

# Left Atrium Volume Reduction Procedure Concomitant With Cox-Maze Ablation in Patients Undergoing Mitral Valve Surgery: A Meta-Analysis of Clinical and Rhythm Outcomes



Massimo Baudo, MD\*, Fabrizio Rosati, MD, Lorenzo Di Bacco, MD, Michele D'Alonzo, MD, Stefano Benussi MD, PhD, Claudio Muneretto, MD

Division of Cardiac Surgery, Spedali Civili di Brescia, University of Brescia, Brescia, Italy

Received 13 February 2023; received in revised form 11 July 2023; accepted 10 September 2023; online published-ahead-of-print 9 October 2023

**Background** The management of an enlarged left atrium (LA) in mitral valve (MV) disease with atrial fibrillation (AF) is still being debated. It has been postulated that a reduction in LA size may improve patient outcomes. This meta-analysis aimed to assess rhythm and clinical outcomes of combined surgical AF treatment with or without LA volume reduction (LAVR) in patients undergoing MV surgery.

**Methods** A systematic review was performed and all available literature to May 2022 was included. The primary endpoint was analysis of early and late mortality and rhythm outcomes. Secondary outcomes included early and late cerebrovascular accident (CVA) and permanent pacemaker implantation.

**Results** The search strategy yielded 2,808 potentially relevant articles, and 19 papers were eventually included. The pooled estimated rate of 30-day mortality was 3.76% (95% CI 2.52–5.56). The incidence rate of late mortality and late cardiac-related mortality was 1.75%/year (95% CI 0.63–4.84) and 1.04%/year (95% CI 0.31–3.53), respectively. At subgroup analysis when comparing the surgical procedure with and without AF ablation, the ablation subgroup showed a significantly lower rate of postoperative CVA ( $p < 0.0001$ ) and higher restoration to sinus rhythm at discharge ( $p = 0.0124$ ), with only a trend of lower AF recurrence at 1 year ( $p = 0.0608$ ). At univariable meta-regression, reintervention was significantly associated with higher late mortality ( $p = 0.0033$ ).

**Conclusion** In enlarged LA undergoing MV surgery, LAVR combined with AF ablation showed a trend of improved rhythm outcomes when compared with AF ablation without LAVR. Each LAVR technique has its advantages and disadvantages, which must be managed accordingly.

**Keywords** Cardiac surgery • Mitral valve surgery • Atrial fibrillation ablation • Left atrium volume reduction surgery • Meta-analysis

\*Corresponding author at: Division of Cardiac Surgery, Spedali Civili di Brescia, Piazza Spedali Civili, 1, 25123, Brescia, Italy; Email: [massimo.baudo@icloud.com](mailto:massimo.baudo@icloud.com); Twitter: @Takotsubo91

## Introduction

Atrial fibrillation (AF) is frequently associated with mitral valve (MV) dysfunction. Significant MV regurgitation or stenosis may lead to a volume/pressure overload, causing left atrial (LA) remodelling, dilation, and fibrosis. However, AF itself may induce LA enlargement, leading to MV annular dilation and worsening regurgitation. As coexisting and self-sustaining pathologies, AF that is not addressed during MV surgery has been identified as an independent predictor of late stroke and cardiovascular mortality [1]. Furthermore, a severely dilated LA is considered a predictor of AF recurrence and a risk factor for early mortality and thromboembolic events [2] in patients who receive concomitant ablation treatment. Although successful MV disease correction reduces LA pressure, fibrosis with an enlarged LA is considered irreversible as time passes [3]. Therefore, it has been postulated that a reduction in LA size may improve patient outcomes [4].

Simultaneous management of a severely dilated LA in patients with AF undergoing concomitant MV surgery and AF ablation is still being debated [5–7]. Several studies have shown that LA volume reduction (LAVR) procedures concomitant with AF ablation significantly increases the incidence of sinus rhythm (SR) restoration [8]; however, most of these studies were limited by retrospective design, small cohorts, and short follow-up. The current meta-analysis aimed to assess rhythm and clinical outcomes of combined LAVR with or without surgical AF treatment in patients scheduled for MV surgery.

## Methods

### Literature Search Strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9], as shown in the PRISMA flow diagram in [Figure 1](#). A search of PubMed, ScienceDirect, Ovid MEDLINE, SciELO, and Cochrane Library databases was performed. Available literature to May 2022 was included, with publications reporting the clinical and rhythm outcomes of patients with AF and severely dilated LA undergoing MV surgery concomitant with LAVR with or without concomitant Cox-Maze AF ablation. The search strategy can be found in [Supplementary Table S1](#). Bibliographies of the included studies and previous reviews were screened to identify further potentially relevant papers (i.e., “backward snowballing”). Studies were independently screened for inclusion by two authors (MB and MD). In case of disagreement, a consensus was reached with the aid of a third author (CM). This review was registered with the PROSPERO register of systematic reviews (ID: CRD42022345226).

