# Heart rhythm monitoring over 1 year following cardiac surgery in patients with permanent atrial fibrillation: A mono centric prospective case study

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Applied Cardiopulmonary Pathophysiology 13: 277-283

Key words: permanent atrial fibrillation, spontaneous conversion rate after heart surgery

#### Abstract

**Background:** Patients with permanent atrial fibrillation have a clearly higher risk for thromboembolic events than people with sinus rhythm. Because also anticoagulant therapy, which is the therapy of choice in chronic atrial fibrillation, has its risks, intra operative ablation therapy as a concomitant procedure has become more and more important. Nevertheless this option is not available for all patients and little is known whether the operation by its self is able to restore sinus rhythm and about the fate of these patients. Therefore we created a registry to follow the clinical course of patients with atrial fibrillation after heart surgery.

**Method:** All consecutive patients with permanent atrial fibrillationwho were operated in our center and who were not eligible for ablation therapy were included into the registry. The patients were monitored up to postoperative month 12 with regard to their clinical outcome especially rhythm course and survival. These data were evaluated during in-hospital visits 30, 90, 180 and 360 days after operation.

**Results:** A total of 287 (151 male/136 female) consecutive patients with permanent atrial fibrillation were included into the registry.

During the follow-up period, approximately 10% of the patients converted to sinus rhythm. 13 patients, or 4.9%, were in stable sinus rhythm, which means that they were in sinus rhythm at every follow-up visit.

30-day mortality was 6.9% (20 of 286 patients) while it was 14.9% after one year (43 of 263 patients). Of the 13 patients who were in stable sinus rhythm after one year, only one patient died (7.7%), while of the 185 patients who where still in atrial fibrillation 43 died (23.2%).

Conclusion: Our results demonstrate that also correction of the heart disease by it self is able to restore sinus rhythm in a few patients. Nevertheless the rate of patients with continuous atrial fibrillation was approximately 90%, the rate of stable sinus rhythm, which is suspected to improve prognosis was only 4.9%. Therefore, an attempt to treat atrial fibrillation with intra operative ablation therapy is strongly justified, respecting the fact that, even if conservatively calculated, a success rate of at least 50% can be accomplished. We believe, that this applies even for endocardial and for the epicardial approach.

# Introduction

Patients with atrial fibrillation exhibit a clearly higher risk for thromboembolic events [17, 18, 23]. The incidence of stroke in these patients is nearly five times higher [13], whereby atrial fibrillation may be respon-

sible for approximately 15% of all cerebral accidents [5]. As a result, both the European and American cardiology societies recommend the therapy with anticoagulants in elderly patients with structural heart disease and atrial fibrillation [6]. However, this anticoagulation treatment is problematic in elderly patients

with intelectual limited capacity without an appropriate social sphere, which in the meantime represent a large portion of patients scheduled for heart surgery [14, 20]. Overdosage poses a risk of hemorrhages [21], whereas underdosage can lead to thromboembolic complications. Additionally, even adequate anticoagulation therapy is not a guarantee of adequate protection [1].

Since only an insufficient amount of data currently exist regarding whether heart surgery alone i.e. bypass and/or valve operations leads to a spontaneous recovery of sinus rhythm, a prospective case study was performed including a sufficiently large group of patients who underwent operations without specific operative antiarrhythmic therapy with preoperative atrial fibrillation. These patients were monitored for up to 12 months postoperatively with regard to rhythm course and survival.

#### Methods

The question was handled by carrying out a prospective monocentric register study. Included into the register were all patients with permanent atrial fibrillation [7] that existed longer than one month prior to operation and had been confirmed by repeated surface EKGs and/or 24-hour Holter monitoring. The indication for heart surgery in these patients was based on clinical, hemodynamic or prognostic criteria.

Patients with the following findings were excluded from the register:

- Emergency operations,
- Stroke or myocardial infarction within the last three months,
- Acute myocarditis,
- Chronic heart failure (NYHA IV),
- Severe obstructive or restrictive ventilation disorders
- Severe endocrine disorders,
- Severe kidney and/or liver function disorders,
- Pregnancy and lactation,
- Known medication and/or drug abuse,
- Paroxysmal and persistent atrial fibrillation,
- Incapacity and/or conditions that do not allow the patient to understand the nature, significance and scope of the study.

