Multiple Procedure Outcomes for Non-Paroxysmal Atrial Fibrillation: Left Atrial Posterior Wall Isolation versus Stepwise Ablation

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Abstract

Objective: To compare multiple-procedure catheter ablation outcomes of a stepwise approach versus left atrial posterior wall isolation (LA PWI) in patients undergoing non-paroxysmal atrial fibrillation (NPAF) ablation. Background: Unfavorable outcomes for stepwise ablation of NPAF in large clinical trials may be attributable to pro-arrhythmic effects of incomplete ablation lines. It is unknown if a more extensive initial ablation strategy results in improved outcomes following multiple ablation procedures. Methods: 222 consecutive patients with NPAF underwent first-time ablation using a contact-force sensing ablation catheter utilizing either a stepwise (Group 1, n=111) or LA PWI (Group 2, n=111) approach. The duration of follow-up was 36 months. The primary endpoint was freedom from atrial arrhythmia >30s. Secondary endpoints were freedom from persistent arrhythmia, repeat ablation, and recurrent arrhythmia after repeat ablation. Results: There was similar freedom from atrial arrhythmias after index ablation for both stepwise and LA PWI groups at 36 months (60% vs. 69%, p=0.1). The stepwise group was more likely to present with persistent recurrent arrhythmia (29% vs 14%, p=0.005) and more likely to undergo second catheter ablation (32% vs. 12%, p<0.001) compared to LA PWI patients. Recurrent arrhythmia after repeat ablation was more likely in the stepwise group compared to the LA PWI group (15% vs 4%, p=0.003). Conclusions: Compared to a stepwise approach, LA PWI for patients with NPAF resulted in a similar incidence of any atrial arrhythmia, lower incidence of persistent arrhythmia, and fewer repeat ablations. Results for repeat ablation were not improved with a more extensive initial approach.

Key Words

Atrial Fibrillation

Catheter Ablation

Contact-Force Sensing

Radiofrequency Ablation

Posterior Wall Isolation

Stepwise

Procedural Outcomes

Condensed Abstract

It is unknown if more extensive initial ablation results in improved outcomes following multiple ablation procedures. We analyzed consecutive patients with non-paroxysmal AF who underwent first-time ablation using stepwise (n=111) or left atrial posterior wall isolation (PWI, n=111) approach. Over 36 months follow-up, compared to a stepwise approach, a PWI approach resulted in similar recurrence of any atrial arrhythmia >30s, but less persistent arrhythmia recurrence, fewer repeat ablations, and fewer recurrences after repeat ablation.

Introduction:

Pulmonary vein antral isolation (PVAI) is an effective strategy for catheter ablation of paroxysmal AF (PAF).[1–5] Various adjunctive ablation strategies have been evaluated for catheter ablation of non-paroxysmal AF (NPAF) and found to have limited success.[2,4,6] Unfavorable outcomes for stepwise linear ablation of NPAF in clinical trials may be attributable to pro-arrhythmic effects of incomplete ablation lines, particularly in the absence of contact-force sensing (CFS) RFA catheters.[4,7,8] It is unknown, however, if a more extensive initial ablation strategy results in improved outcomes following repeat ablation procedures. We compared multiple-procedure catheter ablation outcomes of stepwise linear ablation to left atrial (LA) posterior wall isolation (PWI) in patients undergoing NPAF ablation using a CFS RFA catheter.

Methods:

