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CLINICAL RESEARCH
Ablation for atrial fibrillation

Surgical ablation in patients undergoing mitral valve surgery: impact of lesion set and surgical techniques on long-term success

Sandro Gelsomino[1,2]*, Mark La Meir[1], Henrica N.A.M. Van Breugel[1], Attilio Renzulli[3], Carlo Rostagno[2], Roberto Lorusso[4], Orlando Parise[1], Pieter W.J. Lozekoot[1], Idserd D.G. Klop[1], Narendra Kumar[1], Fabiana Lucà[1,2], Francesco Matteucci[1,2], Filiberto Serraino[3], Pasquale Santè[3], Sabina Caciolli[2], Enrico Vizzardi[4], Monique De Jong[1], Harry J.G.M. Crijns[1], Gian Franco Gensini[2], and Jos G. Maessen[1]

[1]University Hospital Maastricht, Maastricht, The Netherlands; [2]Careggi University Hospital, Florence, Italy; [3]University of Magna Graecia, Catanzaro, Italy; and [4]Ospedali Riuniti Brescia, Brescia, Italy

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Aims To assess the results and impact of lesion set and surgical technique on long-term success of surgical ablation during mitral surgery.

Methods and results The patient population consisted of 685 subjects with persistent and long-standing persistent atrial fibrillation (AF) undergoing cardiac surgery for mitral valve disease as the primary indication and concomitant ablation between January 2003 and January 2012 at three institutions. One hundred and sixty-six underwent unipolar (24.2%), 371 (54.2%) bipolar, and 148 (21.6%) had combined ablation. Median follow-up was 58.4 months (interquartile range 43.3–67.9). To appropriately account for death, a competing risk model was employed to identify predictors of cumulative incidence of recurrent AF among lesion set and surgical techniques. Eight-year freedom from recurrent arrhythmia without antiarrhythmic drugs was 0.60 ± 0.02. Success rate was higher using bipolar radiofrequency (RF) ($P < 0.001$), after performing mitral isthmus line ($P = 0.003$) and following the biatrial technique ($P < 0.001$). Competing risk regression revealed that use of unipolar RF [sub-hazard ratio (SHR) 2.41 (1.52–3.43), $P < 0.001$], combined unipolar/bipolar ablation [SHR 1.93 (0.89–2.57), $P = 0.003$] and the absence of right atrial ablation [SHR 2.79 (1.27–3.48), $P < 0.001$] were predictors of cumulative incidence of long-term recurrence.

Conclusions Our experience suggests that the use of bipolar clamp improves long-term results in surgical treatment of AF and that right-sided ablation should be routinely added. Randomized studies are necessary to confirm our findings.

Keywords Atrial fibrillation • Mitral valve surgery • Surgical ablation

Introduction

Atrial fibrillation (AF) is often associated with mitral valve (MV) diseases and increased rates of cardiac events in the presence of concomitant MV pathology.[1] Therefore, the onset of AF is considered as Class II, an indication for MV surgery in subjects with severe MV regurgitation.[2]

The Cox-Maze III operation has produced excellent results and was considered the gold standard for surgical treatment of AF.[3] However, despite its clinical success, the procedure has been reluctantly employed due to its technical complexity. The Cox-Maze IV has replaced the 'cut-and-sew' technique with lines of ablation created using different energy devices.[4] Nonetheless, the long-term efficacy of associated surgical ablation in a patient population undergoing MV surgery has not yet been fully determined and the role of lesion sets on long-term outcome poorly defined.[5]

This multicentre study analysed the long-term success of radiofrequency (RF) surgical ablation during MV surgery. We also

Corresponding author. Tel +31 43 388 1067; fax +31 43 387 77070; *E-mail address*: sandro.gelsomino@maastrichtuniversity.nl

What's new?

- Long-term efficacy of associated surgical ablation in patient population undergoing mitral valve surgery has not yet been fully determined and the role of lesion sets on long-term outcome poorly defined.
- This is one of the largest series with, at the best of our knowledge, one of the longest follow-ups published in the scientific literature on rhythm outcomes following surgical ablation and analysing the impact of lesion set on late atrial fibrillation recurrence.
- The main message of our study is that right atrial ablations in addition to left-sided lines led to better long-term rhythm outcome with a significantly higher percentage of subjects undergoing standardized biatrial approach in normal sinus rhythm and without antiarrhythmic drugs compared with patients undergoing isolated left atrial ablation.
- Although this message is not completely new, the true relevance of the right atrial lesions included in ablation procedure is still a matter of intense debate among clinicians and the importance of right atrial ablation had never been demonstrated before in a detailed analysis.

assessed the impact of lesion set and surgical technique on late recurrence of arrhythmia.

Methods

Patient population

Ethics committee approval was waived due to the retrospective analysis of the study according to national laws regulating observational retrospective studies (Italian Law No. 11960, released on 13 July 2004; Dutch Law). However, written informed consent was obtained from all the patients prior to the surgical procedure.

The patient population consisted of subjects with persistent or long-standing persistent AF undergoing MV surgery as the primary indication and associated RF surgical ablation between January 2003 and January 2012 at three institutions (Careggi Hospital, Florence, Italy; University Hospital, Catanzaro, Italy; and University Hospital, Maastricht, the Netherlands).

Patients undergoing isolated or associated cryothermy ($n = 296$), or ablation with other energy sources ($n = 156$) were excluded from this study. Atrial fibrillation was defined according to the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society.[6] Data from each centre were checked by three institutional referees and finally approved by an external referee and sent to the core lab (see Appendix 1). Data were randomly split into 'training' (75%) and 'validation' sample to develop and validate the prediction rule, respectively. There was no significant imbalance in terms of technique employed, lesion set, surgical availability and the number of cases among centres.

Surgical technique

A primary MV lesion was the main indication for surgery, and ablation was a standard procedure we used in patients with AF. Ablation surgery was performed as previously described.[7] Ganglia ablation was performed when there was active ganglionated plexi (GP) after mapping and stimulation of ganglia resulting in a doubling of the R–R interval.[8] In these patients, active sites along the Waterston groove—for GP located on the right side along the right pulmonary veins (PVs) and along the left PVs—and the Marshall ligament for GP located on the left side were immediately ablated with the Cardioablate surgical pen (Medtronic, Minneapolis, MN).

The aorta was then cross-clamped, the heart was arrested and the left atrium (LA) accessed through a left atriotomy. Pulmonary veins ablation was carried out with the unipolar Cardioablate surgical pen (Medtronic, Minneapolis, MN) or bipolar Cardioablate (Medtronic, Minneapolis, MN) or Atricure clamp (Atricure, West Chester, OH). Additional left atrial lesions were performed as schematized in *Figure 1*.

