

The Belgian experience with concomitant surgical ablation of atrial
fibrillation: a multi-centre prospective registry

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The Belgian Experience with Concomitant Surgical Ablation of Atrial Fibrillation: a Multi-Centre Prospective Registry

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Abstract:	<p>Background The Belgian 'National Institute for Health and Disability Insurance (RIZIV-INAMI)' requested prospective collection of data on all ablations in Belgium to determine the outcomes of surgical ablation of atrial fibrillation (AF) during concomitant cardiac surgery.</p> <p>Methods 890 patients undergoing concomitant ablation for AF between 2011 and 2016 were prospectively followed. Freedom from AF with and without anti-arrhythmic drugs was calculated for 817 patients with follow-up beyond the 3-month blanking period and for 574 patients with sufficient rhythm-related follow-up consisting of at least one Holter registration or a skipped Holter due to AF being evident on ECG. Besides preoperative AF type, concomitant procedure and ablation, potential covariates were entered into uni- and multivariable regression models to determine predictors of outcome.</p> <p>Results The overall freedom from AF beyond 3 months was 69.9% (571/817) and without anti-arrhythmic drugs at last follow-up 51.0% (417/817), respectively 61.3% (352/574) and 44.4% (255/574) for patients with sufficient rhythm-related follow-up. Using a Kaplan-Meier estimate, freedom from AF was 89.3%, 74.9% and 59%, without antiarrhythmic drugs 74.4%, 47.8% and 32.3% at 6, 12 and 24 months, respectively. In-hospital mortality was 1.7% (15/890) and overall survival was 95.0% at 1 year and 92.3% at 2 years. Preoperative left atrial diameter and AF type were significant predictive factors of freedom from AF in a multivariable analysis.</p>

	<p>Conclusion</p> <p>Analysis of the Belgian national registry shows that concomitant surgical ablation of atrial fibrillation is safe, achieves favorable freedom from AF and therefore deserves to be performed in accordance to the guidelines.</p>
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The Belgian Experience with Concomitant Surgical Ablation of Atrial Fibrillation: A Multi-Centre Prospective Registry

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Author Statement and Conflicts of Interest

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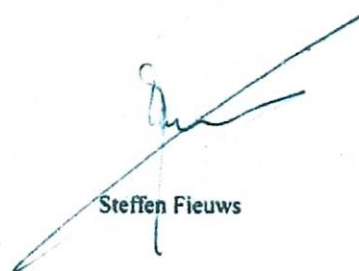
None of the authors have a conflict of interest to declare.



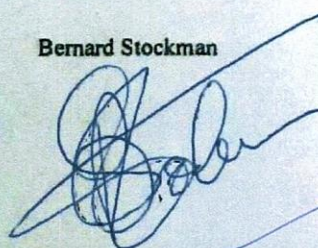
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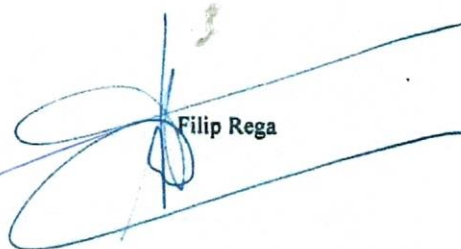
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Background

The Belgian 'National Institute for Health and Disability Insurance (RIZIV-INAMI)' requested prospective collection of data on all ablations in Belgium to determine the outcomes of surgical ablation of atrial fibrillation (AF) during concomitant cardiac surgery.

Methods

890 patients undergoing concomitant ablation for AF between 2011 and 2016 were prospectively followed. Freedom from AF with and without anti-arrhythmic drugs was calculated for 817 patients with follow-up beyond the 3-month blanking period and for 574 patients with sufficient rhythm-related follow-up consisting of at least one Holter registration or a skipped Holter due to AF being evident on ECG. Besides preoperative AF type, concomitant procedure and ablation, potential covariates were entered into uni- and multivariable regression models to determine predictors of outcome.

Results

The overall freedom from AF beyond 3 months was 69.9% (571/817) and without anti-arrhythmic drugs at last follow-up 51.0% (417/817), respectively 61.3% (352/574) and 44.4% (255/574) for patients with sufficient rhythm-related follow-up. Using a Kaplan-Meier estimate, freedom from AF was 89.3%, 74.9% and 59%, without antiarrhythmic drugs 74.4%, 47.8% and 32.3% at 6, 12 and 24 months, respectively. In-hospital mortality was 1.7% (15/890) and overall survival was 95.0% at 1 year and 92.3% at 2 years. Preoperative left atrial diameter and AF type were significant predictive factors of freedom from AF in a multivariable analysis.

Conclusion

Analysis of the Belgian national registry shows that concomitant surgical ablation of atrial fibrillation is safe, achieves favorable freedom from AF and therefore deserves to be performed in accordance to the guidelines.

Keywords

Ablation; Arrhythmia surgery; Atrial fibrillation; Maze procedure; Surgical ablation

Abbreviations

AAD = antiarrhythmic drug; ACD = anticoagulant drug; AF = atrial fibrillation; CM-IV = Cox-Maze IV ablation; LAA = left atrial appendage; LAD = left atrial diameter; LVEF = left ventricular ejection fraction; RF = radiofrequency; STAF = surgical treatment of atrial fibrillation; SR = sinus rhythm

Word count: 5251

Introduction

Since the first results of surgical treatment of atrial fibrillation (STAF) were published by James Cox in 1987 using the ‘cut-and-sew’ technique, STAF has evolved through multiple iterations [1,2]. Concomitant STAF using modern ablation devices has proven to increase long-term survival and decrease the incidence of stroke without increasing short-term mortality [3–6]. The Cox maze IV procedure, currently the gold standard for the treatment of AF, consisting of bipolar radiofrequency lesions and cryothermal ablation, produces equivalent rates of freedom of AF with less perioperative complications and shorter bypass and cross-clamp times than the ‘cut-and-sew’ Cox maze III procedure [7]. Both the most recent Heart Rhythm Society (HRS) and Society of Thoracic Surgeons (STS) guidelines recommend STAF with variable levels of evidence depending on, amongst others, the concomitant procedure [8,9]. Various renditions of the Cox-Maze procedure and derived lesion sets are still in use, complicating comparison of outcomes between clinical trials. Furthermore, the effectivity of commercially available ablation devices and their mutual differences remain uncertain. The safety and efficacy of STAF as performed throughout Belgium had never been investigated. Aforementioned considerations led to the inception of the ‘Belgian Atrial Fibrillation Management Database’, initiated by the National Institute for Health and Disability Insurance (RIZIV-INAMI) and carried out by the Belgian Association for CardioThoracic Surgery (BACTS). The retrospective analysis of this multi-centric, prospectively collected database is hereby presented.

Methods

Study design

Data was collected in 28 centres performing cardiac surgery throughout Belgium between November 2011 and June 2016 after obtaining informed consent from all patients. All

patients with preoperative AF undergoing cardiac surgery were eligible while ablations were performed at the indication of the referring cardiologist or the performing surgeon without central protocol prescription or limit to the extent of concomitant surgery. Permanent AF for more than 5 years, preoperative left atrial diameter (LAD) > 65mm, a percutaneous ablation during the same hospitalization and isolated right-sided ablations were exclusion criteria. Three follow-up visits (6, 12, 24 ± 3 months), at least one transthoracic echocardiography and one 24-hour Holter monitoring were mandatory.

Surgical techniques and postoperative care

Devices using bipolar or unipolar radiofrequency, cryotherapy or microwave ablation, and combinations were used. Procedural data, ablation lines and Left Atrial Appendage (LAA) management were registered. Postoperative management of anti-arrhythmic drugs (AADs) and anticoagulant drugs (ACDs) was up to the surgeon and after discharge, up to the referring cardiologist.

Study end-points

End-points were defined retrospectively while adhering to the 2017 HRS/EHRA/ECAS guidelines [8]. The primary efficacy end-point was freedom from AF beyond a 3-month blanking period with recurrence defined as the detection of AF or flutter lasting greater than 30 seconds on 24-hour Holter monitoring, ECG or rhythm strip, or by documented cardioversion or additional percutaneous ablation. The secondary efficacy end-point was freedom from AF beyond 3 months without the need for class I or III AADs. The primary safety end-point was in-hospital mortality. Additional secondary end-points are the incidence of postoperative complications, permanent pacemaker implantation both in-hospital and during follow-up, and AAD and ACD status at follow-up.

Data analysis

Demographic and procedural variables and in-hospital outcomes were registered for the total population (n=890). Freedom from AF was first calculated for patients with follow-up beyond 3 months (n=817), referred to as “patients beyond blanking period”. Freedom from AF was also calculated in patients with at least one Holter registration beyond 3 months or for whom a scheduled Holter was skipped due to AF being evident on ECG (n=574), referred to as “patients with rhythm follow-up”. The primary and secondary efficacy end-point were calculated in 2 ways. First, recurrences beyond 3 months were analyzed regardless of when recurrence occurred, resulting in an observed percentage for freedom from AF with and without taking AAD at last follow-up. Next, a Kaplan-Meier analysis was performed using the first detection of AF beyond 3 months to estimate freedom from AF with and without continuation of AADs.

We considered three variables to be the main possible determinants of the primary end-point: type of atrial fibrillation being paroxysmal or non-paroxysmal (persistent and long-standing persistent) as specified by the referring cardiologist, the concomitant procedure being mitral or non-mitral and the type of lesion set used. Based on the registered ablation lines, ablations were retrospectively divided into three categories: a true full Cox Maze IV ablation with the coronary sinus lesion being optional [10], ablations including a Box lesion regardless of additional left- or right-sided lesions and ablations including PVI only. LAA management was not mandatory and therefore not used to categorize patients. We reported outcomes of the total population and for subgroups based on these three variables.

Comparison of categorical variables between subgroups was performed using χ^2 or Fisher's exact tests while continuous variables were analyzed using Mann-Whitney U and Kruskal-Wallis tests.

Uni- and multivariable regression analyses were performed to identify variables associated with freedom from AF. Cox regression and logistic regression were used with and without taking into account the timing of the first recurrence, respectively. The three main variables were entered into the model together with patient age, sex, preoperative duration of AF, preoperative LAD and LVEF, preoperative pacemaker status, previous rhythm related intervention and energy source used for ablation. No model reduction strategies were considered. Via the multivariable regression models, we investigated whether the potential effect of the three main determinants was maintained when correcting for these covariates and additionally, by adding interactions in the model, whether the effect of each of the three main predictors depended on the level of another variable. Patient survival during follow-up was plotted using a Kaplan-Meier curve. All analyses were performed using SAS software, version 9.4 of the SAS System for Windows.

Results

Baseline characteristics

Between November 2011 and June 2016, 890 patients were included in 28 cardiac centers. 817 patients had follow-up beyond 3 months and 42.1% (344/817) received 3 or more follow-up assessments. 70.3% (574/817) had sufficient rhythm follow-up as they underwent at least one 24h Holter monitoring (64.3%, 525/817) or skipped a scheduled Holter due to AF being evident on ECG (14.2%, 116/817). The average age at operation was 68.4 ± 9.4 years, 59.9% (533/890) of all patients were male and 52.4% (467/890) of patients undergoing ablation presented with paroxysmal AF. A full overview of preoperative characteristics for the total population (n=890), patients beyond blanking period (n=817) and patients with rhythm follow-up (n=574) is shown in Table 1. Demographic tables for subgroups are presented in the supplementary appendix.

Surgical procedure and postoperative care

63.6% (566/890) underwent a concomitant mitral operation. The type of lesion set was a true CM-IV in 24.8% (221/890) of cases while 45.8% (408/890) underwent an ablation including a box lesion and 29.4% (261/890) underwent an ablation including PVI. A true CM-IV was performed significantly more often in patients with non-paroxysmal AF (33.8% vs 16.9% for paroxysmal AF, $P < 0.001$) and in patients undergoing concomitant mitral valve surgery (31.6% vs 13% for non-mitral, $P < 0.001$). For patients undergoing non-mitral operations, mainly ablations including PVI (65.1%, 211/324) were performed. A bipolar RF energy source (with or without adjuncts) was used in 69.4 % (618/890) while cryoablation alone was used in 27.4% (244/890). Left atrial appendage closure was performed in 69.1% (615/890) of patients and external closure was used most frequently (38.9%, 239/615). A complete overview of procedural variables is provided in Table 2 with data on the subgroups available in the supplementary appendix. 32.1% (281/875) of in-hospital survivors were discharged on prophylactic AADs while not taking them preoperatively and ACDs were given for the first time postoperatively in 25.9% (227/875). On the whole, 62.5% (547/875) of all patients were discharged on AADs and 77.1% (675/875) on ACDs.

Adverse events and survival

For the total population, in-hospital mortality was 1.7% (15/890) and postoperative bleeding requiring revision occurred in 1.4% (12/890) while acute conduction block was seen in 2.3% (20/890). When looking within subgroups, both reoperation for bleeding and acute conduction block were more frequent in patients with non-paroxysmal AF, in those undergoing mitral operations and those undergoing a full CM-IV lesion set. All in-hospital results are shown in Table 3, with tables for the subgroups in the appendix. Using a Kaplan-Meier curve, overall survival during follow-up was 96.5%, 95% and 92.3% at 6, 12 and 24

months with N at risk 731, 527 and 170, respectively. There were no significant differences for in-hospital mortality and overall survival within any subgroup based on preoperative AF classification, concomitant operation or extent of the ablation (supplementary appendix).

Rhythm-related outcomes

At discharge, significantly more patients in the total population and all subgroups were in sinus rhythm (SR) compared to preoperatively (75.5 versus 46.6%, $P < 0.001$). In-hospital, 4.6% (41/890) of patients underwent a postoperative cardioversion and 3.7% (33/890) received a permanent pacemaker. After discharge, 8.0% (65/817) of patients beyond blanking period, underwent an additional cardioversion, 6.4% (52/817) received a permanent pacemaker and 4.2% (34/817) of all patients required an additional percutaneous ablation. When combining hospital stay and follow-up period, implantation of a permanent pacemaker was performed in 9.8% of all patients (80/817). The total pacemaker implantation rate was significantly greater for patients with non-paroxysmal AF and for those undergoing mitral surgery or a full CM-IV ablation when combined to their respective counterparts. An overview of rhythm-related events during follow-up for all groups is shown in the supplementary appendix.

Freedom from AF beyond 3 months regardless of precise timing (Figure 1) was 69.9% (571/817) and without taking AADs at last follow-up 51.0% (417/817). For patients with rhythm follow-up (Figure 1', supplementary appendix), overall freedom from AF was 61.3% (352/574) and without need for AADs 44.4% (255/574). Using a Kaplan-Meier estimate, freedom from AF for patients beyond blanking period was 89.3%, 74.9% and 59% and without AADs 74.4%, 47.8% and 32.3% at 6, 12 and 24 months respectively. For patients beyond blanking period, Kaplan-Meier estimates for freedom from AF were 87.3%,

69.8% and 51.4% and without AADs 72.3%, 44.0% and 27.4% at 6, 12 and 24 months, respectively.

Patients with paroxysmal AF displayed greater overall freedom from AF than those with non-paroxysmal AF (75.7% vs 63.4% overall, $P<0.001$) for overall freedom from AF and the difference was also significant between the Kaplan-Meier curves. Patients undergoing mitral surgery displayed lower overall freedom from AF than those undergoing non-mitral surgery (65.6% vs 77.5% overall, $P<0.001$), also significantly different between Kaplan-Meier curves. For the mixed group of patients beyond blanking period, the more extensive ablations did not show significantly greater overall freedom from AF. Overall percentages and Kaplan-Meier curves for freedom from AF are available in the supplementary appendix.

Results from the uni- and multivariable logistic regression models for overall freedom from AF and from the Cox regression models are shown in Tables 4 and 5, respectively, for patients with follow-up beyond blanking period and in the appendix for patients with rhythm follow-up. Preoperative LAD and type of AF consistently emerge as significantly associated with freedom from AF both with and without continuation of AADs. No interactions were withheld between the effect of the three main predictors or between each of the main predictors and covariates.

At last follow-up, 29.6% (242/817) was still taking AADs, compared to 40.9% (364/890) preoperatively and 62.5% (547/875) at discharge. At last follow-up, patients free from AF were on AADs less frequently compared to those with recurrent AF (27% (154/571) versus 35.5% (87/245), $P=0.014$). 55.9% (457/817) was still taking ACDs at last follow-up, compared to 58.3% (519/890) preoperatively and 77.1% (675/875) at discharge. Patients free from AF were on ACDs less frequently at last-follow-up compared to those with recurrent AF (50.8% (290/571) versus 67.7% (166/245), $P<0.001$).

Discussion

We have presented the outcomes of surgical ablation for atrial fibrillation of a large and heterogeneous cohort employing data collected throughout 28 centres in Belgium over a period of nearly 5 years. Our data show that STAF as performed throughout Belgium is safe and effective. In our subgroup and regression analyses, we reveal factors associated with AF recurrence and enable extrapolation of our data to multiple patient populations with regards to AF classification, concomitant procedures and lesion sets. Our stratification of AF type and concomitant procedure follows recent guidelines that use these variables to determine the indication for concomitant ablation [8,9]. We limit our division of AF type into only paroxysmal and non-paroxysmal and this seems reasonable as 2017 HRS guidelines have identical recommendations for persistent and long-standing persistent AF. We focus on 3 frequently investigated lesion sets: a full CM-IV, a Box lesion and only PVI. Additional left- or right-sided lesions were disregarded for the last 2 groups as preliminary analysis revealed pronounced heterogeneity in these lesions, limiting the ability to draw useful conclusions.

Baseline characteristics and surgical procedures

With regards to both preoperative patient characteristics and procedural variables, our cohort approaches previous reports [5,10–16]. Of note, we observe a heterogeneous mix of ablations with 45.8% (408/890) using a Box lesion and a lesser proportion of full CM-IV ablations (24.8%, 221/890) while the latter is overrepresented in the literature. Although LAA exclusion is recommended by recent STS guidelines and by other authors in all cases of STAF as it reduces stroke incidence and increases overall survival after STAF, it is performed in only 69.1% (615/890) of all patients in our database with variable percentages for subgroups [9,17].

Safety and Survival

Untreated AF decreases postoperative survival whereas concomitant STAF performed in recent times has shown to increase long-term survival and lower stroke incidence without increasing short-term morbidity or mortality [3–6]. Although only a limited number of complications were registered, we observe a low incidence of reoperation for bleeding and in-hospital mortality, 1.35% (12/890) and 1.7% (15/890) respectively, in the total population compared to an incidence of 4-8.9% for reoperation due to bleeding and 1.2-5.9% for early mortality in trials with diverse populations [3,4,13,15,16,18]. As we have limited information about the preoperative functional status, selection bias and our trial setup may influence results. We estimated overall survival to be 95.0% at 1 year and 92.3% at 2 years using a Kaplan-Meier analysis, parallel with the 94.9% survival at 1 year and 91.1% survival at 2 years reported by Pecha [18] and Attaran [3] respectively for similar mixed cohorts undergoing concomitant ablation [3,18]. There was no significant difference between any of the subgroups with regards to in-hospital mortality, reoperation for bleeding or overall survival despite significant differences in demographic and procedural variables related to increased perioperative risk.

Freedom from AF and other rhythm-related outcomes

Other trials with similar populations as well as a meta-analysis, report freedom from AF at 1 year between 59.9% and 76%, similar to our 69.9% overall for the total population and 74.9% at 1 year in the Kaplan-Meier analysis [4,16,18,19]. As in our study, preoperative paroxysmal AF is often withheld as being predictive of freedom from AF [13,18,19].

Throughout the literature, preoperative LAD also emerges as a predictive factor related to the substrate of AF and along with AF type, it was the only variable consistently associated with freedom from AF in the regression analyses [12,13,20].

Commonly cited rates for freedom from AF at 1 year for patients undergoing a CM-IV ablation during mitral valve surgery vary between 66 and 93% [10–14,21,22]. In a meta-analysis including trials with variable ablations during mitral valve surgery, 75.5% of patients were free from AF at 1 year, similar to our 73% at 1 year for all patients undergoing mitral valve surgery [15]. For patients undergoing non-mitral surgery, published numbers vary between 58.7% and 86.2%, compared to our 78.4% freedom from AF at 1 year [16,23]. This effect based on AF type and concomitant procedure is likely related to the worse substrate of AF in these groups.

