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Impact of the left common ostium following pulmonary vein isolation in AF: Systematic review and meta-analysis

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Abstract

Purpose: Pulmonary vein isolation (PVI) through catheter ablation is the basis for the treatment of atrial fibrillation (AF). The left common ostium (LCO) is a high prevalence anatomical variation and has conflicting results in the effects on the prognosis following ablation. We undertook a systematic review and meta-analysis of studies that compared the arrhythmia recurrence rate after radiofrequency ablation or cryoablation balloon between patients with normal pattern pulmonary vein and patients with LCO.

Methods and Results: Results were pooled using a fixed or random effect, at the discretion of heterogeneity (>25%), in addition, we associated subgroup analysis in these cases and when clinically indicated. Fourteen non-randomized studies totaling 3278 patients were included. In analyses using the two energies all patients: OR 1.01 (95% CI 0.84–1.23; $P = .90$, $I^2 = 67\%$) and excluding patients with any type of persistent AF (PeAF) and those submitted to linear atrial lesion (LAL) OR 0.80 (95% CI 0.52–1.22; $P = .30$, $I^2 = 71\%$). Using CRYO: all patients OR 1.34 (95% CI 1.03–1.74; $P = .03$, $I^2 = 0\%$). Using RF: all patients—OR 0.55 (95% CI 0.32–0.95; $P = .03$, $I^2 = 49\%$); excluding studies with long duration PeAF and the performance of LAL concomitant—OR 0.45 (95% CI 0.23–0.91; $P = .03$, $I^2 = 44\%$).

Conclusion: The results suggest a better prognosis in patients with LCO, submitted to PVI without additional LAL under RF energy in paroxysmal AF and short-duration PeAF. In patients undergoing CRYO, the presence of LCO suggests a worse prognosis.

KEYWORDS
arrhythmia, atrial fibrillation, meta-analysis, pulmonary vein isolation, systematic review

1 | INTRODUCTION

The extrasystoles of the pulmonary veins (PV) are the most significant trigger of atrial fibrillation (AF), and PV isolation through catheter ablation is the basis for the treatment of symptomatic AF and cases that are refractory to drug therapy.[1] The complete isolation of the veins in relation to the atrium is the desired outcome of the ablation and this can be achieved through radiofrequency energy (RF) (point-to-point or by linear lesions surrounding the veins under three-dimensional mapping) or by insertion of a cryoablation balloon (CRYO), with similar results experienced with the two techniques.[1] Despite the continuous evolution of ablation techniques, recurrence still reaches 20%–30% in paroxysmal cases and is strongly associated with electrical reconnection between the left atrium (LA) and the PVs.[2]

The identification of factors related to the post-PVI prognosis is of fundamental clinical importance and a variation in pulmonary venous anatomy is one of the topics studied. With the exception of the accessory PVs, the left common ostium (LCO) is the most common abnormality and can affect 37% of the population.[3] There are conflicting results in the literature concerning the effects of the presence of the LCO on the prognosis following AF ablation.[2–19]

Comparisons of the effectiveness of the two ablation modalities (RF and CRYO) among patients with the LCO have already been published, however, a meta-analysis has the potential to optimize the statistical power and precision of the respective analyses.[15,17] Therefore, we conducted a systematic review and meta-analysis of studies that determined the pulmonary venous anatomy in patients undergoing AF ablation. We specifically seek to assess the evolution (arrhythmia recurrence rate) of LCO patients compared to non-LCO patients, in the clinical follow-up, post-AF ablation.

2 | METHODS

2.1 | Research strategy

The study was registered with *PROSPERO* (International Prospective Register of Systematic Reviews)—CRD42020199382 and was conducted according to the *MOOSE* guidelines for systematic review and meta-analysis of observational studies. The Medline, Embase, and Lilacs databases were used, using the search system in accordance with the guidelines according to PICOS (Population, Intervention, Comparison, Outcomes, and Study design), for studies included by July 2020. The following keywords were used in the methodology—Table 1.

The bibliographic references of the review articles and that of the observational studies included were analyzed in order to detect publications that may be relevant.

2.2 | Study selection

Two independent reviewers (RMR and TLS) performed the searches and subsequently the selection of the appropriate references, based on the quality of the publication. In cases where there was disagreement, the evaluations, and resolutions of the pending issues were made by a third senior reviewer (TLLL). Our research was limited to human studies in peer-reviewed journals. There were no restrictions on language, sample number, or minimum clinical follow-up time included. As for studies originating from the same population, only those that presented the most complete pre-determined outcomes were included.

The studies had to meet the following inclusion criteria:

(a) Patients undergoing AF ablation with assessment of pulmonary venous anatomy, using cardiac angiotomography, cardiac resonance, three-dimensional transesophageal echocardiogram, venography, or three-dimensional reconstruction with electroanatomical mapping. It was necessary to provide sufficient detail to determine LCO and non-LCO patients.

(b) Description of the treatment energy source and the presence of lesions in addition to the PVI.

(c) Inclusion of clinical outcomes in patients with LCO and non-LCO as the primary or secondary outcome in the studies analyzed.

