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Association of the left common ostium with clinical outcome after pulmonary vein isolation in atrial fibrillation



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ABSTRACT

Introduction: Electrical pulmonary vein isolation (PVI) is used for the invasive treatment of atrial fibrillation (AF). However, despite the procedure's technical evolution, the rate of AF recurrence due to electrical reconnection of the PVs is high. The aims of this study was to assess the influence of left common pulmonary venous ostium (LCO) on clinical outcomes following PVI.

Methods: Retrospective cohort of 254 patients who underwent the first procedure of PVI from the years 2013–2018 was assessed. Patients with persistent AF of long duration and extra-pulmonary focus associated with triggers for arrhythmia were excluded. Patients were stratified into two groups according to the presence of a LCO and received follow up for atrial tachyarrhythmia-free survival. The mean follow-up period was 28 ± 1.73 months.

Results: The majority were men (68.5%), with a mean age of 54 ± 12 years. With respect to the atrial anatomy, LCO occurred in 23.6% of cases after pulmonary venous angiotomography. The arrhythmia-free survival rate was 79.5% in the follow-up period. The Cox regression model was utilized and the adjusted hazard ratio for LCO was 0.36 (95% CI 0.15–0.87; $p = 0.02$) in terms of age, body mass index, left atrium diameter, bi-directional blocking of the cavotricuspid isthmus, persistent AF, left ventricular ejection fraction adjusted model.

Conclusion: Anatomic abnormality with the presence of the LCO is present in a quarter of patients undergoing AF ablation, which is associated with a lower rate of arrhythmia recurrence in our population.

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1. Introduction

Atrial fibrillation (AF) is the most common sustained form of arrhythmia. AF has a strong impact on the quality of life and increases the morbidity and mortality of the patients affected [1]. Invasive treatment of AF consists of electrical pulmonary vein isolation (PVI). The pulmonary veins (PVs) contain ectopic foci and

anisotropic conduction zones, which are responsible for starting and maintaining AF [2]. Despite the continuous evolution of the ablation technique, the recurrence rate is 20%–30% in paroxysmal AF and is strongly associated with electrical reconnection between the left atrium (LA) and the PVs [3].

The identification of factors associated with post PVI prognosis is of fundamental importance, and pulmonary venous anatomical abnormality is one of the topics studied. With the exception of accessory pulmonary veins, the left common pulmonary venous ostium (LCO) (Fig. 1) is the most common anatomic abnormality, and may affect 37% of the population [4–7]. Anatomically the LCO lacks the pulmonary carina that separates the ostia of the upper and lower PV, that is, fusion of the 2 left PVs in the LCO [8]. The studies

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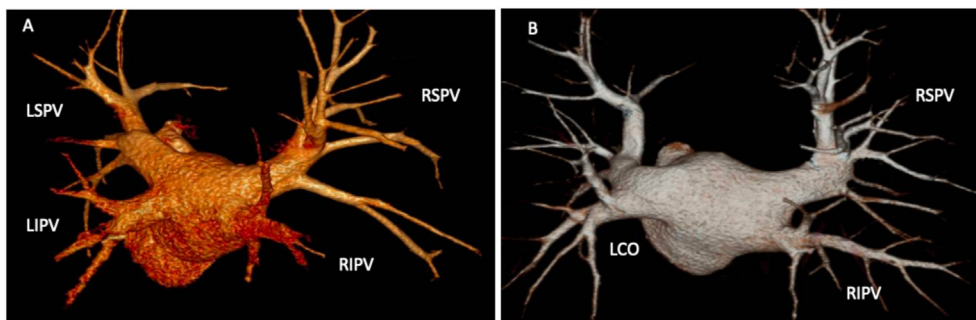


Fig. 1. (A) An example of a normal left venous anatomy. (B) An example of a left common ostium. Left pulmonary veins coalesce at least 5 mm before insertion into the left atrium. (A, B) Show different projections of the posterior wall of the left atrium after performing angiotomography with three-dimensional reconstruction.

LSPV: left superior vein pulmonary.
LIPV: left inferior vein pulmonary.
RSPV: right superior vein pulmonary.
RIPV: right inferior vein pulmonary.
LCO: left common ostium.

on the effects of the presence of a LCO on the prognosis following AF ablation are conflicting in the literature [3,6,9–11].

The aims of this study were to assess the influence of this abnormality on clinical outcomes following PVI.

