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Strategies to Improve the Efficacy of Epicardial Linear Ablation on the Beating Heart

Yoshiyuki Watanabe, MD, PhD^{*}, Matthew R. Schill, MD[†], Toshinobu Kazui, MD, PhD[‡], Spencer J. Melby, MD[†], Richard B. Schuessler, PhD[†], and Ralph J. Damiano Jr, MD[†]

^{*}Department of Cardiovascular Surgery, Nippon Medical School, Chiba Hokusoh Hospital, Tokyo, Japan

[†]Division of Cardiothoracic Surgery, Washington University School of Medicine, Barnes-Jewish Hospital, St Louis, MO USA

[‡]Division of Cardiothoracic Surgery, University of Arizona Medical Center, Tucson, AZ USA

Abstract

Objective—Creating transmural linear lesions on the beating heart is an important component of minimally invasive surgical ablation for atrial fibrillation. Animal studies have shown poor efficacy for surface bipolar radiofrequency ablation (RFA). Clinicians have developed strategies including multiple device applications and vena caval occlusion (VCO) to improve ablation efficacy. These techniques were evaluated in an acute porcine model.

Methods—In the first experiment, an RFA device was used to perform two 40-second epicardial ablations on the right atrium of six pigs. Ablations were performed with and without VCO. Ultrasonic flow probes were used to verify VCO. In the second experiment, an RFA device was used to perform two 40-second epicardial ablations at six locations on the left and right atria of six pigs. All animals were sacrificed. The hearts were removed and stained with 2,3,5-triphenyltetrazolium chloride. Sections were examined using digital photography.

Results—With VCO, 42 (81%) of 52 sections were transmural; without VCO on the RA, only 12 (24%) of 50 sections were transmural ($P < 0.01$). In thick (>2 mm) tissue, 10 (59%) of 17 VCO sections were transmural compared with only two (8%) of 24 with normal caval blood flow. Compared with a single ablation, multiple device applications improved transmural on the LA but not the RA (92% vs 71%, $P < 0.05$).

Conclusions—In an acute animal model, VCO improved the efficacy of beating-heart RFA on the RA. Multiple device applications improved the efficacy of RFA on the LA.

Address correspondence and reprint requests to Ralph J. Damiano, Jr, MD, Division of Cardiothoracic Surgery, Department of Surgery, Washington University School of Medicine, 660 S Euclid Ave, Campus Box 8234, St Louis, MO 63110 USA. damianor@wustl.edu.

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Keywords

Epicardial ablation; Atrial fibrillation; Radiofrequency ablation; Vena caval occlusion; Multiple ablations

Surgical ablation has become an established treatment for atrial fibrillation (AF), whether performed concomitantly with other cardiac operations or as a stand-alone operation for symptomatic patients.¹ Multispecialty consensus guidelines recommend surgical ablation for patients with AF who are undergoing other cardiac operations and for symptomatic patients with lone AF who have failed antiarrhythmic drugs and catheter ablation or who desire a surgical approach.² The efficacy of the Cox-Maze IV procedure performed either as a stand-alone operation or concomitantly with other cardiac surgical procedures is well established.³ Both bipolar radiofrequency clamps and cryoablation devices have been successfully used. Despite the growing evidence in favor of an aggressive strategy for atrial ablation at the time of cardiac surgery,⁴ many patients are still not treated, even during valve procedures.⁵ Surgeons cite several reasons for withholding concomitant AF ablation at the time of coronary artery bypass grafting or aortic valve procedures, including increased procedure time and increased invasiveness. Specifically, the need for left atriotomy has been a concern. Efforts to eliminate the need for atriotomy have resulted in left atrial ablation procedures using purse-string sutures, but these have not been widely adopted and still require opening the left atrium, posing a risk of air embolism and bleeding if cardiopulmonary bypass is not used.^{6,7} For minimally invasive atrial ablation, surgeons have introduced a variety of techniques that can be performed using minimal access on the beating heart.^{8,9} To replicate a left atrial Maze lesion set, they require performing linear epicardial ablation on the beating heart.

Ideally, the need for atriotomy and cardiopulmonary bypass for performance of an effective atrial ablation could be eliminated by the use of an effective device applied epicardially to the beating heart. Unfortunately, several factors reduce the efficacy of this approach. These include the depth of penetration achievable with available ablation devices and the heat sink effect of circulating blood. In previous work from our laboratory, decreasing intracavitary blood flow was found to improve the efficacy of epicardial ablation.¹⁰ The percentage of transmural lesions increased from 46% at normal cardiac output to 90% in animals without intracavitary blood flow; the percentage of transmural ablations was 100% with no intracavitary blood flow and a longer duration of ablation. We have also previously tested a linear surface bipolar radiofrequency ablation (RFA) device on the beating heart and found that it failed to produce transmural lesions up to 30% of the time when applied epicardially.^{11,12} These devices were found to be unable to create lesions that resulted in chronic conduction block in experimental models. In these studies, it was noted that ablation was least effective in the region of the superior vena cava (SVC) and inferior vena cava (IVC) and on thick tissue.^{11,12} Longer duration of ablation seemed to improve the device's effectiveness. In clinical practice, surgeons frequently use ablation devices multiple times when conduction block is not established acutely.¹³ We tested two strategies to improve the efficacy of epicardial RFA in an acute animal model: occlusion of the superior and inferior

vena cavae to reduce intracavitary blood flow and multiple applications of an ablation device to the same site.