2.3 | Quality assessment, data extraction, and definitions

The quality of the studies was assessed using the Newcastle-Ottawa scale (NOS) and classified into three categories (high, satisfactory, and unsatisfactory)—Table 2. A spreadsheet was used to compile data on characteristics of the venous anatomy sample, technical data of the procedure, and the outcomes of interest. The main data of interest in the characteristics of the sample: percentage of AF subtypes (paroxysmal, persistent, and long-standing persistent AF), mean age, gender, and dimension of the LA. Regarding venous anatomy: acquisition method, definition used, and prevalence of

TABLE 1 search system in accordance with the guidelines according to PICOS

PICOS	Keywords	
Population	*("atrial fibrillation" OR "AF")*	AND
Intervention	*("ablation" OR "isolation" OR "pulmonary vein isolation" OR "catheter ablation")*	AND
Comparison	*("outcomes" OR "results" OR "success" OR "follow-up" OR "freedom")*	AND
Outcomes	*("pulmonary venous anatomy" OR "pulmonary veins anatomy" OR "pulmonary vein anatomy" OR "pulmonary veins anatomical" OR "pulmonary vein anatomical" OR "pulmonary venous anatomical" OR "pulmonary vein variations" OR "pulmonary veins variations" OR "pulmonary venous variations" OR "Pulmonary vein variants" OR "Pulmonary veins variants" OR "Pulmonary venous variants" OR "left atrial anatomical" OR "left atrial anatomy" OR "left common pulmonary vein" OR "Common left pulmonary vein" OR "Left common ostium" OR "pulmonary venous drainage" OR "pulmonary veins drainage" OR "pulmonary vein drainage" OR "pulmonary veins branching" OR "pulmonary vein branching" OR "pulmonary venous branching" OR "variants left atrial" OR "variants pulmonary vein" OR "variants pulmonary veins" OR "variants pulmonary venous" OR "variant pulmonary vein" OR "variant pulmonary veins" OR "variant pulmonary venous" OR "left common trunk").*	
Study design	All included	

TABLE 2 Summary of the quality of the studies included, assessed using the Newcastle-Ottawa scale (NOS)

Study	Selection	Comparibility	Outcome	Classification
McLellan et al., 2014[3]	4	1	5	High
Odozynski et al., 2010[4]	3	1	5	High
Anselmino et al., 2010[5]	3	1	5	High
Heeger et al., 2017[6]	3	1	5	High
Kubala et al., 2011[19]	3	1	5	High
Yorgun et al., 2019[7]	3	1	5	High
Beiert et al.,[8] 2018	2	1	5	Satisfactory
Shigeta et al., 2017[9]	3	1	5	High
Huang et al., 2018[10]	3	1	5	High
Khoueiry et al., 2016[15]	3	1	5	High
Wei et al, 2019[16]	3	1	5	High
Ronsoni et al., 2020[23]	4	1	5	High
Larsen et al., 2020[17]	4	1	5	High
Ströker et al., 2017[18]	3	1	5	High

Note: Selection: maximum of four points, Comparability: maximum of two points, Outcome: maximum of five points.

LCO. Procedure data: energy used, type of catheter, PVI confirmation method by blocking the entry and exit of the PV and additional test with adenosine, presence of additional lesion in addition to the PVI and total procedure time. The number of study outcomes was extracted precisely and directly, without needing to extract data indirectly through Kaplan–Meier curves. The clinical outcomes were the presence of AF or atrial tachycardia after 3 months of follow-up after the procedure: electrocardiogram detection, Holter detection for a minimum of 30 s, detection in an implantable event monitor lasting 120 s in the asymptomatic type or 30 s in the symptomatic type.

Studies using remote navigation, PVAC catheters, laserballon catheters, HotBalloon catheters, and partial use of 3D mapping were not included in the meta-analysis, with the objective being to standardize the point-to-point technique with 3D mapping with RF. This selection was made to standardize the technology traditionally used in ablation among the studies used, in addition to using an exclusive sample of patients with recurrence after the first.[2,11–14]

2.4 | Statistical analysis

Statistical analysis was performed using the RevMan 5.4 program (The Cochrane Collaboration). The data were described in terms of relative risk (RR) and at 95% confidence intervals (CI) for dichotomous outcomes and with a $P<.05$ considered to be statistically significant. Descriptive statistics were presented in means and standard deviations (SD) for continuous variables or number of cases (*n*) and as a percentage (%) for categorical variables.

We assessed the effect of heterogeneity using the Higgins *I*-squared (I^2) statistical formula.[20] When heterogeneity was low ($I^2 <25\%$) using the fixed effects of the Mantel–Haenszel method, this model was maintained for the final analysis. In cases of high heterogeneity ($I^2 >25\%$), the model of the analysis of choice was of random effects, in addition, we associate subgroup analysis in these cases and when clinically indicated.[21] The presence of publication bias was assessed by a funnel chart when more than ten studies were included.[22]

3 | RESULTS

3.1 | Characteristics of the studies

The articles identified through our systematic literature search are illustrated in Figure 1. The relevant characteristics of the studies included in the meta-analysis are in Table 3. The main data of the studies are summarized below. For the assessment of the presence of the LCO in the clinical outcome of patients undergoing AF ablation (by RF or CRYO), 14 non-randomized studies totaling 3278 patients were included.[3–10,15–19,23]

Eleven studies only used PV isolation as an ablation strategy associated with cavotricuspid isthmus block in the presence of atrial flutter. In the remaining three studies, linear ablations in the LA and RA were present in all of them, and in one of them, there was a mapping of fractional potentials with associated ablation.

Six studies only included patients with paroxysmal AF, two studies included patients with paroxysmal and persistent AF of short duration (<1 year) and six studies included patients with paroxysmal AF and persistent AF and long-standing persistent AF.

