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Influence of Cardiovascular Risk Factors on Prevalence of Left Atrial Accessory Appendages and Diverticula in Patients with Atrial Fibrillation

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Abstract

Background: *Left atrial accessory appendages (LAAA) and left atrial diverticula (LAD) may be caused by structural remodeling. The aim of our study is therefore to investigate the relation between the occurrence of LAAA/LAD, different types of atrial fibrillation (AF) and cardiovascular risk factors affecting the atrial structure including age, diabetes mellitus, hypertension, and hypercholesterolemia, body mass index (BMI) and sex. To our knowledge, the relation between the occurrence of LAAA and LAD and cardiovascular risk factors has not yet been studied.*

Methods: *Cardiac CT scans were obtained from patients with sinus rhythm (N=402, SR) and a history of AF (N=422, AF) for evaluation of either coronary artery disease or atrial anatomy prior to pulmonary vein isolation (PVI) and were screened for the presence of LAD and LAAA. Clinical characteristics including cardiovascular risk factors were retrieved from the electronic medical records and correlated with the presence of LAAA/LAD.*

Results: *In 91 (22.6%) SR patients, a total of 90 LAAA and 4 LAD were detected and in the AF group (N=74, 17.5%), 75 LAAA and 2 LAD. LAAA/LAD prevalence did not differ between SR and AF patients (P=.067) nor between patients with paroxysmal and persistent AF (P=0 .924) Also, there was no relation was detected between LAAA/LAD prevalence and cardiovascular risk factors (P > .05).*

Conclusion: *The prevalence of LAAA/LAD in a large patient cohort was not associated with clinical profiles including AF subtypes and cardiovascular risk factors affecting atrial structure. Hence, it is unlikely that LAAA/LAD play an important role in the pathophysiology of AF.*

Abbreviations: *A: Anterior, AF: Atrial Fibrillation, AO: Aorta, BMI: Body Mass Index, CT: Computed Tomography, L: Left, LA: Left Atrium, LAA: Left Atrial Appendage, LAAA: Left Atrial Accessory Appendage, LAD: Left Atrial Diverticula, LSPV: Left Superior Pulmonary Vein, LIPV: Left Inferior Pulmonary Vein, P: Posterior, R: Right, RSPV: Right Superior Pulmonary Vein, RIPV: Right Inferior Pulmonary Vein, SR: Sinus Rhythm.*

Keywords: Electrophysiology; Atrial Fibrillation; Pathophysiology; Left Atrial Accessory Appendages; Left atrial Diverticula; CT imaging

Introduction

Left atrial accessory appendages (LAAA) and left atrial diverticula (LAD) are frequent findings on cardiac computed tomography (CT) images obtained from patients with atrial fibrillation (AF) acquired prior to pulmonary vein isolation[1-2]. Diverticula are structures with an ostium and a sac like body, whereas LAAA are trabeculated structures with a distinct neck. LAD are commonly found at the superior part of the left atrium towards the right superior pulmonary vein (RSPV) [3-6]. It is generally assumed that both LAAA and LAD are acquired and caused by local weakening of the left atrial wall due to structural remodeling [6]. Prior studies have demonstrated that structural remodeling is associated with example: Age, BMI, Diabetes mellitus, Hypertension, Hypercholesterolemia and Sex. However it is unknown whether these cardiovascular risk factors are associated with the presence of LAAA or LAD. The aim of this study is therefore to investigate the relation between the occurrence of LAAA, LAD, different types of AF and patient characteristics, including cardiovascular risk factors.

Methods

Patient population

Patients were included in both the Maasstad Hospital and the Erasmus Medical Center. The AF group consisted of patients

with paroxysmal or persistent AF who were referred for pulmonary vein isolation. A cardiac CT scan was obtained prior to the ablation procedure as recommended in HRS guidelines [7]. The SR control group consisted of successive patients referred to the Maasstad Hospital for CT screening for detection of coronary artery disease.