METHODS

Two different strategies for improving ablation efficacy were evaluated: caval occlusion and multiple device applications. Twelve domestic pigs weighing 72 to 94 kg were used in this study. They were divided into two groups of six animals to separately test each strategy. All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals (National Academy Press, Washington, DC USA) under a protocol approved by our institution's animal studies committee.

For both groups, the animals were prepared in similar fashion. Each animal was premedicated with ketamine, anesthetized with isoflurane, and monitored continuously throughout the procedure with electrocardiogram and a femoral arterial pressure line. A median sternotomy was performed, and the heart was suspended in the pericardial cradle. The superior and inferior venae cavae were dissected circumferentially. Intravenous heparin was given, and the activated clotting time was maintained at greater than 350 seconds throughout the ablation procedure. Epicardial surface bipolar ablation using a commercial linear surface bipolar device (Coolrail; AtriCure, Inc, West Chester, OH USA) was then performed using caval occlusion and multiple device applications as described hereafter.

Six pigs were used in the caval occlusion group. In these animals, the Coolrail device was first applied epicardially without caval occlusion for 40 seconds at one location each on the SVC and the IVC (Fig. 1). The SVC and IVC were then occluded using vessel loops and a snare. An ultrasonic flow probe device (Transonic Systems, Inc, Ithaca, NY USA) was used to confirm vena caval occlusion (VCO). The Coolrail device was then applied for 40 seconds parallel to the previous SVC lesion (Fig. 1). The SVC and IVC flow was then restored, and the animal was allowed to recover. The Coolrail device was then applied for 40 seconds parallel to the previous IVC lesion (Fig. 1). A suture was placed to mark the end of each lesion to facilitate identification at the time of sacrifice.

Six pigs were used in the multiple device applications group. In these animals, the Coolrail device was applied epicardially for 40 seconds at each of six locations: two on the right atrial free wall, one each on the SVC and IVC, and two on the left atrial free wall (Fig. 2). The tissue was allowed to cool, and then the ablation device was applied to the tissue for 40 seconds a second time. A suture was placed to mark the end of each lesion to facilitate identification at the time of sacrifice.

After performance of the study lesion sets, the animals were sacrificed by cross-clamping the aorta and injection of concentrated potassium chloride into the aortic root. After asystole, 60 mL of 1% 2,3,5-triphenyltetrazolium chloride (TTC) was injected into the aortic root to perfuse the coronary circulation. The hearts were removed for examination.

Histologic Assessment

Each heart was grossly examined for evidence of charring, clot formation, or tissue disruption at the lesion sites. After this, each heart was bathed in TTC at room temperature for 45 minutes to stain viable myocardium. Each epicardial lesion was then examined and excised. Sections were taken every 5 mm along each lesion, perpendicular to the long axis of the lesion. A high-resolution digital photograph was taken of each lesion next to a caliper set at 1 cm for calibration. Lesion width, lesion depth, and tissue thickness were determined using commercial software (Photoshop; Adobe, San Jose, CA USA). This technique has been shown to be accurate to within ± 0.03 mm.¹⁴ Lesion depth and width were measured from the unstained area to the pink halo region surrounding each lesion. A total of five to eleven sections from each lesion were analyzed.

Statistical Analysis

Differences in the proportion of transmural sections were evaluated using the χ^2 test, Fisher exact test, and Pearson correlation. Differences in wall thickness and lesion depth were evaluated using one-way analysis of variance or Student *t* test. Data were expressed as mean $\pm$ standard deviation, and comparisons were considered significant if a *P* value is less than 0.05.

RESULTS

Gross examination revealed that all lesions were discrete and identifiable. No tissue disruption or endocardial clot was noted. Some epicardial charring was present but did not obscure any lesion. Examples of transmural and nontransmural sections are shown in Figure 2.

Vena Caval Occlusion

With caval occlusion, 42 (81%) of 52 sections were transmural; however, without caval occlusion, only 12 (24%) of 50 sections were transmural ($P < 0.01$, Fig. 3). In thick (>2 mm) tissue, 10 (59%) of 17 caval occlusion sections were transmural compared with only two (8%) of 24 with normal caval blood flow (Fig. 4). In thin (<2 mm) tissue, 32 (91%) of 35 caval occlusion sections were transmural compared with 10 (42%) of 24 without caval occlusion. In the nonocclusion group, the difference in transmurality between thick (2/24, 8%) and thin (10/25, 42%) tissue was also significant ($P < 0.01$, Fig. 4).