The vast majority of studies used cardiac angiotomography to assess pulmonary venous anatomy; other methods used were cardiac MRI and venography mainly in cases of CRYO energy. Less frequent were 3D echocardiography and 3D mapping in isolation (see Table 3). The prevalence varied between 10.1% and 41.2% and these extremes occurred in studies that used a distance of ≥5 mm.[5,16]

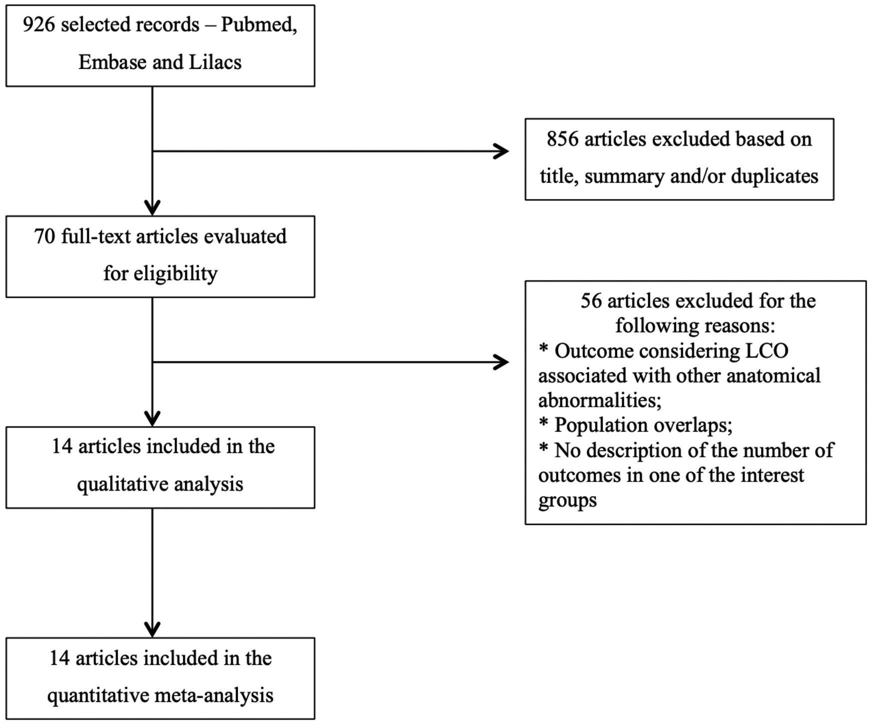

FIGURE 1 Study flow diagram. LCO, left common ostium

Minimum clinical follow-up of the studies included was 12 months. The clinical outcome used by all studies was the detection of any atrial tachyarrhythmia (AF/TA) with a minimum duration of 30 s determined by non-invasive diagnostic methods. One of the studies used application of an implantable monitor and any atrial tachyarrhythmia (AF/TA) with a minimum duration of 120 s being used as the outcome,[17] while for the purpose of the analysis, the detection of clinical recurrence was considered using non-invasive and invasive methods. In two studies, the suspension of antiarrhythmic drugs after the blanking period was at the discretion of the attending medical team, therefore, drug therapy may have been maintained during the clinical follow-up of these studies.[7,9]

3.2 | Technical characteristics

In procedures with RF in general, irrigation ablation catheters without contact force were used, except in two studies, one of which was variable.[15,17] Regarding the power of the RF application, it varied according to each institution, and some studies did not report this datum. Average procedure time ranged from 50.44 min for studies with cryoablation to 185.11 min in RF studies applying extended atrial lesions to the PVI.[7,19]

In the CRYO procedures, most cases were used with a Second generation 28 mm balloon, with one that had varied between first and Second generation[24] and in two studies the first generation balloon was utilized.[10,19] In one of the studies was used adjuvantly, in case of failure to obtain vein isolation with the CRYO applications and catheter irrigated with RF.[19] The application protocol had a significant amount of variation between studies, ranging from 2 to 5 min with or without bonus.

Most studies used the strategy of proving the pulmonary vein isolation (PVI) by blocking the entry and exit, with the minority using adenosine to detect early recurrence.[3,17,23]

Regarding complications, there were a significant number of studies that did not describe the complication rate or when cited, it was not segregated by the venous anatomy, which made it impossible to conduct a reliable analysis for this item.

3.3 | Clinical outcomes

In the analysis of the influence of the presence of the LCO in the clinical follow-up of patients with AF submitted to ablation by RF or CRYO, 14 studies were included. In all analyses using the two energies, no statistically significant result was found, in relation to patients and without LCO: the entire population studied OR 1.01 (95% CI 0.84–1.23; $P = .90$, $I^2 = 67\%$) (Figure 2A), excluding patients with long-standing persistent AF and those that underwent linear atrial lesion (LAL) OR 0.87 (95% CI 0.62–1.2; $P = .40$, $I^2 = 72\%$) (Figure 2B), excluding patients with any type of persistent AF and those submitted to LAL OR 0.80 (95% CI 0.52–1.22; $P = .30$, $I^2 = 71\%$) (Figure 2C).

In the analysis using CRYO energy under the LCO and non-LCO groups (eight studies), a statistically significant result was found, with heterogeneity absent, which resulted in a worse clinical outcome for patients with LCO—OR 1.34 (95% CI 1.03–1.74; $P = .03$, $I^2 = 0\%$) (Figure 3A). Whereas, when the patients with long-standing persistent AF are excluded from the studies, there is a tendency toward a worse clinical outcome with the absence of statistical significance, with an OR of 1.60 (95% CI 1.00–2.58; $P = .05$, $I^2 = 0\%$) (Figure 3B). When including only second generation cryoballon studies, there is a worse clinical outcome, with heterogeneity absent, with an OR of 1.33 (95% CI 1.01–1.74; P = .04, I^2 =0%) (Figure 3C) and when the patients with long-standing persistent AF are excluded with an OR of 1.81 (95% CI 1.07–3.06; P = .03, I^2 =0%) (Figure 3D).

