Preliminary Results of a Limited Thoracotomy: New Approach to Treat Atrial Fibrillation

JAMES H. MCCLELLAND, M.D., DAVID DUKE, M.D., and RAMAKOTA REDDY, M.D.

From the Oregon Heart and Vascular Institute and Oregon Cardiology, Eugene, Oregon, USA

Epicardial Ablation of Atrial Fibrillation. ***Objective:*** **To determine efficacy of a new procedure combining epicardial bipolar radiofrequency (RF) pulmonary vein (PV) antrum isolation and ganglionated plexus (GP) ablation for treatment of atrial fibrillation (AF).**

Background: **PV antrum electrical isolation and GP ablation have each been associated with elimination of AF. Both of these can be performed epicardially in a single combined surgical procedure, which may have advantages over endocardial ablation.**

Methods and Results: **Twenty-one subjects entered a prospective evaluation of limited thoracotomy epicardial bipolar PV antrum isolation, verified by PV recordings, with GP ablation, guided by GP mapping. Procedural success was defined as freedom from AF and antiarrhythmic agents during 1 year of follow-up, including evaluation by prolonged continuous monitoring capable of detecting asymptomatic arrhythmias. All subjects had recordable PV potentials and GP activity prior to ablation. Circumferential epicardial bipolar RF eliminated PV potentials in 18 of 20 right and 14 of 20 left PV antra. This concurrently eliminated 79% of GP activity (125 of 159 active sites); nearly all remaining GP activity could then be eliminated using epicardial bipolar RF forceps. Fifteen of 20 (75%) subjects overall, and 14 of 16 (87.5%) subjects with paroxysmal or persistent AF had a successful procedure.**

Conclusion: **Limited thoracotomy epicardial bipolar RF antrum isolation, verified by PV recordings, with GP ablation, guided by GP mapping, is effective treatment for AF and should be considered in patients with paroxysmal or persistent AF.** *(J Cardiovasc Electrophysiol, Vol. 18, pp. 1289-1295, December 2007.)*

atrial fibrillation, ablation, ganglionated plexus, epicardial, bipolar, radiofrequency, surgery

Introduction

Both endocardial[1] and epicardial[2,3] pulmonary vein (PV) antrum isolation have been shown to eliminate atrial fibrillation (AF), and ablation of ganglionated plexi (GP) has been reported to reduce recurrence of or eliminate AF.[4-6] AF has also been shown to originate from the ligament of Marshall.[7,8] A procedure which adds GP ablation and division of the ligament of Marshall to epicardial PV isolation has recently been reported.[9] We describe findings during this combined procedure, and 1 year follow-up, in a prospective study of consecutive patients.

Methods

Patient Selection

Between January 1, 2005 and July 3, 2006, patients aged 30–85 years with documented recurrent symptomatic paroxysmal, persistent, or long-standing persistent AF[10] unresponsive to medical therapy, with failure of or intolerance to at least one class IC or Class III antiarrhythmic agent (generally two or more) were considered for entry. Exclusion criteria included left atrium (LA) $>$ 5.0 cm by transthoracic echocardiography, ejection fraction (EF) $<$ 40%, inability to give informed consent, comorbid conditions with a life expectancy less than 1 year. IRB approval of the protocol, including GP mapping and ablation, and written informed consent were obtained. The study was terminated when all subjects were classified as either ***Failed*** (at least 30 seconds of AF[10] detected at any time following the blanking period of 3 months) or ***Success*** (free of class 1 and class III antiarrhythmic agents and AF by all electrocardiographic recordings including long-term continuous monitoring capable of detecting asymptomatic arrhythmias at 1 year following the procedure) Student's *t*-test and the chi-square test were used for comparisons.

Description of the Procedure

Presurgical and surgical aspects

All patients were anticoagulated with warfarin for at least 1 month prior to the procedure. Transesophageal echocardiography was performed 1 week prior to surgery to exclude LA thrombus. Warfarin was then discontinued and low molecular weight heparin instituted through the morning prior to the procedure. Antiarrhythmics were continued through surgery, and were discontinued 3 months postoperatively; no subject was taking amiodarone. Through bilateral limited thoracotomy incisions (Fig. 1A), patients underwent off-pump video-assisted PV antrum isolation and GP ablation using an epicardial bipolar radiofrequency (RF) clamp (Fig. 1B) (MIR1, MIL1 patients 1–17; EMR1, ELR1 patients 18–20; Atricure Inc.; Cincinnati, OH, USA), and left atrial appendectomy,[2] with division of the ligament of Marshall (Fig. 1C) guided by mapping of PV potentials and GP activity (Fig. 1D), as described below. A standard protocol was followed regarding pain management including oral agents

Address for correspondence: James H. McClelland, M.D., 677 E. 12th Avenue, Suite N400, Eugene, OR 97401, USA. Fax: 541-242-6770; E-mail: jmcclelland@oregoncardiology.com

Manuscript received 26 April 2007; Revised manuscript received 21 July 2007; Accepted for publication 30 July 2007.

