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Microwave Ablation in Mitral Valve Surgery for Atrial Fibrillation (MAMA)

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Abstract

Objective: Microwave ablation in conjunction with open heart surgery is effective in restoring sinus rhythm (SR) in patients with atrial fibrillation (AF). In patients assigned for isolated mitral valve surgery no prospective randomized trial has reported its efficacy.

Methods: 70 patients with longlasting AF where included from 5 different centres. They were randomly assigned to mitral valve surgery and atrial microwave ablation or mitral valve surgery alone.

Results: Out of 70 randomized, 66 and 64 patients were available for evaluation at 6 and 12 months. At 12 months SR was restored and preserved in 71.0 % in the ablation group vs 36.4 % in the control group (P=0.006), corresponding figures at 6 months was 62.5 % vs 26.5 % (P=0.003). The 30-day mortality rate was 1.4 %, with one death in the ablation group vs zero deaths in the control group. At 12 months the mortality rate was 7,1 % (Ablation n=3 vs Control n=2). No significant differences existed between the groups with regard to the overall rate of serious adverse events (SAE) during the perioperative period or at the end of the study. 16 % of patients randomized to ablation were on antiarrhytmic drugs compared to 6 % in the control group after 1 year (p=0.22)

Conclusion: Microwave ablation of left and right atrium in conjunction with mitral valve surgery is safe and effectively restores sinus rhythm in patients with longlasting AF as compared to mitral valve surgery alone.

Introduction

Atrial fibrillation (AF) has a prevalence of 1% in the general population,[1] with a dramatic increase reaching 30-50 % in patients scheduled for mitral valve surgery.[2] Growing evidence has emerged showing that restoration of SR at the time of cardiac surgery is associated with an improvement in Quality of Life (QoL) and clinical parameters,[3, 4] and although not yet supported in prospective,

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randomized trials, reduced mortality and morbidity.[5] In patients with preoperative continous AF > 3 months or longstanding persistent AF, valve surgery alone restores SR in only 5% to 43 % of the patients, as compared to 44 % to 80 % when performing adjunctive left or biatrial ablation using microwave, radiofrequency or cryoenergi.[6-10] By employing the classical cut and sew Maze operation in patients scheduled for mitral valve surgery and chronic AF, restoration of SR is achived in a higher degree, 74% to 90 %.[11] However, even if the Maze technique is regarded as the gold standard it is considered too complicated and has gradually been replaced by surgical ablation methods where endo and/or epicardial ablation lines replaces surgical incisions. Concomitant microwave ablation of AF has succesfully been used in cardiac surgery, with SR at follow up in the range of 52% to 87 %,[11-14] including one randomized, prospective trial.[10] We wanted to study how effectively microwave ablation restores SR in a homogenous population, i.e. patients assigned for mitral valve surgery with longlasting AF, and therefore performed a multicenter, prospective, randomized, controlled clinical trial comparing microwave ablation in conjunction with mitral valve surgery versus mitral valve surgery alone.

1.Materials and Methods

1.1 Patient population

The study was performed at five different University Hospitals, with two centres situated in Sweden and three centres situated in Finland, during the period between November 2002 and December 2006. Patients aged over 18 years old primarily scheduled for mitral valve surgery with longlasting atrial fibrillation of more than twelve months duration prior to surgery were considered eligble. Longlasting atrial fibrillation was defined as continous atrial fibrillation without clinically or by electrocardiogram (ECG) documented evidence of sinus rhythm, also including a 24-hour Holter ECG performed within the last three months without any signs of sinus rhythm. One attempt of previous cardioversion resulting in immediate recurrence of atrial fibrillation (IRAF) or subacute recovery of atrial fibrillation (SRAF) was however allowed.

