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● *Original Contribution*

COMPARISON OF DIFFERENT METHODS OF VALSALVA MANEUVER FOR RIGHT-TO-LEFT SHUNT DETECTION BY CONTRAST-ENHANCED TRANSCRANIAL DOPPLER

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Abstract—We evaluated 298 patients for right-to-left shunt (RLS) detection by contrast-enhanced transcranial Doppler at rest state (RS), during the conventional Valsalva maneuver (CM), and during the modified Valsalva maneuver (BM: blowing into the connecting tube of a sphygmomanometer at 40 mm Hg for 10 s) in random order, and the degree of RLS along the time of the first microbubble occurrence was recorded. The positive rates were 21.8%, 36.9% and 47.3% for RS, CM and BM, respectively ($p < 0.001$). BM resulted in a significantly higher positive rate ($p = 0.010$), and there was a significant difference between the two different methods of VM in terms of the degree of RLS detection ($p < 0.001$). Further, the first microbubble occurred later during BM than CM (10.22 ± 3.77 s vs. 9.44 ± 4.36 s, $p < 0.05$). This modified maneuver is an alternative to the conventional one, especially for those who cannot perform the conventional maneuver adequately, but are highly suspected of having RLS. (E-mail: xingyq2009@sina.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Contrast-enhanced transcranial Doppler, Right-to-left shunt, Valsalva maneuver.**

INTRODUCTION

Right-to-left shunt (RLS) is likely to play a causal role in patients with cryptogenic stroke, migraine, and myocardial infarction (Anzola 2002; Diener et al. 2005; Sastry et al. 2006). One theory states that RLS permits emboli or neurotransmitters such as serotonin to bypass the pulmonary circulation and go directly to the systemic circulation. Currently, invasive transesophageal echocardiography (TEE) is still considered the gold standard for the diagnosis of cardiac RLS. However, contrast-enhanced transcranial Doppler (cTCD) has been reported to be a more reliable and reproducible screening method for RLS detection, with higher sensitivity, for both cardiac and extracardiac RLS (Angeli et al. 2001; Droste et al. 2002; Nedeltchev and Mattle 2006; Van et al. 2010). In addition, cTCD has also been found to be superior in quantification of RLS compared with TEE.

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Although cTCD has been widely used during the last two decades, no consensus on a standard examination protocol for the detection of RLS using cTCD has yet been reached. The results of studies using cTCD for RLS detection vary considerably, depending largely on methodologic factors such as the contrast agent (Gentile et al. 2014; Hao et al. 2014; Lange et al. 2012; Shariat et al. 2011), injection mode, timing with respect to the Valsalva maneuver (VM) (Droste et al. 2000) and effects of posture (Agustin et al. 2011; Caputi et al. 2008; Lao et al. 2007; Wu et al. 2015). There is a general consensus that a VM is necessary to increase the sensitivity of RLS detection. However, the latest International Consensus Meeting did not provide explicit instructions regarding the standard procedure of VM (Jauss and Zanette 2000). Accordingly, several different procedures for provocation in cTCD have been reported (Droste et al. 1999), including conventional VM, "standardized" or modified VM, repetitive VMs and coughing and confusion remains regarding the optimal method of VM for RLS detection by cTCD. With this in mind, the aim of our study was to compare two different methods of VM for RLS detection by cTCD.

METHODS

Participants

The study design was approved by the First Hospital of Jilin University ethics committee, and informed consent was obtained from all patients. From November to December 2014, 298 consecutive patients were recruited from the Department of Neurology of our hospital. Among these patients, 193 (64.8%) were women and 105 (35.2%) were men, with a mean age of 37 ± 12.1 y. Of these, 291, 5 and 2 patients reported varying degrees of headache, dizziness and ineffective limb activity, respectively.

The exclusion criteria were as follows: a temporal "window" that could not be penetrated by ultrasound; inability to perform the VM because of severe heart or lung disease or impaired cognition or coordination; and follow-up patients who had undergone transcatheter closure of a patent foramen ovale.

