

Atrial septal pouch – Morphological features and clinical considerations



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ARTICLE INFO

Article history:

Received 26 April 2016

Received in revised form 12 June 2016

Accepted 24 June 2016

Available online 28 June 2016

Keywords:

Interatrial septum

Stroke

Left atrium

Left atrial appendage

Patent foramen ovale

ABSTRACT

Background: The atrial septal pouch (SP) is a new anatomical entity within the interatrial septum. The left-sided SP may be the source of thrombus and contribute to ischemic stroke. The aim of this study was to provide a detailed morphometric description of the SP.

Methods: Two hundred autopsied hearts (23% deriving from females) with a mean age of 46.7 ± 19.1 years were investigated. We assessed the morphology of the interatrial septum. We obtained measurements and casts of the SPs, and we conducted histological staining of the left-sided SPs.

Results: Patent foramen ovale was observed in 25% of hearts. We found a left SP in 41.5%, right in 5.5% and a double SP in 5.5% of hearts. We found the patent foramen ovale (PFO) more often in younger hearts, and the SP and smooth septum were more prevalently found in older hearts ($p = .0023$). The mean volume of the left-sided SP was 0.31 ± 0.11 ml, which represented $13.6 \pm 9.4\%$ (range: 3.1–44.9%) of the left atrial appendage volume. The SP shape resembled a cone or a cylinder with some smaller diverticula originating from the main body. The SP free wall was composed of two layers of endocardium, transverse muscle fibers and connective tissue.

Conclusions: A left-sided SP was present in 47% of individuals. The SP arises as a result of PFO channel closure. The anatomy of left-sided SP may promote blood stasis and thrombus formation. The universal formula for SP volume was calculated.

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1. Introduction

Atrial septal pouch (SP) is a new anatomical entity within the interatrial septum that was first described in 2006 by Breithardt et al. [1] and developed in 2010 by Krishnan and Salazar [2]. Embryologically, the interatrial septum is composed of the septum primum and the septum secundum. During fetal life, the interatrial septum is incomplete and physiologically fuses after birth. In approximately 10–35% of adults, a nonadherent flap valve of the septum and the rims of the fossa ovalis form a channel across the interatrial septum that connects both atria known as the patent foramen ovale (PFO) [3,4]. By definition, a SP is a kangaroo pouch-like structure that occurs when the PFO is absent but the septum primum and septum secundum are partially fused [2]. The diverticulum may be located either on the right or left side of the interatrial septum.

The morphological nature and clinical significance of this mysterious structure remain unclear. Only one anatomical study has focused on the prevalence of SP and its depth. Also its clinical significance is uncertain. Over a dozen case reports have noted that SPs located in the left atrium

(LA) are a site of origin of thrombus formation and a source of embolism [1,5–14]. A case–control study by Tugcu et al. reported no association between left-sided SP and cryptogenic ischemic stroke in a subgroup of elderly patients [15]. Also, Wayangankar et al. reported no correlation between left-sided SP and cryptogenic stroke [16]. On the other hand, a recent study by Wong et al. conducted on population of relatively young patients suggests that left-sided SP is associated with cryptogenic stroke [17]. Also the paper by Sun, et al. reported that the risk of ischemic stroke was twice more among patients with LSSP than cases without LSSP [18].

The question of left-sided SP clinical significance still remains controversial. However, everything seems to indicate that left-sided SP may be a serious player on the stage of ischemic stroke. Therefore, in this study, we attempt to answer fundamental questions: what the SP is, where it is located and why it is formed.

2. Methods

2.1. Study population

We focused on a total of 200 randomly selected autopsied human hearts from Caucasian individuals of both sexes (23% females) aged from 1 to 94 (mean = 46.7 ± 19.1 years). The average measured

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body mass index (BMI) of the individuals was $26.6 \pm 4.8 \text{ kg/m}^2$, and the average body surface area was $1.9 \pm 0.3 \text{ m}^2$. The hearts were collected during routine forensic medical autopsies. The primary causes of death included suicide, murders, traffic accidents and home accidents. The difference in sex distribution (F = 23% vs M = 73%) results from the forensic nature of death which is more common in males. The exclusion criteria included severe anatomical defects, heart grafts, evident severe macroscopic pathologies of the heart or vascular system found during autopsy, heart trauma and macroscopic signs of cadaver decomposition. No death due to heart failure was observed. There were no cases with a past medical history of atrial fibrillation. This study was approved by the Bioethical Committee of Jagiellonian University Medical College, Cracow, Poland (No 122.6120.37.2016). In our study we personally collected hearts only from deceased person who did not express objection, when alive, and if family did not express objection. Also our Bioethical Committee waived the need for consent. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Dissection and measurements

The hearts were dissected together with the proximal portions of the great vessels: the ascending aorta, pulmonary trunk, superior and inferior vena cava, and all of the pulmonary veins. We weighed the hearts before fixation using a 0.5 g precision electronic laboratory scale (SATIS, BSA-L Laboratory, Poland). After dissection, all of the hearts were fixed by immersion in 10% paraformaldehyde solution for a maximum of two months until the time of measurement.