There is considerable evidence indicating that a more complete left-sided ablation as well as the addition of right-sided lesions [13,16,18,19,21,23,24] yields lower recurrence rates, especially for persistent or permanent AF or AF related to mitral valve pathology. However, it remains uncertain which specific lesion set is indicated based on a patient's preoperative AF type and concomitant procedure [9,16,18,19]. In our study, the more extensive ablations were not consistently associated with greater freedom from AF. Nonetheless, our results appear to favour more extensive ablations as these were not associated with increased morbidity or mortality while producing similar or better results for patients with more severe forms of AF.

While surgical ablation appears to increase the need for postoperative pacemaker implantation [5,6,13,22], more so for biatrial ablations [24], this effect is also related to the substrate of AF as ablation can unmask underlying sinus node dysfunction [1]. Need for in-hospital implantation of a permanent pacemaker was favourable in our study at 3.7% (33/890), compared to rates between 6.8 and 22.9% after CM-IV ablation [5,10,13,14] and 3.1-6% after left-sided ablations [16,20]. Overall need for a permanent pacemaker was 9.7% (87/890) and significantly higher in patients with non-paroxysmal AF, patients undergoing mitral valve surgery and those undergoing a full CM-IV ablation.

Postoperative management and follow-up

At last follow-up, only 29.6% (242/817) was on AADs and 55.9% (457/817) on anticoagulant drugs, compared to 62.5% (547/875) and 77.1% (675/875) respectively at discharge. This is in accordance with current guidelines and shows that ablation allows a significant proportion of patients to quit AADs and ACDs [8,9].

Strengths and limitations

The strength of this study lies in the size of the database and while data registry and follow-up violated protocol, our study reflects real life clinical practice in a complicated domain, emphasizing the need for further investigation with attention to subgroups. Our definition of the primary end-point considers any episode of AF beyond 3 months as permanent treatment failure while we do not know if some patients display durable freedom from AF after an initial recurrence[8]. Inadvertently, some event times were treated as actual event times in the construction of the Kaplan-Meier curves while in reality they were interval-censored, occurring somewhere between two follow-up visits. While guidelines advocate regular Holter assessment or monitoring of AF burden in all patients, only 64.3% (525/817) were evaluated by 24h Holter [9]. When calculating freedom from AF for all patients beyond blanking period, absent follow-up implies the absence of recurrence, potentially underestimating recurrence. However, we also report freedom from AF for patients with rhythm follow-up and we believe this second approach overestimates the true AF recurrence because patients in AF are likely overreported in the database. As shown in Tables 1-3, no differences in preoperative and procedural variables were observed between the total population, patients beyond blanking period and patients with rhythm follow-up. As expected, freedom from AF was 5-10% lower for the 574 patients with rhythm follow-up in both calculations yet the relationships between subgroups are comparable and the same predictors of freedom from AF

are withheld. We believe that when combined, both approaches reliably represent the true spectrum of freedom from AF in our population.

Conclusion

This retrospective analysis of the prospectively collected 'Belgian Atrial Fibrillation Management Database' proves that on the whole, surgical treatment of atrial fibrillation as performed throughout Belgium is safe both in the short- and long-term and achieves favourable freedom from AF between 6 and 24 months in a cohort with various types of preoperative AF, concomitant procedures and types of ablation. Preoperative left atrial diameter and AF type were predictive of freedom from AF in regression analysis. None withstanding its limitations, we believe this report, when correlated with other recent data on the safety of STAF, reliably supports the message that concomitant STAF should be performed in accordance with the guidelines. Our study emphasizes the need for centralized, accurate registry of follow-up and analysis of outcomes according to relevant subgroups.

Table and table captions

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow-Up (n=574)
Age	68.9 ± 9.4	68.7 ± 9.3	68.7 ± 9.2
Male	59.9 (533)	60.1 (491)	61.2 (351)
AF duration (y)	2.4 ± 3.3	2.4 ± 3.3	2.4 ± 3.3
Paroxysmal AF	52.5 (467)	53.5 (437)	51.9 (298)
LVEF	55.0 ± 13.8	55.2 ± 13.7	55.7 ± 13.6
LAD (mm)	47.9 ± 8.6	47.8 ± 8.7	47.7 ± 8.8
Previous embolism	9.1 (81)	8.8 (72)	9.4 (54)
Previous ablation	4 (36)	4.2 (34)	4.2 (24)
Using AADs	40.9 (364)	40.6 (332)	39.2 (225)
Using ACDs	58.3 (519)	58.4 (477)	62.0 (356)
SR preop	46.6 (415)	47.6 (389)	46.9 (269)
Mitral surgery	63.6 (566)	64.1 (524)	63.2 (363)
Ablation			
Full Cox Maze IV	24.8 (221)	25.5 (208)	25.4 (146)
Box ± more	45.8 (408)	45.5 (372)	45.6 (262)
PVI ± more	29.3 (261)	29.0 (237)	28.9 (166)

Table 1. Preoperative characteristics of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow-Up (n=574)
Sternotomy	80.8 (719)	80.7 (659)	80.8 (464)
Operation time (min)	253 ± 81.2	253 ± 80.5	252.4 ± 80.6
Bypass time (min)	144 ± 57	143 ± 57.2	144.3 ± 57.9
Cross clamp time (min)	97 ± 45.8	96 ± 44.9	97.1 ± 45.8
LAA exclusion	69.1 (615)	69.2 (565)	72.7 (417)
LAA management			
External Closure	38.9 (239)	39.3 (222)	38.6 (161)
Internal Closure	31.7 (195)	31.2 (176)	30.9 (129)
Resection	29.4 (181)	29.6 (167)	30.5 (127)
Energy source			
Bipolar RF	50.3 (448)	50.2 (410)	50.5 (290)
Cryotherapy	27.4 (244)	27.9 (228)	25.1 (144)
Bipolar RF and Cryotherapy	10.6 (94)	10.8 (88)	11.7 (67)
Bipolar and Unipolar RF	8.5 (76)	8.1 (66)	9.2 (53)
Other	3.2 (28)	3.1 (25)	3.5 (20)

Table 2. Procedural variables of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow- Up (n=574)
Length of stay (d)	13.8 ± 18.2	13.2 ± 17	13.2 ± 18.1
Bleeding	1.4 (12)	1.4 (11)	1.1 (6)
Block	2.3 (20)	2.1 (17)	2.1 (12)
In-hospital mortality	1.7 (15)		
Cardioversion	4.6 (41)	4.5 (37)	3.7 (21)
New permanent pacemaker	3.7 (33)	3.4 (28)	3.3 (19)
SR at discharge	75.5 (661)	75.6 (618)	75.4 (433)

Table 3. In-hospital outcomes of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Univariable model		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	0.99 (0.98-1.01)	0.283	0.99 (0.98-1.01)	0.705
Female	1.17 (0.86-1.59)	0.307	0.99 (0.71-1.4)	0.974
AF duration (y)	0.98 (0.93-1.02)	0.313	0.98 (0.93-1.03)	0.446
Paroxysmal AF	0.55 (0.41-0.75)	<.001	0.6 (0.43-0.84)	0.003
LVEF	0.999 (0.99-1.01)	0.886	1 (0.99-1.02)	0.559
LAD (mm)	1.05 (1.02-1.07)	<.001	1.03 (1.01-1.05)	0.004
Previous ablation	0.97 (0.46-2.07)	0.943	1.19 (0.53-2.68)	0.671
Pacemaker pre-op	1.64 (0.75-3.58)	0.218	1.72 (0.76-3.91)	0.194
Mitral surgery	1.79 (1.29-2.48)	<.001	1.52 (0.95-2.43)	0.079
Ablation		0.026		0.445
Box ± more	1.62 (1.12-2.33)	0.010	1.12 (0.69-1.8)	0.656
Full Cox Maze IV	1.2 (0.78-1.83)	0.411	0.83 (0.47-1.48)	0.533
Energy source		0.002		0.013
Bipolar	0.35 (0.16-0.79)	0.012	0.43 (0.18-1.02)	0.055
Bi- and unipolar	0.82 (0.33-2.06)	0.669	0.74 (0.29-1.92)	0.539
Bipolar and Cryo	0.28 (0.11-0.7)	0.007	0.31 (0.11-0.85)	0.023
Cryo	0.39 (0.17-0.89)	0.026	0.33 (0.14-0.79)	0.013

Table 4. Results of uni- and multivariable logistic regression models for overall freedom from AF for patients with follow-up beyond the 3-month blanking period (n=817) with odds ratios for recurrence of AF.

	Univariable model		Multivariable model	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Age	0.99 (0.98-1.01)	0.669	0.99 (0.99-1.01)	0.914
Female	1.12 (0.87-1.45)	0.383	1.04 (0.78-1.38)	0.781
AF duration (y)	0.98 (0.94-1.02)	0.273	0.98 (0.94-1.03)	0.441
Paroxysmal AF	0.66 (0.51-0.85)	0.001	0.67 (0.51-0.89)	0.005
LVEF	0.99 (0.99-1.01)	0.888	1.00 (0.99-1.01)	0.432
LAD (mm)	1.03 (1.02-1.05)	<.001	1.03 (1.01-1.04)	0.004
Previous ablation	0.77 (0.41-1.46)	0.421	0.90 (0.46-1.76)	0.761
Pacemaker pre-op	1.59 (0.87-2.92)	0.131	1.65 (0.89-3.05)	0.111
Mitral surgery	1.41 (1.06-1.87)	0.019	1.40 (0.95-2.07)	0.093
Ablation		0.436		0.541
Box ± more	1.18 (0.86-1.61)	0.301	0.87 (0.59-1.30)	0.501
Full Cox Maze IV	0.99 (0.69-1.44)	0.988	0.77 (0.48-1.23)	0.269
Energy source		0.068		0.096
Bipolar	0.66 (0.37-1.18)	0.164	0.75 (0.41-1.38)	0.360
Bi- and unipolar	0.99 (0.51-1.90)	0.971	0.92 (0.47-1.80)	0.817
Bipolar and Cryo	0.47 (0.23-0.95)	0.036	0.49 (0.23-1.03)	0.061
Cryo	0.65 (0.36-1.18)	0.159	0.60 (0.32-1.11)	0.103

Table 5. Results of uni- and multivariable Cox regression models for Kaplan-Meier estimate of freedom from AF for patients with follow-up beyond the 3-month blanking period (n=817) with hazard ratios for recurrence of AF.

Figures

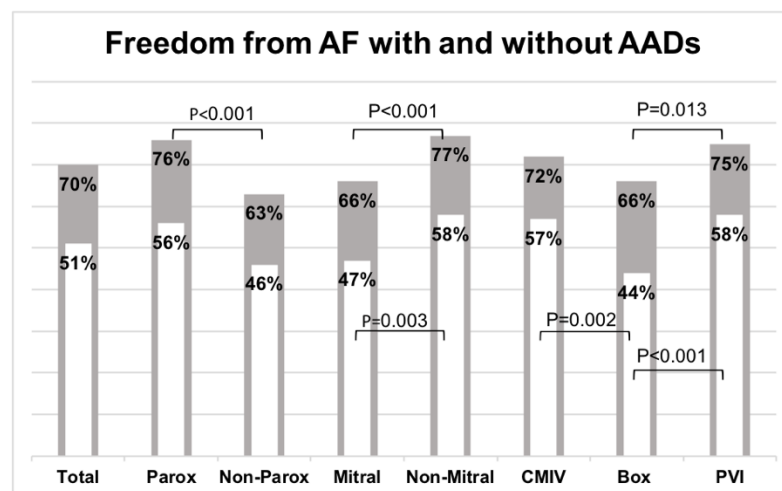


Figure 1. Overall freedom from AF with and without (inlaying white bars) continuation of AADs for patients with follow-up beyond the 3-month blanking period (n=817). Statistical comparison was performed using a Fisher's Exact test and significant differences are indicated with brackets.

The Belgian Experience with Concomitant Surgical Ablation of Atrial Fibrillation: A Multi-Centre Prospective Registry

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The Belgian Experience with Concomitant Surgical Ablation of Atrial Fibrillation: A Multi-Centre Prospective Registry

Background

The Belgian 'National Institute for Health and Disability Insurance (RIZIV-INAMI)' requested prospective collection of data on all ablations in Belgium to determine the outcomes of surgical ablation of atrial fibrillation (AF) during concomitant cardiac surgery.

Methods

890 patients undergoing concomitant ablation for AF between 2011 and 2016 were prospectively followed. Freedom from AF with and without anti-arrhythmic drugs was calculated for 817 patients with follow-up beyond the 3-month blanking period and for 574 patients with sufficient rhythm-related follow-up consisting of at least one Holter registration or a skipped Holter due to AF being evident on ECG. Besides preoperative AF type, concomitant procedure and ablation, potential covariates were entered into uni- and multivariable regression models to determine predictors of outcome.

Results

The overall freedom from AF beyond 3 months was 69.9% (571/817) and without anti-arrhythmic drugs at last follow-up 51.0% (417/817), respectively 61.3% (352/574) and 44.4% (255/574) for patients with sufficient rhythm-related follow-up. Using a Kaplan-Meier estimate, freedom from AF was 89.3%, 74.9% and 59%, without antiarrhythmic drugs 74.4%, 47.8% and 32.3% at 6, 12 and 24 months, respectively. In-hospital mortality was 1.7% (15/890) and overall survival was 95.0% at 1 year and 92.3% at 2 years. Preoperative left atrial diameter and AF type were significant predictive factors of freedom from AF in a multivariable analysis.

Conclusion

Analysis of the Belgian national registry shows that concomitant surgical ablation of atrial fibrillation is safe, achieves favorable freedom from AF and therefore deserves to be performed in accordance to the guidelines.

Keywords

Ablation; Arrhythmia surgery; Atrial fibrillation; Maze procedure; Surgical ablation

Abbreviations

AAD = antiarrhythmic drug; ACD = anticoagulant drug; AF = atrial fibrillation; CM-IV = Cox-Maze IV ablation; LAA = left atrial appendage; LAD = left atrial diameter; LVEF = left ventricular ejection fraction; RF = radiofrequency; STAF = surgical treatment of atrial fibrillation; SR = sinus rhythm

Word count: 5251

Introduction

Since the first results of surgical treatment of atrial fibrillation (STAF) were published by James Cox in 1987 using the ‘cut-and-sew’ technique, STAF has evolved through multiple iterations [1,2]. Concomitant STAF using modern ablation devices has proven to increase long-term survival and decrease the incidence of stroke without increasing short-term mortality [3–6]. The Cox maze IV procedure, currently the gold standard for the treatment of AF, consisting of bipolar radiofrequency lesions and cryothermal ablation, produces equivalent rates of freedom of AF with less perioperative complications and shorter bypass and cross-clamp times than the ‘cut-and-sew’ Cox maze III procedure [7]. Both the most recent Heart Rhythm Society (HRS) and Society of Thoracic Surgeons (STS) guidelines recommend STAF with variable levels of evidence depending on, amongst others, the concomitant procedure [8,9]. Various renditions of the Cox-Maze procedure and derived lesion sets are still in use, complicating comparison of outcomes between clinical trials. Furthermore, the effectivity of commercially available ablation devices and their mutual differences remain uncertain. The safety and efficacy of STAF as performed throughout Belgium had never been investigated. Aforementioned considerations led to the inception of the ‘Belgian Atrial Fibrillation Management Database’, initiated by the National Institute for Health and Disability Insurance (RIZIV-INAMI) and carried out by the Belgian Association for CardioThoracic Surgery (BACTS). The retrospective analysis of this multi-centric, prospectively collected database is hereby presented.

Methods

Study design

Data was collected in 28 centres performing cardiac surgery throughout Belgium between November 2011 and June 2016 after obtaining informed consent from all patients. All

patients with preoperative AF undergoing cardiac surgery were eligible while ablations were performed at the indication of the referring cardiologist or the performing surgeon without central protocol prescription or limit to the extent of concomitant surgery. Permanent AF for more than 5 years, preoperative left atrial diameter (LAD) > 65mm, a percutaneous ablation during the same hospitalization and isolated right-sided ablations were exclusion criteria. Three follow-up visits (6, 12, 24 ± 3 months), at least one transthoracic echocardiography and one 24-hour Holter monitoring were mandatory.

Surgical techniques and postoperative care

Devices using bipolar or unipolar radiofrequency, cryotherapy or microwave ablation, and combinations were used. Procedural data, ablation lines and Left Atrial Appendage (LAA) management were registered. Postoperative management of anti-arrhythmic drugs (AADs) and anticoagulant drugs (ACDs) was up to the surgeon and after discharge, up to the referring cardiologist.

Study end-points

End-points were defined retrospectively while adhering to the 2017 HRS/EHRA/ECAS guidelines [8]. The primary efficacy end-point was freedom from AF beyond a 3-month blanking period with recurrence defined as the detection of AF or flutter lasting greater than 30 seconds on 24-hour Holter monitoring, ECG or rhythm strip, or by documented cardioversion or additional percutaneous ablation. The secondary efficacy end-point was freedom from AF beyond 3 months without the need for class I or III AADs. The primary safety end-point was in-hospital mortality. Additional secondary end-points are the incidence of postoperative complications, permanent pacemaker implantation both in-hospital and during follow-up, and AAD and ACD status at follow-up.

Data analysis

Demographic and procedural variables and in-hospital outcomes were registered for the total population (n=890). Freedom from AF was first calculated for patients with follow-up beyond 3 months (n=817), referred to as “patients beyond blanking period”. Freedom from AF was also calculated in patients with at least one Holter registration beyond 3 months or for whom a scheduled Holter was skipped due to AF being evident on ECG (n=574), referred to as “patients with rhythm follow-up”. The primary and secondary efficacy end-point were calculated in 2 ways. First, recurrences beyond 3 months were analyzed regardless of when recurrence occurred, resulting in an observed percentage for freedom from AF with and without taking AAD at last follow-up. Next, a Kaplan-Meier analysis was performed using the first detection of AF beyond 3 months to estimate freedom from AF with and without continuation of AADs.

We considered three variables to be the main possible determinants of the primary end-point: type of atrial fibrillation being paroxysmal or non-paroxysmal (persistent and long-standing persistent) as specified by the referring cardiologist, the concomitant procedure being mitral or non-mitral and the type of lesion set used. Based on the registered ablation lines, ablations were retrospectively divided into three categories: a true full Cox Maze IV ablation with the coronary sinus lesion being optional [10], ablations including a Box lesion regardless of additional left- or right-sided lesions and ablations including PVI only. LAA management was not mandatory and therefore not used to categorize patients. We reported outcomes of the total population and for subgroups based on these three variables.

Comparison of categorical variables between subgroups was performed using χ^2 or Fisher's exact tests while continuous variables were analyzed using Mann-Whitney U and Kruskal-Wallis tests.

Uni- and multivariable regression analyses were performed to identify variables associated with freedom from AF. Cox regression and logistic regression were used with and without taking into account the timing of the first recurrence, respectively. The three main variables were entered into the model together with patient age, sex, preoperative duration of AF, preoperative LAD and LVEF, preoperative pacemaker status, previous rhythm related intervention and energy source used for ablation. No model reduction strategies were considered. Via the multivariable regression models, we investigated whether the potential effect of the three main determinants was maintained when correcting for these covariates and additionally, by adding interactions in the model, whether the effect of each of the three main predictors depended on the level of another variable. Patient survival during follow-up was plotted using a Kaplan-Meier curve. All analyses were performed using SAS software, version 9.4 of the SAS System for Windows.

Results

Baseline characteristics

Between November 2011 and June 2016, 890 patients were included in 28 cardiac centers. 817 patients had follow-up beyond 3 months and 42.1% (344/817) received 3 or more follow-up assessments. 70.3% (574/817) had sufficient rhythm follow-up as they underwent at least one 24h Holter monitoring (64.3%, 525/817) or skipped a scheduled Holter due to AF being evident on ECG (14.2%, 116/817). The average age at operation was 68.4 ± 9.4 years, 59.9% (533/890) of all patients were male and 52.4% (467/890) of patients undergoing ablation presented with paroxysmal AF. A full overview of preoperative characteristics for the total population (n=890), patients beyond blanking period (n=817) and patients with rhythm follow-up (n=574) is shown in Table 1. Demographic tables for subgroups are presented in the supplementary appendix.