The enrollment process became noticeably prolonged due to a scarcity of patients with a duration of atrial fibrillation of more than twelve months. Therefore, the initial inclusion criteria was modified, with the amendment approved by the ethics committee, to the following wording; ″Longlasting atrial fibrillation for at least six months prior to surgery or atrial fibrillation ongoing for at least three months prior to surgery and a history of previously failed cardioversion or relapse after initially successful cardioversion″. The exclusion criteria were as follows, prior valve surgery, concomitant aortic valve surgery, prior catheter ablation for atrial fibrillation, documented torsade de pointes, permanent pacemaker treatment, hyperthyroidism ruled out by blood-test, active endocarditis, severe calcifications of the mitral anulus, unforeseen events developing during the surgical procedure whereby adding ablation imposes an unproportional risk to the procedure or inability, unwillingness to follow the protocol. Written informed consent was received from all patients. The protocol was approved the by the ethics committee in each participating institution.

1.2 Study Design, Endpoints, Randomization Procedure and Sample Size

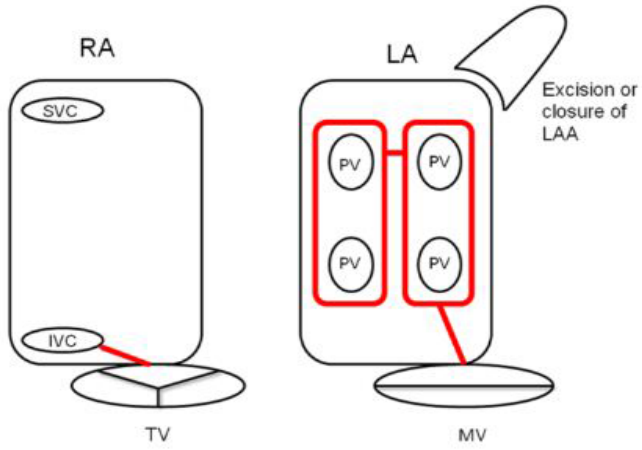
Patients were randomly assigned to either mitral valve surgery and concomitant atrial microwave ablation or mitral valve surgery alone. The primary endpoint was defined as evidence of preserved sinus rhythm at the 12 month Follow Up (F/U) determined by 12-lead ECG. Preserved sinus rhythm was defined as follows; SR on 12 lead-ECG without any documented episodes (or cardioversion) of atrial fibrillation (AF), atrial flutter (AFL) or atrial tachycardia (AT) since previous F/U. Secondary endpoints consisted of freedom from AF, AFL and AT at the 12 month F/U determined by 24-hour Holter ECG, at 6 months after surgery determined by 12-lead ECG, pacemaker requirement, antiarrhythmic treatment, QoL, and incidence of adverse events according to protocol. The computer-based randomization was performed by an external resource and stratified by hospital. Accordingly each hospital received sealed envelopes in numbered series with a balance between patients assigned for ablation vs. controls. At the day of surgery the cardiac surgeon opened the envelope in order, designating the allocated study treatment. Information regarding the latter was

during the time of the study kept out of the patient chart, i.e., all patients and with the exception of the surgical team, all personnel involved in the follow-up was blinded to the assigned treatment. The conversion rate from atrial fibrillation to sinus rhythm was estimated to 20 % in the group of patients undergoing mitral valve surgery alone, versus 60 % in the group of patients where intraoperative ablation was added to mitral valve surgery. To reach a power of 90 % with a type I error of 5 % it was calculated that 35 patients was needed in each group.

1.3 Preoperative Screening and Evaluation

Consecutive patients scheduled for mitral valve surgery was screened and enrolled if they met the inclusion and exclusion criterias. Data was prospectively recorded regarding patient demography, clinical history and QoL Atrial and ventricular dimensions, left ventricular function and cardiac valve function was obtained by transthoracic echocardiography. The duration of longlasting atrial fibrillation was determined by data in the patient chart. A 24-hour Holter ECG was performed to rule out any periods of sinus rhythm. Heart failure was defined as clinical symtoms of heart failure and depressed left ventricular function on echocardiography. Presence of coronary artery disease (CAD) was defined as previous myocardial infarction, previous or planned percutaneous coronary intervention (PCI) or coronary artery by-pass grafting (CABG), respectively. Before surgery all patients were put on treatment with a beta-blocker, Bisoprolol, in a dose to maintain adequate rate control.