Clinical characteristics, including cardiovascular risk factors: Age, BMI, diabetes mellitus: hemoglobin A1c (HbA1c) >6.5%, hypercholesterolemia: (LDL-C) ≥160 mg/dl and hypertension: systolic BP (SBP) ≥130 or diastolic BP (DBP) ≥80 mm Hg, and sexwere retrieved from the electronic medical records and related with the presence of LAAA/LAD. Patients with congenital heart disease and heart failure were excluded. This retrospective study was approved by the institutional medical ethical committee (MEC2015-673) and written informed consent was therefore not obliged.

CT Technique and Imaging Protocol Analysis

All patients underwent a non–contrast-enhanced calcium scan (dual-source 64-slice Somatom. Definition Flash, Siemens Healthineers, Forchheim, Germany) and received sublingual nitroglycerin before CT studies. If indicated (heart rate >65/min), beta-blockers were administered. Prospective electrocardiographically triggered axial scan mode was used, with an exposure window during diastole and/or systole depending on the heart rate. Tube current and voltage were selected semi-automatically based on body size. A test bolus acquisition was performed using 15 ml of contrast medium followed by a 40 ml saline chaser. For CT, a contrast bolus of 50 to 60 ml (depending on iodine concentration) was injected to achieve an iodine delivery rate of 2.2 g/s, followed by a 40-ml saline bolus chaser. Images were reconstructed with a medium-smooth kernel (B26, Bv40), a slice thickness of 0.5 mm and an increment of 0.3 mm. All CT images of LAAA and LAD were analyzed by two experienced investigators in reviewing cardiovascular CT images. Sac like structures located at sites originating from the pulmonary venous atrium were labelled as LAD, whereas trabeculated structures located at sites originating from the primitive atrium (like the left atrial appendage (LAA) arelabelled as a LAAA).

Figure 1 shows a typical example of a LAD located at the posterior wall. The location of LAAA and LAD was determined by the LA segmenting methodology [8]. As demonstrated in Figure 1, the LA is divided into an anterior-superior wall, posterior wall, septum, vestibulum and lateral wall. Medical data (electrocardiograms (ECG), history of AF, classification of AF, Age, BMI, Diabetes mellitus, Hypercholesterolemia, Hypertension, Sex) were collected from digital patient records.

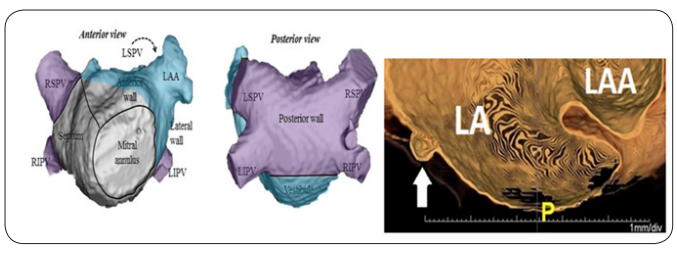

Figure 1: Atrial origin and diverticulum example

Left Panel: Schematic anterior and posterior view of the left atrium. The LAA has its origin in the primitive atrium (blue). Structures sharing the same origin as the LAA should only be labeled as LAAA. Structures located in the purple area, which have a pulmonary venous origin, can therefore not be labeled as LAAA. Right panel: cardiac Computed Tomography image showing a typical example of a left atrial cyst shaped diverticulum (white arrow) at the posterior wall., LA: Left Atrium, LAA: Left Atrial Appendage, LAAA: Left Atrial Accessory Appendage, LSPV: Left Superior Pulmonary Vein, LIPV: Left Inferior Pulmonary Vein, P: Posterior, RSPV: Right Superior Pulmonary Vein, RIPV: Right Inferior Pulmonary Vein.

Statistical analysis

All data were tested for normality. Normally distributed data is expressed as mean ± standard deviation, whereas skewed data is depicted as median (minimum-maximum). Dichotomous variables were analyzed using Pearson's Chi squared test and the Mann Whitney rank test was used to compare means for not equally distributed continuous variables. Associations between cardiovascular variables and the prevalence of LAAA/LAD were tested using a multivariate binary logistic regression. A P-value < .05 was considered statistically significant. Tests were performed by SPSS 24.