Surgical procedure and postoperative care

63.6% (566/890) underwent a concomitant mitral operation. The type of lesion set was a true CM-IV in 24.8% (221/890) of cases while 45.8% (408/890) underwent an ablation including a box lesion and 29.4% (261/890) underwent an ablation including PVI. A true CM-IV was performed significantly more often in patients with non-paroxysmal AF (33.8% vs 16.9% for paroxysmal AF, $P < 0.001$) and in patients undergoing concomitant mitral valve surgery (31.6% vs 13% for non-mitral, $P < 0.001$). For patients undergoing non-mitral operations, mainly ablations including PVI (65.1%, 211/324) were performed. A bipolar RF energy source (with or without adjuncts) was used in 69.4 % (618/890) while cryoablation alone was used in 27.4% (244/890). Left atrial appendage closure was performed in 69.1% (615/890) of patients and external closure was used most frequently (38.9%, 239/615). A complete overview of procedural variables is provided in Table 2 with data on the subgroups available in the supplementary appendix. 32.1% (281/875) of in-hospital survivors were discharged on prophylactic AADs while not taking them preoperatively and ACDs were given for the first time postoperatively in 25.9% (227/875). On the whole, 62.5% (547/875) of all patients were discharged on AADs and 77.1% (675/875) on ACDs.

Adverse events and survival

For the total population, in-hospital mortality was 1.7% (15/890) and postoperative bleeding requiring revision occurred in 1.4% (12/890) while acute conduction block was seen in 2.3% (20/890). When looking within subgroups, both reoperation for bleeding and acute conduction block were more frequent in patients with non-paroxysmal AF, in those undergoing mitral operations and those undergoing a full CM-IV lesion set. All in-hospital results are shown in Table 3, with tables for the subgroups in the appendix. Using a Kaplan-Meier curve, overall survival during follow-up was 96.5%, 95% and 92.3% at 6, 12 and 24

months with N at risk 731, 527 and 170, respectively. There were no significant differences for in-hospital mortality and overall survival within any subgroup based on preoperative AF classification, concomitant operation or extent of the ablation (supplementary appendix).

Rhythm-related outcomes

At discharge, significantly more patients in the total population and all subgroups were in sinus rhythm (SR) compared to preoperatively (75.5 versus 46.6%, $P < 0.001$). In-hospital, 4.6% (41/890) of patients underwent a postoperative cardioversion and 3.7% (33/890) received a permanent pacemaker. After discharge, 8.0% (65/817) of patients beyond blanking period, underwent an additional cardioversion, 6.4% (52/817) received a permanent pacemaker and 4.2% (34/817) of all patients required an additional percutaneous ablation. When combining hospital stay and follow-up period, implantation of a permanent pacemaker was performed in 9.8% of all patients (80/817). The total pacemaker implantation rate was significantly greater for patients with non-paroxysmal AF and for those undergoing mitral surgery or a full CM-IV ablation when combined to their respective counterparts. An overview of rhythm-related events during follow-up for all groups is shown in the supplementary appendix.

Freedom from AF beyond 3 months regardless of precise timing (Figure 1) was 69.9% (571/817) and without taking AADs at last follow-up 51.0% (417/817). For patients with rhythm follow-up (Figure 1', supplementary appendix), overall freedom from AF was 61.3% (352/574) and without need for AADs 44.4% (255/574). Using a Kaplan-Meier estimate, freedom from AF for patients beyond blanking period was 89.3%, 74.9% and 59% and without AADs 74.4%, 47.8% and 32.3% at 6, 12 and 24 months respectively. For patients beyond blanking period, Kaplan-Meier estimates for freedom from AF were 87.3%,

69.8% and 51.4% and without AADs 72.3%, 44.0% and 27.4% at 6, 12 and 24 months, respectively.

Patients with paroxysmal AF displayed greater overall freedom from AF than those with non-paroxysmal AF (75.7% vs 63.4% overall, $P<0.001$) for overall freedom from AF and the difference was also significant between the Kaplan-Meier curves. Patients undergoing mitral surgery displayed lower overall freedom from AF than those undergoing non-mitral surgery (65.6% vs 77.5% overall, $P<0.001$), also significantly different between Kaplan-Meier curves. For the mixed group of patients beyond blanking period, the more extensive ablations did not show significantly greater overall freedom from AF. Overall percentages and Kaplan-Meier curves for freedom from AF are available in the supplementary appendix.

Results from the uni- and multivariable logistic regression models for overall freedom from AF and from the Cox regression models are shown in Tables 4 and 5, respectively, for patients with follow-up beyond blanking period and in the appendix for patients with rhythm follow-up. Preoperative LAD and type of AF consistently emerge as significantly associated with freedom from AF both with and without continuation of AADs. No interactions were withheld between the effect of the three main predictors or between each of the main predictors and covariates.

At last follow-up, 29.6% (242/817) was still taking AADs, compared to 40.9% (364/890) preoperatively and 62.5% (547/875) at discharge. At last follow-up, patients free from AF were on AADs less frequently compared to those with recurrent AF (27% (154/571) versus 35.5% (87/245), $P=0.014$). 55.9% (457/817) was still taking ACDs at last follow-up, compared to 58.3% (519/890) preoperatively and 77.1% (675/875) at discharge. Patients free from AF were on ACDs less frequently at last-follow-up compared to those with recurrent AF (50.8% (290/571) versus 67.7% (166/245), $P<0.001$).

Discussion

We have presented the outcomes of surgical ablation for atrial fibrillation of a large and heterogeneous cohort employing data collected throughout 28 centres in Belgium over a period of nearly 5 years. Our data show that STAF as performed throughout Belgium is safe and effective. In our subgroup and regression analyses, we reveal factors associated with AF recurrence and enable extrapolation of our data to multiple patient populations with regards to AF classification, concomitant procedures and lesion sets. Our stratification of AF type and concomitant procedure follows recent guidelines that use these variables to determine the indication for concomitant ablation [8,9]. We limit our division of AF type into only paroxysmal and non-paroxysmal and this seems reasonable as 2017 HRS guidelines have identical recommendations for persistent and long-standing persistent AF. We focus on 3 frequently investigated lesion sets: a full CM-IV, a Box lesion and only PVI. Additional left- or right-sided lesions were disregarded for the last 2 groups as preliminary analysis revealed pronounced heterogeneity in these lesions, limiting the ability to draw useful conclusions.

Baseline characteristics and surgical procedures

With regards to both preoperative patient characteristics and procedural variables, our cohort approaches previous reports [5,10–16]. Of note, we observe a heterogeneous mix of ablations with 45.8% (408/890) using a Box lesion and a lesser proportion of full CM-IV ablations (24.8%, 221/890) while the latter is overrepresented in the literature. Although LAA exclusion is recommended by recent STS guidelines and by other authors in all cases of STAF as it reduces stroke incidence and increases overall survival after STAF, it is performed in only 69.1% (615/890) of all patients in our database with variable percentages for subgroups [9,17].

Safety and Survival

Untreated AF decreases postoperative survival whereas concomitant STAF performed in recent times has shown to increase long-term survival and lower stroke incidence without increasing short-term morbidity or mortality [3–6]. Although only a limited number of complications were registered, we observe a low incidence of reoperation for bleeding and in-hospital mortality, 1.35% (12/890) and 1.7% (15/890) respectively, in the total population compared to an incidence of 4-8.9% for reoperation due to bleeding and 1.2-5.9% for early mortality in trials with diverse populations [3,4,13,15,16,18]. As we have limited information about the preoperative functional status, selection bias and our trial setup may influence results. We estimated overall survival to be 95.0% at 1 year and 92.3% at 2 years using a Kaplan-Meier analysis, parallel with the 94.9% survival at 1 year and 91.1% survival at 2 years reported by Pecha [18] and Attaran [3] respectively for similar mixed cohorts undergoing concomitant ablation [3,18]. There was no significant difference between any of the subgroups with regards to in-hospital mortality, reoperation for bleeding or overall survival despite significant differences in demographic and procedural variables related to increased perioperative risk.

Freedom from AF and other rhythm-related outcomes

Other trials with similar populations as well as a meta-analysis, report freedom from AF at 1 year between 59.9% and 76%, similar to our 69.9% overall for the total population and 74.9% at 1 year in the Kaplan-Meier analysis [4,16,18,19]. As in our study, preoperative paroxysmal AF is often withheld as being predictive of freedom from AF [13,18,19].

Throughout the literature, preoperative LAD also emerges as a predictive factor related to the substrate of AF and along with AF type, it was the only variable consistently associated with freedom from AF in the regression analyses [12,13,20].

Commonly cited rates for freedom from AF at 1 year for patients undergoing a CM-IV ablation during mitral valve surgery vary between 66 and 93% [10–14,21,22]. In a meta-analysis including trials with variable ablations during mitral valve surgery, 75.5% of patients were free from AF at 1 year, similar to our 73% at 1 year for all patients undergoing mitral valve surgery [15]. For patients undergoing non-mitral surgery, published numbers vary between 58.7% and 86.2%, compared to our 78.4% freedom from AF at 1 year [16,23]. This effect based on AF type and concomitant procedure is likely related to the worse substrate of AF in these groups.

There is considerable evidence indicating that a more complete left-sided ablation as well as the addition of right-sided lesions [13,16,18,19,21,23,24] yields lower recurrence rates, especially for persistent or permanent AF or AF related to mitral valve pathology. However, it remains uncertain which specific lesion set is indicated based on a patient's preoperative AF type and concomitant procedure [9,16,18,19]. In our study, the more extensive ablations were not consistently associated with greater freedom from AF. Nonetheless, our results appear to favour more extensive ablations as these were not associated with increased morbidity or mortality while producing similar or better results for patients with more severe forms of AF.

While surgical ablation appears to increase the need for postoperative pacemaker implantation [5,6,13,22], more so for biatrial ablations [24], this effect is also related to the substrate of AF as ablation can unmask underlying sinus node dysfunction [1]. Need for in-hospital implantation of a permanent pacemaker was favourable in our study at 3.7% (33/890), compared to rates between 6.8 and 22.9% after CM-IV ablation [5,10,13,14] and 3.1-6% after left-sided ablations [16,20]. Overall need for a permanent pacemaker was 9.7% (87/890) and significantly higher in patients with non-paroxysmal AF, patients undergoing mitral valve surgery and those undergoing a full CM-IV ablation.

Postoperative management and follow-up

At last follow-up, only 29.6% (242/817) was on AADs and 55.9% (457/817) on anticoagulant drugs, compared to 62.5% (547/875) and 77.1% (675/875) respectively at discharge. This is in accordance with current guidelines and shows that ablation allows a significant proportion of patients to quit AADs and ACDs [8,9].

Strengths and limitations

The strength of this study lies in the size of the database and while data registry and follow-up violated protocol, our study reflects real life clinical practice in a complicated domain, emphasizing the need for further investigation with attention to subgroups. Our definition of the primary end-point considers any episode of AF beyond 3 months as permanent treatment failure while we do not know if some patients display durable freedom from AF after an initial recurrence[8]. Inadvertently, some event times were treated as actual event times in the construction of the Kaplan-Meier curves while in reality they were interval-censored, occurring somewhere between two follow-up visits. While guidelines advocate regular Holter assessment or monitoring of AF burden in all patients, only 64.3% (525/817) were evaluated by 24h Holter [9]. When calculating freedom from AF for all patients beyond blanking period, absent follow-up implies the absence of recurrence, potentially underestimating recurrence. However, we also report freedom from AF for patients with rhythm follow-up and we believe this second approach overestimates the true AF recurrence because patients in AF are likely overreported in the database. As shown in Tables 1-3, no differences in preoperative and procedural variables were observed between the total population, patients beyond blanking period and patients with rhythm follow-up. As expected, freedom from AF was 5-10% lower for the 574 patients with rhythm follow-up in both calculations yet the relationships between subgroups are comparable and the same predictors of freedom from AF

are withheld. We believe that when combined, both approaches reliably represent the true spectrum of freedom from AF in our population.

Conclusion

This retrospective analysis of the prospectively collected 'Belgian Atrial Fibrillation Management Database' proves that on the whole, surgical treatment of atrial fibrillation as performed throughout Belgium is safe both in the short- and long-term and achieves favourable freedom from AF between 6 and 24 months in a cohort with various types of preoperative AF, concomitant procedures and types of ablation. Preoperative left atrial diameter and AF type were predictive of freedom from AF in regression analysis. None withstanding its limitations, we believe this report, when correlated with other recent data on the safety of STAF, reliably supports the message that concomitant STAF should be performed in accordance with the guidelines. Our study emphasizes the need for centralized, accurate registry of follow-up and analysis of outcomes according to relevant subgroups.

Table and table captions

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow-Up (n=574)
Age	68.9 ± 9.4	68.7 ± 9.3	68.7 ± 9.2
Male	59.9 (533)	60.1 (491)	61.2 (351)
AF duration (y)	2.4 ± 3.3	2.4 ± 3.3	2.4 ± 3.3
Paroxysmal AF	52.5 (467)	53.5 (437)	51.9 (298)
LVEF	55.0 ± 13.8	55.2 ± 13.7	55.7 ± 13.6
LAD (mm)	47.9 ± 8.6	47.8 ± 8.7	47.7 ± 8.8
Previous embolism	9.1 (81)	8.8 (72)	9.4 (54)
Previous ablation	4 (36)	4.2 (34)	4.2 (24)
Using AADs	40.9 (364)	40.6 (332)	39.2 (225)
Using ACDs	58.3 (519)	58.4 (477)	62.0 (356)
SR preop	46.6 (415)	47.6 (389)	46.9 (269)
Mitral surgery	63.6 (566)	64.1 (524)	63.2 (363)
Ablation			
Full Cox Maze IV	24.8 (221)	25.5 (208)	25.4 (146)
Box ± more	45.8 (408)	45.5 (372)	45.6 (262)
PVI ± more	29.3 (261)	29.0 (237)	28.9 (166)

Table 1. Preoperative characteristics of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow-Up (n=574)
Sternotomy	80.8 (719)	80.7 (659)	80.8 (464)
Operation time (min)	253 ± 81.2	253 ± 80.5	252.4 ± 80.6
Bypass time (min)	144 ± 57	143 ± 57.2	144.3 ± 57.9
Cross clamp time (min)	97 ± 45.8	96 ± 44.9	97.1 ± 45.8
LAA exclusion	69.1 (615)	69.2 (565)	72.7 (417)
LAA management			
External Closure	38.9 (239)	39.3 (222)	38.6 (161)
Internal Closure	31.7 (195)	31.2 (176)	30.9 (129)
Resection	29.4 (181)	29.6 (167)	30.5 (127)
Energy source			
Bipolar RF	50.3 (448)	50.2 (410)	50.5 (290)
Cryotherapy	27.4 (244)	27.9 (228)	25.1 (144)
Bipolar RF and Cryotherapy	10.6 (94)	10.8 (88)	11.7 (67)
Bipolar and Unipolar RF	8.5 (76)	8.1 (66)	9.2 (53)
Other	3.2 (28)	3.1 (25)	3.5 (20)

Table 2. Procedural variables of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Total population (n=890)	Beyond Blanking Period (n=817)	Rhythm Follow- Up (n=574)
Length of stay (d)	13.8 ± 18.2	13.2 ± 17	13.2 ± 18.1
Bleeding	1.4 (12)	1.4 (11)	1.1 (6)
Block	2.3 (20)	2.1 (17)	2.1 (12)
In-hospital mortality	1.7 (15)		
Cardioversion	4.6 (41)	4.5 (37)	3.7 (21)
New permanent pacemaker	3.7 (33)	3.4 (28)	3.3 (19)
SR at discharge	75.5 (661)	75.6 (618)	75.4 (433)

Table 3. In-hospital outcomes of total population, patients beyond blanking period and patients with rhythm follow-up. Continuous variables are presented as % (n) and categorical variables are presented as mean ± Std.

Variable	Univariable model		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	0.99 (0.98-1.01)	0.283	0.99 (0.98-1.01)	0.705
Female	1.17 (0.86-1.59)	0.307	0.99 (0.71-1.4)	0.974
AF duration (y)	0.98 (0.93-1.02)	0.313	0.98 (0.93-1.03)	0.446
Paroxysmal AF	0.55 (0.41-0.75)	<.001	0.6 (0.43-0.84)	0.003
LVEF	0.999 (0.99-1.01)	0.886	1 (0.99-1.02)	0.559
LAD (mm)	1.05 (1.02-1.07)	<.001	1.03 (1.01-1.05)	0.004
Previous ablation	0.97 (0.46-2.07)	0.943	1.19 (0.53-2.68)	0.671
Pacemaker pre-op	1.64 (0.75-3.58)	0.218	1.72 (0.76-3.91)	0.194
Mitral surgery	1.79 (1.29-2.48)	<.001	1.52 (0.95-2.43)	0.079
Ablation		0.026		0.445
Box ± more	1.62 (1.12-2.33)	0.010	1.12 (0.69-1.8)	0.656
Full Cox Maze IV	1.2 (0.78-1.83)	0.411	0.83 (0.47-1.48)	0.533
Energy source		0.002		0.013
Bipolar	0.35 (0.16-0.79)	0.012	0.43 (0.18-1.02)	0.055
Bi- and unipolar	0.82 (0.33-2.06)	0.669	0.74 (0.29-1.92)	0.539
Bipolar and Cryo	0.28 (0.11-0.7)	0.007	0.31 (0.11-0.85)	0.023
Cryo	0.39 (0.17-0.89)	0.026	0.33 (0.14-0.79)	0.013

Table 4. Results of uni- and multivariable logistic regression models for overall freedom from AF for patients with follow-up beyond the 3-month blanking period (n=817) with odds ratios for recurrence of AF.

	Univariable model		Multivariable model	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Age	0.99 (0.98-1.01)	0.669	0.99 (0.99-1.01)	0.914
Female	1.12 (0.87-1.45)	0.383	1.04 (0.78-1.38)	0.781
AF duration (y)	0.98 (0.94-1.02)	0.273	0.98 (0.94-1.03)	0.441
Paroxysmal AF	0.66 (0.51-0.85)	0.001	0.67 (0.51-0.89)	0.005
LVEF	0.99 (0.99-1.01)	0.888	1.00 (0.99-1.01)	0.432
LAD (mm)	1.03 (1.02-1.05)	<.001	1.03 (1.01-1.04)	0.004
Previous ablation	0.77 (0.41-1.46)	0.421	0.90 (0.46-1.76)	0.761
Pacemaker pre-op	1.59 (0.87-2.92)	0.131	1.65 (0.89-3.05)	0.111
Mitral surgery	1.41 (1.06-1.87)	0.019	1.40 (0.95-2.07)	0.093
Ablation		0.436		0.541
Box ± more	1.18 (0.86-1.61)	0.301	0.87 (0.59-1.30)	0.501
Full Cox Maze IV	0.99 (0.69-1.44)	0.988	0.77 (0.48-1.23)	0.269
Energy source		0.068		0.096
Bipolar	0.66 (0.37-1.18)	0.164	0.75 (0.41-1.38)	0.360
Bi- and unipolar	0.99 (0.51-1.90)	0.971	0.92 (0.47-1.80)	0.817
Bipolar and Cryo	0.47 (0.23-0.95)	0.036	0.49 (0.23-1.03)	0.061
Cryo	0.65 (0.36-1.18)	0.159	0.60 (0.32-1.11)	0.103

Table 5. Results of uni- and multivariable Cox regression models for Kaplan-Meier estimate of freedom from AF for patients with follow-up beyond the 3-month blanking period (n=817) with hazard ratios for recurrence of AF.