Contrast-enhanced TCD protocol

Contrast-enhanced TCD examinations were performed using a Multi-DopX4 TCD detector (DWL, Sipplingen, Germany) with left middle cerebral artery (MCA) monitoring. An 18-gauge needle was inserted into the cubital vein of the patients while in the supine position. The contrast agent was prepared by vigorously mixing 9 mL saline solution, 1 mL air and a drop of the patient's blood (Gentile et al. 2014; Hao et al. 2014) between two 10-mL syringes *via* a three-way stopcock. After 30 mixing cycles, the contrast agent was injected rapidly as a bolus.

All patients underwent the three different tests in random order: (i) In the rest state (RS), there was no VM; (ii) in the conventional method (CM), the patient inhaled deeply and strained against a closed glottis 5 s after the start of the contrast agent injection and expiring 10 s later, that is, 15 s after the beginning of the injection and (iii) in the modified method (BM), the patient blew into the connecting tube of a sphygmomanometer at 40 mm Hg for a 10-s period, 5 s after the start of the contrast agent injection (Jauss and Zanette 2000).

The strength of the CM was measured as the reduction in mean flow velocity of the MCA, whereas in the BM, maintenance of the column of mercury in the sphygmomanometer at 40 mm Hg was required (Fig. 1). The monitored Doppler spectra were stored for offline analyses of the time of occurrence and number of microbubbles (MBs). A MB was defined as a visible and audible (click, chirp or whistle), short-duration, high-intensity signal within the Doppler flow spectrum. To improve detection of the MB track, ultrasound was performed in M-mode. There are several different classification methods (Jauss and Zanette 2000; Lao et al. 2008; Yang et al. 2012); in this study, we adopted the four-level categorization of the International Consensus Criteria according to MB appearance in the cTCD spectrum using unilateral MCA monitoring, as follows: negative = no occurrence of MBs; grade I = 1–10 MBs; grade II > 10 MBs, but no curtain; grade III = curtain, that is, inability to discriminate a single MB within the cTCD spectra (Jauss and Zanette 2000). The numbers of MBs recorded during different methods of VM were respectively taken as estimates of shunt extent in each patient. Tests were performed consecutively; each test required approximately 3 min to perform, and there was an interval of at least 5 min from the last observed MB between the tests.

Two ultrasound technologists assessed the degree of RLS in all patients for both the CM and BM.

Statistical analysis

Statistical analysis was performed with SPSS 17.0 software (SPSS, Chicago, IL, USA). The χ^2 test was used for comparisons of the positive rates of RLS detection between the different tests. McNemar's test was used for comparisons of RLS detection by cTCD between the

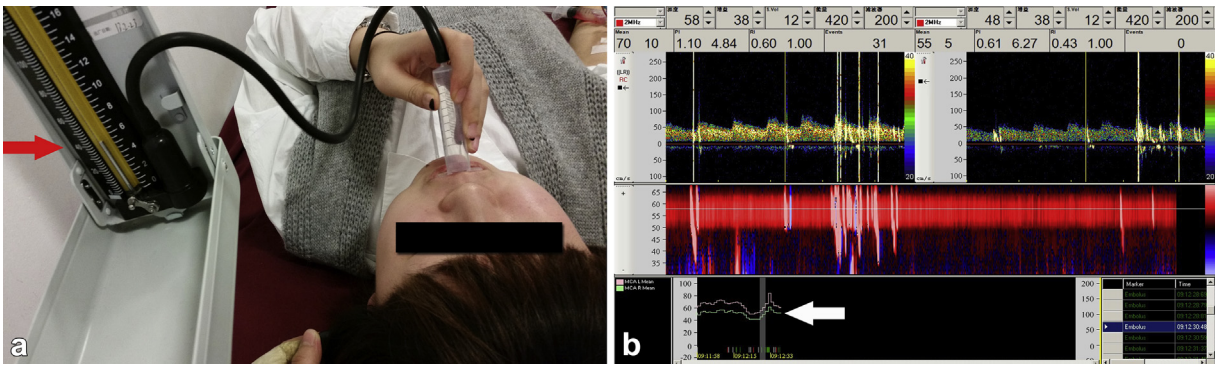

Fig. 1. Quality control of the modified and conventional Valsalva maneuvers. (a) The *red arrow* points to 40 mm Hg on the sphygmomanometer. (b) The *white arrow* points to the Doppler flow velocity curve (first down and then up).