

Predictive factors of sustained sinus rhythm and recurrent atrial fibrillation after a radiofrequency modified Maze procedure

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Abstract

Background: Preoperative atrial fibrillation (AF) in patients scheduled for elective open-heart surgery is a well-known phenomenon. The cut and sew Maze procedure or variant Maze procedures abolish AF in 45–95% of patients during short- to intermediate-term follow-up. We determined preoperative and postoperative factors predictive of sustained sinus rhythm (SR) and recurrent AF in an elderly cohort of patients with structural heart disease who underwent cardiac surgery. **Patients and methods:** From November 1995 to November 2003, 285 patients with structural heart disease and permanent AF were scheduled for elective cardiac surgery. All patients underwent a radiofrequency (RF) modified Maze procedure as an adjunct to the open-heart operation. Patients were followed in the outpatient clinic or follow-up data were obtained from attending doctors. Patients are being followed in an ongoing registry; however for the patients who are the subject of this paper follow-up ended November 2006. Preoperative factors predicting recurrent AF postoperatively were assessed, as were factors associated with sustained SR. **Results:** Two hundred and eighty-five patients (mean age 68.0 ± 9.6 years) underwent a total of 655 open-heart procedures and concomitant RF Maze surgery. In-hospital mortality was 4.6% (13 patients). Mean and median duration of AF were 60.9 ± 68.7 months and 26 months (range 6–396), respectively. Median follow-up was 36.5 months (range 27–114 months). Sustained SR, including atrial rhythm or an atrial-based paced rhythm was present in 59% of patients at 1 year, in 54.4% at 3 years, in 53.4% at 5 years and in 57.1% of patients at the latest follow-up. Stroke was reported in six patients (2.1%). Factors predictive of postoperative AF recurrence were duration of permanent AF, preoperative atrial fibrillation wave and preoperative left atrial (LA) size. Postoperative angiotensin converting enzyme (ACE) inhibitor therapy was associated with SR during follow-up. LA size decreased during follow-up in patients with sustained SR, whereas LA size increased in case of recurrent AF. **Conclusions:** In this group of elderly patients with permanent AF in the setting of structural heart disease who underwent cardiac surgery and a RF Maze procedure as a concomitant procedure, the duration of AF, preoperative atrial fibrillation wave and preoperative LA size were predictive of recurrent AF, whereas left ventricular ejection fraction, left ventricular diameters and invasive hemodynamic parameters were not. Postoperative ACE inhibitor therapy was associated with sustained SR. Furthermore, sustained SR after RF Maze surgery was associated with decreased LA dimensions.

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Keywords: Chronic atrial fibrillation; RF Maze; Predictors of sinus rhythm

1. Introduction

In patients with mitral valve disease preoperative atrial fibrillation (AF) is present in 30–50% [1,2] and surgical correction of the underlying cardiac abnormality usually will not abolish AF that has been present for 6 months or more. Maze surgery using the cut and sew technique or alternative

means of creating linear lesions of electrical block in both atria, results in sinus rhythm (SR) or an atrial rhythm in 44–95% of patients [3–15]. Restoration of SR is a consistent and highly significant finding in match controlled and randomized controlled trials of Maze and Maze-related surgical procedures. An important and largely unanswered question remains: which group of patients benefits from this type of surgery? This report of the long-term follow-up of elderly patients with structural heart disease who underwent a radiofrequency (RF) modified Maze procedure as an adjunct to elective cardiac surgery identifies preoperative risk factors for recurrence of AF and postoperative factors predictive of sustained SR.

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2. Patients and methods

2.1. Patients

From November 1995 to November 2003, 285 patients with structural heart disease and permanent AF were included in a registry (Table 1). All patients consented to their data being registered and used for publication, as did the board of hospital administrators. Preoperative atrial fibrillation wave (AFW) amplitude in millimetres was measured in lead V₁ of a 12-lead electrocardiogram obtained 1–7 days before surgery (1 mm = 0.1 mV). The measurements were made from the peak to the trough of the AFW and all AFW measurements in V₁ were averaged. A division was made of the AFW <0.1 mV or ≥0.1 mV. All patients underwent an RF Maze procedure as an adjunct to the primary surgery. All patients were operated by a single surgeon (HTS). Patients were followed in the outpatient clinic and follow-up data were obtained from attending doctors. Follow-up ended November 2006. All available EKGs per patient starting at 6 months post-operatively and ending November 2006 were scored as showing SR, atrial based paced rhythm, atrial flutter/atrial tachycardia or AF. Preoperative non-invasive and invasive parameters were scored as predictive for sustained SR or recurrent AF post surgery and also postoperative non-invasive factors predicting sustained SR using multivariate analysis.

