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## Endocardial microwave ablation in patients following mitral valve surgery

Michael Knaut<sup>1</sup>, Theresa Link<sup>1</sup>, Friedrich Jung<sup>2</sup>, Stefan Brose<sup>1</sup>, Klaus Matschke<sup>1</sup>

<sup>1</sup>Department of Cardiac Surgery, University of Technology Dresden, Germany; <sup>2</sup>Institute of Clinical Haemostaseology and Transfusion Medicine, University Hospitals of Saarland, Homburg, Germany

### Abstract

Atrial fibrillation not only impairs the quality of life but is also associated with higher mortality and morbidity caused by embolic events or therapeutic anticoagulation treatment. The present prospective registry study evaluated the conversion rates and the influencing factors on outcomes of mitral valve surgery and concomitant microwave ablation in 191 patients with permanent atrial fibrillation.

In approximately 60% of the patients it was possible to establish stable sinus rhythm during the postoperative period whereas, conversion rates between 4% and 33.5% have been reported after cardiac surgery alone without additional surgical ablation therapy. Significant influencing factors on postoperative sinus rhythm were the presence of diabetes mellitus or a history of myocardial infarction, the preoperative atrial size, and tendentially, operation time. There were no ablation-related complications. During the 1.5-year follow-up it became evident that longer operation time (in most cases due to operative complexity with higher risk) and postoperative recurrence of atrial fibrillation were significant factors influencing mortality.

**Key words:** atrial fibrillation, surgical ablation, mitral valve surgery

### Introduction

Atrial fibrillation is the most common and clinically relevant form of supraventricular arrhythmia. The prevalence is as follows: people between 50-59-years is 0.5%, between 60-69-years it is 1% and 4%, between 70-79-year it is 7%, and finally in individuals between 80 to 89 years it is more than 10% [Kannel, 1982; Go, 2001]. The risk of developing atrial fibrillation is increased in patients with underlying cardiovascular disease and is often associated with hypertension, heart insufficiency, coronary heart disease [Quader,

2004; Knaut, 2005; Knaut, 2006], heart attack and valvular heart diseases [Kannel, 1982]. In association with rheumatic mitral valve disease the incidence of atrial fibrillation can even reach 60% to 80% [Kannel, 1982].

Atrial fibrillation doubles the cardiovascular mortality [Kannel, 1982, Jung 2009]. The major causes of death are stroke (sixfold higher risk [Kannel, 1982; Laupacis, 1996]) or peripheral embolism [Atrial Fibrillation Investigators, 1994; Wolf, 1998; Sack, 2002; Quader, 2004]. Anticoagulation may reduce the risk of embolic events [Fuster, 2001] but

at the same time it can increase the risk of cerebral hemorrhage by 300% [Taylor, 2001; Leithäuser 2009].

The present prospective study has investigated the influence of pre-, intra- and perioperative parameters on postoperative rhythm in patients who underwent mitral valve surgery and concomitant ablation and looked for risk factors influencing the postoperative course.

## Material and Methods

The registry study was conducted in accordance with the Declaration of Helsinki/Somerset West 1996 and the Guidelines of the European Forum for Good Clinical Practice (GCP) [WHO, 2000]. Approval was obtained from the Ethics Committee of the University of Dresden if the cardiosurgical procedure included an additional rhythm intervention. All patients with permanent atrial fibrillation who had undergone mitral valve surgery in combination with an endocardial microwave ablation between 1999 and 2004 were consecutively entered in the prospective registry. The criteria for inclusion into the registry were permanent atrial fibrillation with a duration of at least three months, elective mitral valve surgery and performed endocardial microwave ablation.

Exclusion criteria were paroxysmal or persistent atrial fibrillation, emergency operations, stroke or myocardial infarction within the last three months, severe obstructive or restrictive disorders of pulmonary function, severe endocrine disease, severe renal and/or hepatic failure, pregnancy and nursing, known prescription or illegal drug abuse, and incapacity to understand the nature and scope of the study.

Only patients who fulfilled all inclusion criteria and met none of the exclusion criteria were included in the study. Patients were informed at least 24 hours before surgery about the risks and benefits of the planned operation and the associated ablation indication procedure and their written informed

consent was obtained. Consent to the transfer of postoperative follow-up data provides by their general practitioner and cardiologist was also obtained as well as consent to the entry of their personal data in a database. Data collection was initiated after the Ethics Committee of the University of Dresden gave its approval.

This data collection included demographic data (age at time of surgery, height, weight, gender) and clinical parameters (diabetes mellitus, hyperlipidemia, hyperuricemia, arterial and pulmonary hypertension, hyperthyroidism, nicotine abuse, NYHA and CCS status, CHD, history of stroke or heart attack, duration of preoperative atrial fibrillation, echocardiographic data (size of atrium parasternal, ejection fraction), mitral, aortic, tricuspid and pulmonary valve insufficiency or stenosis).

Preoperative antiarrhythmic drug therapy was discontinued; any other cardiovascular medications and antiplatelet drug treatments were left unchanged. The microwave ablation probes used were manufactured by AFx (Freemont, CA, USA), since 2004 by Guidant (Santa Clara, CA, USA) and after 2006 by Boston Scientific. The lesion line concept is shown in Figure 1. It is analogous to the box lesions and other connection lines proposed by Cox [Cox, 1995] and Melo [Melo, 1999].

The left and right pulmonary vein pair was each separately encircled by a so-called box lesion. Half of the encircling line around the right pulmonary veins is predefined by the atriotomy of the left atrium. Both pulmonary vein pairs boxes were then connected with a lesion line at the posterior wall of the left atrium. The left atrial appendage, thus included in the ablation scheme, was connected with a lesion line that started at the lower left pulmonary vein and led to the mitral valve annulus. This was followed by the classic valve procedure and the additionell LAA closure or resection.

