Epicardial microwave ablation for the treatment of permanent atrial fibrillation: 1-year results of a prospective registry study

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Abstract

Background: Atrial fibrillation (AF) which is one of the most common arrhythmias is responsible for a high percentage of strokes. Recently simplified ablation procedures became more relevant in the surgical treatment of AF. One advantage of microwave ablation (MW) is, that it can be used epicardially. We report our first clinical results of the use of epicardial MW as a concomitant procedure during cardiac surgery where opening of the left atrium was not required.
Methods: Patients who were scheduled for aortic valve replacement and/or coronary artery bypass grafting suffering from permanent AF, were included into the registry. They received epicardial MW as a concomitant procedure during their operation and were followed over a period of one year. The results were compared to the outcome of a historical patient group with equivalent operations without ablation therapy. Epicardial MW was done on extracorporeal circulation on the beating heart creating box lesions around the pulmonary veins with a connection line on the roof of the left atrium and an additional line to the left atrial appendage.
Results: 40 patients were treated with epicardial MW in combination with aortic valve replacement and/or coronary artery bypass grafting. Their preoperative data were as follows: age: 69.6±7.8 years, ejection fraction: 55.7±14.2%, left atrial diameter: 46.2±6.0 mm, duration of AF 6.8±9.8 years. The control group comprised 145 patients (age: 72.6±6.9 years, ejection fraction: 49.7±14.8%, left atrial diameter: 47.4±6.6 mm, AF history: 3.7±5.7 years). One year survival rate was 92.5 % in the ablation group and 86.9 % in the control group. We observed no device-related complications. During the follow-up the sinus rhythm rate ranged between 71.4 and 65.7% in the ablated patients in contrast to 7.4 to 9.6% in the control group (p=0.00001).
Conclusion: Our results demonstrate that epicardial ablation, in this study with a microwave ablation device, is an effective treatment option for patients with permanent AF. The procedure is less invasive then the endocardial approach and prolongs concomitant heart surgery only minimally without lengthening ischemic time. Epicardial ablation has become part of the daily routine in our institution for the treatment of AF in patients scheduled for bypass grafting and/or aortic valve replacement.

1. Introduction

After atrial and ventricular extrasystoles, atrial fibrillation is the most common heart rhythm disorder [1]. Atrial fibrillation has been estimated to affect about 0.4% of the worldwide population [2, 3]. Its prevalence in people under the age of 60 years is approximately 1%, in those older than 80 years about 6% [2], and in 90-year olds it reaches even 15% [4]. The incidence of atrial fibrillation in patients with structural

heart disease is markedly higher. For example, 30% to 60% of the patients who require mitral valve surgery suffer from atrial fibrillation [1].

Especially in the left atrial appendage blood stasis occurs in case of atrial fibrillation when the atrium is no longer capable to actively eject blood into the ventricle by contraction. This results in the formation of thrombi that may embolize. Atrial fibrillation is made responsible for about 15% of all cases of strokes [5, 6]; these patients thus have significantly higher mortality rates than patients without atrial fibrillation [7, 8].

Both in surgical and interventional ablation procedures, the endocardial approach is the method of choice. It can be performed using different energy sources. However, several cardiac surgery procedures do not require opening of the atria (patients with coronary artery bypass grafting and/or aortic valve surgery). An additional opening of the left atrium to perform the endocardial ablation would necessitate additional bicaval cannulation and prolong the entire operation. In order to avoid this and still be able to treat atrial fibrillation, ablation strategies have been developed for epicardially ablation in recent years. Not all endocardially utilized energy sources are suitable for the epicardial approach, the microwave technique, however, has proved to be usable in the endocardial and epicardial approach. In this study we investigated the efficacy of epicardial microwave ablation during one year of follow-up in patients with permanent atrial fibrillation who were scheduled for coronary artery bypass grafting and/or aortic valve surgery.