Clinical outcomes were evaluated in 222 patients undergoing first-time catheter ablation of NPAF with a CFS RFA catheter (SmartTouch, Biosense Webster) at New York University (NYU) Langone Health. Group 1 included 111 patients that underwent PVAI followed by stepwise linear ablation between July 2014 and September 2015, while Group 2 included 111 patients that underwent PVAI followed by LA PWI between October 2015 and August 2016. Our group changed ablation strategies from a linear stepwise approach to LA PWI and this research evaluates the effectiveness of this change. Index and repeat ablations were performed by the same five high-volume (>150 AF ablations per year) operators in each cohort. NPAF was defined as AF lasting more than seven days or a duration of greater than 48 hours requiring cardioversion.[9] The incidence of atrial arrhythmia recurrence of >30 seconds in duration was evaluated in each cohort and stratified by AF or atrial tachycardia (AT) as well as by persistence of the arrhythmia. Amiodarone was discontinued at least one month prior to ablation and any antiarrhythmics started after the ablation were discontinued within 4 to 8 weeks after the procedure. After the index ablation, patients were scheduled for follow up in-office visits at 3, 6, 9, and 12 months, and every 6 months thereafter. At each visit, study assessments included a detailed medical history, physical exam, and 12-lead ECG. A 2-week mobile cardiac outpatient telemetry (MCOT) monitor was performed prior to each scheduled in-office visit in patients without implanted arrhythmia monitoring. Arrhythmia recurrence was defined as either (1) a sustained atrial arrhythmia within the 90-day blanking period that required a repeat ablation or (2) an atrial arrhythmia that occurred after the 90-day blanking period and was captured on a resting 12-lead ECG or lasted longer than 30 seconds on an ambulatory monitor. Persistence of AF or AT after index ablation was defined by the need for direct current cardioversion after the blanking period or sustained AF or AT at the time of repeat ablation. Patient follow-up was censored for the purposes of survival analyses at time of last follow up if less than 3 years after their first procedure, but did not have a second ablation.

Electrophysiology Study and Ablation

Data collection and analysis were performed according to protocols approved by the NYU Langone Health Institutional Review Board. Surface and intracardiac electrograms (ECGs) were digitally recorded and stored (EP Workmate, Abbott Medical, Inc.,). Non-fluoroscopic 3-dimensional mapping was performed using the Carto 3 (Biosense-Webster, Inc.,) mapping system.

All procedures were performed under general anesthesia with standard mechanical ventilation using weight-based tidal volumes. A 7-French 20-pole catheter (Daig DuoDeca 2-10-2, Abbott Medical, Inc.) was used with the distal poles placed within the coronary sinus and the proximal electrodes located along the tricuspid annulus in the lateral and inferior right atrium. For left atrial mapping and recording, a 10- or 20-pole circumferential PV mapping catheter (Lasso, Biosense-Webster, Inc.), or a five-spline mapping catheter

(PentaRay Nav, Biosense-Webster, Inc.) was utilized. Left atrial three-dimensional anatomy and voltage mapping was created with manipulation of the multi-electrode mapping catheter. Low-voltage areas were defined as bipolar voltage <0.5 mV either during AF or atrial pacing.

Ablation was performed in each group with an open-irrigated, 3.5-mm RFA catheter (ThermoCool SmartTouch, Biosense Webster Inc.). Ablation lesions were generated in a power-controlled mode applying 20 to 35 W for 20 to 40 seconds per lesion during irrigation at a rate of 17 to 30-mL/min while maintaining a goal ACT of > 350 seconds. All electroanatomic map lesion markers were created using automated lesion annotation (VisiTag, Biosense Webster, Inc.) with settings at the discretion of each operator.

A stepwise linear ablation approach, as previously described by O'Neill et al, [10] was utilized in Group 1. PVAI was performed as the initial step with wide area circumferential lesions created approximately 1 cm proximal to the ostium of each of the right veins and posterior left veins. When AF terminated during this step, entrance and exit block was assessed with the ablation catheter during sinus rhythm and confirmed with a multielectrode mapping catheter at the end of the procedure as described below. If AF persisted, only entrance block was confirmed and additional linear ablation was performed. The second step was ablation along the LA roof creating a line between the isolated left and right pulmonary veins at approximately the 12 o'clock (superior) position. The next step was targeting complex LA activity while the patient remained in AF, which included regions of continuous electrical activity, complex fractionated atrial electrograms, and locally short cycle lengths. These regions included the posterior interatrial septum, posterior LA, base of LAA, inferior LA, coronary sinus, anterior LA, and mitral isthmus at the discretion of the operator. The goal of ablation in each of these regions was to organize local activity, decrease amplitude of atrial signals, and to achieve a line of block when a mitral line was created. When electrogram-based ablation of the LA did not result in organization of the coronary sinus, electrogram-based ablation was performed in the right atrium (RA) if the RA appendage demonstrated a shorter cycle length than the LA appendage targeting areas of complex electrograms in the RA. If the patient remained in atrial fibrillation, decision to perform electrical cardioversion due to procedure length or extensive atrial ablation was at the discretion of the operator. LA PWI was utilized in Group 2, which included PVAI, as described above, followed by isolation of the LA posterior wall. PWI was achieved by creating linear lesions along the posterior LA roof and posterior-inferior LA between the isolated pulmonary veins.