Figure 1: Schematic view of the left and right atria demonstrating the lesionset. Abbreviations: RA, right atrium; LA, left atrium; TV, Tricuspid valve; MV, mitral valve; PV, pulmonary vein; SVC, superior vena cava; IVC inferior vena cava; LAA, left atrial appendage.



1.4 Surgical and Microwave ablation procedure

All patients underwent mitral valve surgery during cardioplegic arrest and on cardiopulmonary bypass (CBP). The route into the left atrium was made according to the surgeon's preference, ie, either by transeptal approach or via Sondergaard's groove. Mitral valve repair or mitral valve replacement and additional surgical procedures was performed according to clinical routine. In the group randomised to concomitant ablation the left atrial appendage was either excised or excluded. After valve surgery was completed ablation took place using a microwave ablation system (Afx Inc., Fremont, CA), including a microwave generator connected to an ablation probe. The microwave generator produced electromagnetic waves with a fixed frequency of 2.45Ghz, however, with a variable power output. The ablation probe consisted of a malleable shaft with the ablation antenna emmitting the microwave radiation located in the distal end of the probe. Two different probes were used, either the FLEX 2 with an 2.5 cm long antenna with a power output of 40 W for 25 seconds or the FLEX 4 with an 4 cm long antenna with a power output of 65 W for 60 seconds. Ablation lines were under visual guidance created en bloc around the left upper and lower pulmonary vein (PV) and around the right upper and lower PV, respectively. In addition one interconnecting line between the two PV pairs and a second line connecting the left PV pair to the mitral anulus were created (Figure 1). In the right atrium a line between the inferior vena cava and the tricuspid anulus was performed. All individual ablation lesions were performed endocardially and furthermore in an overlapping manner to avoid gaps. If AF persisted after the completion of surgery, epicardial electrical cardioversion was performed.

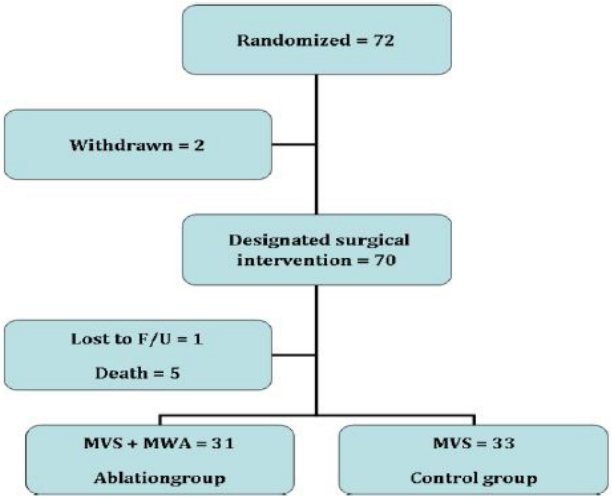
1.5 Postoperative management and follow-up

According to protocol, atrial overdrive pacing (AODP) was performed during the first five post-

operative days in all patients with SR. Pacing mode was AAI, or if needed DDD using the epicardially placed pacing electrodes. The pacing rate was kept 10 beats above the average native heart rate up to a maximum of 105 bpm. If postoperative atrial fibrillation appeared AODP was paused. Continous telemetry and daily 12-lead ECG were performed during the first five postoperative days, thereafter a 12 lead ECG was taken before discharge. Bisoprolol was the only antiarrhythmic drug used during the postoperative period, ie, no Class I or III drugs were given at this time. All patients with persistent atrial fibrillation underwent cardioversion the day before disharge. For patients with recurrence of paroxysmal AF during discharge to 4 months postoperative period, antiarrhythmic treatment with Sotalol, or Amiodarone if contraindications against Sotalol existed, was recommended including at least two attempts of cardioversion in patients with persistent AF. All Class III drugs were discontinued at 6 months after surgery if previously sinus rhytm ensued. Warfarin was administered according to the local guidelines during the in-hospital period and continued for at least three months.