Right atrial ablation was carried out as follows: a purse-string suture was stitched in front of the coronary sinus, a RF clamp (Cardioblate, Medtronic, Minneapolis, MN) was introduced through the purse string into the right atrial cavity, and two lesions were made directing the clamp first between the inferior vena cava and the coronary sinus and then rotating it towards the atrio-ventricular groove and making a lesion above the coronary sinus. Subsequently, the bipolar clamp was rotated upwards to create an ablation line connecting the purse string to the right appendage. An additional purse-string suture was carried out on the tip of the right atrial appendage, which allowed us to make a connection line between the superior vena cava and the inferior and to perform the ablation of the terminal crest. Ablation of the right appendage completed the procedure.

Postoperative management

Twelve-lead electrocardiogram (ECG) recordings were performed on admission to the intensive care unit (ICU), and daily thereafter whenever necessary until hospital discharge. All patients underwent continuous ECG monitoring for at least the first 72 h postoperatively.

An intravenous amiodarone bolus (150 mg), followed by continuous intravenous infusion at 1 mg/kg/h for 12 h and then 0.5 mg/kg/h until patients tolerated oral intake, was routinely administered intraoperatively. Patients then received oral amiodarone (200 mg twice daily for 1 week, and subsequently 200 mg daily) until 6 months postoperatively. Oral anticoagulation was given to maintain the international normalized ratio between 2.5 and 3.5 for the first 6 months in all patients, and lifelong in patients who received mechanical valves or who had AF persistence, or both.

Follow-up

Patients were seen at the outpatient clinic 3, 6, and 12 months after the surgical procedure, and annually thereafter. Between visits, patients were followed by their referring physician on a regular basis and routine ECGs were obtained at each clinic visit regardless of symptoms. Event monitors were prescribed for patients who complained of palpitations or symptoms compatible with AF during follow-up. Between visits, all patients were encouraged to seek 12-lead ECG documentation for any symptom suggestive of AF/atrial flutter (AFL) recurrence and a physician routinely performed trans-telephonic monitoring of any symptoms and complications.

At each follow-up, patients underwent an ECG or 24 h cardiac monitoring (CM) in the form of Holter monitoring, pacemaker interrogation, or interrogation of implantable loop recorders, whereas, starting in 2008, 24 h Holter was routinely obtained in all patients.

Any episode of symptomatic or asymptomatic atrial tachyarrhythmia [AF, atrial tachycardia (AT), AFL] after the 6-month blanking period that lasted 30 s or longer was considered as arrhythmia recurrence.

The primary endpoint was the recurrence of arrhythmia, but since it might be composed of multiple events, only the earliest event following the 6-month blanking period in the absence of Class I and III

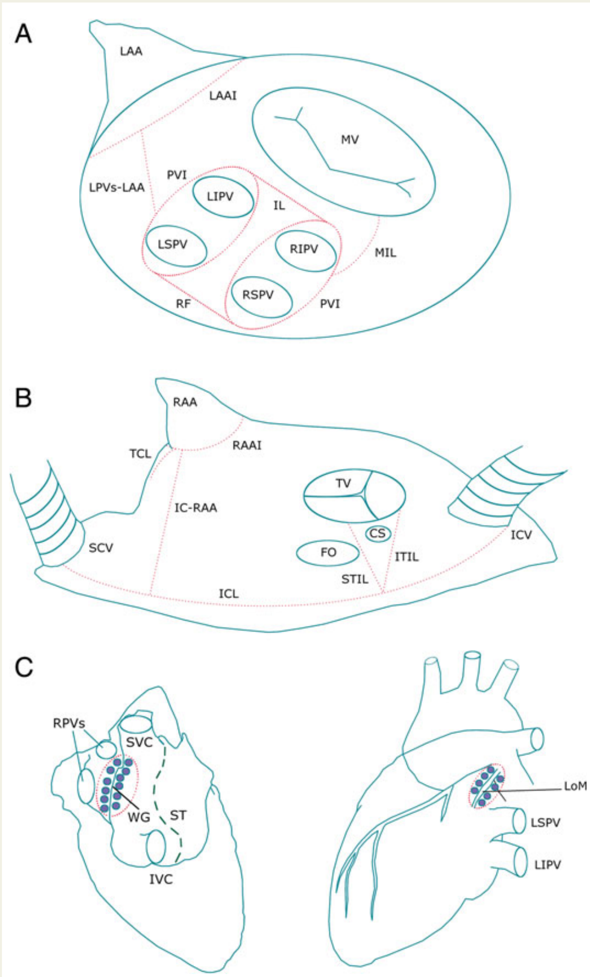

Figure 1 Schematic surgical lesion sets. (*A*) Left atrial lesions. MV, mitral valve; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; LAA, left atrial appendage; PVI, pulmonary veins isolation, RF, roof line; IL, inferior line; LPVs-LAA, left pulmonary vein to left atrial appendage line; LAAI, left atrial appendage isolation; MIL, mitral isthmus line. (*B*) Right atrial lesions. SCV, superior caval vein; ICV, inferior caval vein; TV, tricuspid valve; CS, coronary sinus; FO, fossa ovalis; RAA, right atrial appendage; ICL, intercaval line; ITIL, inferior tricuspid isthmus line (between the inferior caval vein and the tricuspid valve); STIL, superior tricuspid isthmus line (above the coronary sinus); IC-RAA, intercaval to left atrial appendage line; RAAI, right atrial appendage isolation; TCL, terminal crest line. (*C*) Ganglia ablation. Ganglia are shown as solid grey circles. On the left, ablation of the ganglia along the Waterston groove, between the LA and the RA. On the right, isolation of left ganglia along the left PVs and the ligament of Marshall. RPVs, right pulmonary veins; SCV, superior caval vein; ICV, inferior caval vein; WG, Waterston groove; TC, terminal crest; LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; LoM, ligament of Marshall.

antiarrhythmic drug (AAD) therapy was counted, and patients were censored after that point in the analysis.

Echocardiographic examinations were carried out at discharge and at every follow-up appointment and were stored on a magneto-optical disk. Offline analysis was performed by two expert echocardiographers (E.V. and S.C.) following the American Society of Echocardiography recommendations.[9] The reliability of echocardiographic measurements was assessed by the Bland–Altman method calculating inter-observer and intra-observer intervals of agreement of three main measures used in this study in 20 subjects randomly chosen among cohort patients. The difference was <5% in all parameters chosen with excellent agreement for both low and high values (see Appendix 1).