If the patient converted to an atrial tachycardia in either group, the arrhythmia was mapped and targeted with ablation. Ablation of the CTI was performed at the discretion of the operator in both groups. A waiting period of 30 minutes, followed by administration of adenosine, was utilized to confirm entrance and exit block. If prior ablation sites were still excitable with bipolar pacing output of 10 mA at 2 msec after PVAI or LA PWI, additional ablation lesions were delivered until loss of pace capture was achieved at that location. [11,12] All sites of adenosine elicited dormant PV or LA posterior wall conduction were also ablated.

Statistical Analysis

The statistical analysis was performed using Stata version 14.0 (StataCorp LLC, College Station, TX). Descriptive statistics were used to summarize demographic characteristics. Continuous variables were assessed for normality with the Kolmogorov-Smirnov test. All normally distributed data were analyzed using an unpaired Student t test. A 2-tailed P value < 0.05 was considered statistically significant. Data found to be non-normally distributed were analyzed using Mann–Whitney U test. Comparisons of proportions between different groups of patients were carried out using a Chi square and Fisher's exact test. Kaplan-Meier survival curves were utilized to compare time to primary outcomes (arrhythmia recurrence) between groups. Uni- and multivariable logistic regression models were used to assess relationships between variables of interest and arrhythmia recurrence. Cox proportional hazards were used to determine the association between variables of interest and time to the primary outcome.

Results

Baseline characteristics in each group were similar (Table 1). Compared to patients undergoing stepwise linear ablation, patients undergoing LA PWI had a shorter procedure duration (220 min vs 190 min, p<0.001,

respectively), shorter fluoroscopy time (34 min vs 17 min, p<0.001), a lower fluoroscopy dose (956 mGy vs 390 mGy, p<0.001), and a lower radiofrequency time (93 min vs 81 min, p=0.011) (table 2).

Single Procedure Outcomes

AF was terminated with ablation more frequently in the stepwise group compared to the LA PWI group (49% vs. 20%, p<0.001). There was similar freedom from any atrial arrhythmia >30s in duration after index ablation for both the stepwise and LA PWI groups at 12 months (69% vs. 78%, p=0.1), 24 months (60% vs. 71%, p=0.09), and 36 months (60% vs. 69%, p=0.1) (Figure 1). There was no significant difference between stepwise and LA PWI Kaplan-Meier estimated freedom from AF >30s alone at 12 months (88% vs. 87%, p=0.8), 24 months (87% vs. 81%, p=0.6), or 36 months (86% vs. 80%, p=0.5) (Figure 2). In contrast, stepwise patients were less likely to remain free from recurrent AT > 30s when compared to LA PWI patients at 12 months (71% vs. 87%, p=0.008), 24 months (66% vs. 85%, p=0.002), and 36 months (66% vs. 84%, p=0.003) (Figure 3). Stepwise group patients were over twice as likely to experience persistent AF or AT after index ablation at 36 months (29% vs 14%, p=0.005) (Figure 4).