Follow up was conducted at 1, 3, 6 and 12 months after hospital discharge by a dedicated cardiologist in each participating center's outpatient clinic. The medical history was reviewed including medications, cardioversions, documented arrhythmia events, serious adverse events, unscheduled visits/hospitalisations. A physical examination including a 12-lead ECG was performed. Transthoracic echocardiography was performed at 6 and 12 months, complemented by a bicycle exercise test at 6 months and a 24-hour Holter ECG at 12 months. QoL assessment using SF-36 was performed at baseline, and at the 6 and 12 month F/U.

Figure 2: Flow chart through the study. Abbreviations: F/U, follow-up; MVS, mitral valve surgery; MWA,micro wave ablation.



1.6 Statistical analysis

Data are presented as mean ±SD or percentages. Fisher's exact test or Chi-square test were used for categorial variables, while continous variables were analyzed by unpaired t test or Mann-Whitney test. All P-values were two-sided and considered significant if below 0.05.

2. Results

2.1 Study implementation

A flow chart describing the implementation of the study is shown in Figure 2. 72 patients were randomized. Two patients designated to the ablation group were withdrawn, one met the surgeons exclusion criteria; unforeseen events developing during the surgical procedure whereby adding ablation imposes an unproportional risk to the procedure, the other patient was withdrawn due to technical problems at the time of surgery with the microwave ablation system, i.e. 70 patients underwent the designated surgical intervention and are included in the analysis for morbidity and mortality. During the study five patients died and one was lost to follow up, resulting in 64 patients included in the analysis for primary and secondary endpoints.

2.2 Baseline characteristics

Baseline characteristics are given in Table 1. There were significantly more men and a lower frequency of tricuspid valve regurgitation in the ablation group, otherwise the two groups did not differ with regard to demographical and echocardiographic data, New York Heart Association classification, concomitant diseases or pre-operative medication.

2.3 Operative procedures, Perioperative (≤30 days) Morbidity and Mortality

Reflecting the lower incidence of tricuspid valve regurgitation in the ablation group, a significantly

Table 1 Baseline Patient Characteristics

Characteristics	Ablation Group (n=31)	Control group (n=33)	P-value
Male, n (%)	26 (84)	18 (54)	0.011
Age, (years)	66 ± 7.7	67 ± 9.2	n.s.
History of AF (months)	87 ±110 (6-240)	65 ±62 (6-432)	n.s.
Duration of longlasting AF (months)	53 ±83 (4-360)	34 ±49 (4-240)	n.s
Previous DC cardioversion, n (%)	18 (58)	17 (52)	n.s.
Hypertension, n (%)	12 (39)	11 (33)	n.s.
Coronary artery disease, n (%)	5 (16)	7 (21)	n.s.
Previous stroke/TIA, n (%)	2 (6)	4 (12)	n.s.
Diabetes, n (%)	3 (10)	1 (3)	n.s.
Pulmonary disease, n (%)	2 (6)	2 (6)	n.s.
Heart failure, n (%)	5 (16)	5 (15)	n.s.
NYHA class, n (%)			
I	2 (7)	1 (3)	n.s.
II-III	28 (90)	29 (88)	n.s.
IV	1 (3)	3 (9)	n.s.
LVEF < 50 %, n (%)	3 (10)	4 (12)	n.s.
Left atrial size (cm)	5.8 ±0.7	5.8 ±0.6	n.s.
Mitral valve regurgitation, n (%)	29 (94)	30 (91)	n.s.
Combined mitral valve disease, n (%)	2 (6)	3 (9)	n.s.
Tricuspid valve regurgitation, moderate or severe	7 (23)	15 (46)	0.054
Medication, n (%)			
Beta-blocking agents	24 (77)	28 (85)	n.s.
Calcim channel blocking agents	2 (6)	1 (3)	n.s.
Digoxin	17 (55)	18 (54)	n.s.
Class I and III antiarrhythmic agents	2 (6)	0	n.s.
Diuretics	14 (45)	17 (52)	n.s.
ACE-inhibitors/ARB	19 (61)	22 (67)	n.s.
Warfarin	29 (94)	32 (97)	n.s.
Aspirin	2 (6)	2 (6)	n.s.