2.2. Radiofrequency ablation procedure

RF energy was used to create continuous endocardial lesions mimicking most of the lesion set as described in the Cox maze III procedure [3]. RF energy was delivered as a continuous sinusoidal unmodulated waveform of 500 kHz in a unipolar mode between a hand-held electrode and a dispersive pad at the patient's back. In the first 173 patients a custom-made radiofrequency probe with a saline irrigation system incorporated to cool the tip of the probe was used along with a HAT 200S generator (Sulzer-Osypka GmbH, Grenzach-Wyhlen, Germany). In 112 patients who had undergone surgery after

November 2000 the Medtronic cooled tip Cardioblate pen was used. The tip of both types of RF probe was irrigated with saline at room temperature at a flow rate of 4–6 ml/min.

2.3. Surgical procedure

In all patients cardiopulmonary bypass was used with standard aortic cannulation, bicaval cannulation, and moderate hypothermia. Part of the RF Maze was performed during cross-clamping of the aorta and cardioplegic arrest with cold crystalloid cardioplegia. The RF Maze procedure and postoperative management were described in detail previously [9]. In brief the radiofrequency ablation part of the surgical procedure was as follows: most of the atrial incisions currently used in the Cox maze III were replaced by RF ablation lines except for an incision in the right atrium and a standard left atrial incision in Waterston's groove: these incisions were used to enter the atrial cavities. Both the right atrial appendage (RAA) and the left atrial appendage (LAA) were excised. In redo operations the LAA was electrically isolated by a circumferential RF ablation line around the orifice and subsequently the cul-de-sac was closed at the endocardial site with polypropylene. In contrast to the Cox maze III procedure the right and left pulmonary vein islands were isolated separately and interconnected with a RF linear lesion in the left atrial (LA) roof to preserve contractile posterior wall tissue in between them. Isolation of the coronary sinus was performed endocardially with radiofrequency ablation at the posterior wall of the LA, guided by a round metal probe which was introduced into the CS through the right atrium (Fig. 2). This ablation line is then connected to the posterior annulus of the mitral valve at the posteromedial commissure, thus creating a left isthmus block and obviating the need for an additional cryo-ablation.

3. Postoperative management

Postoperative care was similar to routine cardiac surgical procedures. Postoperative atrial arrhythmias were treated with sotalol 80–160 mg daily or amiodarone 200 mg daily and with direct-current cardioversion if deemed necessary. Antiarrhythmic drugs were usually continued at discharge and further antiarrhythmic therapy was managed by the patient's (referring) doctor. Anticoagulation therapy was given for at least 3 months and discontinuation of medication was at the discretion of the (referring) cardiologist.

4. Statistical analysis

All data are reported as mean and standard deviation. Analysis of variance was applied to compare effects over time and effects per time point. Multivariable logistic regression analysis was performed to test the independent association between several preoperative variables and postoperative SR. The arrhythmia-free survival curves were constructed by using the Kaplan–Meier method; differences between groups were investigated with the log-rank test. Cox proportional hazards regression models were used to estimate adjusted hazard ratios of postoperative SR with

Table 1
Patient characteristics

	Total (n = 285 patients)
Age (years)	68.04 ± 9.56
Male gender	143/285 (50.2%)
Duration AF (months)	60.87 ± 68.70
Duration AF (median, range, months)	26 (13–89)
Prolapse	46/285 (16.1%)
Rheumatic	62/285 (21.8%)
Degenerative (MS)	84/285 (29.5%)
Annulus dilatation	43/285 (15.1%)
Ruptured chordae	14/285 (4.9%)
Av disease	43/285 (15.1%)
Ischemic	51/285 (17.9%)
Hypertension	25/285 (8.8%)
Ischemic and/or hypertension	67/285 (23.5%)
More than 1 etiology	107/285 (37.5%)
NYHA class 3 or 4	250/285 (87.7%)
F-wave <0.1	111/250 (44.4%)
LVEF normal	113/259 (43.6%)
LVEF moderate	114/259 (44.0%)
LVEF poor	32/259 (12.4%)

regard to survival. A confidence level of 95% was considered statistically significant.