In analyses using RF energy to assess the influence of the presence of LCO, using a fixed model, a statistically significant result was found, but with high heterogeneity: the entire population studied OR 0.64 (95% CI 0.46–0.89; P = .008, I^2 =49%) (Figure 4A), while following the protocol of this meta-analysis we applied a random method and a statistically significant result was found of OR 0.55 (95% CI 0.32–0.95; P = .03, I^2 =49%) (Figure 4B). From this point on, it was decided to perform a subgroup analysis excluding studies with persistent long-duration AF and the performance of linear ablations concomitant with the PVI was obtained by the fixed method with an OR of 0.44 (95% CI 0.27–0.73; P = .001, I^2 =44%) (Figure 4C). As a result of the high heterogeneity, a random analysis was performed, while maintaining a statistical significance with an OR of 0.45 (95% CI 0.23–0.91; P = .03, I^2 =44%) (Figure 4D).

4 | DISCUSSION

This is the first meta-analysis that studied the influence of the presence of LCO in clinical follow-up after AF ablation, performed under RF and CRYO energy. Applying a standardization of patient selection (paroxysmal AF), our results showed that patients with LCO submitted to RF have a better arrhythmia-free survival. On the other hand, when undergoing CRYO ablation, patients with LCO have a higher rate of clinical recurrence compared to non-LCO patients.

One reason for the choice stems from the results published by Schwartzman et al.,[25] which demonstrated that in the majority of patients with AF and LCO the arrhythmic triggers had originated from an anatomical abnormality. In addition, we must consider its high prevalence, which together with accessory PVs are the main anatomical abnormalities. In the studies included in our meta-analyses we found wide prevalence variability between 8% and 41% for those with LCO, although the opposite studies used the same anatomical definition (distance from the confluence of the branches ≥5 mm to the LA) and imaging methods that are considered the gold standard for anatomy evaluation (MRI and CT).[26] We suggest that a single anatomical definition be used in future studies on the subject in order to standardize the data, pointing out that the majority adopts a cutoff point of 5 mm.[24]

When analyzing the overall influence of the LCO, under both energies, no statistical significance was found, even when applied to the predefined subgroup analyses, despite the degree of heterogeneity always remaining high. This can be explained by the possible different clinical responses between RF and CRYO energies in the presence of LCO. Regarding the sample selection criteria, it is noteworthy that, for example, the variation in the percentage of long-standing persistent AF may be responsible for the generation of foci that trigger extra-pulmonary AF, which could affect the success of the procedure. Regarding the ablation strategy extended beyond the PVs, it may explain scar or macrorrentrant arrhythmias in the clinical follow-up.[2] Therefore, our subgroup analysis policy was based on these data, which was applied in all scenarios studied.

We found that patients with LCO undergoing RF ablation have a better clinical outcome compared to controls, when analyzed excluding patients with long-standing persistent AF and those with an ablation strategy extended beyond the PVs. The exclusion of these items is important in terms of attempting to standardize the population studied and eliminating possible biases influencing extra-pulmonary triggering mechanisms.

As justifications for these findings, we could suggest certain mechanisms: the left ridge (left anterosuperior region) is a region of reduced contact between the catheter and myocardial tissue and is consequently associated with the formation of flaws in the ablation lines as demonstrated by Neuzil et al.,[27] and Makimoto et al.,[28] and the presence of LCO can enable an optimization of contact in this region and justify the better outcome in the group with LCO. Currently, with the technology of catheters with contact-force sensors, this anatomical superiority of LCO may be limited nowadays. Another suggestion was demonstrated by Barrio-Lopez et al.,[29] who described that the presence of LCO has an inverse relationship with the detection of epicardial connections. These results may provide an explanation of the protection of LCO patients in the clinical follow-up after PVI, since the presence of these connections confers a worse clinical prognosis.

On the other hand, patients with LCO submitted to the procedure under CRYO energy, when we analyzed it in general without sample restrictions, we found a worse clinical prognosis with an increase of 34% in the recurrence in relation to those without LCO. It noteworthy that in the cryoablation procedure, the lesions are restricted to the PVI, which could determine a worse prognosis, especially in patients with long-standing persistent AF. In the presence of this selection, that is, exclusion of studies with long-standing persistent AF, we identified a trend of worse evolution, although without statistical significance. Even analyzing only the second generation cryoballon, a worse prognosis was maintained with statistical significance.

It is important to describe the forms of PVI approach by CRYO energy in the presence of LCO: standard approach (when the cryoballoon obtains the total occlusion of the LCO antrum and ablation occurring in this region); sequential approach (ablation of the upper/lower branch of the LCO); consecutive approach (ablation of a continuous antral lesion by consecutive overlapping applications at each quadrant of the PV-ostium).[6–8,10,15,18]

As LCO usually has a wider ostium, it would be perhaps more difficult to have the complete antral occlusion, which justifies the less practical use of the standard approach.[10] Analyzing the sequential approach, the most used among the studies, the antral region is not reached by the balloon, especially in LCO with length >12 mm.[6–8,10,15,18] Consecutive ablation approach was previously suggested instead of the sequential ablation approach in the setting of large PV-diameters. However, the efficacy might be questionable because of the limited temperature drop caused by incomplete antral occlusions, consecutively less minimal temperatures, and thus less effective freeze cycles and lesion formation.[6] Previous studies