### Selection Criteria

The included studies analysed patients with dilated LA and AF who underwent MV surgery and LAVR with or without concomitant surgical Cox-Maze AF ablation. Only articles

written in English language were included. Exclusion criteria were: studies with a description of hybrid procedures, transcatheter procedures, MV surgery without LAVR surgery; studies with <10 patients; case reports, reviews, abstracts, letters, and comments. If there were multiple papers from the same institution, the study period was assessed; if the study period overlapped, the paper with the largest sample size was considered.

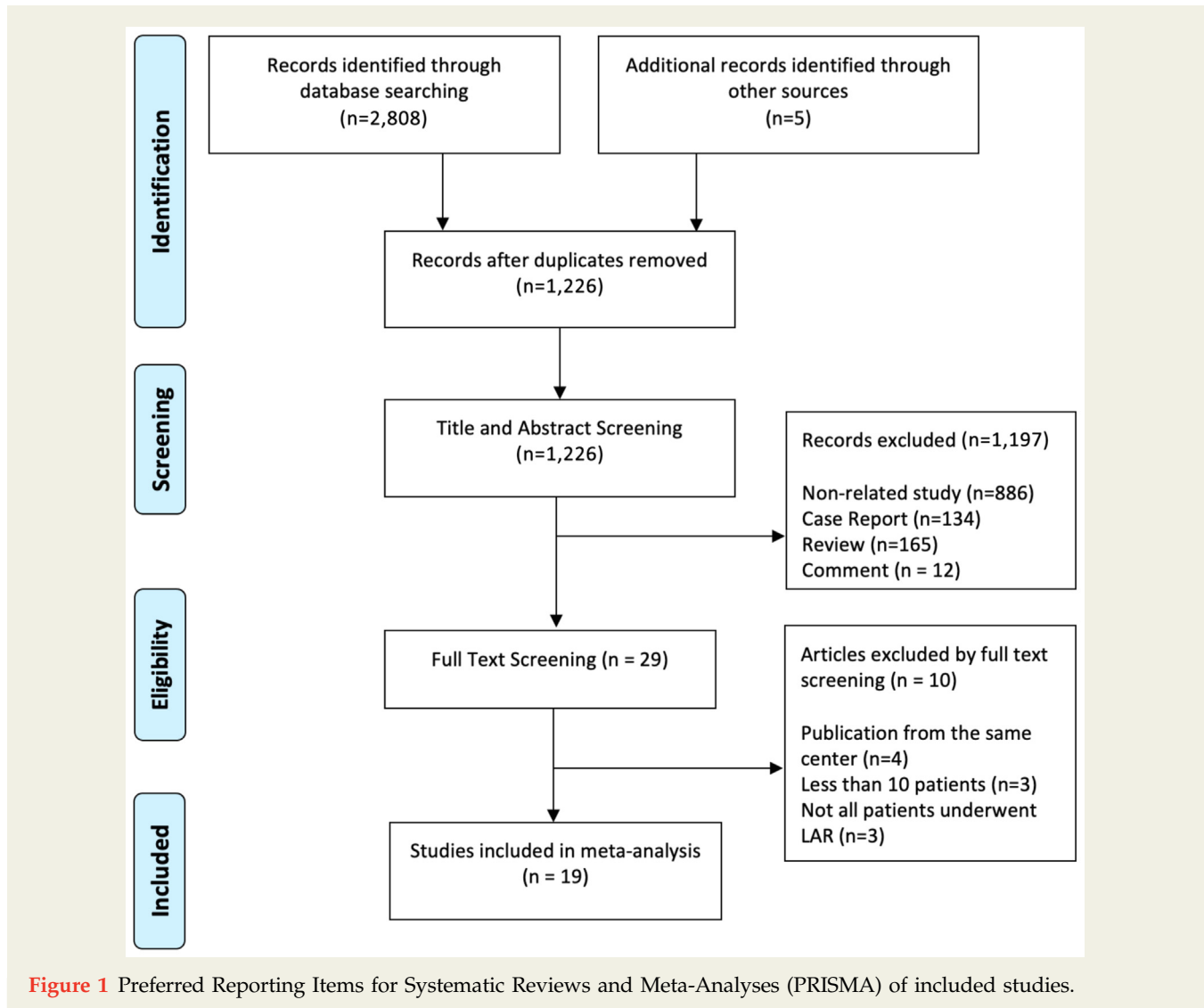
### Data Extraction and Critical Appraisal

Data extraction was performed with the aid of Microsoft Office 365 Excel software (Microsoft, Redmond, Washington, USA). Categorical variables were reported as numbers, while continuous variables were expressed as mean  $\pm$  standard deviation. Data on study period, study centre, country, sample size, and type of cohort grouping were retrieved. The following patient characteristics were extracted: mean age, sex, mean body mass index, AF, cut-off of LA diameter for study inclusion, mean LA diameter, left ventricular ejection fraction, and reintervention status. Data regarding intraoperative, early and late surgical, and rhythm outcomes were recorded. The Newcastle-Ottawa Quality Assessment Scale for Cohort Studies was used for critical appraisal of the quality of included non-randomised studies [10], while the Cochrane Collaboration’s Risk of Bias Tool was adopted for randomised controlled trials (RCTs) [11]. The certainty of the conclusions drawn from comparison meta-analyses was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool [12].

