Avoiding Microbubbles Formation During Radiofrequency Left Atrial Ablation Versus Continuous Microbubbles Formation and Standard Radiofrequency Ablation Protocols: Comparison of Energy Profiles and Chronic Lesion Characteristics

SEIL OH, M.D., Ph.D., FETHI KILICASLAN, M.D., YOUHUA ZHANG, M.D., PH.D., OUSSAMA WAZNI, M.D., TODOR N. MAZGALEV, PH.D., ANDREA NATALE, M.D., and NASSIR F. MARROUCHE, M.D.

From the Section of Pacing and Electrophysiology, Department of Cardiovascular Medicine, The Cleveland Clinic Foundation, Cleveland, Ohio, USA

Avoiding Microbubbles During RF Ablation. **Background:** Radiofrequency (RF) energy parameters and chronic lesion characteristics associated with the microbubbles formation have not been yet fully elucidated.

**Objectives:** The objective of this study was to compare the energy profiles and chronic lesion characteristics associated with RF ablation of the pulmonary vein antrum using three different ablation protocols: (1) avoiding microbubbles; (2) continuous microbubble formation; (3) temperature-guided ablation.

**Methods:** A 4-mm tip ablation catheter was used for creating RF ablation lesions in 15 adult mongrel dogs. All ablation lesions were created at the posterior aspect of the PV antrum in each animal. Avoiding microbubbles (group 1, n = 5 dogs, 23 lesions), continuous microbubble formation (group 2, n = 5 dogs, 22 lesions), and temperature-guided (group 3, n = 5 dogs, 19 lesions, target temperature 60°C/power limit 50 W) ablation lesions were analyzed.

**Results:** Group 1 showed significantly lower power (19 ± 8.6 W), lower temperature (50 ± 4.8°C), higher efficiency-of-heating index (2.9 ± 0.8°C/W), and lower impedance (109 ± 24.4 Ω) than groups 2 (38 ± 8.4 W; 63 ± 10°C; 1.8 ± 0.8°C/W; 148 ± 34.4 Ω) and 3 (44 ± 12 W; 57 ± 2.4°C; 1.4 ± 0.5°C/W; 139 ± 23.1 Ω) (P < 0.001 vs groups 2 and 3). During ablation, no significant events were detected in group 1, but 11 cases of audible pop, 11 cases of catheter tip charring, and 1 case of fatal myocardial perforation were observed in groups 2 and 3. Transmural lesions were more frequently created in group 1.

**Conclusion:** RF energy delivery applying “avoiding microbubbles” protocol seems to be associated with higher degree of safety and efficacy when compared to temperature-guided and continuous microbubble-formation ablation protocols. (J Cardiovasc Electrophysiol, Vol. 17, pp. 72-77, January 2006)

Introduction

Radiofrequency (RF) energy for catheter ablation has been widely applied as a safe and effective therapeutic modality for a variety of cardiac arrhythmias. Ablation catheter tip temperature monitoring has been traditionally used to guide RF energy delivery. Nevertheless, this strategy could be inaccurate especially in high flow areas such as pulmonary veins (PVs). Intracardiac echocardiography (ICE) has been shown to be helpful in guiding ablation lesion creation and evaluating procedural complications. In dog experiments, microbubbles formation during RF catheter ablation was associated more frequently with poor perpendicular contact and higher power delivery. In humans, RF power titration guided by direct visualization of microbubbles reduced the risk of complications and improved long-term outcome in patients undergoing PV isolation for the treatment of AF. Nevertheless, RF energy parameters and chronic lesion characteristics associated with the microbubbles titration protocol have not yet been fully elucidated.

The objective of this study was to analyze the RF energy profile and chronic lesion characteristics associated with radiofrequency ablation of the PV antrum comparing three different RF delivery protocols: (1) avoiding microbubbles; (2) continuous microbubble formation; (3) temperature-guided ablation.