TABLE 3 Characteristics of the studies

Study	Year	Design	*N*	Type of AF[a]	Definition of de LCO (mm)	LCO (%)	Diagnosis	Age	Male (%)	Left atrium	Energy	Catheter
McLellan et al.[3]	2014	Prospective multicenter	102	PAF 100%	≥5	37	CMR or CT	59 ± 9	67	59.87[c]	RF	RF—Irrigated
Odozynski et al.[4]	2018	Retrospective unicenter	172	PAF 100%	≥10	17	CT	58.8	70.3	38.7[a]	RF	RF—Irrigated
Anselmino et al.[5]	2017	Retrospective unicenter	330	PAF 62.7% + PeAF 25.5% + LSPAF 11.8%	≥5	41.20	CMR	60 ± 9.8	83	45.7 ± 7[a]	RF	RF—Irrigated
Heeger et al.[6]	2017	Retrospective multicenter	147	PAF 55% + PeAF/LSPAF 45%	≥5	11	Venography	64.8 ± 11	71	44 ± 5[a]	CRYO	Second generation cryoballoon
Kubala et al.[19]	2011	Retrospective unicenter	118	PAF 72% + PeAF/LSPAF 28%	≥5	25	CT	55 ± 9	77	23.75[c]	CRYO and RF	First—generation cryoballoon (RF—Irrigated)
Yorgun et al.[7]	2019	Retrospective unicenter	82	PAF 62.5% + PeAF/LSPAF 37.5%	≥5	12.20	CT	59.48	52.5	38.1[a]	CRYO	Second generation cryoballoon
Beiert et al.[8]	2015	Retrospective unicenter	68	PAF 42.6% + PeAF 57.4%	≥5	13.70	Venography	66.5	60.3	80[c]	CRYO	Second generation cryoballoon
Shigeta et al.[9]	2017	Retrospective unicenter	324	PAF 100%	≥10	8	CT	65	67.2	39.25[a]	CRYO	Second generation cryoballoon
Huang et al.[10]	2018	Retrospective unicenter	78	PAF 100%	≥5	23.10	CT	60.7 ± 10.9	64.1	39.1 ± 3.6[a]	CRYO	First generation cryoballoon
Khoueiry et al.[15]	2015	Retrospective unicenter	687	PAF 100%	≥5	18.63	CT	60.8 ± 10	70.3	40.7 ± 15.4[c]	RF or CRYO	RF—Irrigated[d] or Second generation cryoballoon
Wei et al.[16]	2019	Retrospective unicenter	424	PAF 77.1% + PeAF/LSPAF 22.8%	≥5	10.10	CT	56.25	63.6	38.6 ± 5.3[a]	CRYO	Second generation cryoballoon
Ronsoni et al.[23]	2020	Prospective multicenter	254	PAF 88.1% + PeAF 11.8%	≥5	23.60	CT	54 ± 12	68.5	41 ± 5[a]	RF	RF—Irrigated
Larsen et al.[17]	2020	Multicenter, prospective, parallel-group, single-blinded randomized clinical trial (sub-analysis)	346	PAF 100%	≥10	13.60	CT, CMR, Echo, 3D mapping systems	59 ± 10	67	37.7[a]	RF or CRYO	RF—Irrigated or Second generation cryoballoon
Ströker et al.[18]	2017	Retrospective unicenter	146	PAF 78.4% + PeAF/LSPAF 21.5%	≥5	34	CT	55.5	69	42.6[a]	CRYO	Second generation cryoballoon

[a]Left atrial volume.

[b]Ablation strategies—sequential: ablation of the superior/inferior branch, without treatment of the antral aspect of the LCPV—standard: CB with antral occlusion of the LCPV—consecutive ablation: Ablation of a continuous antral lesion by consecutive overlapping applications at each quadrant of the PV-ostium. AF: atrial fibrillation; PAF: paroxysmal atrial fibrillation; PeAF: persistent atrial fibrillation; LSPAF: long-standing persistent atrial fibrillation; LCO: left common ostium; CMR: cardiac magnetic resonance; CT: computed tomography; Echo: echocardiogram; RF: radiofrequency: CRYO: Cryoablation; PVAC: pulmonary vein ablation catheter; LA: Left atrial; CTI: cavo-tricuspid isthmus; PV: pulmonary vein; EKG: electrocardiogram.

[c]Left atrial diameter.

[d]Irrigation catheters with contact force—variable.

If CRYO, ablation strategies in LCO[b]	Additional lesions	Entrance block in PV	Exit block in PV	Adenosine test	Time	Complication	Follow-up	Method of follow-up	Outcome criteria
—	Absent	Yes	Yes	Yes	165.38	Not detected	12 ± 4 months	EKG—Holter (24 h and 7 days) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
—	Absent	Yes	Yes	No	Not Detected	Not detected	32.65 months	EKG—Holter (5 days) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
—	Linear lesions + complex fractionated atrial	Yes	Yes	No	Not Detected	Not detected	15.6 ± 7.2 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Standard (50%) and sequential (50%)	Absent	Yes	No	No	105	No difference	1.9 ± 0.9 years	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Consecutive (100%)	LA linear lesions + CTI block in Persistent	Yes	No	No	185.5	No difference	13 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Standard (22%) and sequential (78%)	Absent	Yes	Yes	No	50.44	No difference	31 ± 15 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods (suspension occurred by decision assistant team)
Standard (11%) and sequential (89%)	Absent	Yes	No	No	100	No difference	77 weeks	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Majority sequential	Absent	Yes	Yes	No	143.48	No difference	454 ± 195 days	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods (suspension occurred by decision assistant team)
Standard (26%) and sequential (74%)	Absent	Yes	No	No	112.28	No difference	689.5 ± 103.8 days	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Sequential (100%)	Varied lesions not specific	Yes	No	No	123	Not detected	14 ± 8 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
Consecutive (100%)	Absent	Yes	No	No	49.59	No difference	16.1 ± 3.3 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
—	CTI block if flutter	Yes	Yes	Yes	142.41	No difference	28 ± 1.7 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods
No data	Absent	Yes	Yes	Yes	143.38	Not detected	12 months	EKG—(24 h) and exams guided by symptoms + deployed event monitor	After 3 months—30 s in non-invasive methods and 120 s with implanted monitor
Standard (19%) and sequential (81%)	Absent	Yes	No	No	66	No difference	19.1 months	EKG—(24 h) and exams guided by symptoms	After 3 months—30 s in non-invasive methods

