Mitral valve surgery plus concomitant atrial fibrillation ablation is superior to mitral valve surgery alone with an intensive rhythm control strategy

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Abstract

Objective: Prospective randomised study comparing patients with atrial fibrillation (AF) of more than 6 months duration after mitral valve surgery plus biatrial modified radiofrequency Maze procedure using Medtronic Cardioblate System (Cardioblate group, n = 24) vs mitral valve surgery plus intensive rhythm control strategy (control group, n = 25). Methods: Patients were blinded to randomisation. Preoperatively, at discharge, and at 3-month and 1-year follow-up, echocardiography, quality of life assessments and ECGs were done. In both groups, sinus rhythm (SR) restoration was attempted by intra- and postoperative DC cardioversion and class III antiarrhythmic medication. All patients received warfarin. Amiodarone and warfarin was considered for discontinuation after 3 months in SR, 24-h Holter or event monitor excluding AF. Results: Both groups underwent mitral valve replacement or repair (Cardioblate vs control: 16:8 vs 10:15), had similar gender (male: 33% vs 56%), age (66 ± 8 years vs 68 ± 9 years), additional aortic valve replacement (7 vs 6 patients), tricuspid annuloplasty (13 vs 13 patients), and CABG (10 vs 16 patients). There was 0% operative mortality, 0% postoperative cerebrovascular accidents, but 2 late deaths in the control group. At discharge, 3- and 12-month follow-up, more patients in the Cardioblate group returned to normal SR compared to control (29%, 57% and 75% vs 20%, 43% and 39%; p = 0.030). Return of functional atrial contraction in patients in SR at 1 year was comparable between groups (63% vs 89%, NS), and more likely in non-rheumatic pathology and preoperative AF of shorter duration. The effectiveness of atrial contraction was 36 ± 14% vs 43 ± 18% of transmural flow and there was no difference between groups. Amiodarone treatment decreased more in Cardioblate group over time (92%, 55% and 29% vs 52%, 52% and 21%; p = 0.003), whereas warfarin decrease was comparable (100%, 100% and 71% vs 100%, 95% and 82%; NS). Conclusions: Radiofrequency Maze ablation additional to mitral valve surgery resulted in a higher SR conversion rate (75%), despite control group treatment with intensive rhythm control strategy having a higher SR conversion rate (39%) compared to literature (~25%). Maze ablation resulted in normalisation of atrial function in 63% of patients converted to SR.

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Keywords: Cardiac surgery; Mitral valve; Atrial fibrillation; Radiofrequency ablation; Rhythm control

1. Introduction

In general, atrial fibrillation (AF) is associated with a doubling of cardiovascular mortality [1], an increased risk of systemic emboli and stroke [1] (4- to 5-fold increased risk in non-rheumatic patients and 18-fold increase in patients with rheumatic valve disease [2]), and a deterioration in cardiac function due to a combination of loss of atrial transport, irregular or rapid ventricular rates, and progressive cardiomyopathy. The increased mortality associated with AF is independent to the underlying cardiovascular condition [3]. The detrimental effects of AF are exacerbated by mitral valve disease. At present approximately half of all patients undergoing mitral valve surgery have AF preoperatively [4,5]. Although mitral valve repair (valvuloplasty) or replacement improves transmural haemodynamics, studies have shown that on long-term follow-up only 25% of those in AF preoperatively remain in sinus rhythm (SR) at one year [6,4,7]. Moreover, even after otherwise successful cardiac surgery, patients with persisting AF often remain symptomatic, experience little improvement in exercise capacity and require life-long anticoagulation [6].

Long-term outcome studies after mitral valve repair surgery have shown no significant difference in survival...
between preoperative SR patients and preoperative AF patients. However, postoperative maintenance of SR is associated with improved survival as compared to postoperative AF [1,5,8]. Hence, it can be assumed that patients undergoing mitral valve repair surgery in combination with successful AF treatment will have an increased survival as compared to the 75% of patients with preoperative AF who do not maintain postoperative SR after mitral valve repair surgery alone.

The surgical cut-and-sew Maze procedure, as described by Cox and co-workers [9], has been established as an effective mechanism of surgically curing AF. The majority of his patients underwent AF surgery alone (Maze III procedure using only surgical incisions and cryosurgical lesions) and did not require concomitant cardiac surgery; perioperative mortality was 2.3% and SR was maintained in 98% of patients. Furthermore, health-related quality of life improved significantly after Maze surgery in patients refractory to antiarrhythmic therapy [10]. Combining Maze or modified Maze procedures with other open heart surgery (valvular surgery) is associated with maintenance of SR on follow-up of 75—90% [11,12,13] and potentially allows discontinuation of both anticoagulation and antiarrhythmic therapy. The cut-and-sew Maze operation though is not without problems, as the surgery is technically difficult, time consuming and therefore potentially increases morbidity of the total procedure. The demanding nature of the surgery, the risk of perioperative complications and uncertainties regarding atrial mechanical function explain why the procedure has not been more widely adopted.

