Abstract

We sought to determine if early recurrence of atrial fibrillation (AF) after surgical ablation is a risk factor of late failure. Between February 2004 to May 2009, 106 patients underwent surgical ablation of concomitant permanent AF with radiofrequency. Operations primarily consisted of valve surgery in 85% of patients. Hospital mortality was 2.8% (n=3). The median follow-up was 37 months (interquartile rank 12–77), and was complete in 99% of patients. Freedom from AF was 82%, 76% and 68% at one, two and three years, respectively. Patients with early recurrence of AF had less prevalence of sinus rhythm in late follow-up (P<0.001). Multivariate Cox regression analysis showed that AF duration [hazard ratio (HR) 1.014, 95% CI 1.009–1.020, P<0.001] and early recurrence of AF (HR 3.45, 95% CI 1.50–7.95, P=0.004) were independent risk factors for failure. In conclusion, in our series, early recurrence of AF after surgical ablation is a strong predictor of late failure.

Keywords: Atrial fibrillation surgery; Failure; Risk factors

1. Introduction

Preoperative atrial fibrillation (AF) among patients undergoing cardiac surgery is an independent risk factor for late morbidity and reduced survival [1–3]. Surgical procedures to cure atrial fibrillation seem to improve its outcomes [4, 5]. New sources of energies, which are capable of reproducing the same pattern of Cox-maze III lesions in a safer and faster way, have led to a new increasing interest in surgical AF correction in the past few years [6].

The main risk factors for surgical ablation failure have been widely reported; i.e. age, arrhythmia duration and left atrium (LA) size [7, 8]. Postoperative recurrence of AF is not considered a failure after the Cox-maze III procedure [9]. It was our focus to investigate if the early postoperative recurrence after radiofrequency (RF) ablation is a late failure predictor.

2. Materials and methods

2.1. Study group

Every patient undergoing surgical ablation of permanent AF between February 2004 to May 2009 was included in this study. Decisions to perform a surgical ablation or not depended on the surgeon criteria, but high-risk patients or those with severely dilated left atria (>70 mm) or long standing AF (>20 years) were usually rejected.

2.2. Surgical technique

Irrigated mono and bipolar RF (Cardioblate, Medtronic, Minneapolis, MN, USA) was the source of energy used in all procedures. After aorta cross-clamping, bipolar RF was epicardially applied to left and right pulmonary veins and to the LA appendage. Afterwards, LA was opened through the interatrial groove. Left and right pulmonary veins were connected through the left atrial roof with one blade of the bipolar device on the epicardial side and the other on the endocardial side. Two more line lesions were performed using the monopolar pen: one connecting the right pulmonary veins to the mitral annulus, and another one connecting the left pulmonary veins to the appendage. A right atrial maze procedure with both monopolar and bipolar devices was performed only in those cases when surgery for the tricuspid valve was necessary. For every lesion, at least three applications were made. Electric conduction blockage was not checked. Atrial appendage was always excluded using a polipropilene 4/0 running suture.

2.3. Postoperative management and follow-up

All patients were treated with oral anticoagulants and antiarrhythmic drugs (amiodarone or sotalol) at the moment of discharge, except for those with any contrain-
dication or previous history of allergy or intolerance. Patients were evaluated at three, six and 12 months after surgery; and then, every year. At every follow-up visit, a 12 lead electrocardiogram (ECG) and a 24-hour Holter were performed. Transthoracic echocardiography was performed at three months and every year. Antiarrhythmic drugs were withdrawn at six to 12 months if no recurrence was detected (AF episodes longer than 30 s in the 24-hour Holter). Anticoagulation was stopped 12 months after surgery if stable sinus rhythm was recorded in a 24-hour Holter and atrial contraction plus complete left appendage exclusion were verified in the echocardiography.

AF recurrences were treated aggressively (Fig. 1). During the postoperative period, patients suffering AF underwent an electric cardioversion in case they did not return to sinus rhythm (SR) after a 48-hour administration of intravenous antiarrhythmic drugs. If cardioversion was not possible (low international normalized ratio, thrombus or spontaneous smoke in the LA, or patient refusal), cardioversion was delayed until the sixth postoperative week. Every AF recurrence during the first postoperative year was treated using either electric or pharmacological cardioversion. If any further recurrence was detected after the first year, one attempt of electric cardioversion was performed at least.

