Featured Article

Effectiveness of Maze IV procedure versus thoracoscopic ablation for atrial fibrillation: a propensity score-matched analysis

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Background: Thoracoscopic ablation (TA) has emerged as a promising treatment for atrial fibrillation (AF), with the Cox-Maze IV Procedure (CMP-IV) as the current gold-standard intervention. This study aims to evaluate and compare the outcomes of TA and CMP-IV in treating AF.

Methods: Patients with AF underwent either CMP-IV or TA through a left-side chest approach. The CMP-IV entailed bi-atrium ablation, whereas the TA involved creating three circular plus three linear ablations in the left atrium. We analyzed baseline characteristics, perioperative outcomes and recurrence rates using propensity score matching (PSM) at a 1:1 ratio, to ensure comparability between the two treatment groups.

Results: A total of 459 patients underwent either CMP-IV (n=93) or TA via left chest (n=366) and 174 patients were deemed eligible for 1:1 PSM. The TA group experienced significantly shorter intensive care unit (ICU) and hospital stays. The mean follow-up period was 31.5±22.1 months. Pre- and post-matching analysis showed that CMP-IV had a higher rate of freedom from recurrence compared to TA, particularly in non-paroxysmal AF patients. Multivariable Cox regression analysis revealed that CMP-IV was associated with a reduced risk of recurrence, while an increased left atrial size emerged as an independent predictor of postoperative recurrence, regardless of the use of CMP-IV or TA.

Conclusions: Our study suggests that while the therapeutic efficacy of TA for "lone" AF may fall short of the classic CMP-IV, its less invasive nature results in significantly shorter ICU and hospital stays. To enhance patient outcomes following TA, it is essential to improve the quality of ablation, refine the ablation route, and focus on careful patient selection.

Keywords: Atrial fibrillation (AF); thoracoscopic ablation (TA); Cox-Maze IV procedure (CMP-IV); outcomes

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Introduction

The burden of disease from atrial fibrillation (AF) has been on the rise since the beginning of the 21st century. It is estimated that there are over 33 million cases of AF worldwide, with over 10 million in China alone (1,2). AF carries a significant health burden and can lead to complications such as stroke, heart failure, and sudden death (3). While surgical interventions for "lone" AF, such as the Cox-Maze IV procedure (CMP-IV) and thoracoscopic ablation (TA) procedure, boast a high success rate, the overall efficacy of AF treatment remains unsatisfactory. The quest for optimal treatment strategies in managing AF has been a subject of ongoing contention. The CMP-IV procedure, a classic treatment for AF, is highly successful, but as an open surgical procedure may potentially limit its acceptance among patients (4). In China, the use of CMP-IV to treat "lone" AF is also limited. The TA procedure, on the other hand, adopts minimally invasive technology and reduces

surgical trauma. However, the simplification of the ablation route (5) prompts inquiry into whether this modification has impacted the curative efficacy of TA for AF and how it compares to CMP-IV. The lack of relevant controlled studies has made it difficult to provide an answer. In this study, data were gathered from two distinct patient groups, and we assessed the outcomes of these groups through the application of propensity score matching (PSM).

Methods

Patient population

We collected data from 459 patients with "lone" AF who underwent either CMP-IV (n=93) or TA via the left chest (n=366) between January 2015 and June 2022. To enhance the comparability of both treatment groups, we measured the baseline characteristics of all patients, including demographic characteristics such as age, gender, body mass index (BMI), and echocardiographic data containing left atrium diameters (LAD), left ventricular ejection fraction (LVEF), and left atrial appendage thrombus (LAAT). We also considered clinical characteristics including hypertension, diabetes, heart failure, coronary artery disease (CAD), previous cerebrovascular accidents, and previous catheter ablation history.

We prioritized the CMP-IV procedure for patients presenting with LAAT, previous left chest surgeries, or unsuccessful catheter ablations. Alternatively, the TA procedure was advised for individuals with significantly compromised cardiac function, or for frail and/or elderly patients. In other instances, we ensured that patients' wishes were paramount and thoroughly honored.

