Mortality after Cardiac Surgery with or without Microwave Ablation in Patients with Permanent Atrial Fibrillation

Michael Knaut[1], Sems M. Tugtekin[1], Stefan Spitzer[2], Friedrich Jung[3], Klaus Matschke[1]

[1]Department of Cardiac Surgery, University of Technology Dresden, Dresden, [2]Praxisklinnik Herz-und Gefäße, [3]Institute for Heart and Circulation Research, Hoyerswerda, Germany

Background and aim of the study: **The surgical treatment of atrial fibrillation (AF) by Cox and other ablation methods shows a 50-90% conversion rate to sinus rhythm. However, to date no study has addressed the influence of ablation on the mortality rate.**

Methods: **The perioperative and postoperative mortalities of 210 consecutive patients with permanent AF was investigated for up to two years after cardiac surgery with (n = 111) or without (n = 99) endocardial microwave ablation within the framework of a prospective register study. All patients were followed up.**

Results: **In the ablation group, one patient (0.9%) died perioperatively, seven died during the first year of follow up (6.3%), and nine in the second year of follow up (8.1%). In the control group, five patients died perioperatively (5.1%), 12 died in the first year of follow up (12.1%), and 22 in the second year of follow up (22.2%). During the two-year follow up period, significantly more patients died in the control group than in the ablation group (Log-Rank test: p = 0.0051).**

Conclusion: **The results of this register study showed that among patients with permanent AF who underwent cardiac surgery with ablation, mortality was significantly lower than in those who underwent comparable surgery but without ablation. The marked difference in mortality was essentially based on the typical clinical consequences of AF (e.g. thromboembolic complications, cardiac arrhythmias and bleeding complications due to anticoagulation therapy), which occurred less often in the ablation group.**

The Journal of Heart Valve Disease 2005;14:531-537

Worldwide, the maze procedure is recognized as being the 'gold standard' in the surgical therapy of atrial fibrillation (AF). However, due to its complexity this procedure could not be established as a routine cardiosurgical therapy. Since the spontaneous conversion rate into sinus rhythm was less than 10%, Raine et al. (1) concluded that an additional ablation procedure should be performed in order to obtain a postoperative sinus rhythm in all cases of mitral valve surgery. There are similar opinions regarding coronary bypass surgery (2,3). The introduction of ablation procedures has led to a renewed interest in the treatment of AF.

An increasing number of study groups are currently performing intraoperative ablation of permanent AF (4). Until now, the most frequently used method has been that of radiofrequency ablation, which was introduced into the clinical scenario in 1986 (5), though further procedures are based on cryotherapy and laser ablation.

One possible alternative to these methods is to use microwave energy for ablation. To date, approximately 2,500 patients have been treated in this way worldwide (6), with a total of 330 receiving treatment at the Dresden center since the procedure was introduced in 1998. While severe complications (lesions of the left coronary artery) have been reported with the epicardial use of microwave ablation (7), there have been no reports of complications with endocardial use. Therefore, the procedure appears to be very safe and to have few complications. Indeed, the results with regard to the restoration of sinus rhythm and atrial transport function are comparable to those obtained with other ablation methods (8).

In the initial randomized studies using this technique, there was shown to be a clear advantage for the ablated group in terms of restoration of the sinus rhythm compared to the non-ablated group (9,10). However, as yet insufficient investigations have been made as to whether the patients also had an advantage

Address for correspondence:
Michael Knaut MD, Dept. of Cardiac Surgery, Heart Center Dresden University Hospital, Fetscherstr. 76, D-01307 Dresden, Germany
e-mail: M.Weber@herzzentrum-dresden.com

J Heart Valve Dis
Vol. 14. No. 4
July 2005

Table I: Patient characteristics at baseline.