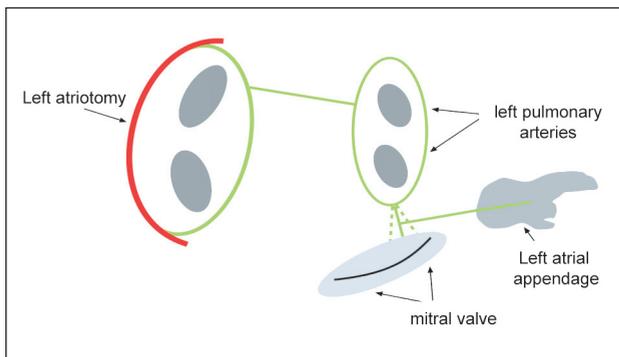


Figure 1: Line concept (red = left atriotomy, green = microwave ablation lines, dashed green = possible ablation line variation)

### Follow-up parameters

Postoperative data were collected at day 10, 30, 90, 180 and 360 and 1.5 years after surgery. The type of rhythm, echocardiographic parameters, any antiarrhythmic or anticoagulation medication and implantations of a new cardiac pacemaker were assessed at each follow-up date. The number of performed cardioversions and any complications (including death) occurring during the intervals between each follow-up visit date were also documented. 24-Holter-ECG was used to document heart rhythm. Rhythm was divided into sinus rhythm, atrial fibrillation, typical and atypical atrial flutter (according to the definition by Della Bella [Della Bella, 2002]).

The size of the left atrium and the ejection fraction were assessed by a transthoracic echocardiogram (except at day 10 of follow-up).

Rhythm related medications such as antiarrhythmics and anticoagulants were documented. All patients received sotalol to stabilize rhythm (initial dose: 2 x 40 mg/d, followed by 3 x 80 mg/d (< 75 kg) or 2 x 160 mg/d (> 75 mg). Due to its side-effects and its high antiarrhythmic potential, amiodarone was rarely used for rhythm control as it would have obscured the actual effectiveness of the ablation therapy.

Oral anticoagulation therapy was established in all patients. A target INR between two and three or, in patients with mechanical valve prosthesis, of three to four was targeted. In patients with stable sinus rhythm (sinus

rhythm at all control time points, [Knaut, 2005]) three months after their operation, anticoagulation treatment was discontinued in case of the patient had undergone either biological valve replacement or valve repair and that there were no further indications for anticoagulation therapy.

Sotalol also was discontinued three months postoperatively in patients with stable sinus rhythm. Patients with structural heart disease received instead conventional beta-blocker. This decision was finally made the general practitioner. Patients with postoperative atrial fibrillation and those in whom no conversion to sinus rhythm could be achieved by medication or cardioversion received heart-rate controlling medication. Rhythm control and anticoagulation medication was recorded at each follow-up date and any changes were documented.

In case of persistent atrial fibrillation up to two cardioversions were performed around the eighth postoperative day. This strategy was followed mainly in the early phase of the study. Later on, this approach of early cardioversion treatment was abandoned after it became obvious that at least six to eight weeks are necessary to get a definitive transmural lesion after cardiac ablation. Within this period conversion into sinus rhythm may occur spontaneously could be avoided. If a new cardiac pacemaker was implanted, the date and reason for the implantation and the mode of implantation were recorded.

Also data from any postoperative complications or other diseases that occurred postoperatively were collected. If available, hospital medical records from the concerned hospitals were requested. Special attention was given to any thromboembolic events that occurred.

When a patient died, the reason was evaluated, survival time was assessed and the follow-up for this patient was terminated.

### Statistics

Continuous data are presented as mean values with standard deviations, categorical data as frequencies in terms of percentages. Survival probability and rates are described using Kaplan-Meier estimates and calculated by log-rank test. For statistical analysis, probabilities ( $p$  values)  $< 0.05$  were considered as significant.

Multivariate regression analysis was used for data evaluation. Surgical data and factors that may have had an influence on the clinical outcome of the ablation treatment were used as confounding variables.

## Results

### Patient cohort

191 patients (male: 64; female: 127) were included in the registry and followed for 1.5 years. Mean patient age at the time of sur-

gery was  $67.4 \pm 8.2$  years and mean duration of permanent atrial fibrillation was  $6.6 \pm 9.1$  years. Table 1 shows the incidence of cardiovascular risk factors.

69 patients (36%) had a manifest CHD, 18 patients (9%) had a history of myocardial infarction. A history of stroke was seen in 17 patients (9%), thromboembolic events occurred in 16 patients (8%). 18 patients (9%) had a medical history of rheumatic fever. Pulmonary hypertension was observed in 140 patients (73%).

Preoperative diameters of the left atrium of  $55.1 \pm 9.1$  mm were obtained in echocardiography. 27 patients (14%) had a left atrium larger than 65 mm. Ejection fraction was between 20% and 80% ( $56.6 \pm 11.2$ ). Six patients (3.1%) already had an implanted pacemaker (two patients a DDD (dual-chamber) pacemaker and four patients a VVI (single-chamber) pacemaker. On average, the surgical procedure took  $196 \pm 50$  minutes (ablation time was 15 minutes). The performed mitral valve procedures are listed in Table 2.

20 of the 94 mitral valve reconstructions were performed as isolated procedures and 74 in combination with other interventions. 44 of the 93 mitral valve replacements were performed as isolated procedures and 49 in combination with other interventions. Mitral valve replacement with a mechanical valve was performed in 67 patients (72%) (43 Carbomedics (46%), 19 Baxter Mira (20%), 4 ATS (4%) and one Edwards Mira (1%)). 26 biological valves were implanted (28%): nine Carpentier Edwards Perimount (9.5%), 13 St.