5. Results

5.1. Preoperative data

Between November 1995 and November 2003 a total of 285 patients underwent a radiofrequency modified Maze procedure for permanent AF as concomitant surgery. The patients' characteristics are outlined in Table 1. All patients had structural heart disease, which was the primary indication for surgery in 276 patients. In nine patients arrhythmia surgery was the primary reason for cardiac surgery. A total of 655 procedures were performed in these patients. There were 142 female patients (49.8%) and the mean age of the whole group was 68 ± 9.6 years (range, 30–86). The mean LA dimension was 52.5 ± 9.6 mm (range, 31–96 mm) as measured on an M-mode tracing taken from a two-dimensional parasternal long-axis view (Table 2).

5.2. Operative data

The 285 patients with chronic AF (duration >6 months) underwent a total of 655 cardiac surgical procedures and concomitant RF Maze surgery. Of these patients, 227 (79.1%) underwent mitral valve surgery as part of the surgical procedure and 213 (82.5%) underwent a multiple procedure. Extra corporeal circulation time (ECC) and aortic cross-clamp (ACC) time were 226.1 ± 59.0 and 122.6 ± 43.7 min, respectively.

5.3. Postoperative data

For the 285 patients with chronic AF (duration >6 months) in-hospital mortality was 4.2% (12 patients) and during a mean follow-up of 43.6 ± 25.4 months (median follow-up 40.4 months, range 27–61) 78 patients died (27.4%). Neither NYHA class nor left ventricular ejection fraction (LVEF) was predictive for recurrent AF. SR, atrial rhythm (AR) or an atrial-based paced rhythm (ABPR) was present in 69% of patients at 1 year, in 58% at 3 years, in 55% at 5 years and in 56% of patients at the latest follow-up (Fig. 1). The presence of SR did not influence cardiac mortality, total mortality and stroke rate (Fig. 2). Antiarrhythmic drugs were used in 66% of

Table 2
Echocardiographic and hemodynamic characteristics

LA (parasternal long axis view, mm)	52.47 ± 9.56
LA (apical 4-chamber view, mm)	76.55 ± 11.21
RA (apical 4-chamber view, mm)	68.23 ± 10.09
Systolic blood pressure (mmHg)	134.31 ± 28.45
Diastolic blood pressure (mmHg)	72.67 ± 14.13
RAP (mmHg)	8.50 ± 9.14
RVP (mmHg)	40.56 ± 14.66
PAP (mmHg)	5.66 ± 5.35
PAP systolic (mmHg)	40.90 ± 13.95
PAP diastolic (mmHg)	18.56 ± 7.30
Pulmonary capillary wedge (mmHg)	19.16 ± 7.81
LVED (mm)	55.30 ± 8.97
LVES (mm)	38.93 ± 9.61

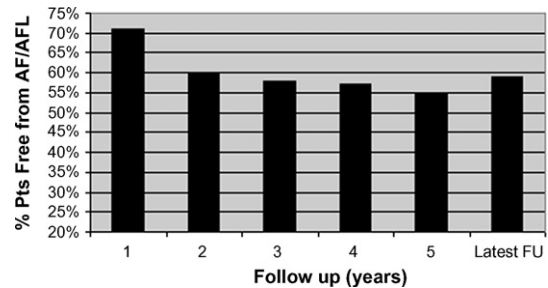


Fig. 1. Bar graph showing freedom from AF/Afl at 1, 2, 3, 4, 5 years and at the latest follow-up. Latest follow up ranged from 27 to 114 months.

survivors who were free of atrial fibrillation. Oral anticoagulation was taken by 99.6% of patients. Stroke was reported in six patients (2.1%). At the time of stroke two were in SR and four were in AF (Table 3).

5.4. Predictive factors of sinus rhythm after RF Maze procedure

Factors predictive of postoperative AF recurrence were duration of permanent AF, preoperative AFW and preoperative LA size. LA size >60 mm was associated with a high incidence of postoperative AF (Fig. 3). Underlying cardiac abnormality, NYHA class, LVEF, pulmonary artery pressure (PAP), mean pulmonary capillary wedge pressure (PCWP), left ventricular (LV) end diastolic diameter and LV end systolic diameter were not predictive of postoperative AF. LA size decreased during follow-up in patients with sustained sinus rhythm, whereas LA size increased in case of recurrent AF (Table 4).