We obtained linear measurements using 0.03-mm YATO (YT-7201) precision electronic calipers. All of the measurements were made by two independent researchers in order to reduce bias. If the differences in the results between the two researchers were greater than 10%, both of the measurements were repeated. The mean of the two measurements was calculated, with approximation to the tenth decimal place.

We evaluated the morphology of the interatrial septum from the left and right atrial sides. The septum was classified as one of the following (Fig. 1):

- PFO – channel connecting the left and right atrium;
- left SP – pouch opened into the left atrial cavity without a connection between the left and right atrium;
- right SP – pouch opened into the right atrial cavity;
- double SP – two pouches with openings into both atria;
- smooth septum – neither PFO nor SP was observed.

The term “left-sided SP” was used when a diverticulum was observed on the left side of the interatrial septum (left and double SP);

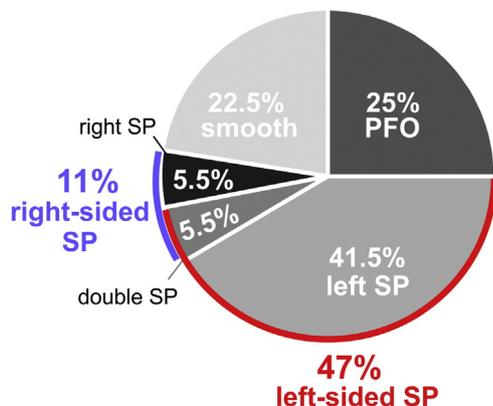


Fig. 1. Pie chart showing the prevalence of observed interatrial septum variations (n = 200). PFO = patent foramen ovale; SP = septal pouch.

“right-sided SP” was used when the pouch was present on the right side of the septum (right and double SP).

We measured the length of the PFO channel and the SP depth (D), its ostium height (H) and its width (W). We measured D as the maximum distance from the SP ostium to its apex. The ostium height (H) was defined for left-sided SPs as the maximum distance between its free wall and LA wall and for right-sided SPs as the largest distance between the fossa ovalis floor and the left surface of the antero-superior rim. The ostium width (W) was defined for left-sided SPs as the maximum distance from the attachment points of SP free walls to the LA wall and for right-sided SPs as the maximum distance between the attachment points of the fossa ovalis floor and the antero-superior rim.

2.3. Histology

Ten hearts with left SPs were intended for histological processing. Ten days after the hearts were placed in 10% paraformaldehyde, we sectioned fragments of the interatrial septum. We stained 5- μm thick sections routinely with Mayer's hematoxylin and eosin for general morphology. We examined the stained sections using an Axio Lab.A1 microscope (ZEISS, Germany) in bright-field mode and acquired images using an AxioCam ERC5s digital CCD camera (ZEISS).

2.4. SP and left atrial appendage casting

The SPs and left atrial appendages (LAAs) were injected with the acrylic mass Duracryl Plus (Spofa, Dental, Czech Republic) dyed with pigments (n = 105). The mass was made by mixing the powdered Duracryl Plus with liquid Duracryl Plus in a 1:3 volume ratio to slow down solidification and enable the structures to be filled adequately. After solidification of the mass, the tissue was microdissected to release the cast from the specimen. We measured the volume (V) of the casts in a graduated cylinder using Archimedes' principle.

2.5. Statistical analysis

We present the data as mean values and the corresponding standard deviations or percentages. We used the Shapiro-Wilk test to determine if the quantitative data were normally distributed. We relied on Levene's test to verify the homogeneity of variance. The Student's *t*-test and Mann-Whitney U test were used to statistically compare the two groups. We performed analysis of variance (ANOVA) with the Bonferroni post-hoc test for multiple comparisons to determine a significant difference in mean age between groups with different types of interatrial septa (PFO, SP, smooth). We calculated correlation coefficients to measure the statistical dependence between the parameters of the measured hearts. We performed multiple regression analysis on the depth and width of the SP set as independent variables and the cast volume of the SP set as the dependent variable to determine the extent to which these parameters predicted the size of the SP. We conducted our statistical analyses using STATISTICA v12 (StatSoft Inc., Tulsa, OK, USA). A p value of less than 0.05 was considered to be statistically significant.