Figures

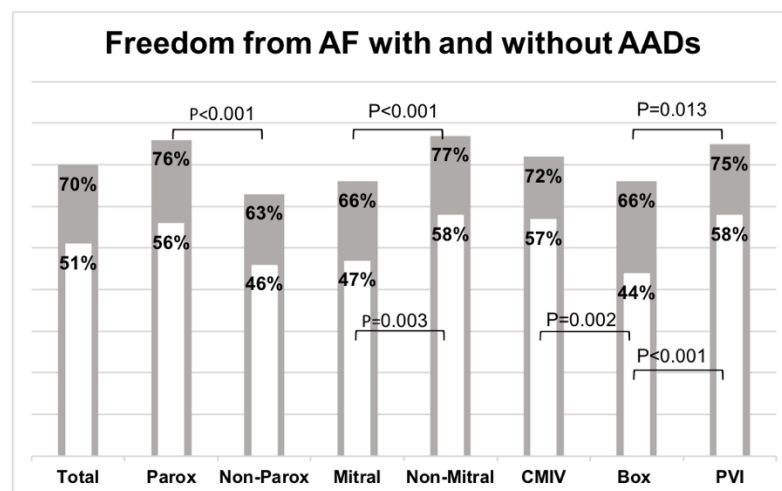


Figure 1. Overall freedom from AF with and without (inlaying white bars) continuation of AADs for patients with follow-up beyond the 3-month blanking period (n=817). Statistical comparison was performed using a Fisher's Exact test and significant differences are indicated with brackets.

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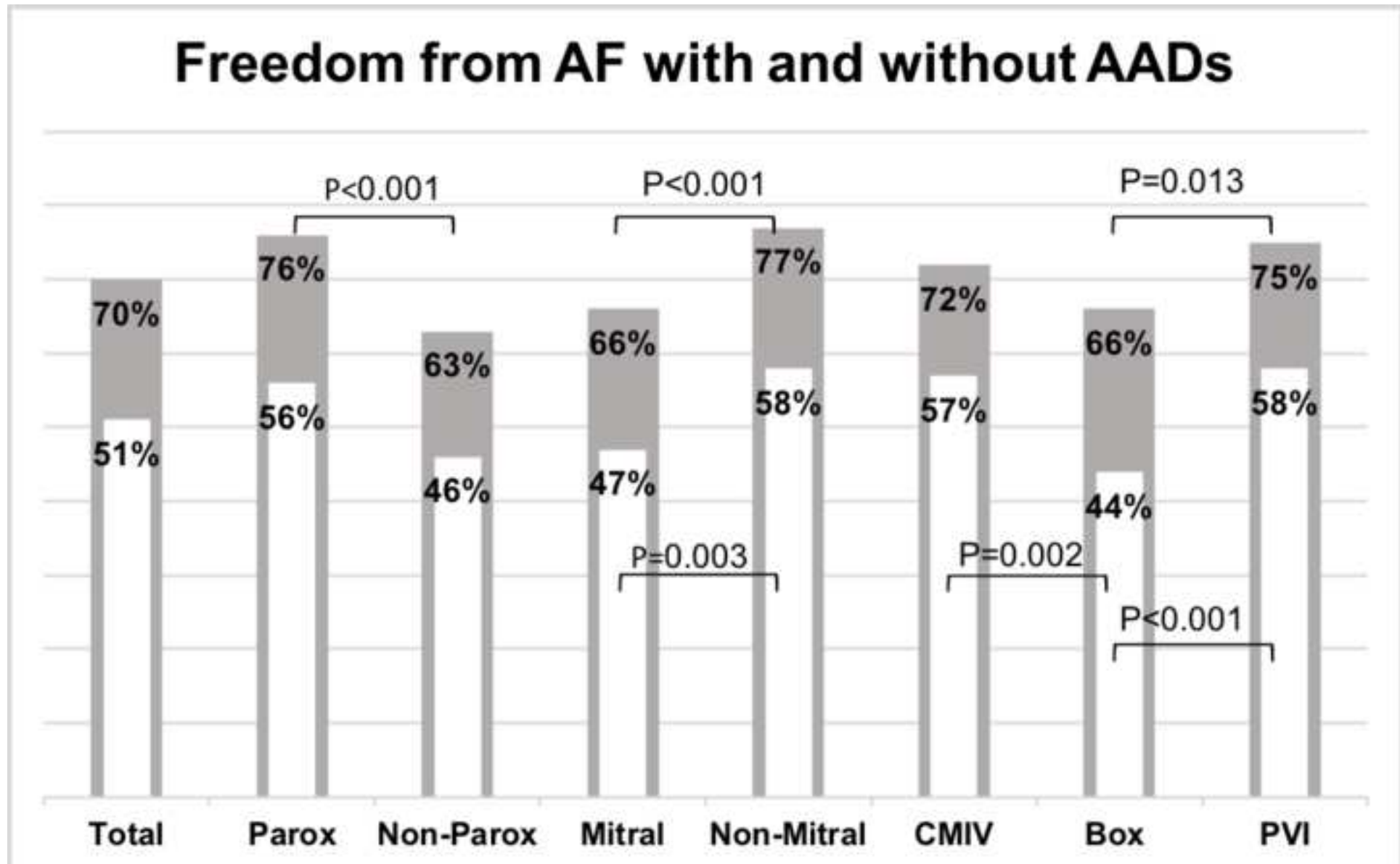
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Supplementary Tables

Tables 1'-3': Preoperative characteristics of total population (n=890), patients beyond blanking (n=817) and patients with rhythm follow-up (n=574) and subgroups.

Tables 4'-6': Procedural variables of total population (n=890), patients beyond blanking (n=817) and patients with rhythm follow-up (n=574) and subgroups.

Tables 7'-9': In-hospital outcomes of total population (n=890), patients beyond blanking (n=817) and patients with rhythm follow-up (n=574) and subgroups.

Tables 10'-12': Rhythm-related events in-hospital and during follow-up of total population (n=890), patients beyond blanking (n=817) and patients with rhythm follow-up (n=574) and subgroups.

Table 13': Freedom from AF with and without dependence on AADs and use of ACDs for patients with follow-up beyond the 3 month blanking point (n=817)

Table 14': Freedom from AF with and without continuation of AADs and use of ACDs for patients with rhythm follow-up (n=574)

Table 15': Results of uni- and multivariable logistic regression models for overall freedom from AF in patients with rhythm follow-up (n=574) with odds ratios for recurrence of AF.

Table 16': Results of uni- and multivariable Cox regression models for Kaplan-Meier estimate of freedom from AF in patients with rhythm follow-up (n=574) with hazard ratios for recurrence of AF.

Table 1'. Preoperative characteristics of total population (n=890) and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Total population (n=890)	Paroxysmal (n=467)	Non-Paroxysmal (n=417)	P-value
Age	68.9 \pm 9.4	68.9 \pm 9.2	68.9 \pm 9.3	0.922
Male	533/890 (59.89%)	288/467 (61.67%)	243/417 (58.27%)	0.303
AF duration (y)	2.4 \pm 3.3	2.4 \pm 3.3	2.4 \pm 3.3	0.234
Paroxysmal AF	467/890 (52.47%)			
LVEF	55.0 \pm 13.8	57.3 \pm 13.4	52.5 \pm 12.9	<.001
LAD (mm)	47.9 \pm 8.6	46.7 \pm 8.4	49.4 \pm 8.5	<.001
Previous embolism	81/890 (9.10%)	31/467 (6.64%)	50/417 (11.99%)	0.006
Previous ablation	36/890 (4.04%)	20/467 (4.28%)	16/417 (3.84%)	0.738
Using AADs	364/890 (40.90%)	217/467 (46.47%)	147/417 (35.25%)	<.001
Using ACDs	519/890 (58.31%)	230/467 (49.25%)	288/417 (69.06%)	<.001
SR preop	415/890 (46.63%)	350/467 (74.95%)	62/417 (14.87%)	<.001
Mitral surgery	566/890 (63.60%)	264/467 (56.53%)	296/417 (70.98%)	<.001
Ablation				<.001
Full Cox Maze IV	221/890 (24.83%)	79/467 (16.92%)	141/417 (33.81%)	
Box \pm more	408/890 (45.84%)	206/467 (44.11%)	198/417 (47.48%)	
PVI \pm more	261/890 (29.33%)	182/467 (38.97%)	78/417 (18.71%)	

Variable	Total population (n=890)	Mitral (n=566)	Non-Mitral (n=324)	P-value
Age	68.9 ± 9.4	68.5 ± 9.7	69.5 ± 8.6	0.302
Male	533/890 (59.89%)	268/566 (47.35%)	265/324 (81.79%)	<.001
AF duration (y)	2.4 ± 3.3	2.4 ± 3.3	2.5 ± 3.2	0.966
Paroxysmal AF	467/890 (52.47%)	264/566 (46.64%)	203/324 (62.65%)	<.001
LVEF	55.0 ± 13.8	55.2 ± 13.7	54.6 ± 14	0.507
LAD (mm)	47.9 ± 8.6	49.3 ± 8.5	45.5 ± 8.3	<.001
Previous embolism	81/890 (9.10%)	43/566 (7.60%)	38/324 (11.73%)	0.039
Previous ablation	36/890 (4.04%)	21/566 (3.71%)	15/324 (4.63%)	0.503
Using AADs	364/890 (40.90%)	239/566 (42.23%)	125/324 (38.58%)	0.287
Using ACDs	519/890 (58.31%)	337/566 (59.54%)	182/324 (56.17%)	0.327
SR preop	415/890 (46.63%)	237/566 (41.87%)	178/324 (54.94%)	<.001
Mitral surgery	566/890 (63.60%)			
Ablation				<.001
Full Cox Maze IV	221/890 (24.83%)	179/566 (31.63%)	42/324 (12.96%)	
Box ± more	408/890 (45.84%)	337/566 (59.54%)	71/324 (21.91%)	
PVI ± more	261/890 (29.33%)	50/566 (8.83%)	211/324 (65.12%)	

Variable	Total population (n=890)	Full Cox Maze IV (n=221)	Box ± more (n=408)	PVI ± more (n=261)	P-value	1 vs 2	1 vs 3	2 vs 3
Age	68.9 ± 9.4	68.3 ± 8.2	68.9 ± 10.1	69.2 ± 9.1	0.305	0.178	0.161	0.848
Male	533/890 (59.89%)	125/221 (56.56%)	204/408 (50.00%)	204/261 (78.16%)	<.001	0.116	<.001	<.001
AF duration (y)	2.4 ± 3.3	3.0 ± 4	2.2 ± 3	2.2 ± 2.9	0.004	<.001	0.022	0.324
Paroxysmal AF	467/890 (52.47%)	79/221 (35.75%)	206/408 (50.49%)	182/261 (69.73%)	<.001	0.001	<.001	<.001
LVEF	55.0 ± 13.8	54.3 ± 14	54.5 ± 13.7	56.3 ± 13.6	0.177	0.749	0.093	0.116
LAD (mm)	47.9 ± 8.6	48.1 ± 7.9	48.7 ± 9.7	46.6 ± 7.2	<.001	0.112	0.031	<.001
Previous embolism	81/890 (9.10%)	17/221 (7.69%)	35/408 (8.58%)	29/261 (11.11%)	0.379	0.700	0.203	0.277
Previous ablation	36/890 (4.04%)	14/221 (6.33%)	14/408 (3.43%)	8/261 (3.07%)	0.134	0.092	0.087	0.796
Using AADs	364/890 (40.90%)	99/221 (44.80%)	159/408 (38.97%)	106/261 (40.61%)	0.363	0.156	0.355	0.672
Using ACDs	519/890 (58.31%)	151/221 (68.33%)	225/408 (55.15%)	143/261 (54.79%)	0.002	0.001	0.002	0.928
SR preop	415/890 (46.63%)	78/221 (35.29%)	178/408 (43.63%)	159/261 (60.92%)	<.001	0.042	<.001	<.001
Mitral surgery	566/890 (63.60%)	179/221 (81.00%)	337/408 (82.60%)	50/261 (19.16%)	<.001	0.617	<.001	<.001

Table 2'. Preoperative characteristics of patients with follow-up beyond the 3 month blanking period (n=817) and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Beyond Blanking Period (n=817)	Paroxysmal (n=437)	Non-Paroxysmal (n=374)	P-value
Age	68.7 \pm 9.3	68.9 \pm 9.2	68.6 \pm 9.2	0.525
Male	491/817 (60.10%)	270/437 (61.78%)	219/374 (58.56%)	0.349
AF duration (y)	2.4 \pm 3.3	2.3 \pm 3.3	2.5 \pm 3.4	0.204
Paroxysmal AF	437/817 (53.49%)			
LVEF	55.2 \pm 13.7	57.5 \pm 13.9	52.6 \pm 12.9	<.001
LAD (mm)	47.8 \pm 8.7	46.6 \pm 8.4	49.3 \pm 8.7	<.001
Previous embolism	72/817 (8.81%)	27/437 (6.18%)	45/374 (12.03%)	0.003
Previous ablation	34/817 (4.16%)	20/437 (4.58%)	14/374 (3.74%)	0.555
Using AADs	332/817 (40.64%)	204/437 (46.68%)	128/374 (34.22%)	<.001
Using ACDs	477/817 (58.38%)	216/437 (49.43%)	260/374 (69.52%)	<.001
SR preop	389/817 (47.61%)	328/437 (75.06%)	58/374 (15.51%)	<.001
Mitral surgery	524/817 (64.14%)	246/437 (56.29%)	272/374 (72.73%)	<.001
Ablation				<.001
Full Cox Maze IV	208/817 (25.46%)	76/437 (17.39%)	131/374 (35.03%)	
Box \pm more	372/817 (45.53%)	189/437 (43.25%)	179/374 (47.86%)	
PVI \pm more	237/817 (29.01%)	172/437 (39.36%)	64/374 (17.11%)	

Variable	Beyond Blanking Period (n=817)	Mitral (n=524)	Non-Mitral (n=293)	P-value
Age	68.7 ± 9.3	68.4 ± 9.7	69.2 ± 8.6	0.562
Male	491/817 (60.10%)	251/524 (47.90%)	240/293 (81.91%)	<.001
AF duration (y)	2.4 ± 3.3	2.4 ± 3.3	2.4 ± 3.2	0.874
Paroxysmal AF	437/817 (53.49%)	246/524 (46.95%)	191/293 (65.19%)	<.001
LVEF	55.2 ± 13.7	55.3 ± 13.5	54.9 ± 14.2	0.726
LAD (mm)	47.8 ± 8.7	49.2 ± 8.5	45.4 ± 8.4	<.001
Previous embolism	72/817 (8.81%)	38/524 (7.25%)	34/293 (11.60%)	0.035
Previous ablation	34/817 (4.16%)	21/524 (4.01%)	13/293 (4.44%)	0.768
Using AADs	332/817 (40.64%)	220/524 (41.98%)	112/293 (38.23%)	0.294
Using ACDs	477/817 (58.38%)	311/524 (59.35%)	166/293 (56.66%)	0.453
SR preop	389/817 (47.61%)	223/524 (42.56%)	166/293 (56.66%)	<.001
Mitral surgery	524/817 (64.14%)			
Ablation				<.001
Full Cox Maze IV	208/817 (25.46%)	168/524 (32.06%)	40/293 (13.65%)	
Box ± more	372/817 (45.53%)	310/524 (59.16%)	62/293 (21.16%)	
PVI ± more	237/817 (29.01%)	46/524 (8.78%)	191/293 (65.19%)	

Variable	Beyond Blanking Period (n=817)	Full Cox Maze IV (n=208)	Box ± more (n=372)	PVI ± more (n=237)	P-value	1 vs 2	1 vs 3	2 vs 3
Age	68.7 ± 9.3	68.1 ± 8.4	68.8 ± 10	68.9 ± 9.1	0.300	0.130	0.242	0.840
Male	491/817 (60.10%)	118/208 (56.73%)	188/372 (50.54%)	185/237 (78.06%)	<.001	0.152	<.001	<.001
AF duration (y)	2.4 ± 3.3	3.1 ± 4	2.1 ± 3	2.2 ± 2.9	0.001	<.001	0.012	0.292
Paroxysmal AF	437/817 (53.49%)	76/208 (36.54%)	189/372 (50.81%)	172/237 (72.57%)	<.001	0.002	<.001	<.001
LVEF	55.2 ± 13.7	54.1 ± 14.3	54.8 ± 13.5	56.6 ± 13.7	0.102	0.494	0.040	0.107
LAD (mm)	47.8 ± 8.7	48.0 ± 7.9	48.6 ± 9.8	46.4 ± 7.2	<.001	0.124	0.025	<.001
Previous embolism	72/817 (8.81%)	17/208 (8.17%)	31/372 (8.33%)	24/237 (10.13%)	0.697	0.946	0.477	0.452
Previous ablation	34/817 (4.16%)	13/208 (6.25%)	14/372 (3.76%)	7/237 (2.95%)	0.193	0.173	0.094	0.593
Using AADs	332/817 (40.64%)	90/208 (43.27%)	145/372 (38.98%)	97/237 (40.93%)	0.598	0.313	0.618	0.632
Using ACDs	477/817 (58.38%)	142/208 (68.27%)	205/372 (55.11%)	130/237 (54.85%)	0.004	0.002	0.004	0.951
SR preop	389/817 (47.61%)	75/208 (36.06%)	164/372 (44.09%)	150/237 (63.29%)	<.001	0.060	<.001	<.001
Mitral surgery	524/817 (64.14%)	168/208 (80.77%)	310/372 (83.33%)	46/237 (19.41%)	<.001	0.437	<.001	<.001

Table 3'. Preoperative characteristics of patients with rhythm follow-up (n=574) and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Rhythm Follow-Up (n=574)	Paroxysmal (n=298)	Non-Paroxysmal (n=273)	P-value
Age	68.7 \pm 9.2	69.2 \pm 8.7	68.4 \pm 9.6	0.460
Male	351/574 (61.15%)	187/298 (62.75%)	163/273 (59.71%)	0.456
AF duration (y)	2.4 \pm 3.3	2.4 \pm 3.3	2.4 \pm 3.3	0.499
Paroxysmal AF	298/574 (51.92%)			
LVEF	55.7 \pm 13.6	58.4 \pm 13.7	53 \pm 12.6	<.001
LAD (mm)	47.7 \pm 8.8	46.6 \pm 8.1	48.9 \pm 9.3	<.001
Previous embolism	54/574 (9.41%)	17/298 (5.70%)	37/273 (13.55%)	0.001
Previous ablation	24/574 (4.18%)	14/298 (4.70%)	10/273 (3.66%)	0.538
Using AADs	225/574 (39.20%)	132/298 (44.30%)	93/273 (34.07%)	0.012
Using ACDs	356/574 (62.02%)	155/298 (52.01%)	201/273 (73.63%)	<.001
SR preop	269/574 (46.86%)	223/298 (74.83%)	44/273 (16.12%)	<.001
Mitral surgery	363/574 (63.24%)	170/298 (57.05%)	190/273 (69.60%)	0.002
Ablation				<.001
Full Cox Maze IV	146/574 (25.44%)	54/298 (18.12%)	91/273 (33.33%)	
Box \pm more	262/574 (45.64%)	133/298 (44.63%)	128/273 (46.89%)	
PVI \pm more	166/574 (28.92%)	111/298 (37.25%)	54/273 (19.78%)	

Variable	Rhythm Follow-Up (n=574)	Mitral (n=363)	Non-Mitral (n=211)	P-value
Age	68.7 ± 9.2	68.6 ± 9.6	69.1 ± 8.6	0.838
Male	351/574 (61.15%)	177/363 (48.76%)	174/211 (82.46%)	<.001
AF duration (y)	2.4 ± 3.3	2.4 ± 3.4	2.4 ± 3.2	0.918
Paroxysmal AF	298/574 (51.92%)	170/363 (46.83%)	128/211 (60.66%)	0.003
LVEF	55.7 ± 13.6	55.9 ± 13.7	55.4 ± 13.5	0.516
LAD (mm)	47.7 ± 8.8	49.1 ± 8.7	45.3 ± 8.3	<.001
Previous embolism	54/574 (9.41%)	30/363 (8.26%)	24/211 (11.37%)	0.218
Previous ablation	24/574 (4.18%)	14/363 (3.86%)	10/211 (4.74%)	0.611
Using AADs	225/574 (39.20%)	151/363 (41.60%)	74/211 (35.07%)	0.123
Using ACDs	356/574 (62.02%)	229/363 (63.09%)	127/211 (60.19%)	0.491
SR preop	269/574 (46.86%)	156/363 (42.98%)	113/211 (53.55%)	0.014
Mitral surgery	363/574 (63.24%)			
Ablation				<.001
Full Cox Maze IV	146/574 (25.44%)	116/363 (31.96%)	30/211 (14.22%)	
Box ± more	262/574 (45.64%)	218/363 (60.06%)	44/211 (20.85%)	
PVI ± more	166/574 (28.92%)	29/363 (7.99%)	137/211 (64.93%)	

