A modified Cox maze IV procedure: a simpler technique for the surgical treatment of atrial fibrillation

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OBJECTIVES: To determine the effectiveness of a simplified surgical treatment method for atrial fibrillation (AF).

METHODS: Between September 2012 and October 2013, 120 patients (mean age, 52.3 ± 8.8 years) underwent valve surgery and concomitant bipolar radiofrequency ablation for the treatment of AF. Patients were randomized to a Cox maze IV procedure (CMP-IV) group (n = 60) or a modified CMP-IV (MCMP-IV) group (n = 60). Freedom from AF was defined as freedom from any left atrial arrhythmia lasting <30 s and no requirement of antiarrhythmic drugs after 6 months. Data were recorded at postoperative follow-up examinations, which were scheduled at 1, 3, 6 and 12 months, and annually thereafter.

RESULTS: No ablation-related complications occurred in either group. The mean ablation time was longer in the CMP-IV group than in the MCMP-IV group (18.5 ± 1.7 vs 16.6 ± 1.6 min, P < 0.001). The mean follow-up time was 32.4 ± 3.6 months (range, 26–39 months).

Freedom from AF tended to be higher, but not significantly so, among the MCMP-IV group than among the CMP-IV group over the entire follow-up period.

CONCLUSIONS: The MCMP-IV is an effective surgical procedure for the treatment of AF. In certain patients, such as those with anatomic variations of the pulmonary veins, the MCMP-IV is simpler than the CMP-IV. CLINICAL TRIALS REGISTRATION ID: ChiCTR-TRC-12002742.

INTRODUCTION

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in clinical practice, with an estimated prevalence rate of 0.4–1% in the general population [1, 2]. The prevalence rate of AF increases with age, from 0.5% at the ages of 50–59 years to almost 9% at the ages of 80–89 years [3]. Approximately 50% of patients who have mitral valve disease also have AF [4]. The crude rate of AF prevalence is 0.77% in China, where it affects about 10 million patients [5, 6]. AF is associated with an increased risk of stroke, aggravation of heart failure and an increased risk of overall mortality [7, 8].

The maze procedure was developed by James Cox in 1987. Since then, two improvements to the original technique have led to the Cox maze III procedure (CMP-III), which has become the gold standard for the surgical treatment of chronic AF [9]. However, the complexity of this procedure has limited its adoption by cardiac surgeons. In recent years, the development of alternative energy sources has enabled surgeons to create lines of ablation that replace most incisions of the CMP-III. This has simplified the procedure and led to the establishment of the Cox maze IV procedure (CMP-IV) [10], in which bipolar radiofrequency devices are commonly used as an alternative energy source.

In our clinical experience, the CMP-IV still has areas for improvement. For example, avoiding the dissection around the pulmonary veins (PVs) may reduce the risk of rupture that is caused by their blunt dissection, especially in some patients with PV anatomic variations or partial adhesion of the left atrial (LA) posterior wall. Another potential improvement is that single-layer ablation can be used for each of the lesion sets, which reduces the thickness of the ablated tissues and can improve the transmurality of the lesions. We termed this new procedure the modified Cox maze IV (MCMP-IV) procedure. This study was conducted to determine the effectiveness of the MCMP-IV.

MATERIALS AND METHODS

Study design

A randomized, prospective study was conducted on patients who had AF for more than 6 months and were undergoing valvular
The study was approved by the ethics committee of West China Hospital, Sichuan University (2012 183). The trial was registered with the Chinese Clinical Trial Register (ChiCTR-TRC-12002742). Patients were enrolled between September 2012 and October 2013 at the West China Hospital of Sichuan University, Chengdu, China. Written informed consent was obtained from each participant preoperatively, and all research was performed in accordance with the Declaration of Helsinki. All procedures for this trial were performed by one experienced surgeon (Ying-qiang Guo).

The exclusion criteria were as follows: LA diameter >60 mm, pregnancy, history of cardiac surgery via the median sternotomy approach, requirement of additional coronary bypass surgery, age <18 years, severe tricuspid regurgitation and the patient being unwilling or feeling unable to complete the follow-up.