Dr. McClelland and Dr. Duke receive honoraria from Atricure Inc.

doi: 10.1111/j.1540-8167.2007.00977.x

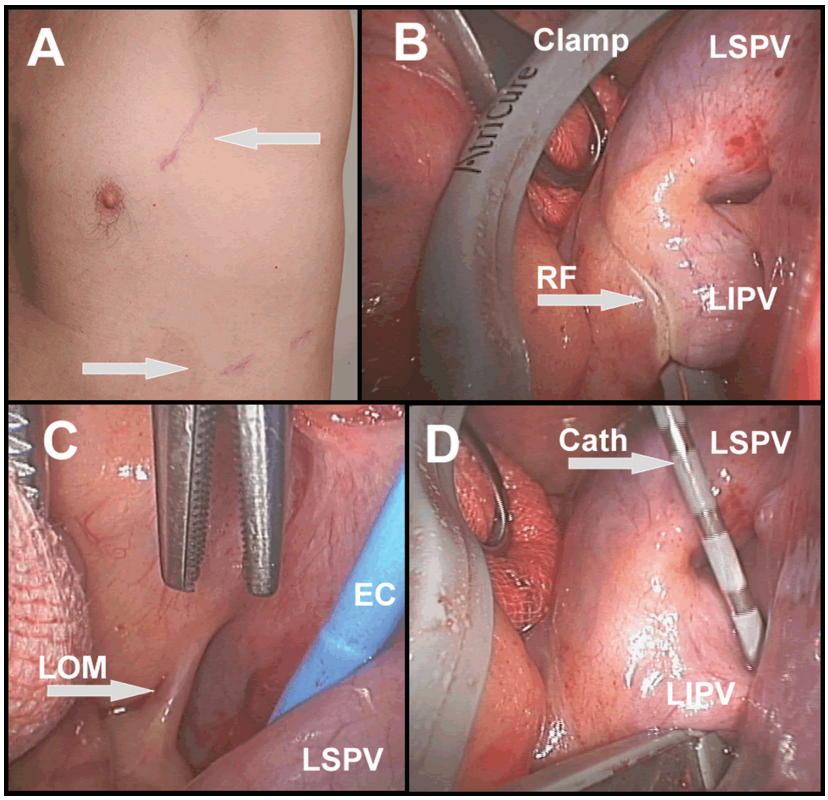

Figure 1. *Surgical epicardial PV antrum isolation and GP ablation. Panel A: One 5 cm and two 1 cm incisions (arrows) are required on each side of the chest. Panel B: Epicardial surface of the left antrum immediately following application of RF using the clamp (Clamp). Note linear lesion (RF), which is relatively far from the crux of the left superior (LSPV) and left inferior pulmonary veins (LIPV). Panel C: Superior aspect of the ligament of Marshall (LOM), immediately prior to transection and ablation by electrocautery tool (EC). Panel D: Epicardial testing for PV potentials using a standard EP catheter (Cath) prior to delivery of RF via the clamp.*

and epidural or subcutaneous infusions. All received intravenous hydrocortisone and oral prednisone for prophylaxis of pericarditis.

Mapping and elimination of PV potentials

PV potentials were recorded (30–500 Hz, 2500 gain CardioLab System, Pruka Engineering Inc., Houston, TX, USA) epicardially by maneuvering a standard 4 pole electrode catheter (Fig. 1D) to 12 sites around the pulmonary veins (Right A–F and Left A–F), using a diagram (Fig. 2) adapted from University of Oklahoma (personal communication). Potentials were mapped prior to application of RF via the clamp, and after RF application. The clamp is positioned anatomically, without reference to results of mapping. If PV potentials remained following RF, additional applications were given, and mapping repeated. The end-point for RF applications was elimination of PV potentials at all mapped sites; one additional application of RF was generally given when this was demonstrated. No RF clamp lesions were given in any other locations. After the seventh patient, animal studies demonstrating the safety of up to 15 applications of RF using the clamp became known, and the methods were altered to deliver up to a maximum of 10 applications of RF.