Variable	Rhythm Follow-Up (n=574)	Full Cox Maze IV (n=146)	Box ± more (n=262)	PVI ± more (n=166)	P-value	1 vs 2	1 vs 3	2 vs 3
Age	68.7 ± 9.2	68.2 ± 8	69 ± 10	68.8 ± 8.9	0.365	0.157	0.408	0.590
Male	351/574 (61.15%)	85/146 (58.22%)	134/262 (51.15%)	132/166 (79.52%)	<.001	0.170	<.001	<.001
AF duration (y)	2.4 ± 3.3	3.2 ± 4.1	2.1 ± 3.1	2.2 ± 2.8	<.001	<.001	0.020	0.141
Paroxysmal AF	298/574 (51.92%)	54/146 (36.99%)	133/262 (50.76%)	111/166 (66.87%)	<.001	0.027	<.001	0.004
LVEF	55.7 ± 13.6	53.6 ± 14	55.9 ± 13.2	57.2 ± 13.7	0.024	0.056	0.007	0.278
LAD (mm)	47.7 ± 8.8	47.7 ± 8.3	48.6 ± 9.6	46.3 ± 7.5	0.003	0.096	0.132	<.001
Previous embolism	54/574 (9.41%)	12/146 (8.22%)	24/262 (9.16%)	18/166 (10.84%)	0.718	0.748	0.433	0.568
Previous ablation	24/574 (4.18%)	9/146 (6.16%)	9/262 (3.44%)	6/166 (3.61%)	0.381	0.198	0.293	0.922
Using AADs	225/574 (39.20%)	67/146 (45.89%)	94/262 (35.88%)	64/166 (38.55%)	0.136	0.047	0.190	0.576
Using ACDs	356/574 (62.02%)	107/146 (73.29%)	153/262 (58.40%)	96/166 (57.83%)	0.005	0.003	0.004	0.908
SR preop	269/574 (46.86%)	54/146 (36.99%)	114/262 (43.51%)	101/166 (60.84%)	<.001	0.199	<.001	<.001
Mitral surgery	363/574 (63.24%)	116/146 (79.45%)	218/262 (83.21%)	29/166 (17.47%)	<.001	0.346	<.001	<.001

Table 4'. Procedural variables for total population and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Total population (n=890)	Paroxysmal (n=467)	Non-Paroxysmal (n=417)	P-value
Sternotomy	719/890 (80.79%)	385/467 (82.44%)	328/417 (78.66%)	0.155
Operation time (min)	253 \pm 81.2	249 \pm 78.8	259 \pm 84	0.104
Bypass time (min)	144 \pm 57	137 \pm 54.2	152 \pm 58.4	<.001
Cross clamp time (min)	97 \pm 45.8	92 \pm 44	102 \pm 47.2	0.003
LAA exclusion	615/890 (69.10%)	308/467 (65.95%)	306/417 (73.38%)	0.017
LAA management				<.001
External Closure	239/615 (38.86%)	140/308 (45.45%)	99/306 (32.35%)	
Internal Closure	195/615 (31.71%)	75/308 (24.35%)	120/306 (39.22%)	
Resection	181/615 (29.43%)	93/308 (30.19%)	87/306 (28.43%)	
Energy source				<.001
Bipolar RF	448/890 (50.34%)	266/467 (56.96%)	178/417 (42.69%)	
Cryotherapy	244/890 (27.42%)	119/467 (25.48%)	124/417 (29.74%)	
Bipolar RF and Cryotherapy	94/890 (10.56%)	36/467 (7.71%)	57/417 (13.67%)	
Bipolar and Unipolar RF	76/890 (8.54%)	32/467 (6.85%)	44/417 (10.55%)	
Other	28/890 (3.15%)	14/467 (3.00%)	14/417 (3.36%)	

Variable	Total population (n=890)	Mitral (n=566)	Non-Mitral (n=324)	P-value
Sternotomy	719/890 (80.79%)	398/566 (70.32%)	321/324 (99.07%)	<.001
Operation time (min)	253 \pm 81.2	268 \pm 79.4	228 \pm 78.3	<.001
Bypass time (min)	144 \pm 57	159 \pm 54.6	118 \pm 51.4	<.001
Cross clamp time (min)	97 \pm 45.8	110 \pm 42.2	74 \pm 42.8	<.001
LAA exclusion	615/890 (69.10%)	384/566 (67.84%)	231/324 (71.30%)	0.284
LAA management				<.001
External Closure	239/615 (38.86%)	76/384 (19.79%)	163/231 (70.56%)	
Internal Closure	195/615 (31.71%)	180/384 (46.88%)	15/231 (6.49%)	

Resection	181/615 (29.43%)	128/384 (33.33%)	53/231 (22.94%)	<.001
Energy source				
Bipolar RF	448/890 (50.34%)	187/566 (33.04%)	261/324 (80.56%)	
Cryotherapy	244/890 (27.42%)	232/566 (40.99%)	12/324 (3.70%)	
Bipolar RF And Cryotherapy	94/890 (10.56%)	69/566 (12.19%)	25/324 (7.72%)	
Bipolar and Unipolar RF	76/890 (8.54%)	59/566 (10.42%)	17/324 (5.25%)	
Other	28/890 (3.15%)	19/566 (3.36%)	9/324 (2.78%)	

Variable	Total population (n=890)	Full Cox Maze IV (n=221)	Box ± more (n=408)	PVI ± more (n=261)	P-value	1 vs 2	1 vs 3	2 vs 3
Sternotomy	719/890 (80.79%)	208/221 (94.12%)	263/408 (64.46%)	248/261 (95.02%)	<.001	<.001	0.662	<.001
Operation time (min)	253 ± 81.2	296 ± 88.4	245 ± 72.8	230 ± 73.6	<.001	<.001	<.001	0.002
Bypass time (min)	144 ± 57	170 ± 53.5	145 ± 51.5	120 ± 57.9	<.001	<.001	<.001	<.001
Cross clamp time (min)	97 ± 45.8	112 ± 39.9	101 ± 43.3	78 ± 48	<.001	0.001	<.001	<.001
LAA exclusion	615/890 (69.10%)	191/221 (86.43%)	242/408 (59.31%)	182/261 (69.73%)	<.001	<.001	<.001	0.006
LAA management					<.001	0.028	<.001	<.001
External Closure	239/615 (38.86%)	54/191 (28.27%)	60/242 (24.79%)	125/182 (68.68%)	<.001	<.001	<.001	<.001
Internal Closure	195/615 (31.71%)	57/191 (29.84%)	102/242 (42.15%)	36/182 (19.78%)				
Resection	181/615 (29.43%)	80/191 (41.88%)	80/242 (33.06%)	21/182 (11.54%)				
Energy source								
Bipolar RF	448/890 (50.34%)	69/221 (31.22%)	156/408 (38.24%)	223/261 (85.44%)				
Cryotherapy	244/890 (27.42%)	40/221 (18.10%)	187/408 (45.83%)	17/261 (6.51%)				
Bipolar RF and Cryotherapy	94/890 (10.56%)	87/221 (39.37%)	7/408 (1.72%)	0/261 (0.00%)				
Bipolar and Unipolar RF	76/890 (8.54%)	21/221 (9.50%)	41/408 (10.05%)	14/261 (5.36%)				
Other	28/890 (3.15%)	4/221 (1.81%)	17/408 (4.17%)	7/261 (2.68%)				

Table 5'. Procedural variables for patients with follow-up beyond 3 months (n=817) and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Beyond Blanking Period (n=817)	Paroxysmal (n=437)	Non-Paroxysmal (n=374)	P-value
Sternotomy	659/817 (80.66%)	360/437 (82.38%)	293/374 (78.34%)	0.148
Operation time (min)	253 \pm 80.5	249 \pm 78.7	257 \pm 82.8	0.210
Bypass time (min)	143 \pm 57.2	136 \pm 54.6	152 \pm 58.7	<.001
Cross clamp time (min)	96 \pm 44.9	92 \pm 44.4	102 \pm 45.1	0.003
LAA exclusion	565/817 (69.16%)	289/437 (66.13%)	275/374 (73.53%)	0.023
LAA management				<.001
External Closure	222/565 (39.29%)	133/289 (46.02%)	89/275 (32.36%)	<.001
Internal Closure	176/565 (31.15%)	68/289 (23.53%)	108/275 (39.27%)	
Resection	167/565 (29.56%)	88/289 (30.45%)	78/275 (28.36%)	
Energy source				
Bipolar RF	410/817 (50.18%)	250/437 (57.21%)	156/374 (41.71%)	
Cryotherapy	228/817 (27.91%)	113/437 (25.86%)	114/374 (30.48%)	<.001
Bipolar RF and Cryotherapy	88/817 (10.77%)	35/437 (8.01%)	52/374 (13.90%)	
Bipolar and Unipolar RF	66/817 (8.08%)	27/437 (6.18%)	39/374 (10.43%)	
Other	25/817 (3.06%)	12/437 (2.75%)	13/374 (3.48%)	
Variable	Beyond Blanking Period (n=817)	Mitral (n=524)	Non-Mitral (n=293)	P-value
Sternotomy	659/817 (80.66%)	368/524 (70.23%)	291/293 (99.32%)	<.001
Operation time (min)	253 \pm 80.5	266 \pm 79	228 \pm 77.4	<.001
Bypass time (min)	143 \pm 57.2	158 \pm 55.2	116 \pm 50.6	<.001
Cross clamp time (min)	96 \pm 44.9	109 \pm 42.6	73 \pm 39	<.001
LAA exclusion	565/817 (69.16%)	351/524 (66.98%)	214/293 (73.04%)	0.072
LAA management				<.001
External Closure	222/565 (39.29%)	70/351 (19.94%)	152/214 (71.03%)	<.001
Internal Closure	176/565 (31.15%)	163/351 (46.44%)	13/214 (6.07%)	
Resection	167/565 (29.56%)	118/351 (33.62%)	49/214 (22.90%)	

Energy source				<.001
Bipolar RF	410/817 (50.18%)	173/524 (33.02%)	237/293 (80.89%)	
Cryotherapy	228/817 (27.91%)	217/524 (41.41%)	11/293 (3.75%)	
Bipolar RF and Cryotherapy	88/817 (10.77%)	65/524 (12.40%)	23/293 (7.85%)	
Bipolar and Unipolar RF	66/817 (8.08%)	51/524 (9.73%)	15/293 (5.12%)	
Other	25/817 (3.06%)	18/524 (3.44%)	7/293 (2.39%)	

Variable	Beyond Blanking Period (n=817)	Full Cox Maze IV (n=208)	Box ± more (n=372)	PVI ± more (n=237)	P-value	1 vs 2	1 vs 3	2 vs 3
Sternotomy	659/817 (80.66%)	197/208 (94.71%)	238/372 (63.98%)	224/237 (94.51%)	<.001	<.001	0.927	<.001
Operation time (min)	253 ± 80.5	296 ± 88.1	244 ± 70.8	229 ± 73.1	<.001	<.001	<.001	0.003
Bypass time (min)	143 ± 57.2	170 ± 54	144 ± 51.1	118 ± 58.1	<.001	<.001	<.001	<.001
Cross clamp time (min)	96 ± 44.9	112 ± 40	99 ± 41.1	78 ± 48.6	<.001	<.001	<.001	<.001
LAA exclusion	565/817 (69.16%)	181/208 (87.02%)	215/372 (57.80%)	169/237 (71.31%)	<.001	<.001	<.001	<.001
LAA management					<.001	0.042	<.001	<.001
External Closure	222/565 (39.29%)	52/181 (28.73%)	53/215 (24.65%)	117/169 (69.23%)				
Internal Closure	176/565 (31.15%)	53/181 (29.28%)	89/215 (41.40%)	34/169 (20.12%)				
Resection	167/565 (29.56%)	76/181 (41.99%)	73/215 (33.95%)	18/169 (10.65%)				
Energy source					<.001	<.001	<.001	<.001
Bipolar RF	410/817 (50.18%)	66/208 (31.73%)	143/372 (38.44%)	201/237 (84.81%)				
Cryotherapy	228/817 (27.91%)	37/208 (17.79%)	174/372 (46.77%)	17/237 (7.17%)				
Bipolar RF and Cryotherapy	88/817 (10.77%)	82/208 (39.42%)	6/372 (1.61%)	0/237 (0.00%)				
Bipolar and Unipolar RF	66/817 (8.08%)	19/208 (9.13%)	33/372 (8.87%)	14/237 (5.91%)				
Other	25/817 (3.06%)	4/208 (1.92%)	16/372 (4.30%)	5/237 (2.11%)				

Table 6'. Procedural variables for patients with rhythm follow-up (n=574) and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Chi-square test. Continuous variables are presented as mean \pm Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Rhythm Follow-Up (n=574)	Paroxysmal (n=298)	Non-Paroxysmal (n=273)	P-value
Sternotomy	464/574 (80.84%)	247/298 (82.89%)	214/273 (78.39%)	0.173
Operation time (min)	252.4 \pm 80.6	247.1 \pm 79.8	258.3 \pm 81.5	0.128
Bypass time (min)	144.3 \pm 57.9	139.6 \pm 56.6	150.4 \pm 57.8	0.028
Cross clamp time (min)	97.1 \pm 45.8	93.6 \pm 45	101.3 \pm 46.3	0.048
LAA exclusion	417/574 (72.65%)	207/298 (69.46%)	210/273 (76.92%)	0.045
LAA management				
External Closure	161/417 (38.61%)	92/207 (44.44%)	69/210 (32.86%)	0.004
Internal Closure	129/417 (30.94%)	49/207 (23.67%)	80/210 (38.10%)	
Resection	127/417 (30.46%)	66/207 (31.88%)	61/210 (29.05%)	
Energy source				
Bipolar RF	290/574 (50.52%)	170/298 (57.05%)	118/273 (43.22%)	0.006
Cryotherapy	144/574 (25.09%)	72/298 (24.16%)	72/273 (26.37%)	
Bipolar RF and Cryotherapy	67/574 (11.67%)	28/298 (9.40%)	38/273 (13.92%)	
Bipolar and Unipolar RF	53/574 (9.23%)	19/298 (6.38%)	34/273 (12.45%)	
Other	20/574 (3.48%)	9/298 (3.02%)	11/273 (4.03%)	

Variable	Rhythm Follow-Up (n=574)	Mitral (n=363)	Non-Mitral (n=211)	P-value
Sternotomy	464/574 (80.84%)	254/363 (69.97%)	210/211 (99.53%)	<.001
Operation time (min)	252.4 \pm 80.6	268.7 \pm 79.4	224.3 \pm 74.8	<.001
Bypass time (min)	144.3 \pm 57.9	158.8 \pm 57.2	119.2 \pm 50.1	<.001
Cross clamp time (min)	97.1 \pm 45.8	109.4 \pm 45.3	76 \pm 38.4	<.001
LAA exclusion	417/574 (72.65%)	258/363 (71.07%)	159/211 (75.36%)	0.267
LAA management				
External Closure	161/417 (38.61%)	47/258 (18.22%)	114/159 (71.70%)	<.001
Internal Closure	129/417 (30.94%)	119/258 (46.12%)	10/159 (6.29%)	
Resection	127/417 (30.46%)	92/258 (35.66%)	35/159 (22.01%)	

Energy source								
Bipolar RF	290/574 (50.52%)	121/363 (33.33%)	169/211 (80.09%)	<.001				
Cryotherapy	144/574 (25.09%)	137/363 (37.74%)	7/211 (3.32%)					
Bipolar RF and Cryotherapy	67/574 (11.67%)	50/363 (13.77%)	17/211 (8.06%)					
Bipolar and Unipolar RF	53/574 (9.23%)	41/363 (11.29%)	12/211 (5.69%)					
Other	20/574 (3.48%)	14/363 (3.86%)	6/211 (2.84%)					
Variable	Rhythm Follow-Up (n=574)	Full Cox Maze IV (n=146)	Box ± more (n=262)	PVI ± more (n=166)	P-value	1 vs 2	1 vs 3	2 vs 3
Sternotomy	464/574 (80.84%)	136/146 (93.15%)	167/262 (63.74%)	161/166 (96.99%)	<.001	<.001	0.114	<.001
Operation time (min)	252.4 ± 80.6	304.3 ± 88.2	241.7 ± 69.1	223.9 ± 69.3	<.001	<.001	<.001	0.002
Bypass time (min)	144.3 ± 57.9	174 ± 56.3	143.4 ± 51	119.5 ± 57.7	<.001	<.001	<.001	<.001
Cross clamp time (min)	97.1 ± 45.8	112.5 ± 40.3	99.5 ± 43.1	79.7 ± 48.9	<.001	<.001	<.001	<.001
LAA exclusion	417/574 (72.65%)	128/146 (87.67%)	164/262 (62.60%)	125/166 (75.30%)	<.001	<.001	0.005	0.006
LAA management								
External Closure	161/417 (38.61%)	30/128 (23.44%)	40/164 (24.39%)	91/125 (72.80%)	<.001	0.029	<.001	<.001
Internal Closure	129/417 (30.94%)	37/128 (28.91%)	69/164 (42.07%)	23/125 (18.40%)				
Resection	127/417 (30.46%)	61/128 (47.66%)	55/164 (33.54%)	11/125 (8.80%)				
Energy source								
Bipolar RF	290/574 (50.52%)	44/146 (30.14%)	101/262 (38.55%)	145/166 (87.35%)	<.001	<.001	<.001	<.001
Cryotherapy	144/574 (25.09%)	21/146 (14.38%)	115/262 (43.89%)	8/166 (4.82%)				
Bipolar RF and Cryotherapy	67/574 (11.67%)	62/146 (42.47%)	5/262 (1.91%)	0/166 (0.00%)				
Bipolar and Unipolar RF	53/574 (9.23%)	16/146 10.96%)	28/262 (10.69%)	9/166 (5.42%)				
Other	20/574 (3.48%)	3/146 (2.05%)	13/262 (4.96%)	4/166 (2.41%)				

Table 7'. In-hospital outcomes for total population and subgroups.