2.4. Objective

The main focus of this study was to investigate if early postoperative AF recurrence is a predictor of late failure after AF surgical ablation. Early AF recurrence was defined as any AF episode during postoperative stay. Procedure late failure was considered when AF or atrial flutter were persistent after one or more electric cardioversions in the follow-up.

2.5. Statistical analysis

Data were collected prospectively. Categorical variables are shown with absolute and relative frequency [n (%)]; while quantitative are presented using mean and standard deviation (S.D.), or median plus interquartile range (IQR) if not normal. A Shapiro–Wilk test was applied to check normality of quantitative variables. Qualitative variables were compared using $\chi^2$ or exact Fisher’s test. Quantitative ones were compared using Student’s $t$, or non-parametric tests (Mann–Whitney $U$-test) for not normal. Follow-up AF incidence is shown using cumulative risk curves (Kaplan–Meier method). Survival differences were detected using Mantel–Haenszel ‘log-rank’ test. Multivariate Cox proportional risks analysis was performed in order to detect independent predictors of late failure. In the multivariate analysis, two types of variables were included: a) those asymmetrically distributed between patients with or without AF early recurrence ($P<0.05$); and b) those related to late recurrence in a univariate Cox analysis ($P<0.1$). Multivariate models log-linearity was checked by verifying the lineality of the martingale residuals. Statistically significance was set at $P<0.05$. PASW 18.0 (SPSS, Chicago, IL, USA) was used for statistical analysis.

3. Results

One hundred and six patients were included in the present study. Sixty-two percent were women, with a mean age of 63.3 years (S.D. 10.2; ranking 34–85). Associated surgical procedures were: valve surgery [85%, 13% associated coronary artery bypass grafting (CABG)], thoracic aorta surgery (9%), and isolated CABG (6%). Mean AF duration was 59 months (S.D. 57; ranking 3–240), and mean LA size was 54 mm (S.D. 7, ranking 38–74). Mean left ventricle ejection fraction (LVEF) was 60% (S.D. 10.2, ranking 25–85).

Early postoperative mortality was 2.8% ($n=3$), and logistic EuroSCORE was 6.4%. The main adverse postoperative outcomes were: permanent cerebrovascular accident ($n=2$, 1.9%), surgical site re-exploration because of bleeding ($n=8$, 7.5%), renal failure requiring haemofiltration ($n=3$, 2.8%), and definitive pacemaker implantation ($n=12$, 11.3%). Complete follow-up was achieved in 99% of surviving patients.

Sixty-three patients (59%) had at least one postoperative AF episode. Seventy patients (68%) were either on sinus or
two patients denied an electric cardioversion (both after unsuccessful pharmacological treatment): one of them remained in permanent asymptomatic flutter and the other one reverted to sinus rhythm spontaneously 12 months later. Ten patients had a second episode of atrial flutter and six suffered a third episode. Three of them were referred for cardiac electrophysiological study after several unsuccessful cardioversions. In all those three cases, an atypical left sided flutter was detected. In one case, an AV node ablation and pacemaker implantation were performed due to the high comorbidity. Incomplete ablation lines were detected in the remaining two cases during the endocavitary electrical mapping of the LA: the atrial roof line in one case, and the right pulmonary veins and the left isthmus line in the other case (Fig. 4). Lesion lines were completed during the electrophysiological study, and both remained in SR during the rest of the follow-up.

Age, AF duration, LVEF and early postoperative recurrence (Table 1) were associated to late AF recurrence in univariate Cox analysis. Patients who suffered an early recurrence episode had a longer preoperative AF duration (Table 2). Multivariate analysis detected that AF duration (HR 1.014, 95% CI 1.009–1.020, \( P < 0.001 \)), and early AF recurrence (hazard ratio (HR) 3.44, 95% CI 1.49–7.95, \( P = 0.004 \)) were both independently associated to late failure (Table 3).
Early recurrence

