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Left atrial accessory appendages, diverticula, and left-sided septal pouch in multi-slice computed tomography. Association with atrial fibrillation and cerebrovascular accidents

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ABSTRACT

Background: The aim of this study is to provide a morphometric description of the left-sided septal pouch (LSSP), left atrial accessory appendages, and diverticula using cardiac multi-slice computed tomography (MSCT) and to compare results between patient subgroups.
Methods: Two hundred and ninety four patients (42.9% females) with a mean of 69.4 ± 13.1 years of age were investigated using MSCT. The presence of the LSSP, left atrial accessory appendages, and diverticula was evaluated. Multiple logistic regression analysis was performed to check whether the presence of additional left atrial structures is associated with increased risk of atrial fibrillation and cerebrovascular accidents.
Results: At least one additional left atrial structure was present in 51.7% of patients. A single LSSP, left atrial diverticulum, and accessory appendage were present in 35.7%, 16.0%, and 4.1% of patients, respectively. After adjusting for other risk factors via multiple logistic regression, patients with LSSP are more likely to have atrial fibrillation (OR = 2.00, 95% CI = 1.14–3.48, $p = 0.01$). The presence of a LSSP was found to be associated with an increased risk of transient ischemic attack using multiple logistic regression analysis after adjustment for other risk factors (OR = 3.88, 95% CI = 1.10–13.69, $p = 0.03$).
Conclusions: In conclusion LSSPs, accessory appendages, and diverticula are highly prevalent anatomic structures within the left atrium, which could be easily identified by MSCT. The presence of LSSP is associated with increased risk for atrial fibrillation and transient ischemic attack.

1. Introduction

Left atrial anatomical abnormalities, such as accessory appendages and diverticula, are focal outpouchings of the left atrium wall from the heart cavity to the outside. Their origins are not quite clear and could be either congenital or acquired [1]. Clinically, they are generally asymptomatic. Ectopic electrical activity, as well as thrombi formations, has been described in patients with left atrial accessory appendages and diverticula [2–5]; however, the exact relation between the left atrial abnormalities and atrial arrhythmias or thromboembolic events remains uncertain.

The atrial septal pouch is a new anatomical entity within the interatrial septum. This kangaroo pouch-like structure occurs when the patent foramen ovale is absent but the septum primum and septum secundum are incompletely fused [6,7]. The blind-ending pouch may be located either on the right or left side of the interatrial septum. The clinical significance of this structure remains unclear. Over a dozen case reports have noted that the left-sided septal pouch (LSSP) is a site of origin of thrombus and a source of embolism [8–19]. Wong et al. suggest that LSSP may be associated with cryptogenic stroke [20], and Sun et al. reported that the risk of ischemic stroke was twice more among patients with LSSP than cases without LSSP [21].

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Concurrently, the use of cardiac multi-slice computed tomography (MSCT) in the diagnosis and invasive treatment of various cardiac diseases has continued to grow. The contrast-enhanced electrocardiogram-gated MSCT has enabled visualization of the left atrium in high resolution and depicts anatomical structures in detail [22]. As the LSSP and other left atrial anatomic abnormalities may be a source of systematic embolisms, their proper radiographic identification is essential to enhance their management and reduce potential complications [3,21].

The first aim of this study is to present the prevalence and morphological characteristics of the LSSP, accessory appendages, and diverticula that could be identified in cardiac MSCT. We also aimed to assess whether the presence of analyzed additional left atrial structures may be associated with other medical conditions.