Categorical variables are presented as n/N (%) and analysed using a Fisher's exact test. Continuous variables are presented as mean \pm Std (n) and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Total population (n=890)	Paroxysmal (n=467)	Non-Paroxysmal (n=417)	P-value
Length of stay (d)	13.8 \pm 18.2	12.9 \pm 19.2	14.9 \pm 17.2	0.006
Bleeding	12/890 (1.35%)	3/467 (0.64%)	9/417 (2.16%)	0.078
Block	20/890 (2.25%)	5/467 (1.07%)	14/417 (3.36%)	0.021
In-hospital mortality	15/890 (1.69%)	6/467 (1.28%)	9/417 (2.16%)	0.435
Cardioversion	41/890 (4.61%)	20/467 (4.28%)	21/417 (5.04%)	0.633
New permanent pacemaker	33/890 (3.71%)	10/467 (2.14%)	23/417 (5.52%)	0.012
SR at discharge	661/875 (75.5%)	373/461 (80.91%)	283/408 (69.36%)	<.001

Variable	Total population (n=890)	Mitral (n=566)	Non-Mitral (n=324)	P-value
Length of stay (d)	13.8 \pm 18.2	14.4 \pm 15.6	12.8 \pm 22.2	<.001
Bleeding	12/890 (1.35%)	9/566 (1.59%)	3/324 (0.93%)	0.552
Block	20/890 (2.25%)	16/566 (2.83%)	4/324 (1.23%)	0.160
In-hospital mortality	15/890 (1.69%)	9/566 (1.59%)	6/324 (1.85%)	0.791
Cardioversion	41/890 (4.61%)	32/566 (5.65%)	9/324 (2.78%)	0.066
New permanent pacemaker	33/890 (3.71%)	26/566 (4.59%)	7/324 (2.16%)	0.068
SR at discharge	661/875 (75.5%)	425/557 (76.3%)	236/318 (74.21%)	0.490

Variable	Total population (n=890)	Full Cox Maze IV (n=221)	Box ± more (n=408)	PVI ± more (n=261)	P-value	1 vs 2	1 vs 3	2 vs 3
Length of stay (d)	13.8 ± 18.2	17.2 ± 29.8	13.2 ± 14.2	11.9 ± 7.8	<.001	0.004	<.001	0.159
Bleeding	12/890 (1.35%)	6/221 (2.71%)	3/408 (0.74%)	3/261 (1.15%)	0.131	0.073	0.313	0.683
Block	20/890 (2.25%)	10/221 (4.52%)	6/408 (1.47%)	4/261 (1.53%)	0.053	0.031	0.060	0.99
In-hospital mortality	15/890 (1.69%)	4/221 (1.81%)	8/408 (1.96%)	3/261 (1.15%)	0.794	1000	0.708	0.542
Cardioversion	41/890 (4.61%)	11/221 (4.98%)	25/408 (6.13%)	5/261 (1.92%)	0.028	0.595	0.075	0.012
New permanent pacemaker	33/890 (3.71%)	14/221 (6.33%)	12/408 (2.94%)	7/261 (2.68%)	0.083	0.057	0.071	0.99
SR at discharge	661/875 (75.5%)	179/217 (82.49%)	301/400 (75.25%)	181/259 (69.88%)	0.006	0.039	0.001	0.129

Table 8'. In-hospital outcomes for patients with follow-up beyond the 3 month blanking period (n=817)

Categorical variables are presented as n/N (%) and analysed using a Fisher's exact test. Continuous variables are presented as mean ± Std and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Beyond Blanking Period (n=817)	Paroxysmal (n=437)	Non-Paroxysmal (n=374)	P-value
Length of stay (days)	13.2 ± 17	12.8 ± 19.7	13.7 ± 13.3	0.028
Bleeding	11/817 (1.35%)	3/437 (0.69%)	8/374 (2.14%)	0.075
Block	17/817 (2.08%)	5/437 (1.14%)	11/374 (2.94%)	0.067
In-hospital mortality				
Cardioversion	37/817 (4.53%)	18/437 (4.12%)	19/374 (5.08%)	0.513
New permanent pacemaker	28/817 (3.43%)	8/437 (1.83%)	20/374 (5.35%)	0.006
SR at d/c	618/817 (75.6%)	355/437 (81.24%)	258/374 (68.98%)	<0.001

Variable	Beyond Blanking Period (n=817)	Mitral (n=524)	Non-Mitral (n=293)	P-value
Length of stay (days)	13.2 ± 17	13.5 ± 12.5	12.6 ± 23	<.001
Bleeding	11/817 (1.35%)	8/524 (1.53%)	3/293 (1.02%)	0.550
Block	17/817 (2.08%)	13/524 (2.48%)	4/293 (1.37%)	0.284
In-hospital mortality				
Cardioversion	37/817 (4.53%)	29/524 (5.53%)	8/293 (2.73%)	0.065
New permanent pacemaker	28/817 (3.43%)	22/524 (4.20%)	6/293 (2.05%)	0.105
SR at d/c	618/817 (75.6%)	397/524 (75.76%)	221/293 (75.43%)	0.932

Variable	Beyond Blanking Period (n=817)	Full Cox Maze IV (n=208)	Box ± more (n=372)	PVI ± more (n=237)	P-value	1 vs 2	1 vs 3	2 vs 3
Length of stay (days)	13.2 ± 17	17.0 ± 30.4	12.2 ± 9	11.5 ± 7	<.001	0.003	<.001	0.117
Bleeding	11/817 (1.35%)	6/208 (2.88%)	3/372 (0.81%)	2/237 (0.84%)	0.083	0.052	0.106	0.960
Block	17/817 (2.08%)	9/208 (4.33%)	5/372 (1.34%)	3/237 (1.27%)	0.032	0.025	0.047	0.934
In-hospital mortality								
Cardioversion	37/817 (4.53%)	9/208 (4.33%)	24/372 (6.45%)	4/237 (1.69%)	0.022	0.289	0.099	0.006
New permanent pacemaker	28/817 (3.43%)	11/208 (5.29%)	12/372 (3.23%)	5/237 (2.11%)	0.177	0.222	0.072	0.415
SR at d/c	618/817 (75.6%)	170/208 (81.73%)	278/372 (74.74%)	170/237 (71.73%)	0.040	0.063	0.014	0.451

Table 9'. In-hospital outcomes for patients with rhythm follow-up (n=574) and subgroups

Categorical variables are presented as n/N (%) and analysed using a Fisher's exact test. Continuous variables are presented as mean \pm Std (n) and are analysed using a Mann-Whitney U test or Kruskal-Wallis test when comparing multiple groups. All reported p-values are two-sided.

Variable	Rhythm Follow-Up (n=574)	Paroxysmal (n=298)	Non-Paroxysmal (n=273)	P-value
Length of stay (d)	13.2 \pm 18.1	13.3 \pm 23	13.1 \pm 10.5	0.339
Bleeding	6/574 (1.05%)	0/298 (0.00%)	6/273 (2.20%)	0.012
Block	12/574 (2.09%)	3/298 (1.01%)	8/273 (2.93%)	0.129
In-hospital mortality				
Cardioversion	21/574 (3.66%)	8/298 (2.68%)	13/273 (4.76%)	0.188
New permanent pacemaker	19/574 (3.31%)	4/298 (1.34%)	15/273 (5.49%)	0.006
SR at discharge	433/574 (75.4%)	240/298 (80.5%)	191/273 (70%)	0.004

Variable	Rhythm Follow-Up (n=574)	Mitral (n=363)	Non-Mitral (n=211)	P-value
Length of stay (d)	13.2 \pm 18.1	13.3 \pm 9.8	13 \pm 27	<.001
Bleeding	6/574 (1.05%)	5/363 (1.38%)	1/211 (0.47%)	0.422
Block	12/574 (2.09%)	10/363 (2.75%)	2/211 (0.95%)	0.226
In-hospital mortality				
Cardioversion	21/574 (3.66%)	17/363 (4.68%)	4/211 (1.90%)	0.086
New permanent pacemaker	19/574 (3.31%)	15/363 (4.13%)	4/211 (1.90%)	0.149
SR at discharge	433/574 (75.4%)	274/363 (75.5%)	159/211 (75.4%)	0.999

Variable	Rhythm Follow-Up (n=574)	Full Cox Maze IV (n=146)	Box ± more (n=262)	PVI ± more (n=166)	P-value	1 vs 2	1 vs 3	2 vs 3
Length of stay (d)	13.2 ± 18.1	17.1 ± 33	12 ± 8	11.7 ± 7.6	0.003	0.006	0.001	0.422
Bleeding	6/574 (1.05%)	3/146 (2.05%)	2/262 (0.76%)	1/166 (0.60%)	0.494	0.354	0.343	0.999
Block	12/574 (2.09%)	4/146 (2.74%)	5/262 (1.91%)	3/166 (1.81%)	0.810	0.727	0.710	0.999
In-hospital mortality								
Cardioversion	21/574 (3.66%)	5/146 (3.42%)	14/262 (5.34%)	2/166 (1.20%)	0.083	0.378	0.186	0.028
New permanent pacemaker	19/574 (3.31%)	6/146 (4.11%)	9/262 (3.44%)	4/166 (2.41%)	0.696	0.729	0.395	0.547
SR at discharge	433/574 (75.4%)	119/146 (81.5%)	196/262 (74.8%)	118/166 (71.1%)	0.095	0.140	0.034	0.433

Table 10'. Rhythm-related events in-hospital and during follow-up for total population (n=890)

Variables are presented as n/N (%) and analysed using a Fisher's Exact test. All reported p-values are two-sided.

	Variable	Total population (n=890)	Paroxysmal (n=467)	Non- Paroxysmal (n=417)	P-value
In-hospital	Early cardioversion	41/890 (4.61%)	20/467 (4.28%)	21/417 (5.04%)	0.633
	New pacemaker	33/890 (3.71%)	10/467 (2.14%)	23/417 (5.52%)	0.012
During follow-up	Cardioversion	65/890 (7.3%)	20/467 (4.3%)	45/417 (10.8%)	<0.001
	Percutaneous ablation	34/890 (3.8%)	16/467 (3.4%)	17/417 (4.1%)	0.723
	New pacemaker	54/890 (6.1%)	22/467 (4.7%)	32/417 (7.7%)	0.069
Combined	New PM total	87/890 (9.7%)	32/467 (6.9%)	55/417 (13.2%)	0.0021

	Variable	Total population (n=890)	Mitral (n=566)	Non-Mitral (n=324)	P-value
In-hospital	Early cardioversion	41/890 (4.61%)	32/566 (5.65%)	9/324 (2.78%)	0.066
	New pacemaker	33/890 (3.71%)	26/566 (4.59%)	7/324 (2.16%)	0.068
During follow-up	Cardioversion	65/890 (7.3%)	45/566 (8.0%)	20/324 (6.2%)	0.352
	Percutaneous ablation	34/890 (3.8%)	31/566 (5.5%)	3/324 (0.9%)	<0.001
	New pacemaker	54/890 (6.1%)	43/566 (7.6%)	11/324 (3.4%)	0.013
Combined	New PM total	87/890 (9.7%)	69/566 (12.2%)	18/324 (5.6%)	0.0014

	Variable	Total population (n=890)	Full Cox Maze IV (n=221)	Box ± more (n=408)	PVI ± more (n=261)	P-value	1 vs 2	1 vs 3	2 vs 3
In-hospital	Early cardioversion	41/890 (4.61%)	11/221 (4.98%)	25/408 (6.13%)	5/261 (1.92%)	0.028	0.595	0.075	0.012
	New pacemaker	33/890 (3.71%)	14/221 (6.33%)	12/408 (2.94%)	7/261 (2.68%)	0.083	0.057	0.071	0.999
During follow-up	Cardioversion	65/890 (7.3%)	18/221 (8.1%)	33/408 (8.1%)	14/261 (5.4%)	0.349	0.99	0.271	0.215
	Percutaneous ablation	34/890 (3.8%)	6/221 (2.7%)	15/408 (3.7%)	13/261 (5.0%)	0.441	0.645	0.245	0.433
	New pacemaker	54/890 (6.1%)	30/221 (13.6%)	15/408 (3.7%)	9/261 (3.4%)	<0.001	<0.001	<0.001	0.99
Combined	New PM total	87/890 (9.7%)	44/221 (19.9%)	27/408 (6.6%)	18/261 (6.9%)	<0.001	<0.001	<0.001	0.88

Table 11'. Rhythm-related events in-hospital and during follow-up for patients with follow-up beyond 3 months (n=817)
Variables are presented as n/N (%) and analysed using a Fisher's Exact test. All reported p-values are two-sided.

	Variable	Beyond Blanking Period (n=817)	Paroxysmal (n=437)	Non-Paroxysmal (n=374)	P-value
In-hospital	Early cardioversion	37/817 (4.53%)	18/437 (4.12%)	19/374 (5.08%)	0.613
	New pacemaker	28/817 (3.43%)	8/437 (1.83%)	20/374 (5.35%)	0.007
During follow-up	Cardioversion	65/817 (8.0%)	20/437 (4.6%)	45/374 (12.0%)	<0.001
	Percutaneous ablation	34/817 (4.2%)	16/437 (3.7%)	17/374 (4.6%)	0.594
Combined	New pacemaker	52/817 (6.4%)	21/437 (4.8%)	31/374 (8.3%)	0.0453
	New PM total	80/817 (9.8%)	29/437 (6.6%)	51/374 (13.6%)	<0.001

	Variable	Beyond Blanking Period (n=817)	Mitral (n=524)	Non-Mitral (n=293)	P-value
In-hospital	Early cardioversion	37/817 (4.53%)	29/524 (5.53%)	8/293 (2.73%)	0.079
	New pacemaker	28/817 (3.43%)	22/524 (4.20%)	6/293 (2.05%)	0.113
During follow-up	Cardioversion	65/817 (8.0%)	45/524 (8.6%)	20/293 (6.8%)	0.420
	Percutaneous ablation	34/817 (4.2%)	31/524 (5.9%)	3/293 (1.0%)	<0.001
Combined	New pacemaker	52/817 (6.4%)	42/524 (8.0%)	10/293 (3.4%)	0.0105
	New PM total	80/817 (9.8%)	64/524 (12.2%)	16/293 (5.5%)	0.0019

	Variable	Beyond Blanking Period (n=817)	Full Cox Maze IV (n=208)	Box ± more (n=372)	PVI ± more (n=237)	P-value	1 vs 2	1 vs 3	2 vs 3
In-hospital	Early cardioversion	37/817 (4.53%)	9/208 (4.33%)	24/372 (6.45%)	4/237 (1.69%)	0.016	0.352	0.156	0.005
	New pacemaker	28/817 (3.43%)	11/208 (5.29%)	12/372 (3.23%)	5/237 (2.11%)	0.188	0.268	0.08	0.462
During follow-up	Cardioversion	65/817 (8.0%)	18/208 (8.7%)	33/372 (8.9%)	14/237 (5.9%)	0.386	0.99	0.276	0.214
	Percutaneous ablation	34/817 (4.2%)	6/208 (2.9%)	15/372 (4.0%)	13/237 (5.5%)	0.386	0.644	0.24	0.431
Combined	New pacemaker	52/817 (6.4%)	29/208 (13.9%)	15/372 (4.0%)	8/237 (3.4%)	<0.001	<0.001	<0.001	0.828
	New PM total	80/817 (9.8%)	40/208 (19.2%)	27/372 (7.3%)	13/237 (5.5%)	<0.001	<0.001	<0.001	0.502

Table 12'. Rhythm-related events in-hospital and during follow-up for patients with rhythm follow-up (n=574)

Variables are presented as n/N (%) and analysed using a Fishers Exact test. All reported p-values are two-sided.

		Rhythm Follow-Up (n=574)	Paroxysmal (n=298)	Non- Paroxysmal (n=273)	P-value				
In-hospital	Early cardioversion	21/574 (3.66%)	8/298 (2.68%)	13/273 (4.76%)	0.188				
	New pacemaker	19/574 (3.31%)	4/298 (1.34%)	15/273 (5.49%)	0.006				
During follow-up	Cardioversion	48/574 (8.4%)	12/298 (4.03%)	36/273 (13.19%)	<0.001				
	Percutaneous ablation	30/574 (5.23%)	14/298 (4.70%)	15/273 (5.49%)	0.706				
Combined	New pacemaker	37/574 (6.45%)	15/298 (5.03%)	22/273 (8.06%)	0.174				
	New PM total	56/574 (9.76%)	19/298 (6.38%)	37/273 (13.55%)	0.005				
		Rhythm Follow-Up (n=574)	Mitral (n=363)	Non-Mitral (n=211)	P-value				
In-hospital	Early cardioversion	21/574 (3.66%)	17/363 (4.68%)	4/211 (1.90%)	0.086				
	New pacemaker	19/574 (3.31%)	15/363 (4.13%)	4/211 (1.90%)	0.149				
During follow-up	Cardioversion	48/574 (8.4%)	30/363 (8.26%)	18/211 (8.53%)	0.999				
	Percutaneous ablation	30/574 (5.23%)	27/363 (7.44%)	3/211 (1.42%)	0.001				
Combined	New pacemaker	37/574 (6.45%)	28/363 (7.71%)	9/211 (4.27%)	0.115				
	New PM total	56/574 (9.76%)	43/363 (11.85%)	13/211 (6.16%)	0.029				
		Rhythm Follow-Up (n=574)	Full Cox Maze IV (n=146)	Box ± more (n=262)	PVI ± more (n=166)	P-value	1 vs 2	1 vs 3	2 vs 3
In-hospital	Early cardioversion	21/574 (3.66%)	5/146 (3.42%)	14/262 (5.34%)	2/166 (1.20%)	0.083	0.378	0.186	0.028
	New pacemaker	19/574 (3.31%)	6/146 (4.11%)	9/262 (3.44%)	4/166 (2.41%)	0.696	0.729	0.395	0.547
During follow-up	Cardioversion	48/574 (8.4%)	14/146 (9.59%)	22/262 (8.40%)	12/166 (7.23%)	0.732	0.717	0.539	0.717
	Percutaneous ablation	30/574 (5.23%)	5/146 (3.42%)	13/262 (4.96%)	12/166 (7.23%)	0.336	0.617	0.211	0.398
Combined	New pacemaker	37/574 (6.45%)	21/146 (14.38%)	9/262 (3.44%)	7/166 (4.22%)	<0.001	<0.001	0.002	0.795
	New PM total	56/574 (9.76%)	27/146 (18.49%)	18/262 (6.87%)	11/166 (6.63%)	<0.001	<0.001	0.002	0.999

Table 13'. Freedom from AF with and without dependence on AADs and use of ACDs for patients with follow-up beyond the 3 month blanking point (n=817)

Variables are presented as n/N (%) and analysed using a Fisher's exact test. All reported p-values are two-sided.

Variable	Beyond Blanking Period (n=817)	Paroxysmal (n=437)	Non-Paroxysmal (n=374)	P-value
Free from AF	571/817 (69.89%)	331/437 (75.74%)	237/374 (63.37%)	<.001
Free from AF and off AAD	417/817 (51.0%)	243/437 (55.6%)	172/374 (46.0%)	0.007
Free from AF and off ACD	281/817 (34.4%)	163/437 (37.3%)	116/374 (31.0%)	0.060

Variable	Beyond Blanking Period (n=817)	Mitral (n=524)	Non-Mitral (n=293)	P-value
Free from AF	571/817 (69.89%)	344/524 (65.65%)	227/293 (77.47%)	<.001
Free from AF and off AAD	417/817 (51.0%)	247/524 (47.2%)	170/293 (58.0%)	0.003
Free from AF and off ACD	281/817 (34.4%)	155/524 (29.6%)	126/293 (43.0%)	<0.001

Variable	Beyond Blanking Period (n=817)	Full Cox Maze IV (n=208)	Box ± more (n=372)	PVI ± more (n=237)	P-value	1 vs 2	1 vs 3	2 vs 3
Free from AF	571/817 (69.89%)	149/208 (71.63%)	244/372 (65.59%)	178/237 (75.11%)	0.038	0.140	0.452	0.015
Free from AF and off AAD	417/817 (51.0%)	118/208 (56.7%)	162/372 (43.5%)	137/237 (57.8%)	<0.001	0.00245	0.8479	<0.001
Free from AF and off ACD	281/817 (34.4%)	77/208 (37.0%)	109/372 (29.3%)	95/237 (40.1%)	0.016	0.056	0.508	0.006

Table 14'. Freedom from AF with and without continuation of AADs and use of ACDs for patients with rhythm follow-up (n=574)

Variables are presented as n/N (%) and analysed using a Fisher's exact test. All reported p-values are two-sided.

Variable	Rhythm Follow-Up (n=574)	Paroxysmal (n=298)	Non- Paroxysmal (n=273)	P-value
Free from AF	352/574 (61.32%)	205/298 (68.79%)	147/273 (53.85%)	<.001
Free from AF and off AAD	255/574 (44.4%)	149/298 (50%)	106/273 (38.83%)	0.007
Free from AF and off ACD	176/574 (30.1%)	100/298 (33.56%)	76/273 (27.84%)	0.139

Variable	Rhythm Follow-Up (n=574)	Mitral (n=363)	Non-Mitral (n=211)	P-value
Free from AF	352/574 (61.32%)	201/363 (55.37%)	151/211 (71.56%)	<.001
Free from AF and off AAD	255/574 (44.4%)	143/363 (39.40%)	112/211 (53.10%)	0.001
Free from AF and off ACD	176/574 (30.1%)	95/363 (26.20%)	81/211 (38.39%)	0.002

Variable	Rhythm Follow-Up (n=574)	Full Cox Maze IV (n=146)	Box (n=262)	PVI (n=166)	P- value	1 vs 2	1 vs 3	2 vs 3
Free from AF	352/574 (61.32%)	95/146 (65.07%)	144/262 (54.96%)	113/166 (68.07%)	0.014	0.059	0.631	0.008
Free from AF and off AAD	255/574 (44.4%)	76/146 (52.05%)	91/262 (34.73%)	88/166 (53.01%)	<.001	<.001	0.866	<.001
Free from AF and off ACD	176/574 (30.1%)	52/146 35.6%	68/262 (25.95%)	56/166 (33.73%)	0.076	0.040	0.727	0.084

Table 15'. Results of uni- and multivariable logistic regression models for overall freedom from AF in patients with rhythm follow-up (n=574) with odds ratios for recurrence of AF.

