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The Impact of Previous Catheter-Based Ablation on the Efficacy of the Cox-Maze IV Procedure

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Abstract

Background—Failed catheter-based ablation for the treatment of atrial fibrillation is an indication for the Cox-Maze procedure. Many patients are referred for the Cox-Maze IV procedure with recurrent atrial fibrillation following a previous catheter-based ablation, but the efficacy and safety of surgical management in these patients remains unclear.

Methods—Data were collected prospectively on 129 consecutive patients who underwent a stand-alone Cox-Maze IV procedure. Patients were grouped by the presence ($n = 61$; 47%) or absence ($n = 68$; 53%) of previous catheter ablation history. Follow-up was conducted at 3, 6, and 12 months (94% complete, mean 15.1 ± 15.6 months) with electrocardiograms and 24-hour Holter monitoring.

Results—In patients with no ablation history compared to those with, freedom from atrial tachyarrhythmias and antiarrhythmic drugs were similar at 3 months (73% vs 67%), 6 months (85% vs 83%), and 12 months (81% vs 87%); $p < 0.05$ for all. Those who had failed previous catheter ablation had significantly smaller left atria, longer durations of atrial fibrillation, and were more likely to have persistent atrial fibrillation compared to the group without prior ablation history. All analyzed baseline patient characteristics and comorbidities were similar between the groups. No differences were found in complication rates or surrogate measures of operative difficulty.

Conclusion—The Cox-Maze IV procedure is safe and effective in treating recurrent atrial fibrillation regardless of previous catheter ablation history. Surgical management should be considered in patients who have failed catheter ablation for the treatment of their atrial fibrillation.

Keywords

Ablative therapy; Atrial fibrillation/flutter; Surgical techniques; Outcomes

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Introduction

Atrial fibrillation (AF) is estimated to affect 2.7 to 6.1 million people in the United States alone and its incidence continues to rise. While hemodynamic compromise and tachycardia-induced cardiomyopathy impart significant morbidity and mortality, stroke remains the most feared complication of AF. The risk of stroke is increased by 4 to 5-fold with AF, and almost a quarter of strokes in octogenarians are attributable to AF.[1] Drug-refractory AF is managed by either catheter-based or surgical ablation therapy. One of the most effective techniques in the management of symptomatic drug-refractory atrial fibrillation (AF) originated in the operating room with the introduction of the Maze procedure (CMP) by Dr. Cox at Washington University in 1987.[2,3] Iterative improvements to the procedure have culminated in the current CMP-IV procedure which utilizes bipolar radiofrequency and cryotherapy to recreate the original lesions with linear ablation lines while maintaining the procedural efficacy.[4-8]

The advancements in ablation technology have not been restricted to the surgical arena and multiple technologies now allow for catheter-based percutaneous endocardial ablation. Following Haissaguerre's initial reports on the role of pulmonary veins in AF initiation, innovations in three-dimensional mapping systems and evolving ablation strategies have resulted in widespread adoption of this treatment modality.[9-14] Consequently, the less invasive catheter ablation has become the interventional treatment of choice for many patients with symptomatic and drug-refractory lone AF, relegating surgical ablation for patients who have failed one or more catheter ablation, who are not candidates for catheter intervention, or who prefer a surgical approach.[15]

Results of catheter ablation, however, continue to remain variable and certain patient subgroups, particularly patients with longer duration AF, persistent AF or large atria, have done poorly.[16-18] This has led to a number of patients being referred for surgery following previously failed catheter ablation. However, data documenting the outcome of surgical ablation in these patients is limited. In this report, prospectively collected data was analyzed to evaluate the long-term results of a stand-alone CMP-IV in patients with a history of at least one previous catheter-based ablation (PCBA) for AF or atrial flutter.