Surgical method

The CMP-IV group underwent general anesthesia with endotracheal intubation, using median sternotomy or right mini-thoracotomy. After systemic heparinization, extracorporeal circulation was established through the aorta/vena cava or femoral vessels. Antegrade perfusion was achieved with cardioprotective solution, and the aortic root was used for cardiac arrest with bladder temperature of 32–35 degrees. The ablation route included the standard Maze IV route for both the left and right atrium, with all ablation lines completed using bipolar radiofrequency ablation clamps (AtriCure, Mason, OH, USA). Cryoablation or ablation pen was used to ablate the mitral valve isthmus and cavotricuspid isthmus. The left atrial appendage (LAA) was resected using a stapler, or the orifice was closed with continuous suturing from the endocardial double layer. The TA procedure via the left chest was performed as described previously (6), using three ports near the midaxillary line of the left chest wall. Three circular and three linear ablation lesions were made on the left atrium. The LAA was excluded using an Endo GIATM stapler (Covidien, Mansfield, MA, USA). The ganglion plexus (GPs) and ligament of Marshall (LOM) were ablated epicardially. If AF persisted, immediate cardioversion was performed.

Postoperative follow-up

Oral anticoagulation and antiarrhythmic drugs (AADs) were continued for 3 months post-operation. During this blank period, the onset of AF was not counted. Follow-up visits were conducted in-person or via telephone, including physical examinations, transthoracic echocardiogram, electrocardiogram, and 24 h Holter at 6- and 12-month post-ablation, and every 6 months thereafter. Holter monitoring was performed for any cardiac symptoms. Any documented episodes of atrial tachyarrhythmias lasting for 30 seconds or longer, were considered as recurrence. Head magnetic resonance imaging (MRI), cardiac computed tomography (CT), and echocardiography were performed at least once during postoperative follow-up.

Statistical analysis

Descriptive statistics were calculated to show the differences in baseline characteristics of patients in the CMP-IV and TA procedure cohorts. Categorical variables, expressed in percentages or frequencies, were analyzed using chi-squared test or Fisher's exact test as appropriate. Continuous variables, such as age, were expressed as mean ± standard deviation and compared using the unpaired Student's *t*-test. However, if continuous variable was not normally distributed, it was shown as median and interquartile range (IQR), as well as being compared using Mann-Whitney test. To reduce selection bias and expressed standardized mean difference, we performed a PSM for the patients of both groups using the R package 'MatchIt': 1-to-1 pairing and nearest neighbor methods, with a caliper of 0.2. The propensity score was calculated using baseline characteristics, including age, gender, BMI, duration of AF, type of AF, CHA_2DS_2-VASc score (congestive heart failure, hypertension, age, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age, and sex category),

Table 1 Comparison of baseline characteristics before and after matched: TA *vs.* CMP-IV

Characteristics	All included patients				PSM patients		
	TA (n=366)	CMP-IV (n=93)	P value	SMD	TA (n=87)	CMP-IV (n=87)	SMD
Age, year	61.0 [54.3, 68.0]	58.0 [54.0, 64.0]	0.027	0.214	59.0 [52.0, 66.5]	58.0 [54.0, 64.0]	0.040
Male	244 (66.7)	62 (66.7)	>0.999	<0.001	58 (66.7)	58 (66.7)	<0.001
BMI, kg/m^2	26.3±3.2	26.0±3.5	0.503	0.076	25.9±2.9	26.2±3.5	0.085
Hypertension	239 (65.3)	68 (73.1)	0.191	0.170	59 (67.8)	63 (72.4)	0.101
Diabetes	78 (21.3)	19 (20.4)	0.965	0.022	22 (25.3)	16 (18.4)	0.168
Previous cerebrovascular accident	37 (10.1)	15 (16.1)	0.146	0.179	9 (10.3)	15 (17.2)	0.201
Coronary artery disease	55 (15.0)	9 (9.7)	0.245	0.163	15 (17.2)	9 (10.3)	0.201
NYHA class III–IV	128 (35.0)	31 (33.3)	0.808	0.035	24 (27.6)	28 (32.2)	0.101
CHA_2DS_2-VASc score	2.0 [1.0, 3.0]	2.0 [1.0, 3.0]	0.455	0.097	2.0 [1.0, 3.0]	2.0 [1.0, 3.0]	0.024
Previous catheter ablation	57 (15.6)	21 (22.6)	0.147	0.179	13 (14.9)	19 (21.8)	0.220
Non-paroxysmal AF	292 (79.8)	79 (84.9)	0.527	0.136	75(86.2)	73 (83.9)	0.163
Duration of AF, months	48.0 [24.0, 72.0]	48.0 [24.0, 72.0]	0.123	0.159	48.0 [24.0, 72.0]	48.0 [24.0, 72.0]	0.117
LAD, mm	44.1±5.0	46.9±5.8	<0.001	0.522	45.8±5.0	46.3±5.4	0.105
LVEF (%)	56.0 [51.0, 60.0]	57.0 [53.0, 61.0]	0.036	0.281	57.3±6.3	56.8±5.8	0.097
Left atrial appendage thrombus	8 (2.2)	65 (69.9)	<0.001	1.989	2 (2.3)	59 (67.8)	1.888