### Statistical Analysis

The primary endpoint was analysis of early and late mortality and rhythm outcomes. Secondary outcomes included early and late cerebrovascular accident (CVA) and permanent pacemaker implantation. Poisson regression modelling was used for late outcomes, to account for differences in follow-up times, assuming a constant event rate. The total number of events and mean follow-up time were used to calculate the total person-time of follow-up in years. The pooled event rates (PER) and pooled event means were used for the early outcomes, while a log transformation to model the overall incidence rate (IR) and incidence rate ratio were used for late outcomes. All results were calculated with a 95% Confidence Interval (CI).

Subgroup analyses were performed considering whether surgical AF ablation was performed or not, and the technique of LA reduction surgery (plication or resection). In all analyses, studies were weighted by the inverse of the variance of the estimate for that study, and between-study variance was estimated with DerSimonian-Laird method with random effects model. Studies with double zeros were included in the meta-analysis and treatment arm continuity correction was applied in studies with zero cell frequencies. Univariate meta-regression was performed to explore the relation between early and late mortality and patient’s



**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) of included studies.

characteristics. The results were reported as regression coefficient (i.e., beta), standard error, and p-value.

Heterogeneity was based on the Cochran's Q test, with  $I^2$  values. In case of heterogeneity ( $I^2 > 50\%$ ), individual study inference analysis was performed through a "leave-one-out" sensitivity analysis. Funnel plots by graphical inspection and Egger's test, when feasible, were used for assessment of publication bias. In case of asymmetry positivity, visual assessment and Duval and Tweedie's trim and fill methods were used for further assessment.

Hypothesis testing for equivalence was set at the two-tailed 0.05 level. All statistical analyses were performed using R, version 4.2.0 (R Project for Statistical Computing, Wien, Austria) and RStudio version 2022.02.3. Build 492, using the "meta" and "metafor" packages.

## Results

The search strategy yielded 2,808 potentially relevant articles, with five additional articles included through backward

snowballing. Exclusion of duplicated articles kept 1,226 articles for screening. After evaluation of titles and abstracts, 29 studies were considered for full-text screening. Nineteen studies [13–32] met the meta-analysis inclusion criteria with a total of 1,658 patients. Publication year ranged 1988–2021, and sample size ranged 11–876 patients. Details of the individual studies are shown in [Supplementary Table S2](#). Among the included studies there were four RCTs, two prospective studies, one inverse probability treatment weighting study, and 12 retrospective studies. The demographics of the included studies are summarised in [Supplementary Table S3](#). Of note, different LA diameter cut-offs were adopted by the included studies, with a mean cut-off of 61.3 mm. The actual mean LA diameter of the patients was 72.4 mm. A critical appraisal of the non-randomised and randomised studies is shown in [Supplementary Tables S4 and S5](#).

## Meta-analysis of the Outcomes

The PER of 30-day mortality was 3.76% (95% CI 2.52–5.56). The IR of late mortality and late cardiac-related mortality

**Table 1** Meta-analysis of the outcomes.

Outcome	Studies, n	Estimate (95% CI)	Heterogeneity (I <sup>2</sup> , P-Value)	Egger's test	Bias-adjusted* estimate
<b>Early outcomes</b>					
LAA exclusion	18	96.92% (91.73–98.89)	90.1%, p<0.0001	p<0.0001	74.71% (53.75–88.25)
CPB time	14	135.60 min (107.98–170.28)	99.3%, p<0.0001	p=0.0002	91.75 min (73.49–114.56)
CXC time	14	93.83 min (72.92–120.72)	99.1%, p<0.0001	p=0.0223	61.18 min (46.56–80.39)
Postop atrial diameter	10	47.21 mm (41.96–53.13)	99.5%, p<0.0001	p=0.7080	–
Postop CVA	9	3.16% (1.10–8.73)	78.4%, p<0.0001	NA	–
Postop bleeding	12	6.84% (5.53–8.44)	0%, p=0.5334	p=0.0182	7.23% (5.13–10.10)
Postop PPM	11	4.24% (2.36–7.49)	50.0%, p=0.0293	p=0.5214	–
Discharged with SR	10	70.18% (47.54–85.94)	91.1%, p<0.0001	p=0.2103	–
30-day mortality	18	3.76% (2.52–5.56)	22.7%, p=0.1848	p=0.7889	–
<b>Late outcomes</b>					
Follow-up	17	2.24 years (1.72–2.92)	99.1%, p<0.0001	p=0.2578	–
Late death	14	1.75%/year (0.63–4.84)	90.3%, p<0.0001	p=0.5658	–
Late cardiac death	11	1.04%/year (0.31–3.53)	83.3%, p<0.0001	p=0.4434	–
AF at 1 year	14	30.16% (16.23–49.05)	89.2%, p<0.0001	p=0.5794	–
Late CVA	10	1.26%/year (0.65–2.43)	26.9%, p=0.1965	p=0.2715	–
Late atrial diameter	10	47.14 mm (44.22–50.25)	97.7%, p<0.0001	p=0.1694	–

\*Estimate were adjusted according to publication bias from Egger's test.