2. Methods

2.1. Study population

We focused on a total of 294 consecutive patients who underwent contrast-enhanced electrocardiogram-gated MSCT of the heart from January 2013 to December 2016. Patients with previous cardiac surgery, transseptal puncture, or left atrial interventions were excluded from the study. The subjects were comprised of 168 (57.1%) males and 126 (42.9%) females. The MSCT was performed due to: evaluation of the aortic root before the aortic valve repair or implantation (31.3%); evaluation of the coronary artery disease (24.1%); left atrial anatomy assessment before ablation procedures (23.2%); and other reasons (24.4%). We performed a chart review (history, physical exam, consultations, and outpatient notes) for all patients to determine demographic data and history of atrial fibrillation (AF), coronary artery disease, congestive heart failure (CHF), diabetes mellitus, hyperlipidemia, hypertension, carotid artery disease, syncope, ischemic stroke, transient ischemic attack (TIA) and smoking. The mean age of patients was 69.4 ± 13.1 (range: 22–91) years, mean body mass index was 26.3 ± 4.5 kg/m^2 and mean ejection fraction (EF) was 51.6 ± 17.5%. This study was approved by the Bioethical Committee of Jagiellonian University Medical College, Cracow, Poland (No. 122.6120.37.2016). The Bioethical Committee waived the need for obtaining the informed consent. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The methods were carried out in accordance with the approved guidelines.

2.2. Cardiac multi-slice computed tomography protocol

Before the cardiac MSCT examination procedure, every patient had their pulse checked. If the heart rate was over 70 bpm, 10 or 40 mg of propranolol or 40 mg of verapamil were administered to the patient, according to medical indications. The MSCT was performed using a 64-row dual-source scanner (Somatom Definition, Siemens, Erlangen, Germany and Aquilion 64, Toshiba Medical Systems, Tokyo, Japan). The contrast-enhanced electrocardiogram-gated image acquisitions were performed during inspiratory breath hold. The imaging parameters for dual-source MSCT were a tube voltage of 100–120 kV and an effective tube current of 350–400 mA. The collimation and temporal resolution were 2 × 32 × 0.6 mm and 165 ms, respectively. The arrival time of the contrast agent to the ascending aorta was determined at the level of the carina with the use of a test bolus method (volume of 15 ml of contrast agent, followed by 20 ml of saline). Contrast agent was injected at a dose of 1.0 ml/kg and a rate of 5.5 ml/s followed by 40 ml of saline at the same rate. The acquisition delay was the time of maximum density of the ascending aorta in the test bolus with an additional 6 s of delay. Images were reconstructed with a B26f and B46f kernel and an image matrix of 512 × 512 pixels. Multiphase reconstruction (from 10% to 100%) was performed. The post-processing and study evaluation were performed using a dedicated workstation (Aquarius, TeraRecon, San Mateo, United States). Multiplane- and volume-rendered technique reconstructions were used to investigate left atrial and interatrial septum morphology.

2.3. Image interpretation

All MSCT data sets were retrospectively reviewed and independently evaluated by at least two researchers, mostly during the 70% phase using transverse projection and multiplane reconstruction, as needed. The investigators were blinded to the patients' clinical histories. All linear measurements were taken using virtual calipers. Firstly, the left atrial appendage and all pulmonary vein ostia were identified, then all focal left atrium wall contour abnormalities were recorded. The presence and location of accessory appendages and diverticula were documented in each case. The accessory appendage was defined as an outpouching with irregular contours, suggesting the presence of pectinate muscle (Fig. 1a–c). The diverticulum was identified if the outpouching had a smooth contour (Fig. 1d–h). The maximum ostium diameter and maximum length (distance between ostium and the apex) of the accessory appendages and diverticula were measured in multiplane reconstruction. The shape of accessory appendages and diverticula were assessed and classified as a cone, pyramid, cylinder, half ball or cuboid and the volume was calculated using formulas for selected solid geometry. The interatrial septum area was also investigated in all cases. The LSSP was identified as the blind-ending pouch located on the left side of the interatrial septum, filled with the contrast agent (Fig. 2). The maximum depth and ostium height of the LSSP were measured in the multiplane reconstruction. The LSSP volume was calculated using the formula [7]:

$$V[\mathrm{ml}] = 0.013 \times (\mathrm{LSSP\ depth\ [mm]}) + 0.038 \times (\mathrm{LSSP\ ostium\ height\ [mm]}).$$

The patent foramen ovale was identified when the jet flow of contrast agent was seen from the right to the left atrium through the interatrial septum. The presence of a thrombus formation within the LSSP, accessory appendages, and diverticula were also recorded.