Radiofrequency (RF) ablation is a newer technology that allows the surgeon to perform the Maze procedure using RF energy instead of a scalpel/surgical incision, thereby reducing both the time required and risks associated with this concomitant surgery. The principle of RF energy ablation is to produce a confluent transmural linear line of cellular death by raising tissue temperature to greater than 55 °C thereby, similar to a surgical incision, preventing electrical conduction [14]. A systematic review of the surgical treatment of atrial fibrillation has also not shown any significant difference in the success rate between the classical cut-and-sew and alternative ablation devices techniques [15].

The potential benefits of RF Maze surgery are restoration of atrial mechanical function, improved cardiac haemodynamics and a decreased risk of thromboembolism. In addition, maintenance of SR should decrease long-term requirements of antiarrhythmic drugs, rate controlling drugs and anticoagulants. Potential risks of additional RF Maze surgery are a more complicated postoperative course due to longer cardiopulmonary bypass and aortic cross-clamp times. Risk factors for failure to achieve SR include large left atrial size (usually due to associated mitral valve disease) and associated tricuspid valve disease [8]. However, our hypothesis is that the potential benefit to risk ratio favours patients with cardiac disease and AF undergoing cardiac surgery plus RF modified Maze surgery compared to conventional cardiac surgery alone, but this required confirmation by means of a prospective randomised trial.

The goal of this clinical study was to test the hypothesis that patients with persistent or permanent AF and mitral valve disease requiring surgical treatment have a significantly better outcome after cardiac surgery plus RF modified Maze surgery with the Medtronic Cardioblate Surgical Ablation System as compared to conventional cardiac surgery alone with intense rhythm control postoperatively.

2. Materials and methods

2.1. Study design

This investigation was set up as a prospective, randomised, single-blind, single-centre study comparing the outcome of mitral valve surgery plus RF modified Maze surgery with conventional cardiac surgery alone. Patients enrolled were randomised to receive either RF ablation with the Medtronic Cardioblate Surgical Ablation System (Medtronic Inc, Minneapolis, MN) in addition to their cardiac surgery (Cardioblate group) or alternatively only their planned cardiac procedure (control group). The ablation pattern in the left atrium (LA) included RF isolation of the left and right pulmonary veins, an interconnecting line between them, a left pulmonary vein to atrial appendage line, and a mitral annulus to pulmonary vein line. In the right atrium (RA), a transverse ablation line was made across the free wall, then connecting lines to the superior vena cava, inferior vena cava and right atrial appendage as well as to the tricuspid annulus and coronary sinus were made. Postoperatively, both groups received an intense rhythm control strategy.

To determine study size, it was assumed that 55% of patients in the Cardioblate group and 20% of patients in the control group would convert to normal sinus rhythm. Assuming a level of significance of 5% and a power of 80%, a minimal sample size of 23 patients per group was required. After continuity correction a sample size of 28 patients per group was recommended.

The study was approved by the South East Wales local research ethics committee and all patients signed a patient informed consent form.

Data was collected in the immediate preoperative period, during surgery, prior to discharge from hospital, and at 3 months and 1 year after surgery. Data collection included NYHA functional class, changes in antiarrhythmic and anticoagulant medication, 12-lead ECG recordings, trans-thoracic echocardiographies and determination of perceived adverse events. In addition, patients completed the SF-36 survey form at each visit, except at discharge. Patients were blinded with regard to which group they were randomised to prevent bias during completion of quality of life questionnaires. The key outcome of the study was normal SR, and success was defined as stable normal SR at 1-year follow-up. Atrial pacing with atrial capture was also considered a success.

Recruitment of patients into the trial was difficult, as we were already an established centre for the treatment of atrial fibrillation and the majority of eligible patients were not recruitable as they had been specifically referred by their
physicians for concomitant atrial fibrillation surgery. At the end of 3 years, we closed the trial after achieving the minimal sample size.

2.2. Treatment strategy

Postoperatively, unless contraindicated, all patients in the Cardioblate group received amiodarone, and patients in the control group received amiodarone only if internal DC cardioversion restored SR intraoperatively. Otherwise these control group patients received rate control agents only. Patients were put on antiarrhythmic therapy for at least 3 months. Antiarrhythmic drugs were discontinued if patients were in stable SR for 3 months, after a 24-h Holter tape ruled out asymptomatic AF in patients with no history of postoperative palpitations or an event monitor proved absence of AF in patients with a history of postoperative palpitations. In addition, all patients were put on anticoagulation therapy (warfarin) for at least 3 months. Patients who were in stable SR for 3 months had their warfarin discontinued unless otherwise indicated.