2. Methods

2.1. Sample

A total of 324 patients underwent ablation due to symptomatic AF from July 2013 to December 2018. Of this sample, after the application of the exclusion criteria were included 254 patients retrospectively with a minimum follow-up period of 6 months, extracted from the database of the *Instituto de Ritmologia Cardíaca (IRC)*, Brazil.

All procedures were performed by the IRC in four Brazilian hospital centers. Patients with paroxysmal AF (PAF), persistent AF (PeAF) with less than 1 year of evolution were included [12]. A total of 69 patients with long-term persistent AF and patients with non-pulmonary vein foci were excluded from follow-up. Data obtained included clinical characteristics, electrophysiological measurements during AF ablation, imaging examinations and clinical follow-up measurements.

2.2. Definition of venous anatomy

Patients underwent pulmonary venous angiotomography using a 160-channel multi-slice computed tomography system before AF ablation. The presence of an LCO was defined when the superior and inferior PV joined ≥ 5 mm before entering the left atrium resulting in a single atriopulmonary venous junction [5,13].

2.3. PVI by catheter ablation

The exclusion criteria were the presence of intracavitary thrombus on transesophageal echocardiography performed on the day of AF ablation. The patients underwent ablation under therapeutic levels of oral anticoagulant therapy. The patients taking vitamin K antagonists had an international normalized ratio of 2.0–2.5. The direct-acting oral anticoagulant rivaroxaban was taken on the day before ablation, although this was at an interval longer than 12 h from the predicted start of the procedure. Apixaban or dabigatran were not used in the morning before ablation. All patients were subjected to general anesthesia in association with an esophageal thermometer at the level of the LA. After venous

punctures were performed, a decapolar catheter was placed into the coronary sinus and an irrigated ablation catheter in the His bundle region for fluoroscopic guidance for the *trans*-septal punctures. The double *trans*-septal punctures were performed using a SL-1 sheath and a BRK-1 needle (*St. Jude Medical, St Paul, USA*) followed by therapeutic heparinization. A circular duodecapolar catheter was used for mapping the LA, and an irrigated-tip ablation catheter was placed into the LA. Atrial mapping was performed by three-dimensional *EnSite mapping* (*St. Jude Medical, St. Paul, USA*). Radiofrequency (RF) was applied circumferentially around in the ipsilateral PVs until electrical isolation was achieved (defined by entrance and exit block in each vein 20 min after the last RF application and after bolus infusion with up to 18 mg of adenosine) and investigation of extra-pulmonary focus occurred with isoproterenol infusion starting at 3 mg and incrementing to 6 mg, 12 mg, and 20 mg–30 mg on the basis of the heart rate response. In patients with typical atrial flutter, ablation was performed with the objective being to achieve bi-directional blocking of the cavotricuspid isthmus.

In the immediate postoperative period, anticoagulant therapy regimens were initiated 6 h after the withdrawal of the introducer sheaths and maintained for, at least, 60 days. All patients were maintained with sucralfate, a proton pump inhibitor, for 30 days, and an antiarrhythmic drug (previously used in the preoperative period) for 90 days.

2.4. Postoperative follow-up and definition of recurrence

The follow-up included regular visits at 1 month, 3 months and 6 months, followed by subsequent annual visits. The patients underwent minimal investigation with 24-h Holter in the chronology of the consultations, that means all patients performed at least 3 monitoring (1, 3 and 6 months). All patients were instructed to contact the electrophysiology team when symptoms occur, at which time additional electrocardiographic and Holter examinations were provided. There was no loss of patients until the 6-month follow-up. Recurrence was defined as the presence of atrial tachycardia (AT) and/or AF with duration of at least 30 s after the blanking period of 3 months.

2.5. Statistical analysis

The data were stored and analyzed using the Statistical Package for the Social Sciences (SPSS) software version 22.0 (*SPSS Inc., Chicago, IL, USA*). Continuous variables are expressed as the

means ± standard deviation or medians and interquartile ranges, according to the normality or asymmetry of the distribution, respectively, with categorical variables being expressed as percentages. Kaplan–Meier analysis was used to assess the cumulative percent of arrhythmia events (sustained AT/AF) between LCO and non-LCO groups by follow-up time, and then the log-rank test was used to assess the difference between the two groups. Multivariate Cox regression analysis was utilized to estimate the hazard ratio (HR) and 95% CI for the effects of LCO on risk of an arrhythmic event.