Mapping and elimination of GP activity

Sites of GP activity were mapped epicardially by stimulating via the same 4-pole electrode catheter, using 1 ms pulse width, 10 V (delivered to the subject assuming 100 Ω load; 100 V output), 20 Hz (Grass Telefactor S88, Grass Technologies, West Warwick, RI, USA) for 3 seconds; a positive response was defined as ventricular asystole for 3 seconds or more. GP mapping was performed at 15 right (R0–R14) and 12 left (L0–L11) antrum sites (Fig. 2). Only sites R1–R13 and L1–L10 were in the first three patients, after which the more posterior sites (R0, R14, L0, L11) were added to the tested mapping procedure. GP mapping

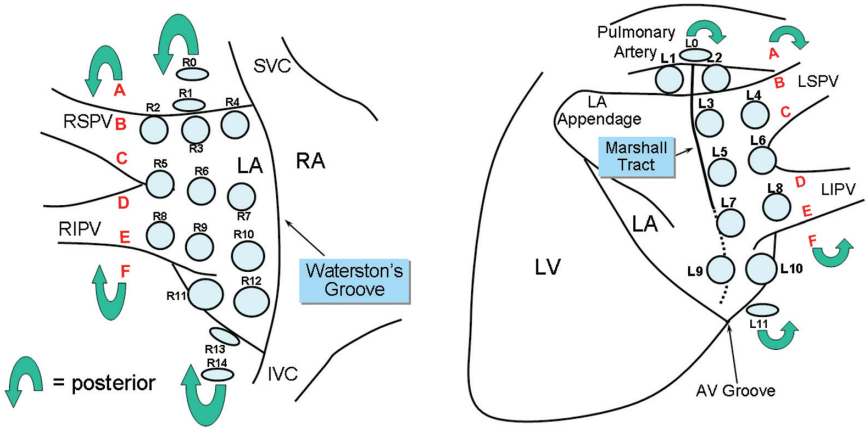

Figure 2. *Diagram of mapping of PV potentials and GP activity. The schematic used to map the ganglionated plexi and pulmonary vein antrum potentials. Six sites on each antrum (Right A–F and Left A–F) were tested for PV potentials; 15 right antral sites (R0–R14) and 12 left antral sites (L0–L11) were used to map the ganglionated plexi. Sites marked with a green arrow are located posteriorly (A, F, R0, R14, L0, L11). RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LA = left atrium; SVC = superior vena cava; IVC = inferior vena cava; RA = right atrium; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein.*

was performed prior to the initial RF application, and following the final application of epicardial RF via the clamp. If GP activity remained, then bipolar epicardial RF forceps were used to eliminate it, and GP mapping was then repeated.

Evaluation and management following discharge

Patients were seen and EKGs performed at 1 week, 2 weeks, 3 weeks, 6 weeks, 3 months, 6 months, and then every 6 months, and as needed for management of surgical or arrhythmia issues. A 3 month blanking period followed surgery, during which arrhythmia was ignored for outcome classification purposes. Symptoms suggestive of arrhythmia were evaluated by ECG, 24 or 48 hour ambulatory ECG monitoring, or event monitoring, as clinically indicated. At 1 year of follow-up, subjects underwent prolonged continuous monitoring (30 days in all but one patient, who was monitored for 15 days) capable of detecting asymptomatic arrhythmias (CardioPal SAVI, Medicomp Inc., Melbourne, FL, USA), unless AF had already been documented otherwise. Warfarin was continued for at least 1 year; it was then discontinued and aspirin instituted if patients so requested, and were classified as "failed" or were without an indication for warfarin.

Patients with recurrent arrhythmia were offered catheter ablation. Patients requiring catheter ablation solely of right atrial flutter or a well-organized right atrial tachycardia were not considered to have failed; rather, they were considered to have a separate right atrial arrhythmia. If atrial fibrillation or left atrial arrhythmias were demonstrated, subjects were classified as ***Failed***.

Results

Patient Characteristics and Outcomes

Twenty-one patients underwent this procedure; one protocol violation occurred (EF $< 40\%$) and was excluded from the analysis. Eleven had paroxysmal AF (PAF), five persistent AF and four long-standing persistent AF (Table 1). None had severe left atrial enlargement by 2D criteria, although five did by volume criteria of ≥ 39 cc/m^2 (area/length method). Five failures occurred during follow-up (mean 17 ± 3.5 months). Success was much more likely in subjects with paroxysmal (10 of 11, 91%) or persistent (4 of 5, 80%) than long-standing persistent AF (1 of 4, 25%) (Table 2). Two had right atrial flutter in follow-up; this was successfully ablated in both. One patient required transfusion for hemothorax related to the procedure. There were no other major complications, including death, neurological events, cardiovascular events, renal failure, or pacemaker implantation.

Elimination of PV Potentials

Pulmonary vein potentials were recordable at all sites in all subjects prior to application of RF, including one (DZ) who had undergone prior catheter ablation of AF at our institution in 1999. Following application of RF using the clamp, the presence or absence of electrograms was usually clear, but in some circumstances diminutive potentials were noted (Fig. 3); in all cases, RF was delivered until an end-point of either elimination of all recordable potentials or 10 applications was reached. These are generally all given to precisely the same site, or within a few millimeters of one another, as the clamp positioning is restricted by the site of the thoracotomy through which the clamp (Fig. 1A) passes, and the anatomy at the antrum (Fig. 1B).