Table 1: Cardiovascular risk factors

	Total (n)	Percent
Diabetes mellitus	64	34
Arterial hypertension	131	69
Hyperlipidemia	97	51
Hyperuricemia	52	27
Smoker	2	1
Ex-smoker	32	17

Table 2: Performed mitral valve interventions

Intervention	Number (n)
Mitral valve replacement	93
Mitral valve repair	94
Cleaning of mitral prosthesis	1
Refixation of mitral prosthesis	1
Decalcification of mitral prosthesis	2

Table 3: Interventions performed in addition to mitral valve surgery

Intervention	Number (n)
Bypass operation	44
Aortic valve replacement	32
Tricuspid valve repair	68
Closure of an atrial septal defect	22
Other	12

Table 4: Number of performed surgical combinations

Number of combinations	Number (n)	Percent (%)
2 combinations	85	44.5
3 combinations	32	16.8
4 combinations	7	3.7
5 combinations	2	1.0

Jude Medical (14%), two St. Jude Medical Quattro (2%), one Edwards CE S.A.V. (1%) and one Edwards Perimount Plus Mitral valve (1%).

Table 3 shows the additional interventions performed together with mitral valve surgery.

Aortic valves were replaced with 18 biological (56%) and 14 mechanical valves (44%). 34% of the interventions were performed as isolated procedures, 66% in combination with other cardiac procedures (Table 4).

### Follow-up

Follow-up was 100% complete up to 180 days. At the one-year follow-up, one patient was lost (99%). At the 1.5-year follow-up drop out rate was 6% (12 patients). 179 patients (94%) remaining available for evaluation.

Rhythm was not evaluated in two patients who died on the first postoperative day. Figure 2 shows that 79 of 191 patients reached stable sinus rhythm (sinus rhythm at all time points), while 110 of 191 patients were not in sinus rhythm at least one follow up visit during the 1.5-year period.

While 59% of the patients (n=112) were perforation cardioversions during the ten-day

Table 5: Course of rhythm during follow-up

Total number: 191	Follow-up date					
	10 d	30 d	90 d	180 d	360 d	1.5 years
Patients alive (n)	189	184	176	172	167	153
Patients dead (n)	2	7	15	19	23	26
Dropouts (n)	0	0	0	0	1	12
SR (n)	119 (63 %)	112 (60.9 %)	105 (59.7 %)	107 (62.2 %)	99 (59.3 %)	91 (59.5 %)
AA (n)	66(34.9 %)	68 (37.0 %)	67 (38.1 %)	61 (35.5 %)	65 (38.9 %)	57 (37.2 %)
Aflut (n)	3 (1.6 %)	4 (2.1 %)	1 (0.6 %)	3 (1.7 %)	2 (1.2 %)	3 (2.0 %)
Atyp. Aflut (n)	1 (0.5 %)	0 (0 %)	3 (1.7 %)	1 (0.6 %)	1 (0.6 %)	2 (1.3 %)

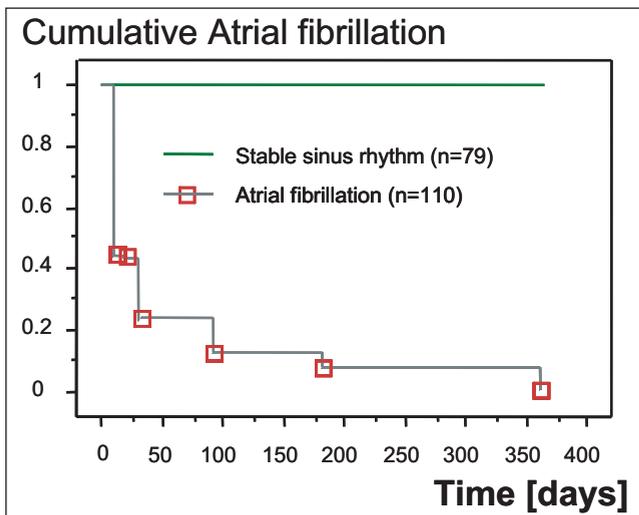


Figure 2: Cumulative assessment of the time to first occurrence of postoperative atrial fibrillation

follow-up, only 24% (n=45) and 6% (n=11) of the cardioversions were done later during the 30-day and 90-day follow-up respectively.

In the whole 1.5-year follow-up period, 61 patients (31.9%) required pacemaker implantation (VVI pacemaker: 15 patients (24.6%), DDD pacemaker: 46 patients (75.4%)). The most frequent indications were bradyarrhythmia absoluta (19.7%), AV block II or III (16.4%) or sick sinus syndrome (18%).

The influence of various variables on postoperative sinus rhythm rate was evaluated by covariate analysis. Preoperative atrium

size (p=0.0185), history of myocardial infarction (p=0.011) and presence of diabetes mellitus (p=0.0296), and tendentially, also surgery duration (p=0.0601) and a reduced ejection fraction (p=0.0976) proved to be major significant influencing factors on success rates (SR). All remaining parameters had no influence in this model (Table 7). Patients with a history of myocardial infarction had higher sinus rhythm rates after the operation. Eight of the 18 patients (44.4%) who had previously suffered from a heart attack and 103 of the patients without myocardial infarction

(58.5%) had a recurrence of atrial fibrillation postoperatively. Patients without diabetes mellitus achieved a better postoperative success rates. Atrial fibrillation recurred in 62.5% (n=40) of 64 patients with diabetes mellitus compared to 55.9% (n=71) of 127 patients without diabetes.

