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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  $69.4 \pm 13.1$  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.

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### 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, transeptal 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  $69.4 \pm 13.1$  (range: 22–91) years, mean body mass index was  $26.3 \pm 4.5$  kg/m<sup>2</sup> and mean ejection fraction (EF) was  $51.6 \pm 17.5\%$ . 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  $2 \times 32 \times 0.6$  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  $512 \times 512$  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]:

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

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  $\pm$  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  $\chi^2$  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

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