All patients got detailed instructions about the purpose and use of the register prior to the operation. After informed consent the patients were included only if all inclusion criteria were met, if none of the exclusion criteria existed.

The study was conducted in accordance with the Declaration of Helsinki and EU guidelines [22].

All required data was recorded by a study nurse using a survey form and then entered into a database. In addition, patients were monitored over the course of one year. After their discharge from the heart center, the patients treatment was continued by their general practitioners, cardiologists or directly by the heart center for adjustments of medication and monitoring anticoagulation therapy and heart rhythm. They were reexamined after 1, 3, 6 and 12 months. A 24-hour Holter EKG was usually recorded on those occasions. The existence of a sinus rhythm was judged as a criterion of success. If a patient was in sinus rhythm at all examination appointments over a period of one year, this fullfilled the criteria for stable sinus rhythm.

The antiarrhythmic medicine was interrupted immediately before the operation, while the cardiovascular drug therapy (including thrombocyte aggregation inhibitors) was continued.

Following the operation, the patients initial received Sotalol exclusively and in the beginning of summer 2003, received metoprolol exclusively for purposes of rhythm stabilization. Phenprocoumon was used in a standardized manner for anticoagulation in instances of mechanical mitral valve replacement with a target INR of 2.5 to 3.5 and in instances of mechanical aortic valve replacement with a target INR of 2.0 to 3.0.

Sotalol/metoprolol was discontinued in all patients who were in sinus rhythm after six months and it was recommended to stop of anticoagulation. Beta-blocker therapy with metoprolol was continued in patients with structural heart disease. However, if the attending physician/cardiologist decided to continue or stop the ongoing therapeutic procedure, this decision was recorded.

#### **Statistics**

The mean and standard deviation are indicated for all continuous data and percent frequency is indicated for classified variables.

Survival probabilities and survival rates in comparison between patients with and without sinus rhythm were described by means of Kaplan-Meier curves and calculated by means of a log rank test. Probabilities smaller than 0.05 were evaluated as significant.

Operative data (duration; type: bypass, aortic valve, mitral valve), accompanying illnesses (stroke, myocardial infarction, rheumatic illnesses, diabetes mellitus, arterial hypertonus, pulmonary hypertension) and factors that may possibly influence the clinical outcome of the operation (diameter of the left atrium, left ventricular ejection fraction, duration of the preoperative atrial fibrillation) were taken into consideration as variables for a confounder analysis. The analysis itself was conducted as a multivariate regression analysis.

#### Results

# Study population

Over the span of three years, a total of 287 consecutive patients with permanent atrial fibrillation were included. 151 of the patients were male, 136 were female. The mean age of the patients was  $71.3 \pm 6.4$  years, average height was  $168 \pm 10$  centimeters, and mean weight was  $75 \pm 14.2$  kg. All patients showed permanent atrial fibrillation, on average for  $5.1 \pm 7.8$  years. Left ventricular ejection fraction equalled  $52.1 \pm 13.9\%$  and the diameter of the left atrium in the parasternal acoustic window of the echocardiography was  $50.9 \pm 9.3$  millimeters. Demographic and clinical data are summarized in Table 1.

There were myocardial infarction and stroke in the medical histories of 62 and 39 patients, respectively. 122 patients had diabetes mellitus, 222 arterial hypertension, 159 pulmonary hypertension, 169 hyperlipidemia and 94 hyperuricemia. Eleven patients were smokers at the time of the operation, and 74 had ceased smoking. 172 patients were obese. Table 2 shows the operations that were conducted.

An isolated operation was conducted in 164 cases. Combined interventions were performed on 123 patients (93 patients underwent a double combined operations, 21 patients underwent a triple combined operations, six patients underwent a quadruple combined operations, two patients underwent fivefold combined operations and one patient underwent sixfold combined operations). The mean duration of the operation was  $2.85 \pm 1.0$  hours (range: 1.3 - 7.95 hours).