Patients in both groups underwent internal cardioversion prior to leaving the operating theatre, if necessary. In the Cardioblate group, if AF persisted in the early postoperative period, external DC cardioversion was performed prior to discharge or at 4–6 weeks following discharge. If recurrence of AF was diagnosed after discharge but within the first 6 months after surgery, patients underwent an external DC cardioversion with a maximum of two attempts. In the control group, if internal DC cardioversion was unsuccessful, then no further external DC cardioversions were done postoperatively as the success rate would be negligible. In both groups, each patient was assessed following each external DC cardioversion. If SR was unlikely to be restored or the risks of amiodarone treatment were thought to outweigh any potential benefit, then further attempts at maintaining SR were abandoned and the patient was switched to a rate control strategy. This decision was at the discretion of the individual consultant surgeon provided that all reasonable attempts were made to restore and maintain SR.

2.3. Data analysis

Statistical analysis was performed using SAS® statistical software, version 9.1. Descriptive statistics were used to report patient population characteristics, and intra- and postoperative data. For continuous variables, the number of patients, mean, standard deviation (SD), minimum and maximum is provided. The effect of Cardioblate treatment was analysed by two-way repeated measurements ANOVA and post-hoc testing was done by Student’s unpaired t-test. Post-hoc testing between time points was done with a paired t-test. Log transformation was applied prior to the ANOVA analysis in case data were not normally distributed. For categorical variables, the number and percentage of patients is provided. The effect of Cardioblate treatment was analysed by categorical repeated measures analysis (CAT-MOD) and post-hoc testing was done by chi-square or exact testing. All post-hoc testing was corrected according to Bonferroni’s inequalities.

A p-value <0.05 was regarded as statistically significant.

3. Results

3.1. Patients

Between January 2004 and November 2006, 49 patients were enrolled in the study. Twenty-four patients (8 male and 16 female) were randomised to the Cardioblate group and 25 patients (14 male and 11 female, NS) to the control group. Mean age was 66 ± 8 (mean ± SD) years (range: 45–78 years) and 68 ± 9 years (range: 43–79 years) and mean body mass index was 25.8 ± 4.5 kg/m² (range: 17.5–39.3 kg/m²) and 27.3 ± 4.0 kg/m² (range: 18.7–36.4 kg/m²) in the Cardioblate and control group, respectively (both NS). In the Cardioblate group, 22 patients suffered from permanent AF and two patients from persistent AF. In the control group, 22 patients suffered from permanent AF and three patients from persistent AF. Patients in the Cardioblate group experienced AF for 7 ± 10 years (range: 0.5–40 years) prior to surgery, whereas patients in the control group experienced AF for 5 ± 4 years (range: 0.5–15 years; NS). Left atrial dimensions were 52 ± 8 mm (range: 33–67 mm) and 55 ± 8 mm (range: 41–27 mm) in the Cardioblate and control group respectively (NS).

Table 1 provides an overview of the patients’ cardiac disease history. Most common valvular disease in both groups was mitral valve insufficiency, mitral valve prolapse and tricuspid insufficiency, and there was no difference between groups. Regarding non-valvular disease history, about half of the patients per group suffered from coronary artery disease,
congestive heart failure and rheumatic heart disease, and similarly there was no difference between groups. However, significantly less patients in the Cardioblate group suffered from hypertension requiring therapy as compared to the control group (p = 0.021).

3.2. Surgery

In the Cardioblate group, 16 patients underwent mitral valve replacement (11 biological/5 mechanical) and 8 patients underwent mitral valve repair. In addition, tricuspid valve repair was done in 13 patients, aortic valve replacement (6 biological/1 mechanical) in 7 patients, and CABG was done in 10 patients. In the control group, 10 patients underwent mitral valve replacement (7 biological/3 mechanical) and 15 patients underwent mitral valve repair. In addition, tricuspid valve repair was done in 13 patients, aortic valve replacement and repair in 5 and 1 patients, and CABG was done in 16 patients. The distribution of mitral valve replacement and repair, or other coexistent surgery was not significantly different between groups.

All patients in the Cardioblate group underwent a complete Maze procedure and had their LA appendix excised. Initially, the ablation pattern was made only with the bipolar device in six patients. However, concerns as to the completeness of the mitral annular line led us to use both the monopolar and bipolar Cardioblate devices in the subsequent 18 patients. In addition, we also tended to subsequently apply 'double' ablations when ablating the thicker pulmonary vein regions.

In the control group, 20 out of 25 patients had their LA appendix excised (p = 0.05 vs Cardioblate group).