2.4. Statistical analysis

Categorical results are presented as numbers and percentages. The Shapiro–Wilk test was performed to determine if the quantitative data were normally distributed. Quantitative results are presented as mean ± standard deviation and quantiles (Q1, Me, Q3). Comparisons were performed using *t*-test or Mann–Whitney test for two groups depending on normality. The qualitative variables were compared using the χ^2 test of proportions for categorical variables. Three sets of groups were created: (1) presence or absence of LSSP, (2) presence or absence of accessory appendages or diverticula, and (3) presence or absence of any of additional left atrial structure. Multiple logistic regression analysis was performed to check whether the effect of each set of analyzed groups on AF and cerebrovascular accidents was modified by adjusting for age, sex, CHF, coronary artery disease, hypertension, dyslipidemia, smoking and diabetes mellitus. Statistical analyses were conducted using STATISTICA v12 (StatSoft Inc., Tulsa, OK, USA). A p value of <0.05 was considered statistically significant.

3. Results

Patient characteristics are summarized in Table 1. Among the patients, 152 (51.7%) had at least one additional left atrial structure (LSSP or left atrial outpouching). LSSPs were present in 105 (35.7%), left atrial diverticula in 47 (16.0%), and accessory appendages in 12 (4.1%) patients. In 140 (47.6%) cases, only one additional structure was found. The LSSP was observed together with a diverticulum in 12 (4.1%) patients. In two cases (0.7%), the accessory appendage and diverticulum coexisted. In one patient, 4 diverticula were observed (Fig. 1i). The most common location for diverticula was the antero-superior left atrium wall (31 of 47; 66.0%), followed by the lateral wall (9 of 47; 19.1%). The accessory appendages were mainly found on the anterior wall near the interatrial septum (8 of 12; 66.7%) and on the lateral wall (4 of 12; 33.3%). The patent foramen ovale was identified in 12 (4.1%) cases. No thrombi were found within LSSPs, left atrial diverticula, and accessory appendages, as well as no thrombi or contrast mixing was seen in left atrial appendage in all cases. There were no differences in the presence of LSSP, accessory appendages or diverticula between sexes ($p > 0.05$). Also no differences in age between patients with and without analyzed left atrial structures were found ($p > 0.05$).

Table 2 presents the results of the performed measurements and calculations. There were no significant differences in any of measured parameters as functions of sex or age. No correlations were found between any of the investigated parameters, both when analyzing the study group as a whole and in subgroup analyses. No statistically significant differences were found in the sizes and volumes of LSSPs, diverticula, and accessory appendages between the patients with and without AF, CHF or cerebrovascular accidents.

In univariable analysis patients with any of the additional left atrial structures (LSSP or accessory appendages or diverticula) are more likely to have AF (OR = 3.04, 95% CI = 1.83–5.05, $p = 0.00$). It was confirmed after adjusting for age, sex, CHF, coronary artery disease, hypertension, dyslipidemia, smoking and diabetes mellitus via multiple logistic regression (OR = 2.62, 95% CI = 1.49–4.62, $p = 0.00$). Also the presence of the LSSP was associated with the increased risk of AF both in univariable analysis (OR = 2.51, 95% CI = 1.52–4.15, $p = 0.00$) and in a multiple logistic regression model (OR = 2.00, 95% CI = 1.14–3.48, $p = 0.01$).

The presence of a LSSP was found to be associated with increased risk of TIA in univariable analysis (OR = 4.86, 95% CI = 1.48–16.01, $p = 0.00$) and it was confirmed after adjustment for age, sex, AF, CHF, coronary artery disease, hypertension, dyslipidemia, smoking, carotid artery disease and diabetes mellitus via multiple logistic regression