Multiple Device Applications

Using multiple device applications, 76% (160/211) of the total sections were transmural (Fig. 5). There was a lower rate of transmural lesion formation on the RA near the SVC/IVC than on the LA or RA [61/71 (86%) RA, 65/71 (92%) LA, 33/69 (48%) SVC/IVC, $P < 0.01$, Fig. 6]. When compared with a single ablation using the same device in previously published data from our laboratory (Fig. 7),¹¹ multiple device applications improved transmurality on the LA but not on the RA or near the SVC/IVC (92% vs 71%, $P < 0.05$).

DISCUSSION

In our acute porcine model, caval occlusion improved the efficacy of linear surface bipolar ablation on the right atrial surface. This is consistent with our group's previous findings; Melby et al¹⁰ showed that the depth and width of lesions produced with an epicardially applied microwave device were dependent on cardiopulmonary bypass flow rate in an acute porcine model. These results validate the concept that the heat sink effect of circulating blood via convective cooling is responsible for the previously observed poor efficacy of epicardial surface bipolar RFA. Eliminating this effect resulted in a 91% rate of transmural lesion formation on thin tissue. Unfortunately, ablation efficacy was still limited by tissue thickness. Caval occlusion or other strategies to decrease cardiac output were effective in improving the efficacy of right atrial ablation.

Furthermore, multiple applications of a linear surface bipolar device improved performance on the LA but not on the RA or near the SVC/IVC. Manufacturers limit the duration of device application to prevent charring, popping, and disruption of the atrial tissue, which can be caused by excessive ablation. Repeated ablation is one way to deliver additional energy to the tissue while avoiding these potential problems. The reason for the inefficacy of multiple ablations on the RA is uncertain but may be due to unique anatomic features such as trabeculations and thick muscle bundles.

The present study showed that VCO is an effective method for increasing the efficacy of epicardially applied surface bipolar RFA on the right atrium in an acute porcine model. In addition, multiple applications of the ablation device improved its efficacy on the left atrium in our model. Both of these maneuvers could conceivably be applied clinically. However, it is acknowledged that caval occlusion is impractical and may lead to hemodynamic instability. The physiological effect of caval occlusion, that is, decreasing intracavitary blood flow, theoretically could be replicated by pharmacological asystole or by going on cardiopulmonary bypass with an empty, beating heart.¹⁰ It may be that additional maneuvers and better devices will be needed for epicardial surgical ablation to match the efficacy of bipolar radiofrequency clamps and cryoablation devices on the empty heart. At this time, we would not recommend off-pump epicardial surface bipolar RFA, except in the context of a clinical trial or if the surgeon feels that the patient would be subjected to undue risk by undergoing a procedure with cardiopulmonary bypass.

Limitations

This study has several limitations. First, the results of the ablations were evaluated in the acute setting. Previous studies have shown that chronic results with this and other ablation devices may differ from acute results.¹² However, TTC staining has been shown in previous work from our laboratory and others to be an accurate method for evaluating the size of ablation lesions and has correlated well with chronic histology.¹⁵ Second, this study was conducted in healthy, normal pigs. The results of ablation on fibrotic, diseased, human atrial tissue in patients with AF may be different. Epicardial fat deposition also has been shown to affect the efficacy of radiofrequency devices.¹⁶ The lesions in this study were not placed over epicardial fat pads. Third, the lesion sets used for this study were optimized for placement of a maximal number of lesions on the atrial surface and do not match clinical

lesion sets. In addition, complete VCO would be difficult to accomplish using a minimally invasive approach. Finally, lesions were sectioned only every 5 mm; the continuity of the lesions was not evaluated along their entire length.

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FIGURE 1.

A, Linear lesion pattern used for the caval occlusion study. SVC (A) and IVC (B) lesions performed without (1) and with (2) caval occlusion. B, Linear lesion pattern used for multiple device applications. RA (A, B), SVC (C), IVC (D), and LA (E, F) lesion sites are labelled. IVC, inferior vena cava; LA, left atrium; RA, right atrium; SVC, superior vena cava.

FIGURE 2.
Examples of a transmural lesion in thin tissue (A) and a nontransmural lesion in thick tissue (B). Caliper set at 5 mm. Stained with 1% TTC.

FIGURE 3.

Lesion depth plotted against wall thickness for lesions created with (A) and without (B) caval occlusion. Transmural lesions lie along the plotted line (lesion depth = wall thickness); nontransmural lesions lie below this line.

FIGURE 4.

Wall thickness and lesion transmurality stratified by wall thickness for the caval occlusion animals. Asterisk denotes $P < 0.05$ by Fisher exact test. VCO, Vena caval occlusion. Dagger denotes $P < 0.05$ by the χ^2 test.

FIGURE 5. Lesion depth plotted against wall thickness for lesions created using multiple device applications. Transmural lesions lie along the plotted line (lesion depth = wall thickness); nontransmural lesions lie below this line.

FIGURE 6.
Percentage of transmural lesions stratified by location for multiple device applications.
Asterisk denotes $P < 0.01$.

FIGURE 7.

Percentage of transmural lesions created with multiple device applications versus a single device application stratified by location. Asterisk denotes $P < 0.05$.