6. Discussion

6.1. Main findings

This study of 285 elderly patients with structural heart disease and permanent AF who underwent an open heart operation and concomitant RF Maze surgery found preoperative duration of AF, preoperative left atrial size,

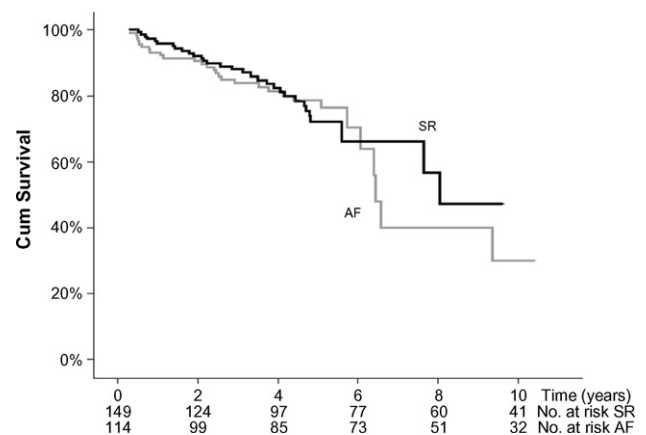


Fig. 2. Kaplan–Meier curve showing the survival in patients with postoperative SR and AF. There was no difference in survival between these two groups ($p = 0.81$). See text for details.

Table 3
Mortality and stroke

	Total
In-hospital death	12/284 (4.2%)
In-hospital cardiac death	6/284 (2.1%)
Death	78/284 (27.5%)
Cardiac death	40/280 (14.3%)
CVA or TIA	6/285 (2.1%)

preoperative F-wave and postoperative angiotensin converting enzyme (ACE) inhibitor therapy prognostic factors for recurrence of AF or sustained SR after RF Maze surgery. Underlying cardiac abnormality, preoperative invasive hemodynamic parameters, NYHA class and LVEF were not predictive of postoperative rhythm. Our findings are in agreement with many other studies, although most often these studies included a much younger patient population. Furthermore, this study does not show a lower incidence of (cardiac) mortality or stroke in those with postoperative sinus rhythm. Potential benefit of postoperative sinus rhythm could not be observed in any subgroup.

6.2. Previous studies

An important and not fully answered question regarding Maze surgery is which patient benefits most from this procedure. From previous reports one may conclude that in the majority of Maze studies patients are between 50 and 60 years of age, have normal or moderately decreased LVEF, permanent AF >12 months and 75% or more have structural heart disease, AF not being the primary reason for surgery. Short-term and intermediate term SR post classical Maze or variant Maze varies widely and is reported between 44% and 95%, respectively. Mortality benefit for Maze over non-Maze has not yet been proven and in the six trials that have randomized patients to Maze or non-Maze stroke rate is not significantly lower in the Maze group compared with the non-Maze group [12–14]. Maze surgery for lone PAF improves quality of life significantly, as does catheter ablation for paroxysmal or persistent AF [15,16]. Even though it is not proven that SR post Maze surgery in patients with structural heart disease decreases mortality, it is reasonable to assume that SR improves quality of life. Knowledge of prognostic factors remains important for individual patient counseling.

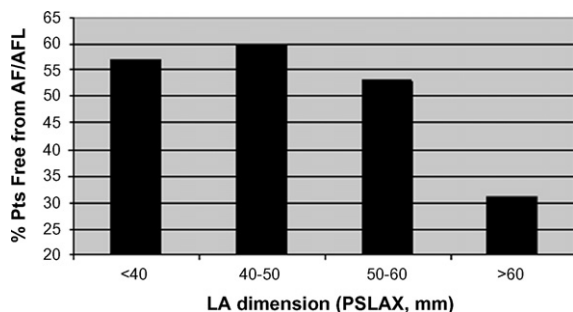


Fig. 3. Bar graph showing the relationship between left atrial dimension and the rhythm outcome at the latest follow up. Percentage patients free from atrial fibrillation or atrial flutter is significantly lower in the patients with a left atrial dimension >60 mm compared with the remaining groups with a left atrial dimension <60 mm. $p = 0.008$.

