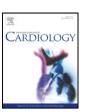
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## Prevalence of atrial septal pouch and risk of ischemic stroke



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#### ABSTRACT

*Background:* It has been postulated that atrial septal pouch (ASP) may favor the stasis of blood and predispose to thromboembolic complications. We sought to evaluate the prevalence of ASP, and its association with ischemic stroke.

Methods: We retrospectively studied 500 patients, who underwent transesophageal echocardiography (TEE) due to clinical indications. Seventy two patients due to image quality, and 104 patients with atrial septal defect or PFO were excluded. The remaining 324 patients were included in the analysis. The depth of ASP was measured. Results: ASP was detected in 98 patients [left side ASP (LASP) in 58 (59.2%), and right side ASP (RASP) in 40 (40.8%) patients]. LASPs were significant deeper than RASPs (10.1  $\pm$  5.2 vs 4.4  $\pm$  1.4 mm, p < 0.0001). Patient characteristics were categorized by the presence or absence of LASP. The age (61  $\pm$  12 vs 61  $\pm$  12), gender and stroke risk factors were no significant difference between patients with or without LAPS. Ischemic stroke occurred in 21 patients without LASP, 10 patients with LASP. The presence of a LASP was found to be associated with an increased risk of ischemic stroke, in either univariable analysis (17.2 vs. 7.9%, p = 0.03; OR = 2.43, 95% CI = 1.1–5.5, p = 0.033) or after adjustment for other stroke risk factors using multiple logistic regression analysis (OR = 2.45, 95% CI 1.1–5.8, p = 0.036).

*Conclusions*: This study demonstrated evidence of association between LASP and ischemic stroke. Among 324 patients, the risk of ischemic stroke was twice more among patients with LASP than cases without LASP.

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#### 1. Introduction

The diagnosis of cryptogenic stroke remains presumptive in a vast majority of patients. Recently, a new anatomical entity, the atrial septal pouch (ASP), has been defined in a pathology study. ASP was described as an incomplete fusion in the cranial segment of the overlap between the septum primum (SP) and septum secundum (SS), resulting in a recess that opens into the left (LASP) or right atrium (RASP), with no interatrial shunting [1]. LASP might serve as a nidus for thrombus formation in the presence of low flow states, and therefore predispose to embolic events. There are a number of case reports demonstrating a thrombus arising from the cavity of LASP, [2–3] but the association between LASP and cryptogenic strokes from several retrospective studies is controversial. The aim of the present study was, therefore, to assess the incidence of atrial septal pouch and the existence of an association between LSP and ischemic stroke.

#### 2. Methods

In this cross-sectional study, we retrospectively evaluated 500 consecutive patients (with or without stroke) who underwent a transesophageal echocardiogram (TEE) between July 2011 and June 2014 at our hospital. The patients' atrial septa were not adequately visualized (n = 72), and the patients with an atrial septal defect (ASD) or PFO were excluded from analysis. The remaining 324 subjects were included in the analysis. The study was approved by the Institutional Review Board of Tongji University.

We performed a chart review (history, physical exam, consultations, and outpatient notes) for the remaining 324 eligible patients to determine history of hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation/flutter, ischemic stroke or TIA, coronary artery disease, and congestive heart failure. The diagnosis of ischemic stroke was based on clinical evidence and CT or MRI.

All TEEs were interpreted by one of our cardiology fellow. The cardiologists were blinded to all patient information, including whether or not the patient experienced a stroke. The interatrial septum was inspected using 2-dimensional echocardiography: fused septum, LASP, RASP, PFO, or ASD. A ASP was defined as fusion at the caudal limit of the zone of overlap between the septum primum and septum