Abbreviations: AF, atrial fibrillation; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; CXC, cross-clamp; LAA, left atrial appendage; NA, not applicable; PPM, permanent pacemaker; SR, sinus rhythm.

was 1.75%/year (95% CI 0.63–4.84) and 1.04%/year (95% CI 0.31–3.53), respectively. The IR of AF at 1-year follow-up was 30.16% (95% CI 16.23–49.05). Of note, the LAA was closed with a PER of 96.92% (95% CI 91.73–98.89) and the IR of late CVA was 1.26%/year (95% CI 0.65–2.43). The results of the meta-analysis can be seen in [Table 1](#). The GRADE evaluation of the outcomes can be seen in [Supplementary Table S6](#).

The subgroup analysis showed a significantly lower rate of postoperative CVA (1.56%, 95% CI 0.96–2.51 vs 12.42%, 95% CI 6.13–23.54; subgroup difference p<0.0001) and a higher incidence of SR restoration at discharge (83.40%, 95% CI 60.56–94.26 vs 34.63%, 95% CI 12.55–66.15; subgroup difference p=0.0124) in patients who received MV surgery concomitant with LAVR and AF ablation when compared with a no concomitant ablation strategy, respectively. There was only a non-significant trend of lower AF recurrence at 1 year between the ablation and no ablation subgroups (23.49%, 95% CI 10.40–44.82 vs 53.46%, 95% CI 30.17–75.34; subgroup difference p=0.0608) ([Table 2](#)).

The subgroup analysis between the LA reduction techniques showed a trend of lower rate of postoperative bleeding in favour of plication (3.19%, 95% CI 1.39–7.16 vs 7.24%, 95% CI 5.81–8.99; subgroup difference p=0.0551), and a significantly lower IR of late CVA in favour of resection (2.56%/year, 95% CI 0.99–6.65 vs 0.80%/year, 95% CI 0.58–1.11; subgroup difference p=0.0240) ([Table 3](#)).

### Meta-analysis of the Outcomes in RCTs

The outcomes were further evaluated by analysing only the RCTs. Of note, the RCTs only performed plication as a

surgical technique; therefore, no data regarding the resection technique were available in this subset of studies. The PER of 30-day mortality was 3.11% (95% CI 0.94–9.81). The IR of late mortality and late cardiac-related mortality was 0.35%/year (95% CI 0.03–4.95) and 0.33%/year (95% CI 0.02–5.49), respectively. The PER of AF at 1 year was 30.16% (95% CI 16.23–49.05). The results are summarised in [Table 4](#).

### Meta-regression

At univariable meta-regression, reintervention was significantly associated with higher late mortality and late cardiac-related mortality (p=0.0033 and p=0.0290, respectively). Moreover, age was significantly and positively associated with late mortality (i.e., older age was associated with higher late mortality). Interestingly, the type of reduction technique was not associated with early and late mortality. There was a trend between higher rates of AF ablation and lower 30-day mortality (p=0.0766). The meta-regression results are summarised in [Table 5](#).

### Discussion

This study analysed rhythm and clinical outcomes of combined LAVR in AF patients undergoing MV surgery with or without surgical AF treatment. The results showed: 1) satisfactory postoperative clinical outcomes (CVA PER: 3.16%, permanent pacemaker PER: 4.24%, bleeding PER: 6.84%, and 30-day mortality PER: 3.76%); 2) satisfactory early and late rhythm outcomes (SR at discharge: 70.18%, SR at 1-year

**Table 2** Subgroup analysis by atrial fibrillation ablation.

Outcome	Subgroup	Studies, n	Estimate (95% CI)	Subgroup difference P-Value
<b>Early outcomes</b>				
Postop CVA	Ablation	6	1.56% (0.96–2.51)	<b>p&lt;0.0001</b>
	No Ablation	3	12.42% (6.13–23.54)	
Postop bleeding	Ablation	9	6.84% (5.49–8.50)	p=0.7502
	No Ablation	3	5.71% (1.86–16.23)	
Postop PPM	Ablation	9	4.54% (2.37–8.53)	p=0.3633
	No Ablation	2	2.07% (0.42–9.36)	
Discharged with SR	Ablation	7	83.40% (60.56–94.26)	<b>p=0.0124</b>
	No Ablation	3	34.63% (12.55–66.15)	
30-day mortality	Ablation	12	3.08% (2.27–4.17)	p=0.4931
	No Ablation	6	4.45% (1.62–11.67)	
<b>Late outcomes</b>				
Late death	Ablation	10	1.44%/year (0.47–4.43)	p=0.6537
	No Ablation	4	2.62%/year (0.25–27.57)	
Late cardiac death	Ablation	7	0.72%/year (0.16–3.19)	p=0.4916
	No Ablation	4	1.81%/year (0.21–15.58)	
AF at 1 year	Ablation	11	23.49% (10.40–44.82)	p=0.0608
	No Ablation	3	53.46% (30.17–75.34)	
Late CVA	Ablation	6	0.90%/year (0.58–1.39)	p=0.3343
	No Ablation	4	1.80%/year (0.47–6.99)	

Bold values denote statistical significance at the  $p<0.05$  level.