The larger the preoperative size of the left atrium, the lower the rate of postoperative sinus rhythm. The mean parasternal atrium diameter in patients with postoperative stable sinus rhythm was  $53 \pm 8$  cm, whereas in patients with postoperative atrial fibrillation it was  $56 \pm 9$  cm. Up to atrium sizes of 60 millimeters, the incidence of postoperative sinus rhythm was the same. With larger atrium sizes, success rates for sinus rhythm dropped to approx. 40%. For this reason, a separate evaluation of the influence of a giant left atrium on sinus rhythm was done. A giant left atrium was defined as an atrial size greater or equal than 65 millimeters (parasternal measurement) [Beppu, 1982]. It was clearly shown that patients with a giant left atrium rarely achieve postoperative sinus rhythm. In the evaluation of surgery duration as an influencing factor on postoperative sinus rhythm, tendential significance ( $p = 0.06$ ) was observed.

### *Echocardiographic parameters*

Table 6 demonstrates the development of left atrial sizes and ejection fractions along the follow-up period.

Ejection fraction was reduced for up to one year after surgery, but thereafter it increased, reaching the preoperative value. The diameter of the left atrium, however, remained markedly decreased (from 55.1 mm to approx. 49 mm).

### *Postoperative complications*

There were no ablation-related complications.

From the 191 operations 16 patients required a rethoracotomy (8.4%). In six cases the reason was a pericardial tamponade and in four cases high drainage volumes.

Postoperative apoplexy was seen in five patients (3%). Four of these patients had stable sinus rhythm. At last patient was still in stable atrial fibrillation in his control ECGs. Two of the patients with apoplexy (40%) were receiving the anticoagulation with Phenprocoumon at the time of the event. One patient took Phenprocoumon together with ASA 100 mg, one heparin and ASA 100 mg and one heparin alone (12.5% each).

In total there were five thrombotic/embolic events (2.6%). Three patients (60%) the thrombosis or embolism occurred were in sinus rhythm and in two while had atrial fibrillation (40%). In two cases the thrombosis or embolism occurred under anticoagulation with Phenprocoumon (40%), in one case each under heparin in combination with ASA 100 mg (20%) and heparin in combination with Phenprocoumon (20%) respectively.

*Table 6: Postoperative course of left atrial size and ejection fractions at the follow-up time points*

<b>Time point</b>	<b>Size of left atrium (mm)</b>	<b>Ejection fraction (%)</b>
Preoperative	$55.1 \pm 9.1$	$56.6 \pm 11.2$
30 days	$50.7 \pm 8.7$	$54.6 \pm 7.9$
90 days	$49.1 \pm 7.9$	$52.2 \pm 11.4$
180 days	$48.7 \pm 7.7$	$53.1 \pm 10.5$
1 year	$49.6 \pm 7.5$	$53.9 \pm 9.3$
1.5 years	$48.5 \pm 6.4$	$56.0 \pm 11.3$

One patient had no anticoagulation at the time of the event.

There were a total of eleven bleeding events during follow-up (5.8%), all of which occurred under anticoagulation treatment; nine under Phenprocoumon (81.8%) and two under heparin (18.2%). Eight of these patients were in sinus rhythm (72.7%) and three in atrial fibrillation (27.3%).

### Mortality analysis

Two patients (1%) died within the first ten postoperatively days. One patient died in the operating room when an intraoperative rupture of the cardiac skeleton. The second patient died on the first postoperative day due to acute left heart failure.

In total, 26 patients (18 female, 8 male) died during the 1.5-year follow-up. The mean age of the deceased patients at the time of surgery was 71 (group mean 67.4 years) and mean preoperative duration time of fibrillation was 8.4 years (group mean 6.6 years). These differences were not statistically significant. In four patients the operation was the second intervention. Two patients had a mitral valve commissurotomy, one an ASD closure and another one an aortic valve replacement before. Six of the deceased patients

had a postoperative cardiac pacemaker implantation.

Mortality rate was significantly higher in the 110 patients with postoperative atrial fibrillation (permanent or intermittend), than in the group of patients with stable sinus rhythm (n=79) (Figure 3).

Recurrent atrial fibrillation ( $p=0.0059$ ) and surgery duration ( $p=0.0382$ ) were identified as major risk factors (covariate-adjusted Kaplan-Meier statistics) influencing survival. Surgery duration was  $210 \pm 61.8$  minutes in patients who died postoperatively and  $193.1 \pm 47.8$  minutes in those who survived.

### Medication

All patients received antiarrhythmic medication postoperatively. In 70% this was sotalol. According to the study protocol, sotalol was discontinued after three months of stable sinus rhythm and in patients with structural heart disease it was exchanged to conventional beta-blocker. An overview about the postoperative antiarrhythmic medication is given in Figure 4.

All patients received Phenprocoumon postoperativ. Remarkably, only 63% of the patients received preoperative anticoagulation therapy despite they suffered from per-

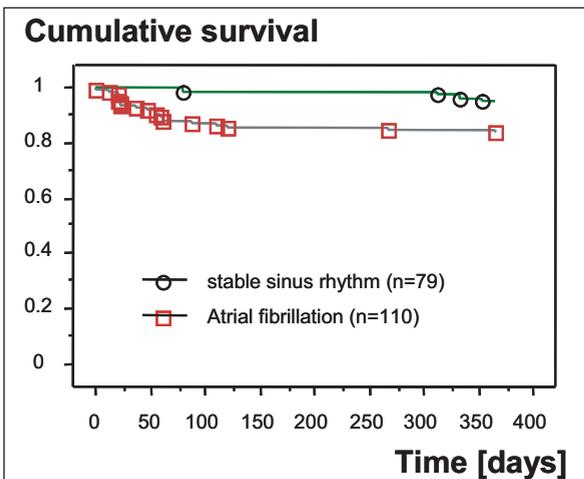


Figure 3: Cumulative survival data of patients with stable sinus rhythm compared to patients with atrial fibrillation