Statistical analysis

Variables were tested for normal distribution by the Kolmogorov–Smirnov test. Continuous data are expressed as mean ± standard deviation, whereas non-normally distributed data are presented as median and interquartile range (IQR) and frequencies as proportions. Missing values (<15%) on covariates were imputed with multiple imputation ($n = 5$) of the entire dataset. The autocorrelation between the imputed datasets was checked and excluded. Between-group differences were assessed by the unpaired *t*-test, Mann–Whitney *U* test, or Pearson's χ^2 test. The Kaplan–Meier (KM) method was used to estimate survival and freedom from recurrent arrhythmia.

A competing risk model was employed to identify predictors of cumulative incidence of recurrent AF among lesion sets and surgical techniques. The Gray test, implemented to assess differences between these functions in multiple groups, was used to check equality of cumulative incidence functions among groups.

Significant (<0.005) and borderline (≤0.1) covariates were tested for their association with AF recurrence employing competing risk regression based on Fine and Gray's proportional hazards model using sub-hazard ratios (SHRs) as measures of association. The model was adjusted for age, gender, duration of AF, type of AF, LA diameter, LA area, concomitant procedures, cardiothoracic centre of origin, and surgeon performing the operation. The potential for covariate multiple colinearity was tested using the variance inflation factor (VIF) and condition number (CN) with VIF < 10 and CN < 30 as reference values.

As standard errors of the Fine–Gray model are robust (heteroscedasticity consistent), model selection was carried out by Akaike's information criteria (AIC) and Bayesian information criterion (BIC) and the model with the lowest values was chosen. The model specification was established by residual analysis and standardized difference of the beta measures of influence across each model covariate.

For analysis, SAS statistical software release 9 (SAS Institute, Inc., Cary, NC) and related specific macros were used.

Results

Patients and ablation procedures

The patient population consisted of 685 subjects, and their preoperative characteristics are shown in *Table 1*. Surgery details are displayed in *Table 2*. Ganglia ablation was carried out in 279 cases (40.7%). One hundred and sixty-six patients (24.2%) underwent unipolar PV ablation, whereas 519 patients (75.8%) underwent bipolar PV ablation. Furthermore, 437 (63.7%) subjects underwent a LA connecting lesion with a bipolar clamp (819 lines), or a unipolar pen (669 lines). Four hundred and thirty-seven patients (67.7%) had a mitral isthmus (MI) line from the left atrial appendage (LAA) to the posterior mitral annulus performed with a unipolar pen in 144 cases (32.9%), a bipolar clamp in 132 patients (30.3%), and a bipolar clamp completing the ablation with a unipolar pen in 161 patients (36.8%). The LAA was always excluded by external ligation

Table 1 Baseline characteristics (*n* = 685)

Age (years)	65.0 ± 9.3
Sex (M/F)	454/231 (66.2/33.8)
Diabetes	163 (23.7)
Hypertension	450 (65.6)
COPD	245 (35.7)
CVD	97 (14.1)
Redo cardiac surgery	32 (4.6)
NYHA	2.9 [2.1–3.4]
Additive EuroScore	6.3 [4.9–7.5]
$CHADS_2$ score	1.6 [1.1–2.1]
Type of AF	
Long-standing persistent	287 (41.9)
Persistent	398 (58.1)
Duration of AF (months)	35.6 ± 40.3
Previous ECV	247 (36.0)
MV disease	
Degenerative	249 (36.3)
Rheumatic	150 (21.9)
Ischaemic	161 (23.5)
Functional	89 (13.0)
Other/unknown	36 (5.3)
Associated cardiac disease	
CAD	103 (15.0)
AVD	171 (24.9)
TVD	289 (42.1)
Other	30 (4.3)
AADs	
Amiodarone	487 (71.0)
Dronedarone	63 (9.2)
Sotalol	135 (19.8)
LVEF (%)	49.7 ± 10.4

Values are shown as mean ± standard deviation for normally distributed data, median [interquartile range] for not normally distributed data or number (percentage) for categorical data. COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; NYHA, New York Heart Association; CHADS, congestive heart failure, hypertension, age, diabetes, prior stroke; AF, atrial fibrillation; ECV, electrical cardioversion; CAD, coronary artery disease; AVD, aortic valve disease; TVD, tricuspid valve disease; LVEF, left ventricular ejection fraction; LA, left atrium; RA, right atrium; PAP, pulmonary artery pressure; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.

Table 2 Surgery (*n* = 685)

Unipolar	166 (24.2)
Bipolar	371 (54.2)
Combined bipolar/unipolar	148 (21.6)
LA connecting lesions	
Roof line	552 (80.5)
Inferior line	483 (70.5)
LAA to LPV line	453 (66.1)
MI line	437 (63.7)
RA ablation	318 (46.4)
LAA isolation	212 (30.9)
LAA ligation/stitching	
Ligation	534 (77.9)
Stitching	151 (22.1)
Ablation system/equipment employed	
Cardio ablate system	531 (77.5)
Atricure system	154 (22.4)
GP ablation	279 (40.7)
CPB time	96.4 ± 14.3
CCT	74.2 ± 13.1
Main procedure	
MV repair	316 (46.1)
MV replacement	
Biological	247 (36.0)
Mechanical	122 (17.9)
Concomitant procedures	
AV repair	34 (4.9)
AV replacement	
Biological	74 (10.8)
Mechanical	37 (5.4)
TVR	264 (38.5)
CABG	97 (14.1)
Other	22 (3.2)

Values are shown as mean ± standard deviation for normally distributed data or number (percentage) for categorical data.
PVs, pulmonary veins; LA, left atrium; LAA, left atrium appendage; LPV, left pulmonary veins; RA, right atrium; GP, ganglionated plexi; CPB, cardiopulmonary bypass; CCT, cross clamp time; MV, mitral valve; AV, aortic valve; TVR, tricuspid valve repair; CABG, coronary artery bypass graft.

(*n* = 534, 77.9%) or internal stitching (*n* = 151, 22.1%). Bipolar right atrial lesions were performed in 318 patients (46.4%).

Early results

There were 6 early deaths (0.9%). Causes of death were low cardiac output (*n* = 2), septic shock (*n* = 2), myocardial infarction (*n* = 1), and cerebral haemorrhage (*n* = 1). Hospital morbidity included re-operation for bleeding in 12 patients (1.7%), respiratory failure in 9 patients (1.4%), renal failure in 8 (1.1%), acute myocardial infarction in 6 patients (0.8%), low cardiac output in 2 (0.4%), deep sternal wound infection in 2 (0.4%), and in 2 (0.4%) transient ischaemic attacks. Overall in-hospital morbidity was 5.9% (*n* = 41). Median ICU and hospital length of stay were 2.5 days (IQR 1.3–4.5) and 9.1 days (IQR 6.1–11.8), respectively.