On the right side, complete elimination of recordable potentials was attained in 18 of 20 subjects utilizing a median of 3.5 applications. On the left side, potentials were completely eliminated in 14 of 20 cases, utilizing a median of 5 applications; diminutive potentials remained in 6 subjects (Table 1). PV potentials were much more difficult to eliminate in patients with paroxysmal AF (13.2 applications, total of right and left sides) than persistent (8.6 applications) or long-standing persistent (6.8 applications); failure to eliminate PV potentials occurred almost exclusively in subjects with paroxysmal AF (Table 2). AF, usually transient, was often initiated by GP stimulation, occasionally making comparison of pre-RF and post-RF electrograms difficult.

GP Response Mapping and Ablation

GP activity was noted in all subjects prior to ablation; it was almost always manifest as complete heart block beginning about 1 second after onset of stimulation, persisting for several seconds after termination of stimulation. It was far more prevalent on the right side (125 active sites) than the left (34 active sites), and was most prevalent in two regions on the right antrum and two regions on the left antrum (Fig. 4). Note that the right side of the chest was entered first in all subjects, which may affect GP activity on the contralateral side. Subjects demonstrated GP activity at 2 to 12 (median 6, average 6.25) of the 15 sites (R0–R14) tested on the right side, and 0 to 6 (median 1, average 1.7) of the 12 sites (L0–L11) tested on the left side, or 125 of 294 (43%) of right-sided and 34 of 234 (15%) of left-sided sites that were mapped. Following attainment the end-point of elimination of PV potentials or 10 applications of RF using the clamp, 125 of the 159 previously active sites (79%) were then without GP activity, but 30 sites on the right and 4 sites on the left remained active (Fig. 4C). Following the use of the epicardial RF forceps to eliminate these areas of GP activity, 8 sites on the right remained active; all were eliminated on the left (Fig. 4D). GP activity was similar in those with paroxysmal, persistent, and long-standing persistent AF (Table 2).

Clinical Outcomes of Failures

Failures were almost always identified immediately after the blanking period ended, although one (WH) had a single episode of AF 7 months postoperatively and underwent cardioversion; he remains clinically free of AF. Another (DM) failed shortly after the blanking period, though noted marked reduction of duration and frequency of symptoms. The 3 others (RM, LS, DZ) failed early, had no clinical improvement and were offered catheter ablation. One (DZ) declined, as catheter ablation had failed previously, while two (RM, LS) underwent catheter ablation at other institutions without success.

Discussion

Pulmonary vein isolation is established therapy in both surgical[2,11] and catheter-mediated[1] procedures for treatment of AF. Newer procedures target autonomic activity specifically.[5,6] The procedure described in this report is designed to perform both, minimizing RF applications by using epicardial

TABLE 1

Patient Characteristics and Outcomes

									Right PV Antrum				Left PV Antrum			
											# of GP Sites				# of GP Sites¶	
ID	Sex	Age	AF Type†	FU (days)	Outcome‡	LA (cm)	LA vol (cc/m^2)	EF EF	# of RF Applications	Elim PV Potentials§	Pre-RF	Post-RF	# of RF Applications	Elim PV Potentials	Pre-RF	Post-RF
SO	F	54	PX	712	Suc	4.1	24	57	6	1	6	0	11	0	2	0
ML	F	33	PX	712	Suc	3.6	22	57	7	1	5	0	8	0	0	0
BS	F	66	PX	642	Suc	4.3	42	57	3	1	8	0	3	1	2	0
FW	M	71	LSPers	614	Suc	4.1	310	52	4	1	9	0	4	1	0	0
IK	M	71	PX	600	Suc	4.2	23	62	7	0	6	0	7	0	5	0
GK	M	71	Pers	567	Suc	4.2	44	57	2	1	6	0	6	1	2	0
MN	M	55	PX	565	Suc	4.3	24	67	2	1	3	1	9	1	5	0
ED	M	51	PX	525	Suc	3.6	17	62	4	1	11	1	5	1	0	0
PK	M	62	Pers	497	Suc	3.6	25	57	2	1	4	0	8	1	1	0
HM	M	82	Pers	495	Suc	3.9	21	52	2	1	2	0	2	1	1	0
WO	M	70	PX	490	Suc	4.3	25	42	7	1	2	0	8	1	0	0
PN	F	62	PX	462	Suc	4.5	38	57	6	1	9	0	8	1	3	0
DP	M	71	PX	453	Suc	4.7	39	62	10	0	6	0	10	0	1	0
WE	M	71	PX	446	Suc	4.1	21	62	10	1	12	2	10	0	4	0
GJ	M	44	Pers	411	Suc	4.1	26	57	4	1	7	4	8	1	0	0
Mean		62		546		4.1	28	57	5		6	1	7		2	0
S.D.		13		95		0.3	9	6	3		3	1	3		2	0
RM	M	51	LSPers	663	Fail	4.9	37	57	2	1	8	0	5	0	2	0
LS	F	51	LSPers	628	Fail	4.5	42	47	2	1	11	0	4	1	6	0
DZ	M	60	LSPers	504	Fail	4.2	43	57	3	1	5	0	3	1	0	0
DM	F	70	PX	364	Fail	4	31	57	2	1	3	0	2	1	0	0
WH	M	62	Pers	348	Fail	4.4	25	62	4	1	2	0	5	1	0	0
Mean		59		501		4.4	36	56	3		6	0	4		2	0
S.D.		8		145		0.3	8	5	1		4	0	1		3	0
p		0.29				0.049	0.048	0.329	0.035		0.360	0.156	0.008		0.449	NS