Table 7: p values of the key factors influencing survival

	Standard error	Standard coefficient	t value	p value
Age	0.919	-0.089	-1.086	0.2790
AA since	0.780	-0.028	-0.358	0.7205
Obesity	1.856	0.136	1.763	0.0797
aHt	15.444	-0.087	-1.117	0.2654
pHt	15.945	0.086	-1.121	0.2640
Apoplexy	23.886	0.051	0.664	0.5077
Heart attack	26.659	0.137	1.630	0.1049
DM	15.839	0.061	0.749	0.4551
LA parasternal	0.816	0.069	0.845	0.3993
EF	0.664	0.048	0.609	0.5431
Duration of surgery	0.161	-0.184	-2.089	<b>0.0382</b>
CAB	20.006	0.011	0.120	0.9050
AKE	19.241	0.034	0.424	0.6719
Stable SR	14.449	0.217	2.792	<b>0.0059</b>

manent atrial fibrillation. About 80 percent received Phenprocoumon postoperatively for one year, so that it can be assumed that Phenprocoumon was not discontinued even if stable sinus rhythm was apparent. Only a small proportion of the patients did not receive platelet function inhibitors (contrary to the present study concept).

## Discussion

The volume overload that occurs in cases of mitral valve insufficiency or stenoses leads to a consecutive dilatation of the left atrium. This is a important trigger to the development of atrial fibrillation. Circling electrical impulses are more easily sustained, because dilatation causes a shortening of the atrial refractory period. There for a conversion into sinus rhythm rarely occurs after mitral valve operations [Fukada, 1998; Izumoto, 1998; Kosakai, 1994; Knaut, 2004]. It is therefore recommended to additionally treat atrial fibrillation in patients who require mitral valve surgery [Raine, 2004]. Overall 60 percent of

the study population were in sinus rhythm in the long term. Many of the included patients not only received a mitral valve replacement or repair but, 66% also received additional interventions. 44 patients got coronary bypass grafting and over one quarter of patients (n=68) a tricuspid valve repair. The rate of sinus rhythm is very low especially after tricuspid valve interventions and left atrial isolation procedures [Vigano, 1996].

In the present study confirms surgery duration (mean duration time for microwave ablation is approx. 15 minutes, the traditional MAZE procedure in contrast requires additional 30 - 60 minutes [Damiano 2004]) was tendentially ( $p=0.0601$ ) a factor influencing for postoperative sinus rhythm.

Valve replacement itself may lead to postoperative complications. The implantation of mechanical valves requires permanent oral anticoagulation to prevent thrombus formation [Jung, 2010] at the exogenous valve surface [Ad, 2002; Leithäuser, 2009].

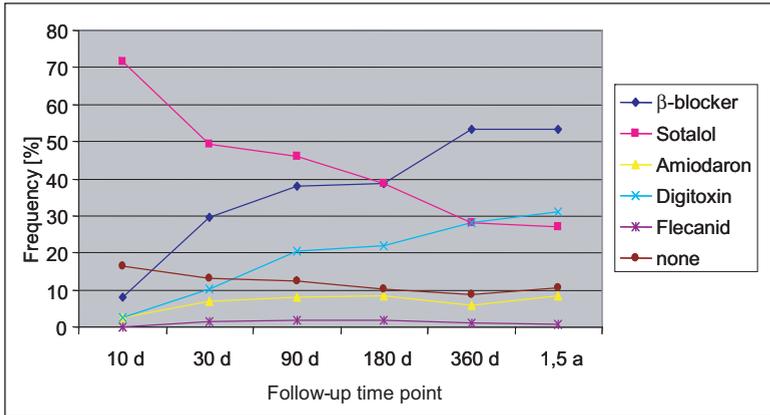


Figure 4: Antiarrhythmic medication

### Follow-up

At 1.5 years approx. 60% of the patients were in sinus rhythm, 65% of them presented stable sinus rhythm (sinus rhythm at all follow-up visits). Zembala has reported sinus conversion rates of 84% (assessed, however, only on the day of discharge, so that these data cannot be compared with the results of the present study) [Zembala, 2002]. Schuetz [Schuetz, 2003] achieved a success rate of 80% for postoperative sinus rhythm after one year, with nine of the 22 patients converting to sinus rhythm over time after initially being in atrial fibrillation. These patients were younger (64.57 vs. 67.4 years) than in the present study group and with mean preoperative atrial fibrillation duration of 3.8 years vs. 6.6 years in our cohort.

Microwave ablation treatment combined with aortic valve intervention resulted in the highest success rate (85%). In the combination of bypass surgery and ablation a success rate of 60% was observed [Knaut, 2001].

The present study shows that sinus rhythm restoration is much more probable after ablation treatment performed concomitantly with mitral valve surgery than after cardio-surgical intervention without rhythm surgery. Table 8 shows the conversion rates after mitral valve operations without surgical ablation therapy.

Kalil et al. studied the risk factors for permanent atrial fibrillation after mitral valve op-

erations. He showed that the incidence of atrial fibrillation is higher in patients with mitral valve stenosis (17% in postoperative sinus rhythm) while sinus rhythm is more frequent in patients with mitral insufficiency (44% in postoperative sinus rhythm) [Kalil, 1999]. Large et al. similarly found that patients with mitral valve stenosis were more likely to develop atrial fibrillation [Large, 1997]. According to the study of Kalil other factors as age, gender, duration of atrial fibrillation, left atrial size, ejection fractions or re-operations had no influence on postoperative rhythm. The patient population of the Kalil study, however, was markedly younger (mean age 46 years versus 67.4 years in the present study population) [Kalil, 1999].

Jessurun et al. found that age at the time of surgery and interventions involving the tricuspid valve were risk factors for the occurrence of postoperative atrial fibrillation [Jessurun, 2000]. In our study age had no significant influence.