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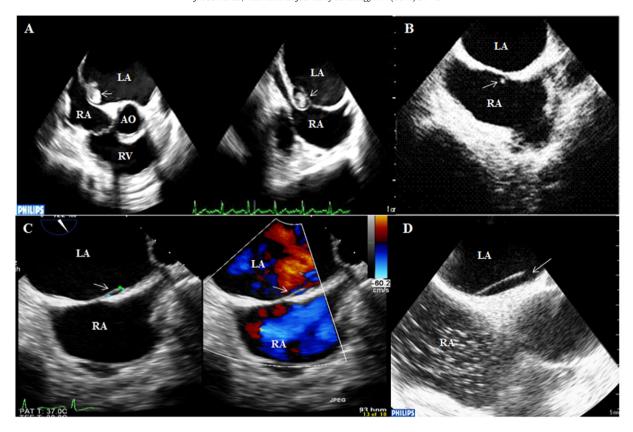


Fig. 1. Transesophageal echocardiogram (TEE) image of the left atrial septal pouch. A. This images was obtained from one case, which showed a thrombus within the left atrial (LA) septal pouch (arrow). B. The image showed a tiny thrombus arising from right atrial (RA) septal pouch (arrow). C. TEE Color Doppler image showed the complete fused septum with LA septal pouch. D. TEE with normal saline contrast demonstrated the complete fused septum with LA septal pouch.

secundum, where a blind-ending pouch is formed that communicates exclusively with the LA (Fig. 1).

The depth of the pouch was measured and defined as from the tip of the septum pouch to the junction between the pouch and septum.

The presence of a PFO was determined if microbubbles were seen in the LA after agitated saline injections and Valsalva maneuver was performed by the patient. The presence of a PFO was also confirmed by the original echocardiography report. Any differences in interpretation between the cardiology fellow and cardiologist were adjudicated by a second cardiologist.

#### 2.1. Statistical analysis

We compared differences in stroke risk factors in patients with and without LASP using the Chi-square test of proportions for categorical variables and t-tests for continuous variables.

Multiple logistic regression analysis was performed to see if the effect of LASP on stroke risk was changed by adjusting for age (continuous), gender, and the stroke risk factors of atrial fibrillation/flutter, congestive heart failure, coronary artery disease, diabetes mellitus, hypertension, and prior history of ischemic stroke. Predictors were included in the final model if the p value was <0.05. A p value of <0.05 was considered statistically significant for other analyses. All analyses were performed using SPSS (IBM SPSS Statistics 21.0, Chicago USA).

#### 3. Results

The distribution of demographic information and ischemic stroke risk factors by the presence of LASP is shown in Table 1. No variable was statistically different between the two groups.

The mean age of all 324 subjects (including stroke and non-stroke) was  $61 \pm 12$  years. The overall prevalence of ASP was 30.2% (n = 98), and the LASP was 17.9% (n = 58), RASP was 12.3 (n = 40)(Fig. 2).

The depth of LASP was significantly deeper than RASP (1.00  $\pm$  0.52 cm vs 0.44  $\pm$  0.14 cm, p < 0.0001).

The presence of a LSP was found to be associated with an increased risk of ischemic stroke, in either univariable analysis (OR = 2.43, 95% CI = 1.1–5.5, p = 0.033) or after adjustment for other stroke risk factors using multiple logistic regression analysis (OR = 2.45, 95% CI = 1.1–5.8, p = 0.036).

We also found a thrombus within the LASP, and a tiny thrombus arising from RASP (Fig. 1A and B; Videos 1, 2).

**Table 1**Patient characteristics categorized by the presence or absence of LASP.

Parameters	LASP $(n = 58)$	No LASP ( $n = 266$ )	P value
Demographics			
Age years(mean $\pm$ SD)	$61 \pm 12$	$61 \pm 12$	0.77
Male (%)	38 (66)	64 (58)	0.24
Stroke risk factors (%)			
Atrial fibrillation/flutter (%)	29 (50)	142 (53)	0.73
Myocardial infarction (%)	1 (1.7)	23 (8.6)	0.17
Diabetes mellitus (%)	6 (15.8)	42 (10.3)	0.29
Hypertension	17 (30)	117 (44)	0.06
Warfarin	19 (33)	79 (30)	0.43
Systemic embolic event (%)	1 (1.7)	3 (1.1)	0.55
Prior ischemic stroke (%)	10 (17.2)	21 (7.9)	0.028

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