†AF Type: PX = paroxysmal; Pers = persistent; LSPers = long-standing persistent. ‡Outcome: Suc = success. §Elim PV Potentials: 1 = yes; 0 = no. ¶# of GP sites = number of sites tested that showed positive GP activity manifest as 3 seconds of asystole following stimulation; Pre-RF = number positive prior to delivering RF via the clamp; Post-RF = number positive after application of RF clamp; and RF forceps; PV = pulmonary vein; GP = ganglionated plexus; ID = identification; AF = atrial fibrillation; FU = follow-up; LA = left atrium; RF = radiofrequency.

TABLE 2
Findings Stratified by Atrial Fibrillation Type

	Atrial Fibrillation Type			
	Paroxysmal	Persistent	Long-standing Persistent	P value*
n	11	5	4	
Success	10	4	1	
Fail	1	1	3	0.01*
LA (cm)	4.2	4.0	4.4	0.056*
LA vol (cc/m2)	27.8	28.2	38.4	0.15*
RF Applications (right)	5.8	2.8	2.8	
RF Applications (left)	7.4	5.8	4	
RF Applications (total)	13.2	8.6	6.8	
Elim PV Potentials (right)	9/11	5/5	4/4	
Elim PV Potentials (left)	6/11	5/5	3/4	
GP Pre (right + left) per subject	8.45	5	10.25	
GP Post RF Clamp	1.82	2.4	0.5	
GP Post RF Clamp + Forceps	0.36	0.8	0	

*P value comparing paroxysmal and persistent versus long-standing persistent. PV: pulmonary vein; GP: ganglionated plexus; LA: left atrium; RF: radiofrequency.

Figure 3. *Recordings at the time of surgery. Composite diagram of recordings during epicardial RF ablation procedure. A: ECG leads. B: Bipolar electrograms recorded from the surface of the left atrium. C: Recordings from the pulmonary vein antrum prior to application of RF energy. D: Recordings following elimination of PV antrum potentials. E and F: Diminutive potentials recorded following delivery of RF using the clamp.*

recording to determine PV isolation, and by guiding GP ablation via GP mapping. This combined procedure results in success in 15 of 20 subjects overall (75%), and 14 of 16 subjects with paroxysmal or persistent AF (87.5%). These findings are noteworthy because follow-up included prolonged (30 days) continuous ECG monitoring for detection of asymptomatic arrhythmias,[12] and because of the limited lesion set that was utilized: a single encircling lesion around each antrum, with additional epicardial RF using bipolar forceps to eliminate the 1.3 ± 2.0 sites of GP activity per patient that remained.

This is a very limited lesion set (Fig. 1B) when compared to other surgical procedures and catheter ablation, which may require more than 100 lesions,[13] including roof lesions, connecting lesions to the mitral annulus, within the coronary sinus, atrial septum, vena cavae and at sites of complex fractionated atrial electrograms. These additional lesions, which were unnecessary for elimination of most paroxysmal or persistent AF in these subjects, incur additional risks,[14-16] and may contribute to the high (approximately 30%) incidence of left atrial arrhythmias following catheter ablation of AF, probably by causing gaps or areas of slow conduction.[17-19] Left atrial flutter occurred in only 1 of 20 subjects (5%) (RM) in this study; it is interesting to speculate that this low incidence may be due to the continuous linear nature of the RF lesion. It is also noteworthy that extensive endocardial ablation was ineffective in the two subjects who failed this procedure and underwent subsequent catheter ablation.

The bipolar epicardial approach has advantages and disadvantages in comparison to a unipolar endocardial one. Among the advantages are that continuous linear lesions can be made[20,21] (Figure 1B) and that the GPs are easily approached, as they reside in epicardial fat pads.[22] Bipolar RF has been reported to be the most effective and safest method to attain conduction block and limit remote injury when compared to other common energy sources in animal models.[20] Because a correctly positioned clamp lies within the pericardial space, injury to structures outside the pericardium, such as the esophagus, should not occur, and as the clamp is positioned on the antrum, far from the veins (Fig. 1B), PV stenosis is unlikely. Other potential advantages are that fluoroscopy is not required, no equipment is required in the left atrium,[23] the ligament of Marshall is eliminated[8] (Fig. 1C), and the LA appendage can be removed.[24] Disadvantages of this procedure include risks of surgery including general anesthesia, median hospital stay of 4 days, cosmetic issues, and incisional discomfort that may remain for weeks in some cases.