Results

Study Population

The study population consisted of 422 AF patients (290 male, age: 65±9 years) and 402 SR patients (163 male, age 54±10 years). Within the AF group, 329 patients had episodes of paroxysmal AF and 93 had persistent AF. Baseline characteristics of both groups are summarized in Table 1.

Prevalence of LAAA and LAD

In the SR group, the majority of the patients (N=311, 77.4%) had no LAAA or LAD. A total of 90 LAAA and 4 LAD were found in the remaining 91 (22.6%) patients, of which 21.9 % had either one LAAA or LAD only 1 patient had two LAD.

Similar to the SR control group, in most patients (N=348, 82.5%) of the AF group, no LAAA or LAD were detected. LAAA or LAD were found in 74 (17.5%) AF patients (LAAA: N=75, LAD: N=2), including 58 (17.6%) patients with paroxysmal AF and 16 patients with persistent AF (17.2%). Thus, no significant difference in the presence of LAAA or LAD between the SR and AF group (P=.067) was detected. Also, within the AF group, the prevalence of LAAA and LAD in patients with paroxysmal and persistent AF was similar (P=0 .924) (table 1).

	AF	SR	P value
No. of patients (N)	422 (329 PAF, 93 Persistent)	402	
Age, years	65 ± 9.0	54 ±10.2	p=0.740
Male gender (%)	290 (68.7)	163 (40.5)	p=0.000
Diabetes (%)	31 (7.3)	31 (7.7)	p=0.129
Hypertension (%)	186 (44)	146 (36.3)	p=0.279

Hypercholesterolemia (%)	52 (12.3)	21 (5.2)	p=0.751
BMI	27 (17-46)	28(15-47)	p=0.002
BMI N.A.	32	4	
Patients with LAAA/LAD (N,%)	74 (18) PAF: (58 (18) Persistent: 16 (17)	91 (23)	
Male patients with LAAA/LAD (N, %)	51 (69) PAF: (38 (66) Persistent: 13 (81)	39 (43)	
Total No. of LAAA/LAD	77 (LAAA:75, LAD:2) PAF: (58 (17.6)(LAD:1) Persistent: 16 (17.2)(LAD:1)	94 (LAAA: 90, LAD:4)	
Total No. of LAAA/LAD in male patients (N,%)	53 (69) PAF: (40 (67) Persistent: 13 (77)	39 (41)	

Table: Baseline Characteristics

AF = Atrial Fibrillation, BMI = Body Mass Index, SR = Sinus Rhythm, LAAA= Left Atrial Accessory Appendages, LAD = Left Atrial Diverticulum, AF = Atrial Fibrillation, SR = Sinus Rhythm.

Distribution of left atrial diverticula and left atrial accessory appendages

In the SR group, LAAA were located at the antero-superior wall (N=90, 95.74%) and the remaining LAD were found at either the pulmonary venous area (N=2, 2.13%) and left atrial vestibulum (N=2, 2.13%). In the AF group, LAAA were also located at the antero-superior wall (N=75, 97.4%) and only two LAD were found (2.6%) at the pulmonary venous area. Thus, the anatomical distribution of LAAA and LAD did not differ between the AF and SR control group (P=0.127). In patients with paroxysmal AF, 58 LAAA (96.6%) were located at the left antero-superior wall and 2 LAD (3.4%) at the pulmonary venous area. In the persistent AF group, only 17 LAAA were detected at the antero- superior wall.

Relation between cardiovascular risk factors and prevalence of left atrial diverticula

In patients with SR or AF, there was no relation between LAAA or LAD prevalence and cardiovascular risk factors including age (P= 0.931), BMI (P=0.670), diabetes mellitus (P= 0.641), hypertension (P= 0.932), hypercholesterolemia (P= 0.465) and sex (P= 0.901), and likewise for patients with either paroxysmal or persistent AF, cardiovascular risk factors; age (P=0.482), BMI (P=0.585), diabetes mellitus (P=0.831), hypertension, (P=0.721), hypercholesterolemia (P=0.464), and sex (P= 0.968) did not relate with the prevalence of LAD. Within the SR group, patients with or without LAAA/LAD were compared on the prevalence of prior strokes or transient ischemic attacks. However, no significant differences were detected (P= 0.087).