n indicates number of patients (%). Figures are mean ±SD with ranges in brackets, unless otherwise stated. Abbreviations: TIA, transient ischemic attack; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; Class I and III, refers to Vaughan Williams classification of antiarrhythmic agents; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor antagonist.

lower proportion 3/31 (9.7%) underwent tricuspid valve repair as compared to the control group 12/33 (36.4 %), (P = 0.01). Otherwise there were no significant differences in the type or number of surgical procedures, cardio pulmonary by-pass (CPB) and aortic cross clamp (AOC) times or hospital stay. The time needed for completing the microwave ablation was 17.5 ± 5.1 min (Table 2). The overall 30-day in-hospital complication rate was 31.4% (11/35) in the control group and 45.7 % (16/35) in the ablation group, (P = 0.220) (Table 3). There were no significant differences between the groups with regard to the specified complications. In one patient bleeding from an area in the right atrium (RA) close to the inferior vena cava occurred during weening from ECC. The right atrial wall was on gross examination unusually thin and the perforation probably resulted from two microwave lesions overlapping. The perforation was succesfully managed by patched sutures. One patient died in the ablation group resulting in a total in-hospital mortality rate of 1.4 % (1/70). Death occurred after surgery was completed when weaning of by-pass. Autopsy revealed the cause of death related to heart failure, perioperative myocardial infarction and prolonged surgery due to bleeding. No rela-

Table 2 Surgical data

Parameter	Ablation Group (n=31)	Control group (n=33)	P-value
Mitral valve replacement	3 (9.7)	8 (24.2)	0.123
Mitral valve repair	28 (90.3)	25 (75.8)	0.123
Tricuspid valve repair	3 (9.7)	12 (36.4)	0.012
CABG	5 (16.1)	5 (15.1)	0.914
ASD closure	1 (3.2)	2 (6.1)	0.592
CPB (min)	146.1 ± 35.5 (90-248)	132.5 ± 35.8 (76-248)	0.136
AOC (min)	109.0 ± 30.1 (56-212)	95.0 ± 28.4 (49-177)	0.061
Microwave ablation time (min)	17.5 ± 5.1 (8-28)	-	-
Hospital stay	15.4 ± 10.4 (7-57)	12.0 ± 5.7 (5-36)	0.108

n indicates number of patients (%). Figures are mean ±SD with ranges in brackets, unless otherwise stated. Abbreviations: CABG, coronary artery bypass grafting; CPB, cardio pulmonary by-pass; AOC, aortic cross-clamp.

tion with the microwave ablation was seen. One patient in the ablation group needed implant of an permanent pacemaker due to sinus node disease (SND).

2.4 Rhythm outcome, prediction of rhythm and postoperative medication

The primary endpoint, preserved SR on the 12 lead ECG at 12 months F/U, was seen in 22/31 patients (71.0%) in the ablation group as compared to 12/33 (36.4%) in the control group (P=0.006). The corresponding figures at 6 months was 20/32 patients (62.5%) versus 9/34 (26.5%), respectively (P = 0.003). When analyzing 24-hour Holter ECG at 12 months, 21/30 (70.0%) in the ablation group versus 9/27 (33.3%) in the control group showed no episodes of AF, atrial flutter (AFL) or atrial