Mean cardiopulmonary bypass time (CPB) and aortic cross-clamp (ACC) time were 176 ± 42 min and 143 ± 35 min in the Cardioblate group, including an additional CPB time of 14 ± 4 min and an additional ACC time of 13 ± 3 min for performing the Maze procedure. In the control group, mean CPB time and ACC time were 160 ± 55 min (NS) and 119 ± 44 min (p = 0.040 vs Cardioblate group). After cross-clamp removal, cardioversion was required in 11 patients in the Cardioblate group (1 for AF and 10 for VF) and 10 patients in the control group (6 for AF and 4 for VF) (NS). On transfer to the intensive care unit, 14 patients in the Cardioblate group and 15 patients in the control group were in normal SR (NS).

Patients were discharged after 15 ± 7 days (range: 7–28 days) in the Cardioblate group and 12 ± 6 days (range: 4–25 days) in the control group (NS).

3.3. Morbidity and mortality

The predicted mortality by logistic EuroSCORE was 7.8 ± 12.6% for the Cardioblate group and 9.0 ± 6.5% for the treatment group (NS); nevertheless there was no inhospital operative mortality in either group.

No RF ablation device-related adverse events were reported. All significant adverse events were classed as ‘related to cardiac surgery’ or to ‘pre-existing disease’. Notably there were no peri- or postoperative cerebrovascular accidents in either group. As cardiac surgery in general and the Maze procedure in particular influence the conduction system of the heart, it was important to know how many patients received a pacemaker. During this study, 1 patient in the Cardioblate group received a DDD pacemaker 49 days after surgery for intermittent, complete heart block, most likely related to the valvular surgery and not to arrhythmia surgery. In the control group, 1 patient received a VVI pacemaker 12 days after surgery for bradycardia and AF.

In the Cardioblate group, all patients were alive at the end of the 1-year follow-up period. In the control group, 2 patients died. The first patient died 35 days after surgery due to a colonic diverticular abscess. The second patient died 163 days after surgery due to unknown cause.

3.4. Clinical status

Preoperatively, 19 patients (79%) in the Cardioblate group and 20 patients (80%) in the control group were in NYHA class III or IV (NS). Two patients in the Cardioblate group and 3 patients in the control group missed their 3-month follow-up visit, whereas no patient missed their 1-year follow-up visit. NYHA class improved significantly after surgery in both groups. At 3-month follow-up, 19 patients (96%) in the Cardioblate group and 20 patients (95%) in the control group were in NYHA class I or II. At 1-year follow-up, 22 patients (92%) and 22 patients (96%) were in NYHA class I or II respectively. The incidence of NYHA functional class I or II improved equally in both groups (CATMOD: group: NS, time: p < 0.001, group × time: NS).

Preoperatively, 23 patients in each treatment group (96% vs 92%, respectively) were using antiarrhythmic medication; mainly digoxin and beta-blockers (NS). Interestingly, only 1 patient in the Cardioblate group and 3 patients in the control group were using amiodarone at that time. At discharge, 22 Cardioblate patients (92%) and 13 control patients (52%, p = 0.004 vs Cardioblate group) were prescribed amiodarone. Over time, amiodarone use decreased to 7 patients (29%) in the Cardioblate group and 5 patients (22%) in the control group (CATMOD: group NS, time: p < 0.001, group × time: p = 0.003). Eight Cardioblate patients (33%), but none of the control patients was using beta-blockers at 1-year follow-up, whereas digoxin use was comparable between groups (6 patients (25%) vs 6 patients (26%), respectively).

Prior to surgery, 23 patients (96%) in the Cardioblate group and 22 patients (88%) in the control group were using warfarin. Warfarin use did not change over time (CATMOD: group NS, time: NS, group × time: NS). At 1-year follow-up, 17 patients (71%) in the Cardioblate group were still using warfarin: 3 patients for prophylactic reasons, 8 patients for AF, 5 patients due to a mechanical valve, and 1 patient due to coronary artery disease. In the control group, 19 patients (83%, NS vs Cardioblate group) were still using warfarin: 1 patient for prophylactic reasons, 15 patients for AF and 3 patients due to a mechanical valve.

3.5. Electrocardiography

Over time, conversion to SR as measured by 12-lead ECG changed significantly (CATMOD: group: p = 0.030, time: p < 0.001, group × time: NS) (Fig. 1). In the Cardioblate
group, SR incidence increased progressively from discharge, 3-month and 1-year follow-up; 7 patients (29%), 12 patients (55%) and 18 patients (75%), respectively. At 1-year follow-up, 4 patients (17%) remained in permanent AF or AFL, 1 patient (4%) was documented to have episodes of paroxysmal AF and 1 patient (4%) had atrial tachycardia. Whilst in the control group, an initial increase in SR plateaued after 3 months; 5 patients (20%), 9 patients (43%) and 9 patients (55%) and 18 patients (75%), respectively. At 1-year follow-up; 7 patients (29%), 12 patients (55%) and 18 patients (75%), respectively. At 1-year follow-up (43% in normal SR at 1-year follow-up with echocardiographic examinations were shown to have functioning atrial contraction, whereas 6 patients in normal SR did not have functional atrial contraction; SR patients with atrial contractions had less rheumatic disease (30% vs 100% of patients, p = 0.011), less coronary artery disease (10% vs 67%, p = 0.036) and tended to have a shorter preoperative duration of AF (28 ± 29 vs 178 ± 163 months, p = 0.074). There were no significant differences in the device used for the Maze procedure, type of mitral valve surgery (replacement vs repair), presence of congestive heart failure, and preoperative LA dimension and volume. Interestingly, SR patients with functional atria had a smaller LA dimension at 1-year follow-up (43 ± 4 vs 49 ± 5 mm, p = 0.015).

