The effect of ablation technology on surgical outcomes after the Cox-maze procedure: A propensity analysis

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Supported in part by National Institutes of Health grants RO1-HL032257 and T32-HL007776. Ralph Damiano reports consulting and lecture fees from Atricure and Medtronic and grant support from Atricure.

Read at the Eighty-sixth Annual Meeting of The American Association for Thoracic Surgery, Philadelphia, Pa, April 29-May 3, 2006.

Received for publication April 27, 2006; revisions received Sept 22, 2006; accepted for publication Oct 9, 2006.

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J Thorac Cardiovasc Surg 2007;133:389-96 0022-5223/\$32.00

Copyright © 2007 by The American Association for Thoracic Surgery doi:10.1016/j.jtcvs.2006.10.009 **Objectives:** Since its introduction in 1987, the Cox-maze procedure has been the gold standard for the surgical treatment of atrial fibrillation. At our institution, this procedure has evolved from the cut-and-sew technique (Cox-maze III procedure) to one using bipolar radiofrequency energy and cryoablation as ablative sources to replace most incisions (Cox-maze IV procedure). This study compared surgical outcomes of patients undergoing the Cox-maze III procedure versus those of patients undergoing the Cox-maze IV procedure by using propensity analysis.

Methods: From April 1992 through July 2005, 242 patients underwent the Coxmaze procedure for atrial fibrillation. Of these, 154 patients had the Cox-maze III procedure, and 88 had the Cox-maze IV procedure. Logistic regression analysis was used to identify covariates among 7 baseline patient variables. Using the significant regression coefficients, each patient's propensity score was calculated, allowing selectively matched subgroups of 58 patients each. Operative outcomes were analyzed for differences. Late follow-up was available for 112 (97%) patients. Freedom from atrial fibrillation recurrence and survival was calculated at 1 year by using Kaplan-Meier analysis.

Results: The Cox-maze III procedure had significantly longer crossclamp times. There was no significant difference in intensive care unit and hospital stay, 30-day mortality, permanent pacemaker placement, early atrial tachyarrhythmias, late stroke, and survival. Freedom from atrial fibrillation recurrence was greater than 90% in both groups at 1 year.

Conclusions: The use of bipolar radiofrequency ablation has simplified the Coxmaze procedure, making it applicable to virtually all patients with atrial fibrillation undergoing concomitant cardiac surgery. The Cox-maze IV procedure produces similar surgical outcomes to the Cox-maze III procedure at 1 year of follow-up.

trial fibrillation (AF) affects more than 2.2 million persons in the United States, with an increased incidence within the elderly population.¹ The presence of AF is an independent risk factor for stroke. When compared with AF-free patients, there is a 5-fold increase in the incidence of stroke.² Even after adjusting for preexisting cardiovascular conditions, AF is associated with a 1.5- to 1.9-fold increase in mortality risk.³ Additional consequences of AF include increased hospitalizations, thromboembolic events, hemodynamic compromise, and decreased quality of life.⁴ In addition to the increased patient morbidity and mortality, AF is associated with significant hospital costs.⁵

The Cox-maze (CM) procedure was introduced in 1987. It is a set of atrial incisions aimed at interrupting the macrore-entrant circuits within the atrial tissue, which were believed to be the cause of AF.⁶ The final iteration of the procedure was the CM III procedure.⁷ Although the CM III procedure produced excellent results and was considered the gold standard for curing AF,^{8,9} its technical complexity

Abbreviations and Acronyms

AF = atrial fibrillation

CABG = coronary artery bypass graft

CM = Cox-maze

- ICU = intensive care unit
- NYHA = New York Heart Association
- RF = radiofrequency

prevented it from being incorporated in the daily practice of the majority of cardiac surgeons.

A variety of energy sources have been used to replace the incisions and simplify the CM III procedure, including unipolar and bipolar radiofrequency (RF), microwave, cryoablation, laser, and ultrasonography.¹⁰⁻¹⁸ At our institution, bipolar RF ablation was chosen to replace many of the CM incisions. Our preference for this energy source was based on experimental data from our laboratory showing that bipolar RF always created reliable transmural lesions, had short ablation times, and resulted in a focused delivery of energy that prevented collateral injury, enhancing the safety margin of ablation.¹⁰⁻¹² Early results in a multicenter trial showed bipolar RF ablation to safely and effectively electrically isolate atrial tissue.¹⁹ This newest version, the CM IV procedure, combined bipolar RF ablation and cryoablation to replace most of the incisions of the CM III procedure. In a small group of 40 patients, this new operation was found to be simpler and shorter than the CM III procedure, with equivalent short-term efficacy.²⁰ However, no direct comparison of matched patients undergoing the CM IV versus the CM III procedure has been performed. The objective of this study was to compare the outcomes of patients undergoing the CM IV procedure with propensitymatched cohorts from the historical CM III group.