Acute restoration of sinus rhythm

After aortic declamping, 472 patients (68.9%) recovered normal sinus rhythm (NSR), 137 (20%) were in junctional rhythm requiring temporary pacemaker stimulation, and 76 (11.1%) displayed AF. Twenty-four patients (5.0% of survivors) underwent successful direct current (DC) cardioversion.

At hospital discharge, 602 (88.6% of survivors) were in NSR, 65 (9.5% of survivors) were in AF, and 12 (2.5% of survivors) required definitive pacemaker implantation. Indications for pacemaker implantation included sinus node dysfunction (*n* = 7), complete heart block (*n* = 4), and bradycardia with second-degree heart block (*n* = 1).

Follow-up

Median follow-up was 58.4 months (IQR 43.3–67.9) with 1865 patient-years available for analysis.

Six hundred and two (87.8%) patients survived. Deaths included 47 cardiac-related deaths and 30 (38.9%) non-cardiac-related or unknown-cause deaths. Ten-year freedom from death was 0.75 ± 0.03. One hundred and twenty-one patients experienced 168 (27.9%) hospital readmissions: 54 (32.2%) for non-cardiac-related events and 114 (67.8%) for cardiac-related events. Among the latter, 44 (38.5%) readmissions were related to rhythm disturbance. Cerebrovascular events were reported in 6 patients (0.9%) during the follow-up: 4 of them had complete resolution of neurological deficits, 1 remained with a slight right paresis, and 1 died.

At the latest control, 55 patients (26.7%) who underwent MV repair experienced mitral regurgitation (MR) recurrence ≥ slight and 34 (10.6%) who had a MV prosthesis implanted a para/periprosthetic leak.

Heart rhythm at follow-up

Eleven patients (1.8%) underwent permanent pacemaker implantation (all for sinus node dysfunction). Excluding deaths and patients with pacemaker implantations, 579 subjects were available for long-term rhythm evaluation. Three hundred and sixty-one patients (62.3%) were in NSR and off-AAD at the latest control. This figure was 73.9 (428/579) considering patients in NSR on-AAD. Eight-year freedom from recurrent arrhythmia without AAD was 0.60 ± 0.02 (see Supplementary material online, *files*). Among the 151 patients experiencing recurrent arrhythmia at follow-up, 101 had AF (66.9%), 36 AT (23.8%), and 14 (9.3%) AFL. Patients who were not in NSR were treated as follows: 37 underwent transcatheter ablation [$n = 7$, recovery conduction around PVs (all unipolar RF); $n = 15$, recovery coronary sinus conduction, $n = 15$, right atrial foci (10 LA procedures)], which was successful in 26 (70.2%), 29 had DC cardioversion (17 successful, 58.6%), and 85 underwent pharmacological cardioversion (success, 63.5%, $n = 54$).

Overall, 221 patients (38.1) were on AAD at the latest follow-up: cordarone 19.9%, dronedarone 6.7%, sotalol 3.6%, atenolol 33.9%, bisoprolol 15.8%, carvedilol 10.8%, digoxin 7.6%, and verapamil 8.5%.

In *Table 3*, long-term successes by surgical procedure are displayed. Success rate was higher using bipolar RF, after performing a MI line and following a biatrial technique. No other significant difference was detected.

Predictors of atrial fibrillation recurrence

Cumulative incidence of recurrent arrhythmia was higher following unipolar or combined procedures and in the absence of a MI line and right atrium (RA) ablation (*Figure 2*). Other factors were not significant, and noteworthy, patients with MR recurrence after mitral repair or who showed a prosthetic leak at late echocardiography did not show a significant higher cumulative incidence (*Figures 2–3*).

Predictors of cumulative incidence of arrhythmia recurrence (*Table 4*) were unipolar RF ($P < 0.001$), combined unipolar/bipolar ablation ($P = 0.003$), and the absence of right atrial ablation ($P = 0.001$). The model was well specified with no unduly influential observations across the covariates, and no significant interactions were demonstrated.

Table 3 Long-term success rate following a single procedure

	Yes Success rate	No Success rate	*P*
Unipolar	60/145 (41.3)	301/434 (63.2)	<0.001
Bipolar	239/319 (74.9)	122/260 (46.9)	<0.001
Combined bipolar/ unipolar	62/115 (53.9)	299/464 (64.4)	0.03
Roof line	289/463 (62.4)	72/116 (62.0)	0.83
Inferior line	255/411 (62.0)	106/168 (63.0)	0.81
MI line	238/358 (66.4)	123/221 (55.6)	0.003
LAA to LPV	240/382 (62.8)	121/197 (61.4)	0.74
RA ablation	212/283 (77.6)	249/296 (50.3)	<0.001
LAA ligation	243/405 (50.1)	118/174 (67.8)	0.08
LAA stitching	118/174 (67.8)	243/405 (50.1)	
GP ablation	154/237 (64.9)	207/342 (60.5)	0.27
Cardio ablate system	279/445 (72.6)	82/134 (61.1)	0.75
Atricure system			
MV repair	206/318 (64.7)	155/261 (59.3)	0.18
MV replacement	155/261 (59.3)	206/318 (64.7)	
Concomitant procedures	284/453 (62.6)	77/126 (61.1)	0.74
Post-repair recurrent MR	34/55 (61.8)	123/206 (59.7)	0.78
Post-replacement leakage	22/35 (62.8)	177/283 (62.5)	0.98

Values are shown as number (percentage) for categorical data. NSR, normal sinus rhythm; AAD, antiarrhythmic drugs; LAA, Left, atrium appendage; LPV, left pulmonary veins; LAA, left atrial appendage; RA, right atrium; GP, ganglionated plexi; LA, left atrium; MV, mitral valve; MR, mitral regurgitation.

Echocardiographic results

In *Table 5*, the echocardiographic data of patients in NSR and with AF recurrence are reported. Baseline parameters did not differ between NSR and AF. At the latest control, LA diameter ($P = 0.02$), LA area ($P > 0.001$), RA area ($P < 0.001$), and systolic pulmonary artery pressure (PAP) (<0.001) significantly decreased in patients with NSR. In contrast, in those with recurrent AF, LA diameter increased ($P < 0.001$), whereas the other parameters did not change. However, all these parameters were significantly higher in patients with recurrence of the arrhythmia. Finally, left ventricular diameter did not show any significant variation in either subgroup.

Discussion

This multicentre study explored long-term rhythm outcomes of patients undergoing RF surgical ablation during MV surgery. In our previous experience,[10] we have demonstrated that associated surgery increases AF recurrence threshold and sensitivity to AADs and DC cardioversion, both attributable to substrate modification caused by surgical lesions. The main objective of this study was to assess long-term rhythm outcomes and the impact of lesion set and surgical technique on late AF recurrence. Our population was formed by patients with persistent and long-standing persistent AFs including a small minority with AF for longer than 2 years who were referred to surgery because of their favourable echocardiographic features (small atria).