6.3. Predictive factors of postoperative sustained SR

Experimental AF causes changes in electrophysiological properties of the atria, a process called electrical remodeling [17]. Allesie et al. have elegantly demonstrated in the goat model that this process is accompanied by a reduction in atrial contractility, called contractile remodeling, which results in an increase of atrial compliance, leading to atrial enlargement during the first days of AF. Six to eight weeks of rapid atrial pacing in a dog model resulted in marked atrial dilatation. Atrial dilatation in itself is a cause of AF, although the mechanisms effective are not completely understood [17,18]. Chronic experimental AF leads to extensive changes in atrial (ultra) structure and increased vulnerability to AF induction. These structural changes may interfere with local conduction and thus promote the perpetuation of AF. In animal studies duration of (artificially maintained) AF therefore is a factor in the stabilization of AF. In humans duration of AF is also associated with perpetuation of the arrhythmia. Spontaneous or electrical conversion of AF to SR is inversely related to duration of AF. AF duration also is an independent predictor of LA size. In the clinical setting LA size and AF are significantly and mutually related to each other. Many clinical investigations have recognized LA dilatation as a cause of AF. LA dilatation on the other hand may also be a consequence of AF [19,20]. Why preoperative AFW is a predictor for recurrence of AF is unknown. Some studies have shown a correlation between AFW amplitude and LA size and AFW amplitude and rheumatic AF or non-valvular AF, however others have not corroborated these findings. It is likely that a combination of the changes in atrial architecture caused by ageing, AF and CHF play an important role [21].

Several studies have assessed the impact of preoperative and postoperative AF on outcome. From previous non-randomized studies it appears that preoperative AF confers an increased long-term mortality risk [22–24]. Postoperative AF is not related to increased mortality, unless preoperatively SR had been present. Preoperative SR translates to low long-term mortality rates. Conflicting opinions remain about Maze induced SR conferring the same benefits as pre- and postoperative spontaneous SR.

The Maze procedure was pioneered by Cox et al. who designed the procedure in the laboratory as an open-heart operation through a median sternotomy (Maze I) and subsequently made two modifications culminating in the Maze III procedure [3]. The cut and sew Cox Maze procedure abolishes AF in 74–97% of patients. Some investigators report a significantly lower stroke rate in Maze versus non-Maze patients in matched cohorts [13]. Mortality benefit for Maze over non-Maze has not yet been proven.

The present study of 285 patients (mean age 68.04 ± 9.56 years, median 70.65 years), all with structural heart disease, permanent AF and poor to moderately decreased LVEF in 50%, who underwent a RF Maze procedure as concomitant surgery does not show an advantage of postoperative SR over AF with regard to cardiac mortality, all cause mortality and stroke. No subgroup, as defined by preoperative LVEF and NYHA class profited from sustained SR with regard to cardiac mortality, total mortality and stroke.

Table 4
Multivariate analysis

Predictors of postoperative SR	Odds ratio	95% CI	p value
Duration AF	0.91	0.89; 0.90	0.002
LA (ps)	0.93	0.86; 0.94	0.041
F-wave <0.1	0.32	0.17; 0.62	0.001
Discharge ACE	1.80	0.99; 3.51	0.054

Collagen formation in atrial tissue may contribute to structural remodeling and fibrosis leading to the development of AF. Angiotensin II is one of the substances responsible for collagen formation. Previous work has shown increased atrial expression of ACE and angiotensin II in fibrillating human tissue. In experimental models of AF both ACE inhibitors and angiotensin receptor blockades appear to have a useful role in reducing AF. This mechanism is complex and thought to be involved in the prevention of atrial electrical and structural remodeling that promotes AF.

In a clinical setting, both ACE inhibition and specific antagonism at the angiotensin II receptor level decrease the recurrence of AF following cardioversion. ACE inhibition also reduces the incidence of AF following myocardial infarction (MI) in patients with LV systolic dysfunction. Data in hypertensive patients have shown a reduction in new onset AF in patients treated with ACE inhibitors and angiotensin II receptor antagonists. The antifibrotic effects of ACE inhibitors seem to be mediated via TGF β .

7. Limitations

This was not a randomized controlled study (RCT) and hence harbors all the shortcomings thereof. A major problem of all studies or registries of treatment of AF is the fact that the burden of atrial arrhythmia cannot reliably be determined unless a pacemaker with a specific algorithm to detect atrial arrhythmia is in situ.

8. Clinical implications

At the present time there is not enough available evidence for clinicians to answer the question as to who is to profit from Maze surgery. Up until now randomized clinical trials have not been able to document superiority of the Maze procedure over non-Maze with regard to all-cause mortality and stroke reduction.

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