Original Research

A Case-Matched Comparative Study of Surgical Radiofrequency (RF) Ablation for Patients with Persistent or Long-Standing Atrial Fibrillation Undergoing Concomitant Heart Surgery

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Introduction: Recent guidelines from the European Society of Cardiology suggest that surgical ablation should be considered in patients with atrial fibrillation (AF) who present for concomitant surgically correctable disease. This is a case-matched study of radiofrequency ablation during concomitant cardiac surgery versus lone surgery on patients with persistent and long-standing permanent AF.

Methods: Surgical ablation was performed in 21 patients, 14 with persistent and 7 with long-standing permanent AF. Patients with paroxysmal AF, recent onset persistent AF (<6 months), duration >6 years or left atrial diameter >8 cm were excluded. The study patients were matched 1-2 for age, sex, type of operation, type and duration of atrial fibrillation with 42 patients operated during the same period in the same department without ablation. The catheters used deliver continuously monitored radiofrequency energy, creating linear lesions on the inside of the arrested left and/or right atrial wall. Follow up was with regular outpatients' appointments and 24-hour ECG recordings at 6 and 12 months.

Results: Sinus rhythm maintenance rate at discharge and 12-month follow up was significantly higher in the ablation group (12 months: 71% vs. 5%, p<0.01). The ablation group had significantly longer operative times. Mean ablation duration was 15.5 minutes (CI: 12-20). There were no deaths. There were no statistically significant differences in postoperative in-hospital stay, NYHA class, left atrial size, or left ventricular ejection fraction. All patients who maintained sinus rhythm during the ablation had echocardiographically confirmed left atrial systole at follow up.

Conclusion: Epicardial radiofrequency ablation in patients with persistent and long lasting permanent AF, who are being operated for concomitant cardiac surgical disease, is a safe, reproducible method with acceptable sustainability of sinus rhythm at medium-term follow up.

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The presence and post-operative persistence of atrial fibrillation (AF) is clearly associated with significant comorbidities and a higher long-term mortality in patients presenting with surgically correctable heart disease.[1,2] Being the commonest arrhythmia in ages >65, it imposes a notable financial burden on the health system.[3] Surgical correction of AF with cut-and-sew lines has established its efficacy, but also its complexity, for many years now. The efficacy of interventional cardiology in the endovascular treatment of paroxysmal and persistent standalone AF has become more widely adopted and is also well established. Evolution in the understanding of the pathogenetic mechanisms of AF in valvular heart disease, as well as advances in medical technology, have refined and continue to ameliorate catheter-

based energy-delivering modalities that allow concomitant surgical treatment of AF when it presents in combination with other cardiac surgical disease. In fact, in the recent ESC guidelines, surgical treatment combined with catheter ablation is a class IIa, evidence level A, recommendation for patients with symptomatic AF undergoing cardiac surgery.[4]

We present here a case-matched study of patients with long-lasting permanent (chronic) or persistent AF, who underwent radiofrequency surgical ablation concomitant with cardiac surgery for their primary surgical disease and were compared to matched AF patients treated with surgery alone.

Methods

Patients

From February 2009 to March 2010 patients scheduled for mitral valve surgery who had a history of long-standing persistent or permanent AF-chronic (definitions as per ESC) were assessed as potential candidates for ablation. Full history and echocardiography data were recorded. Type of AF, time in months since arrhythmia initiation, number of cardioversions with medication or defibrillation, medication (β-blockers, sotalol, propafenone, amiodarone), echocardiography data, left atrial (LA) dimensions, history of hypertension and diabetes, were recorded. Patients with a history of paroxysmal AF, or <6 months' history of persistent AF, as well as patients with a history of chronic AF with duration >6 years and/or an excessive LA size (>8 cm) were excluded. Twenty-one patients who fulfilled the inclusion criteria were treated with radiofrequency (RF) ablation of the left and/or right atrium (Group A).