Methods

From April 1992 through July 2005, 242 patients underwent the CM procedure for AF at Barnes-Jewish Hospital. Of these, 154 patients had the CM III procedure, and 88 had the CM IV procedure. Propensity score analysis was performed to select a matched control group of patients.

Propensity Score Analysis

The nonrandomness of procedure assignment was addressed by propensity matching to provide a more reliable assessment of outcomes based on procedure type. Logistic regression analysis was used to identify covariates among 7 baseline patient variables that were imbalanced in the 2 groups of interest (SPSS 11.0 for Windows; SPSS Inc, Chicago, Ill). Variables included age, sex, preoperative left ventricular ejection fraction, New York Heart Association (NYHA) classification, diagnosis of AF (persistent, permanent, or paroxysmal AF), duration of AF before surgical intervention, and type of operative procedure performed (lone CM, CM with a concomitant coronary artery bypass graft [CABG], or CM with a concomitant valve procedure with or without a CABG). Persistent AF was defined as continuous AF. Permanent AF was defined as persistent AF of more than a 6-month duration that had failed either electrical or chemical cardioversion. Paroxysmal AF was defined as sinus rhythm with intermittent episodes of AF. By using the significant regression coefficients, a propensity score was calculated for each of the 242 patients who underwent a CM III or IV procedure. The total population was ranked by propensity score, and the patients were closely matched on the basis of this score. The short- and long-term outcomes of the patients were blinded during the matching process. Resulting matched patients were analyzed for differences in selected early and late outcomes: crossclamp time, cardiopulmonary bypass time, intensive care unit (ICU) length of stay, hospital length of stay, 30-day operative mortality, postoperative permanent pacemaker placement, incidence of early tachyarrhythmias, late stroke, survival, and late recurrence of AF.

Surgical Technique

The surgical procedure for the CM III procedure has previously been described in detail.²¹ Most patients underwent a median sternotomy and cardiopulmonary bypass with bicaval cannulation. On the beating heart, right atrial incisions included excision of the right atrial appendage, followed by a free wall incision, a linear incision from the orifice of the superior vena cava to the orifice of the inferior vena cava, and a perpendicular, or T, incision to the level of the tricuspid valve annulus. A second incision to the tricuspid annulus was made from the right atrial appendage. At the tricuspid annulus, a 3-mm cryoprobe (Frigitronics CCS200, Trumbell, Conn) was applied.

The heart was arrested, and access to the left atrium was through a standard left atriotomy with amputation of the left atrial appendage. The remaining left atrial incisions included an atrial septal incision and encirclement of the pulmonary veins with extension to the mitral valve annulus. A cryoprobe was used between the appendage amputation site and the 2 ends of the pulmonary vein encircling the incision, as well as over the coronary sinus, and at the mitral valve annulus.

The bipolar RF system consisted of the ablation-sensing unit and the Atricure Isolator (n = 57; Atricure, Inc, Cincinnati, Ohio) or the Medtronic Cardioblate BP Surgical Ablation System (n = 1; Medtronic, Inc, Minneapolis, Minn). For the Atricure device, the energy was applied at 75 W and 750 mA between the jaws of the instrument. The generator continuously monitored voltage, current, temperature, and conductance. Tissue temperature was measured 1 mm from the electrode edge. Two seconds after conductance decreased to less than 0.025 siemens, an indicator light flashed, and an audible tone was heard, signifying full-thickness coagulation and termination of the ablation. Total ablation time and maximum tissue temperature were recorded for every lesion.

The Medtronic irrigated bipolar RF surgical ablation device consisted of a hand piece with embedded electrodes and an RF generator. The device was irrigated with saline solution to improve conduction of the delivered energy. The RF generator continuously monitored tissue impedance, current, voltage delivered, and the duration of ablation. Tissue was considered fully ablated when impedance reached a stable plateau. Initially, moderate power was applied to the tissue. The derivative of impedance (dZ/dt) was calculated every 200 ms. When impedance achieved a stable plateau, the power was increased by a step function of 5 W. If the plateau in impedance was not sustained, then the algorithm determined that transmurality had not been achieved, and ablation continued until another plateau in impedance was detected. This process was repeated until an impedance plateau was sustained after an increase in power. When this end point was reached, the microprocessor determined that transmurality had been achieved, and a signal was provided to the user.