Parameter	Microwave ablation	Control	p-value
No. of patients	111	99	-
Gender ratio (M/F)	51/60	53/46	NS
Age (years)*	68.5 ± 7.5 (45.1-83.5)	72.3 ± 9.3 (36.6-86.9)	NS
pAF before surgery	111 (100)	99 (100)	-
Duration of pAF (years)*	6.5 ± 8.4 (0.1-50.8)	4.2 ± 6.9 (0.1-38.5)	NS
Ejection fraction (%)*	56.1 ± 12.1 (32-80)	52.4 ± 2.1 (30-78)	NS
LAD (mm)*	52.6 ± 9.9 (30-102)	51.9 ± 9.4 (24-90)	NS
Diabetes mellitus	41 (36.9)	32 (32.3)	NS
Arterial hypertension	83 (74.8)	61(61.6)	0.0677
Pulmonary hypertension	23 (20.7)	51(55.5)	<0.0001
Preop. stroke	11 (9.9)	15 (15.2)	NS
Preop. MI	21 (18.9)	25 (25.3)	NS
Rheumatic disease	27 (24.3)	3(3.0)	<0.0001

*Values are mean ± SD (range).
Values in parentheses are percentages.
LAD: Left atrial diameter; MI: Myocardial infarction; NS: Not significant; pAF: Permanent atrial fibrillation.

in survival rate as a result of ablation. The present study included an analysis of mortality rate after microwave ablation compared to a non-ablated control group, and covered the initial two-year period following surgery.

Clinical material and methods

Patient population

A total of 370 patients was entered into the study register. All patients were followed up for two years, with follow up being 100% complete in both the ablation group (n = 111) and the control group (n = 104) at a mean of 2.0 ± 0.1 years. In the control group, five patients were excluded due to exclusion criteria (ejection fraction <30%); thus, data from 99 patients were evaluated. The two groups did not differ in either demographic, anatomical or hemodynamic data and preoperative duration of the permanent AF. With respect to cardiovascular risk factors, both groups were similar, though the incidence of pulmonary hypertension in the control group was significantly higher (55.5% versus 20.7%). In contrast, the incidence of rheumatic disease in the ablation group was 24.3% compared to only 3% in the control group. The incidence of preoperative stroke and myocardial infarction were similar in both groups (Table I).

The average duration of surgery for both groups was comparable (ablation group 3.19 ± 1.12 h; control group 2.58 ± 0.46 h). In addition, the frequency of isolated and combined procedures was comparable (Table II). The frequency of coronary artery bypass grafting (CABG) was also similar in both groups, but more aortic valve replacements were performed in the control group. In contrast, more mitral valve operations were performed in the ablation group (66.6% versus 32.3%). The frequency of isolated procedures performed in both groups are listed in Table III, while details of combined cardiac operations are listed in Table IV.

Study design

All patients who underwent endocardial microwave ablation in the same session as the primary surgical procedure (n = 111) were registered consecutively. Within the framework of this prospective register study, a control group (n = 104) who underwent comparable surgery but without concomitant ablation was also registered. The selection of the patients for either group was carried out before the operating schedule was completed, because all ablation procedures were performed by the same surgeon (M.K.). All patients in both groups had permanent AF (11). For clinical, hemodynamic or prognostic reasons, cardiac surgery was already decided on for all patients in the study. The only exclusion criterion was an ejection fraction <30%. The end point of the study was death (from whatever cause).

Further treatment of patients after discharge was carried out by either the family doctor or the cardiologist to adjust medication, the clotting screen, and to check heart rhythm. Follow up examinations were carried out on all patients after one, three, six, 12 and 24 months; this involved conducting 24-h Holter electrocardiography and transthoracic echocardiography. A study nurse followed up all patients, the data for whom were entered into the study register for the mortality statistics.

Table II: Intraoperative data.

Parameter	Microwave ablation (n = 111)	Control (n = 99)
Duration of surgery (h)*	3.19 ± 0.59 (1.47-12.22)	2.58 ± 0.46 (1.36-4.47)
CABG	49 (44.14)	49 (49.49)
Aortic valve replacement	12 (10.8)	38 (38.38)
Mitral valve replacement	48 (43.24)	26 (26.26)
Mitral valve repair	26 (23.42)	6 (6.06)
Tricuspid valve repair	10 (9)	1 (1.01)
Tricuspid valve replacement	-	1 (1.01)
Atrial septal defect closure	13 (11.7)	7 (7.07)
Isolated procedure	68 (61.3)	66 (67.3)
Combined procedure	43 (38.7)	33 (32.8)

*Values are mean ± SD (range).
Values in parentheses are percentages.
CABG: Coronary artery bypass grafting.

The benefits and risks of ablation were explained to all patients, and informed consent was obtained from each patient prior to surgery. The patients also agreed that their data could be entered anonymously into a register for scientific evaluation.

Medication

Patients were admitted to hospital before surgery, and all anti-arrhythmic drugs were discontinued on the day of surgery (but re-continued on the first post-operative day); all other cardiovascular medication was continued.