2. Materials and methods

This registry study was conducted following the rules of the Declaration of Helsinki, Somerset West 1996 and the guidelines of the European Forum for Good Clinical Practice [9]. The Ethics Committee of the Dresden University gave approval for the study. The purpose of this pilot study was to investigate the feasibility and efficacy of epicardial microwave ablation. The obtained data were compared to the outcomes of patients with permanent atrial fibrillation who had undergone comparable operations without an ablation procedure (Dresden registry). Primary endpoints of the study were restoration of sinus rhythm and death.

The general inclusion criteria to the study for both groups were: permanent atrial fibrillation with duration of at least one month, patients older than 18 years, and indication for coronary bypass graft and/or aortic valve surgery. Patients with paroxysmal or persistent atrial fibrillation were excluded.

The preoperative medication regimen was continued until the day of surgery (including aspirin and clopidogrel). Only patients on oral anticoagulation therapy were switched to low molecular weight heparin at the appropriate time.

2.1 Peri-operative protocol

Left atrial dimensions were measured by transthoracic or transoesophageal echocardiography prior to the operation. Furthermore, thrombus formation in the left atrial appendage was excluded by an intraoperative transesophageal echocardiogram.

2.2 Ablation procedure

All patients were operated using extracorporeal circulation. The ablation treatment was performed on-pump on the beating heart before aortic cross-clamping.

The pericardial reflections at the pulmonary veins, superior and inferior vena cavae and the fibro-fatty tissue of the interatrial groove were bluntly dissected.

Then the transverse pericardial sinus was exposed. Epicardial microwave ablation was performed using a FLEX 4® probe. A continuous box lesion was created around each pulmonary vein pair. These two box lesions were connected by an ablation line along the left atrial roof through the transverse pericardial sinus. The ablation procedure was completed by a lesion line from the left-sided box lesion to the apex of the left atrial appendage (see Figure 1).

2.3 Microwave ablation system

The FLEX 4™ microwave surgical ablation device (Guidant Corp.; Santa Clara, CA, USA) was used to produce linear lesions on the epicardial surface. Ablations were performed for 90 s each with an output of 65 W. Details of the endocardial method have been described previously [10].

2.4 Postoperative protocol

Starting from the first postoperative day, patients received metoprolol to stabilize rhythm and, after re-

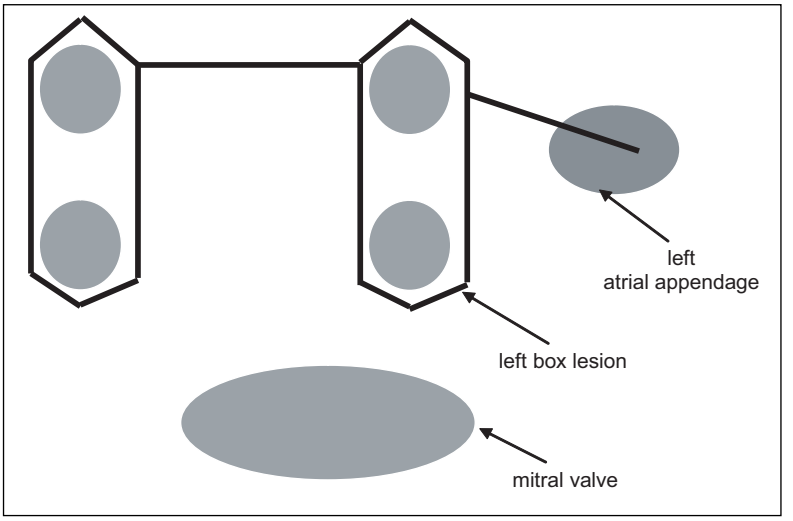

Figure 1. Lesion line concept for epicardial ablation concept.

moval of the chest tubes, anticoagulation therapy was switched from heparin to phenprocoumon aiming at a target INR of 2.0 to 2.5 for at least 6 months.