Second Procedure Frequency and Outcomes

Stepwise patients more frequently underwent second catheter ablation within 36 months compared to LA PWI patients (32% vs. 11%, p<0.001) (Figure 5). Patients who experienced a persistent recurrent arrhythmia were nearly twice as likely to undergo second ablation when compared to patients that experience only paroxysmal arrhythmia recurrence (36 of 46; 78% vs 13 of 32; 40%, p=0.001). After a second ablation, there was a higher rate of recurrence of AF or AT in the stepwise group when compared to the LA PWI group (15% vs 4%, p=0.003). Patients who underwent stepwise ablation as an initial strategy were more likely to undergo a third ablation at 36 months (8 of 111; 7% vs 1 of 111; 1%, p=0.02).

Discussion:

The main findings of the present analysis are that we observed no significant reduction in recurrence of any atrial arrhythmia >30s in duration after index ablation between patients undergoing RF ablation of NPAF with a contact-force sensing catheter using a stepwise linear ablation strategy vs. a LA PWI strategy, however there was a statistically significant reduction in recurrence of AT, recurrence of any persistent atrial arrhythmia, and need for repeat ablation in the LA PWI group. The divergence of these significant differences in outcomes is striking given the null result for the traditional primary endpoint for AF ablation trials (AF or AT >30s in duration). Furthermore, the present analysis provides no evidence that a more extensive initial ablation strategy provides a benefit related to outcomes following a repeat ablation procedure, and that the need for a third ablation procedure may in-fact be greater following a more extensive initial procedure.

A patient-centered evaluation of procedural success should place less emphasis on short episodes of asymptomatic atrial arrhythmia relative to more persistent and symptomatic arrhythmias that require intervention.[13,14] The Circa-Dose study recently highlighted the shortcoming of considering arrhythmia recurrence as a binary condition since arrhythmia recurrence rates of 53% were associated with reduction of arrhythmia burden >99%. [15] A more meaningful representation of arrhythmia recurrence would better guide treatment choices. [16] In our study, the persistence of arrhythmia was an important determinant of need for repeat ablation, and more extensive ablation was strongly associated with an increased risk of persistent arrhythmia. The majority of recurrent ATs following stepwise linear ablation of AF have previously been shown to be macroreentrant ATs related to incomplete linear lesions,[17] and the primary mode of recurrence remains AT despite utilization of CFS catheters.

Limitations

Our study is a retrospective analysis of a consecutive cohort of patients undergoing first time ablation for NPAF, thus reported results may be confounded by other changes in practice over time. Patient cohorts were consecutive, so differences in technique were also separated by differences in times when procedures were performed. Procedures for both cohorts of patients were completed over a 25-month period, and no other significant change in practice besides transition to the more limited lesion set occurred during this

time. Ablation lesions were generated in a power-controlled mode applying 20 to 35 W for 20 to 40 seconds per lesion, thus results may not be applicable to higher power, shorter duration approaches. The recurrence of atrial arrhythmias could be underestimated in patients with asymptomatic episodes not captured on 2-week monitors or during their scheduled follow-up, although intensity of monitoring in the present cohort compares favorably to intensity of monitoring in recent clinical trials.[2,4–6,18–21] In patients that underwent repeat ablation, ablation approach was at the discretion of the operator.

Conclusion:

LA PWI utilizing a CFS ablation catheter for NPAF patients resulted in a similar incidence of any atrial arrhythmia >30s, but lower incidence of recurrent AT, lower incidence of persistent AT/AF, and lower likelihood of requiring repeat ablation compared to a stepwise linear ablation approach. Our results are consistent with prior literature showing lack of benefit for more extensive ablation strategies for NPAF after a single procedure, and find no evidence that more extensive initial ablation is beneficial for subsequent procedures.