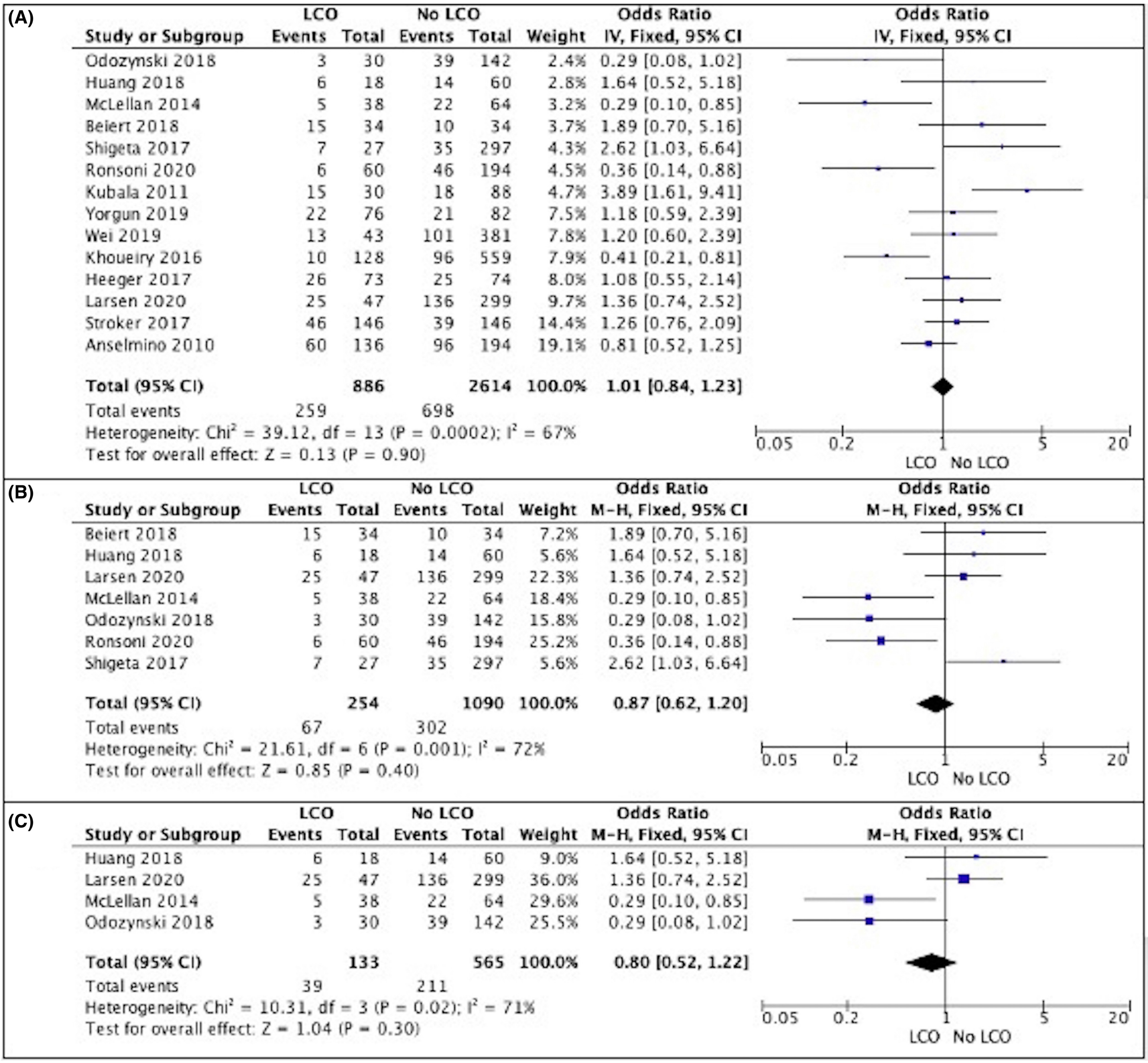

FIGURE 2 (A) Analyses using the two energies; (B) analyses using the two energies, excluding patients with long-standing persistent AF and those that underwent linear atrial lesion; (C) analyses using the two energies, excluding patients with any type of persistent AF and those submitted to linear atrial lesion. AF, atrial fibrillation; LCO, left common ostium

reported conflicting results between the approaches, therefore there is still no recommended technique in this clinical situation.[6–10,19]

Our hypotheses for these results are because of lower maneuverability of balloon to adapt to the PV ostium compared with an RF ablation catheter in order to achieve an optimal antral PVI and CRYO energy is delivered more distally into the venous system not affecting the triggers of the arrhythmia (non-antrum area).[30,31] In opposition to the meta-analysis of Vincenzo et al.,[32] that showed no statistical difference in the clinical follow-up of patients with LCO submitted to PVI with second-generation CRYO balloon, probably the different result was because of the smaller number of patients included in Vincenzo et al.[32]