The CM IV procedure differed from the CM III procedure because it isolated the right and left pulmonary veins as 2 islands, preserved the right atrial appendage, and in some cases left the posterior left atrium in electrical continuity with the remaining atrium.²² After either median sternotomy or right thoracotomy, patients underwent a pericardiotomy and were started on cardio-pulmonary bypass. If patients were not in normal sinus rhythm, intraoperative direct-current cardioversion was performed. Before the ablation procedure, the pacing threshold was recorded from the pulmonary veins. Bipolar RF ablations were completed around the right and the left pulmonary veins. After ablation, electrical isolation was confirmed by means of bipolar pacing at 20 mA from both the superior and inferior pulmonary veins. If atrial capture was present, the ablation was repeated until electrical isolation was achieved. The remainder of the operation has been described in a prior publication.²³

In summary, the right-sided lesions were created by making a simple atriotomy that extended from the intra-atrial septum to near the atrioventricular groove at the acute margin of the heart (Figure 1). All the other incisions of the traditional cut-and-sew method were replaced with bipolar RF ablation lines. Two cryolesions were placed at the tricuspid annulus by using a linear cryoprobe. The left-sided lesions involved only a simple atriotomy extending onto the dome of the left atrium and inferiorly around the orifice of the right inferior pulmonary vein. It intersected the encircling right pulmonary vein ablation. A connecting lesion was performed from the inferior aspect of the left atrium into the left inferior pulmonary vein. In atria larger than 5 cm in diameter, a second connecting lesion was placed from the superior aspect of the incision into the left superior pulmonary vein. A bipolar RF ablation line was performed from the inferior end of the incision down to the mitral annulus. A final cryolesion was placed at the mitral annulus with a 15-mm bell probe. The left atrial appendage was amputated, and a final bipolar RF ablation was performed between the left atrial appendage and the left superior pulmonary vein.

Postoperative Care and Follow-up

After the operation, all patients were monitored continuously for arrhythmias. Patients were started prophylactically on antiarrhythmic drugs, unless they were in heart block or junctional rhythm. The drug of choice was amiodarone, which was continued for the first 2 or 3 months postoperatively and then was discontinued if the patient was in normal sinus rhythm. If patients experienced postoperative atrial tachyarrhythmias, they were cardioverted between 1 to 4 weeks after the procedure. Unless there was a contraindication, all patients were anticoagulated with warfarin for the first 3 months, at which point it was discontinued if the patient was in normal sinus rhythm.

Follow-up for the patients in the CM III group consisted of a retrospective cross-sectional analysis performed in 2001. This

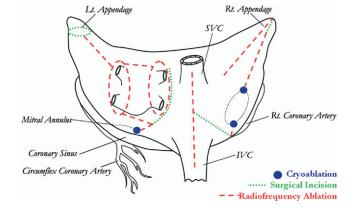


Figure 1. Cox-maze IV procedure lesion set. *Lt. Appendage*, Left atrial appendage; *SVC*, superior vena cava; *Rt. Appendage*, right atrial appendage; *IVC*, inferior vena cava; *Rt. Coronary Artery*, right coronary artery.

included a mailed questionnaire or telephone interview, as well as contact with either their cardiologist or primary care physician regarding recurrence of AF. In patients who complained of arrhythmia recurrence, copies of an electrocardiogram and Holter monitoring were obtained. Patients in the CM IV group were followed prospectively and had visits scheduled for 1, 3, 6, and 12 months postoperatively. Patients were then followed annually. At all follow-up visits, a history, physical examination, and electrocardiogram were obtained. For patients who could not return to our institution, telephone questionnaires were performed, and electrocardiograms were obtained from referring physicians to document the heart rhythm. In patients with symptoms of palpitations, an electrocardiogram or prolonged Holter recording (>24 hours) was obtained to assess their rhythm status.

Recurrence of AF was documented if a patient required a cardioversion or atrial ablation greater than 3 months after the procedure or the presence of AF was seen on prolonged Holter monitoring or electrocardiography. Any episode of recurrent AF after 3 months was classified as a permanent failure.

Data Analysis

Data were represented as frequency distributions and percentages. All continuous data were expressed as means \pm standard deviation. Categoric data were expressed as counts and proportions. Comparisons were done with paired, 2-tailed *t* tests for means of normally distributed continuous variables and the Wilcoxon rank sum test for skewed data. Fisher exact or χ^2 tests were used to analyze differences among the categoric data. Freedom from AF recurrence and survival was calculated at 1 year by using Kaplan-Meier analysis. Statistical analysis of data was conducted with the SPSS system for statistics (SPSS 11.0 for Windows, SPSS Inc).

Results

Patient Demographics

Five variables were not significant in the logistic regression analysis in predicting group assignment, including sex, pre-

Table 1. Preoperative clinical characteristics of the propensity-matched cut-and-sew (CM III) versus ablationassisted (CM IV) groups

Characteristic	CM III	CM IV
No. of patients	58	58
Age, mean \pm SD (y)	58 ± 11	60 ± 11
Male sex	34 (60%)	37 (63%)
Left ventricular ejection fraction, mean \pm SD	52 ± 10	48 ± 14
Preoperative diagnosis		
Persistent AF	1 (2%)	1 (2%)
Permanent AF (>6 mo)	29 (50%)	22 (38%)
Paroxysmal AF	28 (47%)	35 (61%)
Preoperative atrial fibrillation duration, mean \pm SD (y)	7.3 ± 7.0	7.1 ± 8.2
Operative procedure		
Lone Cox-maze	28 (49%)	29 (51%)
Cox-maze, concomitant CABG	14 (25%)	8 (14%)
Cox-maze, concomitant valve \pm CABG	16 (26%)	21 (36%)
NYHA classification		
Class I	17 (30%)	19 (32%)
Class II	26 (44%)	20 (34%)
Class III	11 (19%)	15 (27%)
Class IV	4 (7%)	4 (7%)