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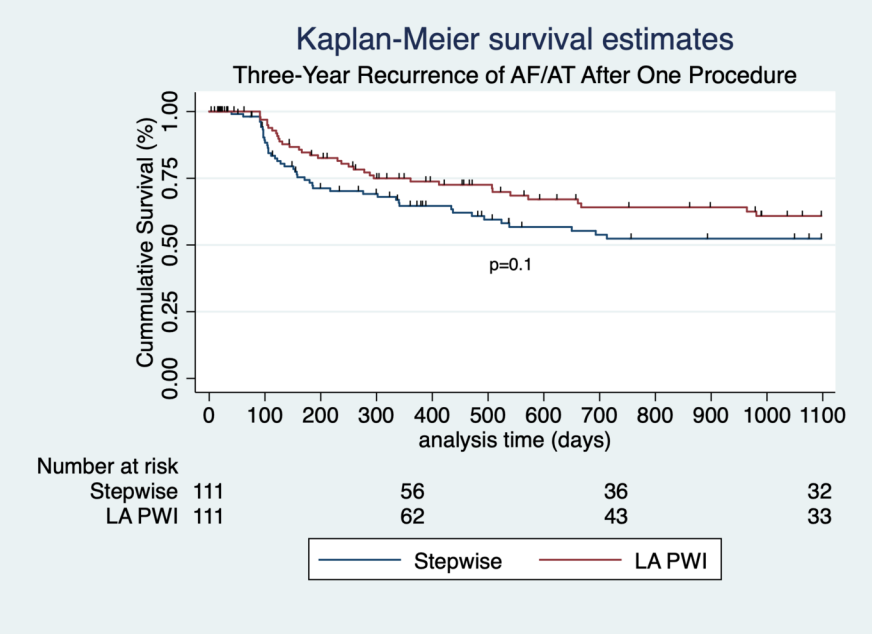

Figure 1: Single Procedure Freedom from Atrial Fibrillation or Atrial Tachycardia

Kaplan–Meier estimates of three-year freedom from documented atrial fibrillation or atrial tachycardia more than 30 seconds after a single procedure. There was no significant differences between groups (P=0.1).

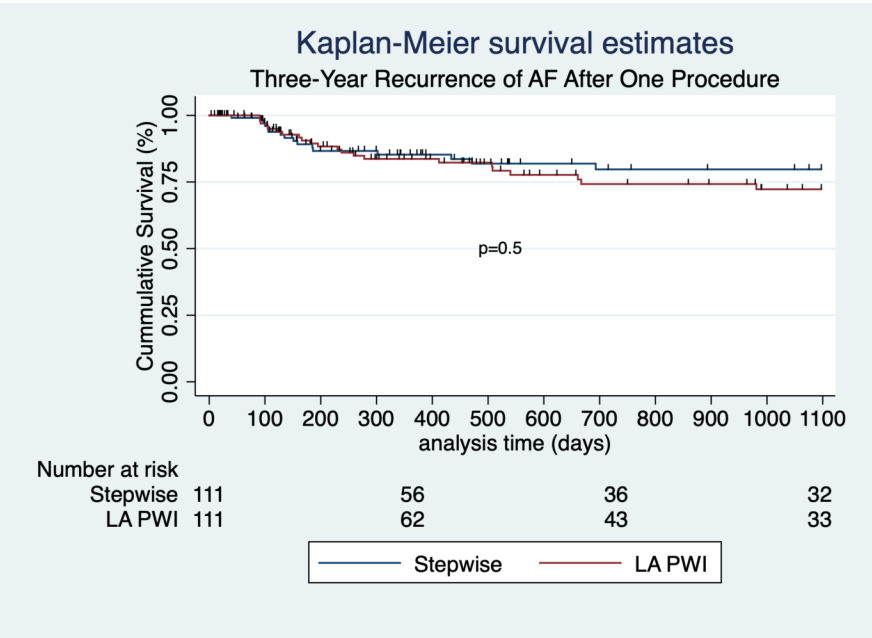

Figure 2: Single Procedure Freedom from Atrial Fibrillation

Kaplan–Meier estimates of three-year freedom from documented atrial fibrillation more than 30 seconds after a single procedure. There was no significant differences between groups (P=0.5).