Table 1: Patient demographic and clinical data

No. of patients:	287	
Male/female	151/136	
Age [years]	$71.3 \pm 6.4$	Range: 36 - 88
LVEF [%]	$52.2 \pm 13.9$	Range: 20 - 85
Duration of pAF [years]	$5.1 \pm 7.8$	Range: 0.2 - 37.2
LA [mm]	$50.9 \pm 9.03$	Range: 24 - 99
BMI [Kg/m <sup>2</sup> ]	$26.6 \pm 4.1$	Range: 16.7 - 42.5

BMI: body mass index; LVEF: left ventricular ejection fraction; pAF: permanent atrial fibrillation; LA: left atrium diameter – parasternal

Table 2: Types of heart surgery conducted

ACB	148	51.6%
AVRp	112	39.0%
MVRp	71	24.7%
MVRe	29	10.1%
TCRe	24	8.4%
other	54	18.8%

ACB: aortocoronary bypass; AVRp: aortic valve replacement; MVRp: mitral valve replacement; MVRe: mitral valve reconstruction; TCRe: tricuspid valve reconstruction; multiple categories possible

# Rhythm course

The main attention was focused on the postoperative rhythm course, i.e. recovery of sinus rhythm without ablation treatment. Table 3 shows the number of patients in sinus rhythm at day 30, 90, 180 and 360 "follow-up." Rhythm data could not be obtained during the follow-up period approximately 8% of the patients.

Approximately 10% of the patients were in sinus rhythm at one or more of the follow-up appointments. 13 patients, or 4.9%, were in stable sinus rhythm (those patients who exhibited a sinus rhythm at each examination). Therefore, the remaining 5.1% of patients exhibited paroxysmal atrial fibrillation over the first year after the operation.

A total of 47 patients had a pacemaker after one year (VVI: 42 patients, DDD: 5 patients). Since 29 patients already had pacemakers prior to the operation (10.1%), the rate of new implants was 6.2%. Five cardioversions were performed during the stay at the heart center. Nine further electric cardioversions were

	Postoperative day				
	30	90	180	360	
no. of patients (n = 287)	266	233	223	219	
deceased	20	29	39	43	
absent	1	25	25	25	
sinus rhythm	22	20	21	23	
atrial fibrillation	239	209	197	188	
atrial flutter					
- typical	3	1	2	5	
- atypical	0	0	0	0	
cumulative VVI-SM	32	26	21	24	
cumulative DDD-SM	1	2	3	3	
no. of CV	9	1	0	1	
spontaneous sinus rhythm	9.0%	9.5%	9.5%	11.5%	

Table 3: Rhythm course of the patients of the control group after 30, 90, 180 and 360 days

VVI-SM: Single chamber pacemaker; DDD-SM: dual chamber pacemaker; CV: electric cardioversion

performed in the ensuing rehabilitation, all these patients remained in sinus rhythm for only a short period of time.

The vast majority of patients exhibited atrial fibrillation within the first 10 days following the operation. A few patients, however, were in sinus rhythm during the immediate post operative period but then later exhibited atrial fibrillation once again. Figure 1 shows the time of the first recorded atrial fibrillation following early postoperative atrial or av-sequential stimulation as an expression of the loss of the sinus rhythm or the inability to continue atrial stimulation.

## Mortality

Figure 2 shows cumulative survival of the patients over time. After 30 days, mortality was 6.99% (20 of 286 patients) and 14.98% after one year (43 of 263 patients).

Of the 13 patients who were in stable sinus rhythm after one year, no patient died (0%), while from the 185 patients who continued to exhibit atrial fibrillation after the operation, 43 died (23.2%). Statistical analysis by means of rank tests cannot be performed be-

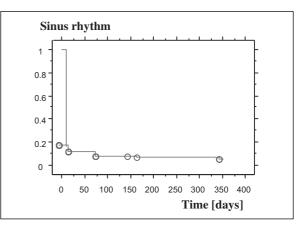


Figure 1. Time of the first recorded postoperative atrial fibrillation (Kaplan-Meier analysis)

cause no events occurred in the "stable sinus rhythm" group.

# Preoperative factors influencing mortality

A further analysis investigated which factors influenced postoperativ mortality after the operation. Pre-

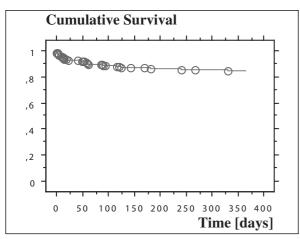


Figure 2. Cumulative survival for patients up to one year after the operation (Kaplan-Meier analysis)