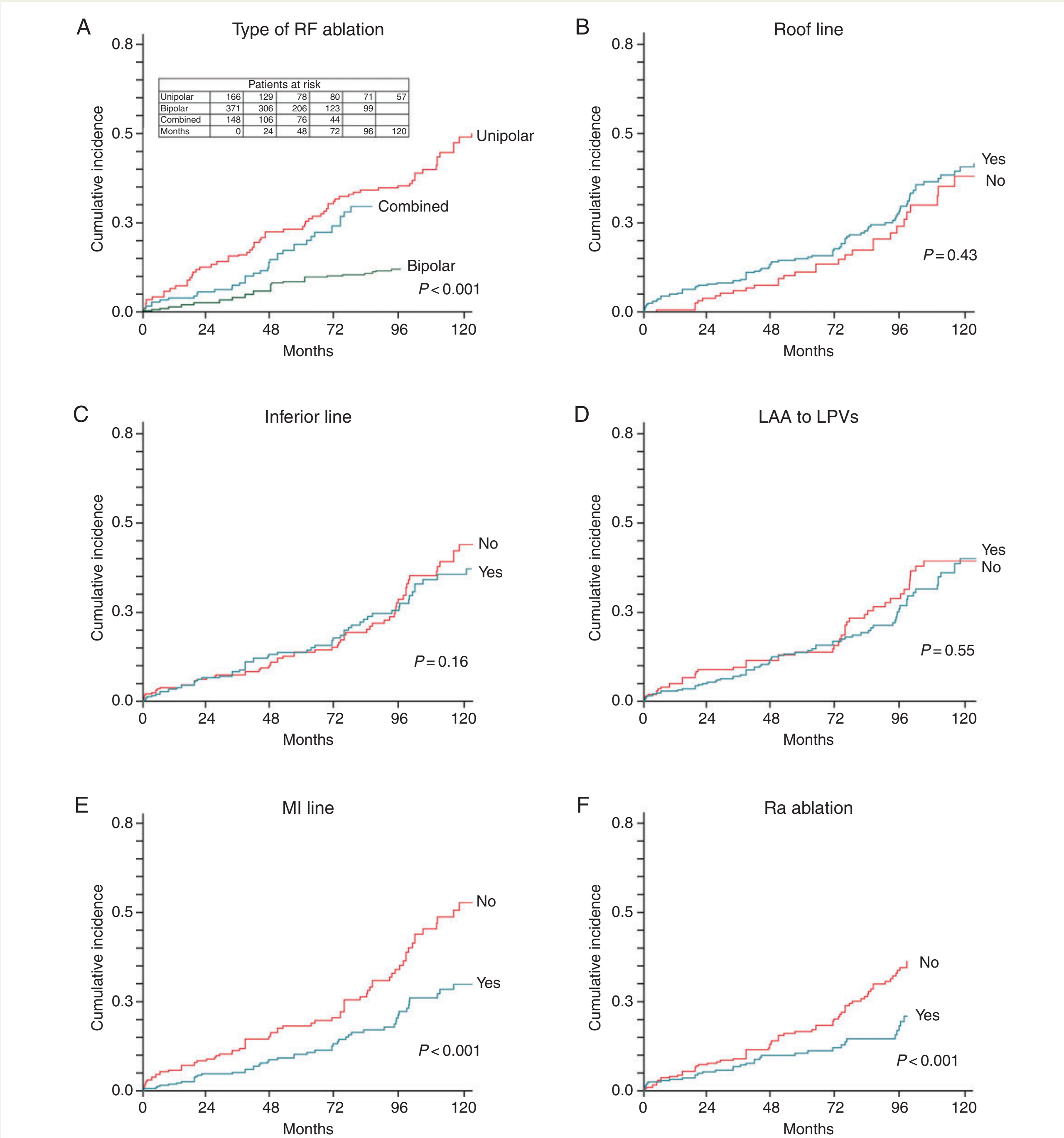

Figure 2 Cumulative incidence of recurrent AF by type of RF ablation (*A*), left atrial roof line (*B*), left atrial inferior line (*C*), LAA-to-LPV line right atrial ablation (*D*), mitral isthmus line (*E*), right atrium ablation (*F*). RF, radiofrequency; AF, atrial fibrillation; LAA, left atrial appendage; LPVs, left pulmonary veins; MI, mitral isthmus; RA, right atrium.

Rhythm outcome

At the latest follow-up, 8-year freedom from recurrent arrhythmias-off-AAD was, in our experience, 0.60 ± 0.02 (Supplementary material online, *Figure*). Bipolar biatrial ablation performed during MV surgery showed a recurrence of AF rate very close to the more invasive and surgically challenging Cox-Maze III cut-and-sew technique, which is still considered the reference gold standard for the surgical treatment of AF.[11]

Importance of the energy source employed

Our findings confirm the superiority of the bipolar sources. Indeed, the complete bipolar RF lesion set resulted to be the technique with the highest long-term success rate ($P < 0.001$) and the use of unipolar RF ($P < 0.001$) or combined unipolar/bipolar ablation ($P = 0.003$) were predictors of increased cumulative incidence of