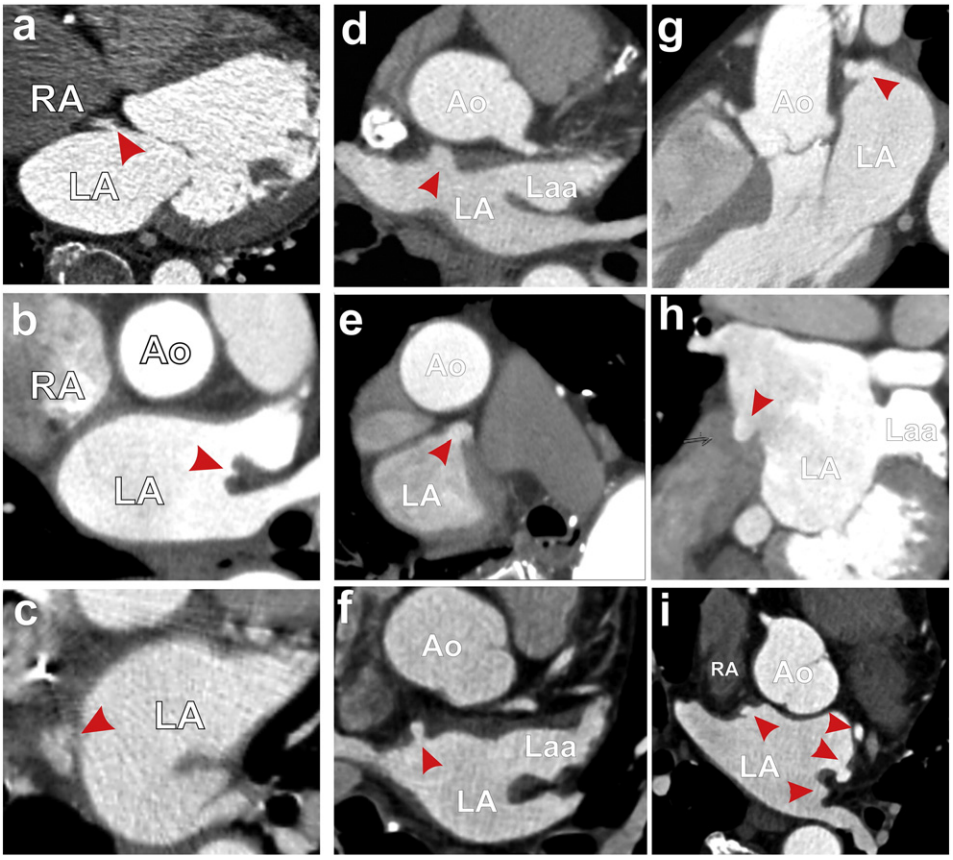

Fig. 1. Multiplane reconstruction view of the left atrium. a–c: Accessory appendages (solid arrows). Visible are the outpouchings of the left atrium wall with irregular contours suggesting the presence of pectinate muscle. d–h: Left atrial diverticula (solid arrows). Outpouchings of the left atrium wall with a smooth contour are observed. i: The left atrium with 4 coexisting left atrial diverticula (solid arrows). Ao — aorta, Laa — left atrial appendage, LA — left atrium, RA — right atrium.

(OR = 3.88, 95% CI = 1.10–13.69, $p = 0.03$). The presence of the LSSP was also associated with increased risk of cerebrovascular accident (TIA and stroke) in univariable analysis (OR = 2.04, 95% CI = 1.09–3.82, $p = 0.03$), but it was not found in the multiple logistic regression model. The prevalence of the LSSP alone, as well as the sum of analyzed structures, was significantly lower in the CHF group than in the remaining patients ($p = 0.01$).

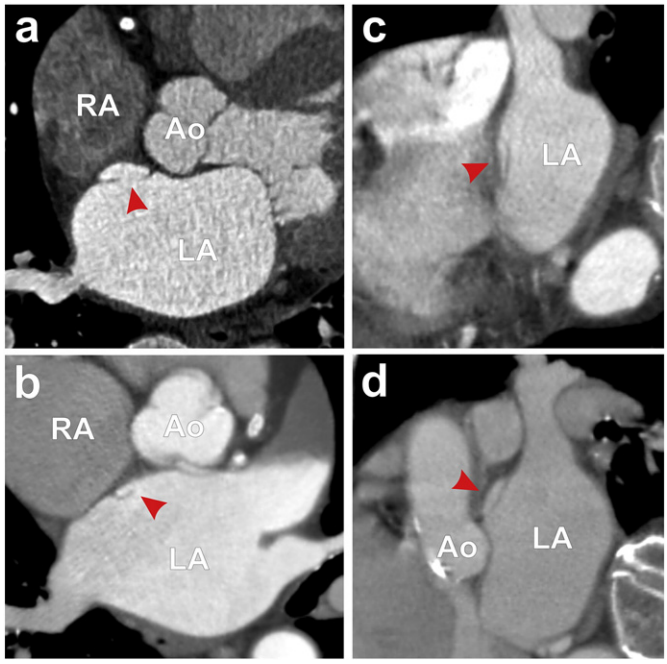

Fig. 2. Multiplane reconstruction view of the left atrium with left-sided septal pouch (solid arrows). The blind-ending pouch located on the left side of the interatrial septum, filled with the contrast could be found. RA — right atrium, LA — left atrium, Ao — aorta.