A comparison to catheter ablation will inevitably be made. We performed catheter ablation of AF from 1998 to 2004 and offer the observation that a successful surgical program for AF utilizing this procedure requires a skilled cardiothoracic surgeon with thoracoscopic experience and a means for recording electrograms and stimulating GPs, but not the infrastructure, equipment, expertise, or case volume that may be required for an effective program of catheter ablation of AF. For this reason, this procedure may be particularly suited for lower volume centers.

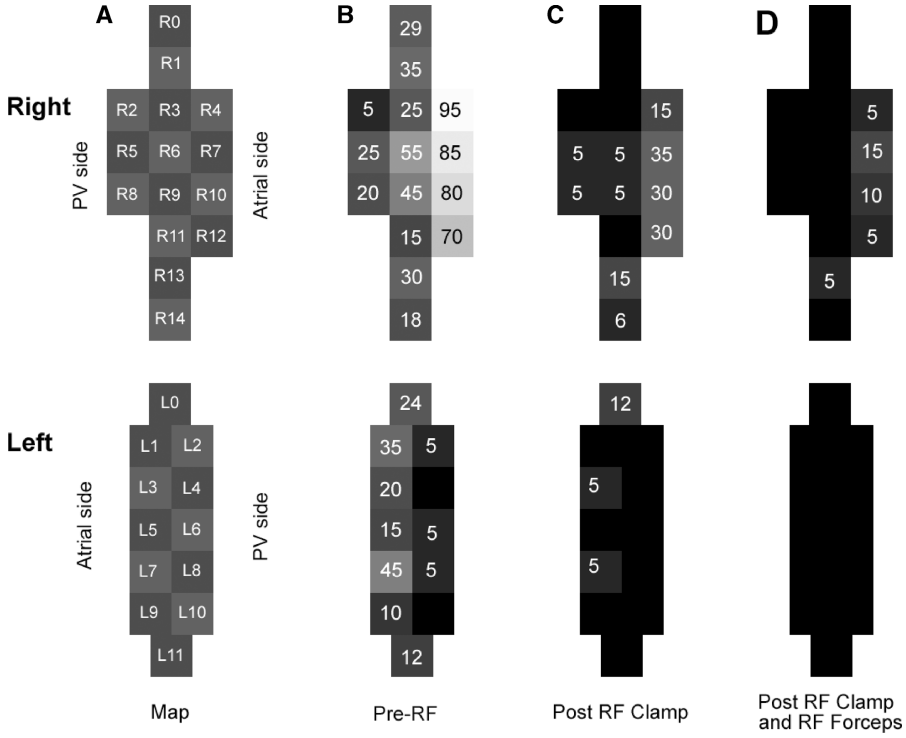

Figure 4. *Epicardial mapping of GP acitivty and after ablation. GP mapping. Panel A: Diagram of the GP sites mapped using the diagram shown in Figure 2, reorganized in a grid pattern. Panel B: Percent of sites tested showing GP activity prior to the delivery of RF, represented as numeric percentages, as well as by grayscale (black = 0%; white = 100% of sites showing GP activity). Activity on the right is localized to one large region anteriorly (R0, R1, R4, R6, R7, R9, R10, R12 area), and a smaller region inferiorly (R13 R14). On the left side, activity is localized superiorly (L0, L1, L3), and inferiorly (L7). Panel C: Following delivery of RF energy by the clamp, 125 of 159 (79%) of the active GP sites are eliminated. Panel D: Handheld epicardial bipolar RF forceps eliminated all but 8 of 159 sites; none remained on the left antrum.*

Limitations

A major limitation of this study is that the methods may not have been adequate to always clearly determine PV isolation. Elimination of PV potentials is verified at only three sites per vein; this may not be equivalent to "PV isolation." Pacing was not regularly utilized to confirm isolation, as many of our patients were in AF at the time of the procedure, or AF was initiated by GP stimulation at the time, making this impossible in many subjects. Most importantly, the diminutive potentials often recorded following ablation may represent "far-field" left atrial potentials.

This study was designed without a comparison group, and for that reason the incremental value of ligament of Marshall division or GP ablation over PV isolation alone cannot be determined. When compared to a similar procedure, without additional GP mapping and ablation,[2] the results are similar; perhaps this is to be expected in light of the finding in the current study that 79% of the mapped GPs are eliminated by the clamp alone during the process of attaining PV antrum electrical isolation, without directed mapping. The long-term effects of eliminating GPs are unknown.