3. Results

The mean heart weight was $433.0 \pm 112.9 \text{ g}$. The PFO was observed in 50 cases (25%) with a mean channel length of $9.2 \pm 3.9 \text{ mm}$ (range: 2.7–17.4 mm). A left SP was observed in 83 individuals (41.5%), and we observed a right SP in 11 individuals (5.5%); we noted a double SP in 11 individuals (5.5%) (Figs. 1, 2). No interatrial septal aneurysms or atrial septal defects were observed. There was a statistically significant difference in the prevalence of PFO, SP and smooth septum as a function of age ($p = .0098$). We found the PFO more often in a younger age group; the SP and smooth septum were more prevalently found among older individuals (Fig. 3).

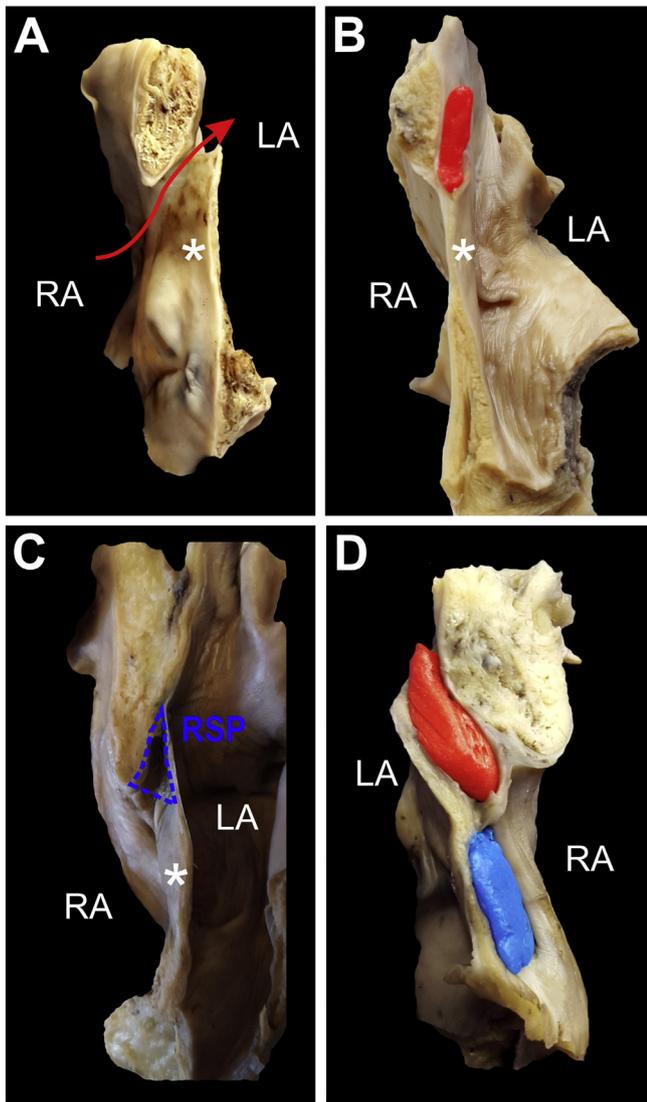


Fig. 2. Photograph showing cadaveric heart specimens. Cross-sections of the interatrial septum area. (A) Patent foramen ovale – channel connecting the left and right atrium. (B) Left septal pouch (SP) – diverticula opening into the left atrial cavity without a connection between the atria. (C) Right SP – diverticula opening into the right atrium without a connection between the atria. (D) – double SP – coexistence of left-sided and right-sided SP without a connection between the atria. LA = left atrium; RA = right atrium; RSP = right septal pouch; * = fossa ovalis.

The measurements of the SPs are presented in Table 1. There was no difference in the size of both the left-sided and right-sided SPs when they existed as a single pouch or coexisted as a double SP. The right-sided SP ostium width was strongly correlated with the right atrioventricular ring diameter ($r = .91$; $p = .00$). All of the measured parameters of left-sided SPs exceeded those of right-sided SPs ($p < .05$). None of the measured SP parameters were correlated with BMI, age or heart weight.

The left-sided SP is located on the border of the left-sided interatrial septum and the LA anterior wall and is always bounded by its free wall (remnant of PFO valve) from the posterior and left side and the LA wall from the anterior and right side. The left-sided SP contour is projected onto the transverse pericardial sinus and then onto the aortic valve non-coronary sinus. It does not overlap with any of the true interatrial septum components [19]. The left-sided SP apex is always directed downward with the ostium positioned at an angle of 10–50° (relative to the horizontal) toward the left. The right-sided SP is always bounded by the antero-superior rim from the right side and by the floor of fossa ovalis from the left side with the apex directed upward and forward (Fig. 4).