4. Discussion

The morphology and possible clinical importance of left atrial outpouchings are still not fully understood. The reported prevalence of accessory appendages in computed tomography varies from 6.5% to 28.0% and the prevalence of diverticula from 16.7% to 38.2% [23–26]. The prevalence of left atrial outpouchings ranges from 10.0% to 50.0% [1,23–32].

The idea of the atrial septal pouch is new with the potential for embolic complications [20,21]. It was first described as a case report in 2006 by Breithardt et al. [8] and developed in an anatomical study in 2010 by Krishnan and Salazar [6]. LSSP occurs in structurally normal autopsied human hearts 44.6% of the time [6,7,33]; when comparing autopsied material with imaging studies, the prevalence of LSSP is significantly lower. MSCT studies found a LSSP prevalence from 24.7% to 38.4% [26,34]. Using transesophageal echocardiography, LSSPs could be detected in 10.6% to 29.1% of cases [20,21,35–37]. In the current study, LSSPs were present in 35.7% of cases, which do not differ from the results of other MSCT studies but is still lower than in autopsied material. This may indicate that some LSSPs could be hemodynamically inactive or it could be the result of insufficient MSCT resolution.

The main finding of this study is that patients with LSSP, as well as with any of the additional left atrial structures have increased risk for AF. However other studies do not confirm this association [24–26,31,37]. Only Vehian et al. reported that in a group of 242 patients, after adjusting for other risk factors accessory appendages were associated

Table 1
Patients characteristic categorized by the presence or absence of additional left atrial structures.

	All ($n = 294$)	LSSP ($n = 105$)	No LASP ($n = 189$)	*p*-Value	Accessory appendages or diverticula ($n = 57$)	No accessory appendages or diverticula ($n = 237$)	*p*-Value	Any of additional left atrial structure[a] ($n = 152$)	No additional left atrial structures[a] ($n = 142$)	*p*-Value
Male/female (%)	57.1%/42.9%	54.3%/45.7%	58.7%/41.3%	0.47	61.4%/38.6%	56.1%/43.9%	0.47	55.3%/44.7%	59.2%/40.8%	0.50
Age (years; mean ± SD)	69.4 ± 13.1	69.5 ± 12.5	69.3 ± 13.5	0.90	68.5 ± 14.6	69.6 ± 12.8	0.57	69.0 ± 13.5	69.7 ± 12.8	0.65
Atrial fibrillation (%)	35.7%	49.5%	28.0%	**0.00**[b]	42.1%	34.2%	0.27	47.4%	23.2%	**0.00**[b]
Coronary artery disease (%)	55.8%	44.8%	61.9%	**0.01**[b]	64.9%	53.6%	0.12	50.7%	61.3%	0.07
Carotid artery disease (%)	21.8%	20.0%	22.8%	0.58	22.8%	17.5%	0.36	19.7%	23.9%	0.38
Congestive heart failure (%)	27.2%	17.1%	32.8%	**0.00**[b]	24.6%	27.8%	0.63	19.7%	35.2%	**0.00**[b]
Diabetes mellitus (%)	24.8%	24.8%	24.9%	0.98	21.1%	25.7%	0.47	23.7%	26.1%	0.63
Ever-smoker (%)	19.4%	18.1%	20.1%	0.68	19.3%	19.4%	0.99	17.8%	21.1%	0.48
Hyperlipidemia (%)	57.8%	58.1%	57.7%	0.95	61.4%	57.0%	0.55	58.6%	57.0%	0.78
Hypertension (%)	63.6%	58.1%	66.7%	0.14	54.4%	65.8%	0.11	59.9%	67.6%	0.17
Syncope (%)	5.8%	8.6%	4.2%	0.12	5.3%	5.9%	0.86	7.2%	4.2%	0.27
Ischemic stroke (%)	11.6%	13.3%	10.6%	0.49	14.0%	11.0%	0.53	13.2%	9.9%	0.38
Transient ischemic attack (%)	4.8%	9.5%	2.1%	**0.00**[b]	1.8%	5.5%	0.24	7.2%	2.1%	**0.04**[b]
Cerebrovascular accident (%)[c]	16.3%	22.9%	12.7%	**0.02**[b]	15.8%	16.5%	0.90	20.4%	12.0%	>0.05