The equipment and methods utilized to map GPs differ between centers, as do methods of anesthesia, which may affect GP responses. The protocol used in this study was adapted from methods utilized at the University of Oklahoma, in conjunction with our experience with intracardiac GP mapping and ablation during catheter ablation of AF; it identified multiple sites of GP activity in all patients. This is much more than is detected using some other methods, which may find no active sites in up to half of all patients (D. Oakes, personal communication); the significance of these differences is unknown.

The method of detection of recurrent AF included frequent routine ECGs, Holter or event monitor follow-up of symptoms, and prolonged continuous monitoring (30 days in all but one patient, for whom it took 15 days) using a device designed to detect asymptomatic arrhythmias (CardioPal SAVI). The effectiveness of such systems is high[12,25,26] but this particular device has no published data regarding efficacy.

Subjects in this trial had an LA size of 4.2 ± 0.3 cm and ejection fraction of $57 \pm 6\%$; results would likely be less favorable in a less carefully selected population. The right chest was entered and right GPs ablated before the left in all patients, which may affect autonomic findings on the left. Transection of the ligament of Marshall occurred before testing for GPs on the left, and may affect left GP activity. Although nearly all of *mapped* GPs can be eliminated using epicardial RF as described here, mapping is not performed at all sites at which GPs may be present, including posteriorly and at the interatrial septum. If subjects were taking antiarrhythmic agents, these were continued through the time of surgery, and could affect determination of PV isolation.

Conclusions

Limited thoracotomy circumferential epicardial bipolar RF antrum isolation, verified by epicardial recordings, with GP ablation, guided by epicardial GP mapping, is effective treatment for AF and should be considered in patients with paroxysmal or persistent AF, good left ventricular function, and a left atrium less than 5 cm. Patients with long-standing persistent AF are less likely to have a successful procedure; hence, a more extensive procedure, such as catheter ablation or the Maze procedure may be more appropriate for them.

Acknowledgments: The authors would like to acknowledge Deborah Lockwood, M.D., and Benjamin J. Scherlag, Ph.D., of the Cardiac Arrhythmia Research Institute, University of Oklahoma, Health Sciences Center, Oklahoma City, OK, and Donna Cash, ARNP, Michele O'Connor, R.N., Bryan Burke, CVT, and Adrienne Davis for their assistance in the preparation of this manuscript.