Variable	Univariable model		Multivariable model	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	0.99 (0.97-1.01)	0.384	0.99 (0.98-1.02)	0.732
Female	1.18 (0.83-1.66)	0.355	0.94 (0.63-1.40)	0.765
AF duration (y)	0.97 (0.91-1.02)	0.189	0.96 (0.91-1.02)	0.219
Paroxysmal AF	0.53 (0.38-0.75)	<.001	0.59 (0.40-0.86)	0.006
LVEF	0.99 (0.98-1.01)	0.78	1.00 (0.99-1.02)	0.792
LAD (mm)	1.06 (1.03-1.08)	<.001	1.04 (1.02-1.07)	0.002
Previous ablation	1.16 (0.50-2.65)	0.733	1.61 (0.63-4.08)	0.319
Pacemaker pre-op	1.48 (0.62-3.55)	0.376	1.67 (0.66-4.20)	0.281
Mitral surgery	1.99 (1.38-2.87)	<.001	1.85 (1.10-3.12)	0.022
Ablation		0.012		0.349
Box ± more	1.77 (1.17-2.66)	0.007	1.05 (0.61-1.82)	0.861
Full Cox Maze IV	1.14 (0.71-1.84)	0.579	0.71 (0.37-1.38)	0.314
Energy source		0.005		0.049
Bipolar	0.36 (0.14-0.91)	0.031	0.41 (0.15-1.09)	0.073
Bi- and unipolar	0.87 (0.31-2.48)	0.794	0.70 (0.24-2.09)	0.524
Bipolar and Cryo	0.27 (0.09-0.76)	0.014	0.31 (0.10-0.97)	0.045
Cryo	0.44 (0.17-1.14)	0.089	0.32 (0.12-0.88)	0.027

Table 16'. Results of uni- and multivariable Cox regression models for Kaplan-Meier estimate of freedom from AF in patients with rhythm follow-up (n=574) with hazard ratios for recurrence of AF.

	Univariable model		Multivariable model	
	HR (95%CI)	P-value	HR (95%CI)	P-value
Age	1.00 (0.99-1.02)	0.462	1.00 (0.99-1.012)	0.637
Female	1.28 (1.04-1.58)	0.021	1.22 (0.96-1.54)	0.103
AF duration (y)	0.98 (0.95-1.01)	0.229	0.98 (0.95-1.02)	0.379
Paroxysmal AF	0.76 (0.62-0.94)	0.011	0.76 (0.61-0.96)	0.019
LVEF	1.00 (0.99-1.01)	0.616	1.00 (0.99-1.01)	0.423
LAD (mm)	1.02 (1.01-1.04)	0.001	1.02 (1.00-1.03)	0.029
Previous ablation	0.86 (0.51-1.44)	0.568	1.00 (0.57-1.76)	0.997
Pacemaker pre-op	1.12 (0.67-1.89)	0.659	1.23 (0.72-2.09)	0.453
Mitral surgery	1.26 (1.01-1.58)	0.04	1.11 (0.81-1.51)	0.521
Ablation		0.013		0.161
Box ± more	1.38 (1.07-1.78)	0.014	1.26 (0.90-1.76)	0.185
Full Cox Maze IV	1.02 (0.75-1.37)	0.924	0.96 (0.64-1.44)	0.838
Energy source		0.179		0.145
Bipolar	0.82 (0.47-1.41)	0.464	1.07 (0.60-1.87)	0.828
Bi- and unipolar	1.05 (0.57-1.91)	0.883	1.12 (0.61-2.08)	0.714
Bipolar and Cryo	0.61 (0.33-1.13)	0.117	0.76 (0.38-1.49)	0.42
Cryo	0.80 (0.46-1.41)	0.441	0.79 (0.45-1.40)	0.418

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Supplementary Figures

Figure 1, as seen in the article. Overall freedom from AF with and without (inlaying white bars) continuation of AADs for the total population with follow-up beyond 3 months (n=817). Statistical comparison was performed using a Fisher's Exact test and significant differences are indicated with brackets.

Figure 1'. Overall freedom from AF with and without (inlaying white bars) continuation of AADs for patients with sufficient follow-up beyond 3 months (n=574). Statistical comparison was performed using a Fisher's Exact test and significant differences are indicated with brackets.

Figures 2'-5': Kaplan-Meier curves for freedom from atrial fibrillation for the total population with follow-up beyond 3 months (n=817). The overall, mixed population as well as subgroups are shown. Statistical comparisons are performed using the log-rank test.

Figure 6'-9': Kaplan-Meier curves for freedom from atrial fibrillation for patients with sufficient follow-up beyond 3 months (n=574). The overall, mixed population as well as subgroups are shown. Statistical comparisons are performed using the log-rank test.

Figure 10'-13': Kaplan-Meier curves for overall survival for the total population (n=890). The overall, mixed population as well as subgroups are shown. Statistical comparisons are performed using the log-rank test.

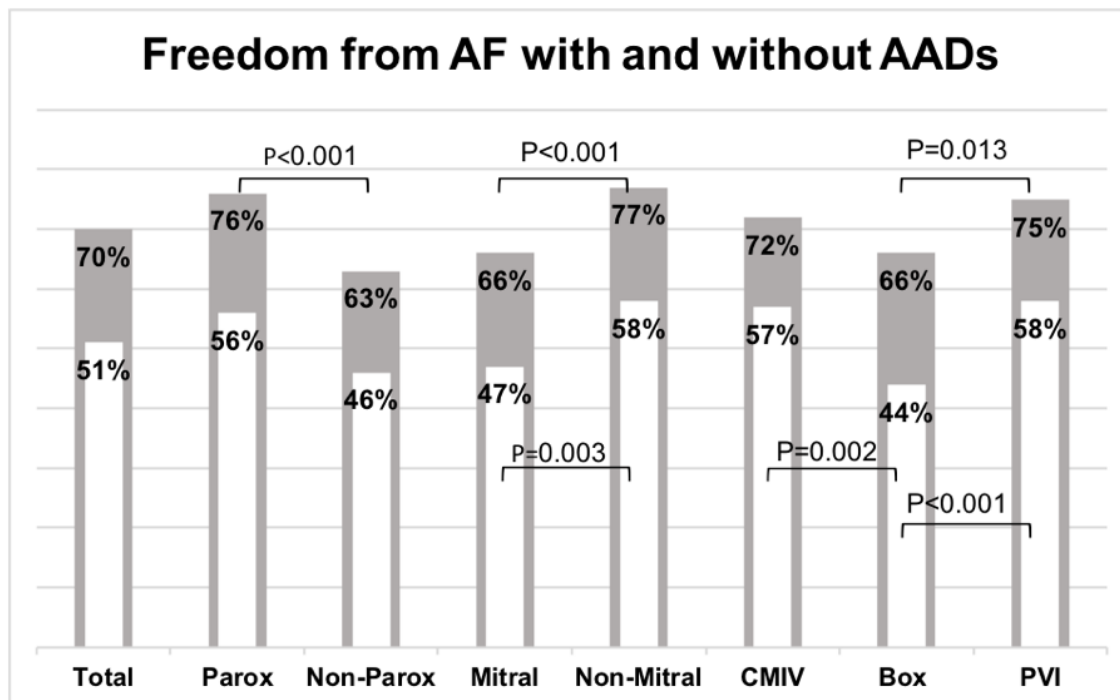


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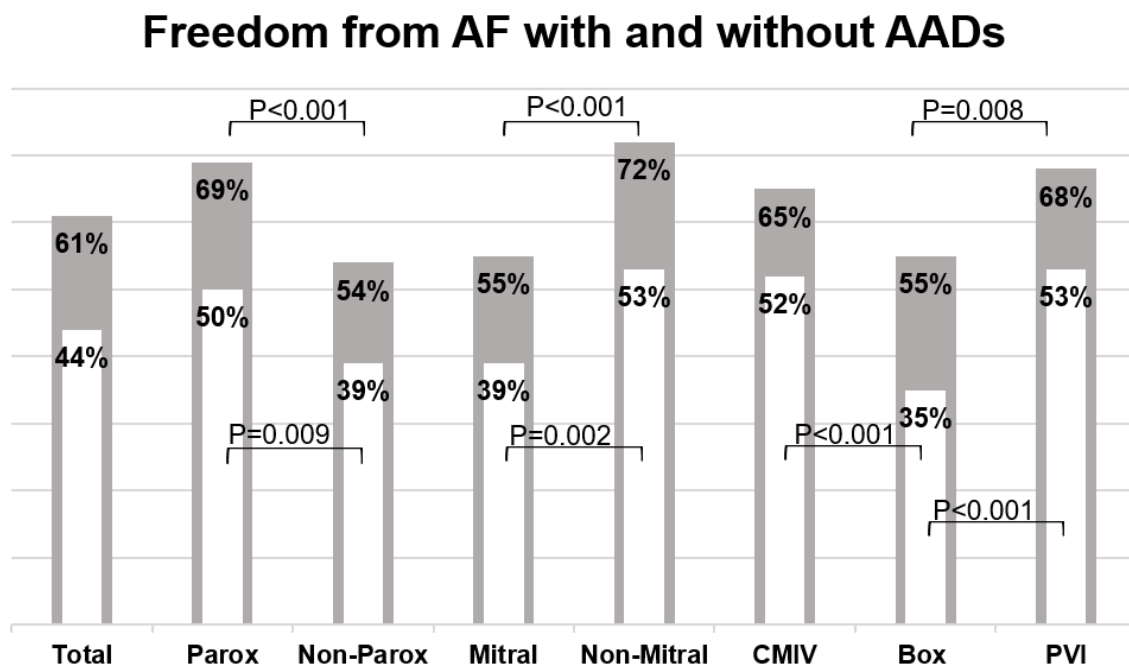


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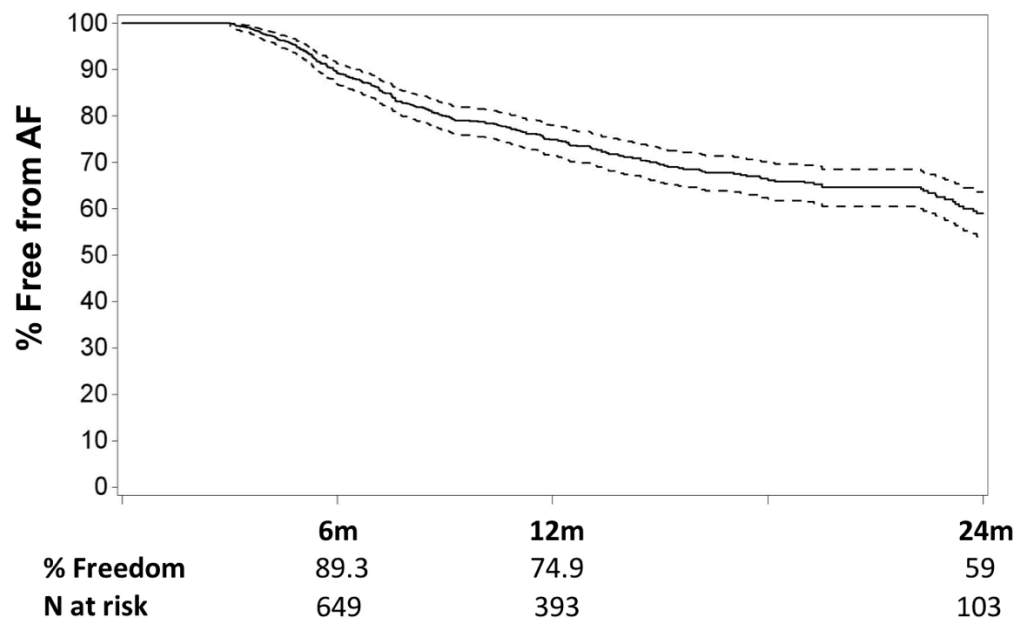


Figure 2'. Kaplan-Meier curve for freedom from atrial fibrillation for the total population with follow-up beyond 3 months (n=817).

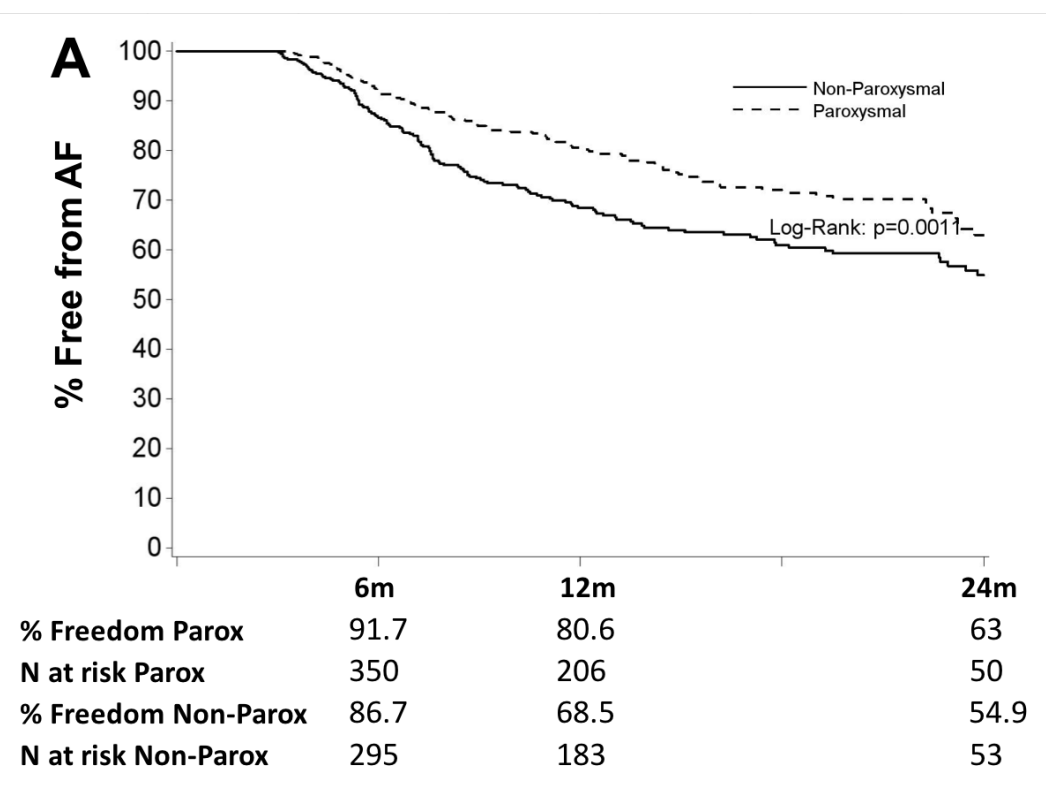


Figure 3'. Kaplan-Meier curve illustrating a significant difference in freedom from atrial fibrillation beyond 3 months when comparing patients with preoperative paroxysmal AF (n=437) versus non-paroxysmal AF (n=374).

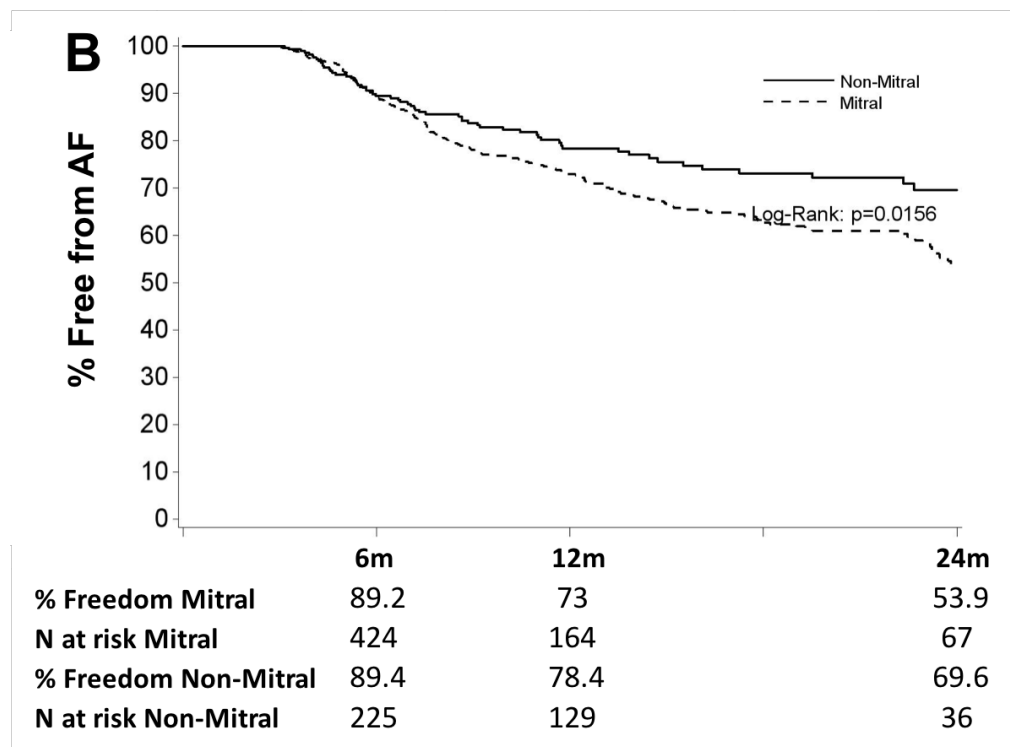


Figure 4'. Kaplan-Meier curve illustrating a significant difference in freedom from atrial fibrillation beyond 3 months between patients undergoing mitral surgery (n=524) compared to those undergoing non-mitral surgery (n=293).

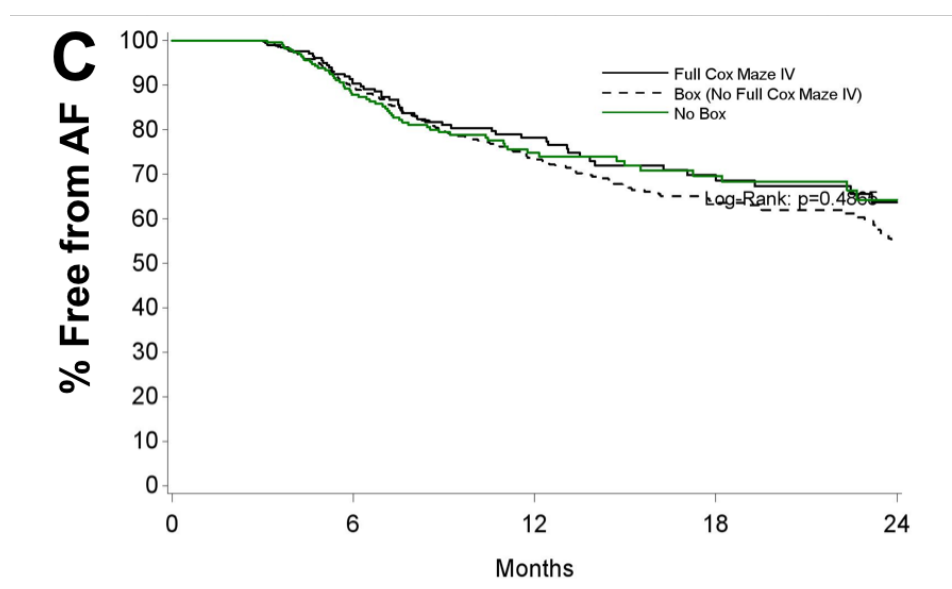


Figure 5'. Kaplan-Meier curve showing freedom from atrial fibrillation beyond 3 months for patients undergoing CMIV ablations (n=208), Box ablations (n=372) and PVI ablations (n=237). No significant difference was observed.