Data are presented as median [interquartile range], n (%), or mean ± standard deviation. TA, thoracoscopic ablation; CMP-IV, Cox-Maze IV procedure; PSM, propensity score matching; SMD, standardized mean difference; BMI, body mass index; NYHA, New York Heart Association; CHA_2DS_2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age, and sex category; AF, atrial fibrillation; LAD, left atrium diameter; LVEF, left ventricular ejection fraction.

LAD and LVEF. The log-rank test was performed to assess if there was a significant difference in Kaplan-Meier survival curves between the CMP-IV and TA procedure groups. We use R package "ComparisonSurv" to compare the cumulative survival rates at a fixed time point by "log-rank" statistical inference method. In all comparisons, P values <0.05 indicated statistical significance. Factors associated with recurrence were determined using univariate and multivariable Cox regression. In the matched cohort, the time of recurrence event at 1 and 3 years were assessed using a Cox proportional hazards model, and the estimates were presented as hazard ratios along with 95% confidence intervals (CIs). These statistical analyses were performed using the R language (R version 4.1.1).

Ethical review

This study has been approved by the Medical Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (XHEC-D-2022-004), and informed consent was obtained from all participants.

Results

Unmatched population

A total of 459 patients were enrolled in the study, of whom 366 had undergone TA, and 93 underwent CMP-IV. The median age of TA patients was 61 years, significantly older than CMP-IV (58 years, P=0.027). There was a higher proportion of paroxysmal AF in TA group (74/366, 20.2%) than those in CMP-IV group (14/93, 15.1%). In echocardiographic data compared to the TA group, CMP-IV group were noted for larger LAD (46.9±5.8 *vs.* 44.1±5.0, P<0.001) and better cardiac function [LVEF 57.0% (53.0%, 61.0%) *vs.* 56% (51.0%, 60.0%), P=0.036]. In addition, 69.9% (65/93) of CMP-IV group had LAAT compared to only 2.2% (8/366) of patients undergoing TA. Baseline characteristics are presented in *Table 1*.