In contrast, in the control group, functional atrial contraction was present in 8 of the 9 patients (89%) who were in normal SR at 1-year follow-up (NS vs Cardioblate group).

There was no difference between treatment groups as to the effectiveness of the atrial contraction in those patients having functioning atria at 1 year (36 ± 14% vs 43 ± 18%, NS).

3.7. Quality of life

All patients completed an SF-36 — Health Survey preoperatively and 3 months and 1 year after surgery. Preoperatively, there was no significant difference in health profile between groups (Fig. 3). Overall, patients’ physical well being as measured by the SF-36 scores for physical functioning, role-physical, general health, vitality and social functioning increased significantly after surgery (all p < 0.001), but did not differ between treatment groups (Fig. 3). Scores for bodily pain (p = 0.014), role-emotional (p = 0.021) and mental health (p = 0.037) were overall lower group had his AF confirmed. All other patients had no episodes of AF on their recording and were free of AF.

3.6. Echocardiography

Preoperatively, there were no significant differences between treatment groups for left ventricular (LV) size and functional assessment, LA and RA size, LV diastolic function and atrial contribution to transmitral flow (Table 2).

One year after mitral valve surgery, no changes in LV size or functional assessment could be found. Overall, LA dimension and RA area were significantly lower (p = 0.011 and p = 0.003) in the Cardioblate group compared to the control group. LA dimension (p = 0.039), LA volume (p = 0.024), tricuspid annulus (p = 0.001), maximum E velocity (p = 0.049) and E-wave deceleration (p = 0.032) decreased significantly over time, but the decline was comparable between groups. Maximum A velocity, peak E/A ratio and the number of patients with an A-wave were not significantly different between groups over time (Table 2).

With regard to atrial contribution to transmitral flow, TotalVTI (p = 0.007) decreased significantly over time, but was comparable between groups. Atrial fraction (if present) remained stable over time (NS). The overall number of patients having effective atrial contraction significantly increased over time (p < 0.001) (Table 2).

Notably, in the Cardioblate group, 10 of the 16 patients (63%) in normal SR at 1-year follow-up with echocardiographic examinations were shown to have functioning atrial contraction, whereas 6 patients in normal SR did not have functional atrial contraction; SR patients with atrial contractions had less rheumatic disease (30% vs 100% of patients, p = 0.011), less coronary artery disease (10% vs 67%, p = 0.036) and tended to have a shorter preoperative duration of AF (28 ± 29 vs 178 ± 163 months, p = 0.074). There were no significant differences in the device used for the Maze procedure, type of mitral valve surgery (replacement vs repair), presence of congestive heart failure, and preoperative LA dimension and volume. Interestingly, SR patients with functional atria had a smaller LA dimension at 1-year follow-up (43 ± 4 vs 49 ± 5 mm, p = 0.015).

In contrast, in the control group, functional atrial contraction was present in 8 of the 9 patients (89%) who were in normal SR at 1-year follow-up (NS vs Cardioblate group).

There was no difference between treatment groups as to the effectiveness of the atrial contraction in those patients having functioning atria at 1 year (36 ± 14% vs 43 ± 18%, NS).
Table 2
Echocardiography data.