Patients and Methods

This study was approved by the Washington University School of Medicine Institutional Review Board. Informed consent and permission for release of information were obtained from all patients. Between January 2002 and December 2011, 129 patients underwent a stand-alone CMP-IV for the treatment of AF. Of these patients, 61 had a history of one or more PCBA with a mean of 2.2 ± 1.2 and range of 1 to 5 ablative procedures per patient. Outcomes for these patients were compared to 68 patients without PCBA.

Surgical Technique

All procedures were performed by one of two surgeons (R.J.D. and H.S.M.) via either a median sternotomy or a right mini-thoracotomy utilizing cardiopulmonary bypass. The CMP-IV has been previously described in detail.[19] Prior to 2005, the linear ablation connecting the left and right superior pulmonary veins (roof line) to form the box lesion, was performed selectively in patients with large atria. Our group has since recognized the importance of isolating the entire posterior left atrium, and the box lesion has routinely been performed in all patients starting in 2005.[20] Schematics of the lesions sets are shown in Figures 1-2. All patients underwent intraoperative transesophageal echocardiography and cardioversion as needed after the presence of a left atrial appendage thrombus was excluded. For PCBA patients, exit block of individual pulmonary veins was assessed before and after

any surgical ablation. In patients undergoing a right mini-thoracotomy, testing was performed for the right pulmonary veins only. Exit block was not assessed with respect to the posterior left atrium as the box lesion was performed on the arrested heart in all cases.

Follow-up

Follow-up was conducted at 3, 6, and 12 months and annually thereafter. At each visit a history, a physical examination, and electrocardiogram were obtained. Since 2006, in accordance with the updated Heart Rhythm Society guidelines, 24-hour Holter monitoring and/or pacemaker interrogation was obtained routinely.[21] In this series, 72% of patients received prolonged monitoring during the first year of follow-up. Patients were considered a success if they were free of both antiarrhythmic medications and atrial tachyarrhythmias (ATAs) defined as any episode of AF, atrial flutter, or atrial tachycardia lasting longer than 30 seconds after the initial 3 month blanking period.

Statistical Analysis

Patients were divided into two groups depending on whether they had undergone previous catheter-based ablation (PCBA) or were never ablated (NA). Continuous variables were expressed as mean $\pm$ one standard deviation and were compared using the unpaired t-test (if distribution was Gaussian) or the Mann-Whitney test (if distribution was non-Gaussian). For categorical data, the Fisher's test was used for comparison between two groups, and the Chi-squared test for multiple groups. In all cases, a p-value < 0.05 was considered to be statistically significant. All statistical analyses were performed using InStat 3.0, (GraphPad Software Inc., La Jolla, CA).

Results

Follow-up at 3, 6, and 12-months was 94% complete with a mean duration of 15.1 ± 15.6 months. No differences in freedom from ATAs was seen between the two groups at any time interval. Freedom from ATAs indiscriminate of the use of antiarrhythmic drugs is demonstrated (Figure 3A). Figure 3B demonstrates freedom from both ATAs and antiarrhythmic drugs which were also no different between the two groups at any time point.

Patient Characteristics

Patient characteristics are shown in Table 1. Baseline characteristics of both groups with respect to demographics and comorbidities were similar. Comparing parameters specific to AF, failed PCBA patients had smaller left atrial diameters, AF of longer duration, and less likely to have paroxysmal AF when compared to the NA group.

Intraoperative Parameters

Table 2 summarizes the intraoperative parameters examined. No differences in operative approach or procedural time were seen between the two groups. The box lesion set, which isolates the posterior left atrium, was performed in significantly fewer of the NA group compared to the PCBA group. This reflects the increasing number of the patients receiving catheter-based ablations since 2005.