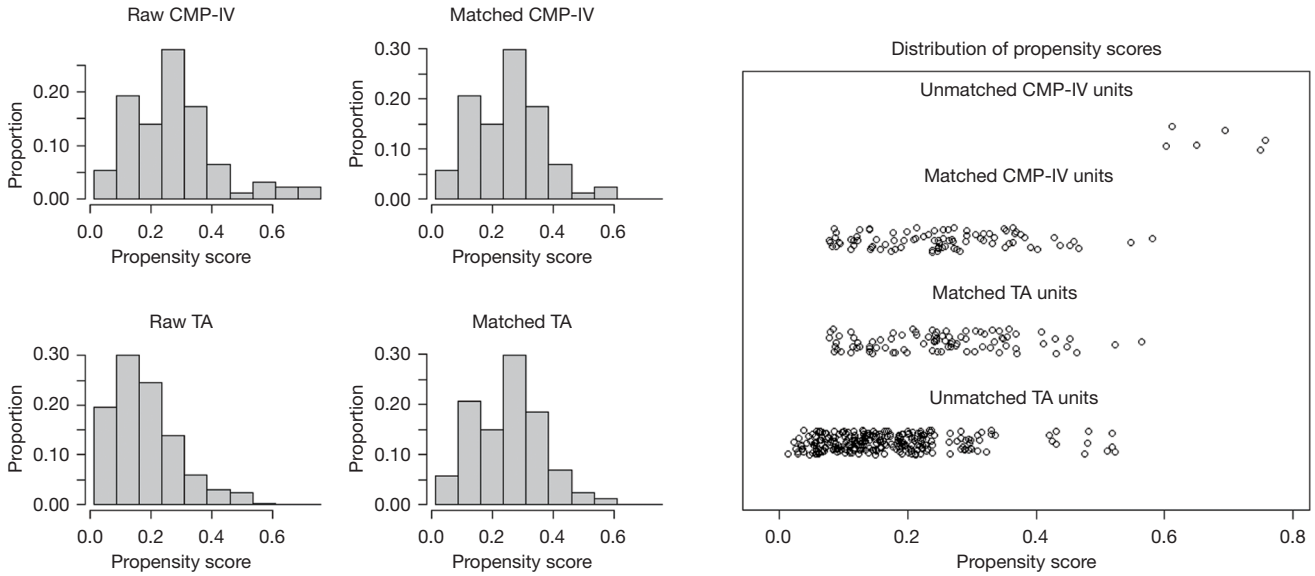

Figure 1 The propensity score distribution of the CMP-IV and TA before and after matching are demonstrated, which shows that the two cohorts were well matched. CMP-IV, Cox-Maze IV procedure; TA, thoracoscopic ablation.

Table 2 Postoperative outcomes before and after matched: TA *vs.* CMP-IV

Postoperative event	All included patients			PSM patients		
	TA (n=366)	CMP-IV (n=93)	P value	TA (n=87)	CMP-IV (n=87)	P value
Stroke	1	0	>0.999	0	0	>0.999
Pneumonia	4	5	0.025	2	4	0.681
Poor wound healing	11	1	0.498	5	1	0.209
Prolonged ventilation	5	4	0.160	1	3	0.620
Acute renal failure	0	1	0.459	0	1	>0.999
Blood product transfusion	4	7	0.001	1	6	0.116
Reoperation for bleeding	1	1	0.867	0	1	>0.999
New pacemaker	2	2	0.389	0	2	>0.999
Mortality within 30 days	0	0	>0.999	0	0	>0.999
ICU time, hour	20.00 [18.00, 28.00]	30.00 [24.00, 36.00]	<0.001	20.00 [18.00, 24.00]	29.00 [24.00, 36.00]	<0.001
Hospital stays, day	6.00 [5.00, 6.00]	10.00 [8.00, 12.00]	<0.001	6.00 [5.00, 6.00]	10.00 [8.00, 11.25]	<0.001

Data are presented as number or median [interquartile range]. TA, thoracoscopic ablation; CMP-IV, Cox-Maze IV procedure; PSM, propensity score matching; ICU, intensive care unit.

Matched population

To minimize these potential biases, a total of 174 patients were eligible for 1:1 PSM from the TA and CMP-IV groups, respectively (*Figure 1*). The baseline characteristics of the matched patients are listed in *Table 1*. After propensity matching, the median age was 58.8±11.1 years in the TA group, higher than 58.4±8.9 years in CMP-IV group (P=0.793). Both groups were similar in gender, BMI, hypertension, diabetes, previous cerebrovascular accident, coronary artery disease, CHA_2DS_2-VASc score, previous catheter ablation, LA diameter, and LVEF.

Postoperative outcomes

Postoperative outcomes for the two groups are listed in *Table 2*. The length of intensive care unit (ICU) (20 *vs.* 30 hours, P<0.001) and hospital stay (6 *vs.* 10 days, P<0.001) was significantly shorter in the TA group. Complications, such as pneumonia, prolonged ventilation, acute renal failure, blood product transfusion, reoperation for bleeding and new pacemaker implantation, were higher in CMP-IV groups but not significantly different.