Postoperatively, sotalol was given to almost all ablation group patients, with the exception of a few treated with metoprolol (13%) or amiodarone (4.5%). Similar proportions of the control patients received either metoprolol, sotalol or amiodarone. Anticoagulation was treated with phenprocoumon, with a target International Normalized Ratio (INR) of 2.0-3.0. If a mechanical mitral or aortic valve was implanted, the target INR was increased to 3.0-4.0. Anticoagulation was stopped for all patients who showed a stable sinus rhythm at the three-month follow up, provided that they had not received a mechanical valve. All control group patients received lifelong anti-arrhythmic therapy.

Microwave ablation system

An AFx microwave surgical ablation device (Flex 2) was used to produce the linear lesions on the endocardial surface. The device was designed to allow the application of microwave energy to the tissue through

Table III: Type and frequency of isolated cardiac operation.

Parameter	Microwave ablation (n = 111)	Control (n = 99)	p-value	Mortality rate (%)*
CABG	22	36	0.0182	3
Aortic valve replacement	5	17	0.0056	4
Biological valve	4	14	-	-
Mechanical valve	1	3	-	-
Mitral valve replacement	32	11	0.0027	6
Biological valve	1	3	-	-
Mechanical valve	31	8	-	-
Mitral valve reconstruction	9	1	-	3
Tricuspid valve replacement	0	1	-	11
Atrial septal defect closure	0	2	-	-

*Based on Society of Thoracic Surgeons (1999).
CABG: Coronary artery bypass grafting.

J Heart Valve Dis
Vol. 14. No. 4
July 2005

an antenna. Details of the method utilized have been published elsewhere (12).

Ablation procedure

The ablation lines followed the concept described by Zarse et al. (13). The procedure was started under visual guidance at the posterior mitral valve annulus, including all pulmonary veins. The lines connecting the pulmonary veins ended 1 cm deep in the veins. The next lesion line was then started at the same depth, but at the contralateral site. The geometry of the lesion lines is shown schematically in Figure 1.

Statistical analysis

The mean ± SD were calculated for all continuous data, and percentage frequency with classified variables. Probability of survival over time and overall survival rate were calculated using Kaplan-Meier curves and compared with the log-rank test. The variables used for confounder analyses included operative data (CABG, aortic valve surgery, mitral valve surgery), concomitant disease (stroke, myocardial infarction, rheumatic disease, diabetes mellitus, arterial hypertension, pulmonary hypertension), and factors which may influence the clinical results of the ablation procedure itself (left atrial diameter, ejection fraction, duration of preoperative AF). This approach aimed to balance out patient preoperative characteristics by incorporating variables that might have related to either systematic bias or simply bad luck.

A p-value <0.05 indicated a statistically significant difference (at the 5% level) between the ablation and control group outcomes.

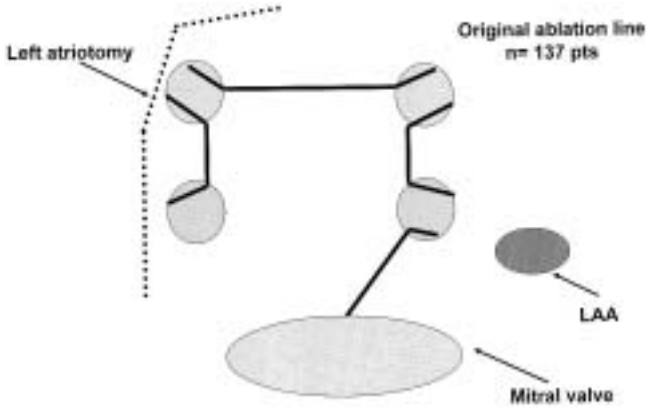

Figure 1: Schematic representation of the lesion lines. LAA: Left atrial appendage.

Results

In the ablation group, one patient (0.9%) died perioperatively (by the 30th postoperative day), and seven died during the one-year follow up period (6.3%). During the two-year follow up period, a total of nine patients died (8.1%). None of the patients died as a result of complications related to the surgical procedure.

Among the control group, five patients died perioperatively (5.1%), 12 died during the one-year follow up period (12.1%), and 22 in the two-year follow up period (22.2%). Significantly more control patients died during the two-year follow up period than did ablation patients (Log-rank (Mantel-Cox) test: p = 0.0051). The Kaplan-Meier curve of survival is shown in Figure 2.