Kaplan–Meier survival curves were compared using the log-rank test and Hazard ratios were determined by Cox regression analysis. A p value < 0.05 in 2-tailed tests was considered to be statistically significant.

2.6. Ethics

The study was approved by the local Institutional Review Board (IRB) and was carried out in concordance with the Declaration of Helsinki. All patients signed an informed consent form prior to study inclusion.

3. Results

3.1. Clinical characteristics

A total of 254 patients underwent electrical isolation of the PVs (Fig. 2), with the majority being men (68.5%), with a mean age of 54 ± 12 years. With regard to atrial anatomy, the LCO occurred in 23.6% of cases. One patient with right common ostium was not included in the study.

Table 1 presents the baseline demographic, clinical characteristics, clinical scores and echocardiographic parameters for the populations grouped according to the respective atrial anatomy (LCO or non-LCO). Variables such age (53 ± 12 vs. 55 ± 11) and gender (61.7% male vs. 70.6% male) showed no differences (LCO vs. non-LCO groups). No statistically significant difference was found in the prevalence of PAF (28.3% vs. 32.5%), hypertension (40% vs. 52.1%), body mass index (28 ± 5 vs. 29 ± 4), coronary artery disease

Table 1
Characteristics of the sample and univariate analysis (n = 254).

Variable	LCO (n = 60)	Non-LCO (n = 194)	P-value
Age, years	53 ± 12	55 ± 11	0.22
Male gender, n (%)	37 (61.7)	137 (70.6)	0.2
Persistent AF, n (%)	17 (28.3)	63 (32.5)	0.40
Comorbidities			
Hypertension, n (%)	24 (40)	101 (52.1)	0.10
BMI	28 ± 5	29 ± 4	0.09
Diabetes Mellitus, n (%)	3 (5)	20 (10.3)	0.31
Coronary Artery Disease, n (%)	2 (3.3)	11 (5.7)	0.73
Stroke, n (%)	2 (3.3)	4 (2.1)	0.62
Heart Failure, n (%)	3 (5)	20 (10.3)	0.3
CHA ₂ DS ₂ VASc score	1.0 ± 0.92	1.3 ± 1.2	0.22
HAS-BLED score	0.15 ± 0.4	0.25 ± 0.53	0.17
Modified EHRA score	2.6 ± 0.7	2.6 ± 0.68	0.51
LVEF	64 ± 6	63 ± 9	0.63
LA diameter (mm)	41 ± 5	41 ± 5	0.44

Data are expressed as mean ± standard deviation or number (%). LCO: left common ostium; AF: atrial fibrillation; BMI: body mass index; LVEF (%): left ventricle ejection fraction; LA: left atrium. Student's t-test and χ^2 for independent samples. P-value indicates a statistically significant difference at the level of 5%.

(3.3% vs. 5.7%), stroke (3.3% vs. 2.1%), heart failure (5% vs. 10.3%) between the LCO vs. non-LCO groups. No difference was noted for echocardiographic parameters (LVEF and LA diameter). Clinical scores (CHA₂DS₂VASc, HASBLED, Modified EHRA) were similar among the samples.

3.2. Procedure

Table 2 shows the characteristics of ablation (complete isolations of all pulmonary veins, need for blocking of the cavo-tricuspid isthmus and durations of procedures) between groups. There was no difference between LCO and non-LCO.

The following complications were observed: pericardial complications (two patients treated with pericardiocentesis due to echocardiographic signs of cardiac reperfusion), femoral vascular complications (two patients with pseudo aneurysm and one patient of fistula), and coronary air embolization (one patient). There were no significant differences between the two groups.