Table 3 30-day and 1-year postoperative morbidity and mortality

	Ablation Group (n=35)	Control group (n=33)	P-value
Perioperative morbidity/mortality, (≤30 days) n (%)		18 (54)	
Re-operation (bleeding)	3 (8.6)	67 ± 9.2	n.s.
Re-operation (MR/PL)	4 (11.4)	65 ±62 (6-432)	0.114
Re-operation (AR)	0	34 ±49 (4-240)	n.s.
Perioperative bleeding	1 (2.9)	17 (52)	n.s.
Low cardiac output syndrome	2 (5.7)	11 (33)	n.s.
Renal failure/hemofiltration	1 (2.9)	7 (21)	n.s.
Sepsis	0	4 (12)	n.s.
Pneumonia/Urinary tract infection	1 (2.9)	1 (3)	n.s.
Pericardial effusion	4 (11.4)	2 (6)	0.356
Pleural effusion	0	5 (15)	n.s.
Heart failure	1 (2.9)		n.s.
Myocardial infarction	1 (2.9)	1 (3)	n.s.
Sustained VT/VF	1 (2.9)	29 (88)	n.s.
Permanent pacemaker implantation (SND)	1 (2.9)	3 (9)	n.s.
Brainoedema	0	4 (12)	n.s.
Superficial skin infection	1 (2.9)	5.8 ±0.6	n.s.
Nerve entrapment	0	30 (91)	n.s.
Infection, without known agent	0	3 (9)	n.s.
Hematoma (leg)	0	15 (46)	n.s.
Mortality	1 (2.9)		n.s.
Late postoperative morbidity/mortality, (>30 days) n (%)		28 (85)	
Re-operation (MR)	0	1 (3)	n.s.
Pericardial effusion	0	18 (54)	n.s.
Permanent pacemaker implantation (SND)	0	0	n.s.
TIA/Stroke	1 (2.9)	17 (52)	n.s.
Pneumonia	1 (2.9)	22 (67)	n.s.
Infection, without known agent	1 (2.9)	32 (97)	n.s.
Chestpain and sternotomy wire removal	1 (2.9)	2 (6)	n.s.
Heart failure	0		n.s.
Atrial tachycardia requiring catheter ablation	0		n.s.
Gastrointestinal bleeding	0		n.s.
Mortality	2 (5.7)		n.s.

n indicates number of patients (%). Abbreviations: MR, mitral regurgitation; PL, paravalvular leakage; AR, Aortic regurgitation; VT, ventricular tachycardia; VF, ventricular fibrillation; SND, sinus node disease; TIA, transient ischemic attack.

tachycardia (AT) (P = 0.012). Table 5 shows the baseline characteristics, surgical data and postoperative medication of the patients in the ablation group with or without preserved SR at 12 month F/U. The history and duration of longlasting AF was significantly shorter in the group with preserved SR. The left atrial size was smaller but this difference did not reach statistical significance. Logistic regression analysis of the variables in table 5 found that the only independent predictor for establishment of SR by microwave ablation was duration of longlasting AF, with an OR for AF after the procedure of 1.015 for each 1-month increment in duration of longlasting AF(95% CI 1.000 to 1.029, P = 0.043).

The only antiarrhythmic agent in use at the one year F/U was Sotalol (Table 4), without any significant difference in usage between the two treatment groups. The proportion of patients on Sotalol and in sinus rhythm was 3/22 (13.6%) in the ablation group. versus 3/12 (25.0%) in the control group.

2.5 Late postoperative (> 30 days) Morbidity and Mortality

The complication rate during the remaining follow-up period was after one year, 34.3 % (12/35) in the control group and 14.3 % in the ablation group (5/35), (P = 0.051) (Table 3). The mortality rate was identical for the two groups, 5.7 % (2/35). In the ablationgroup one patient had an episode of aborted sudden cardiac death (SCD) the day after discharge (postoperative day 16). A secondary severe anoxic brain injury developed and the patient died postoperative day 40 from multiorganic failure. The case was revised by the external Adverse Events Advisory Committee who could not find any link to the microwave ablation. The second patient patient died 6.5 months after surgery due to cerebral infarction and secondary brain herniation. Sinus rhythm without clinical symptoms of paroxysmal AF was seen at the 6 month F/U and Warfarin treatment was stopped. When presenting two weeks later at the emergency room with clinical signs of cerebral infarction, sinusrhythm was still present. A CT scan could not detect any pathological findings. In the control group one patient died from SCD and one from a malignant brain tumor, 3.5 and 9 months after surgery, respectively. One patient in the control group needed implant of an permanent pacemaker due to SND and another patient had a Stroke/Transient ischaemic attack (TIA) resulting in a similar pacemaker implant rate and stroke rate for the two groups (2.9 %).