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Biatrial ablation,

Age

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was considered as a phenomenon explained by the changes

late failure of the procedure. Formerly, early recurrence

4. Discussion

The main finding in the present study is that early AF
recurrence after surgical AF ablation is a risk factor for
late failure of the procedure. Formerly, early recurrence
was considered as a phenomenon explained by the changes
induced in atrial electrophysiology by the inflammatory
response to cardiac surgery [9]. In our experience, the
impact of early recurrence on late failure might be given
by the fact that some RF lesions were incomplete, so new
re-entry circuits should appear. The lack of intraoperative
conduction blockage monitoring in those patients suffering
early failure makes it impossible to accurately define the
mechanism. The high incidence of atrial flutter in the
follow-up would support the mentioned hypothesis of
lesions incompleteness, although most flutters have been
limited to one episode that reverted after antiarrhythmic
drugs or electric cardioversion. Another explanation for
the high incidence of atrial flutter and the early recurrence
could be the lesion set. We do not isolate the posterior LA
and we do not perform routinely biatrial ablation, which
could facilitate the macro re-entry. Endocavitary left atrial
electrical mapping was only performed in two patients who
presented permanent flutter in the follow-up. In both
cases, incomplete LA lesions were detected.

Although it is widely known that monopolar RF is not able
to achieve transmurality as often as bipolar RF, bipolar RF
cannot be easily nor safely applied to some parts of the
atria. Ablation of the left isthmus with the bipolar device,
for example, entails a high risk of circumflex artery dam-
age. Moreover, mitral annulus is difficult to reach because
of the atrioventricular groove fat tissue and left ventricle
myocardium [10]. This is why we preferred to use mono-
polar RF for these lesions.

Previous reports have also identified early recurrence as
a predictor for late failure after surgical AF ablation.
Benussi et al. [11] in a report of 132 patients, found that
age and postoperative supraventricular arrhythmias were
independent predictors for late failure. Hornero et al. [12]
tried to discriminate the type of early recurrence, using
postoperative epicardial unipolar auriculograms. They
detected that less organized auriculograms during post-
operative AF episodes identified patients with high risk of
late recurrence.

Other risk factors have been identified; i.e. age, LA size
and isolated LA ablation [7, 8]. Older age and large LA size
both indicate a long-term AF with profound anatomical,
histological and electric changes, usually irreversible,
which makes the success of the procedure very difficult.
It is widely accepted that, the larger the pattern of lesions
is, the better the outcomes are [10]. In a 5885 patients
meta-analysis [8], those who underwent a biatrial ablation
had better survival freedom from AF at three years than
those who underwent a limited left atrial ablation (87% vs.
73%). However, Khargui et al. [13] reviewed 48 retrospec-
tive studies comprising 3832 patients and found no differ-
ences when they compared the incidence of sinus rhythm
(77% for isolated left side ablation vs. 83% for biatrial
ablation). Recently, a randomized prospective study com-
prising 299 patients comparing left atrial plus cavotricuspid

Table 1. Predictors of late recurrence. Univariate analysis (Cox regression)

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>1.037 (1.001–1.075)</td>
<td>0.046</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.89 (0.46–1.72)</td>
<td>0.73</td>
</tr>
<tr>
<td>Mitral valve surgery</td>
<td>1.21 (0.53–2.76)</td>
<td>0.64</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>1.13 (0.60–2.18)</td>
<td>0.69</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.32 (0.60–2.90)</td>
<td>0.49</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>2.01 (0.71–5.71)</td>
<td>0.19</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>3.34 (0.78–14.35)</td>
<td>0.10</td>
</tr>
<tr>
<td>AF duration (months)</td>
<td>1.014 (1.009–1.019)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left atrial size (mm)</td>
<td>1.001 (0.960–1.045)</td>
<td>0.94</td>
</tr>
<tr>
<td>Left ventricle ejection fraction (%)</td>
<td>0.975 (0.952–0.999)</td>
<td>0.039</td>
</tr>
<tr>
<td>Systolic pulmonary artery pressure (mmHg)</td>
<td>1.003 (0.987–1.020)</td>
<td>0.71</td>
</tr>
<tr>
<td>Logistic euroSCORE</td>
<td>1.000 (1.000–1.001)</td>
<td>0.56</td>
</tr>
<tr>
<td>Early recurrence of AF</td>
<td>4.245 (1.88–9.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biatrial ablation</td>
<td>1.55 (0.81–2.97)</td>
<td>0.18</td>
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</tbody>
</table>

AF, Atrial fibrillation; HR, hazard ratio. Bold values = P > 0.1.