Patients were randomized to either the CMP-IV group or the MCMP-IV group in a 1:1 ratio using computer-generated randomization. The surgical procedures were performed with irrigated bipolar radiofrequency clamps (Cardioblate BP2, Medtronic Inc., Minneapolis, MN, USA). Amiodarone (200 mg orally, once daily) was used postoperatively for 3 months with QTc monitoring.

Surgical technique

A median sternotomy and moderate hypothermic cardiopulmonary bypass with bicaval cannulation were performed. The right atrium (RA) and interatrial septum were incised to manage the mitral and tricuspid valves. After cardioplegic arrest, we created the LA lesion set. The lesion lines were ablated 4–6 times before the valve procedure was performed. The ligament of Marshall was dissected in patients from both groups. The RA lesion set was not performed in this study.

The CMP-IV LA lesion set has been described by Reddy et al. [10]. The right and left PVs were bluntly dissected and contained the following lesions (Fig. 1A): PV ablation (left-sided and right-sided PVs separately), interconnecting lesions between the superior PV pairs, left atrial appendage (LAA) surgical resection, a lesion from the left upper PV to the rim of the LAA, interconnecting lesions between the inferior PV pairs and a connecting lesion from the right lower PV to the mitral annulus.

The MCMP-IV LA lesion set was similar to the CMP-IV, except that it did not require the isolation of the PVs, and each lesion was achieved using single-layer ablation. The MCMP-IV contained the following lesions (Figs 1B and 2): ablation of the anterior wall of the right-side PV through a small incision of the superior right PV antrum, interconnecting lesions between the superior PVs (LA roof line), LAA surgical resection, a connecting lesion from the LAA to the LA roof line, a lesion of the anterior wall of the left-side PVs through the LAA incision, interconnecting lesions between the inferior PVs and a connecting lesion from the PV to the mitral annulus.

Postoperative care and follow-up

Both groups were given the same postoperative care. All patients received amiodarone (200 mg/day, orally) for 3 months. Patients who were in AF at the completion of the surgical procedure underwent immediate cardioversion. Those who remained in AF at 7 days to 6 months underwent cardioversion at those times. If atrial arrhythmia persisted after 6 months or the patient was unable to tolerate amiodarone, a rate-control strategy was used; metoprolol was used to control ventricular rate, maintained between 70 and 100 bpm. Warfarin was administered orally to maintain the international normalized ratio at 1.5–2.5.

Freedom from AF was defined as freedom from any LA arrhythmia lasting <30 s for 24 h Holter electrocardiography (ECG) or freedom from AF or atrial flutter for 12-lead ECG, and no requirement for antiarrhythmic drugs after 6 months. Follow-up information was obtained from office visits at the outpatient clinic. Postoperative follow-ups were scheduled at 1, 3, 6 and 12 months, and annually thereafter. Follow-up appointment included the administration of a questionnaire and 24 h Holter ECG at 12 months or 12-lead ECG at other time points. Patients underwent transthoracic echocardiography (TTE) annually. The data recorded included the following: 24 h Holter ECG, 12-lead ECG, TTE, current medications and recent complications. The patients were offered free 24 h Holter ECG, 12-lead ECG, TTE and INR.

Statistical analysis

Standard descriptive statistics were applied. Continuous data have been presented as means and SDs, and the Student two-sample t-test was used to compare differences in continuous data between

Figure 1: (A) Cox maze IV and (B) modified Cox maze IV procedure lesion sets.
the two groups. The Pearson \( \chi^2 \) test was applied to analyse differences in success rates between the two groups. All statistical tests were treated as two-sided and were evaluated at a significance level of 0.05. Statistical analysis was performed using the statistical software IBM SPSS 20.0 (IBM, Chicago, IL, USA).

**RESULTS**

**Patients**

Between 2012 and 2013, 120 patients were enrolled in the study and were randomized to two groups (Table 1). Preoperatively, there were no significant differences in sex, age, New York Heart Association class, AF duration, LA diameter or AF type between the two groups.

**Operative results, morbidity and mortality**

The lesion sets were performed completely in all patients. No ablation-related complications occurred in either group. Valve surgery procedures were similar in both groups. The mean ablation time was longer in the CMP-IV group than in the MCMP-IV group (18.5 ± 1.7 vs 16.6 ± 1.6 min, \( P < 0.001 \)). Cardiopulmonary bypass time, operative time, length of intensive care unit stay and postoperative hospital stay did not significantly differ between the two groups (Table 1).