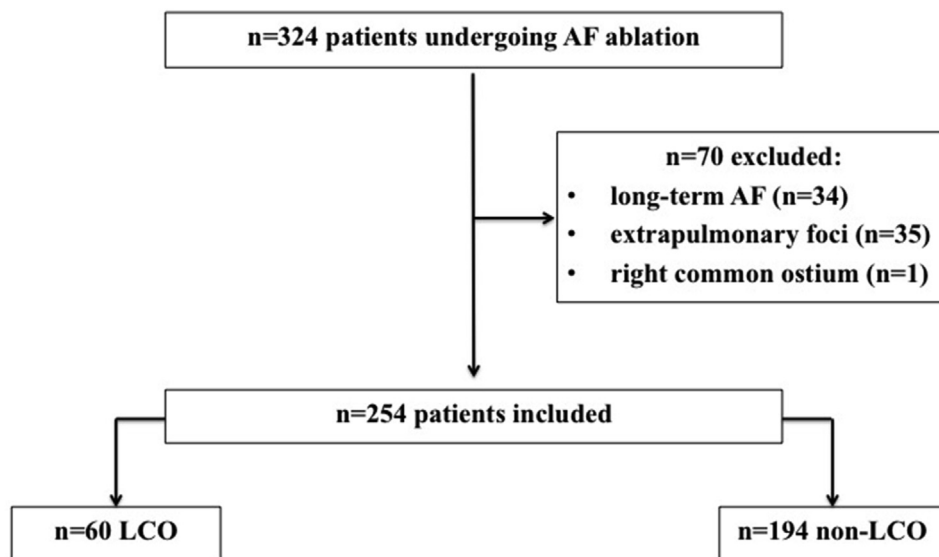


Fig. 2. Flowchart study: patients undergoing ablation of atrial fibrillation categorized of the exclusion criteria and presence of LCO. AF: atrial fibrillation. LCO: left common ostium.

Table 2
Characteristics of the sample and univariate analysis (n = 254).

Variable	LCO (n = 60)	Non-LCO (n = 194)	P-value
Complete isolation of all pulmonary veins, n (%)	58 (96.7)	189 (97.4)	0.67
Bi-directional blocking of the cavotricuspid isthmus, n (%)	6 (10)	26 (13.4)	0.32
Duration of the procedure (minutes)	147 ± 50	141 ± 42	0.87

Data are expressed as mean ± standard deviation or number (%). P-value indicates a statistically significant difference at the level of 5%.

3.3. Long-term follow-up

At a median follow-up of 28 ± 1.73 months, there were no significant differences between the two groups (P = 0.53), 79.5% of the cases were free from recurrent sustained atrial arrhythmias. The results of the Kaplan-Meier analysis indicated that the probability of recurrence in the presence of the LCO was significantly lower (Log rank χ^2 5.51 p = 0.019) than that in the non-LCO group (Fig. 3). The rates of recurrence in patients with and without LCO were 10% and 23.7% respectively (HR, 0.38; 95% CI, 0.16–0.89; p = 0.026). In patients with LCO there was no difference in arrhythmia recurrence between paroxysm AF and persistent AF (p = 0.13).

The Cox regression model was utilized to assess the effects of the presence of a LCO on arrhythmia recurrence. The adjusted HR for LCO was 0.36 (95% CI 0.15–0.87; p = 0.02) in terms of age, body mass index, LA diameter, bi-directional blocking of the cavotricuspid isthmus, persistent AF, LVEF adjusted model. Persistent AF was an independent predictor of arrhythmia recurrence (Table 3).

4. Discussion

The main clinical finding of this retrospective study is that the anatomy of the LCO vein was associated with that of atrial

tachyarrhythmia-free survival independently and controlled by that main variables associates with clinical recurrence. The clinical similarities between the two groups studied at baseline, minimizing a possible selection bias, collaborated with the results. The rational of the findings is derived from results published by Schwartzman D. et al., in which it was demonstrated that in patients with LCO, the majority of arrhythmias triggers have their origins in the anatomic abnormality [14]. In addition, the rate of complications was within the expected range for AF ablation, while not comprising procedure safety [12,15,16].

Some results are of fundamental importance in the discussion of this study; one of them being the anatomic definition of LCO and its prevalence in patients with AF that underwent ablation. We utilized the definition applied to previous studies, that is the confluence of the superior and inferior branches of the left vein at least 5 mm from the outlet in the LA [5,13]. We used angiotomography with three-dimensional reconstruction to study the anatomic abnormality because it is considered, together with resonance, as methods of choice for this purpose [17]. In our cohort it was found in 23.6%, which is consistent with the results of other studies [3,6,9–11].