LSSP — left-sided septal pouch; N — number of patients; SD — standard deviation.
[a] LSSP or accessory appendages or diverticula.
[b] Statistically significant (χ^2 test).
[c] Stroke or transient ischemic attack.

with a history of palpitations (OR: 1.80; CI: 1.03–3.16), but not with the AF [26]. Killeen et al. noted that left atrial accessory appendages may act as sites of focal electrical activity, which explains the increased prevalence of AF in patients with left atrial outpouchings [4]. When not expected, they can also cause serious complications during catheter ablation, as they may be sites of catheter entrapment with a risk of left atrium wall perforation [38]. There is a theory of the LSSP formation in which the patent foramen ovale channel evolves into a septal pouch and then into a smooth septum. Constant friction between the patent foramen ovale valve and the interatrial septum leads to micro-injuries, cicatrization of contacting structures and gradual closing of the channel [7]. So formed scar tissue may be proarrhythmogenic, which may explain the increased risk of AF in patients with LSSP.

There are some case reports indicating that the left atrial diverticula and accessory appendages could be a source of thromboembolism and potential cause of embolic stroke [2,5]. The outpouching within the atrial wall may promote thrombus formation through the mechanism of blood stasis. The same mechanisms could be also taken into account for the LSSP, which could also be considered a site of thrombus formation [8–14,16–18,20]. Despite of direct evidences of LSSP involvement in pathogenesis of cardio-embolic stroke the clinical significance of this mysterious structure remains unclear. The association between the LSSP and cryptogenic stroke from the preliminary epidemiologic retrospective studies is controversial. A case-control study by Tugcu et al. reported no association between LSSP and cryptogenic ischemic stroke in a subgroup of elderly patients [35], and Wayangankar et al. and Strachinaru et al. also reported no correlation between LSSP and stroke [37,39]. The MSCT study by Vehian et al., concluded that left atrial accessory appendages, diverticula, and septal pouches are not associated with cerebrovascular accidents or TIA [26]. On the other hand, recent studies by Wong et al. and Sun et al. conducted on a population of relatively young patients suggested that LSSP is associated with cryptogenic stroke [20,21]. The aforementioned studies have many limitations and were conducted on relatively small groups. In our study the presence of a LSSP was found to be associated with an increased risk of TIA in univariable analysis and it was confirmed after adjustment for other cardiovascular accident risk factors. However, due to the small number of patients with cardiovascular accidents (41 cases) and TIA (14 cases) our analysis may be impaired. Also only cases with cryptogenic stroke or TIA, where the etiology is unknown despite a detailed work up, should be examined in all further studies. There is a great need for large multicenter clinical studies that are devoted to determining whether the LSSP is an independent stroke risk factor [40,41].

Table 2
Results of measurements.

	Mean	SD	Min	Max	Median	Q1	Q3
LSSP depth (mm)	8.7	3.7	2.8	21.9	7.8	6.4	10.7
LSSP ostium height (mm)	2.9	1.2	0.9	7.0	2.7	2	3.4
LSSP volume (ml)	0.22	0.07	0.08	0.47	0.22	0.18	0.25
LA diverticula length (mm)	5.9	2.8	1.7	16.7	5.4	3.9	7.4
LA diverticula ostium diameter (mm)	6.4	3.2	1.9	15.4	6.0	4.1	8.9
LA diverticula volume (ml)	0.26	0.27	0.01	1.12	0.12	0.06	0.44
LA accessory appendages length (mm)	8.8	4.2	2.4	14.1	7.9	5.3	12.4
LA accessory appendages ostium diameter (mm)	6.5	3.4	1.7	15.0	6.2	4.8	8.0
LA accessory appendages volume (ml)	0.34	0.40	0.03	1.38	0.19	0.08	0.38

SD — standard deviation; Q1 and Q3 — lower and upper quartiles; LSSP — left-sided septal pouch; LA — left atrium.