<table>
<thead>
<tr>
<th></th>
<th>Cardioblate group (n = 24)</th>
<th>Control group (n = 25)</th>
<th>ANOVA</th>
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<tbody>
<tr>
<td></td>
<td>Preop</td>
<td>Discharge</td>
<td>3 months</td>
</tr>
<tr>
<td><strong>Left ventricular size and functional assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV end systolic diameter (mm)</td>
<td>36 ± 9</td>
<td>40 ± 12</td>
<td>37 ± 11</td>
</tr>
<tr>
<td>LV end diastolic diameter (mm)</td>
<td>53 ± 8</td>
<td>54 ± 8</td>
<td>51 ± 9</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>31 ± 10</td>
<td>27 ± 14</td>
<td>29 ± 10</td>
</tr>
<tr>
<td>LV end systolic volume (ml)</td>
<td>50 ± 22</td>
<td>58 ± 41</td>
<td>47 ± 29</td>
</tr>
<tr>
<td>LV end diastolic volume (ml)</td>
<td>104 ± 40</td>
<td>106 ± 48</td>
<td>94 ± 34</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>52 ± 12</td>
<td>49 ± 16</td>
<td>53 ± 13</td>
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<tr>
<td><strong>Left and right atrial size</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA dimension (mm)</td>
<td>52 ± 8</td>
<td>50 ± 6</td>
<td>50 ± 8</td>
</tr>
<tr>
<td>LA volume (ml)</td>
<td>141 ± 75</td>
<td>138 ± 79</td>
<td>106 ± 60</td>
</tr>
<tr>
<td>RA area (cm²)</td>
<td>22 ± 6</td>
<td>20 ± 5</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>Tricuspid annulus (mm)</td>
<td>32 ± 7</td>
<td>26 ± 5</td>
<td>27 ± 5</td>
</tr>
<tr>
<td><strong>Left ventricular diastolic function</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Maximum E velocity (cm/s)</td>
<td>170 ± 40</td>
<td>150 ± 25</td>
<td>146 ± 33</td>
</tr>
<tr>
<td>Maximum A velocity (cm/s)</td>
<td>71 (n = 1)</td>
<td>60 ± 20 (n = 2)</td>
<td>74 ± 17 (n = 6)</td>
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<tr>
<td>Peak E/A ratio</td>
<td>1.6</td>
<td>2.4 ± 1.6</td>
<td>1.6 ± 0.5</td>
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<tr>
<td>E wave deceleration time (ms)</td>
<td>366 ± 212</td>
<td>271 ± 92</td>
<td>281 ± 79</td>
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<tr>
<td><strong>Atrial contribution to transmural flow</strong></td>
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<tr>
<td>Total/VTI (cm)</td>
<td>44 ± 24</td>
<td>28 ± 8</td>
<td>33 ± 9</td>
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<tr>
<td>Atrial fraction (%)</td>
<td>27 (n = 1)</td>
<td>28 ± 19 (n = 2)</td>
<td>31 ± 9 (n = 6)</td>
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</table>

a *p = 0.030 Cardioblate vs control group.

b *p = 0.003 vs preoperative measurement.
in Cardioblate group as compared to the control group, but these scores did not change over time. There was no statistical difference in any of the quality of life parameters between success and failure patients in the Cardioblate group or between success and failure patients for the Cardioblate and control group combined.

4. Discussion

The goal of this prospective randomised study was to test the hypothesis that patients with persistent or permanent AF and cardiac disease requiring surgical treatment have a significantly better outcome after mitral valve surgery plus RF modified Maze surgery with the Medtronic Cardioblate Surgical Ablation System as compared to only conventional mitral valve surgery. All patients in the Cardioblate group had atrial ablation lesions in order to have as high a success rate as possible [16].

As the proportion of patients with normal SR in the Cardioblate group (75%) was significantly higher (p = 0.019) compared to the control group (39%; Fig. 1), RF modified Maze surgery with the Medtronic Cardioblate Surgical Ablation System is more effective than only conventional surgery with an intensive rhythm control strategy. A significant number of patients had early atrial fibrillation recurrence in the first 3 months post surgery, similar to that previously being reported at between 36% and 67% [17,18]. Nevertheless, 1-year 75% SR success rate was slightly higher than the 63% success rate reported by the International Registry of AF Surgery [19]. Notably our study population of mitral valve patients were predominantly patients with longstanding permanent atrial fibrillation and 83% required additional concomitant procedures such as coronary revascularisation, which are known predictors of failure of reverting to stable normal sinus rhythm [19]. Higher success rates of 91% have though been reported with the bipolar RF device, but in patient populations having predominant preoperative paroxysmal AF [20]. The addition of the modified RF Maze procedure did not effect operative mortality in our study population, having an overall logistic EuroSCORE predicted mortality of 8.4 ± 9.9%, as has been reported by others [21]. Notably, 20 patients (83%) in the Cardioblate group and 21 patients (84%) in the control group had other concomitant surgery (CABG, AVS or TA, etc.) in addition to their mitral valve surgery.

Enrolment of patients into this study was started at the moment the first bipolar Cardioblate device was introduced on the market in the UK, and all six failures in the Cardioblate group occurred at the beginning of the study (Fig. 2), and could be interpreted as part of our 'learning curve'. However, the first three failure patients were treated only with the bipolar device, and this prompted us to review our technique. It is difficult to ensure a confluent ablation line between the left pulmonary veins and the mitral valve annulus and the tricuspid valve annulus with the bipolar device alone without potentially injuring coronary arteries, and we felt it advisable to use the monopolar pen for these lines for subsequent procedures. Alternative techniques to obtain transmurality to the mitral annulus with only the bipolar device have though been described [22]. In addition, total ablation time between the first 9 and last 18 enrolled patients in the Cardioblate group (success and failure combined) was significantly different with a longer ablation time for the later group (4:03 ± 1:07 vs 5:03 ± 1:12, p = 0.049). Again this might reflect more monopolar pen use and/or 'double' bipolar ablation lines. Bipolar RF devices may not consistently produce complete transmurality depending upon the presence of epicardial fat [23], and following commencement of the study ‘double bipolar ablations’ were usually performed in the latter half of the study, when ablating the pulmonary veins and interconnecting line for these reasons, as well as dissecting large areas of fat away from the AV groove.