During the same period, 161 patients with persistent or chronic AF underwent mitral valve surgery without ablation by the same surgical team. All patients were entered into a logistic regression analysis. Parameters included were type and duration of AF, age, preoperative left ventricular ejection fraction (LVEF), type of operation and New York Heart Association (NYHA) class. In the multiple logistic regression, Group A (RF ablation) patients were older, with a longer duration of AF, higher NYHA class, but similar as regards the other selected covariates (male/female, LVEF). We identified 42 of the non-RF patients who were matched 2-1 to the RF group for all the above parameters; these made up group B. All patients gave written informed consent.

Technique

Ablation was performed with the use of a monopolar catheter (Cobra, Estech, California, USA) delivering radiofrequency energy to the endocardial surface of the left atrium in an arrested heart (Figure 1). This catheter consists of a malleable probe that creates linear lesions that can be up to 12 cm long. No dragging is required, ensuring a thin straight line lesion with no gaps. During transmission of the RF ablation, the energy delivered is continuously monitored and automatically adjusted by seven electrodes spread along the total length of the catheter, which simultaneously measure the resistance of the underlying atrial tissue.

Specifically, our technique is as follows. Following cross-clamp application and cardioplegia administration on an arrested heart the left atrium was incised on its roof through the interatrial groove. The lines performed included isolation of the posterior atrial wall around the pulmonary vein outlet, with one line being the cut-and-sew of the interatrial groove (box lesion), and a minimum of 2 more lines connecting the "box" lesion to the base of the LA appendage, and to the posterior mitral valve annulus towards P3, thus avoiding injury to the circumflex artery (Figure 2). All patients in group A were prescribed amiodarone starting immediately postoperatively and for

Figure 1. The ablation catheter used in our study (Cobra, Estech, California, USA). The catheter is malleable and consists of seven segments that can independently monitor tissue resistance and deliver continuously adjustable RF energy levels.

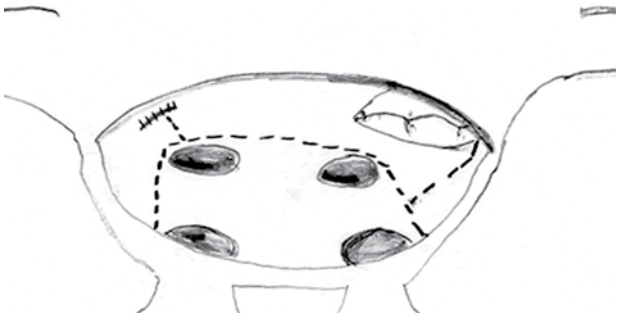

Figure 2. Ablation lines in the left atrium form a "box" in order to isolate the pulmonary veins.

at least 2 months, while in group B the preoperative rate-control medication was continued postoperatively. In cases where sinus rhythm (SR) was restored after surgical ablation and AF recurred during hospitalization, patients underwent cardioversion before discharge. They were all followed up with regular outpatients' visits, echocardiography and 24-hour ECG recordings (Holter).

Patients found to have AF recurrence after 2 months' follow up were considered as "unsuccessful" regarding the procedure; amiodarone was discontinued and they were subsequently treated as per cardiology advice. For the patients in SR, amiodarone was routinely discontinued and they were put on β-blockers. The procedure was considered successful when patients were in sinus rhythm on all postoperative ECGs and 24-hour ECG recordings 12 months postoperatively. A recurrence was considered as reappearance of persistent arrhythmia or episodes longer that 30 s on 24-hour Holter recordings. Patients in both groups were also started on acenocoumarol with a target international normalized ratio of 2-3.

Table 1. Basic patient characteristics and summary of type of ablation.

	Ablation group	Lone MVR surgery	p
Total patients	21	42	<0.05
Persistent AF	14	28	<0.05
Long-standing permanent AF	7	14	<0.05
Mean age, years	62 ± 5	64 ± 3	NS
Duration, months	24 ± 8	25 ± 11	NS
Persistent	4.3 ± 0.6	4.1 ± 0.4	NS
Long-standing permanent	42 ± 5	45 ± 3	NS
LADi, cm/m^2	2.9 ± 0.6	3.1 ± 0.4	NS
LVEF, % (mean)	52 ± 4	51 ± 4	NS

AF – atrial fibrillation; MVR – mitral valve replacement; LADi – left atrial diameter index (maximum atrial diameter divided by body surface area); LVEF – left ventricular ejection fraction; NS non-significant.