Heart rhythm was monitored daily up to postoperative day 10. Follow-up examinations were carried out at day 30, 90, 180 and 360 after surgery. Cardiac rhythm was evaluated with a 12-channel ECG and a continuous 24-hour Holter ECG at day 180 and 360. Early recurrences of atrial fibrillation up to postoperative day 90 were treated with up to two cardioversions.

2.5 Statistical analysis

Mean values and standard deviations were given for all continuous data, and classified variables are presented in percentage frequency.

Probability of survival over time and overall survival rates were calculated using Kaplan-Meier analysis and compared with the (Mantel-Cox) log-rank test. Chi-square and two-tailed, unpaired Student's t-test (exact Fisher's test) were used for two sample analysis. Probability values less than 0.05 indicate a statistically significant difference (at the 5% level) between the ablation and the control group outcome.

3. Results

So far, 40 patients (f: 18 / m: 22) who received epicardial ablation treatment (A) and 145 patients (f: 49 / m: 96) without ablation, as controls (C), have been included into the registry.

Mean age at the time of enrollment was 69.1±6.8 years in the ablation group and 72.6±6.9 years in the control group. The duration of atrial fibrillation was 6.8±9.8 and 3.7±5.7 years, respectively. One patient in the ablation group (2.5%) with bradyarrhythmia had received a single chamber pacemaker 5 years prior to surgery; in the control group this happened in 15 patients (10.3%). Preoperative transthoracic echocardiography showed mean left atrial sizes of 46.2±6.0 mm and 47.4±6.6 mm as well as ejection fractions of 55.7±14.2% and 49.7± 14.8 % in the ablation and control group, respectively. 72.5% and 80.7%, respectively, had a diagnosed coronary heart disease (p= 0.0239). Twenty-five patients of the control group and one patient of the ablation group came with a preoperative stroke while six patients and 49 had a history of myocardial infarction, resp..

The cardiovascular risk profile of both groups is shown in Table 1.

Surgeries conducted and conditions diagnosed are seen in Table 2.

The average duration of the operation was 2 hours and 55 minutes in the ablation group and 2 hours and 30 minutes in the control group.

Follow-up was complete in all but two patients from the ablation group (drop out rate 5%). In the control group the drop out rate was 7.6% (11 patients).

We observed no ablation procedure-related complications.

In the ablation group mortality during follow-up was 7.5% compared to 13.1% in the control group. There was no significant difference between the 1-year mortality rates in both groups (p>0.05, see Figure 2).

Table 1: Comparison of cardiovascular risk factors.

	Ablation group	Control group	p
n	40	145	
Type 2 diabetes mellitus	15 (37.5%)	75 (51.7 %)	0.111
Arterial hypertension	35 (87.5%)	121 (83.4 %)	0.5326
Pulmonary hypertension	13 (32.5%)	59 (40.7%)	0.3469
Hyperlipidemia	32 (80.0%)	105 (72.4%)	0.3325
Obesity	22 (55.0%)	100 (69.0%)	0.0989
Nicotine abuse	11 (27.5%)	56 (38.6%)	0.1951

Table 2: Overview over conducted surgeries and diagnosed conditions with statistical analysis.

	Ablation group (n=40)	Control group (n=145)	p
Coronary artery bypass surgery	25	85	0.0011
Aortic valve replacement surgery	10	42	0.4659
Coronary artery bypass and aortic valve replacement surgery	5	18	0.9883
Biological valve prosthesis	13	40	0.5428

Success rates, defined as maintenance of sinus rhythm at all follow-up dates, were at least more than 5 times higher in patients in the ablation group than in the non-ablated group (Table 3). After one year, 65.7% of the ablated patients were in sinus rhythm compared to 9.6% in the control group (p=0.000001).

Cardioversions performed in 4 patients of the ablation group were successful, i.e. these patients showed stable sinus rhythm at all subsequent follow-up dates. In 5 patients a cardioversion could not be performed (non compliance of the patients). None of the 8 cardioversions performed in the control group, done in the first 30 days, were successful.