CM III, Cox-maze III procedure; *CM IV*, Cox-maze IV procedure; *SD*, standard deviation; *AF*, atrial fibrillation; *CABG*, coronary artery bypass graft; *NYHA*, New York Heart Association.

operative left ventricular ejection fraction, diagnosis of AF (persistent, permanent, or paroxysmal AF), duration of AF before surgical intervention, and type of operative procedure performed (lone CM, CM with a concomitant CABG, or CM with a concomitant valve procedure plus or minus a CABG). In contrast, the logistic regression analysis identified 2 variables, older age and a higher NYHA classification, as significant predictors for the performance of a CM IV procedure.

This process matched 58 of the 154 patients who underwent a CM III procedure with 58 of the 88 patients who underwent a CM IV procedure. Thirty of the 88 patients in the CM IV group were not able to be matched with the patients in the CM III group because their propensity scores were extreme outliers.

Selected preoperative patient characteristics for the CM III and CM IV groups are listed in Table 1. There was no significant difference between the 2 groups in age, sex, left ventricular ejection fraction, preoperative diagnosis (persistent, permanent, or paroxysmal AF), preoperative AF duration, operative procedure (lone CM, CM with concomitant CABG, or CM with concomitant valve and CABG), or NYHA classification. Late follow-up was available for 112 (97%) patients. Late follow-up was 100% in the CM IV group and 93% in the CM III group. Mean follow-up was

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Table 2. Early and late outcomes of the propensity matched					
cut-and-sew	(CM III)	versus	ablation-assisted	(CM	IV)
groups					

Variable	CM III	CM IV	P value
Mean crossclamp time (min)	121 ± 34	76 ± 37	<.001
Median intensive care unit stay (d)	2	2	.97
Median hospital stay (d)	10	9	.77
Pacemaker placement	9 (16%)	6 (10%)	.42
Early atrial tachyarrhythmias	27 (47%)	36 (61%)	.19
30-day mortality	1 (2%)	3 (5%)	.62
Freedom from atrial fibrillation*	96%	93%	.52
Late stroke	0%	0%	1.00

CM III, Cox-maze III procedure; *CM IV*, Cox-maze IV procedure. *Kaplan-Meier analysis at 1 year.

significantly longer in the CM III group $(4.3 \pm 2.7 \text{ years})$ versus that in the CM IV group $(1.2 \pm 0.8 \text{ years})$. Median follow-up was 5.1 years and 1.1 years in the CM III and CM IV groups, respectively.

Early and Late Outcomes

Early and late outcomes are summarized in Table 2. The CM III group had significantly longer crossclamp times (P < .001) than the CM IV group. There was no significant difference in ICU or hospital stay, 30-day mortality, permanent pacemaker placement, early atrial tachyarrhythmias, or late stroke. There was 1 perioperative stroke in the CM IV group and none in the CM III group. There was 1 death in the CM III group caused by multisystem organ failure. The 3 deaths in the CM IV group were due to the following: pulmonary embolism; hepatic failure, sepsis, and heparin-induced thrombocytopenia; and late postoperative tamponade and renal failure.

Survival at 1 year, as determined by means of Kaplan–Meier analysis, was 94% in the CM III group and 89% in the CM IV group (P = .19). Freedom from AF recurrence at 3 and 6 months was 98% in each group. Freedom from AF recurrence at 1 year was 96% and 93% in the CM III and CM IV groups, respectively (P = .52), as determined by using Kaplan–Meier analysis (Figure 2). Antiarrhythmic drug use at last follow-up was 19% in the CM III group and 31% in the CM IV group. However, no statistical comparison was made because of the major difference in follow-up data collection of this variable between groups.

Discussion

The CM procedure originally was developed to control the symptoms and sequelae of AF.⁶ It consisted of a complex set of incisions designed to prevent macrore-entrant circuits from forming in the atria, which was the prominent theory at that time regarding the mechanism of AF.^{6,24,25} The CM procedure was difficult, required long crossclamp times, and was associated with significant morbitiy.⁹ Its technical com-

plexity prevented the CM procedure from being adopted widely by cardiac surgeons.