Discussion

Our study demonstrated in a large cohort of patients that LAAA or LAD are present in a minority of patients with AF. There was no correlation between the prevalence of LAAA/LAD and the presence of AF episodes. In addition, no differences in LAAA or LAD prevalence between patients with paroxysmal and persistent AF were detected, nor could we confirm a relation between LAAA/LAD prevalence and cardiovascular risk factors. Elimination of AF by ablative therapy targeting a LAAA has previously been reported in a 65-years old patient with a history of hypertension who had AF episodes triggered by ectopic activity originating from a LAAA. After ablative therapy, the patient remained free of AF episodes [9].

Investigated the presence of LAAA and LAD in 200 patients undergoing a pulmonary vein isolation procedure for paroxysmal atrial fibrillation (PAF) and in another 200 patients with coronary artery disease who had no AF [10]. They found no differences in LAAA or LAD prevalence between the 2 groups (AF group: 23.5% versus control group: 20.5%, P> .05) similar findings were reported [3]. Who compared the prevalence of LAAA or LAD in 214 patients referred for ablative therapy of PAF to a SR control group with coronary disease, and also found no differences (AF versus SR group: 77 (36%) versus 70 (32.7%) (P= .551). We also investigated the relation between sex and the prevalence of LAAA or LAD.

In both the SR as well as in the AF group, we did not find a difference in prevalence of LAAA or LAD between male and female patients. These results are comparable with observations in larger study populations [2-12].

Only two studies did observe sex differences in LAD prevalence. Found in patients who underwent cardiac CT for evaluation of coronary artery disease, cardiac masses, ARVC and prior to pulmonary vein isolation procedures, more LAD in males (27.3% vs 14.1%). They detected a sex difference in LAD prevalence, but only in their AF group; M more often had LAD (40.1% vs 27.8%, P=.03). From their data, we could not find a plausible explanation for this difference in outcome [5].

Within our SR group we also found no relation between the presence of LAAA/LAD and history of strokes and transient ischemic attacks (P= .087). These results are in line with a prior study [11]. Who found LAD in 74.4% of 212 patients. They also found no significant difference in the prevalence of cerebrovascular events between patients with or without LAD. The results of these large population studies support our study outcomes and in addition, there were also no differences in LAAA or LAD prevalences between patients with paroxysmal and persistent AF. Hence, it seems unlikely that LAAA or LAD play an important role in the pathophysiology of AF.

Conclusion

LAD and LAAA are common findings on cardiac CT scans, however, there was no correlation between the prevalence of LAAA or LAD and the presence of AF episodes. We also did not find a difference in prevalence of LAAA or LAD between patients with paroxysmal and persistent AF, or a difference in the prevalence of strokes or transient ischemic attacks in the SR group between patients with or without LAAA / LAD.

Despite the fact that cardiovascular risk factorsincluding age, BMI, diabetes mellitus, hypertension and hypercholesterolemia may affect atrial structure, and thereby potentially weaken the atrial wall giving rise to LAAA or LAD, we found no impact of these factors on the prevalence of LAAA or LAD. Neither did we find a difference in LAD or LAAA prevalence between male and female patients. A possible explanation could be that LAAA or LAD are more 'congenital' in nature than acquired.

Study Limitations

Features of theinner surface can be also be used to discriminate LAAA from LAD. However, this requires contrast and the timing of contrast administration may differ between patients who had a cardiac CT scan for evaluation of coronary artery disease or prior to pulmonary vein isolation. This difference in timing of contrast administration may hamper evaluation of the inner surface.

Author contributions

Danny Veen mostly contributed to the data collection, complete data analysis and interpretation of the CT scans and drafting the article, Tobias A. Bruning was involved in the analysis and interpretation of the CT scans, and Natasja. M.S. de Groot contributed to the critical revision and approval of the article.

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