The results of the present study showed that, consid-

Table IV: Type and frequency of combined cardiac operation.

Surgery	Microwave ablation (n = 111)	Control (n = 99)
CABG + (MV repl./AV repl.)	8	2
CABG (+ A. carotis/Ao. asc. repl./ASDC/AV repl.)	9	8
CABG + MV reconstruction (+ TV recon./ASDC/AV repl.)	10	3
MV replacement (+ AV repl./TV recon./ASDC)	9	12
MV reconstruction (+ ASDC/TV recon./AV repl.)	7	1
AV replacement (+ ASDC/Ao. asc. enlargement)	0	3
TV reconstruction (+ ASDC)	1	0

Ao. asc.: Aorta ascendens; ASDC: Atrial septal defect closure; AV repl.: Aortic valve replacement; CABG: Coronary artery bypass grafting; MV repl.: Mitral valve replacement; TV recon.: Tricuspid valve reconstruction.

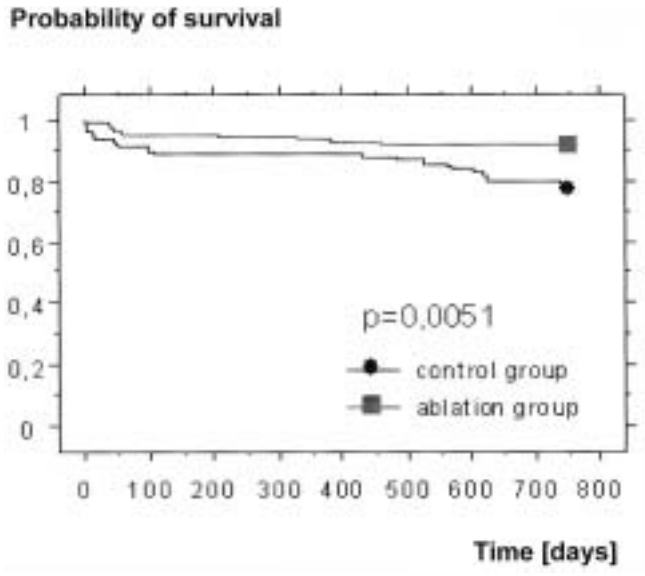

Figure 2: Kaplan-Meier curve for surviving patients of the ablation group compared to the control group.

ering the confounder analyses, the differences in mortality rate during the first two postoperative years between the ablation and control groups remained significantly different (p = 0.0243). The causes of death for all patients are listed in Table V.

For all patients in the ablation group, and for 20 of 22 in the control group, the cause of death was taken from the final epicritical evaluation by the hospital, or provided by the family doctor; in the other two cases, death certificates were used.

Sinus rhythm was restored in 68% of patients in the ablation group after six months, in 58% after 12 months, and in 54% after 24 months. Restoration of sinus rhythm in the control group at similar times were 8%, 10% and 11%, respectively.

Table V: Causes of death for both groups during the two-year follow up period.

Cause of death	Microwave ablation	Controls
Heart failure	3	6
Septic multiorgan failure	2	3
Bilateral pulmonary embolism	-	1
Mesenteric ischemia	-	2
Cardiogenic shock	1	-
Malignant cardiac arrhythmia	-	1
Cranial hemorrhage	1	-
Stroke	-	4
Corpus uteri carcinoma	1	-
Bronchial carcinoma	1	-
Acute subdural hematoma	-	1
Pulmonary embolism	-	1
Colonic carcinoma	-	1
Mesenteric hemorrhage	-	1
Pneumonia	-	1

Discussion

The data obtained in this register study showed that intraoperative microwave ablation, although adding approximately 15 minutes to the duration of the operation (14), does not lead to any increase in perioperative and long-term mortality. Rather, a significant reduction in mortality was achieved (p = 0.0051). This result can be influenced by a number of confounders, these being variables that influence the long-term risk for postoperative mortality. Several such variables are known from the literature. Depending on the type of operation performed, the mortality risks are clearly different: CABG, aortic valve replacement, mitral valve replacement or reconstruction (15,16). Furthermore, the postoperative mortality rate can be influenced by concomitant disease (e.g. stroke, myocardial infarction, rheumatic disease, diabetes mellitus, arterial hypertension, pulmonary hypertension), as well as atrial and ventricular specific confounders (e.g. left atrial diameter, duration of preoperative AF, ejection fraction) (17-20).