A future point to be clarified remains to be the best technique for treating patients with LCO undergoing AF ablation. A subgroup analysis of the CIRCA-*DOSE* study showed no significant difference between the two types of energy. However, we must consider certain points of limitation in the generalization of these results, although the original study was randomized in the subgroup analysis, no randomization occurred, because of the presence of a low number of LCO patients in the study ($n = 47$), thus limiting the statistical power of this study.[33]

5 | LIMITATIONS

One of our limitations already foreseen before the execution of the meta-analysis was related to the high heterogeneity, which was probably related to the different methods of LCO detection,

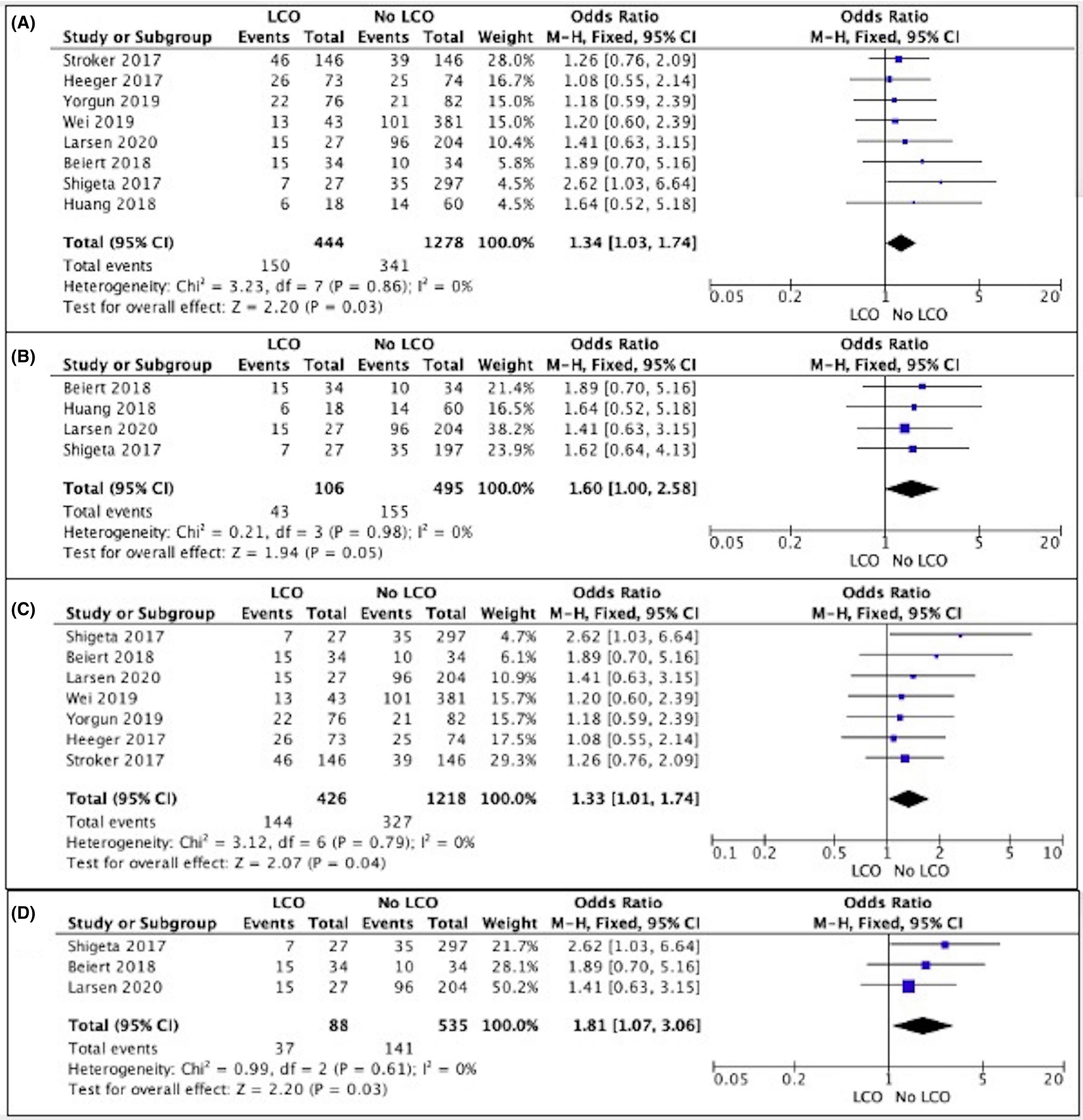

FIGURE 3 (A) Analyses using CRYO energy; (B) analyses using CRYO energy, excluding patients with long-standing persistent AF; (C) analyses using CRYO energy, excluding patients with first generation catheter; (D) analyses using CRYO energy, excluding patients with first generation catheter and with long-standing persistent AF. AF, atrial fibrillation; LCO, left common ostium

different definitions of LCO, heterogeneous groups of patients, different types of ablation energy and ablation techniques restricted to PVI or extended to the LA. Random methods were used in highly heterogeneous analyses and, where possible, we performed subgroup analysis as a way to minimize this effect.

Other limitations were the observational nature of the studies included and a relatively small number of studies, mainly in the performance of sub-analyzes. We opted to exclude studies with catheters involving new technologies such as HotBalloon, laserballon catheter, and PVAC in an attempt to inhibit clinical heterogeneity; perhaps in the future with subsequent studies, this may require future evaluation.