We analysed whether or not there were any obvious differences between success and failure in patients in the Cardioblate group. It was found that there was no significant difference between treatment outcome and Cardioblate device used, type of mitral valve surgery, presence of rheumatic heart disease, use of amiodarone at 1-year follow-up, preoperative duration of AF, or total ablation time.

Table 3

<table>
<thead>
<tr>
<th>Factor</th>
<th>Success (n = 18)</th>
<th>Failure (n = 6)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Preoperative duration of AF (months)</td>
<td>112 ± 123</td>
<td>82 ± 116</td>
<td>NS</td>
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<tr>
<td>Presence of rheumatic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
<td>4</td>
<td>NS</td>
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<tr>
<td>No</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cardioblate device used</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bipolar device only</td>
<td>3</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Both mono- and bipolar device</td>
<td>15</td>
<td>3</td>
<td></td>
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<tr>
<td>Total ablation time (mm:ss)</td>
<td>4:12 ± 1:18</td>
<td>4:49 ± 1:14</td>
<td>NS</td>
</tr>
<tr>
<td>Type of mitral valve surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>13</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Mitral valve repair</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Use of amiodarone at 1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
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<td>4</td>
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</table>
(Table 3). Other studies though have shown that the duration of preoperative AF and LA diameter are independent predictors of success [24].

In addition to conversion to normal SR, Maze surgery should also contribute to return of atrial transport function and improved haemodynamics after surgery. The number of patients having atrial contraction increased significantly over time \((p < 0.001)\), but there was no difference between the Cardioblate and control group (3 months: 6 patients (30%) vs 7 patients (44%); 1 year: 11 patients (52%) vs 8 patients (42%), both NS). As return of atrial contraction is associated with conversion to normal SR, we were surprised to see that with echocardiography of 16 of the 18 successful patients, only 10 patients (63%) in the Cardioblate group had atrial contractions at 1-year follow-up, whereas the other 6 patients (37%) had no atrial contractions associated with their SR. One patient assigned as a Cardioblate failure had atrial contractions during echocardiography, as this patient with a DDD pacemaker had episodes of paroxysmal atrial fibrillation but was in A–V conducted rhythm at the time of his echocardiogram.

We investigated whether the return of atrial contraction was dependent on the duration of AF or whether the patient was suffering from rheumatic heart disease; patients with LA contraction (irrespective of randomisation into Cardioblate group or control group) tended to suffer from AF for a much shorter time as compared to patients in whom LA contraction was not restored \((38 \pm 41 \text{ months} vs 162 \pm 154 \text{ months}, p = 0.077)\). In addition, only 33% of the patients with restored LA contraction suffered from rheumatic heart disease, whereas this was the case in all patients (100%) with no return of LA contraction \((p = 0.014)\). We did not do LA volume reduction procedures in our patients, apart from excision of the left atrial appendage, although this has been reported to increase both SR conversion as well as increasing left atrial contraction recovery [25,26], and may well be of additional benefit.

The restored atrial fraction generated was comparable between the Cardioblate and control group \((34 \pm 14\% \text{ vs } 43 \pm 18\%, \text{NS})\), indicating that the modified RF Maze surgery does not significantly compromise the ability of the atrium to contract effectively. Our ablation pattern did not involve the creation of a ‘box lesion’, which in the cut-and-sew Maze III negates any effective atrial contraction of the posterior isolated atrial wall between the pulmonary veins. Improvement in haemodynamics over time was not significantly better in the Cardioblate group compared to the control group. However, our study population was diverse in terms of AF duration and pre-existing persistent or permanent AF is likely to result in 75% of patients being in normal SR at 1-year follow-up. More than 60% of patients in SR will have restoration of effective left atrial contraction, especially if they have non-rheumatic pathology and if not very long-standing permanent AF preoperatively. Our practice was to do a biatrial ablation pattern, as well as to use the bipolar device with ‘double ablation’ in the presence of epicardial fat and the monopolar device for the lines to the annulus of the mitral and tricuspid valves.

Acknowledgements

We would like to thank Mr P. O’Keefe, RN D. Banner and J. Evans for their assistance in this study.

References


Appendix A. Conference discussion

Dr D. Pagano (Birmingham, UK): Impressive study in terms of results for the atrial fibrillation ablation particularly in a mixed group of patients as you operated on.