Pulmonary Vein Isolation Statistics

Of the 196 individual pulmonary veins tested for exit block, only 69 (35%) were found to be electrically isolated. Moreover, in 41 patients where all four pulmonary veins were available for testing, complete electrical isolation of all pulmonary veins was confirmed in only 8 (20%) patients. There was no difference in the isolation rates of any given pulmonary vein. All four pulmonary veins could not be tested in patients who underwent the CMP-IV via a

right mini-thoracotomy approach and testing was also not possible if cardioversion to sinus rhythm could not be achieved due to persistent AF or the presence of intra-atrial thrombus. (Table 3)

Postoperative Results

Postoperative variables are summarized in Table 4. Compared to NA, PCBA patients had shorter hospital and intensive care unit lengths of stay. Total blood product requirements were significantly higher in NA patients. There was one 30-day mortality in the NA group and one postoperative stroke in the PCBA group, but no significant differences in complication rates between the two groups were detected. Requirement for new postoperative permanent pacemakers was similar. The vast majority of patients were discharged directly home in both groups.

Comment

While improvements in catheter-based ablation strategies have been made during the past decade, the single procedural success rates of catheter ablation in patients with paroxysmal and non-paroxysmal AF have been variable and as low as 20% in a recent meta-analysis. [22] The recent findings from the FAST-2 trial have further clarified patients whose AF is difficult to treat percutaneously which include patients with dilated left atria, hypertension, and failed PCBA.[16] In the present study of highly selected patients after failed PCBA, only a third of pulmonary veins tested intraoperatively demonstrated exit block. In addition, all four pulmonary veins in a given patient were isolated even less frequently. While the mechanism behind AF recurrence following PCBA cannot be determined definitively in these patients, it is likely that the inability of catheter-based procedures to create durable, transmural, electrical isolation is at least partially responsible for the recurrent AF. As a surgical procedure on the arrested heart, the prominent advantage of the CMP-IV over catheter ablation is its ability to reliably create extensive, linear, transmural lesions.[23-25]. The lesion set of the CMP-IV remains based upon the CMP-III whose extensive biatrial lesion set creates atria that are incapable of sustaining AF in the majority of patients.[25] This investigation is the largest to date examining the success of the stand-alone CMP-IV in patients who have failed one or more PCBA. The principal finding of this study is that the efficacy of the CMP-IV is not affected by a history of previous failed catheter ablation and a high success rate between 80-90% is maintained at 12 months.

A hypothesis of this investigation was that previous catheter ablations would increase the difficulty and morbidity of subsequent. There was a theoretical concern that catheter ablations, although endocardially performed, could render surgical dissection of the pulmonary veins and posterior left atrium more difficult. It was also possible that the previous ablations, particularly when multiple, would predispose patients for greater postoperative arrhythmias as suggested by others, or increase the need for permanent pacemakers.[26] This study failed to identify any surrogate measure (operative times, transfusion requirements, use of minimally invasive approaches) as indicative of increased operative difficulty or complexity. Complication rates, including the need for a new postoperative permanent pacemaker were similar in both groups.

The average length of postoperative hospital stay for patients undergoing a stand-alone CMP-IV was 9 ± 6 days in this series. While intensive care unit and hospital stay durations were longer in the NA group, this may be a result of the changing management strategies for CMP-VI patients postoperatively. When compared to NA patients, PCBA patients are a more recent group of patients being referred for AF surgery and are likely benefitting from the streamlining of postoperative care with respect to pacing management, anticoagulation, and transfusion protocols that continue to evolve and result in shorter lengths of stay.

This study has a number of potential limitations. The heterogeneity in the PCBA could not be accounted for as the precise details of catheter ablations were not available for each patient. The box lesion which isolates the posterior left atrium and plays a key role in preventing AF recurrence was not performed in patients earlier in the series and may unfairly bias the results of NA patients with regard to efficacy of their AF treatment.[20] Many of the pulmonary veins in a significant portion of the PCBA group remained untested due to limitations by surgical approach (right mini-thoracotomy) or the presence of left atrial thrombus (n = 1). While this has an impact on the sampling bias of the study, the data remain significant by elucidating the problem of incomplete electrical isolation by PCBA. This is the largest study of its kind, but may still be underpowered to detect small differences in complication rates which are low after a stand-alone CMP-IV. This study also focuses on a highly selective population of recurrent AF patients with relatively few comorbidities, and its results may not be generalizable to all AF patients or those with concomitant structural heart disease.