Postoperative pacemaker implantation was necessary in 5 patients of the ablation group and 15 patients of the control group.

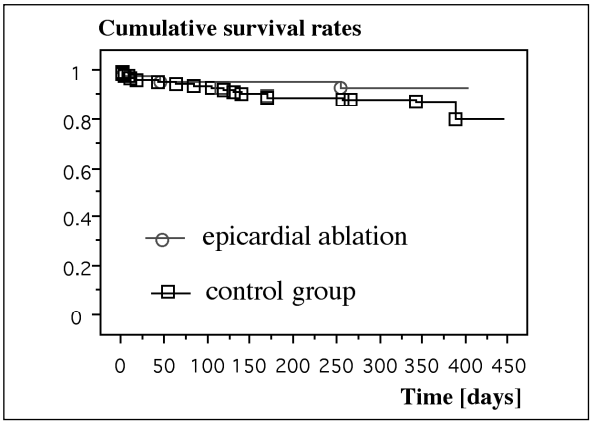

Figure 2. Cumulative survival rates in the ablation group (n=40) and in the control group without ablative treatment (n=145) (Kaplan Meier analysis).

Table 3: Incidence of sinus rhythm in both groups after 90, 180 and 360 days.

	Ablation group	Control group
90 days	71.4 %	7.4 %
180 days	66.7 %	8.0 %
360 days	65.7 %	9.6 %

Sinus rhythm and mortality as well as the number of implanted pacemakers and cardioversions are compiled in Table 4.

4. Discussion

The study demonstrates that epicardial ablation, in this study with a microwave ablation device, is able to restore sinus rhythm with more than acceptable rate (65.7%) in patients with permanent atrial fibrillation. The success rates after ablation (between 65.7 and 71.4%) considerably exceed (p=0.000001) the spontaneous conversion rates of 7.4% to 9.6% at all time points of follow-up.

The rates of restored sinus rhythm after operations without ablation treatment have been reported to be between 0% and 27% [7, 11, 12, 13].

The results of epicardial microwave ablation are not inferior to the 1-year success rates of the endocardial approach using microwave energy (success rates between 52% and 88% [10, 14], depending on the type of heart surgery). Our findings are also able to com-

Table 4: Sinus rhythm maintenance, atrial fibrillation, atrial flutter, pacemaker implantations, cardioversions, mortality and loss of patients (A= 40/C=145).

	Post-operative days			
	30	**90**	**180**	**360**
	A / C	**A / C**	**A / C**	**A / C**
n	39 / 139	38 / 122	38 / 113	37 / 115
Deaths	1 / 6	2 / 9	0 / 17	3 / 19
Absence	0 / 0	3 / 14	2 / 15	2 / 11
Sinus rhythm	22 / 12	25 / 9	24 / 9	23 / 11
Atrial fibrillation	16 / 126	10 / 113	12 / 104	12 / 103
Atrial flutter				
– typical	0 / 1	0 / 0	0 / 0	0 / 1
– atypical	0 / 0	0 / 0	0 / 0	0 / 0
PM implantation	3 / 15	3 / 15	4 / 11	5 / 15
Cardioversion	3 / 7	0 / 0	1 / 0	0 / 1
Sinus rhythm [%]	57.9 / 8.6	71.4 / 7.4	66.7 / 8.0	65.7 / 9.6

pare with results of other ablation studies using other energy sources and vary only slightly from those results achieved with the traditional MAZE procedure [15, 16, 17, 18]. Moreover, the clinical findings of this study clearly disprove conclusions from animal experiments [19] that epicardial microwave ablation is not effective.

The advantage of the epicardial approach is that ablation can be performed on the heart`s surface, leaving the endocardium intact and so minimizing the risk of postoperative thromboembolic or bleeding complications [20]. The microwave probes allow energy delivery in only one direction enabling epicardial ablation at the posterior surface of the heart. Collateral damage of the surrounding tissue can be largely ruled out. A rapid temperature decrease at a distance of 5 mm from the probe prevents the surrounding tissue (especially the circumflex coronary artery) from being involved [21].