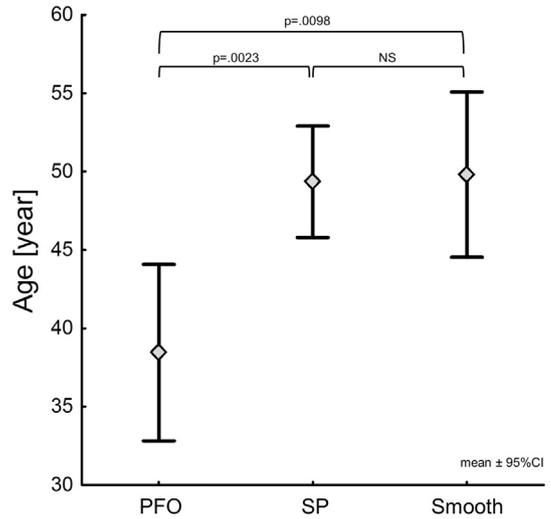


Fig. 3. Mean age values with a 95% confidence interval (CI 95%) for hearts with patent foramen ovale (PFO), septal pouch (SP) and smooth septum ($n = 200$). Left, right and double SPs were all considered to be part of the SP group. We applied analysis of variance with multiple comparisons.

We also made casts of the LAA and SP (Fig. 5). The mean volume of the LAA was 3.2 ± 2.0 ml (range: 0.4–11.1 ml) and was correlated with BMI ($r = .64$; $p = .03$), age ($r = 0.25$; $p = .02$) and the PFO channel length ($r = .38$; $p = .01$). The volumes of the left- and right-sided SPs are presented in Table 1. The right-sided SPs exhibited smaller volumes than the left-sided SPs ($p = .03$). We calculated the left-sided SP/LAA volume ratio. The mean ratio was $13.6 \pm 9.4\%$ (range: 3.1–44.9%). The LAA volume was correlated with both the left-sided SP volume ($r = .32$; $p = .003$) and the right-sided SP volume ($r = .67$; $p = .02$).

Based on the volumes of the SP casts and their morphometric measurements, we created a linear regression model for a universal formula for SP volume. The overall model features were: $R^2 = .315$; adjusted $R^2 = .09$; $p = .109$; the model included SP depth ($p = .08$), SP width ($p = .11$) and a constant variable ($\beta = -.131$; $p = .527$). The last variable was omitted in the final formula:

$$V [ml] = 0.013 \times (SP \text{ depth} [mm]) + 0.038 \times (SP \text{ ostiumheight} [mm]).$$

The SP casts revealed the shape of the SPs; this shape was similar to that of a cone or cylinder with some smaller diverticula originating from the main body (Fig. 5). There were no significant differences in any of measured parameters as a function of sex.

Histological staining of the left SP revealed its primary morphology, which was common among all of the examined samples (Fig. 6). The SP free wall was composed of two layers of endocardium, between which transverse muscle fibers and connective tissue could be observed. The atrial wall of the SP presented classical morphology for LA. At the apex, we observed the accumulation of sub-endocardial tissue.

Table 1
Results of obtained morphometric measurements.

| | Left-sided SP | | | | Right-sided SP | | | |
|------------------------|---------------|------|------|------|----------------|------|------|------|
| | Mean | SD | Min | Max | Mean | SD | Min | Max |
| Depth (D) [mm] | 8.4 | 5.1 | 1.0 | 36.4 | 6.2 | 3.4 | 2.1 | 17.1 |
| Ostium height (H) [mm] | 5.2 | 1.7 | 2.0 | 15.0 | 4.5 | 1.5 | 2.3 | 8.0 |
| Ostium width (W) [mm] | 8.8 | 2.6 | 2.3 | 17.3 | 7.5 | 3.5 | 3.0 | 15.0 |
| Volume (V) [ml] | 0.31 | 0.11 | 0.11 | 1.03 | 0.25 | 0.08 | 0.15 | 0.53 |

SD – standard deviation; SP – septal pouch.

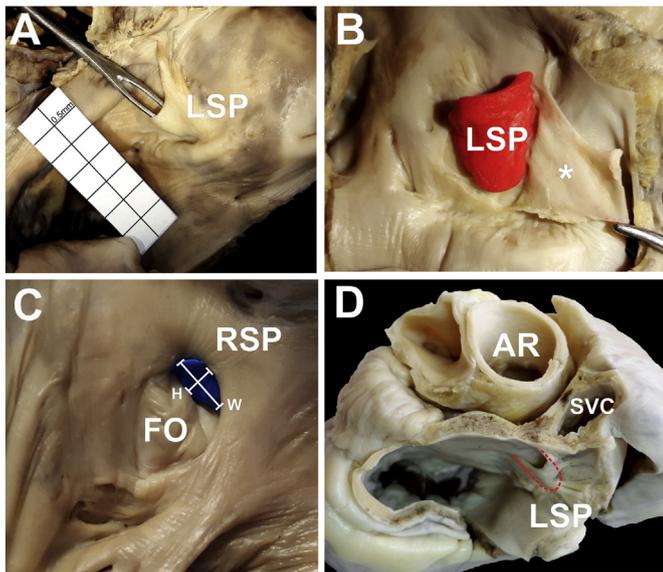


Fig. 4. Intracavitary view of the interatrial septum. (A) Left septal pouch (LSP). The probe is inserted into the diverticula ostium. (B) Left septal pouch cast. The free wall of the pouch (*) is retracted. (C) Right septal pouch (RSP) cast filling the diverticula. (D) View of the LSP and surrounding structures. The close proximity of aortic root (AR) is seen. FO = fossa ovalis; H = ostium height; SVC = superior vena cava; W = ostium width.