However, the clinical results after AF ablation contradicted those of previous studies. Den Uijl et al. demonstrated that the presence of

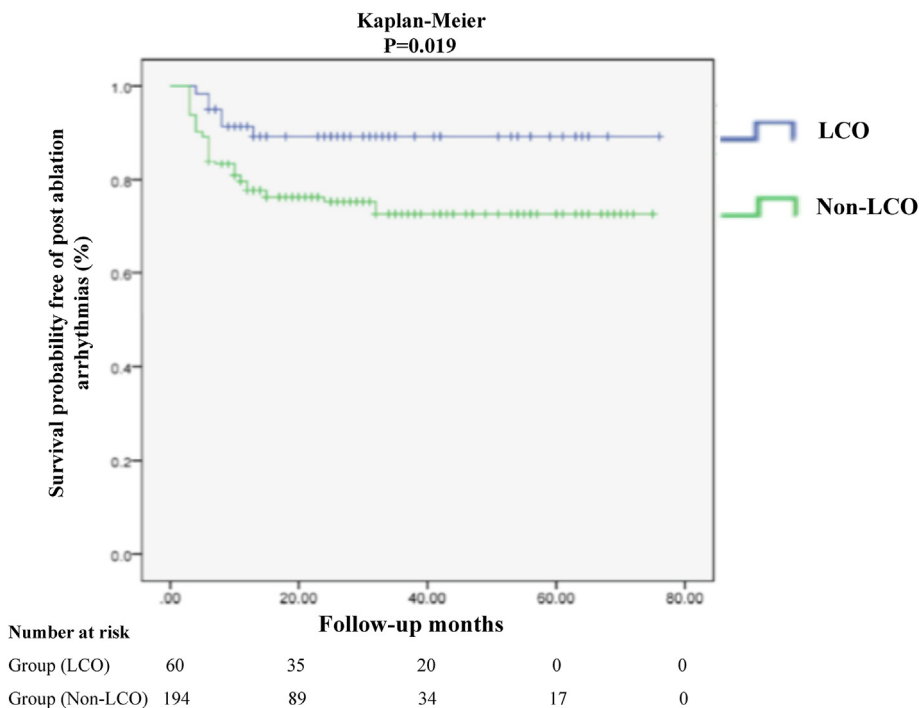


Fig. 3. Freedom from any AT/AF recurrence after the blanking period according to variant PV anatomy (LCO or non-LCO).

AT: atrial tachycardia.
AF: atrial fibrillation.
LCO: left common ostium.
LCO: (blue).
Non-LCO: (green).

Table 3
Multivariate analysis demonstrating the freedom from recurrent AT and/or AF with predictor variables.

Variable	HR	95% CI	P-value
Presence of LCO	0.36	0.15–0.87	0.02
Age, years	0.98	0.96–1.01	0.25
BMI	1.05	0.99–1.11	0.06
Bi-directional blocking of the cavotricuspid isthmus	1.38	0.67–2.81	0.37
LA diameter (mm)	0.98	0.93–1.03	0.58
Persistent AF	1.91	1.01–3.61	0.04
LVEF	1.00	0.97–1.03	0.69

AT: atrial tachycardia; AF: atrial fibrillation; LCO: left common ostium; BMI: body mass index; LA: left atrium; LVEF (%): left ventricle ejection fraction.

a normal right venous anatomy conferred a substantial risk of AF recurrence after ablation (OR, 6.71; 95% CI, 1.73–26.31). Moreover, these authors found that the anatomy of the left PVs did not affect the clinical outcomes ($p = 0.14$) [11].

Hof et al. described the influence of the increase in the LA volume on relapse after AF ablation and observed that the anatomy of the PVs (common trunk and accessory PV) did not affect the post intervention clinical follow-up [9]. Whereby, it is important to emphasize three points: the lower prevalence of a LCO in this study (16%) compared with other studies, persistent AF was present in 45% of patients and these patients received an ablation strategy extending beyond PVI, which may explain the results obtained [9].

McLellan et al. assessed 102 patients and found that 37% presented LCO and had a success rate in the clinical follow-up of 87% compared with 66% in patients with two left PVs, after application of Cox regression multivariate models ($p = 0.03$) [6].

Sohn et al. assessed the influence of PV anatomy in patients undergoing RF ablation with remote magnetic navigation and found that the rates of recurrence were 32% in patients with normal PV anatomy, 41% in patients with a LCO, and 25% in patients with a RCO. In the multivariate analysis, the authors combined patients with LCO and RCO and observed that the probability of relapse in the presence of abnormalities in venous anatomy was 72% [3].