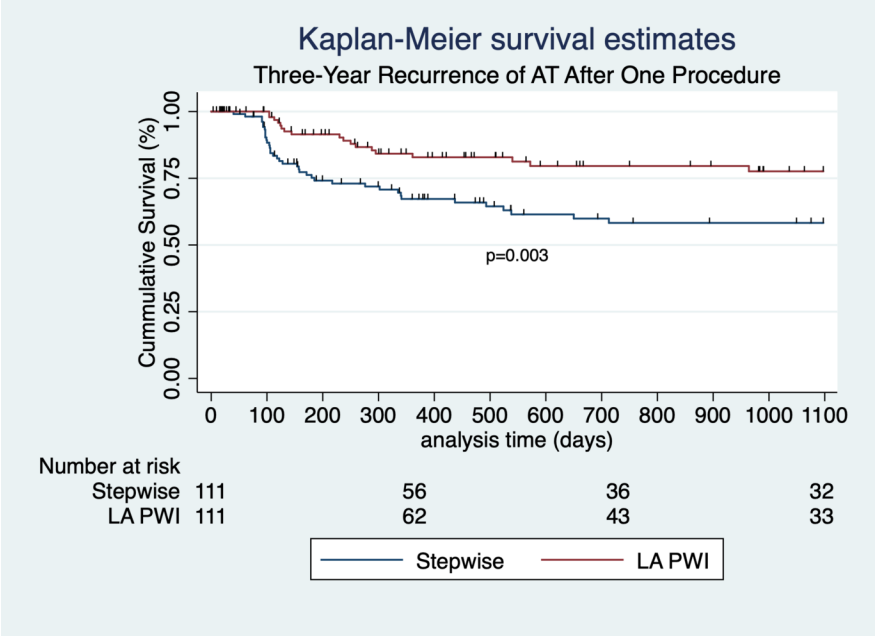

Figure 3: Single Procedure Freedom from Atrial Tachycardia

Kaplan–Meier estimates of three-year freedom from documented atrial tachycardia more than 30 seconds after a single procedure. There was greater incidence of atrial tachycardia in the Stepwise group (P=0.008).

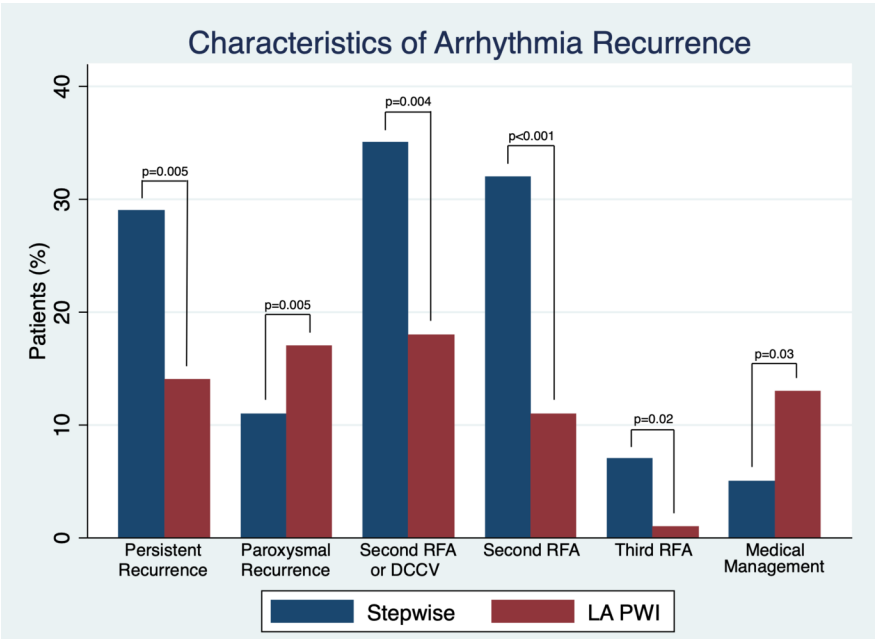

Figure 4 (Central Illustration): Characteristics of Arrhythmia Recurrence

Comparison of three-year outcomes among patients that underwent ablation of non-paroxysmal atrial fibrillation by ablation technique; stepwise versus left atrial posterior wall isolation (LA PWI).