4. Discussion

Table 2. Distribution of variables among patients with and without early recurrence of AF

<table>
<thead>
<tr>
<th></th>
<th>No early recurrence</th>
<th>Early recurrence</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean, S.D.)</td>
<td>61.8 (10.8)</td>
<td>64.4 (9.8)</td>
<td>0.19</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>28 (65)</td>
<td>38 (60)</td>
<td>0.38</td>
</tr>
<tr>
<td>Mitral valve surgery, n (%)</td>
<td>37 (86)</td>
<td>46 (73)</td>
<td>0.086</td>
</tr>
<tr>
<td>Arterial hypertension, n (%)</td>
<td>16 (37)</td>
<td>32 (50)</td>
<td>0.11</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>6 (14)</td>
<td>15 (24)</td>
<td>0.15</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>2 (4)</td>
<td>4 (6)</td>
<td>0.53</td>
</tr>
<tr>
<td>Chronic renal insufficiency, n (%)</td>
<td>0 (0)</td>
<td>4 (6)</td>
<td>0.12</td>
</tr>
<tr>
<td>AF duration (months) (mean, S.D.)</td>
<td>40.3 (47.6)</td>
<td>71.9 (60)</td>
<td>0.004</td>
</tr>
<tr>
<td>LA size (mm) (mean, S.D.)</td>
<td>54.1 (6.7)</td>
<td>53.9 (7.9)</td>
<td>0.94</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62.5 (10.5)</td>
<td>58.4 (13.7)</td>
<td>0.096</td>
</tr>
<tr>
<td>SPAP (mmHg) (mean S.D.)</td>
<td>49 (20.4)</td>
<td>49.3 (17.6)</td>
<td>0.94</td>
</tr>
<tr>
<td>Biaatrial ablation, n (%)</td>
<td>15 (35)</td>
<td>22 (35)</td>
<td>0.58</td>
</tr>
</tbody>
</table>

AF, Atrial fibrillation; S.D., standard deviation; COPD, chronic obstructive pulmonary disease; LA, left atrium; LVEF, left ventricle ejection fraction; SPAP, systolic pulmonary artery pressure. Bold values = P > 0.05

Table 3. Predictors of late recurrence. Multivariate analysis (Cox’s proportional hazard model)

<table>
<thead>
<tr>
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<tr>
<td>Early recurrence of AF</td>
<td>3.45 (1.50–7.95)</td>
<td>0.004</td>
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AF, Atrial fibrillation; HR, hazard ratio.
isthmus vs. biatrial ablation [14] showed no differences in the incidence of SR after a mean follow-up of 28 months (85% vs. 84%). In any case, it has been demonstrated that the right atrium can participate on the genesis and maintenance of AF, especially among those patients with long standing disease. We only performed biatral lesions in those cases when surgical repair of the tricuspid valve was necessary. We did not detect a greater AF/flutter incidence in the isolated left side ablation group during the follow-up, but either an insufficient statistical power or short follow-up could explain it.

Postoperative AF was identified once the patients referred with symptoms or either because a routine ECG coincided with an AF episode. Therefore, it is possible that some postoperative AF recurrences might have not been detected. Rhythm in the follow-up was defined according to a 24-hour Holter, so it is also possible that asymptomatic AF episodes, even long ones, might have not been detected. Several limitations of this study need to be addressed. This is a study comprising patients referred to a single center. The size of the sample and the length of the follow-up may be insufficient. The Kaplan–Meier method to describe the risk of AF in the follow-up may not be the most accurate, given the fact that atrial rhythm is not an event but a state [15], so a continuous registry of the rhythm might be more suitable.

In conclusion, in our experience, early postoperative AF recurrence is a risk factor for the procedure long-term failure.

References


eComment: Early and late atrial fibrillation recurrence after the Cox maze procedure

Author: Ovidio A. Garcia-Villarreal, Department of Cardiovascular Surgery, Hospital of Cardiovascular Disease No.34, IMSS, Monterrey, Mexico
doi:10.1510/icvts.2010.261842A
I have read with interest the article by Maroto et al. [1]. In a series of 106 patients who underwent surgical ablation of concomitant and permanent atrial fibrillation (AF), they found that 59% of cases had at least one postoperative AF episode. At discharge, 32% had AF or VVI pacemaker rhythm. Of interest, multivariate analysis showed that early AF recurrence was associated to late AF recurrence.