In summary, previous studies with radiofrequency energy found 3 different results regarding the influence of LCO in the clinical follow-up after PVI. One study reported that the variability was associated with worse outcomes [3]; two studies found that venous anatomy variability did not significantly affect the outcomes [9,11]; while one study evidenced a positive correlation between the presence of a LCO and better outcomes [6]. It is noteworthy that the heterogeneity between the studies were similar in terms of the selection of samples and techniques of ablation. Regarding the sample selection criteria, i.e. the variation of the percentage of long persistent AF, could generate a variability of extra-pulmonary focus that can affect the success of the procedure. While also being similar in terms of the ablation strategy extending beyond PVI, which may explain cicatricial arrhythmias in the clinical follow-up [8].

With respect to the use with alternate ablation technologies such as cryoablation using the first-generation balloon, Kubala et al. found that the presence of a LCO was a predictor of higher recurrence in clinical follow-up after using a cryoablation balloon catheter. One possible explanation is the difficulty involved in coupling the balloon catheter to the extensive surface of the venous trunk, producing an ineffective myocardial injury [10]. The STOP-AF, using a second-generation cryoballoon, demonstrated the absence of a significant difference in acute, or long-term outcomes, in patients with or without a LCO. In one patient (2.8%), focal ablation was required to obtain the electrical isolation of the LCO [18]. Heeger C–H et al. showed that patients with LCO had a success rate in the clinical follow-up similar to the control group (64% vs. 66% $P = 0.82$) [19].

With respect to the LCO, we hypothesize that:

- It is possible that LCO is a risk factor for developing PV dependent AF. If confirmed, PVI may be more effective in this population;
- The left ridge (anterior-superior left region) is a region where the catheter has reduced contact with the myocardial tissue and consequently associated with gap formation as demonstrated by Neuzil P. et al. and Makimoto et al. [20,21]. The presences of LCO may possibly optimize the contact in the region, and justify a better outcome in the LCO group;
- The absence of the influence of carina in the PVI can also justify the results found in this study.
- Istratoaie et al. suggest a hypothesis that fewer pulmonary veins would be easier to isolate, so the LCO provides a better prognosis differently from the presence of accessory vein [7].
- Barrio-Lopez et al. demonstrated that the presence of epicardial connections reduces the acute and chronic success of PVI. Likewise, they reported that the presence of LCO has a significant inverse relationship with the detection of epicardial connections. These results may help explain the protection that LCO provides in clinical follow-up after PVI [22].

In this context, our results corroborate with those of McLellan et al., who suggested that the presence of the LCO conferred a better prognosis in patients undergoing AF ablation [6]. In these 2 studies we have uniformity as for the absence of inclusion of long-persistent AF and applications of RF in other regions of the LA, which may be a possible justification for the contradictory findings of previous studies.

The major criticism of the PVI is the rate of clinical recurrence, despite the procedure's technical evolution [3]. One way to minimize clinical recurrence would be to determine sub-groups of patients with the best response to the procedure. In this context, the findings of our study may be applied in clinical practice, that is, the presence of LCO may be a factor to consider in terms of predicting success rates of AF ablation. Regarding the ablation strategy, antral isolation of pulmonary veins in patients with LCO remains the standard technique.

4.1. Study limitations

One of the limitations of our study was that we did not use a catheter with a contact sensor due to a lack of availability, due to the health insurance for study subjects, considering that the myocardium-catheter interaction is fundamental for the clinical outcome of the procedure. However, both groups did not use this technology, whereby we can affirm that the association found was due to an anatomical influence and not by the catheter type. Also, the small sample size and small number of events, but with the largest sample in relation to those mentioned in the discussion in radiofrequency ablation. The follow-up was limited to 24h-Holter,

which might overestimate the clinical success rate in both groups. Randomization is the best way to eliminate bias in a study. Although, we believe that it would not be possible to conduct a study with such a design, in a study such as ours because having or not having a LCO would require the same treatment.

5. Conclusion

The variability in pulmonary venous drainage in the form of LCO is found in a significant percentage of patients submitted to PVI for an AF. In patients undergoing radiofrequency ablation, LCO is associated with postoperative success of PVI. The presence of a LCO may be a factor to consider in terms of predicting success rates of AF ablation.

Declaration of competing interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Informed consent

Informed consent form was obtained from all individual subjects included in the study.

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Contributors

R.M.R. and T.L.L.L. participated in the study design. R.M.R. and T.L.L.L. performed the statistical analyses. All authors contributed to the interpretation of results, drafted the manuscript and approved the final manuscript.

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