Raine emphasized that preoperative rhythm is a strong predictor for postoperative rhythm. Of the patients in sinus rhythm before surgery, 91% remained in sinus rhythm also postoperatively. This similarly applies to atrial fibrillation. If patients had had permanent atrial fibrillation for less than twelve months or if atrial fibrillation had even been paroxysmal, 25% converted to sinus rhythm postoperatively without any surgical ablation therapy. If atrial fibrillation history was longer

Table 8: Spontaneous postoperative conversion to sinus rhythm without ablation

Study group	Type of operation	Postoperative sinus rates
Vigano, 1996	Mitral valve operations	16 % (one-year follow-up)
Sueda, 1997	Mitral valve operations	20 % (six-month follow-up)
Large, 1997	Mitral valve operations	21 % (one-year follow-up)
Kaili, 1999	Mitral valve operations	26 % (one-year follow-up)
Jessurun, 2000	Mitral valve operations	4 % (3.3-year follow-up)
Raine, 2004	Mitral valve operations	8.5 % (six-month follow-up)

than twelve months, no conversions to sinus rhythm were observed. In the patient group of the our study with atrial fibrillation durations of 6.6 years on average, one could assume that only a very small part would convert spontaneously. The Raine working group also found that left atrial diameter decreases in presence with sinus rhythm but not in atrial fibrillation [Raine, 2004].

All these studies had the problem that the study cohort consisted of only a small number of patients. It remains to be seen whether larger sample sizes would confirm the observed findings.

Conversions to sinus rhythm after mitral valve operation without surgical rhythm intervention was observed between 4% and 33.3%. The achieved 60% sinus rhythm in the present study thus represents a very successful outcome.

In summary it was shown that atrial fibrillation, once established, rarely could be terminated by valve operation alone.

Six patients came with implanted pacemaker to surgery. Postoperatively, 61 patients (31.9%) required pacemaker implantation in the follow-up period. Implantation rates reported in the literature range between 0% [Lee, 2003], 2.7% [Kim, 1999], 4% [Lemke, 2003], 6% [Sueda, 1997; Musci, 1998], 9% [Gillinov, 2004], 11% [Sie, 2001], 14% [Doll, 2003] and 18.9 % [Ad, 2002]; at different follow-up time points.

At the beginning of the study, cardioversions were done early after the operation when atrial fibrillation recurred. Later, it was understood that scar development has to be

completed and inflammation caused by ablation has to abate before the success of the surgical rhythm treatment can be evaluated [Cox, 1995; Ad, 2002; Schuetz, 2003]. For this reason an increased incidence of atrial fibrillation over a six- to eight-week postoperative period may be observed until final rhythm is established. Also the rate of pacemaker implantations decreased of cardioversion was delayed [Knaut, 2004]. In the early cardioversion approach, bradyarrhythmia requiring pacemaker implantation was more frequent due to irritations of the cardiac conduction system. This could explain the relatively high rate of pacemaker implantations. Furthermore, the patients treated in this study were of a considerably higher age than in other studies and thus higher pacemaker implantation rates were to be expected per se.

Success rates after cardioversion were low. Deneke reported sinus rhythm one year postoperatively in 17% of patients who underwent cardioversion after radiofrequency ablation and no sinus rhythm in patients who had cardioversion after an operation without ablation treatment [Deneke, 2002].

The size of the left atrium decreased in the during follow-up from 55 to 49 mm, and values remained stable from postoperative day 90. This corresponds with conversion processes that continue for two to three months postoperatively. Postoperative reduction in ejection fraction may be a result of surgical trauma, damaged to vessels and cardiac conduction system, and electrical isolation of parts of the left atrium [Feinberg,

1994]. Over time, remodeling processes begins and functionality recovered.

At day 30 postoperatively seven patients were deceased, which is equivalent to a perioperative mortality of 4%. In total, 15 patients had died up to day 90 (8% mortality), 19 patients up to day 180 (10% mortality), 23 patients up to one year (12% mortality) and 26 after 1.5 years (15% total lethality). Lenke et al. described a mortality rate of 12% one year postoperatively following radiofrequency current ablation [Lemke, 2003]; Khargi et al. a rate of 11.3% after an observation period of 19.7 months [Khargi, 2003].

The mean preoperative duration of atrial fibrillation among the deceased was 8.4 years compared to the whole patient cohort, with 6.6 years. The duration of surgery in these patients was also longer compared to the total patient population (3.5 hours vs. 3.16 hours) and was found to be a significant influencing factor ( $p=0.04$ ) for mortality.

There were no deaths that could be attributed to the ablation procedure its self. As we could shown, significantly more patients died within a two-year follow-up in the control group than in the ablation group. This result was found for the perioperative time period as well as during long-term comparison. This effect could be explained by the continuous atrial fibrillation that in the nonablated patients, such as thromboembolic events and bleeding complications, caused by anticoagulation or malignant arrhythmias [Knaut, 2005]. The present study also shows a survival benefit for patients with sinus rhythm compared to those with atrial fibrillation.

Due to the design of the present study there was no randomization. In addition, it was not always possible to perform a Holter monitoring at all follow-up time points so that phases of atrial fibrillation were perhaps missed. The detection of fibrillation phases with Holter ECG is, however, also limited, since intermittent atrial fibrillation phases may occur outside of the 24- to 48-hour monitoring period.

Approximately 60% of the patients who suffered from preoperatively permanent atrial fibrillation were in sinus rhythm during the postoperative period, whereas conversion rates between 4% and 33.5% have been reported after cardiac surgery without additional surgical ablation therapy. Significant influencing factors on postoperative sinus rhythm were the presence of diabetes mellitus, a history of myocardial infarction, the preoperative left atrial size, and tendentially, surgery duration. There were no ablation-related complications. During the 1.5 year follow-up it became clear that prolonged surgery (in most cases due to operative complexity with higher risk) and postoperative recurrence of atrial fibrillation were significant factors influencing mortality.