Results

The case-mix cohort consisted of patients operated for mitral valve pathology with or without other procedures (tricuspid valve, aortic valve, etc.). The two groups were comparable regarding the matching covariates (Table 1). There were also no statistical differences regarding length of hospital stay, postoperative NYHA class, or LA size on follow-up echo (Table 2). There were no major complications, such as thrombotic episodes, hemorrhage, pericardial effusion or prolonging hospitalization. The treatment group's operative times were higher (cardiopulmonary bypass time 104 ± 12 vs. 89 ± 8 min, p<0.05). Both at discharge (80% vs. 10%) and at 12 months' follow up (71% vs. 5%) there was a significantly higher proportion of patients in SR. There was also a trend towards a difference in the LVEF, albeit not statistically significant. At discharge, 17 of 21 (80%) in the ablation group vs. 4 of 42 (10%) of controls were in SR (p<0.01). Specifically,

Table 2. Summary of the intraoperative and postoperative characteristics of the two groups.

	Ablation group Group A	Surgery alone Group B	p
No of patients	21	42	
Sinus rhythm on discharge	17 (80%)	4 (10%)	<0.01
In-hospital AF recurrence	3	0	<0.01
Length of stay	6.8 (CI: 6-9)	7.5 (CI: 7-11)	NS
CPB time	104 ± 12	89 ± 8	<0.05
Sinus rhythm, 12 months' follow up	15 (71%)	2 (5%)	<0.01
LADi, cm/m^2, 12 months' follow up	2.5 ± 0.6	2.8 ± 0.3	NS
LVEF, %, 12 months' follow up	51 ± 3	47 ± 4	NS (p=0.2)

CI – 95% confidence interval; CPB - cardiopulmonary bypass time. Other abbreviations as in Table 1.

11 of 14 patients who had persistent AF and 4 of 7 with chronic AF were in sinus rhythm. Of the 6 remaining patients, 3 had relapsing episodes of AF requiring cardioversion before discharge, which was successful in 2 pts. At 2 months, 2 of the 17 pts in the ablation group who had SR postoperatively were in AF. Amiodarone was discontinued in these 2 patients and in 13 patients in SR. An exception was made in 2 pts with SR in the ablation group who had frequent atrial ectopy, where amiodarone was continued until month 6. At 6 and 12 months, 15 (71%) in the ablation group vs. 2 (5%) of controls remained in SR with no other intervention. An echocardiographic check was performed at 6 and 12 months' follow up. In the postoperative study of 4 of the 17 pts in SR, left atrial mechanical function was not found. At 6 and 12 months' follow up, atrial function (A wave) was present in all patients in sinus rhythm.

Discussion

Well before any of the current knowledge on AF initiation, propagation and perpetuation was available, Cox, based on empirical surgical data, reported on a highly successful operation for AF, thus setting the gold standard. In a cohort that included patients with paroxysmal, as well as persistent and longstanding permanent AF, with cut-and-sew lines across both atria that created an electromechanical maze, he demonstrated a very high rate of SR maintenance (95% at 5 years) and a low rate of thromboembolic events.[5,6] This operation, despite its high success, has not been widely adopted by the surgical community because of the complexity involved. Seminal electrophysiological studies have shed light on the mechanisms that produce, propagate, and perpetuate AF. The discovery of a preponderance of arrhythmogenic triggers in the area of the pulmonary veins (PVs) by Haïssaguerre is one of those.[7] Parasystole, which is automatic activity within a protective surrounding, has also been demonstrated in the atrial sleeves present in the PVs.[8] Ablation lines isolating the PVs from the LA wall have been adopted by electrophysiologists and proved more effective than standard medical treatment in curing at least symptomatic paroxysmal AF.[9] Success rates, however, vary greatly in the literature, but seem to be higher when more than the solitary isolation of the PVs is performed.[10,11] This is in agreement with both the high success of the Cox-maze operation and the evolving theory of AF, shifting from single trigger points when paroxysmal, towards more diffuse, multiple micro–re-entrant circuits, structural and electrochemical biatrial substrate remodeling, as well as a genetic predisposition and neurohormonal modifications in persistent and chronic.[12,13] A recent meta-analysis clearly showed that lone PV isolation resulted in lower success rates.[14] It also has to be kept in mind that AF substrate propagation and the effect of treatment options vary between patients with lone AF and AF in the context of structural heart disease. Furthermore, surgical patients present with a more advanced AF substrate and most surgical series, our own included, do not treat paroxysmal AF. A number of retrospective studies and a few randomized ones have clearly demonstrated the efficacy of RF ablation in maintaining sinus rhythm at mid-term intervals across all groups, albeit with variable results ranging from 65–90%.[15-17] Prognostic factors in the success of achieving SR were the addition of at least one more line from the box lesion towards the mitral annuls[18] and another to the atrial appendage base, the size of the LA, the duration of AF preoperatively, and permanent vs. paroxysmal AF.[19,20]