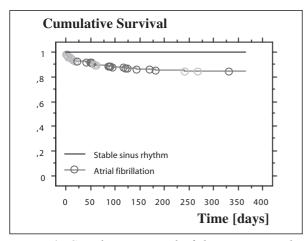


Figure 3. Cumulative survival of those patients who remained in stable sinus rhythm or in atrial fibrillation up to one year (Kaplan-Meier analysis)

operative parameters such as size of the atrium, duration of atrial fibrillation prior to the operation, ejection fraction and patient age, as well as cardiovascular risk factors such as diabetes mellitus, arterial hypertension, obesity and smoking were classified as factors of influence. Further accompanying illnesses such as pulmonary hypertension, as well as intraoperative factors such as the operation duration (indicating the complexity of the intervention), conducting a coronary bypass, an aortic valve operation and a mitral valve operation, were taken into consideration. Significant factors influencing mortality (within the scope of a covariable analysis of the Kaplan-Meier statistics) were found to be:

- Duration of the operation (p < 0.0001),
- Prior stroke (p = 0.0016)
- Ejection fraction (p = 0.0034), and
- Age (p = 0.0246) of the patient.

The duration of the operation of the surviving patients was shorter  $(2.7 \pm 0.8 \text{ hours})$  than of those patients who died later on  $(3.7 \pm 1.6 \text{ hours})$ .

Of the 287 patients in the entire group, 39 (14%) had already experienced a stroke. Eleven of these incidents occurred in the deceased patients (26%), and 28 occurred in the surviving patients (12%).

The surviving patients were a little bit younger than those who died with ages of  $70.9 \pm 8.3$  years and  $72.3 \pm 8.1$  years, respectively, and exhibited a somewhat higher left ventricular ejection fraction of  $52.9 \pm 13.4\%$  (in comparison to  $47.0 \pm 15\%$  for the deceased patient group). The remaining factors did not influence postoperative survival.

## Discussion

In general, it can be assumed that the vast majority of patients suffering from atrial fibrillation preoperatively will continue to experience atrial in other studies fibrillation following heart surgery [2, 8, 9, 12, 24]. In other studies after one year, between 0% [3] and 31.5% [19] of patients were in sinus rhythm. This is a considerable degree of variability that may in fact be mainly due to the small number of cases in these studies. To date, however, there have been no prospective surveys (if one disregards the small control groups of the randomized ablation studies).

As a result, a prospective case register for patients with permanent atrial fibrillation was established in Dresden in order to record and analyze the frequency of sinus rhythm following single heart operations.

The criterion of success at the follow-up of patients who received ablation treatment is differently defined in the various studies. While in some studies the presence of sinus rhythm at the time of the follow-up was considered to be a criterion of success, it was the absence of atrial fibrillation in others. For sure it is difficult to detect a permanent sinus rhythm because not all patients notice the onset of atrial fibrillation. Continuous rhythm monitoring is also not possible (with the exception of patients who have the option of home monitoring). As a compromise, the present survey proceeded in such a way that sinus rhythm was judged as stable if a patient exhibited sinus rhythm on a surface

or 24-hour Holter EKG at all follow-up appointments. These data can only be ascertained when patients are repeatedly asked to return to the hospital during the postoperative period or are closely monitored within the context of a structured collaboration with the cardiologists who are continuing the patient's care.

The results show that for patients who exhibit permanent atrial fibrillation prior to operation, stable sinus rhythms occurred only in very limited number of cases after the operation. Approximately 10% of the patients were in sinus rhythm at one of the follow-up appointment, while only 4.9% exhibited a stable sinus rhythm lasting over the one year period.

In our study, stable sinus rhythms in the postoperative period were observed more frequently in younger patients, with shorter operation time, with good ejection fractions and with patients who had not already suffered a stroke. In particular, age as well as the ejection fraction could be identified as factors for postoperative restoration of sinus rhythm [6].

The mortality rate of 14.9% after one year is comparable to the results reported in other studies ranging from 8 to 19% [4]. In addition, there was a clear advantage for survival for patients who achieved a stable sinus rhythm after the operation [11]. A similar result was reported by Obadia, who likewise found an advantage for survival in patients who were in sinus rhythm following the operation, remarkably whom the difference over time – up to four years – became clearer (15%). 92% of the patients in sinus rhythm were still alive after four years, whereas only 77% of those with atrial fibrillation survived [16].