**Methods**

**Surgical Preparation**

This study protocol was approved by the Cleveland Clinic Foundation Institutional Animal Care and Use Committee. Fifteen adult mongrel dogs of either sex, weighing 25–30 kg, were studied. Following standard and approved protocols,
all dogs were anesthetized with propofol (5–7.5 mg/kg), intubated, respirated, and followed by gaseous anesthesia (1–2% isoflurane). Standard surface electrocardiogram (ECG) was monitored continuously throughout the entire study. Intermittent arterial blood gas measurements were taken and ventilator adjustments were made to correct any metabolic abnormalities. An electrical heating pad under the animal and operating-room lamps were used to maintain body temperature of 36–37°C. Single-lumen sheaths were placed in both femoral veins to insert a RF ablation catheter and an ICE catheter.

**ICE and RF Ablation**

ICE was performed using a 10 F 64-element phased-array ultrasound imaging catheter (AcuNav, Acuson, Mountain View, CA, USA) inserted through 11 F sheath via the left femoral vein. The electroanatomical mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA) with a 4-mm tip ablation catheter (Navistar, Biosense Webster) was used for creating three-dimensional (3D) map of the left atrium, to navigate the catheters, to create ablation lesions, and to tag RF lesion sites. To create RF lesions at the PV antrum, transseptal puncture was performed under ICE guidance. During ablation, an effort was made to keep the ablation catheter tip perpendicular to endocardial surface under ICE guidance.

ICE was used not only to ensure proper catheter positioning and appropriate site of energy delivery but also to guide energy titration by monitoring microbubbles formation. The types of microbubbles observed using ICE has been described elsewhere. Briefly, while type 1 microbubbles represent scattered microbubbles formation, type 2 microbubbles describe dense and brisk showers of microbubbles formation during RF energy delivery.

In group 1 animals (avoiding microbubbles group), power (starting at 20 W) was titrated upward by 5-W increments every 5 seconds, watching for formation of type 1 microbubbles. When type 1 pattern was seen, energy was titrated downward by 5-W decrements until microbubbles generation subsided, and only then RF energy delivery was continued for a total duration of 60 seconds.

In group 2 animals (continuous microbubbles formation), the power (starting at 20 W) was continuously titrated upward by 5 W-increments until either type 2 pattern was seen or the maximum generator power (50 W) was reached.

In group 3 animals (temperature-guided ablation), RF energy was delivered with target temperature of 60°C and power limit of 50 W.

All dogs were randomly assigned one of these three groups (Fig. 1). All lesions in groups 2 and 3 were delivered for 60 seconds. All ablation sites were tagged on the electroanatomical 3D map. Steady-state catheter tip temperature, power, and impedance were used for analyses. Efficiency-of-heating index was defined as the ratio of steady-state temperature to steady-state power.

**Analysis of Ablation Lesion**

All surviving dogs were euthanized 6 weeks after the ablation, and the left atrial RF lesions were analyzed. Long diameter (d1) and short diameter (d2) of each RF lesion were measured using calipers on the endocardial surface. Lesion areas were calculated using the formula \( \pi \times (d_1/2) \times (d_2/2) \). Transmurality of each lesion was assessed by cutting the center of each lesion along the long axis. Two independent investigators blinded to ablation protocol evaluated these dimensions, and the average values were used for the analysis.

**Statistical Analysis**

All numerical data are expressed as mean ± standard deviation. The Student’s t-test was used for comparisons of continuous variables. Pearson chi-square test was used for categorical data comparisons. Values of \( P < 0.05 \) were considered statistically significant.

**Results**

**Ablation Results**

Of fifteen dogs, one dog assigned to group 2 died due to acute myocardial perforation. Fourteen dogs survived successfully 6 weeks after the ablation. Lesions showing catheter tip sliding in ICE monitoring during ablation procedures (n = 2) and linear lesions, which were defined as \( d_1 \) are longer

**Figure 1. Flow chart of each ablation protocol.**
than two times of d2, suggestive of catheter tip sliding (n = 1) were excluded. A total 64 ablation lesions (n = 23, 22, and 19 in groups 1, 2, and 3, respectively) were evaluated for the final analysis.