There were no deaths during the in-hospital or follow-up periods. In the CMP-IV group, 1 patient had low cardiac output; after 40 postoperative days of supportive treatment, she was discharged from the hospital and returned home; 1 patient underwent a redo surgery because of a sternal infection. There were no additional complications related to the ablation procedures, and no patient required the implantation of a permanent pacemaker.

**Follow-up**

Follow-up data were available for all the patients. The mean follow-up time was 32.4 ± 3.6 months (range, 26–39 months). Freedom from AF was higher, but not significantly so, in the MCMP-IV group than in the CMP-IV group over the entire follow-

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**Table 1: Patient characteristics**

<table>
<thead>
<tr>
<th>Group</th>
<th>CMP-IV (n = 60)</th>
<th>MCMP-IV (n = 60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male/female</td>
<td>14/46</td>
<td>18/42</td>
<td>0.96</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.2 ± 9.1</td>
<td>52.3 ± 8.7</td>
<td>0.56</td>
</tr>
<tr>
<td>Mean NYHA class</td>
<td>2.93</td>
<td>2.93</td>
<td>1.00</td>
</tr>
<tr>
<td>AF duration (months)</td>
<td>37.5 ± 14.6</td>
<td>39.1 ± 15.5</td>
<td>0.56</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>51.13 ± 6.23</td>
<td>53.87 ± 7.21</td>
<td>0.12</td>
</tr>
<tr>
<td>Disease aetiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RHD</td>
<td>58</td>
<td>56</td>
<td>0.81</td>
</tr>
<tr>
<td>Non-RHD</td>
<td>2</td>
<td>4</td>
<td>0.81</td>
</tr>
<tr>
<td>Type of AF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>6</td>
<td>6</td>
<td>1.00</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>54</td>
<td>54</td>
<td>1.00</td>
</tr>
<tr>
<td>Surgical procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVR + maze</td>
<td>44</td>
<td>44</td>
<td>0.81</td>
</tr>
<tr>
<td>AVR + maze</td>
<td>2</td>
<td>4</td>
<td>0.81</td>
</tr>
<tr>
<td>DVR + maze</td>
<td>14</td>
<td>12</td>
<td>0.81</td>
</tr>
<tr>
<td>RFT (min)</td>
<td>18.5 ± 1.7</td>
<td>16.6 ± 1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCT (min)</td>
<td>80.0 ± 23.7</td>
<td>79.3 ± 26.0</td>
<td>0.67</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>115.1 ± 31.7</td>
<td>109.9 ± 31.7</td>
<td>0.53</td>
</tr>
</tbody>
</table>

The main goal of our study was to evaluate the effectiveness of a simpler and more effective surgical treatment for AF. Although the CMP-III has been the gold standard for the treatment of AF, its complexity and high rate of postoperative haemostasis have prevented its widespread clinical use [11]. To simplify the procedure, most of the traditional incisions have been replaced with alternative energy sources. Radiofrequency bipolar ablation may be the most widely used device in surgical AF therapy. The bipolar clamps limit the energy between the two clamps and can achieve reliable transmural lesions and avoid damage to the surrounding tissue [12]. This ablative procedure—the CMP-IV [13]—has a success rate of freedom from AF that has been shown to vary between 51 and 86% at the 1-year follow-up [14]. Here, we evaluated the effectiveness of a modified CMP-IV procedure—the MCMP-IV. Our findings show that the modified procedure is associated with a significantly reduced mean ablation time and a strong trend towards an increased duration of freedom from AF.