4. Discussion

The high prevalence of SP (over 50% of the healthy population) ensures that the pouch is not a pathology. Rather, it is an element of normal human anatomy. The left-sided SP is the most common anatomical variation of the human interatrial septum. Our results revealed an increased prevalence of PFO among younger subjects and an increased prevalence of SP among older individuals ($p = .0023$). It leads us to a theory of continuous, lifelong remodeling of the interatrial septum in which the PFO evolves into an SP or smooth septum. The PFO valve fuses with the left side of the interatrial septum. In cases with very short PFO valves (short channel), fusion is completed and results in full channel closure and a smooth septum at an early age. A long PFO valve (long channel) may fuse with the remaining part of the interatrial septum at three levels. Fusion limited to the caudal portion of the zone of overlap leads to left SP, and fusion limited to the central portion of the zone of overlap leads to double SP. Finally, fusion limited to the cranial portion of the zone of overlap leads to right SP (Fig. 7). Further adhesion, especially of small pouches, results in the closure of the SP from its apex to the ostium and the smooth septum in the elderly. Furthermore, closed pouch (bilaminated interatrial septum) may occur (incomplete fusion of the septum without opening into either atrial chamber) [15] as a result of SP involution and closure. Some studies pointed that the decreased prevalence of PFO among older subjects may be the result of selective mortality due to paradoxical embolism [20]. However, authors do not attribute significant effect of this mechanism on current study results.

Our study provides details about the internal structure of the SP. First, the volume of the left-sided SP is relatively small (mean = 0.31 ml), but pouches with volumes above 1 ml were also observed. When compared with the corresponding LAA, the SP represents approximately 14% of the volume, but again it can attain nearly half of the LAA's volume. Furthermore, the shape of the left-sided SP cavity is complex with secondary diverticula. Additionally, the apex of the left-sided SP is oriented downward, like a calyx covered with endocardium filled with blood. All of the SP's anatomical features predispose it to thrombi formation through the mechanism of blood stasis. The SP in many ways resembles the LAA.

One hypothesis as to why thrombi are not routinely found in left-sided SPs is that brisk laminar blood flow of the right pulmonary veins is a protective mechanism against clot formation along the interatrial septum [5]. When this protective mechanism is lost (due to, for example, mitral stenosis, high ventricular pressure, heart failure, anomalies in the pulmonary vein confluence), stasis may occur in the SP. The other, yet unsolved, factor is transverse muscular fibers that surround the left-sided SP cavity. Contraction of these fibers can promote emptying of the pouch, which may function as a protective mechanism against SP thrombosis. In atrial fibrillation this mechanism could be impaired. On the other hand, segmental contraction of muscles in the SP ostium that does not empty the SP but instead inhibits communication between the LA and SP cavity, may favor blood stasis and clot formation. The SP may be also associated with unexplained transient ischemic attacks and ischemic strokes occurring just after transseptal puncture. The intervention within the interatrial septum may release embolic material from the left-sided SP.

When we compare our results with those of the first SP anatomical study, we do not find any significant differences in either SP prevalence or SP depth [2]. However, Krishnan and Salazar [2] did not discuss the presence of double SP, which is described for the first time in autopsied material in the current study. When comparing with imaging studies