Over the past decade, a number of alternatives have been examined to simplify the surgical treatment of AF and reduce the associated morbidity. A central strategy of these efforts has been to replace the surgical incisions with linear lines of ablation by using a variety of energy sources, including unipolar and bipolar RF, microwave, cryoablation, laser, and ultrasonography.¹⁰⁻¹⁷ Although all of these have enjoyed some degree of success, experimental work by our laboratory and others have revealed that bipolar RF ablation resulted in the most consistent transmural lesions.¹⁰⁻¹³ Moreover, lesions were quicker to perform with bipolar RF than other energy sources. The injury also was contained within the jaws of the clamp, preventing the collateral damage seen with other unipolar devices.²⁶⁻²⁸ At our institution, this energy source was adopted to replace the majority of the CM incisions, and the procedure was termed the CM IV procedure.²⁰ Early and late events were compared between the 2 groups to determine whether this new procedure produced similar outcomes as the CM III procedure. A propensity analysis was used to overcome selection bias.

In these matched patients the CM III group had significantly longer crossclamp times when compared with the CM IV group. Bipolar RF ablation replacing the surgical incisions simplified the procedure, allowing for shorter operative times in the CM IV group. The use of this ablation technology removed the major obstacle to widespread adoption of the CM procedure, its complexity and technical difficulty. This has significantly altered our own indication for AF operations in patients with concomitant heart disease. Although in the past the CM procedure was reserved for highly selected patients, it is now offered to virtually all patients with chronic AF referred for valvular or coronary surgery. This change in attitude is testified to by the fact that it took 9.2 years to accumulate the 58 patients in the CM III cohort compared with 3.2 years for the CM IV cohort.

Other outcomes were not significantly different between the 2 groups. ICU and hospital stay, 30-day mortality, permanent pacemaker placement, and atrial tachyarrhythmias and late stoke were similar. Thus the CM IV procedure resulted in similar operative outcomes with a shorter crossclamp time.

There was no difference in freedom from AF recurrence between the 2 groups on the basis of Kaplan–Meier analysis at 1 year. Both procedures yielded success rates of greater than 90%. This agrees with a prior report involving an unmatched comparison of 30 patients who underwent a CM III procedure with 40 patients undergoing a modified RF ablation maze procedure.²⁹

A major difference between the CM III and CM IV procedures is the method of creating the lesions (cut-andsew vs ablation). An incision creates a conduction block across the suture line 100% of the time. Although experimental studies have shown the ability to isolate targeted tissue and produce transmural lesions using the bipolar RF ablation device,¹⁰⁻¹³ it is possible that not all the lesions clinically produced conduction block or were transmural. Studies have shown that gaps as small as or smaller than 1 mm can allow the propagation of AF.³⁰ Isolation of the pulmonary veins can be tested intraoperatively, but the remaining lesions cannot be verified. Furthermore, in the CM IV procedure less left atrial tissue is isolated, leaving more of the left atrium in electrical continuity. Further follow-up is needed to determine whether these small differences between procedures will have any late effect at greater than 1 year.

Antiarrhythmic drug use was different between the study populations at last follow-up. Although the data for the CM IV group at 1 year were available, postoperative data from the CM III group were collected in a cross-sectional manner and did not allow for analysis at 1 year but rather only at last follow-up. The median follow-up was quite different between the 2 groups, making it difficult to compare the CM III and CM IV groups in terms of need for antiarrhythmic drugs.

The limitations of this study included the relatively small number of patients in each group. However, with 116 patients, this series is the largest comparison of matched patients undergoing a cut-and-sew versus an ablationassisted CM procedure in the literature. Moreover, with no prospective randomized studies either published or in process, this might be the most valid way to compare these 2 procedures.

The CM III patient information was retrospectively collected, whereas CM IV patient information was prospectively collected, and follow-up has been more complete. This might have contributed to the slightly higher failure rate. The CM IV procedure was more widely applied to higher-risk patients than the CM III procedure, making retrospective comparison difficult. For this reason, the propensity analysis was used to help overcome this shortcoming.

An additional weakness of this study is the means of assessing recurrence of AF. In the CM IV group an electrocardiogram was obtained at each follow-up appointment. If a patient in either the CM III or CM IV group complained of symptoms of palpitations, an electrocardiogram or prolonged Holter monitoring was obtained. If patients had implanted pacemakers, these were interrogated and used to determine the occurrence of AF. These limitations of follow-up were similar to all previous reports, and one strength of this study was the low percentage of patients lost to follow-up.

In summary, the CM IV procedure, using bipolar RF ablation, has simplified the procedure from a technical standpoint, making it applicable to most patients with

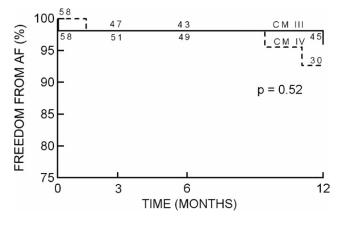


Figure 2. First-year freedom from atrial fibrillation (AF).

AF undergoing concomitant cardiac surgery. Comparing matched populations, the operation can be done with a shorter crossclamp time and produces similar surgical outcomes to the cut-and-sew technique of the original CM procedure.