Abbreviations: AF, atrial fibrillation; CVA, cerebrovascular accident; PPM, permanent pacemaker; SR, sinus rhythm.

**Table 3** Subgroup analysis by surgical technique.

Outcome	Subgroup	Studies, n	Estimate (95% CI)	Subgroup difference P-Value
<b>Early outcomes</b>				
Postop CVA	Plication	3	1.63% (0.33–7.73)	p=0.6642
	Resection	5	2.59% (0.67–9.52)	
Postop bleeding	Plication	5	3.19% (1.39–7.16)	p=0.0551
	Resection	7	7.24% (5.81–8.99)	
Postop new PM	Plication	5	4.27% (2.15–8.31)	p=0.8895
	Resection	6	3.92% (1.45–10.16)	
Discharged with SR	Plication	7	69.14% (41.95–87.41)	p=0.2279
	Resection	2	91.14% (53.15–98.94)	
30-day mortality	Plication	11	3.98% (2.01–7.70)	p=0.4342
	Resection	7	2.94% (2.08–4.14)	
<b>Late outcomes</b>				
Late death	Plication	8	1.35%/year (0.26–6.94)	p=0.4835
	Resection	6	2.67%/year (1.01–7.02)	
Late cardiac death	Plication	8	1.06%/year (0.22–5.12)	p=0.9083
	Resection	3	0.93%/year (0.23–3.73)	
AF at 1 year	Plication	8	30.31% (15.76–50.29)	p=0.5344
	Resection	5	16.61% (1.93–66.84)	
Late CVA	Plication	6	2.56%/year (0.99–6.65)	<b>p=0.0240</b>
	Resection	4	0.80%/year (0.58–1.11)	

Bold value denotes statistical significance at the  $p<0.05$  level.

Abbreviations: AF, atrial fibrillation; CVA, cerebrovascular accident; PPM, permanent pacemaker; SR, sinus rhythm.



**Table 4** Meta-analysis of the outcomes in randomised controlled studies only.

Outcome	Studies, n	Estimate (95% CI)	Heterogeneity (I <sup>2</sup> , P-Value)
<b>Early outcomes</b>			
LAA exclusion	4	97.54% (94.79–98.86)	0%, p=0.7600
CPB time	3	133.79 min (110.39–162.15)	93.5%, p<0.0001
CXC time	3	96.64 min (86.01–112.51)	88.7%, p=0.0001
Postop atrial diameter	2	54.57 mm (47.86–62.21)	98.1%, p<0.0001
Postop CVA	2	1.03% (0.15–6.96)	0%, p=0.7002
Postop bleeding	1	4.29% (1.39–12.46)	NA
Postop PPM	1	5.71% (2.16–14.26)	NA
Discharged with SR	3	82.32% (52.62–95.12)	84.8%, p=0.0014
30-day mortality	4	3.11% (0.94–9.81)	56.5%, p=0.0754
<b>Late outcomes</b>			
Follow-up	4	1.49 years (1.16–1.92)	95.1%, p<0.0001
Late death	3	0.35%/year (0.03–4.95)	81.4%, p=0.0046
Late cardiac death	3	0.33%/year (0.02–5.49)	83.0%, p=0.0028
AF at 1 year	4	17.87% (6.74–39.59)	88.0%, p<0.0001
Late CVA	2	2.81%/year (0.57–12.82)	0%, p=0.5856
Late atrial diameter	4	47.45 mm (41.31–54.51)	98.2%, p<0.0001

Abbreviations: AF, atrial fibrillation; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; CXC, cross-clamp; LAA, left atrial appendage; NA, not applicable; PPM, permanent pacemaker; SR, sinus rhythm.

follow-up: 69.84%); 3) AF ablation concomitant with LAVR and MV surgery significantly reduced the incidence of postoperative CVA and postoperative AF recurrence when compared with the no concomitant AF ablation group (p<0.0001 and p=0.0124, respectively); 4) the LA resection technique was associated with lower CVA at follow-up and a trend of higher postoperative bleeding compared with the plication technique (p=0.0240 and p=0.0551, respectively); 5) advanced age and reintervention were associated with higher incidence of mortality at follow-up (p=0.0071 and p=0.033, respectively).