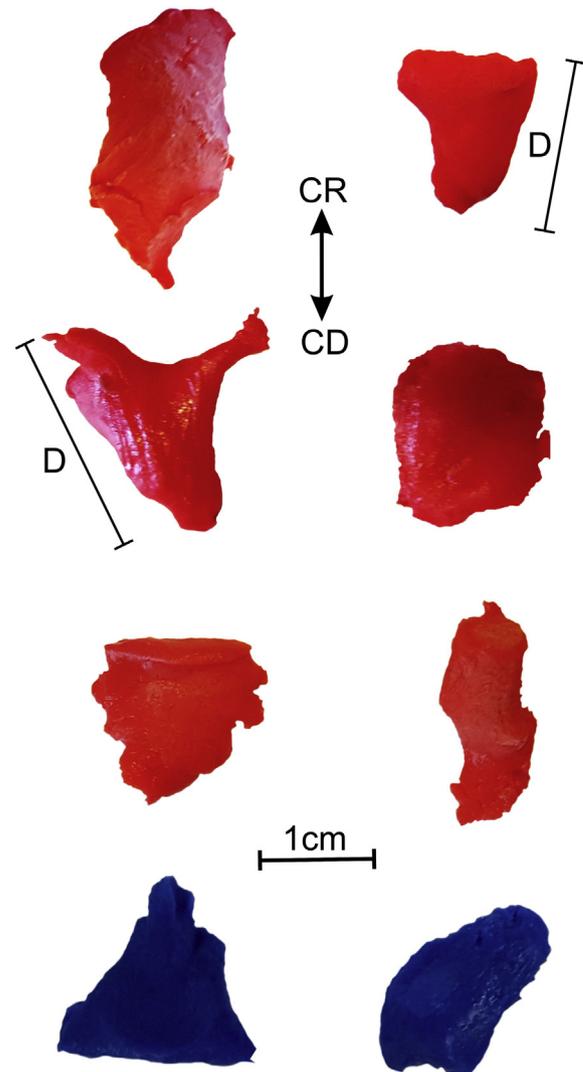


Fig. 5. Casts of left-sided (red; $n = 94$) and right-sided (blue; $n = 22$) septal pouches. CD = caudal; CR = cranial; D = septal pouch depth. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

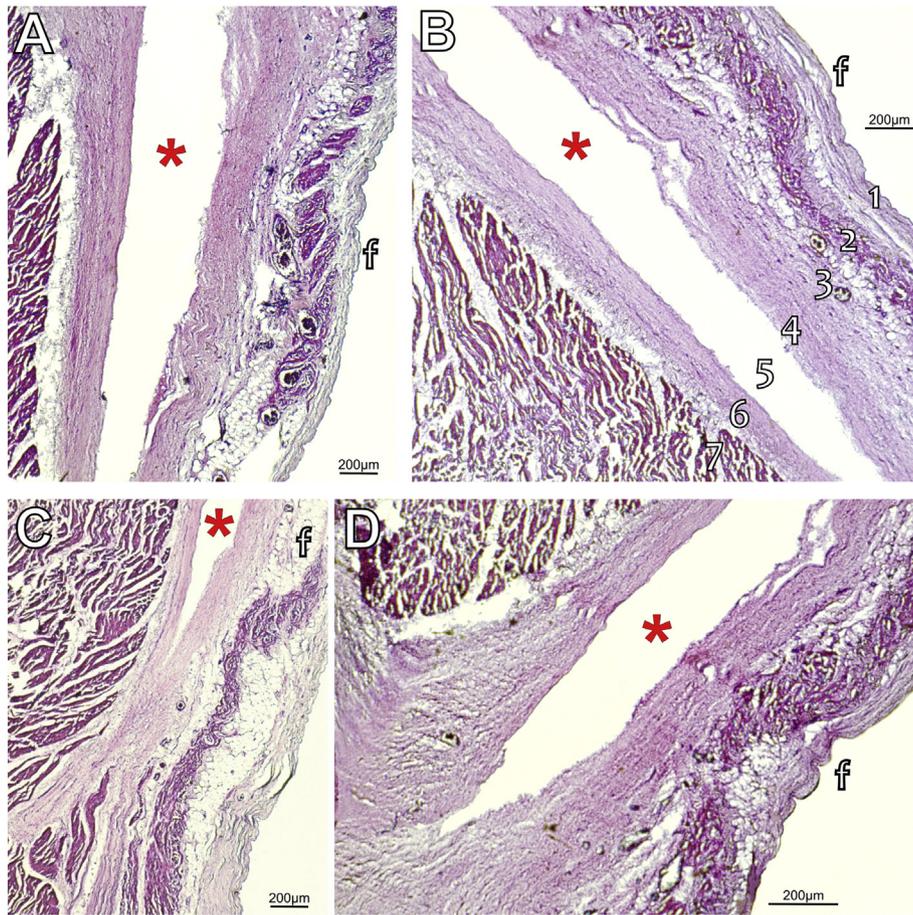


Fig. 6. Histology (hematoxylin and eosin) of the left septal pouch (SP) samples (n = 10). (A, B) Morphology of the routinely stained left septal pouch. Layers from the left atrium cavity: 1 – endocardium; 2 – transverse muscle fibers; 3 – connective tissue; 4 – endocardium; 5 – SP lumen (*); 6 – atrial endocardium; 7 – deep atrial muscle fibers. (C, D) The apex of the left SP is visible. * = septal pouch lumen; f = SP free wall.

(transesophageal echocardiography), the prevalence of left-sided SP is significantly lower: Tugcu et al. found a prevalence of 29.1% [15], Sun et al. found a prevalence of 17.9% [18], Wong et al. found a prevalence of 16.5% [17] and Wayangankar et al. found a prevalence of 10.6% [16]. The prevalence of left-sided SP assessed by multidetector, cardiac-gated computed tomography is higher than that assessed using transesophageal echocardiography; Vehian et al. found a prevalence of

38.4% [21], and Terpenning et al. found a prevalence of 24.7% [22]. It should be noted that the term SP has been misused as describing the interatrial septum in imaging studies in which the presence of the SP and PFO in one heart are described [22,23]. A prerequisite to the formation of the SP is the closure of the PFO channel and no connection between the left and right atria. In other words, coexistence of the PFO and SP cannot be observed.