The morphology of accessory appendages, diverticula, and LSSPs could predispose patients to form thrombi within these structures. In the authors' opinion, LSSP anatomy predisposes patients to form thrombi more than diverticula and small accessory appendages; this is reflected in the number of cases described in the literature, where the thrombi within the LSSP are featured more often. The shape of the LSSP cavity is complex with secondary diverticula. Additionally, its apex is oriented downward, with the ostium positioned at an angle of 10–50° (relative to the horizontal) toward the left, like a calyx covered with endocardium and filled with blood. Also, the segmental contraction of muscles in the LSSP ostium may inhibit communication between the left atrium and septal pouch cavity, which may favor blood stasis and clot formation [7]. The atrial wall outpouchings are usually oriented more horizontally with their long axis and have wide ostia, which may facilitate blood flow between the left atrium and diverticula interior. On the other hand, the presence of trabeculation inside the accessory appendages seems to be the strongest risk factor for clot formation. However, the prevalence of accessory appendages is considerably lower than LSSP and diverticula. The risk of thromboembolism inside the outpouchings seems to be low during sinus rhythms, due to the small size and good contractibility of those structures. Also the low number of reports on thrombi within the left atrial outpouchings and septal pouches could be explained by the fact that they are not routinely

clinically evaluated (for example, with transesophageal echocardiography or MSCT).

Subgroup analysis of the LSSP, accessory appendages, and diverticula prevalence shows that CHF is related to a lower occurrence of the analyzed structures. The explanation of this observation is difficult; this may be a result of sidewall blood stasis in CHF and insufficient contrast penetration into the LSSP or accessory appendages and diverticula, and therefore might be the bias related to the used imaging method. Also, the LSSP could be involved in an eccentric left atrium remodeling process in the course of the CHF with reduced ejection fraction and used pharmacological therapy, which may lead to LSSP closure through the fusion between the LSSP free wall and left atrium [42,43].

This study has some limitations. It is a retrospective imaging study where contrast-enhanced electrocardiogram-gated MSCT was used. The spatial resolution of 64-row MSCT is great, but may still be inadequate to show very small elements; however, the 64-row MSCT is probably the most commonly available imaging modality in cardiologic centers. The use of that typical imaging equipment was intentional; it was used to show that despite all higher-row devices, 64-row MSCT is sufficient to visualize the accessory structures in sizes that may be clinically significant. Also, the authors did not perform dynamic studies to look at left atrium wall motion to investigate the behavior of LSSP, accessory appendages, and diverticula during the cardiac cycle. The MSCT was performed during inspiratory breath hold, which may slightly influence the size of the measured structures. Furthermore, the MSCT is not a dynamic study and the patent foramen ovale might have been incorrectly classified as LSSP in some cases. However, when compared to the prevalence of patent foramen ovale identified in this study with the autopsied material ($n = 50$), that was adjusted for age to the current research group the difference is relatively small (4.1% vs. 8.6%) and thus should not affect the results [7]. No anatomy (shape and size) of the left atrial appendage was assessed and no left atrial size was measured. Due to a relatively small number of patients with the TIA the results of the analysis of the association between the presence of the LSSP and TIA may be faulty. Finally, there was the lack of electrophysiological data that could establish a possible direct association between the analyzed structures and ectopic electrical activity.

The LSSP, accessory appendages, and diverticula are highly prevalent anatomic structures within the left atrium and are easily identifiable by MSCT. The presence of LSSP is associated with increased risk for AF and TIA. The clinical assessment of these structures, especially the LSSP, should not be neglected, particularly in patients with atrial fibrillation and cerebrovascular accidents.

Conflict of interest statement

All authors have no potential conflicts of interest.

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