Patients with MV disease are at higher risk of either new-onset or recurrences of AF, particularly those patients with

larger LA. A dilated LA has increased atrial wall stress, potentially causing metabolic changes and myocardial fibrosis, leading to electrical dishomogeneity sustaining primary foci or re-entrant circuits triggering AF [33,34]. Moreover, the duration of AF plays a major role in the mechanisms sustaining LA remodelling and fibrosis, thereby lowering the efficacy of LA ablation because of an unfavourable anatomical substrate with complex electrical dishomogeneity [35]. In mildly dilated LA, rhythm outcomes of the Cox-Maze procedure have been reported for up to 92% and 77% freedom from AF at 1 and 10 years of follow-up, respectively [36]. The present meta-analysis only considered severely dilated LA, usually associated with higher

**Table 5** Meta-regression analysis.

Outcome	30-Day Mortality		Late Mortality		Late Cardiac Death	
	Beta±SE	P-value	Beta±SE	P-value	Beta±SE	P-value
Age (mean)	0.0289±0.0211	0.1725	0.1371±0.0510	<b>0.0071</b>	0.1071±0.0761	0.1592
Male sex (%)	0.0035±0.0239	0.8826	0.0448±0.0544	0.4107	0.0246±0.0614	0.6882
History of CVA (%)	0.0154±0.0536	0.7735	-0.0400±0.1358	0.7681	-0.1806±0.1498	0.2281
EF (mean)	0.0917±0.0513	0.0737	-0.0799±0.1598	0.6172	-0.1232±0.1974	0.5327
Reintervention (%)	0.0005±0.0343	0.9875	0.3888±0.1322	<b>0.0033</b>	0.3865±0.1770	<b>0.0290</b>
Cut-off value LA diameter (mm)	-0.0067±0.0196	0.7327	-0.0125±0.0375	0.7389	0.0021±0.0417	0.9589
Mean LA diameter (mm)	0.0094±0.0211	0.6572	-0.0187±0.0432	0.6652	0.0014±0.0488	0.9769
AF ablation (yes/no)	-0.7447±0.4206	0.0766	-0.6901±1.1702	0.5554	-0.9300±1.2876	0.4701
Type of LAR (plication/resection)	-0.4427±0.3989	0.2671	0.5602±1.0638	0.5985	-0.0138±1.4763	0.9925

Bold values denote statistical significance at the p<0.05 level.

Abbreviations: AF, atrial fibrillation; CVA, cerebrovascular accident; EF, ejection fraction; LA, left atrium; LAR, left atrial reduction; SE, standard error.

incidence of AF recurrences at follow-up, and found an overall freedom from AF of 70% at 1 year.

It is well known that patients undergoing correction of MV lesions concomitant with arrhythmia surgery have higher potential for postoperative maintenance of stable SR and reverse LA remodelling [37], as the Maze procedure by itself does not influence atrial size [38]. The concomitant addition of LAVR to AF ablation may improve SR restoration by eliminating a potential substrate for the development and perpetuation of AF [8]. However, a limited number of studies have directly compared LAVR with and without AF ablation in patients with dilated LA undergoing MV surgery [16,29–31]. These studies reported a significant advantage of reducing the LA size during AF ablation when compared with AF ablation alone. Nevertheless, recent guidelines and an expert consensus paper do not mention LA reduction procedures in patients with MV disease and dilated LA [5,7,39]. In the current meta-analysis, there was a trend of higher freedom from AF at 1 year in patients with severe LA dilation undergoing MV surgery and LAVR concomitantly with AF ablation when compared with the non-ablation group ( $p=0.0608$ ). Long-term advantages of ablation surgery together with concomitant LAVR and MV surgery could not be demonstrated, even if AF recurrences at 1 year of follow-up occurred in <50% compared with the non-ablation group. Lack of significance was probably due to the limited available data of the non-ablation group, as most of the included studies performed LAVR with concomitant AF ablation. The advantages of performing AF ablation concomitantly with LAVR and MV surgery can also be seen in the postoperative hospital stay. The ablation group showed a significant reduction in postoperative CVA ( $p<0.0001$ ) and an increased number of patients discharged in SR ( $p=0.0124$ ) compared with the non-ablation group.

The available techniques to reduce LA volume can be divided into two categories: plication and resection. The possible disadvantages of the plication techniques include the risk of thrombosis in the plicated portion, injury to posterior structures, and only a modest reduction of the LA. The present study has shown how the plication technique was associated with worse CVA rates at follow-up compared with resection (2.56%/year vs 0.80%/year, respectively;  $p=0.0240$ ). However, this technique is faster and has a reduced risk of postoperative bleeding compared with resection (3.19% vs 7.24%, respectively;  $p=0.0551$ ). The main advantage of the resection technique is that the surgeon has direct vision to free any adhesions and avoid injury behind the posterior wall, but haemostasis may be more challenging. Despite not being significant, a lower recurrence of AF was found at 1 year when compared with the plication technique (16.61% vs. 30.31%;  $p=0.5344$ ). The higher incidence of SR restoration in the resection group might be explained by the resemblance to the original “cut and sew” lesions of the Cox-Maze III. However, the lack of individual patient data did not allow conclusions to be drawn in this regard.

Interestingly, at meta-regression, older age and reintervention were associated with increased late mortality, but AF

ablation and type of atrial volume reduction technique were not. This means that each technique has its own specific complication that the surgeon must manage accordingly, but no survival differences can be seen so far between the two.