The authors gratefully acknowledge the contributions of Bryan F. Meyers, MD, and Richard B. Schuessler, PhD, in the statistical analysis of our data.

References

- Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, et al. Heart disease and stroke statistics—2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113:e85-151.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*. 1991;22:983-8.
- Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation*. 1998;98:946-52.
- Valderrama AL, Dunbar SB, Mensah GA. Atrial fibrillation: public health implications. Am J Prev Med. 2005;29:75-80.
- Wattigney WA, Mensah GA, Croft JB. Increasing trends in hospitalization for atrial fibrillation in the United States, 1985 through 1999: implications for primary prevention. *Circulation*. 2003;108:711-6.
- Cox JL, Schuessler RB, D'Agostino HJ Jr, Stone CM, Chang BC, Cain ME, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure [see comment]. *J Thorac Cardiovasc Surg.* 1991;101:569-83.
- Cox JL, Boineau JP, Schuessler RB, Jaquiss RD, Lappas DG. Modification of the maze procedure for atrial flutter and atrial fibrillation. I. Rationale and surgical results. *J Thorac Cardiovasc Surg.* 1995;110: 473-84.
- Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8 1/2-year clinical experience with surgery for atrial fibrillation [see comment]. *Ann Surg.* 1996;224:267-75.
- Prasad SM, Maniar HS, Camillo CJ, Schuessler RB, Boineau JP, Sundt TM 3rd, et al. The Cox maze III procedure for atrial fibrillation: long-term efficacy in patients undergoing lone versus concomitant procedures. J Thorac Cardiovasc Surg. 2003;126:1822-8.
- Prasad SM, Maniar HS, Schuessler RB, Damiano RJ Jr. Chronic transmural atrial ablation by using bipolar radiofrequency energy on the beating heart. J Thorac Cardiovasc Surg. 2002;124:708-13.
- 11. Prasad SM, Maniar HS, Diodato MD, Schuessler RB, Damiano RJ Jr. Physiological consequences of bipolar radiofrequency energy on the

atria and pulmonary veins: a chronic animal study. *Ann Thorac Surg.* 2003;76:836-41.

- Gaynor SL, Ishii Y, Diodato MD, Prasad SM, Barnett KM, Damiano NR, et al. Successful performance of Cox-Maze procedure on beating heart using bipolar radiofrequency ablation: a feasibility study in animals. *Ann Thorac Surg.* 2004;78:1671-7.
- Bugge E, Nicholson IA, Thomas SP. Comparison of bipolar and unipolar radiofrequency ablation in an in vivo experimental model. *Eur J Cardiothorac Surg.* 2005;28:76-82.
- Gaynor SL, Byrd GD, Diodato MD, Ishii Y, Lee AM, Prasad SM, et al. Microwave ablation for atrial fibrillation: dose-response curves in the cardioplegia-arrested and beating heart. *Ann Thorac Surg.* 2006; 81:72-6.
- Gillinov AM, Smedira NG, Cosgrove DM 3rd. Microwave ablation of atrial fibrillation during mitral valve operations. *Ann Thorac Surg.* 2002;74:1259-61.
- Gammie JS, Laschinger JC, Brown JM, Poston RS, Pierson RN, Romar LG, et al. A Multi-institutional experience with the CryoMaze procedure. *Ann Thorac Surg.* 2005;80:876-80.
- Reddy VY, Houghtaling C, Fallon J, Fischer G, Farr N, Clarke J, et al. Use of a diode laser balloon ablation catheter to generate circumferential pulmonary venous lesions in an open-thoracotomy caprine model. *Pacing Clin Electrophysiol*. 2004;27:52-7.
- Ninet J, Roques X, Seitelberger R, Deville C, Pomar JL, Robin J, et al. Surgical ablation of atrial fibrillation with off-pump, epicardial, highintensity focused ultrasound: results of a multicenter trial. *J Thorac Cardiovasc Surg.* 2005;130:803-9.
- Mokadam NA, McCarthy PM, Gillinov AM, Ryan WH, Moon MR, Mack MJ, et al. A prospective multicenter trial of bipolar radiofrequency ablation for atrial fibrillation: early results. *Ann Thorac Surg.* 2004;78:1665-70.
- Gaynor SL, Diodato MD, Prasad SM, Ishii Y, Schuessler RB, Bailey MS, et al. A prospective, single-center clinical trial of a modified Cox maze procedure with bipolar radiofrequency ablation. *J Thorac Cardiovasc Surg.* 2004;128:535-42.
- Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the maze III procedure. *J Thorac Cardiovasc Surg.* 1995;110:485-95.
- Gaynor SL, Schuessler RB, Bailey MS, Ishii Y, Boineau JP, Gleva MJ, et al. Surgical treatment of atrial fibrillation: predictors of late recurrence. *J Thorac Cardiovasc Surg.* 2005;129:104-11.
- Damiano R, Gaynor S. Atrial fibrillation ablation during mitral valve surgery using the Atricure device. *Oper Tech Thorac Cardiovasc Surg.* 2004;9:24-33.
- Cox JL, Schuessler RB, Boineau JP. The surgical treatment of atrial fibrillation. I. Summary of the current concepts of the mechanisms of atrial flutter and atrial fibrillation. *J Thorac Cardiovasc Surg.* 1991; 101:402-5.
- Cox JL, Canavan TE, Schuessler RB, Cain ME, Lindsay BD, Stone C, et al. The surgical treatment of atrial fibrillation. II. Intraoperative electrophysiologic mapping and description of the electrophysiologic basis of atrial flutter and atrial fibrillation. *J Thorac Cardiovasc Surg.* 1991;101:406-26.
- Doll N, Borger MA, Fabricius A, Stephan S, Gummert J, Mohr FW, et al. Esophageal perforation during left atrial radiofrequency ablation: is the risk too high? *J Thorac Cardiovasc Surg.* 2003;125:836-42.
- Gillinov AM, Pettersson G, Rice TW. Esophageal injury during radiofrequency ablation for atrial fibrillation. *J Thorac Cardiovasc Surg*. 2001;122:1239-40.
- Demaria RG, Page P, Leung TK, Dubuc M, Malo O, Carrier M, et al. Surgical radiofrequency ablation induces coronary endothelial dysfunction in porcine coronary arteries. *Eur J Cardiothorac Surg.* 2003; 23:277-82.
- Chiappini B, Martin-Suarez S, LoForte A, Arpesella G, Di Bartolomeo R, Marinelli G. Cox/Maze III operation versus radiofrequency ablation for the surgical treatment of atrial fibrillation: a comparative study. *Ann Thorac Surg.* 2004;77:87-92.
- Melby SJ, Lee AM, Schuessler RB, Damiano RJ. The effect of residual gaps in ablation lines for the treatment of atrial fibrillation. *Heart Rhythm.* 2005;2:S15.