## References

1. Ad N, Cox JL. The significance of atrial fibrillation ablation in patients undergoing mitral valve surgery. *Seminars in Thoracic and Cardiovascular Surgery* 2002; 14: 193-197
2. Ad N, Cox JL. Combined mitral valve surgery and the maze III procedure. *Seminars in Thoracic and Cardiovascular Surgery* 2002; 14: 206-209
3. Atrial fibrillation investigators. Risk factors for stroke and efficiency of anti-thrombotic therapy in atrial fibrillation: analysis of pooled data from randomised controlled trials. *Arch Internal Med* 1994; 154: 1449-1457
4. Cox JL, Boineau P, Schuessler RB, Jaquiss RD, Lappas DG. Modification of the Maze procedure for atrial flutter and atrial fibrillation. I. Rationale and surgical results. *J Thorac Cardiovasc Surg* 1995; 110: 473-484
5. Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the Maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the Maze III procedure. *J Thorac Cardiovasc Surg* 1995; 110: 485-495
6. Damiano R, Gaynor SL. Atrial fibrillation ablation during mitral valve surgery using the Atricure device. *Operative techniques in Thoracic and Cardiovascular Surgery* 2004; 1: 24-33

## Conclusion

7. Della Bella P, Fraticelli A, Tondo C, Riva S, Fassini S, Carbucicchio C. Atypical atrial flutter: clinical features, electrophysiological characteristics and response to radiofrequency catheter ablation. *Europace* 2002; 4: 241-253
8. Deneke T, Khargi K, Grewe PH, Laczkovics A, vonDryander S, Lawo T, Muller KM, Lemke B. Efficacy of an additional MAZE procedure using cooled-tip radiofrequency ablation in patients with chronic atrial fibrillation and mitral valve disease. *Eur Heart J* 2002; 23: 558-566
9. Doll N, Borger MA, Fabricius A, Stephan S, Gummert J, Mohr FW, Hauss J, Kottkamp H, Hindricks G. Esophageal perforation during left atrial radiofrequency ablation: Is the risk too high? *J Thorac Cardiovasc Surg* 2003; 125: 836-842
10. Feinberg MS, Waggoner AD, Later KM, Cox JR, Lindsay BD, Perez JE. Restoration of atrial function after the Maze procedure for patients with atrial fibrillation. *Circ Assess Doppler Echocardiogr* 1994; 90: 285-292
11. Fukada J, Morishita K, Komatsu K, Sato H, Shiiku C, Muraki S, Tsukamoto M, Abe T. Is atrial fibrillation resulting from rheumatic mitral valve disease a proper indication for the Maze procedure? *Ann Thorac Surg* 1998; 65: 1566-1570
12. Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, Halperin JL, Kay GN, Klein WW, Levy S, McNamara RL, Prys-towsky EN, Wann LS, Wyse DG, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Hiratzka LF, Jacobs AK, Russell RO, Smith SC, Klein WW, Alonso-Garcia A, Blomstrom-Lundqvist C, De Backer G, Flather M, Hradec J, Oto A, Park-homenko A, Silber S, Torbicki A. American College of Cardiology/American Heart Association/European Society of Cardiology Board. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary. *J Am Coll Cardiol* 2001; 38: 1231-66
13. Gillinov AM, McCarthy PM, Blackstone EH, Pettersson G, Calhoun R, Sabik JF, Cosgrove III DM. Bipolar radiofrequency to ablate atrial fibrillation in patients undergoing mitral valve surgery. *The heart surgery forum* 2004; 7: 147-152
14. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA* 2001; 285: 2370-2375
15. Izumoto H, Kawazoe K, Kitahara H, Kamata J. Operative results after the Cox/Maze procedure combined with a mitral valve operation. *Ann Thorac Surg* 1998; 66: 800-804
16. Jessurun ER, van Hemel NM, Kelder JC, Elbers S, de la Rivière AB, Defauw JJAM, Ernst JMPG. Mitral valve surgery and atrial fibrillation: Is atrial fibrillation surgery also needed? *European Journal of Cardio-thoracic Surgery* 2000; 17: 530-537
17. Jung F. Editorial: Atrial Fibrillation. *Applied Cardiopulmonary Pathophysiology* 2009; 13: 275-276
18. Jung F, Wischke C, Lendlein A. Degradable, multifunctional cardiovascular implants: challenges and hurdles. *MRS Bull* 2010; 35: 607-613
19. Kalil RAK, Maratia CB, D`Àvila, Ludwig FB. Predictive factors for persistence of atrial fibrillation after mitral valve operation. *Ann Thorac Surg* 1999; 67: 614-617
20. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation. The Framingham Study. *N Engl Med* 1982; 306: 1018-1022
21. Khargi K, Deneke T, Lemke B, Laczkovics A. Irrigated radiofrequency ablation is a safe and effective technique to treat chronic atrial fibrillation. *Interact Cardiovasc Thorac Surg* 2003; 2: 241-245
22. Kim K-B, Cho KR, Sohn D-W, Ahn H, Rho JR. The Cox-Maze III procedure for atrial fibrillation associated with rheumatic mitral valve disease. *Ann Thorac Surg* 1999; 68: 799-804
23. Knaut M, Tugtekin SM, Matschke K, Gulielmos V. A modified ablation line concept is superior to original microwave ablation for curative treatment of permanent atrial fibrillation. *Heart Surg Forum* 2003; 6: 20
24. Knaut M, Tugtekin SM, Jung F, Matschke K. Microwave ablation for the surgical treatment of permanent atrial fibrillation – a single centre experience. *Eur J Cardiothorac Surg* 2004; 26: 742-746