I, thus, have a number of questions and a number of points or comments to raise.

The first point is that the study includes a very small number of patients. So I’m intrigued to see how you actually powered the study beforehand.

And more importantly, what kind of randomisation schedule did you use? Because it appears that you managed to have two populations which are comparable for the surgical procedure even for aortic valve, the need for aortic valve replacement.

Dr von Oppell: We assumed a significance of 5% and power of 80%, which called for a minimum group size of 23 patients, and after continuity correction a recommended size of 28 patients in each arm of the study.

Recruitment of patients into the trial was quite difficult, as we had already established our centre as a centre for the treatment of atrial fibrillation and had over 100 patients in this period specifically referred for atrial fibrillation surgery. At the end of 3 years, we closed the trial.

Dr Pagano: But what power were you using? What difference were you expecting?

Dr von Oppell: We powered the study to have in the control group 20%, and in the study group a 55% success rate of conversion to sinus rhythm. In terms of the randomisation, this was computer-generated randomisation sealed in blinded envelopes prior to the commencement of the study, and the blinded envelopes were only opened at the time of surgery.

Dr Pagano: Okay. The next point is, it appears that a class III antiarrhythmic in particular amiodarone, was used in the control group only if those patients were in sinus rhythm at the time of surgery.

Now, some people may argue that if you want to treat the control group the same, there should be an aggressive antiarrhythmic during the same period of time, and you perhaps should use cardioversion schedules for all the patients at the same time. Any comment on that?

Dr von Oppell: Every patient who remained in atrial fibrillation post procedure underwent internal cardioversion at the time of surgery.

If they failed internal cardioversion and remained in atrial fibrillation, the chances of converting these patients, who have not had a Maze procedure, into normal sinus rhythm is virtually negligible.

Therefore, in these patients, many of them quite old patients, we elected to not give them amiodarone if they failed the internal cardioversion at the time of surgery.

Dr Pagano: So that brings us to the next question. Can you clarify, what was the predefined protocol to use DC cardioversion? You have may said it, someone, on the slides from the presentation earlier, for the control and for the non-control groups.

Dr von Oppell: The protocol was for patients in both groups if they were in normal sinus rhythm and subsequently reverted to atrial fibrillation, to undergo electrical cardioversion.

We had an equal number of patients in both groups having DC cardioversion if they went back into atrial fibrillation.

However, the defining point in the control group was that the patient must have at least reverted to sinus rhythm by internal cardioversion at the time of surgery.

Dr Pagano: Holter monitoring seems to be used quite sparingly in these patients, and some people may argue that particularly if you intend to stop the warfarin, Holter monitoring is important. And some people, like us, for instance, we use 72-h Holter monitoring. Do you want to add any comments to that?

Dr von Oppell: I fully agree with you. The problem in the study population was the distance to our centre for some of the patients. If there was any warfarin, Holter monitoring is important. And some people, like us, for instance, we use 72-h Holter monitoring. Do you want to add any comments to that?
Therefore doing a Maze procedure, even if you are putting in a mechanical valve, may have some advantages.

However, in our population, as elsewhere, our patients are becoming older and older, so biological valves are becoming the norm. And if you can maintain them in sinus rhythm, so much the better.

**Dr Pagano**: One more point. The conversion rate of patients in AF without ablation is actually quite high despite the fact that you did not use amiodarone and despite the fact that you were not aggressive.

That brings me to the point, any comment on that? Could you have achieved better if you had been more aggressive in that group with antiarrhythmics and AF?

**Dr von Oppell**: In the literature, the control group should have had a conversion rate of about 20% at 1 year, and ours was significantly higher than the literature.

I think it was due to two things, one, the aggressive rhythm control strategy as well as removing the left atrial appendage which has also been shown to assist in maintaining sinus rhythm.

I do not believe, if we had given amiodarone to the control group that failed internal cardioversion and came out of surgery in atrial fibrillation, that it would have changed our results.

**Dr I. Tzanavaros** (Cottbus, Germany): You did not find any difference in secondary end points, survival or thromboembolic events. Can you, please, comment on that?

**Dr von Oppell**: No, we had no difference in secondary end-point survival and thromboembolism. However, in terms of the risk of thromboembolism, all patients were anticoagulated. At the close of the study at 1 year, we still had about 70% and 80% of each patient group on warfarin anticoagulation.

Excluding patients in each group in atrial fibrillation or with mechanical valves, there were still at least 5 patients in each group in sinus rhythm who were taking warfarin prophylactically because the referring physician was still reluctant to withdraw warfarin. In addition our protocol was to first withdraw the amiodarone, and wait for 3 months before then withdrawing the warfarin to make sure that there was no relapse after withdrawal of the antiarrhythmic medication.