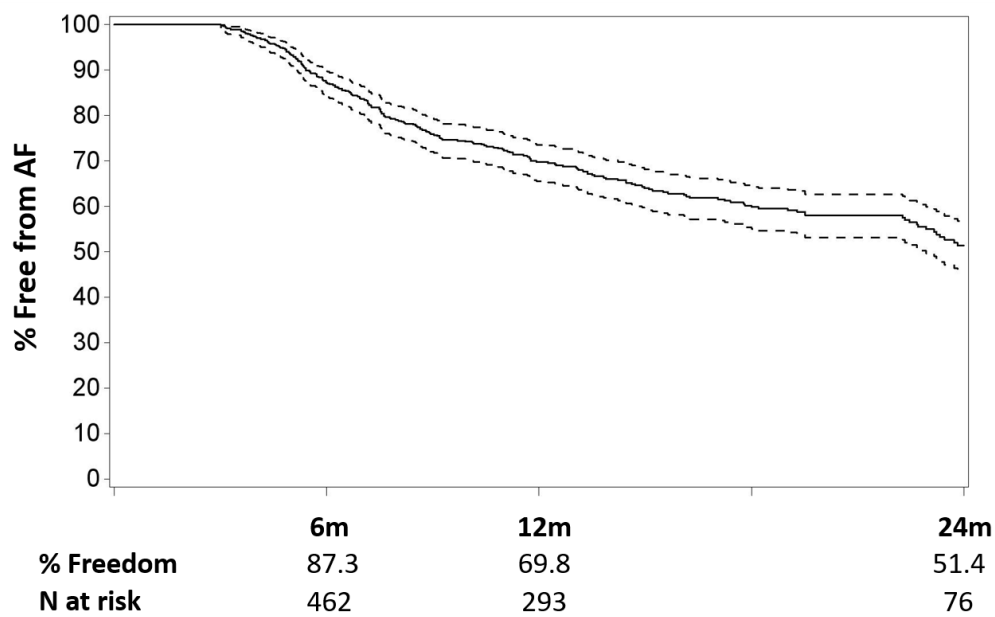


Figure 6’. Kaplan-Meier curve of freedom from atrial fibrillation for all patients with sufficient follow-up beyond 3 months (n=574).

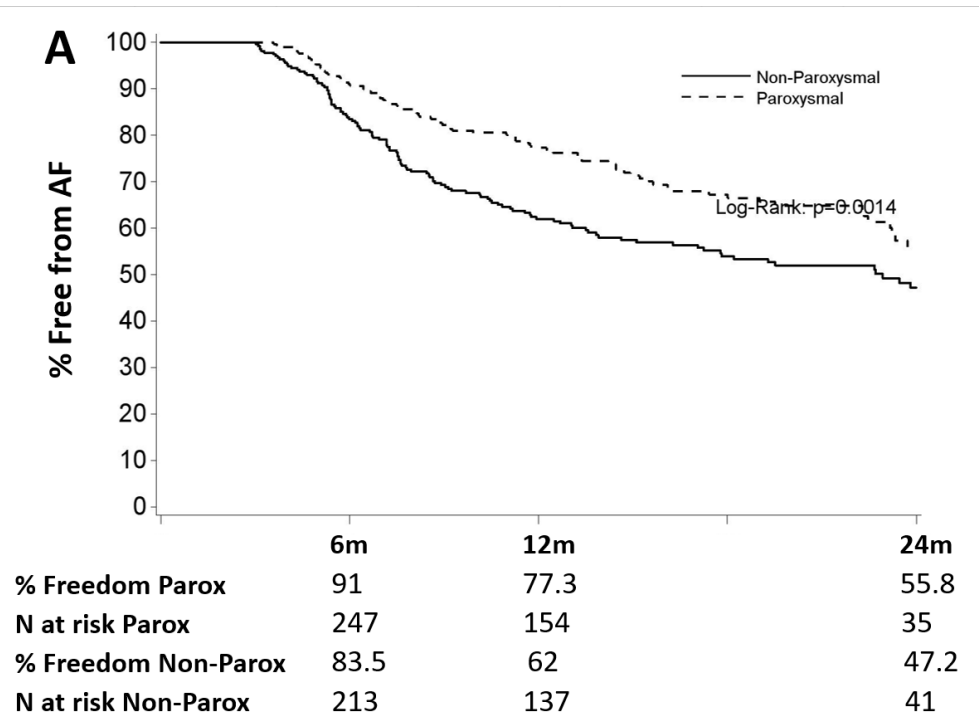


Figure 7’. Kaplan-Meier curve illustrating a significant difference in freedom from atrial fibrillation in patients with sufficient follow-up when comparing those with preoperative paroxysmal AF (n=298) to those with non-paroxysmal AF (n=273).

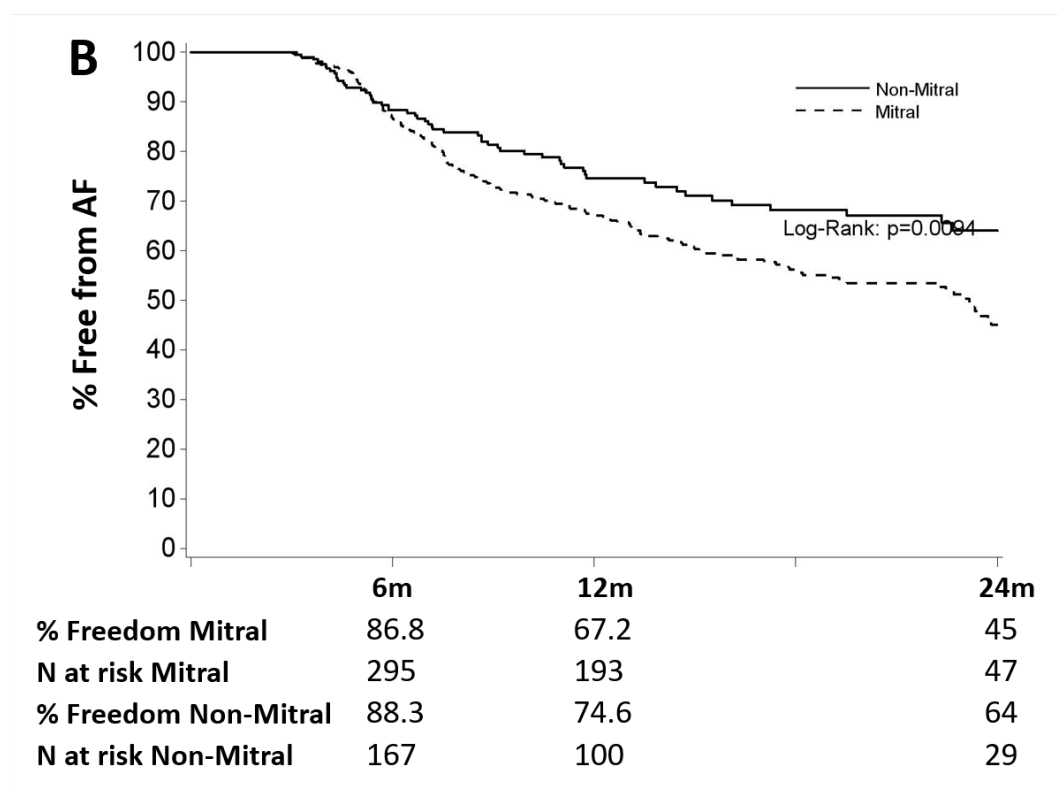


Figure 8’. Kaplan-Meier curve illustrating a significant difference in freedom from atrial fibrillation in patients with sufficient follow-up when comparing those undergoing mitral surgery (n=363) to those undergoing non-mitral surgery (n=211).

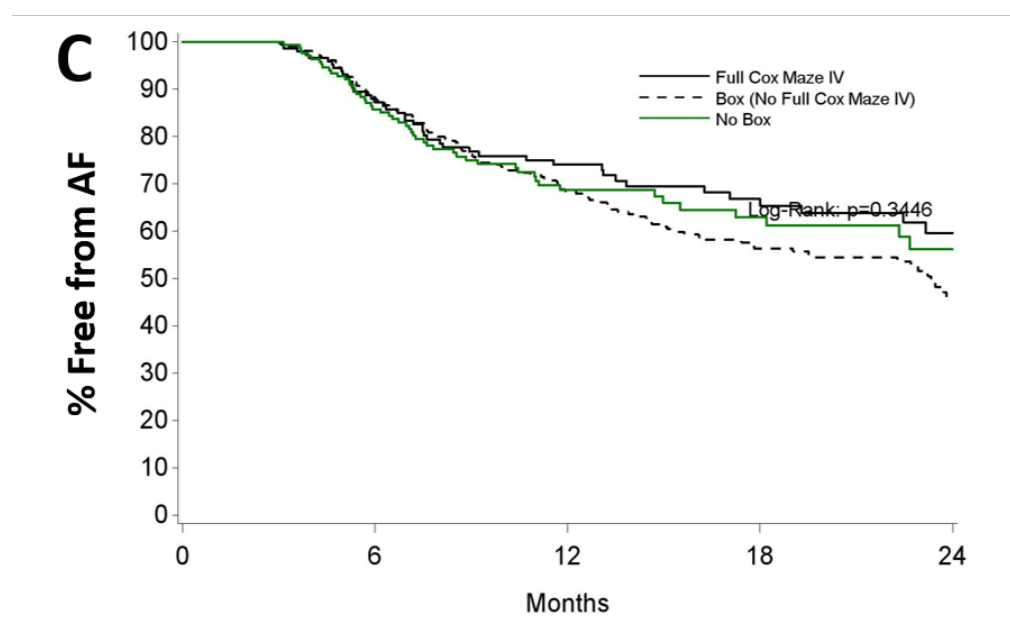


Figure 9’. Kaplan-Meier curve showing freedom from atrial fibrillation in patients with sufficient follow-up for those undergoing CMIV ablations (n=146), Box ablations (n=262) and PVI ablations (n=211). No significant difference was observed.

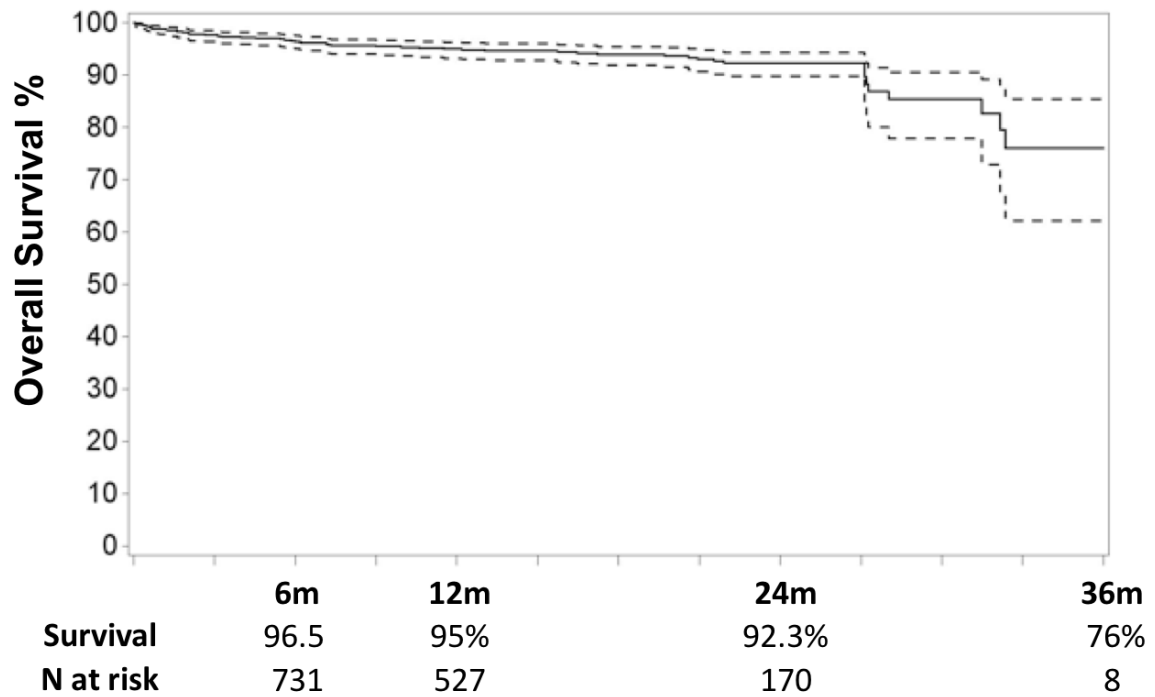


Figure 10’. Kaplan-Meier curve for overall survival of total population (n=890).

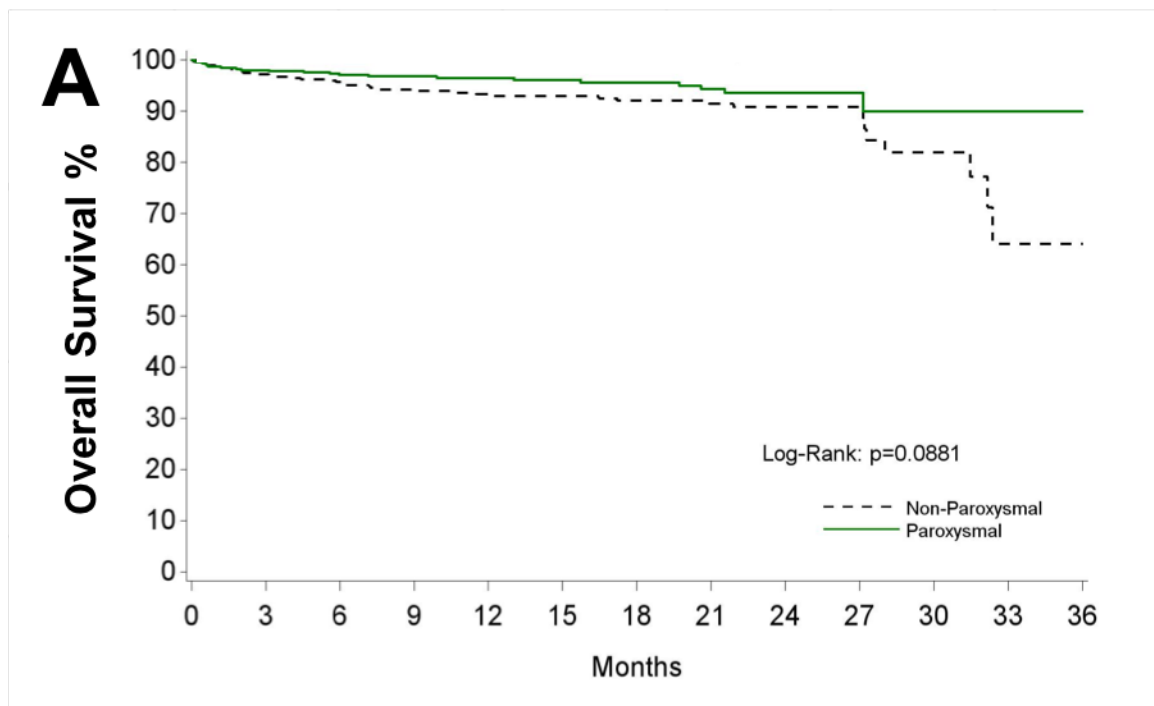


Figure 11’. Kaplan-Meier curve comparing overall survival for patients with preoperative paroxysmal AF (n= 467) versus non-paroxysmal AF (n=417). No significant difference was observed.

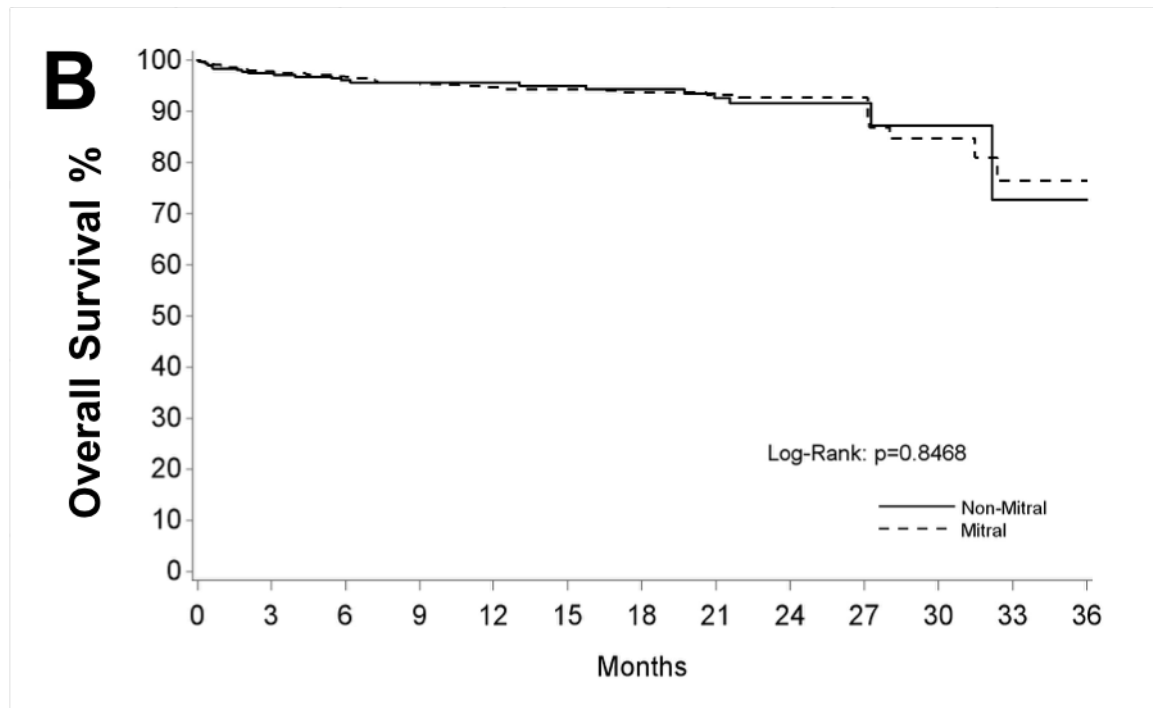


Figure 12'. Kaplan-Meier curve comparing overall survival for patients undergoing concomitant mitral surgery (n=566) versus those undergoing non-mitral surgery (n=324). No significant difference was observed.

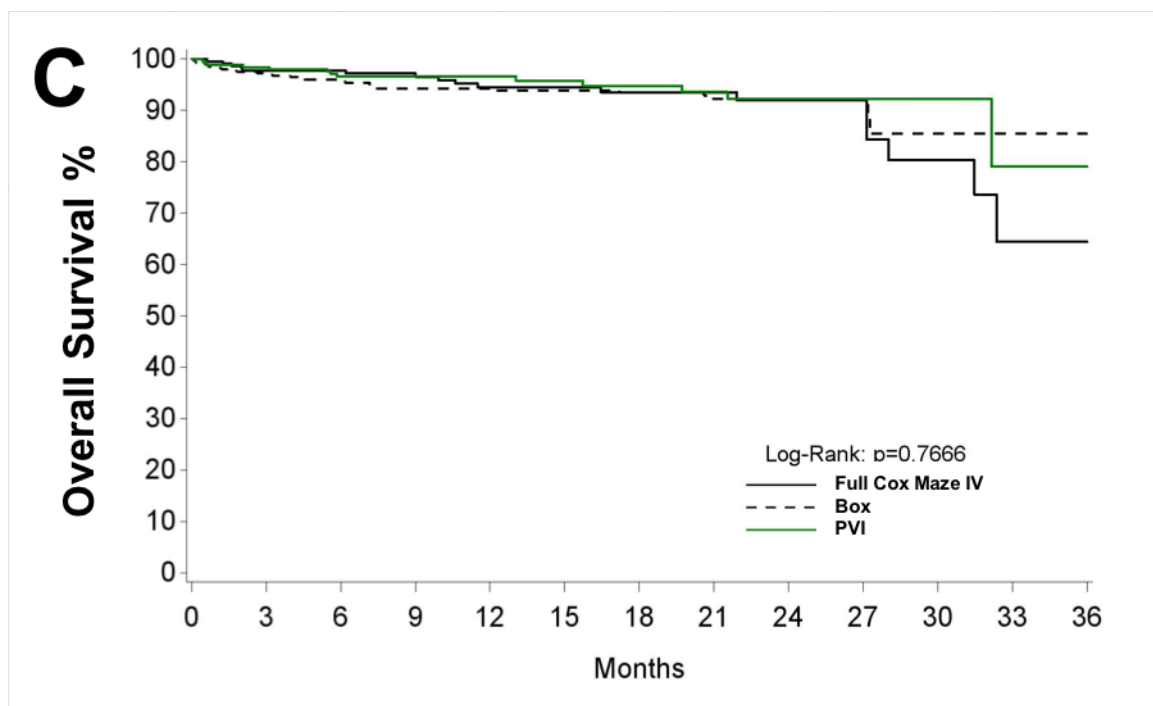


Figure 13'. Kaplan-Meier curve comparing overall survival for patients undergoing CMIV ablations (n=324), Box ablations (n=408) and PVI ablations (n=261). No significant difference was observed.