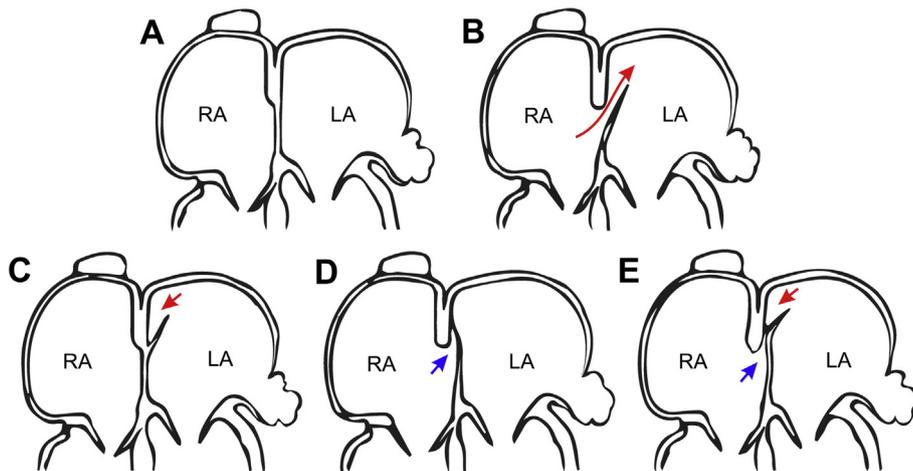


Fig. 7. Schematic view of the interatrial septum. (A) Smooth septum – fusion between the septum primum and secundum occurs along the entire zone of overlap. (B) Patent foramen ovale. (C) Left septal pouch – fusion limited to the caudal portion of the zone of overlap. (D) Right septal pouch – fusion limited to the cranial portion. (E) Double septal pouch – fusion between the septum primum and secundum occurred in the central part. LA = left atrium; RA = right atrium.

The SP is still a new concept. The anatomy of left-sided SP may promote blood stasis and thrombus formation. Additional clinical studies may fill the gap and render the SP a significant player in the story of thromboembolic episodes arising from the LA and an achievable target for catheter-based intervention or surgical therapy. Multicenter clinical studies are strongly required [24,25]. As far there are no criteria for the diagnosis of the SP. Which imaging technique should be used to proper evaluation of the SP? Perhaps in the future the left-sided SP will be treated equally with the LAA. It is necessary to ask: what if the SP proves to be an independent risk factor for thromboembolic events? What kind of invasive management (SP ostium closure or free wall damage) could be applied?

5. Conclusions

A left-sided SP is present in 47% of individuals. The SP arises as a result of PFO channel closure. The anatomy of left-sided SP may promote blood stasis and thrombus formation.

Abbreviations

| | |
|-----|-----------------------|
| SP | atrial septal pouch |
| PFO | patent foramen ovale |
| BMI | body mass index |
| LAA | left atrial appendage |

Funding

The research and Mr. Mateusz K. Hołda were supported by the Ministry of Science and Higher Education Republic of Poland, ESF Operational Program “Knowledge - Education - Development” under the project “Best of the best!” (MNIŚW/2016/DIR/182/NN). The funders had no role in the study's design, data collection, or analysis, decision to publish, or preparation of the manuscript.

Conflict of interest

None declared.