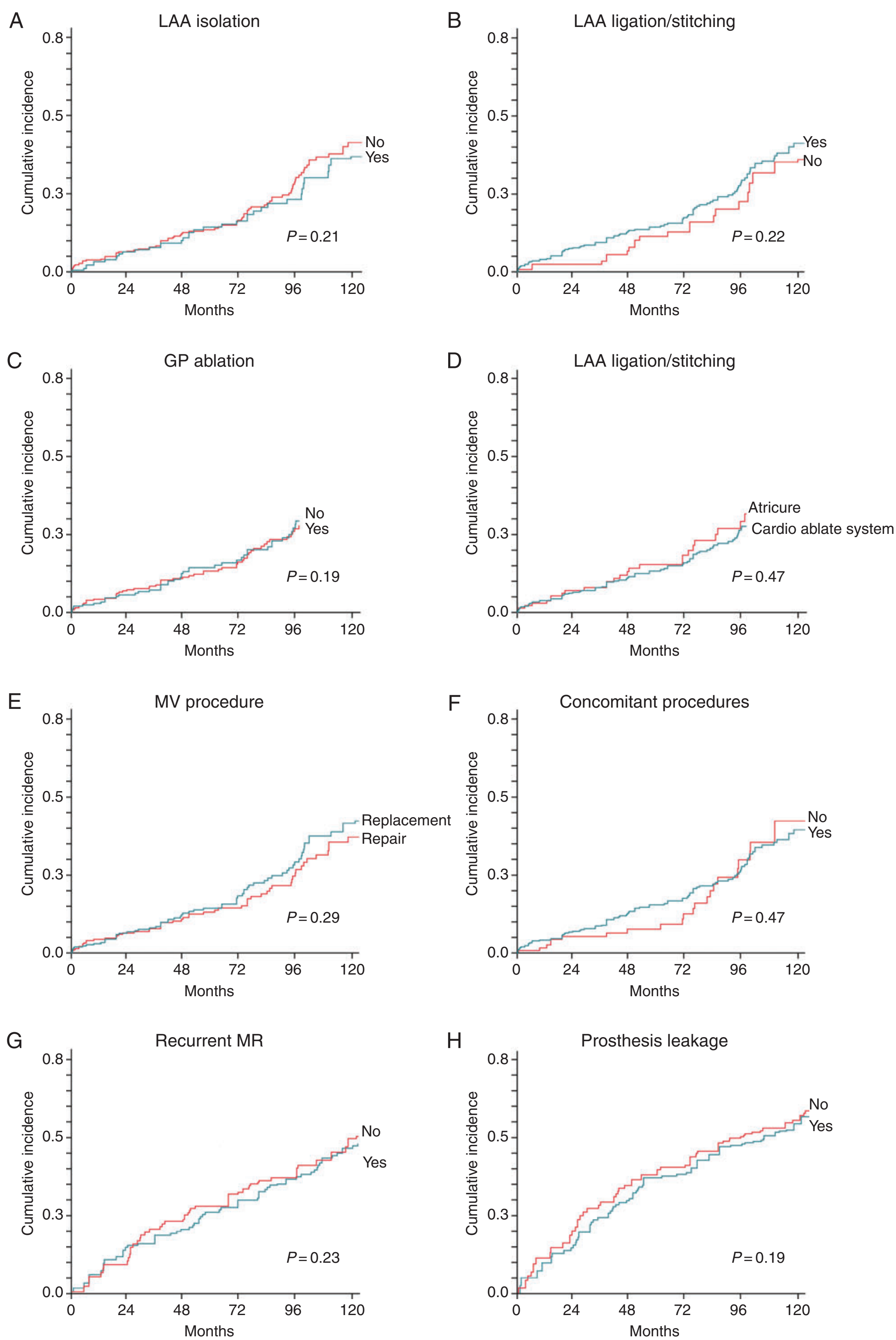

Figure 3 Cumulative incidence of recurrent AF by LAA isolation (*A*), LAA ligation/stitching (*B*), GP ablation (*C*), type of ablation system employed (*D*), type of main procedure performed on MV (*E*), concomitant heart procedures (*F*), post-repair recurrence of mitral regurgitation (*G*), and post MV replacement leakage (*H*). AF, atrial fibrillation; LAA, left atrial appendage; GP, ganglionated plexi; MV, mitral valve.

arrhythmia recurrence. This association was not eliminated after adjusting for potentially influencing baseline factors. This endorses the trend towards the implementation of surgical ablation through the application of the bipolar RF clamp on a pattern of left and right atrial lesions despite technical and positional limitations of clamping devices.[5]

Completeness of the lesion set: right atrial ablation

A key point of our study is that right atrial ablations in addition to left-sided lines led to better long-term rhythm outcome ($P <$ 0.001). Importantly, the absence of right atrial ablation ($P <$ 0.001) was an independent predictor of increased cumulative incidence of recurrence, and this remained unaltered also after adjusting for potentially influencing baseline factors.

The relevance of the right atrial lesions included in the ablation procedure is still a matter of debate. A recent randomized study[12] showed no significant difference in in the rate of freedom from AF between patients who underwent PV isolation and those who underwent the biatrial Maze procedure (61 vs. 66%, respectively, $P = 0.60$). Apart from differences in patient selection and limited length of follow-up (maximum 12 months) in this study, these results might be attributable to the significantly higher percentage of patients undergoing monopolar lesions in the biatrial group, which are more likely not to be transmural. Our findings are in accordance with Lin *et al.*[13] who demonstrated that ablation of the right atrial 'trigger zones' could eliminate AF and prevent the recurrence of AFL or tachycardia, which frequently occur after performing isolated LA lesions. This may also explain the inconsistent results reported for isolated left atrial isolation and confirms previous findings demonstrating that a right-sided ablation interrupts interatrial connections and improves clinical results.[14]

Interestingly, the incidence of pacemaker implantation was low compared with other studies (17), and this might be explained by the lower percentages of patients with long-standing persistent AF $>$ 2 years who received RA ablation (13.2%).

Table 4 **Competing risk regression**

	SHR (95% CI)	*P*
Unipolar	2.41 (1.52–3.43)	<0.001
Combined bipolar/unipolar	1.93 (0.89–2.57)	0.003
Bipolar	0.75 (0.36–1.72)	0.547
Lack of inferior line	1.47 (0.79–3.98)	0.131
Lack of MI line	1.32 (0.54–2.27)	0.114
Lack of RA ablation	2.79 (1.27–3.48)	<0.001
Lack of GP ablation	0.97 (0.44–2.87)	0.684
Post-repair recurrent MR	0.14 (0.09–1.44)	0.91
Post-replacement leakage	0.23 (0.12–1.87)	0.79

SHR, sub-hazard ratio; CI, confidence interval; RA, right atrium; GP, ganglionated plexi.
Values are shown as mean ± standard deviation at baseline and latest follow-up. AF, atrial fibrillation; LA, left atrium; RA, right atrium; PAP, pulmonary artery pressure; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter. *Significance vs. baseline.

Completeness of the lesion set: mitral isthmus ablation

In our experience, a long success rate was comparable between patients with or without a MI line ($P = 0.7$) and MI ablation resulted to be not significant at competing risk regression ($P = 0.1$).