Table 4 | Medication at 12 months follow-up

Drug	Ablation Group (n=31)	Control group (n=33)	P-value
Beta-blocking agents	25 (80.6)	27 (81.8)	0.904
Sotalol (Only Class I/III in use)	5 (16.1)	3 (9,1)	0.395
Digoxin	1 (3.2)	5 (15.2)	0.102
Diuretics	6 (19.4)	9 (27.3)	0.455
ACE-inhibitors/ARB	17 (54.8)	21 (63.6)	0.474
Warfarin	18 (58.1)	29 (87.9)	0.007
Aspirin	10 (32.3)	3 (9.1)	0.021

n indicates number of patients (%). Abbreviations: Class I and III, refers to Vaughan Williams classification of antiarrhythmic agents; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor antagonist.

Discussion

We were in this randomized, controlled trial table to demonstrate that biatrial microwave ablation in conjunction with mitral valve surgery effectively restored sinus rhythm in patients with long lasting atrial fibrillation compared to mital valve surgery alone. We found a conversion rate to stable SR at 12 months (71.0%) which is in the mid-range of the 63,4% reported by the International Registry of AF Surgery [15] and the 78-88.9% reported by the four meta-analysis where both classical cut and sew Maze surgery and Maze like procedures are included.[11, 16-18] The variations in conversion rate are assumed to reflect differences in patient population, AF-type and duration, lesion sets, ablation technology and concomitant surgery.[19] With regard to the nine randomized controlled trials(RCT)[6-9, 20-24] which address the adjunctive value of surgical ablation of AF in patients scheduled for open chest mitral valve surgery, and thus comparable to our study, again differences exists. The two studies using cut and sew Cox Maze III rendered the highest conversion rates to SR after 12 months, 80-92 %, however compared to our study, included younger patients, shorter AF-duration,[22] paroxysmal AF and smaller left atrial size.[21] In the remaining sev-

Table 5 Ablationgroup (n=31) with or without Sinusrhythm at 12 months, Baseline Patient Characteristics, Surgical Data, Medication

Characteristics	Sinusrhythm (n=22)	No sinusrhythm (n=9)	P-value
Male, n (%)	17 (77)	9 (100)	0.118
Age, (years)	66 ±7.9	66 ±7.6	0.938
BMI (kg/m2)	25.7±4.0	27.9±5.1	0.205
Duration of longlasting AF (months)	28 ±50 (4-240)	113 ±114 (11-360)	0.014
Previous DC cardioversion, n (%)	11 (50)	7 (78)	0.155
Hypertension, n (%)	8 (36)	4 (44)	0.675
Coronary artery disease, n (%)	4 (18)	1 (11)	0.627
Previous stroke/TIA, n (%)	2 (9)	0	0.350
Diabetes, n (%)	2 (9)	1 (11)	0.863
Pulmonary disease, n (%)	2 (9)	0	0.350
Heart failure, n (%)	4 (18)	1 (11)	0.627
NYHA class, n (%)			0.351
I	1(5)	1 (11)	
II-III	20 (90)	8 (89)	
IV	1 (5)	0	
LVEF < 50 %, n (%)	19 (86)	9 (100)	0.244
Left atrial size (cm)	5.6 ±0.7	6.1 ±0.7	0.069
Combined mitral valve disease, n (%)	2 (9)	0	0.350
Tricuspid valve regurgitation, mod or severe, n (%)	4 (18)	3 (33)	0.360
MVR performed, n (%)	3 (14)	0	0.244
Microwave ablation time (min)	17.7±5.6	17.0±4.0	0.726
Medication at 12 months F/U, n (%)			
Beta-blocking agents	19 (86)	6 (67)	0.208
Sotalol (Only Class I/III in use)	3 (14)	2 (22)	0.555

n indicates number of patients (%). Figures are mean ±SD with ranges in brackets, unless otherwise stated. Abbreviations: TIA, transient ischemic attack; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; Class I and III, refers to Vaughan Williams classification of antiarrhythmic agents.

