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● *Original Contribution*

CONTRAST TRANSTHORACIC ECHOCARDIOGRAPHY USING 50% GLUCOSE AS A CONTRAST AGENT FOR SCREENING OF A PATENT FORAMEN OVALE

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Abstract—A patent foramen ovale (PFO) is considered a risk factor for neurologic events. The goal of the study described here was to assess the feasibility, advantages, diagnostic sensitivity and accuracy of contrast transthoracic echocardiography examination (cTTE) using 50% glucose as a contrast agent in comparison with the use of agitated saline as contrast to screen for PFO. In our study, we found that the peak time, effective duration and duration of microbubbles produced by 50% glucose were all longer than those produced by the physiologic saline. The sensitivities for detection of PFO with cTTE using physiologic saline and 50% glucose as contrast were 83% (20/24) and 100% (24/24), respectively. TEE suggested a PFO in 24 patients in two groups. Use of 50% glucose as a contrast agent in cTTE examination enables ultrasound technicians to easily observe the right-to-left shunt across the PFO. However, the sensitivities for detection of PFO with cTTE using 50% glucose did not statistically significantly differ from those for physiologic saline. (E-mail: xhm_xq@163.com) © **2018 World Federation for Ultrasound in Medicine & Biology. All rights reserved.**

Key Words: **Contrast, Echocardiography, Echocardiogram, Patent foramen ovale.**

INTRODUCTION

Presence of a patent foramen ovale (PFO) has been correlated with several disease processes, such as stroke, migraine, peripheral arterial embolism and decompression sickness (Calvert et al. 2011). Clinically, closed PFO has been used to prevent the recurrence of stroke events and to treat migraines, platypnea and orthodeoxia, with good curative effect (Kumor et al. 2013). In recent years, the clinical relationship between PFO and migraine, stroke, peripheral arterial embolism and decompression sickness has been subject to considerable controversy (Buchholz et al. 2012).

Transesophageal echocardiography (TEE) is the gold standard for PFO diagnosis. It can determine the size of the foramen ovale and provide the basis for intervention therapy of definitively diagnosed PFO (Fisher et al. 1995; Schuchlenz et al. 2002). Nonetheless, TEE is an inconvenient, semi-invasive, complex diagnostic technique with contraindications and usually causes discomfort in patients during the examination (Rodrigues et al. 2013). These deficiencies of TEE make it difficult to perform for routine clinical diagnosis of PFO. Contrast transthoracic echocardiography (cTTE) is a non-invasive method used to detect the right-to-left shunt across a PFO (Belkin et al. 1994). As early as the 1960s, agitated saline was used as a contrast agent in cTTE examinations (Attaran et al. 2006). Hydrogen peroxide and a preparation of carbon dioxide have also been used in cTTE (Elliott et al. 2011). However, the use of hydrogen peroxide was abandoned because of its side effects; a preparation of carbon dioxide is still used. This contrast agent, made by mixing an acid and an alkali, must be used after preparation. Moreover, the bubbles produced by this contrast agent are large and uneven and cause problems of uniform echo distribution, thick echo and short duration (Muñoz et al. 1984). Therefore, it is very important to determine a simple, tolerable, long-lasting contrast agent for cTTE examination.

It has been reported that the bubbles produced by agitating 50% glucose are more widely distributed and more uniform than those of carbon dioxide (Huber and Handa 1967). In this study, we first assessed the

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advantage of using 50% glucose microbubbles as a contrast agent in cTTE examination compared with agitated saline. Second, we compared the sensitivity and accuracy of cTTE using 50% glucose and with those of TEE in the screening and diagnosis of PFO to optimize the ultrasonic examination and improve the accuracy of ultrasonic diagnosis of PFO.

METHODS

Patients

We enrolled 56 healthy divers as a control group (51 males, 5 females; mean age: 20.3 ± 0.5 y; range: 18–23 y); they received physical examinations between January 2014 and July 2016. We enrolled 56 additional patients (37 males, 19 females; mean age: 36.4 ± 1.2 y; range: 16–59 y) with decompression sickness, cryptogenic stroke or migraine who were screened for PFO by cTTE and TEE as the research group. The baseline characteristics of the two groups are summarized in Table 1. All patients were examined by conventional transthoracic ultrasonography and electrocardiography and exhibited no abnormality in cardiac structure or function.

The study was approved by the Navy General Hospital ethics committee. All patients were informed of the examination content and possible complications before examination, and each signed an informed consent form to participate in this study.

Protocol

The control group and the research group underwent cTTE to detect PFO using agitated saline and then glucose as the contrast agent, respectively. The interval was longer than 10 min to ensure that there was no residual contrast agent. Positive cases were confirmed by TEE examination.

Contrast preparation

In line with a previous study (Komar et al. 2014), saline contrast was produced by mixing 9 mL of 0.9% saline solution with 1 mL of air in two 10-mL syringes connected by a three-way tap, 20 times. Glucose contrast was produced by mixing 4.0 mL of 50% glucose solution with 0.4 mL of air in two 10-mL syringes connected by a three-way tap, 20 times. To reduce the human factor, contrast preparation was performed by two experienced operators. The two operators pushed the syringe back and forth 20 times at a frequency of approximately 80 times/min. The mixture was injected rapidly into the right antecubital fossa *via* a cannula (Fig. 1).

Table 1. Baseline characteristics of the enrolled patients

Group	Control group (n = 56)	Research group (n = 56)
Age (y)	20.3 ± 0.5	36.4 ± 1.2
Male (%)	91.07% (51/56)	66.07% (37/56)
History of migraine (%)	0	55.36% (31/56)
History of stroke (%)	0	48.21% (27/56)
Hypertension (%)	0	3.57% (2/56)
Hyperlipidemia (%)	0	7.14% (4/56)
History of diabetes (%)	0	3.57% (2/56)
Current or prior smoker (%)	5.36% (3/56)	8.92% (5/56)

Fig. 1. Preparation of contrast agent using 50% glucose.

Quantitative analysis of cTTE

The cTTE imaging method was performed with the subject in the left lateral decubitus position using a Philips IE-Elite Ultrasonic diagnostic apparatus (Koninklijke Philips N.V., Eindhoven, Netherlands) fitted with a 3.7- to 5-MHz S5-1 probe. Simultaneously, an electrocardiogram was used to monitor the changes in heart rhythm and rate. After clear visualization of the right and left atria and right and left ventricles by gray-scale ultrasound, each subject was injected with 4.0 mL of 50% glucose contrast and 9 mL physiologic saline contrast *via* the left cubital vein, followed by injection of 5 mL of physiologic saline solution. The interval between the injections of the two contrast agents was >10 min, but was necessary to ensure there was no residual contrast agent in the cardiac chambers before the second cTTE examination. Microbubbles in the cardiac chambers were observed, and continuous dynamic images were stored.