Previous studies have shown that the success rate of the CMP-IV is affected by two important aspects. First, the box lesion should be performed in all patients undergoing the CMP-IV to isolate the LA posterior wall and the PVs. Many studies have suggested that the LA posterior wall plays an important role in the initiation and maintenance of AF [15]. Isolation of the LA posterior wall and the PVs leads to better results than does isolation of only the PVs, and its use has been supported by a number of retrospective and prospective studies [16–19]. In a prospective randomized study of radiofrequency catheter ablation for persistent AF, 83.3% of patients who underwent the LA posterior wall lesion set were found to have normal sinus rhythm at the 1-year follow-up, while the corresponding number among patients who underwent PV isolation alone was only 63.3%. Haissaguerre et al. [20] showed that 94% of foci were in the PVs, suggesting that the PVs are the main AF-triggering source; indeed, PV ablation is the cornerstone of AF ablation. Failure to create transmural lesions may result in recovery of PV conduction, which is the major determinant of clinical AF recurrence [21]. The transmurality of the lesions is affected by the thickness of the myocardium; the thicker the myocardium, the harder it is to achieve transmural lesions [22]. An electrophysiological study of recurrent atrial tachyarrhythmias in patients who had undergone video-assisted thoracoscopic bilateral PV isolation showed that PV gaps were present in the majority of patients with failure of this surgical procedure [23]. Interestingly, all residual PV gaps were distributed in the roof or the bottom of the PV antrum; however, the reason for this is unclear. One possible explanation is that the PV antrum tissue may be thicker at the turnover site of the roof or bottom. An alternative explanation is that, compared with other sites, the PV antrum and thus the turnover site cannot be tightly and completely clipped by the bipolar clamps.

In August 2011, a patient was scheduled to undergo the CMP-IV; however, during surgery, an anatomic variation was identified in the left PVs, which meant that the bipolar clamps could not pass over and clamp the left PVs. This marked the first time that the MCMP-IV was performed. The PV anterior wall and the LA posterior wall were isolated as an entire box in this patient. Subsequently, 2 other patients underwent the same surgical procedure. One of the 2 patients had an enlarged LA (76 mm) and PVs, and the bipolar clamps were not long enough to completely clip the two PVs; however, the patient was willing to undergo the maze procedure. The other patient had partial adhesion of the LA posterior wall. We performed the same surgical procedure. All 3 patients were converted to sinus rhythm. In addition, good results have been achieved even in patients with LA enlargement. In summary, we have found that in certain patients (e.g. those with anatomic variations of the left PVs), the modified surgical procedure is more straightforward and effective than the CMP-IV.

Through the above discussion and our clinical experience, we concluded that the CMP-IV still had room for improvement. One improvement is that the box lesion set can be achieved with four ablation lines, namely, the anterior walls of the left- and rightsided PVs, interconnecting lesions between the superior and inferior PVs and ablation lines that isolate the PVs and LA posterior wall as an entire box. Thus, the dissection around the PVs is prevented, which may reduce the risk of PV rupture caused by blunt dissection, especially in patients who have PV anatomic variations or partial adhesion of the LA posterior wall. Another improvement is that each of the lesion sets involves single-layer ablation, which reduces the thickness of the ablated tissues, can improve the transmurality of the lesions and may also improve the surgical procedure for the treatment of AF.

RA lesions are perhaps important for late atrial flutter, but some studies indicate that RA lesions do not improve the success rate of AF surgery, but do increase the rate of pacemaker implantation [24]. In our institution, right lesions are made only in patients with severe right heart disease, such as severe tricuspid regurgitation. Such patients were excluded from our study. During follow-up, both groups achieved good results at each time point, illuminating the fact that right-sided lesions may not always be needed in patients with mainly left heart disease.

In the present study, the mean ablation time was significantly longer in the CMP-IV group than in the MCMP-IV group; this indirectly reflects that the MCMP-IV is easier to perform. The rate of freedom from AF in the MCMP-IV group was slightly, but not...
significantly, higher than that in the CMP-IV group. Our findings show that the MCMP-IV was at least as efficient as the CMP-IV.

**Limitations**

Because bipolar ablation devices are inadequate for fully ablating the LA isthmus, performing unipolar ablation of the LA isthmus is more reasonable. However, most patients cannot afford this procedure due to its high costs. Therefore, in our institution, unipolar ablation is not routinely performed.

Rhythm success was determined by a 12-lead ECG except for the 12-month time point (24 h Holter ECG). This allowed for excellent follow-up rates but had the risk of underdetection of arrhythmias and therefore overestimation of success rates. Also, as the mean age of the patients was relatively young, it may affect the results.

**CONCLUSION**

The MCMP-IV is an effective surgical procedure for the treatment of AF. It is simpler than the CMP-IV in certain patients, such as those with anatomic variations that prevent clipping or clamping of the PVs. Our findings suggest that the MCMP-IV may be at least as effective as the CMP-IV for the treatment of AF.

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**Conflict of interest:** none declared.

**REFERENCES**