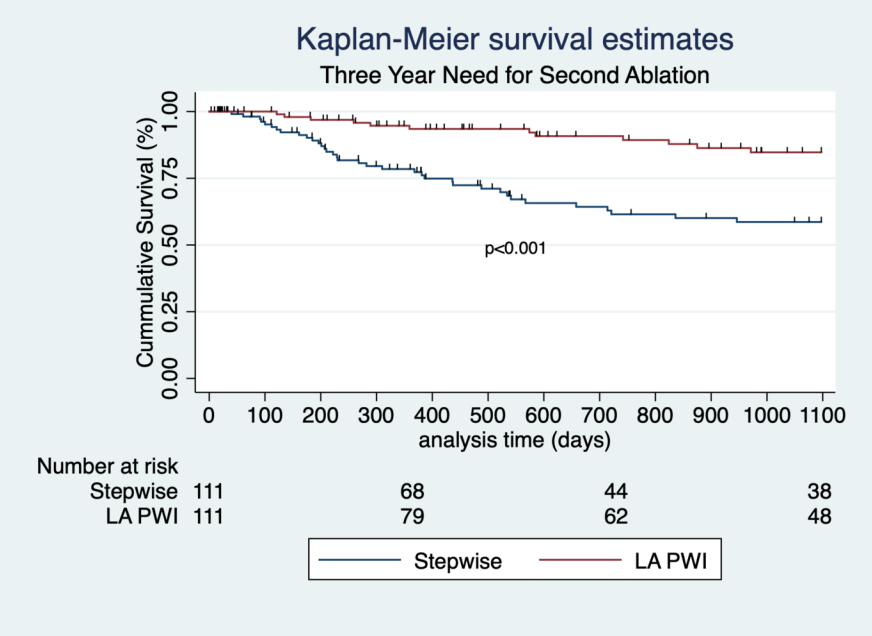

Figure 5: Freedom from Repeat Ablation

Kaplan–Meier estimates of three-year freedom from repeat ablation. There was greater incidence of repeat ablation in the Stepwise group (P<0.001).

Table 1. Characteristics of the Patients at Baseline: Stepwise vs LA Posterior Wall Isolation

Characteristic
Mean Age – years + SD
Male sex – no. (%)
Ejection fraction – % + SD
Left atrial diameter – no. + SD
Mean BSA (m^2) – no. + SD
Mean NPAF Duration – days + SD
Medical history – no. (%)
Hypertension
Diabetes
Coronary disease
Stroke or transient ischemic attack
Heart failure
Baseline Medications – no. (%) Beta-blocker Calcium-channel blocker Digoxin Propafenone Flecainide Sotal
CHA_2DS_2-VASc - no. (%)
0
1
2
> 2

Table 2. Procedural Data: Stepwise vs LA Posterior Wall Isolation

Characteristic	Stepwise (N=111)	LA PWI (N=111)	p-value
Procedure duration – min. + SD	219.9 + 51.5	189.7 + 46.3	<0.001
Fluoroscopy time – min. + SD	33.7 + 14.8	17.2 + 17.5	<0.001
Fluoroscopy dose – mGy + SD	955.7 + 797.6	389.9 + 413.2	<0.001
Radiofrequency time – min + SD	92.8 + 28.5	80.6 + 22.2	0.01
Additional RA Lesions – no. (%)	27 (24.3)	16 (14.6)	0.07
AF terminated with ablation – no. (%)	54 (48.7)	22 (19.8)	<0.001
AF terminated to NSR with ablation – no. (%)	37 (33.3)	19 (17.1)	0.005
AF terminated to AT with ablation – no. (%)	38 (34.2)	6 (5.4)	<0.001
AF/AT terminated with DCCV – no. (%)	66 (59.5)	87 (78.4)	0.002
Complications – no. (%) Hematoma AV Fistula/Pseudoaneurysm Tamponade TIA/Stroke Other	3 1 0 2 0 0	1 0 0 0 0 1	0.3