If the above confounders were to be considered as co-variables in the analysis, the difference between the ablation and control groups remained significant (p = 0.0243).

An analysis of all of the Dresden patients who received microwave ablation included the personal learning curve of the performing surgeon (M.K.), as well as the initial technical difficulties (inhomogeneous energy application) related to the introduction of a completely new ablation device (21).

It was also noteworthy that, in the ablation group, only one patient died during the first 30 days after surgery, in this case from multiple embolisms caused by diffuse atheroma of the aorta. This was caused by insertion of the cardioplegic catheter, which subsequently required complete replacement of the ascending aorta. Although five of the control patients died during the same period, three of these deaths were due to the typical consequences of AF (pulmonary embolism, mesenteric ischemia, continuing malignant arrhythmia) (22). Later during the follow up period of up to two years, 22.2% of the control patients died, which was significantly more than in the ablation group (8.1%; p = 0.0051). The mortality rate of the ablation group in the present study was comparable to that reported by others performing radiofrequency ablation, including Lemke et al. (23), who noted postoperative mortality rates of 12% at one year and 14.2% at three years. Khargi et al. (24) reported a mortality rate of 11.3% at 19.7 months postoperatively, while

Manasse et al. (25), in performing cryotherapy, noted postoperative mortalities of 6.5% after one year and 9.5% after three years.

Mortality rates following CABG surgery without an ablation procedure range from 8% to 19% (26), underlining the consideration that additional intraoperative microwave ablation does not lead to increased mortality among these patients. Indeed, to prove whether these patients benefit from such additional therapy should be the aim of further studies with an appropriate sample size.

Quader et al. concluded, from a risk analysis of 46,984 cases, that all patients with AF undergoing revascularization should undergo an additional intraoperative ablation procedure (2), while Raine et al. (1) advocated additional ablation therapy in all cases of mitral valve surgery. Wolf et al. however, in reporting data from the Framingham study, suggested that the prevention of AF in patients with cardiovascular disease might yield benefits in terms of reduced mortality and stroke (3).

In the present study, nine of the control patients died as a consequence of their continuing AF (from pulmonary embolism, stroke, malignant cardiac arrhythmia, mesenteric ischemia) or as a result of treatment of the AF (mesenteric hemorrhage, acute subdural hematoma), whereas in the ablation group only one patient died. This patient suffered a cranial hemorrhage whilst receiving anticoagulation therapy that had been continued because a mechanical heart valve had been implanted.

Patients suffering from AF, even without any organic heart disease, have a markedly higher risk of thromboembolic events (27). Taylor et al. showed the risk of stroke in the elderly to be five-fold higher compared to patients without AF (28).

Study limitations

Although the present study involved a retrospective review of prospectively collected data, it was likely to suffer from inherent limitations of observational studies on non-randomized patient groups. An attempt was made to control for imbalances between the two patient groups by the statistical analysis of demographic, anatomical and hemodynamic data. However, it was not possible to control for other factors such as inter-patient differences in the extent or distribution of coronary artery disease or valve disease and the differences in performance between individual cardiac surgeons.

In conclusion, additional ablation treatment during surgical procedures proved to be effective in the treatment of AF (9,10,20,25,29,30). In 50-80% of patients, restoration of a stable sinus rhythm was achieved, depending on the type of AF and the efficacy criteria used. The results of the present study have shown that patients with permanent AF undergoing open-heart surgery with concomitant microwave ablation therapy have a significantly lower mortality rate than those not receiving microwave ablation.

