB, a preferred measure may be the presence or absence of RLS, ie, ≤1 mB.

The reason for the finding of higher mB counts or higher frequency of RLS in erect compared to the supine position is unclear. The PFO is located in an anterior-superior location in the interatrial septum.20 The upright posture allows the buoyant mB to rise high into the right atrium close to the PFO and cross it, aided by an increase in the right-side pressures by VM. It is also possible that the upright posture allows gravity to stretch the PFO and this would further increase the opening of the shunt flap, thereby causing RLS to occur.17,18 In addition, the erect posture may allow buoyant mB to reach the superiorly located brain more easily than when in supine position, when the brain and heart are on a similar plane.16,18 Furthermore, VM may be naturally easier to perform in an upright sitting position than in any other position.16

There is controversy about the safety of contrast ultrasound, because stroke and TIA have been reported in some, but not other, studies. We are able to support the safety of repeated injections of agitated saline–air contrast. None of the subjects in our study or in the other 4 studies experienced any adverse event.15–18 Similarly, blood pressure and heart rate did not change significantly in our study.

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### Table 3. Blood Pressure and Heart Rate in Different Body Positions

<table>
<thead>
<tr>
<th>Position</th>
<th>Systolic Blood Pressure, Mean±SD</th>
<th>Diastolic Blood Pressure, Mean±SD</th>
<th>Heart Rate, Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>148.87±25.75</td>
<td>87.58±16.70</td>
<td>71.08±12.18</td>
</tr>
<tr>
<td>Valsalva</td>
<td>148.62±26.88</td>
<td>87.83±18.21</td>
<td>70.78±13.10</td>
</tr>
<tr>
<td>Lateral decubitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>147.04±28.03</td>
<td>83.84±16.80</td>
<td>71.95±12.23</td>
</tr>
<tr>
<td>Valsalva</td>
<td>147.24±29.40</td>
<td>84.62±17.52</td>
<td>72.27±11.45</td>
</tr>
<tr>
<td>Sitting leaning to the right</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal breathing</td>
<td>150.56±28.50</td>
<td>89.06±16.32</td>
<td>73.60±12.60</td>
</tr>
<tr>
<td>Upright sitting</td>
<td>148.69±31.75</td>
<td>88.77±16.64</td>
<td>73.91±11.90</td>
</tr>
</tbody>
</table>

Friedman test = 31.223; degrees of freedom = 7; P < 0.001. SD indicates standard deviation.
Our study has a number of limitations. It is a single-center study. RLS was not confirmed by transesophageal echocardiogram; however, the study was not aimed to compare cTCD with transesophageal echocardiogram. Windows other than the temporal window were also used when necessary; the use of available windows is consistent with real-world clinical practice issues in the assessment of patients with stroke or TIA for RLS. Patients without stroke or TIA were not studied.

Conclusions
In conclusion, our study has shown that position affects the detection of RLS by cTCD, with the highest detection rate found with VM in the upright sitting position. We suggest further validation of our results by other centers performing such a procedure. If verified, then current recommendations for the detection of RLS by cTCD testing only in the supine position may need to be modified.

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Disclosures
None.

References
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