Survival free from recurrence

At discharge, continuous telemetric monitoring confirmed freedom from AF in 85 out of 87 patients in the CMP-IV group and 84 out of 87 patients in the TA group. The mean follow-up period was 31.5±22.1 months. At 1-year follow-up, 93.1% and 86.2% of patients maintained sinus rhythm in the CMP-IV and TA groups, respectively, while 88.5% and 74.7% of patients maintained sinus rhythm at 3-year follow-up. Kaplan-Meier estimation revealed that CMP-IV showed higher cumulative survival free from recurrence than TA both before and after matching (P=0.001, P=0.004) (*Figure 2A*,*2B*). With respect to the type of AF, there was no significant difference in freedom from recurrence of paroxysmal AF between the two groups (P=0.680), while CMP-IV demonstrated a higher freedom from recurrence than TA in non-paroxysmal AF patients (P=0.005) (*Figure 2C*,*2D*). Notably, there was no significant difference in freedom from recurrence between the two groups at only 1 year [0.926 (95% CI: 0.924–0.928) *vs.* 0.857 (95% CI: 0.853–0.860), log-rank test P=0.157] (*Figure 3A*).

Factors associated with postoperative recurrence

Univariable analysis of fourteen preoperative and perioperative variables was performed to determine potential factors contributing to first recurrence probability within the follow-up period. CMP-IV procedure, BMI, failure of catheter ablation, duration of AF and LA diameters were associated with recurrence (P<0.05). Variables deemed significant in univariate analysis and clinically relevant factors associated with AF containing age, gender, hypertension, and CHADS2-VASC scoring factors were included for further multivariable consideration. Using multivariable COX regression to adjust for clinically relevant covariates revealed that CMP-IV [hazard ratio (HR) 0.36, 95% CI: 0.18–0.70, P=0.003] was associated with decreased risk of recurrence, and increased left atrial size (HR 1.16, 95% CI: 1.06–1.26, P=0.001) was an independent predictor of postoperative recurrence (*Figure 3B*). In TA and CMP-IV treatment groups, increased left atrial size was associated with both increased risk of recurrence in TA (HR 1.13, 95% CI: 1.019–1.248, P=0.020) and CMP-IV groups (HR 1.39, 95% CI: 1.131–1.711, P=0.002).

Discussion

Transcatheter ablation is an effective and less invasive option for patients with AF. Unlike traditional surgical methods, TA eliminates the need for extracorporeal circulation or median sternotomy, thereby minimizing surgical trauma and enhancing patient acceptance. Despite numerous clinical studies showing TA's superior success rates compared to catheter ablation (7,8), few studies have directly compared TA and CMP-IV. Our study demonstrates that TA has a faster recovery time and lower incidence of complications compared to CMP-IV. While the long-term effects of TA do not exhibit superiority, both treatments display comparable one-year success rates. In treating paroxysmal AF, CMP-IV and TA demonstrate similar efficacy, but CMP-IV has a higher success rate for non-paroxysmal AF patients. Furthermore, patients with a large left atrium face a relatively poor prognosis irrespective of the chosen treatment method.

The choice between bi-atrial ablation and left atrium box plus mitral isthmus ablation is a topic of debate in clinical practice (9,10). This study aimed to provide data for this discussion. The study's TA group employed the left atrium box plus mitral valve isthmus ablation strategy via a three-circular and three-linear ablation route, while the CMP-IV group underwent standard bi-atrial ablation. The final follow-up results revealed better curative effects for bi-atrial ablation. We attribute this difference to four primary factors. First, TA is performed from the epicardium under the beating heart, with flowing blood dampening the ablation energy, leading to reduced transmurality (11). Second, in CMP-IV, ablation lines are completed entirely using ablation clamps, ensuring ablation quality. In contrast, in TA, some ablation lines can only be made using ablation pens, resulting in lower ablation quality than that of ablation clamps (12,13). Third, due to anatomical constraints, the mitral valve isthmus cannot be ablated from the epicardium, and only the Dallas line is feasible. However, the effect of the Dallas line remains controversial, and some studies show that adding the Dallas line does not increase the ablation