A review of the existing literature in the field of surgical ablation led to the type of energy (i.e. RF) we used, as well as to the ablation lines we performed (over other modes and/or other lines). RF energy seems to offer a greater degree of transmurality in *in vitro* studies in comparison to other modes of energy.[21] Reports of collateral damage are nonexistent with bipolar and infrequent with unipolar catheters. Unipolar catheters are applied under direct vision in a stopped heart and bloodless field. Further evolution of catheters that continuously monitor and automatically adjust the energy delivered, like the one we used, has added safety. Also of significance is that electric signal propagation blockade in RF ablation, as shown by pathology studies, is conveniently not an equitable surrogate of transmurality; i.e. electric blockade is more frequent than the percentage of continuous transmural lesions that surgical RF ablation catheters achieve.[22] Even though there is some evidence that it is not only the gaps[23] in the ablation lines that are responsible for recurrences in unipolar RF ablation, it is evident that gaps are less commonly an issue with long catheters applied under direct vision during surgery.

Surgical ablation studies are still small, underpowered and non-randomized. A meta-analysis of surgical ablations performed during 2006 demonstrated improved freedom from AF but no significant difference in survival,[24] while in a more recent retrospective study of patients treated for mitral valve

disease the addition of conventional Cox-maze and/or RF lines showed a clear long-term survival benefit.[25] Reduction of thromboembolic events has been shown, not only for the "cut-and-sew" surgical Cox-maze, but also for surgical RF ablation cases.[26] An improved quality of life (measured by the Short Form Health Survey, SF-36) was demonstrated in patients who were successfully converted to SR with intraoperative ablation, in comparison to those who had only their primary cardiac surgical disease addressed.[27] Concomitant with mitral valve surgery, ablation was associated with an improvement of the left ventricular ejection fraction following successful ablation.[28] In our study we specifically looked for the atrial systole wave, which was present in all patients in SR. Even though ablation is clearly able to re-establish SR with atrial systole in a high percentage of patients, offering an improved quality of life and decreased risk of cerebrovascular events, the precise long-term benefit of such an approach to patients with concomitant surgical heart disease remains to be quantified.

Limitations

This study is limited both by its small number of patients and by the non-randomized, retrospectively-matched case control group. Also, even though we were more thorough than other studies in acquiring a 24-hour ECG recording, it has to be noted that this is not necessarily capturing all AF episodes.[29] Additionally, a limitation in the interpretation of results is that group B patients were not on amiodarone and there was no attempt at cardioversion. A longer follow up will be required to establish the permanent effect of ablation in the long term.

Conclusions

With increasing knowledge of the complicated mechanisms involved in the pathogenesis of AF related to structural or ischemic heart disease, surgical RF ablation is a safe and highly successful modality. More evidence concerning the potential long-term benefits may shift the recommendations for surgical ablation from the current suggestion towards being a necessary component when AF patients are undergoing concomitant cardiac surgery.

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