References

- [1] O.A. Breithardt, T. Papavassiliu, M. Borggrefe, A coronary embolus originating from the interatrial septum, *Eur. Heart J.* 27 (2006) 2745.
- [2] S.C. Krishnan, M. Salazar, Septal pouch in the left atrium: a new anatomical entity with potential for embolic complications, *JACC Cardiovasc. Interv.* 3 (2010) 98–104.
- [3] D.C. Fisher, E.A. Fisher, J.H. Budd, S.E. Rosen, M.E. Goldman, The incidence of patent foramen ovale in 1000 consecutive patients. A contrast transesophageal echocardiography study, *Chest* 107 (1995) 1504–1509.
- [4] J. Reig, R. Mirapeix, A. Jornet, M. Petit, Morphologic characteristics of the fossa ovalis as an anatomic basis for transseptal catheterization, *Surg. Radiol. Anat.* 19 (1997) 279–282.
- [5] S.V. Gurudevan, H. Shah, K. Tolstrup, R. Siegel, S.C. Krishnan, Septal thrombus in the left atrium: is the left atrial septal pouch the culprit? *JACC Cardiovasc. Imaging* 3 (2010) 1284–1286.
- [6] H. Kuwaki, M. Takeuchi, K. Kaku, N. Haruki, H. Yoshitani, M. Tamura, et al., Thrombus attached to the left atrial septal pouch assessed on 3-dimensional transesophageal echocardiography, *Circ. J.* 75 (2011) 2280–2281.
- [7] I. Elsokkari, E. Reyneke, M. William, Left atrial septal pouch causing an ischaemic stroke in association with aortic coarctation, *Eur. J. Echocardiogr.* 12 (2011) 916.
- [8] M. Strachinaru, M. Morissens, S. Latifyan, I. Costescu, Left atrial septal pouch thrombus assessed on three-dimensional transesophageal echocardiography, *Eur. Heart J. Cardiovasc. Imaging.* 13 (2012) 967.
- [9] S. Buchholz, D. Robaei, N.H. Jacobs, M. O'Rourke, M.P. Feneley, Thromboembolic stroke with concurrent left atrial appendage and left atrial septal pouch thrombus, *Int. J. Cardiol.* 162 (2012) e16–e17.
- [10] M. Strachinaru, P. Wauthy, A. Sanoussi, M. Morissens, I. Costescu, E. Catez, The left atrial septal pouch as a possible location for thrombus formation, *J. Cardiovasc. Med. (Hagerstown)* (2013).
- [11] K. Shimamoto, T. Kawagoe, K. Dai, I. Inoue, Thrombus in the left atrial septal pouch mimicking myxoma, *J. Clin. Ultrasound* 42 (2014) 185–188.
- [12] J.M. Wong, D. Lombardo, J. Handwerker, M. Fisher, Cryptogenic stroke and the left atrial septal pouch: a case report, *J. Stroke Cerebrovasc. Dis.* 23 (2014) 564–565.
- [13] S. Bandyopadhyay, K. Mandana, Left atrial septal pouch: a potential source of systemic thromboembolism: incidental transesophageal echocardiogram findings, *Anesth. Analg.* 121 (2015) 59–61.
- [14] S. Aggarwal, J. Kalavakunta, V. Gupta, Left atrial septal pouch thrombus: a common pathology in an uncommon location, *Int. J. Cardiol.* 212 (2016) 369–370.
- [15] A. Tugcu, K. Okajima, Z. Jin, T. Rundek, S. Homma, R.L. Sacco, et al., Septal pouch in the left atrium and risk of ischemic stroke, *JACC Cardiovasc. Imaging* 3 (2010) 1276–1283.
- [16] S.A. Wayangankar, J.H. Patel, B. Patel, S. Stavrakis, C.A. Sivaram, Clinical and echocardiographic variables associated with LA septal pouch, *JACC Cardiovasc. Imaging* 6 (2013) 833–835.
- [17] J.M. Wong, D.M. Lombardo, A. Barseghian, J. Dhoot, H.S. Hundal, J. Salcedo, et al., Left atrial septal pouch in cryptogenic stroke, *Front. Neurol.* 6 (2015) 57.
- [18] J.P. Sun, F. Meng, X.S. Yang, A.P. Lee, M. Chen, B. Zhang, et al., Prevalence of atrial septal pouch and risk of ischemic stroke, *Int. J. Cardiol.* 214 (2016) 37–40.
- [19] W. Klimek-Piotrowska, M. Hołda, M. Koziej, K. Piątek, J. Hołda, Anatomy of the true interatrial septum for transseptal access to the left atrium, *Ann. Anat. Anat. Anz.* (2016).
- [20] A. Wahl, S. Windecker, B. Meier, Evaluation and treatment of abnormalities of the interatrial septum, *Catheter. Cardiovasc. Interv.* 63 (2004) 94–103.
- [21] A. Vehian, B. Choi, S. Rekhi, H. Young, R. Dusaj, R. Zeman, Clinical significance of left atrial anatomic abnormalities identified by cardiac computed tomography, *Adv. Comput. Tomogr.* 4 (2015) 1–8.
- [22] S. Terpenning, L. Ketai, S. Rissing, S. Teague, Correlation of Left Atrial Septal Pouch with the Prevalence of Patent Foramen Ovale: a Retrospective Review *Cardiology and Angiology: an International Journal*, 32015 122–129.
- [23] Y. Kijima, P. Bokhoor, J.M. Tobis, Patent foramen ovale with right atrial septal pouch, *Catheter. Cardiovasc. Interv.* (2015).
- [24] Y. Chandrashekar, J. Narula, LA septal pouch as a source of thromboembolism: innocent until proven guilty? *JACC Cardiovasc. Imaging* 3 (2010) 1296–1298.
- [25] J.M. Wong, M. Fisher, The potential role of the left atrial septal pouch in cryptogenic stroke, *Expert. Rev. Cardiovasc. Ther.* 14 (2016) 1–3.