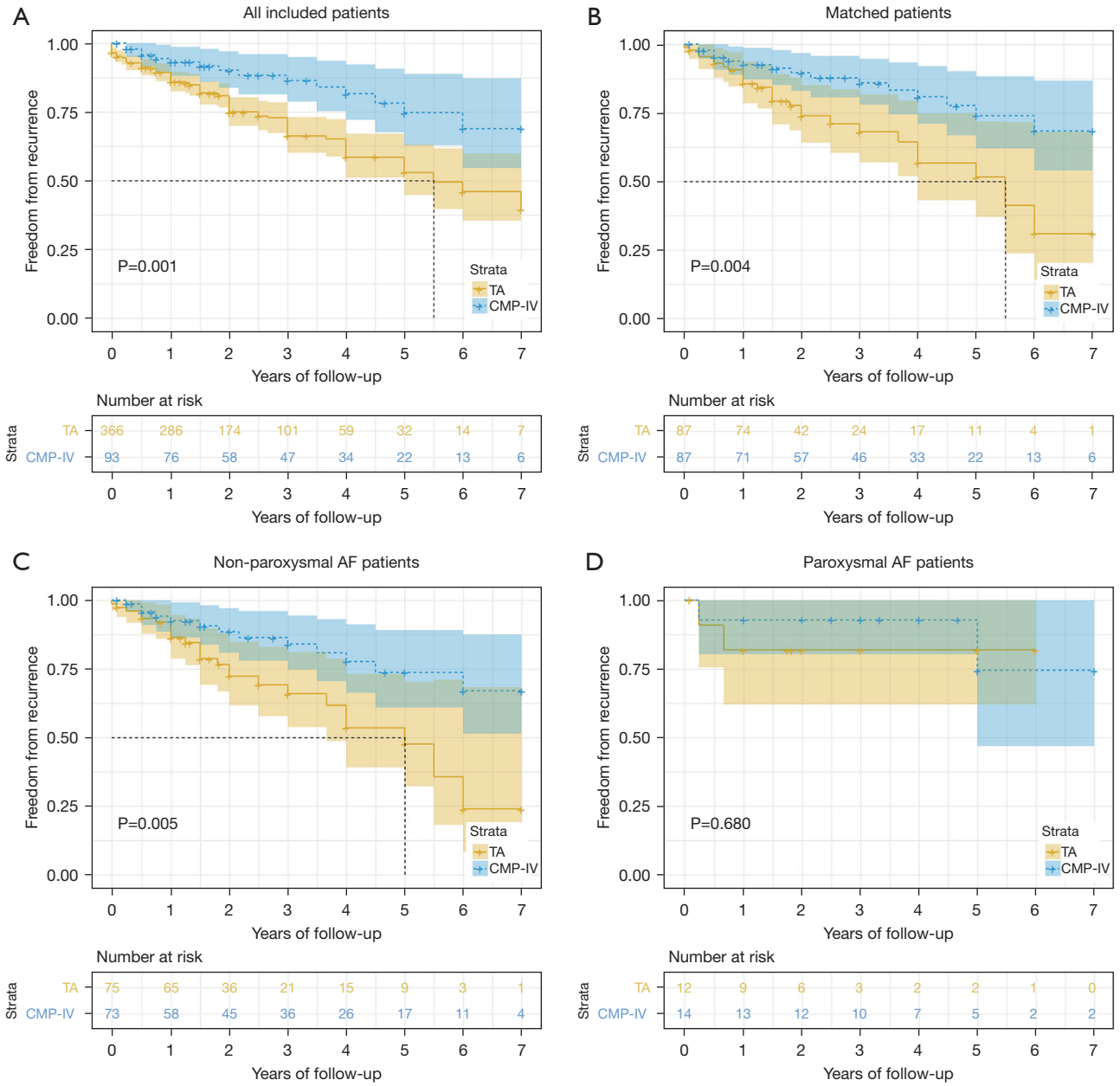

Figure 2 CMP-IV showed higher cumulative survival free from recurrence than TA both before and after matching (A,B). CMP-IV demonstrated a higher freedom from recurrence than TA in non-paroxysmal AF patients (C). No significant difference in freedom from recurrence of paroxysmal AF between the two groups (D). CMP-IV, Cox-Maze IV procedure; TA, thoracoscopic ablation.

success rate (14). Finally, left atrial ablation in TA compared to CMP-IV's bi-atrial ablation differs in whether the right atrium is ablated or not. The role of the right atrium in AF remains disputed. While studies have identified some AF targets in the right atrium, particularly in long-duration patients, some indicate that it is only a bystander and does not lead directly to AF (15,16). Although our study's data indicates that bi-atrial ablation has better curative effects than left atrial ablation, further research is needed to determine the role of the right atrium in AF.