**RF Energy Parameters**

Higher power was needed for creating continuous microbubble-formation lesions (group 2) than avoiding microbubble-formation lesions (38 ± 8.4 W vs 19 ± 8.6 W, P < 0.001; Fig. 2). There was no significant difference in power level between group 2 and group 3. The steady-state catheter tip temperature levels of group 1 (50 ± 4.8°C) were lower than those of groups 2 and 3 (63 ± 10°C and 57 ± 2.4°C, respectively) (Fig. 2). The efficiency-of-heating index was higher in group 1 (2.9 ± 0.8°C/W) than groups 2 and 3 (1.8 ± 0.8°C/W and 1.4 ± 0.5°C/W, respectively) (Fig. 2). The steady-state impedance was lower in group 1 (109 ± 24.4 Ω) than groups 2 and 3 (148 ± 34.4 Ω and 139 ± 23.1 Ω, respectively) (Fig. 2). Figure 3 shows distribution of the lesions over these parameters in each ablation group.

**Events During Ablation**

There were no significant events during ablation in dogs assigned to group 1. However, fatal acute myocardial perforation was developed in one dog assigned to group 2. Perforation site was at the left lower PV antrum and was associated with audible pop, followed instantly by brisk shower of microbubbles, and sudden jump in impedance 2 seconds later. In group 2 audible pop, brisk shower of microbubbles, and impedance jump (mean change 38 ± 25 Ω) were detected during delivery of seven lesions (P = 0.003 vs group 1). In group 3, four lesions were associated with audible pop, followed by brisk shower of microbubbles and impedance jump (mean change 30 ± 32 Ω) (P = 0.021 vs group 1). After every delivered RF lesion the catheter tip was checked for char formation. Char was found on the catheter tip after five lesions in group 2 (P = 0.015 vs group 1), and six lesions in group 3 (P = 0.004 vs group 1).

**Microbubbles Formation**

Type 1 microbubbles pattern was observed in all three groups at a mean power and temperature of 28 ± 20 W and 55 ± 20°C, respectively. In 13% (3/23) of group 1 lesions no type 1 pattern could be observed during RF delivery. In 8.6% (2/23) of group 1 lesions RF delivery was terminated because type 1 microbubbles could not be avoided despite decreasing the power by 10 W. RF was also stopped due to prompt transition of type 1 to type 2 microbubbles during RF delivery of another group 1 lesion. In group 2 animals no type 1 microbubbles were seen in 4.5% (1/22) of lesions, while type 2 microbubbles could not be observed in 36% (8/22) of group 2 lesions. While type 1 microbubbles occurred in 95% (18/19) of group 3 lesions, type 2 microbubbles were detected in 58% (11/19) of lesions (Fig. 4).

**Lesion Characteristics and Pathology**

The remaining 14 dogs were sacrificed 6 weeks after the initial ablation. Endocardial surface lesion dimensions did not show significant differences between group 1 and group 2, but group 1 lesions were significantly larger than group 3 lesions (Table 1). Transmural lesions were more frequently created in group 1 (74%) than group 2 (45%, P = 0.051) and group 3 (26%, P = 0.002). Ablation protocol was different between transmural and nontransmural lesions, but the incidence of audible pop and catheter tip charring during RF ablation was not different between transmural and nontransmural lesions (Table 2).

**Discussion**

Downward power titration to avoid microbubbles when scattered microbubbles are observed during radiofrequency energy delivery at the PV antrum was associated with lower incidence of catheter tip charring/thrombus formation and lack of left atrial perforation when compared with “continuous microbubble formation” and “temperature-guided” RF ablation protocols. Lower power, lower temperature, lower impedance levels, and higher efficiency-of-heating index were documented when comparing the “avoiding microbubbles” with the other two tested protocols. Moreover, transmural lesions were more frequently created by avoiding microbubbles formation during RF energy delivery. These findings suggest that power titration by monitoring microbubbles formation under ICE guidance plays an important role in improving efficiency of energy delivery, creating more appropriate lesions, and preventing complications related to the left atrial ablation procedures such as PV antrum ablation.