## Limitations

This meta-analysis had some limitations. First, non-randomised trials were included in the analysis, thus adding potential risk of bias due to confounding and selection of data for the analysis. Therefore, a selective analysis of the included RCTs was performed, which eventually confirmed the results. There were considerable differences in the surgical strategies among the analysed studies, with a tendency of each institution or surgeon to approach this condition by means of a personalised volume reduction technique. The lack of a standardisation may affect the reliability and generalisability of the comparison between the two main techniques. Some studies performed ablation through a Cox-Maze III approach, while others through a Cox-Maze IV approach. In addition, a different cut-off of LA diameter was used in the included studies. All of these could be a possible source of bias. Despite the higher relevance of LA volume rather than LA diameter to evaluate the left atrium, few of the included studies reported it, thus restricting such analysis. The rhythm follow-up of the included studies was generally very limited, and this significantly limited the final analysis, especially at long-term.

## Conclusions

Clinical and rhythm outcomes of LAVR surgery concomitant with MV surgery and AF ablation in patients with severely dilated LA are encouraging. The combination of LAVR techniques with AF ablation strategies may improve rhythm outcomes in patients with unfavourable LA anatomy otherwise at high risk of arrhythmia recurrences. Further studies are warranted to investigate the outcomes of this meta-analysis.

## Conflict of Interest Statement

Claudio Muneretto: Consulting Fee for Estech, Corcym and Allergan. Stefano Benussi: Consulting Fee for AtriCure Inc., Allergan and Artivion, Medtronic Inc.

## Funding

None.

## Appendices

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.hlc.2023.09.009>.