In conclusion, despite the concern that failing PCBA may select out patients that are more refractory to treatment or more likely to have perioperative complications, the CMP-IV maintains its efficacy in these patients. PCBA, furthermore, does not appear to affect the morbidity or procedural complexity when performing a CMP-IV. The CMP-IV is both safe and efficacious in patients who have had one or more failed PCBA, and such history should not be a deterrent to consideration for surgical management of AF.

Discussion

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Paper presented by Hersh Maniar, MD, St. Louis, MO. maniarh@wudosis.wuslt.edu

Discussion by Richard Lee, MD, St. Louis, MO. rlee@slu.edu

Dr. R. Lee (St. Louis, MO): Hersh, this is a very nice series and an important contribution. If I saw your slides correctly the patients with prior catheter ablation were more likely to have a complete box isolation; is that correct?

Dr. Maniar: Correct.

Dr. Lee: So then obviously the question is: If all the patients had a complete box isolation, do you think there would be a difference between the two groups?

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Response by Hersh Maniar, MD, St. Louis, MO.

Dr. Maniar: It's a good question. The patients with PCBA were more frequent later in the series and as such are more likely to reflect the standardization of posterior left atrial isolation that occurred in 2005. That said, the numbers in the two groups in this series are small and hard to extrapolate from. Perhaps with more numbers we will be able to elucidate a difference.

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Paper presented by Hersh Maniar, MD, St. Louis, MO.

Discussion by Piotr Suwalski, MD, Warsaw, Poland. suwalski.piotr@gmail.com

Dr. P. Suwalski (Warsaw, Poland): I enjoyed this paper. Thank you very much. And just I have one question regarding the group after the EP. Have you seen, after opening the left atrium, any kind of lesion pattern morphologically?

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Response by Hersh Maniar, MD, St. Louis, MO.

Dr. Maniar: That's actually what prompted the interest in this investigation. Despite being an endocardial ablation, EP procedures do create a significant amount of both epicardial and endocardial scarring. So much so that is sometimes difficult to circumferentially dissect the pulmonary veins. As far as can we visualize lesions from previous catheter based ablations, the reality is, more often than not, most atria merely demonstrate wide scarring rather a particular pattern. Lastly, we don't typically alter our lesion sets based on any intraoperative assessment and perform our standard lesion set, regardless of a history of previous ablation.

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Paper presented by Hersh Maniar, MD, St. Louis, MO.

Discussion by H. Kenith Fang, MD, Phoenix, AZ. hkfang@gmail.com

Dr. H. Fang (Phoenix, AZ): We presented at HRS some data of a hybrid procedure that we did in Phoenix with 35 patients. All but one had previous percutaneous ablation. And of the percutaneous ablations, they had either 1 to 4. The interesting thing is that on all of these, when you look at all 4 veins, we had zero that had pulmonary vein isolation. Which is a concern for me, because as a surgeon I like to think that the lineal lines when we do a Cox-Maze IV is the reason why we're getting them out of atrial fibrillation. When there isn't pulmonary vein isolation, then the question becomes one of, well, is the failure of the percutaneous ablation because of the failure of pulmonary vein isolation or the addition of the linear lesion lines? Because as the EP, they can say, well, pulmonary vein isolation was inadequate, we have better technology now where we can get pulmonary vein isolation so therefore our results will be better in the future. Do you have a comment about that?

5. THE IMPACT OF PREVIOUS CATHETER-BASED ABLATION ON THE EFFICACY OF THE COX-MAZE IV PROCEDURE. Response by Hersh Maniar, MD, St. Louis, MO.