The MI refers to the atrial myocardium between the MV annulus and the left-sided PVs. Some anatomical features make this line surgically challenging: (a) the presence of crevices in the isthmus area, which may hinder safe and efficient RF energy delivery; (b) the thickness (up to 8 mm) and the width of this region; (c) the presence of pits and troughs on the MI-endocardial surface where the atrial wall becomes thin; (d) the continuation of atrial myocardium onto the atrial aspect of the MV leaflets; and (e) the epicardial connections (e.g. the ligament of Marshall) across the MI.[15]

Our findings are in contrast with previous reports[16] demonstrating the relevance of a MI line during RF maze procedures. These authors completed the MI line with other energy sources, whereas we included only RF. Therefore, the lack of a transmural lesion following unipolar MI ablation and, on the other hand, the inability of

Table 5 **Echocardiographic results**

	Baseline			Follow-up		
	Sinus rhythm	AF recurrence	*P*	Sinus rhythm	AF recurrence	*P*
LA diameter (mm)	52.4 ± 7.0	51.9 ± 7.4	0.85	48.8 ± 6.4[a]	55.3 ± 8.1[a]	<0.001
LA area (cm^2)	34.2 ± 6.9	35.4 ± 7.0	0.07	30.4 ± 7.1[a]	35.7 ± 8.5	<0.001
RA area (cm^2)	23.1 ± 4.0	22.8 ± 3.9	0.88	19.7 ± 4.4[a]	22.2 ± 6.4	0.001
Systolic PAP (mmHg)	45.2 ± 11.0	45.0 ± 10.6	0.9	40.2 ± 11.4[a]	44.7 ± 14.6	<0.001
LVEDD (mm)	50.8 ± 8.5	51.0 ± 9.0	0.9	50.0 ± 8.8	51.0 ± 9.0	0.09
LVESD (mm)	39.5 ± 9.6	39.0 ± 9.2	0.85	38.0 ± 7.9	39.0 ± 7.4	0.1

Values are shown as mean ± standard deviation at baseline and the latest follow-up. AF, atrial fibrillation; LA, left atrium; RA, right atrium; PAP, pulmonary artery pressure; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter.
[a]Significance versus baseline.

the bipolar clamp to create a reliable lesion all the way to the mitral annulus (probably due to the thickness of the AV groove in that area) may explain such different results. A comparison of RF vs. cryo MI lines is the object of an ongoing study.

Completeness of the lesion set: left atrium connecting lines

In our experience, the application of a roof line, an inferior line, or a LAA to left pulmonary vein (LPV) line failed to show a higher rate of long-term success. Furthermore, the same lesions were not determinant in preventing recurrence at multivariate competing risk analysis. This finding is in accordance with a paper recently published demonstrating that the addition of linear ablation to circumferential PV isolation did not improve clinical outcomes of RF catheter ablation in paroxysmal AF.[17] Nonetheless, the results of our study may have been influenced by the high number of patients in our series receiving a connecting line with a unipolar RF device applied from the endocardial surface. Hence, the success of LA lines might have been hampered by the lack of transmurality of unipolar sources.

Completeness of the lesion set: ganglionated plexi ablation

Differently from previous short-term follow-up studies,[18] we found in patients with or without GP ablation percentages of patients in NSR-off-AAD ($P = 0.7$) at follow-up and the absence of GP ablation was not predictive of increased cumulative incidence of arrhythmia recurrence ($P = 0.6$). The results of Alex *et al.*,[19] who failed to demonstrate any role of cardiac denervation on AF recurrence following coronary revascularization, are in agreement with these figures.

It has been reported that AF inducibility was eliminated immediately after GP ablation, but this denervation effect was reversed within 4 weeks after the ablation due to re-innervations, and this could be a potential explanation for the lack of influence of GP ablation on late outcome in contrast with its proven short-term efficacy.[20]

Finally, we can speculate that if the jaws of the bipolar clamp are placed widely enough to include both PV antra, odds are high that this ablation will target at the same time the two major ganglionated plexuses on the posterior face of the two atria, which are associated with the largest number of ganglia.[15]

This manoeuvre could partially explain the superiority of bipolar clamps and, at the same time, the lack of any beneficial role of adjunctive GP ablation.

Limitations

The present article has certain limitations that need to be addressed. First of all, the retrospective design of the study, its multicentre nature, and the lack of randomization do not provide a definitive causative link between type of surgical ablation technique associated with MV procedures and long-term stable sinus rhythm. However, our study presented a large patient population followed up over a decade and, at the best of our knowledge, it represents one of the most estensive and longest studies published on the topic in the scientific literature.

Another drawback of our study is the heterogeneity of the patient population, although this limitation is shared with other clinical studies on this topic. However, our patient cohort was larger and less heterogeneous compared with most previously published reports. Indeed, we included only persistent and long-standing persistent AF patients undergoing only RF ablation. A key strength of our research is that all patients having right atrial ablation underwent the same bipolar right lesion set including intercaval ablation, cavo-tricuspid isthmus line, isolation of right atrial appendage, and terminal crest.

Third, patients did not undergo continuous rhythm monitoring by an implantable loop recorder which would allow us to identify any AF events that otherwise could have gone unreported. However, all patients met the minimum criteria of 24 h Holter monitoring recording at follow-up.[6]

Fourth, different ablation techniques were employed, and this might have affected our results. However, the single most important variable is the surgeon's experience and technical proficiency with the different procedures, and in our analysis, we did account for the surgeon performing the ablation procedure as well as for the surgical centre.

Fifth, we could speculate that the efficacy of the biatrial approach might be explained by the fact that several areas of active GP localized along the right atrial groove are targeted by the right atrial ablation, whereas they cannot be eliminated by isolated left atrial maze. We did not test possible interactions between RA ablation and GP ablation, which is the object of ongoing research.

Sixth, due to the maintenance in the centres involved in the study of an old protocol foreseeing a postoperative 6-month instead of 3-month amiodarone therapy. This could have affected our results and must be taken into consideration when examining our data.

Seventh, freedom from AF was reported with the KM method, which is not appropriate since it is a condition or intermittent occurrence that cannot meet the criterion of proportional hazard over time like time-related events such as death, for which the KM is appropriate. Nonetheless, this analysis is still widely employed and allows researchers to easily compare results from different studies.

Finally, our findings about the lack of incremental value of targeting cardiac GP during a maze procedure must be interpreted in light of the limitation of the small percentage of patients (18.3%) with GP ablation available at follow-up. Hence, further larger studies are warranted.

Conclusions

Our data suggest that right-sided ablation should be routinely added to LA surgical ablation to achieve reliable long-term NSR and that the use of bipolar clamps improves long-term rhythm outcome. Randomized studies comparing left atrial ablation and biatrial lesions are necessary to confirm our findings.

Supplementary material

Supplementary material is available at *Europace* online.