Discussion

Dr W. Randolph Chitwood (*Greenville*, *NC*). Thank you, Dr Mitchell. I rise first to congratulate Dr Damiano, Dr Lall, and their associates for collating, analyzing and presenting these important data. Dr Lall, your presentation was absolutely excellent. I reviewed the manuscript in detail in advance and have several comments and a few questions.

Clearly, Dr Jim Cox established the gold standard for a procedure to relieve patients of AF, both intermittent and continuous AF. The seminal investigative and clinical work of Dr Cox and Dr Bonieau at Washington University eventuated in the CM III procedure, which was described first in the Journal of Cardiothoracic and Vascular Surgery in 1995, also bears mention. Through detailed intraoperative mapping, he finally settled on an effective right and left atrial incision set that relieved more than 95% of patients from AF. New lesion sets in the CM III procedure at that time improved both right and left atrial transport and decreased the need for pacemakers. Despite these impressive results, the complexity of creating surgical lesions and the morbidity, especially in inexperienced hands, precluded the widespread adoption of the CM III procedure, despite these obvious advantages that Dr Lall has shown us. This is especially true when combined with mitral valve surgery and mitral valve repair.

Dr Damiano's work has continued in this illustrious shadow, with attempts to determine an effective operative method that most surgeons can perform in a reasonable time with minimal complications. The procedure described in this presentation used bipolar RF ablation, with most lesions approximating those of the CM III procedure. However, there were differences in the lesion sets.

The authors have compared 154 patients undergoing traditional cut-and-sew operations with 88 patients undergoing the new operation, which has been dubbed here as the CM IV procedure. Because a serial patient series was reviewed retrospectively, the authors used a propensity score analysis to select matched cohorts for comparison. This method yielded 58 patients in the cut-and-sew group and 58 patients in the bipolar RF or CM IV group. Patients had either lone AF, or it was combined with valvular or coronary disease, and therefore they really were not all the same. They determined that more than 90% in both groups were relieved of AF, suggesting that this new method could supersede the traditional operation as a standard. There was no statistical difference between the groups as far as relief from AF. In the CM IV group 12% more patients continue to receive antiarrhythmics, but follow-up was 4 years less than in the CM III group.

A weakness of this study, of course, is the retrospective review, which we are all forced to do, and the small number of patients in each final comparative cohort. However, these seem inescapable considering the evolutionary nature of these methods.

Our results confirm the data presented. In an attempt to render an effective, minimally invasive, small-incision AF operation, we developed an endoscopic method using cryoablative lesions at -150° C. In 161 patients either with lone AF or combined with mitral valve disease, we approximated the lesion set described by Dr Lall. Of the 41 patients with lone AF, either intermittent or continuous, 92% were AF free 3 months without drugs and 2 continued to receive antiarrhythmics, suggesting that a full lesion set, as you suggested, is optimal and that these operations are safe and efficient. We had no mortality in the lone AF group, and 13% required pacemakers, as you have shown here. I have several questions for you.