6 | CLINICAL IMPLICATIONS

This is the first meta-analysis that studied the influence of the anatomical abnormality of the LCO type in clinical follow-up after AF ablation. In patients undergoing CRYO for atrial fibrillation, the

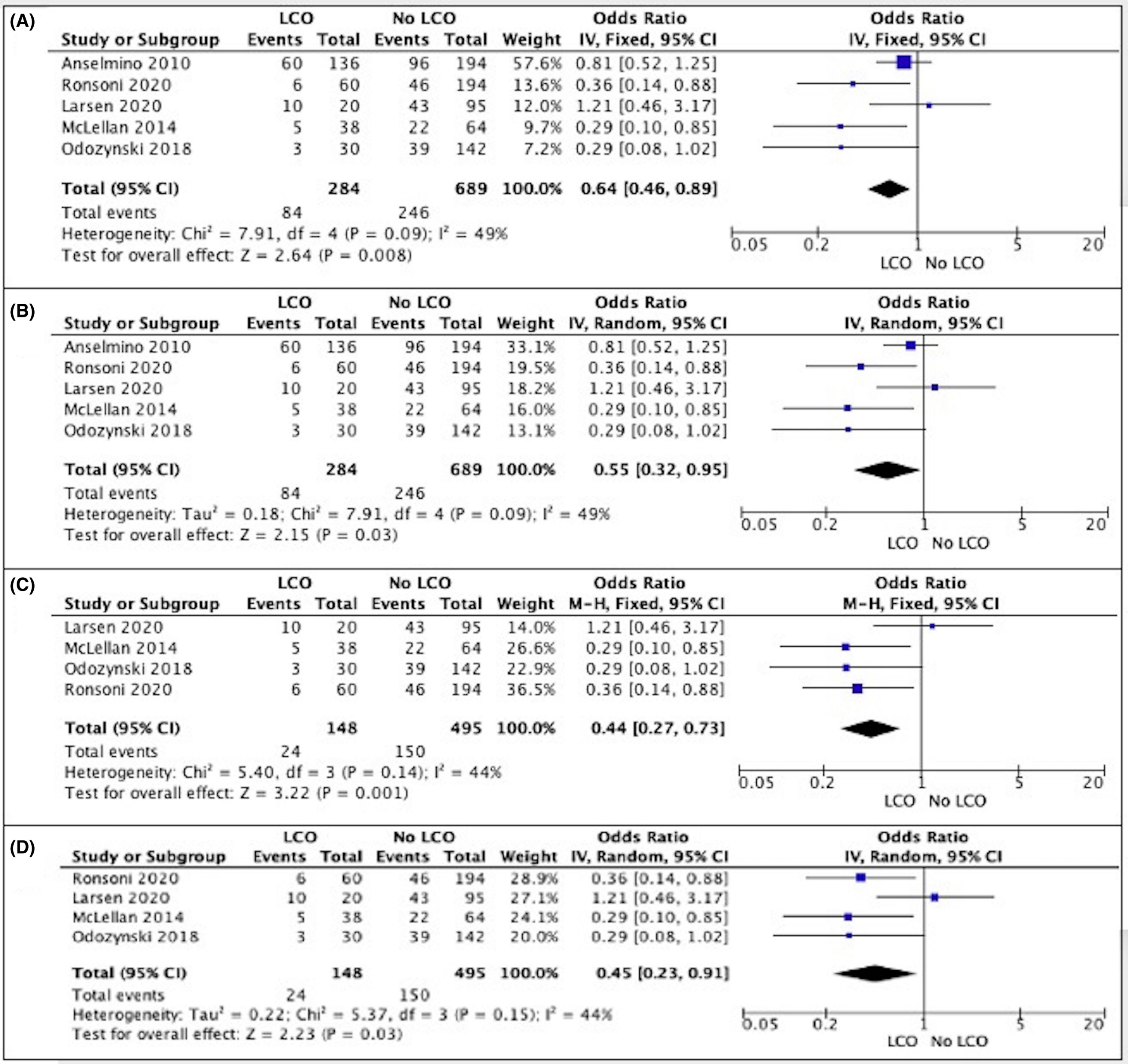

FIGURE 4 (A) Analyses using RF energy, using a fixed model; (B) analyses using RF energy, using a random model; (C) analyses using RF energy, excluding studies with long-standing persistent AF and the performance of linear ablations concomitant with the PVI was obtained by the fixed method; (D) analyses using RF energy, excluding studies with long-standing persistent AF and the performance of linear ablations concomitant with the PVI was obtained by the random method. AF, atrial fibrillation; LCO, left common ostium; PVI, pulmonary vein isolation; RF, radiofrequency

presence of LCO suggests a worse prognosis compared to typical left PVs. Our results suggest that the adoption of anatomical pre-selection of patients may be interesting in the context of choosing between the two ablation modalities in patients with paroxysmal AF.

7 | CONCLUSION

The results of this study suggest a better prognosis in patients with LCO compared to the control group, submitted to PVI without additional lesion under RF energy in paroxysmal AF and short duration persistent AF. In patients undergoing CRYO for AF, the presence of LCO suggests a worse prognosis compared to typical left PV. The ablation strategy in patients with LCO still needs a randomized clinical trial to clarify whether these findings can modify the invasive strategy.

CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

AUTHORSHIP

RMR; TLLL: Conception, design, analysis, and interpretation of the data; RMR; TLS; MALS; TLLL: Contributions to the drafting of the article and critical revision; RMR; TLS; MALS; TLLL: Final approval of the version to be published; RMR; TLS; MALS; TLLL: Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of the article.

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