I would like to emphasize several concepts. One must keep in mind that the basis of the arrhythmia surgery is that the fibrocites that make up scar tissue will not conduct electricity. This has allowed new energy sources producing burn and scar to be adapted for intraoperative use. Thus, the Cox maze procedure (CMP) III classic cut-and-sew evolved into the easiest and fastest CMP IV in which most of the surgical incisions are replaced by lines transmural because one can see it. Nevertheless, one can be absolutely sure that surgical incisions in the atria are completely transmural only after the procedure is done and before patient is discharged from the hospital.

Continuous AF (as in this work) needs electrical CMP must be made biatrial when the aim is to cure a continuous rhythm. Of interest, multivariate analysis showed that early AF recurrence was associated to late AF recurrence.


At the beginning of the CMP, the cut-and-sew method was chosen because one can be absolutely sure that surgical incisions in the atria are completely transmural because one can see it [5]. Continuous AF (as in this work) needs two components to exist: the triggers generating AF located into the pulmonary veins, and the drivers or macro reentrant circuits sustaining AF. Continuous AF requires isolation of the triggers and complete elimination of the macro reentrant circuit.

In other words, even the electrical CMP must be made biatrial when the aim is to cure a continuous or chronic AF. Otherwise, a high rate of AF recurrence might be observed.

In conclusion, early AF recurrence is due to initial myocardial edema. The genesis of late arrhythmias is almost always due to a poor procedure. Obviously, there may be a percentage of recurrent AF whose origin may be an incomplete or poorly executed CMP. In the latter case, the recurrent AF persists in a long-term monitoring.


eComment: Re: The early recurrence is a predictor of late failure in surgical ablation of atrial fibrillation

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doi:10.1510/icvts.2010.261842B

Current, the development of the most effective surgical treatment of concomitant atrial fibrillation (AF) is a priority in modern cardiac surgery. Worldwide trials are studying the effectiveness of different interventions, and also the risk factors affecting the results of operations are clarified. The latter is crucial for determining the indications for surgical ablation and defining the postoperative management of patients. The results of surgical ablation of chronic AF show effectiveness in 60–80% of patients operated on for comorbidity [1, 2]. The factors influencing the success of operations include the size of the left atrium (LA), duration of AF, as well as the choice of method of surgical ablation, which is mostly important in patients with chronic AF [3, 4].

Today, the tactics of postoperative management of patients after surgical ablation of AF do not differ substantially among different medical centers. To restore and maintain normal sinus rhythm in the early postoperative period, aggressive antiarrhythmic therapy is applied, including modern methods of pharmacological and electrical cardioversion. However, after surgical ablation of concomitant chronic forms of AF, more than 60% of patients fail to maintain sinus rhythm in the early postoperative period. Although approximately 30% of patients have AF after discharge, in many of them restoration of sinus rhythm occurs within three months of follow-up. The incidence of postoperative AF is much higher than observed after performance of the classical maze III procedure. Currently, the cause of this phenomenon is unknown.

In an interesting study, Maroto et al. examined the phenomenon of early relapse of AF after surgical ablation of chronic AF as an independent risk factor of unsuccessful surgical ablation in patients with concomitant valvular heart disease and coronary artery disease (CAD) [1]. Operations were performed in 106 patients, most of whom (85%) had valvular pathology. Bipolar and monopolar RF ablation techniques were used to perform surgical ablation. Mean follow-up was 37 months (12–77 months), and was complete in 99% of patients. Sinus rhythm was observed in 82%, 76% and 68% of patients, respectively at one, two and three years of follow-up. The authors found that in the long-term period, sinus rhythm was rarely observed in patients with early postoperative relapse of AF (P < 0.001). Multivariate Cox regression analysis showed that duration of AF and an early relapse of AF were independent risk factors of unsuccessful surgical ablation of concomitant AF. The study design and statistical analysis were of high quality. Nevertheless, for more accurate and reliable evaluation of surgical ablation, it is necessary to study the results in the more remote periods after surgery. In addition, it should be noted that there are obvious disadvantages of monopolar RF ablation, especially in chronic AF patients. Nowadays in our institute the method of intensive ablation using cryotheraphy of areas with limited access is applied. Such areas include the coronary sinus, mitral valve fibrous ring, the base of appendage of the left atrium, as well as the posterior wall of the left atrium [3]. According to our data, which are analogous with studies from other institutions, the use of cryoablation significantly increases the effectiveness of surgical ablation [3].

In conclusion, the article reports the actual issues of surgical treatment of AF. Continuation of research in this area will certainly increase the effectiveness of treatment of this challenging arrhythmia.

References