This commentator applauds you for confirming electrical isolation of pulmonary veins by pacing and mapping for exit block. I think this is important. Would it have been possible to determine isolation of the right side and other parts of the right atrium? Does it matter if we isolate the right atrium? Why do the right side at all if there is no AF?

Would you like me to go ahead and ask all my questions, or let her answer them one at a time?

Dr Mitchell. Let's go one at a time.

Dr Lall. Thank you, Dr Chitwood, for your kind comments and questions. It is an honor to have you discuss our article, and we recognize the many achievements of your group in pioneering minimally invasive AF surgery.

To address your first question on confirmation of conduction block, we can use computerized mapping techniques and multiple electrodes to confirm conduction block, but this is difficult to do in the operative setting; it is very time consuming and not practical. The other way to confirm isolation is with pacing or recording of individual electrocardiograms. This would require a portion of the atrium to be completely electrically isolated from the remainder of the atrium, and in the CM lesion sets, this only occurs around the pulmonary veins.

In terms of the right atrial lesions, we do believe that it is important to perform a biatrial lesion set because mapping studies have shown that between 10% and 30% of patients with AF have a right atrial focus.

Dr Khargi, in the *Journal of European Cardiothoracic Surgery* in 2005, showed in a univariate analysis that sinus rhythm conversion rates were higher in the biatrial lesion set group, and also Dr Niv Ad has shown this in a meta-analysis. Finally, without any right atrial lesions, there will be an incidence of late atrial flutter of about 10% to 20% in most series.

Dr Chitwood. Therefore you are suggesting we always do the right side.

What is the rationale for isolating the pulmonary veins in 2 islands rather than as 1 continual island?

Dr Lall. The bipolar clamp device that we use makes it impossible to encircle all 4 pulmonary veins at once. Therefore we isolate the right and left pulmonary veins separately, and then a lesion across the inferior posterior left atrium is completed. In patients with an atrium larger than 5 cm, we would place a second lesion that would connect with the superior aspect of the pulmonary vein lesions.

Dr Chitwood. Therefore it is mainly related to the device, is that correct?

Dr Lall. Yes.

Dr Chitwood. And I think I will yield my last 2 questions. My last question will be this: What percentage of your patients required a second electrophysiologic study for flutter? Did you have much flutter develop after these procedures?

Dr Lall. We did not have any reoperations for atrial flutter.

Dr Chitwood. Even in the catheterization laboratory?

Dr Lall. Correct.

Dr Chitwood. I thank the Association for the opportunity to discuss this fine article.

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Dr John Stulak (*Rochester, Minn*). What was your method of rhythm assessment for these patients during their clinical follow-up? Was it telephone interview, electrocardiogram, Holter monitor, etc?

Dr Lall. In the CM III group we did a retrospective follow-up through a mailed questionnaire or telephone interview, as well as having contact with either their cardiologist or primary care physician regarding recurrence of AF. In patients who complained of arrhythmia recurrence, copies of an electrocardiogram and Holter monitoring were obtained. In the CM IV group an electrocardiogram was obtained at scheduled 1-, 3-, 6-, and 12-month follow-up appointments. Our study had 100% follow-up in this group. Patients unable to return to our clinic were contacted by telephone, and electrocardiograms from their referring physicians were obtained. A 24-hour Holter monitor or event recorder was obtained on each patient with any symptoms or palpitations.

Dr Syed Tasnim Raza (*Parkersburg, WV*). Dr Lall, I wanted to congratulate you on a very fine presentation. When Dr Cox moved from St Louis to Washington, he changed from doing all cut-and-sew maze procedures to cryoablation, using a long cryoablation probe, the procedure he called cryo-maze, and I wanted to ask, how does your CM IV procedure differ from the cryo-maze procedure? My second question is this: you used 2 separate bipolar

RF technologies, the Medtronic and the Atricure. Was there any difference between the results in those 2, and have you compared them?

Thank you very much.

Dr Lall. I am unsure of how the cryo-maze procedure compares with our CM IV procedure.

For your second question, the Atricure device was used for 57 of the 58 patients, and the Medtronic device was used for only 2 patient. We did not look for any difference between the 2 devices.

Dr Craig R. Smith (*New York, NY*). I am curious how much overlap there was during the period of the study between the 2 procedures. You would think that a procedure with such a dramatically reduced crossclamp time would quickly replace its predecessor if it seemed even close to equivalent. If there was little overlap, I would not think you would need to do a propensity analysis.

Dr Lall. We no longer do the CM III procedure at Barnes-Jewish. There was no overlap between the 2 procedures. Thus to compare these 2 nonrandomized groups, a propensity analysis was done.

Dr Smith. I understand. I just could not see as much of a rationale for it if they were really just one procedure following the other. Point made.