# Conclusion

Knowing the incidence of restoration of sinus rhythm following heart surgery in patients who suffer from permanent atrial fibrillation prior to the operation is absolutely necessary for evaluating the efficacy of ablation treatment. Regarding this topic, we find essentially retrospective analyses [2, 8, 9, 14, 22], smaller prospective surveys [6, 15] or control groups from randomized studies [3, 18] – which nevertheless also have only very small numbers of cases – in the literature.

Our results show that approximately 10% of patients with preoperative permanent atrial fibrillation have sinus rhythm at one are more postoperative monitoring appointments and only 5% achieved a permanent sinus rhythm (the other 5% showed paroxysmal atrial fibrillation).

Conservatively estimated, a stable sinus rhythm can be achieved postoperatively with comparable operations including ablation treatment in at least every second patients. Therefore, this investigation supports the strategy of concomittant ablation therapy during heart surgery in patients with atrial fibrillation.

#### References

- Bernhardt P, Schmidt H, Sommer T, Lüderitz B, Omran H. Atrial fibrillation patients at high risk for cerebral embolism. Clin Res Cardiol 2006: 95: 148-153
- Chua YL, Schaff HV, Orszulak TA, Morris JJ. Outcome of mitral valve repair in patients with preoperative atrial fibrillation. J Thorac Cardiovasc Surg 1994; 107: 408-415
- Deneke T, Khargi K, Grewe PH, Laczkovics A, von Dryander 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
- Eagle KA, Guyton RA, Davidoff R et al. ACC/AHA guidelines for coronary artery bypass graft surgery: executive summary and recommendations: a report of the American College of Cardiology/ American Heart Association Task Force on Practise Guidelines. Circulation 1999; 100: 1464-1480
- Ezekowitz MD, Netrebko PI. Anticoagulation in management of atrial fibrillation. Curr Opin Cardiol 2003; 18: 26-31
- Flugelman MY, Hasin Y, Katznelson N, Kriwisky M, Shefer A, Gotsman MS. Restoration and Maintenance of sinus rhythm after mitral valve surgery for mitral stenosis. Am J Cardiol 1984; 54: 617-619
- 7. Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, Halperin JL, Kay GN, Klein WW, Levy S, McNamara RL, Prystowsky 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, Parkhomenko 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
- Kahn DR, Krish MM, Ferguson PW, Sloan H. Cardioversion after mitral valve operations. Circulation 1967; 35: 182-185
- Kalil RAK, Maratia CB, DÁvila A, Ludwig FB. Predictive factors for persistence of atrial fibrillation after mitral valve operation. Ann Thorac Surg 1999; 67: 614-617
- Knaut M, Tugtekin SM, Jung F, Matschke K. Microwave ablation for the surgical treatment of permanent atrial fibrillation a single center experience. Eur J Cardiothorac Surg 2004; 26: 742-746
- 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
- 12. Knaut M, Tugtekin SM, Spitzer S, Jung F, Matschke K. Intraoperative endocardial microwave ablation for treatment of perma-

- nent atrial fibrillation during bypass surgery: 1 year follow-up. Europace 2006, 8: 16-20
- 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
- Leithäuser B, Jung F, Park J-W. Oral anticoagulation for prevention of cardioembolic stroke in patients with atrial fibrillation: Focusing the elderly. Appl Cardiopulm Pathophysiol 2009; 13 (4): 307-317
- Mohr FW, Fabricius AM, Falk V, Autschbach R, Doll N, Von Oppell U, Diegeler A, Kottkamp H, Hindricks G. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: short-term and midterm results. J Thorac Cardiovasc Surg. 2002; 123: 919-927
- Obadia JF, Farra ME, Bastien OH, Lièvre M, Martelloni Y, Chassignolle JF. Outcome of atrial fibrillation after mitral valve repair. J Thorac Cardiovasc Surg 1997; 114: 179-185
- 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
- Sack S. Epidemiology of atrial fibrillation. Herz 2002; 27: 294-300
- 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

- Spitzer SG. Catheter ablation of atrial fibrillation current status and future directions. Appl Cardiopulm Pathophysiol 2009 13 (4): 291-299
- Taylor FC, Cohen H, Ebrahim S. Systematic review of long term anticoagulation or antiplatelet treatment in patients with nonrheumatic atrial fibrillation. Brit Med J 2001; 322: 321-326
- 22. 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
- 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
- Yang SS, Maranhao V, Monheit R. Cardioversion following open heart valvular surgery. Brit Heart J 1966; 28: 309-315

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