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**ROLE OF TRANSCRANIAL DOPPLER FOR ASSESSMENT OF PERSISTENT FORAMEN OVALE IN PATIENTS WITH STROKE**

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**Abstract:** Transcranial Doppler (TCD) is a noninvasive, portable easy-to perform and easy to interpret technique for evaluating the intracranial vasculature. The indications for a TCD ultrasound examination of adults include detection of right-to-left shunts (RLS). The prevalence of a patent foramen ovale (PFO) in the general population is  $\approx 25\text{-}30\%$ . Thrombus, formed in the venous system could cross the interatrial septum via PFO and provoke paradoxical embolism. The aim of our study was to select those patients, diagnosed with embolic stroke with undetermined etiology (ESUS), who are at higher risk for paradoxical embolism. **Materials and methods:** During one year a total of 21 consecutive patients (14 male and 7 female) with ESUS were directed to cardiology department for further evaluation. They underwent cTCD for detection of RLS. **Results:** In part of the patients another risk factors were found. The most commonly encountered stroke was in vertebro-basilar system and in left middle cerebral artery territory. RLS was detected in 12 patients – 3 females and 9 males. The medium RoPE score in patients with significant RLS was 6.5. Four patients with RoPE score  $\geq 8$  were scheduled for PFO closure and the procedure was performed without any complications. **Conclusion:** TCD is a reliable non-invasive technique to identify ESUS patients with risk for paradoxical embolism.

**Keywords:** Transcranial Doppler, patent foramen ovale, stroke

**INTRODUCTION**

Ischemic stroke occurs as a result of obstruction of the brain arteries. Approximately 25% of all ischemic strokes are of undetermined etiology [1]. They are classified as embolic stroke with unknown source (ESUS). The potential embolic sources include those with minor risk as mitral and aortic valve calcification, covert atrial fibrillation, cancer-associated, atherogenic emboli and paradoxical embolism, mostly by PFO [2]. Paradoxical embolism is identified as a cause 4,5-5% of strokes [3,4]. The most common reason for RLS is the patent foramen ovale. The prevalence of a patent foramen ovale (PFO) in the general population is  $\approx 25\text{-}30\%$  [5,6]. The vast majority of these people have no problems, due to this condition. Rarely thrombus, formed in the venous system or the right atrium could cross the interatrial septum via PFO and provoke paradoxical embolism – stroke or peripheral embolization [7]. The proven methods to detect RLS are contrast transthoracic echocardiography (c-TTE), contrast transesophageal echocardiography (c-TTE) and contrast transcranial Doppler ultrasonography (c-TCD) (al, 2002). Transcranial Doppler (TCD) is a noninvasive, portable technique for evaluating the intracranial vasculature. The latter is easy-to perform and easy to interpret, low-cost technique, which allows a semiquantitative estimation of venous-to arterial circulation shunts. The data for efficacy of PFO closure for stroke prevention has been uncertain. The randomized clinical trials (RCTs) before 2017 failed to demonstrate that the closure of PFO reduces the risk of subsequent stroke [10-12]. Two new trials, published in 2017 [13,14], one in 2018 [15] and one follow-up [16] proved that PFO closure was superior to medical therapy in stroke prevention [17]. The aim of our study was to select those patients, diagnosed with embolic stroke with undetermined etiology (ESUS), who are at risk for paradoxical embolism.

**MATERIALS AND METHODS**

A total of 21 consecutive patients with ESUS – 14 male and 7 female underwent cTCD for detection of RLS during one year. All of them were directed from stroke unit after other reasons for stroke were excluded. TCD was performed as the patient was in supine position using transtemporal approach. 18-G needle was inserted into cubital vein and agitated serum was injected. The middle cerebral artery was insonated at baseline and after Valsalva maneuver. Categorization of shunt was made according to the number of microembolic signals detected, where category 1) (negative result) means 0 microembolic signals, 2) – 1-10 microembolic signals and 4) – curtain or shower of microembolic signals [18]. Shunts category 4 were accepted as significant. The patients were analysed for risk factors such as hypertension, atrial fibrillation, diabetes, dyslipidemia (total cholesterol  $> 5.0$  mmol/l or LDL  $\geq 3.0$  mmol/l or HDL  $< 1.0$  in males and  $< 1.2$  in females or Tg  $> 1.7$  mmol/l), renal function, smoking status and carotid atherosclerosis. The RoPE score was calculated. This score system is based on Risk of Paradoxical Embolism (RoPE) study and was designed to select the patients, who will benefit from the PFO closure [19]. It is calculated from the following variables: history of hypertension, history of diabetes, history of stroke, smoking, cortical infarct

on imaging and age. The youngest patients with cortical infarcts and without risk factors have the highest risk for PFO associated stroke. Data are presented as mean±standard deviation for continuous variables and as numbers and percents for discrete variables.

## RESULTS

The mean age of the patients was 46,48±11,64years. Hypertension was present in 38,1% of the them, diabetes in 14%, dyslipidemia in 76,2%. The most commonly encountered stroke was in vertebro-basilar system and in left middle cerebral artery territory. RLS was detected in 12 patients – 3 females and 9 males. Significant RLS was found in 8. In all of these patients c-TOE confirmed the presence of PFO. Two or more risk factors were found in 25% of the group with significant shunt and in 38% of the group with no or insignificant shunt. The medium RoPE score in patients with significant was 6.5. Four patients with RoPE score ≥ 8 were scheduled for PFO closure and the procedure was performed without complications.

Discussion: Patients, included in our study were at a younger age in comparison with other ESUS studies [20]. Right-to left shunt was found in half of them. Homma et colleagues detected PFO in 38% of their population with cryptogenic stroke [21]. Half of the PFOs in ESUS are incidental – not associated with the stroke [22]. Our study confirms data from previous studies that TCD has a high sensitivity [23], but TEE is needed to confirm the localization of the shunt.

## CONCLUSION

TCD is a reliable non-invasive technique to identify ESUS patients with risk for paradoxical embolism. The selection of patients for PFO closure is difficult, because a vast majority of them have additional risk factors.

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