## References

- [1] Bando K, Kasegawa H, Okada Y, Kobayashi J, Kada A, Shimokawa T, et al. Impact of preoperative and postoperative atrial fibrillation on outcome after mitral valvuloplasty for nonischemic mitral regurgitation. *J Thorac Cardiovasc Surg.* 2005;129:1032–40.
- [2] Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. *Circulation.* 1995;92:835–41.
- [3] Iwasaki Y, Nishida K, Kato T, Nattel S. Atrial fibrillation pathophysiology: implications for management. *Circulation.* 2011;124:2264–74.
- [4] Chen M-C, Chang J-P, Chang H-W. Preoperative atrial size predicts the success of radiofrequency maze procedure for permanent atrial fibrillation in patients undergoing concomitant valvular surgery. *Chest.* 2004;125:2129–34.
- [5] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J.* 2021;42:373–498.
- [6] Sakaguchi T, Totsugawa T, Orihashi K, Kihara K, Tamura K, Hiraoka A, et al. Mitral annuloplasty for atrial functional mitral regurgitation in patients with chronic atrial fibrillation. *J Card Surg.* 2019;34:767–73.
- [7] Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2022;43:561–632.
- [8] Sunderland N, Nagendran M, Maruthappu M. In patients with an enlarged left atrium does left atrial size reduction improve maze surgery success? *Interact Cardiovasc Thorac Surg.* 2011;13:635–41.
- [9] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:m71.
- [10] Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analyses n.d. [https://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp).
- [11] Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ.* 2011;343:d5928.
- [12] Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64:383–94.
- [13] Adalti S, Patel KG, Doshi CP, Ananthnarayanan C, Mehta CN, Wadhawa VA, et al. Concomitant left atrial reduction in rheumatic mitral valve disease with giant left atrium: our technique with midterm results. *Innov Phila Pa.* 2018;13:349–55.
- [14] Aydin U, Sen O, Kadirogullari E, Kahraman Z, Onan B. Robotic Mitral Valve Surgery Combined with Left Atrial Reduction and Ablation Procedures. *Braz J Cardiovasc Surg.* 2019;34:285–9.
- [15] Badhwar V, Rovin JD, Davenport G, Pruiett JC, Lazzara RR, Ebra G, et al. Left atrial reduction enhances outcomes of modified maze procedure for permanent atrial fibrillation during concomitant mitral surgery. *Ann Thorac Surg.* 2006;82:1758–63; discussion 1764.
- [16] Bogachev-Prokophiev AV, Ovcharov MA, Lavinykov SO, Pivkin AN, Sharifulin RM, Afanasyev AV, et al. Surgical atrial fibrillation ablation with and without left atrium reduction for patients scheduled for mitral valve surgery: a prospective randomised study. *Heart Lung Circ.* 2021;30:922–31.
- [17] Chen L-W, Qiu Z-H, Wu X-J. A modified atrial volume reduction technique for a giant left atrium. *Ann Thorac Surg.* 2018;106:e101–3.
- [18] Choi W, Kim HJ, Park SY, Park SJ, Kim JB, Jung S-H, et al. The impact of left atrial reduction during surgical ablation of atrial fibrillation. *Semin Thorac Cardiovasc Surg.* 2022;34:537–46.
- [19] Di Eusanio G, Gregorini R, Mazzola A, Clementi G, Procaccini B, Cavarra F, et al. Giant left atrium and mitral valve replacement: risk factor analysis. *Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg.* 1988;2:151–9.
- [20] Firmansyah DK, Soesanto AM, Hanafy DA, Bono A. Cox maze IV versus left atrial reduction for atrial contraction restoration. *Asian Cardiovasc Thorac Ann.* 2019;27:353–61.
- [21] Hagihara H, Kitamura S, Kawachi K, Morita R, Taniguchi S, Fukutomi M, et al. Left atrial plication combined with mitral valve surgery in patients with a giant left atrium. *Surg Today.* 1995;25:338–42.
- [22] Isomura T, Hisatomi K, Hirano A, Maruyama H, Kosuga K, Ohishi K. Left atrial plication and mitral valve replacement for giant left atrium accompanying mitral lesion. *J Card Surg.* 1993;8:365–70.
- [23] Joshibayev S, Bolatbekov B. Early and long-term outcomes and quality of life after concomitant mitral valve surgery, left atrial size reduction, and radiofrequency surgical ablation of atrial fibrillation. *Anatol J Cardiol.* 2016;16:797–803.
- [24] Kawazoe K, Beppu S, Takahara Y, Nakajima N, Tanaka K, Ichihashi K, et al. Surgical treatment of giant left atrium combined with mitral valvular disease. Plication procedure for reduction of compression to the left ventricle, bronchus, and pulmonary parenchyma. *J Thorac Cardiovasc Surg.* 1983;85:885–92.
- [25] Kim JH, Jang WS, Kim J-B, Lee SJ. Impact of volume reduction in giant left atrium during surgical ablation of atrial fibrillation. *J Thorac Dis.* 2019;11:84–92.
- [26] Marui A, Nishina T, Tambara K, Saji Y, Shimamoto T, Nishioka M, et al. A novel atrial volume reduction technique to enhance the Cox maze procedure: initial results. *J Thorac Cardiovasc Surg.* 2006;132:1047–53.
- [27] Romano MA, Bach DS, Pagani FD, Prager RL, Deeb GM, Bolling SF. Atrial reduction plasty Cox maze procedure: extended indications for atrial fibrillation surgery. *Ann Thorac Surg.* 2004;77:1282–7; discussion 1287.
- [28] Scherer M, Therapidis P, Miskovic A, Moritz A. Left atrial size reduction improves the sinus rhythm conversion rate after radiofrequency ablation for continuous atrial fibrillation in patients undergoing concomitant cardiac surgery. *Thorac Cardiovasc Surg.* 2006;54:34–8.
- [29] Scherer M, Dzemali O, Aybek T, Wimmer-Greinecker G, Moritz A. Impact of left atrial size reduction on chronic atrial fibrillation in mitral valve surgery. *J Heart Valve Dis.* 2003;12:469–74.
- [30] Scherer M, Therapidis P, Wittlinger T, Miskovic A, Moritz A. Impact of left atrial size reduction and endocardial radiofrequency ablation on continuous atrial fibrillation in patients undergoing concomitant cardiac surgery: three-year results. *J Heart Valve Dis.* 2007;16:126–31.
- [31] Wang W, Buehler D, Martland AM, Feng XD, Wang YJ. Left atrial wall tension directly affects the restoration of sinus rhythm after Maze procedure. *Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg.* 2011;40:77–82.
- [32] Yalcinkaya A, Diken AI, Aksoy E, Lafci G, Cicek OF, Kadirogullari E, et al. Effect of left atrial reduction on restoration and maintenance of sinus rhythm in patients undergoing mitral valve replacement: a pilot study. *Thorac Cardiovasc Surg.* 2016;64:441–6.
- [33] Bolca O, Akdemir O, Eren M, Dagdeviren B, Yildirim A, Tezel T. Left atrial maximum volume is a recurrence predictor in lone atrial fibrillation: an acoustic quantification study. *Jpn Heart J.* 2002;43:241–8.
- [34] Chen MC, Chang JP, Guo GB, Chang HW. Atrial size reduction as a predictor of the success of radiofrequency maze procedure for chronic atrial fibrillation in patients undergoing concomitant valvular surgery. *J Cardiovasc Electrophysiol.* 2001;12:867–74.
- [35] Delgado V, Di Biase L, Leung M, Romero J, Tops LF, Casadei B, et al. Structure and function of the left atrium and left atrial appendage: AF and stroke implications. *J Am Coll Cardiol.* 2017;70:3157–72.
- [36] Khiabani AJ, MacGregor RM, Bakir NH, Manghelli JL, Sinn LA, Maniar HS, et al. The long-term outcomes and durability of the Cox-Maze IV procedure for atrial fibrillation. *J Thorac Cardiovasc Surg.* 2022;163:629–41.
- [37] Hyllén S, Nozohoor S, Meurling C, Wierup P, Sjögren J. Left atrial reverse remodeling following valve surgery for chronic degenerative mitral regurgitation in patients with preoperative sinus rhythm: effects on long-term outcome. *J Card Surg.* 2013;28:619–26.
- [38] Jessurun ER, van Hemel NM, Kelder JC, Defauw JAMT, Brutel de la Rivière A, Ernst JMPG, et al. The effect of maze operations on atrial volume. *Ann Thorac Surg.* 2003;75:51–6.
- [39] Calkins H, Hindricks G, Cappato R, Kim Y-H, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. *Heart Rhythm.* 2017;14:e275–444.