25. Knaut M, Tugtekin S M, Spitzer SG, Jung F, Matschke K. Mortality after cardiac surgery with or without microwave ablation in patients with permanent atrial fibrillation. *J Heart Valve Dis* 2005; 14: 531-537
26. Knaut M, Tugtekin SM, Spitzer SG, Jung F, Matschke K. Intraoperative endocardial microwave ablation for treatment of permanent atrial fibrillation during coronary artery bypass surgery: 1-year follow-up. *Europace* 2006; 8: 16-20
27. Kosakai Y, Kawaguchi AT, Isobe F, Sasako Y, Nakano K, Eishi K, Tanaka N, Kito Y, Kawashima Y. Cox-Maze procedure for chronic atrial fibrillation associated with mitral valve disease. *J Thorac Cardiovasc Surg* 1994; 108: 1049-1055
28. Large SR, Hosseinpour AR, Wisbey C, Wells FC. Spontaneous cardioversion and mitral valve repair: A role for surgical cardioversion (Cox-Maze)? *European Journal of Cardiothoracic Surgery* 1997; 11: 76-80
29. Laupacis A, Sullivan K. Canadian atrial fibrillation anticoagulation study: were the patients subsequently treated with warfarin? Canadian Atrial Fibrillation Anticoagulation Study Group. *Can Med Assoc J* 1996; 154: 1669-1674
30. Lee JW, Park NH, Choo SJ, Jo MS, Song H, Song MG. Surgical outcome of the Maze procedure for atrial fibrillation in mitral valve disease: rheumatic versus degenerative. *Ann Thorac Surg* 2003; 75: 57-61
31. Leithäuser B, Jung F, Park J-W. Oral anticoagulation for prevention of cardioembolic stroke in patients with atrial fibrillation: Focussing the elderly. *Applied Cardiopulmonary Pathophysiology* 2009; 13: 307-317
32. Lemke B, Khargi K, Grewe PH, Kuschkowicz F, Lawo T, Calcum B, Mugge A, Laczkovics A, Muller KM, Deneke T. Sicherheit und Effektivität der intraoperativen gekühlten linearen Hochfrequenzstromablation bei Patienten mit Vorhofflimmern während eines kardiochirurgischen Eingriffs. *Z Kardiologie* 2003; 92: 1008-1017
33. Melo JQ, Neves J, Adragão P, Ribeiros R, Ferreira MM, Bruges L, Canada M, Ramos T. When and how to report results of surgery in atrial fibrillation. *Eur J Cardiothorac Surg* 1997; 12: 739-745
34. Melo J, Adragao P, Neves J, Ferreira MM, Pinto MM, Rebocho MJ, Parreira L, Ramos T. Surgery for atrial fibrillation using radiofrequency catheter ablation: assessment of results at one year. *Eur J Cardiothorac Surg* 1999; 15: 851-855
35. Musci M, Pasic M, Siniawski H, Lehmkuhl H, Edelmann B, Hetzer R. "Cox/Maze-III-Operation" als chirurgische Therapie des chronischen Vorhofflimmerns während Mitralklappen- und ASD-II-Operation. *Z Kardiologie* 1998; 87: 202-208
36. Probst P, Galshlager N, Selzer A. Left atrial size and atrial fibrillation in mitral stenosis. *Circulation* 1973; 48: 1282-1287
37. Quader MA, McCarthy PM, Gillinov AM, Alster JM, Cosgrove DM, Lytle BW, Blackstone EH. Does preoperative atrial fibrillation reduce survival after coronary bypass grafting? *Ann Thorac Surg* 2004; 77: 1514-1524
38. Raine D, Dark J, Bourke JP. Effect of mitral valve repair/replacement surgery on atrial arrhythmia behavior. *The Journal of Heart Valve Disease* 2004; 13: 615-621
39. Sack S. Epidemiology of atrial fibrillation. *Herz* 2002; 27: 294-300
40. Schuetz A, Schulze CJ, Sarvanakis KK, Mair H, Plazer H, Kilger E, Reichart B, Wildhirt SM. Surgical treatment of permanent atrial fibrillation using microwave energy ablation: a prospective randomized clinical trial. *Eur J Cardiothorac Surg* 2003; 24: 475-480
41. Sie HT, Beukema WP, Ramdat Misier AR, Elvan A, Ennema JJ, Wellens HJ. The radiofrequency modified MAZE procedure. A less invasive surgical approach to atrial fibrillation during open heart surgery. *Eur J Cardiothorac Surg* 2001; 19: 443-447
42. Spitzer SG, Karolyi L. Catheter ablation of atrial fibrillation - Current status and future directions. *Applied Cardiopulmonary Pathophysiology*, 13, 291-299
43. Sueda T, Nagata H, Orihashi K, Morita S, Okada K, Sueshiro M, Hirai S, Matsuura Y. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. *Ann Thorac Surg* 1997; 63: 1070-1075
44. Taylor FC, Cohen H, Ebrahim S. Systematic review of long-term anticoagulation or antiplatelet treatment in patients with non-rheumatic atrial fibrillation. *Brit Med J* 2001; 322: 321-326
45. Viganò M, Graffigna A, Ressa L, Minzioni G, Pagani F, Aiello M, Gazzoli F. Surgery for

- atrial fibrillation. *Eur J Cardiothorac Surg* 1996; 10: 490-497
46. WHO. The World Medical Association: Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects. Adopted by the 18th World Medical Assembly Helsinki, Finland 1964, 41st World Medical Assembly Hong Kong, September 1989, last amendment 48th General Assembly Somerset West, South Africa, October 1996, Edinburgh 2000
47. Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. *Arch Intern Med* 1998; 158: 229-234
48. Zembala M, Lenarczyk R, Kalarus Z, Puszczewicz D, Przybylski R, Pacholewicz J. Early and late outcome after microwave ablation for chronic valvular atrial fibrillation. *Heart Surg Forum* 2003; 6: 403-408

*Correspondence address*

Michael Knaut, M.D., Ph.D.  
Department of Cardiac Surgery  
University of Technology Dresden  
Fetscherstr. 76  
01307 Dresden  
Germany  
m.knaut@herzzentrum-dresden.com