Given the limitations of surgical ablation, which is not amenable to repeated procedures like catheter ablation, our routine clinical practice involves a CMP-IV procedure with bi-atrial ablation during open heart surgery. In the context of

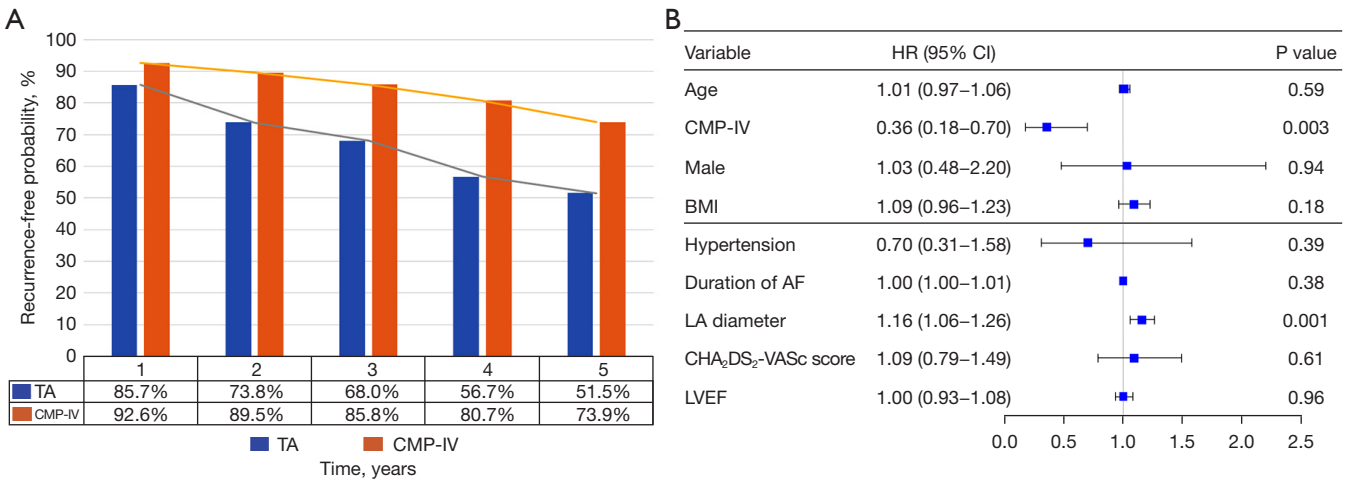

Figure 3 There was no significant difference in freedom from recurrence between the two groups at only 1 year (A). Using multivariable COX regression to adjust for clinically relevant covariates revealed that CMP-IV was associated with decreased risk of recurrence, and increased left atrial size were independent predictors of postoperative recurrence (B). TA, thoracoscopic ablation; CMP-IV, Cox-Maze IV procedure; HR, hazard ratio; CI, confidence interval; BMI, body mass index; AF, atrial fibrillation; LA, left atrium; CHA_2DS_2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, stroke or transient ischemic attack, vascular disease, age, and sex category; LVEF, left ventricular ejection fraction.

minimally invasive AF surgery, where anatomical constraints come into play, left atrial ablation combined with the Dallas lesion is undertaken. Nevertheless, we advocate for proactive exploration of appropriate methods for right atrial ablation in minimally invasive surgery (17). We caution against indiscriminate addition of ablation lines for right atrial ablation, as this has the potential to harm healthy atrial tissue. Such an approach may not necessarily enhance treatment success rates and could contribute to an increased incidence of postoperative atrial tachycardia or persistent AF (18).

The efficacy of TA as a stand-alone treatment for AF is currently inferior to that of the classic Cox-Maze procedure IV. However, this may be improved through several means, including enhancing the quality of ablation, refining the ablation route, and carefully selecting patients for treatment. Furthermore, there remains room for enhancing the minimally invasive nature of CMP-IV, ultimately improving the quality of life for patients with AF.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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