References

1. Natale A, Raviele A, Arentz T, Calkins H, Chen S, HaÏssaguerre M, Hindricks G, Ho Y, Kuck KH, Napolitano C, Packer D, Pappone C, Prystowsky EN, Shah D, Themistoclakis S, Verma A: Venice chart international consensus document on atrial fibrillation ablation. J Cardiovasc Electrophysiol 2007;18:560-580.
2. Wolf RK, Schneeberger E, Osterday R, Miller D, Merrill W, Flege JB, Gillinov AM: Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. J Thorac Cardiovasc Surg 2005;130:797-802.
3. Pak H, Hwang C, Lim HE, Kim JS, Kim Y: Hybrid epicardial and endocardial ablation of persistent or permanent atrial fibrillation: A new approach for difficult cases. J Cardiovasc Electrophysiol 2007; 18:917-923.
4. Pappone C, Santinelli V, Manguso F, Vicedomini G, Gugliotta F, Augello G, Mazzone P, Tortoriello V, Landoni G, Zangrillo A, Lang C, Tomita T, Mesas C, Mastella E, Alfieri O: Pulmonary vein denervation enhances long-term benefit after circumferential ablation for paroxysmal atrial fibrillation. Circulation 2004;109:327-334.
5. Scherlag BJ, Po S: The intrinsic cardiac nervous system and atrial fibrillation. Curr Opin Cardiol 2006;21:51-54
6. Scanavacca M, Pisani CF, Hachul D, Lara S, Hardy C, Darrieux F, Trombetta I, Negrão CE, Sosa E: Selective atrial vagal denervation guided by evoked vagal reflex to treat patients with paroxysmal atrial fibrillation. Circulation 2006;114:876-885.
7. Hwang C, Karaguezian HS, Chen PS: Idiopathic paroxysmal atrial fibrillation induced by a focal discharge mechanism in the left superior pulmonary vein: Possible role of the ligament of Marshall. J Cardiovasc Electrophysiol 1999;10:636-648.
8. Kurotobi T, Ito H, Inoue K, Iwakura K, Kawano S, Okamura A, Date M, Fujii K: Marshall vein as arrhythmogenic source in patients with atrial fibrillation: Correlation between its anatomy and electrophysiologic findings. J Cardiovasc Electrophysiol 2006;17:1062-1067.
9. Mehall JR, Kohut RM, Schneeberger EW, Taketani T, Merrill WH, Wolf RK: Intraopterative epicardial electrophysiologic mapping and isolation of autonomic ganglionated plexi. Ann Thorac Surg 2007;83:538-541.
10. Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJG, Damiano RJ. Jr, Davies DW, Haines DE, Haissaguerre M, Lesaka Y, Jackman W, Jais P, Kottkamp H, Kuck KH, Lindsay BD, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Natale A, Pappone C, Prystowsky E, Raviele A, Ruskin JN, Shemin RJ: HRS/EHRA/ECAS Expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: Recommendations for personnel, policy, procedures and follow-up: A report of the Heart Rhythm Society (HRS) task force on catheter and surgical ablation of atrial fibrillation. Heart Rhythm 2007;4:816-861.
11. Cox JL, Schuessler RB, Lappas DG, Boineau JP: An 8 1/2-year clinical experience with surgery for atrial fibrillation. Ann Surg 1996;224:267-273.
12. Vasamreddy CR, Dalal D, Dong J, Cheng A, Spragg D, Lamiy SZ, Meininger G, Henrikson CA, Marine JE, Berger R, Calkins H: Symptomatic and asymptomatic atrial fibrillation in patients undergoing radiofrequency catheter ablation. J Cardiovasc Electrophysiol 2006;17:134-139.
13. Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T: A new approach for catheter ablation of atrial fibrillation: Mapping of the electrophysiologic substrate. J Am Coll Cardiol 2004;43:2044-2053.
14. Pappone C, Oral H, Santinelli V, Vicedomini G, Lang CC, Manguso F, Torracca L, Benussi S, Alfieri O, Hong R, Lau W, Hirata K, Shikuma N, Hall B, Morady F: Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. Circulation 2004;109:2724-2726.
15. Lemola K, Desjardins B, Sneider M, Case I, Chugh A, Good E, Han J, Tamirisa K, Tsemo A, Reich S, Tschopp D, Igic P, Elmouchi D, Bogun F, Pelosi F, Kazerooni E, Morady F, Oral H: Effect of left atrial circumverential ablation for atrial fibrillation on left atrial transport function. Heart Rhythm 2005;2:923-928.
16. Callans DJ: The effect of catheter ablation for atrial fibrillation on left atrial transport function. J Cardiovasc Electrophysiol 2006;17:747-748.
17. Daoud EG, Weiss R, Augostini R, Hummel JD, Kalbfleisch SJ, Van Deren JM, Dawson G, Bowman K: Proarrhythmia of circumferential left atrial lesions for management of atrial fibrillation. J Cardiovasc Electrophysiol 2006;17:157-165.
18. Wylie JV, Josephson ME: Atrial tachyarrhythmias after atrial fibrillation ablation procedures: Trading one tachycardia for another? J Cardiovasc Electrophysiol 2006;17:374-376.
19. Raviele A, Themistoclakis S, Rossillo A, Bonso A: Iatrogenic postatrial fibrillation ablation left atrial tachycardia/flutter: How to prevent and treat it? J Cardiovasc Electrophysiol 2005;16:298-301.
20. Schwartzman D, Bonanomi G, Zenati MA: Epicardium-based left atrial ablation: Impact on electromechanical properties. J Cardiovasc Electrophysiol 2003;14:1087-1092.
21. Aupperle H, Doll N, Walther T, Ullmann C, Schoon HA, Mohr FW: Histological findings induced by different energy sources in experimental atrial ablation in sheep. Interact Cardiovasc Thorac Surg 2005;4:450-455.
22. Armour JA, Murphy DA, Yuan B-X, MacDonald S, Hopkins DA: Gross and microscopic anatomy of the human intrinsic cardiac nervous system. Anat Rec 1997;247:289-298.
23. Ren JF, Marchlinski FE, Callans DJ, Gerstenfeld EP, Dixit S, Lin D, Nayak HM, Hsia HH: Increased intensity of anticoagulation may reduce risk of thrombus during atrial fibrillation ablation procedures in patients with spontaneous echo contrast. J Cardiovasc Electrophysiol 2005;16:474-477.
24. Blackshear JL, Odell JA: Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg 1996;61:755-759.
25. Rothman SA, Laughlin JC, Seltzer J, Walia JS, Baman RI, Siouffi SY, Sangrigoli RM, Kowey PR: The diagnosis of cardiac arrhythmias: A prospective multi-center randomized study comparing mobile cardiac outpatient telemetry versus standard loop event monitoring. J Cardiovasc Electrophysiol 2007;18:241-247.
26. Olson JA, Fouts AM, Padanilam BJ, Prystowsky EN: Utility of mobile cardiac outpatient telemetry for the diagnosis of palpitations, presyncope, syncope, and the assessment of therapy efficacy. J Cardiovasc Electrophysiol 2007;18:473-477.