References

1. Raine D, Dark J, Bourlee JP. Effect of mitral valve repair/replacement surgery on atrial arrhythmia behavior. J Heart Valve Dis 2004;13:615-621
2. Quader MA, McCarthy PM, Gillinov AM, et al. Does preoperative atrial fibrillation reduce survival after coronary bypass grafting? Ann Thorac Surg 2004;77:1514-1524
3. Wolf PA, Mitchel 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
4. Damiano RJ. Alternative energy sources for atrial ablation: Judging new technology. Ann Thorac Surg 2003;75:329-330
5. Borgrefe M, Budde T, Podczeck A, et al. High frequency alternating current ablation of an accessory pathway in humans. J Am Coll Cardiol 1987;10:576-582
6. Saltman A. Microwave ablation. The endocardial and epicardial experience. In: Fourth Annual Conference on the Surgical treatment of atrial fibrillation. Promedica International. 2004
7. Manasse E, Medici D, Ghiselli S, Ornaghi D, Gallotti R. Left main coronary artery lesion after microwave epicardial ablation. Ann Thorac Surg 2003;76:276-277
8. Viola N, Williams MR, Oz MC, Ad N. The technology in use for the surgical ablation of atrial fibrillation. Semin Thorac Cardiovasc Surg 2002;14:198-205
9. Schuetz A, Schulze CJ, Sarvanakis KK, et al. Surgical treatment of permanent atrial fibrillation using microwave energy ablation: A prospective randomized clinical trial. Eur J Cardiothorac Surg 2003;24:475-480
10. Deneke T, Khargi K, Grewe PH, et al. 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
11. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. J Am Coll Cardiol 2001;18:1
12. Spitzer SG, Richter P, Knaut M, Schüler S. Treatment of atrial fibrillation in open heart surgery. The potential role of microwave energy.

Thorac Cardiovasc Surg 1999;47(Suppl.3):374-378
13. Zarse M, Deharo JC, Allessie MA. Radiofrequency ablation of anatomical atrial circuits in a rabbit model of atrial fibrillation. Circulation 1996;94(Suppl.1):164-171
14. Knaut M, Spitzer SG, Karolyi, et al. Intraoperative microwave ablation for curative treatment of atrial fibrillation in open heart surgery. The MICRO-STAF and MICRO-PASS pilot trial. Thorac Cardiovasc Surg 1999;47(Suppl.II):379-384
15. STS National Database Spring 2003 Executive Summary
http://www.chestnet.org/file/STSNational Database2003ExecutiveSummary.pdf
16. Jamieson WR, Burr LH, Anderson WN, Jr., Chambers JB, Gams JP, Dowd CM. Prosthesis-related complications: First-year annual rates. J Heart Valve Dis 2002;11:758-763
17. Kannel WB, Abbott RD, Savage DD, McNamara PM. Epidemiologic features of chronic atrial fibrillation: the Framingham study. N Engl J Med 1982;306:1018-1022
18. Cox JL, Schuessler RB, D'Agostino HJ, Jr., ET AL. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. J Thorac Cardiovasc Surg 1991;101:569-583
19. Kawaguchi AT, Kosakai Y, Isobe F, et al. Surgical stratification of patients with atrial fibrillation secondary to organic cardiac lesions. Eur J Cardiothorac Surg 1996;10:983-989; discussion 989-990
20. Spitzer SG, Knaut M. Intraoperative Mikrowellen-Ablation zur chirurgischen Behandlung von Vorhofflimmern. Herzschr Elektrophys 2002;13:225-232
21. 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
22. Odell JA, Blackshear JL, Hodge D, Bailey KR. Stroke after coronary artery bypass grafting: Are we forgetting atrial fibrillation? Ann Thorac Surg 2001;71:397-404
23. Lemke B, Khargi K, Grewe PH, et al. Sicherheit und Effektivität der intraoperativen gekühlten linearen Hochfrequenzstromablation bei Patienten mit Vorhofflimmern während eines kardiochirurgischen Eingriffs. Z Kardiol 2003;92:1008-10017
24. 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
25. Manasse E, Gaita F, Ghiselli S, et al. Cryoablation of the left posterior atrial wall: 95 patients and 3 years of mean follow-up. Eur J Cardiothorac Surg 2003;24:731-740
26. 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 Practice Guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). Circulation 1999;100:1464-1480
27. Wolf PA, Dawber TR, Thomas HE, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: The Framingham study. Neurology 1979;28:973-977
28. Taylor FC, Cohan H, Ebrahim S. Systemic review of long term anticoagulation or antiplatelet treatment in patients with non-rheumatic atrial fibrillation. Br Med J 2001;322:321-326
29. Mohr WF, Fabricius AM, Falk V, et al. Curative treatment of atrial fibrillation with intraoperative radiofrequency ablation: Short-term and midterm results. J Thorac Cardiovasc Surg 2002;123:919-927
30. Knaut M, Spitzer S, Tugtekin SM, Schüler S. Microwave ablation: A successful option for treatment of chronic atrial fibrillation. Circulation 2000 (Suppl. II);102:486