Dr. Maniar: Well, I think your comment is a good one but the reality is that it is hard to determine the mechanism of failure for patients with prior ablation. We do know from recent reports from EP literature, that there are significant limitations to pulmonary vein isolation, even when performed well. Many of our EP colleagues are more readily embracing the idea that PVI alone is not sufficient and linear lesions are necessary. The Cox-Maze IV works because of its ability to create transmural lesions and our results, reflect, our bias to perform a full lesion on nearly all patients undergoing arrhythmia surgery.

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Figure 1.
Right atrial lesion set.

Figure 2.
Left atrial lesion set.

Figure 3A.

Freedom from AF at 3, 6, and 12 months. AF = atrial fibrillation, PCBA = patients with previous catheter ablation, NA = patients who were previously never ablated. * denotes $p > 0.1$

Figure 3B.

Freedom from AF and AAD at 3, 6, and 12 months. AAD = antiarrhythmic drugs, AF = atrial fibrillation, PCBA = patients with previous catheter ablation, NA = patients who were previously never ablated. * denotes $p > 0.1$

Table 1

Baseline Characteristics

	NA (n = 68)	PCBA (n = 61)	p-value
Mean age (years)	58 ± 11	57 ± 11	0.65
Gender (% male)	74% (50)	77% (47)	0.68
BMI	31 ± 1	31 ± 6	0.45
NYHA Class III or IV	29% (20)	33% (20)	0.71
LVEF	51 ± 12	52 ± 13	0.45
Diabetes	7% (5)	13% (8)	0.38
PAD	7% (5)	3% (2)	0.45
Severe chronic lung dis	1% (1)	3% (2)	0.6
Previous stroke	19% (13)	10% (6)	0.21
Previous MI	9% (6)	3% (2)	0.28
LA diameter (cm)	5 ± 1.1	4.6 ± 0.8	0.02
AF duration (months)	74 ± 9	121 ± 12	< 0.0001
Persistent AF	57% (39)	79% (48)	0.01

BMI = body mass index, CRI = chronic renal insufficiency, dis = disease, LA = Left atrial, LVEF = left ventricular ejection fraction, MI = myocardial infarction.

Table 2

Operative Parameters

	NA	PCBA	p-value
Thoracotomy	24% (16)	31% (19)	0.43
CPB time (minutes)	131 ± 32	126 ± 30	0.34
Aortic XCT (minutes)	41 ± 12	44 ± 17	0.64
Box lesion performed	76% (52)	93% (57)	0.01

CPB = cardiopulmonary bypass, PVI = pulmonary vein isolation, XCT = crossclamp time

Table 3

Pulmonary Vein Exit Block Testing

PV	checked	isolated	%
Left Inferior	41	13	32
Left Superior	41	15	37
Right Inferior	55	16	29
Right Superior	55	22	40
All four PVs isolated	41	8	20

PV = Pulmonary vein. Chi-squared test of first four rows: $p = 0.64$.

Table 4

Postoperative Results

	NA	PCBA	p-value
Mean; median Hospital LOS (days)	11 ± 7; 8	8 ± 5; 7	0.02
Mean; median ICU LOS (hrs)	75 ± 71; 53	50 ± 40; 27	0.02
Mechanical ventilation duration (hrs)	14 ± 35	5 ± 4	0.59
Postoperative stroke	0	2% (1)	1
Pneumonia	4% (3)	3% (2)	1
Total blood products transfused (units)	2.3 ± 3.2	1.5 ± 3	0.14
30-day mortality	1% (1)	0	1
Early postoperative ATAs[*]	52% (35)	34% (21)	0.07
New postoperative PPM placement	4% (3)	5% (3)	1
Discharge location (% to home)	96% (65)	95% (58)	1

ARF = acute renal failure, ATA = atrial tachyarrhythmias, HD = hemodialysis, ICU = intensive care unit, LOS = length of stay, MI = myocardial infarction, PPM = permanent pacemaker

* within 30 days of surgery.