Nevertheless, complications are imaginable. It is an additional intervention that prolongs operation time compared to a stand-alone heart surgery. However, in contrast to the 60 - 90 minutes of additional cross-clamp time required for the classical MAZE procedure, the 15 - 20 minutes required for epicardial ablation is merely a minor prolongation that does not lengthen ischemic time. Pulmonary vein isolation is technically challenging and comprises the risk of injury of these structures. Atrial perforation with subsequent bleeding or injury of coronary vessels caused by incorrect epicardial application, are possible complications. Finally, with this method the pericardial reflections around the venae cavae and pulmonales must be dissected very carefully which can be difficult in case of a thick layer of fatty tissue. However, none of the described possible procedure-related complications occurred during this pilot study.

The epicardial approach restricts access to the ablation sites usually targeted in classical lesion concepts. This means that the usual ablation line to the posterior mitral valve annulus performed in the endocardial setting can not or only restrictedly be done from the outside due to the coronary arteries located close to the annulus.

The mortality rate in the ablation group was 7.5% at one year. These 3 patients had been classified to have a high risk according to the EuroSCORE risk-stratification model with a mean score of 9.3; one patient had a high EuroSCORE of 13 indicating a markedly higher peri- and postoperative risk. Similar

mortality rates of 7.8%, 12.3% and 13% respectively, have been found in different studies with radiofrequency ablation within a 1-year time period [3, 20, 22]. In one prospective registry study, it could be shown that endocardial microwave ablation treatment does not raise peri- and postoperative mortality. Rather, a significant decrease in mortality after two years was found in comparison to a control group who had undergone similar heart surgeries without additional ablation treatment [23]. Other studies demonstrate similar results [7, 24].

The postoperative pacemaker implantation rate was 10% in the ablation group in correspondence with rates of 9% [25], 11% [3] and 14% [19], that have been reported to date after radiofrequency ablation, and was slightly lower than in the control group (17.2%). Consequently, epicardial microwave ablation did not lead to a higher incidence of pacemaker implantations, as compared to other ablation procedures or stand-alone heart surgeries. However, the need of a dual chamber pacemaker after ablation can be judged as a success, because the patient has regained his sinus rhythm.

5. Limitations of the registry

There was some variance in the preoperative clinical parameters documented for the two patient groups in this study. The mean duration of atrial fibrillation in the control group and the ablation group was 3.7 and 6.8 years, respectively. Hence, atrial fibrillation had been present in patients of the ablation group almost twice as long as in those of the control group. The longer the duration of atrial fibrillation, the more likely it is that structural and electrophysiological changes are manifested [9, 26]. This so called structural and electrical remodeling is made responsible for the development of chronic atrial fibrillation by causing the atrial myocardium to independently maintain circulation of multiple reentry wavelets without the influence of trigger mechanisms. On the other hand, the patients of the control group were on average 3 years older than the patients of the ablation group. It is not possible to estimate to what extent these two inhomogenities may have influenced the outcome. However, one might speculate, that the large difference in atrial fibrillation duration between the two groups is more significant than the comparatively small age difference so that, in a randomized study, the success rate difference between these groups should tend to be larger instead of smaller.

Randomization of the patients for this registry was not possible since all patients of the control group had been enrolled consecutively before the epicardial ablation treatment study functioning as a historical control.

6. Conclusion

Our data of this registry for the first time demonstrate that epicardial microwave ablation is an effective treatment option for patients with permanent atrial fibrillation. The procedure is less invasive then the endocardial approach and prolongs concomitant heart surgery only minimally without lengthening ischemic time. Because this pilot study has excellently shown that epicardial microwave ablation is an effective instrument to restore sinus rhythm without any procedure-related complications or deaths, a prospective, randomized, controlled trial will be carried out to confirm the results of this study.

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