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References

1. Herrmann HC, Gertz ZM, Silvestry FE, Wiegers SE, Woo YJ, Hermiller J *et al.* Effects of atrial fibrillation on treatment of mitral regurgitation in the EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) randomized trial. *J Am Coll Cardiol* 2012;**59**:1312–29.
2. Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr, Faxon DP, Freed MD *et al.* American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the ACC/AHA Task Force on Practice Guidelines. *J Am Coll Cardiol* 2008;**52**:e1–142.
3. Cox JL. Surgical treatment of atrial fibrillation: a review. *Europace* 2004;**1**:S20–9.
4. Damiano RJ Jr, Schwartz FH, Bailey MS, Maniar HS, Munfakh NA, Schuessler RB. The Cox-Maze IV procedure: predictors of late recurrence. *J Thorac Cardiovasc Surg* 2011;**1141**:113–21.
5. Phan K, Xie A, Tian DH, Shaikhrezai K, Yan TD. Systematic review and meta-analysis of surgical ablation for atrial fibrillation during mitral valve surgery. *Ann Cardiothorac Surg* 2014;**3**:3–14.
6. Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA *et al.* 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *Europace* 2012;**14**:528–606.
7. Onorati F, Mariscalco G, Rubino AS, Serraino F, Santini F, Musazzi A *et al.* Impact of lesion sets on mid-term results of surgical ablation procedure for atrial fibrillation. *J Am Coll Cardiol* 2011;**57**:931–40.
8. Mehall JR, Kohut RM Jr, Schneeberger EW, Taketani T, Merrill WH, Wolf RK. Intraoperative epicardial electrophysiologic mapping and isolation of autonomic ganglionic plexi. *Ann Thorac Surg* 2007;**83**:538–41.
9. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA *et al.* Recommendations for chamber quantification: a report from the ASE Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the JASE. *J Am Soc Echocardiogr* 2005;**18**:1440–63.
10. van Breugel HN, Gelsomino S, de Vos CB, Accord RE, Tieleman RG, Lucà F *et al.* Maintenance of sinus rhythm after electrical cardioversion for recurrent atrial fibrillation following mitral valve surgery with or without associated radiofrequency ablation. *Int J Cardiol* 2014;**175**:290–6.
11. Stulak JM, Suri RM, Burkhart HM, Daly RC, Dearani JA, Greason KL *et al.* Surgical ablation for atrial fibrillation for two decades: are the results of new techniques equivalent to the Cox maze III procedure? *J Thorac Cardiovasc Surg* 2014;**147**:1478–86.
12. Gillinov AM, Gelijns AC, Parides MK, DeRose JJ Jr, Moskowitz AJ, Voisine P *et al.* Surgical ablation of atrial fibrillation during mitral-valve surgery. *N Engl J Med* 2015;**372**:1399–409.
13. Lin YJ, Tai CT, Kao T, Tso HW, Huang JL, Higa S.*et al.* Electrophysiological characteristics and catheter ablation in patients with paroxysmal right atrial fibrillation. *Circulation* 2005;**112**:1692–700.
14. Chang SL, Tai CT, Lin YJ, Wongcharoen W, Lo LW, Lee KT *et al.* The role of left atrial muscular bundles in catheter ablation of atrial fibrillation. *J Am Coll Cardiol* 2007;**50**:964–73.
15. Gelsomino S, Corradi D, Lorusso R, Parise O, Callegari S, Macchi E *et al.* Anatomical basis of minimally invasive epicardial ablation of atrial fibrillation. *Eur J Cardiothorac Surg* 2013;**43**:673–82.
16. McCarthy PM, Kruse J, Shalli S, Ilkhanoff L, Goldberger JJ, Kadish AH *et al.* Where does atrial fibrillation surgery fail? Implications for increasing effectiveness of ablation. *J Thorac Cardiovasc Surg* 2010;**139**:860–7.
17. Kim TH, Park J, Park JK, Uhm JS, Joung B, Hwang C *et al.* Linear ablation in addition to circumferential pulmonary vein isolation (Dallas lesion set) does not improve clinical outcome in patients with paroxysmal atrial fibrillation: a prospective randomized study. *Europace* 2015;**17**:388–95.
18. Ware AL, Suri RM, Stulak JM, Sundt TM 3rd, Schaff HV. Left atrial ganglion ablation as an adjunct to atrial fibrillation surgery in valvular heart disease. *Ann Thorac Surg* 2011;**91**:97–102.
19. Alex J, Guvendik L. Evaluation of ventral cardiac denervation as a prophylaxis against atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg* 2005;**79**:517–20.
20. Sakamoto S, Schuessler RB, Lee AM, Aziz A, Lall SC, Damiano RJ Jr. Vagal denervation and reinnervation after ablation of ganglionated plexi. *J Thorac Cardiovasc Surg* 2010;**139**:444–52.

IMAGES IN ELECTROPHYSIOLOGY

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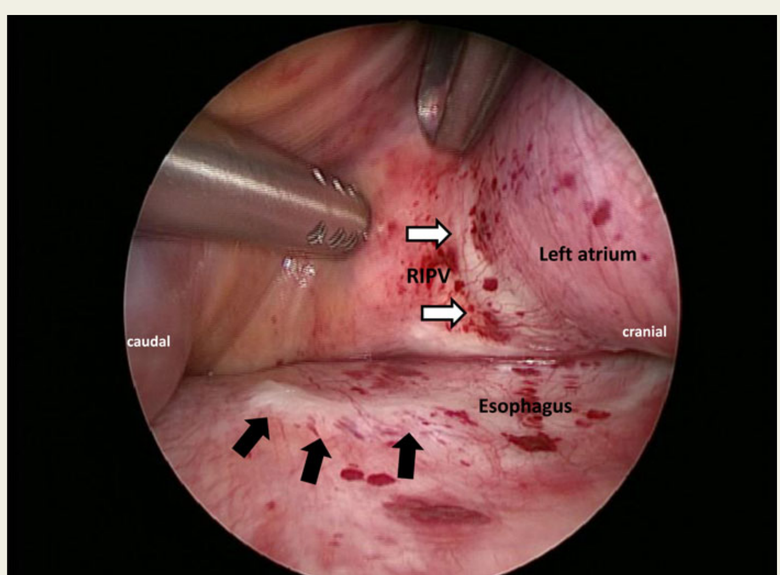
Collateral damage after endocardial catheter ablation

Mindy Vroomen[1]*, Mark La Meir[1,2], and Laurent Pison[1]

[1]Department of Cardiology and Cardiothoracic Surgery, Maastricht University Medical Center, Cardiovascular Research Institute Maastricht, PO Box 5800, Maastricht, The Netherlands and [2]Department of Cardiac Surgery, UZ Brussel, Brussels, Belgium

* Corresponding author. Tel: +31 433875072; fax: +31 433875104. *E-mail address*: mindyvroomen1@gmail.com



The image shows a left-sided thoracoscopic view of the oblique sinus during a hybrid atrial fibrillation ablation (procedure combining an endocardial and epicardial approach), which was performed after two failed endocardial radiofrequency pulmonary vein isolations (PVIs). The posterior left atrium is lifted using two surgical devices. The red spot areas are bleedings due to handling by the surgeon, which is commonly seen, already by gentle handling.

Fibrotic strands are visible at the antrum of the right inferior PV (white arrows) and on the opposite posterior pericardium (black arrows) overlying the oesophagus.

The fibrosis on the posterior pericardium is the result of collateral damage that occurred during previous PVI procedures. More extensive collateral damage could have resulted in oesophageal injury.