en studies, Maze like procedures were performed using alternative energy sources and different lesions sets, RF, Cryo-energy/Biatrial; n=6/5[6, 8, 9, 20, 23, 24] and, Cryo-energy/Biatrial; n=1/0.(7) The sinus conversion rate varied from 44 to 80% and patient characteristics being more uniform with regard to age distribution, AF-duration, AF-type (no paroxysmal AF), left atrial dimensions, with the exception for the study presented by Srivastava et al,[23] and thus comparable with our results with SR in 71% at 12 month F/U. Having said that, differences in definitions, postoperative rhythm strategies, antiarrhythmic treatment at F/U and potential bias due to a non-blinded F/U, still makes direct comparison difficult. To our knowledge only one RCT where microwave energy was used is published.[10] They reported a conversion rate to SR of 80 vs. 33% at 12 months based on 24/41 patients. Compared to our study they had 24% of non-MVS surgery, smaller left atrial diameters, 60% of patients on antiarrhythmic treatment in the ablation group after 12 months which could partially explain the higher efficacy.

The rationale for replacing surgical incisions by alternative ablation techniques depends upon the capability of creating transmural lesions without collateral damage in an easier and faster way. Microwave energy creates lesions as a result of transformation of electromagnetic energy to kinetic

energy and dielectric heating, with lesion depth dependent on power and duration of delivery.[25] The potential advantages offered by microwave energy is consistent penetration, low risk of tissue charring (temperatures < 100ºC) and a high degree of transmurality (>94%) using endocardial ablation.[26] The main drawbacks constitutes of, the risk of collateral damage although to our knowledge only isolated Featured Reviews have been published[27, 28] and lack of a feed-back system assessing transmurality during surgery. The mean lesion depth reported in a dose-response study was 4.1±1.3mm,[26] however they used longer ablation time (90 s) compared to the recommended settings (60 s) that we used in our study. This reason and the fact that ablation in our study was performed in a human diseased atria, with supposedly thicker walls and fibrosis, could potentially have led to lower efficacy due to non-transmural lesions.

The perioperative mortality rate of 1.4 % observed in our study is lower compared to the 5.1-7.1 %, previously reported in mitral valve surgery.[29] No significant difference existed between the groups, even though the control group contained a higher proportion of women and tricuspid valve repair, known risk factors for increased mortality.[29] An increased morbidity rate at 30 days in the ablation group as compared to the control group was detected. The difference was not statistical significant but similar findings has been reported by others.[7] Among our patients, one perioperative complication, perforation of RA, was most likely caused by microwave ablation. Of the remaining complications observed in the ablation group, no obvious link could be established to the ablation procedure. This however does not exclude that such a connection exists. During the remaining follow-up period the mortality and morbidity rate did not differ between the groups. The need for pacemaker implantation, catheter ablation for atrial tachycardia and stroke was low. However, the observation of a stroke in one ablated patient with sinus rhythm and discontinued warfarin treatment supports the prevailing strategy of maintaining warfarin based on clinical risk factors instead of the observed rhythm.[19]

To conclude, sinus rhythm was safely restored and preserved by performing microwave ablation in conjunction with mitral valve surgery in patients with long lasting continuous AF as compared to mitral valve surgery alone. These findings are in accordance with the current guidelines supporting surgical ablation in cardiac surgery.

Limitations

Since we only used 12-lead ECG and 24-hour Holter ECG to determine rhythm outcome, episodes of asymptomatic paroxysmal AF, AT and AFL could have occurred during follow-up, i.e. underestimating the true burden of atrial tachyarrhythmias. The fact that all patients were not of antiarrhythmic drugs (Sotalol) when analyzing the primary endpoint at 12 months could act as a confounding factor. However, the small proportion of patients on Sotalol, without differences between the groups and its modest efficacy ought to limit the influence on the rhythm outcome. The formation of a transmural lesion was not confirmed at surgery by electrophysiological mapping.

Disclosures

- Ulla Walfridsson, RN, for collection of data, input on and participating in statistical analysis and HRQOL interpretation.
- Mats Fredriksson, Ph.D and Kristofer Årestedt, Ph.D for their contribution to the statistical analysis.

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