**Microbubbles Monitoring, Char Formation, and Tissue Overheating**

Heating of myocardial tissue during RF ablation procedure may be thought of as a two-step process: resistive heating followed by conductive heat transfer from the area of resistive heating to surrounding tissue. Resistive heating occurs in a very narrow rim of tissue extending approximately...
The temperature of the region associated with resistive heating (catheter tip-tissue interface) is determined by RF ablation conditions such as energy setup, surrounding blood flow, and tissue contact with the ablation catheter. Overheating of this region could form char or coagulum by tissue desiccation and plasma protein denaturation when the interface temperature approaches or exceeds 100°C. The development of char or coagulum results in impedance jump. The insulating effects of char or coagulum may result in marked decrease in
heat transfer to surrounding tissue and marked discrepancy between catheter tip and tissue temperature. In addition, the denatured protein and desiccated tissue at the interface site are probable sources of thromboembolism.15

Microbubbles also occur when the interface temperature approaches or exceeds 100°C.13 and excessive amounts of microbubbles may also be a possible cause of systemic embolism. Audible pop is thought to be caused by a sudden release of vapor from the tissue just below the ablation catheter tip. This phenomenon is often associated with significant tissue damage such as crater formation and acute cardiac rupture.

The lack of char or thrombus formation in the “avoiding microbubbles” protocol group in this study could suggest a correlation between continuous microbubbles formation and tissue overheating, which would have lead to char or thrombus formation. This was the case in groups 2 and 3 protocols. In these two groups 95% and 61% of lesions showed type A char on catheter tip. This phenomenon is often associated with significant tissue damage such as crater formation and acute cardiac rupture.

Moreover one acute myocardial perforation was detected in group 2.

We recently demonstrated that applying the same “avoiding microbubbles” formation protocol tested in this study during PV isolation procedure in patients with atrial fibrillation did diminish the risk of complications like embolic events and PV stenosis.6 The results of the present study confirmed these findings by showing lack of catheter tip charring, lack of audible pop, and lack of perforation when the “avoiding microbubbles” protocol was applied. In this respect, using ICE to avoid microbubbles formation could be suggested as a reliable method to guide safe RF energy delivery.

Using the in vivo canine model and despite a tissue temperature of >80°C, Bunch et al. showed that microbubbles were not present in 13.2% of RF lesions delivered using an 8-mm tip catheter.1 Theoretically, microbubbles formation indicates overheating because there should be a region with temperature >100°C at the catheter tip-tissue interface. However, “no microbubble” does not always mean “no overheating” because all cases of tissue overheating do not produce microbubbles. If tissue temperature rises above the temperature enough to induce overheating, but less than boiling temperature, tissue will be overheated without microbubbles formation. This may be the major reason that not 100% but 86.8% of RF lesions associated with tissue temperature >80°C showed microbubbles formation in Bunch et al.’s report. In addition, they demonstrated that RF lesions associated with microbubbles formation had significantly higher tissue temperature than those without microbubbles.1 Therefore, and due to the fact that no tool is available to reliably measure myocardial tissue temperature in a “closed-chest” animal or human model, microbubbles formation during RF energy delivery might be considered as an indicator for tissue overheating to avoid further complications during RF energy delivery such as char/thrombus formation and perforations as demonstrated in this study.

Microbubble Monitoring and Lesion Size

The degree of tissue contact is one of the major determinants of the lesion size during RF ablation.14 Other factors related to the lesion size are the magnitude and duration of RF energy delivery, the characteristics of ablating catheter, the orientation of the catheter, the RF energy delivery protocol, and the heat dissipation characteristics of the cardiac tissue.8,13-20 In a controlled in vitro setting, the catheter tip temperature is known to be a very firm predictor of the depth of the ablation lesion.8,12 However, catheter tip temperature monitoring may be unreliable in the situation developing high convective heat loss such as high blood flow area, a large tip electrode, or an actively cooled-tip catheter. In the present study, RF ablation with power titration to avoid microbubbles created transmural lesions more frequently than continuous microbubbles formation and temperature-guided RF ablations. We demonstrated that microbubbles monitoring improved long-term outcome of PV isolation for treatment of patients with AF.6 This higher success rate could be explained by the higher transmurality achieved applying the “avoiding microbubbles” protocol shown in the current study. Areas of RF ablation avoiding microbubbles were also larger than those of temperature-guided ablation lesions in the present study. Therefore, titrating RF energy using microbubbles formation as guidance could not only be suggested to

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lower complications associated with left atrial procedures, but also to improve lesion transmurality and enhance procedural outcomes.21

**Study Limitation**

The three studied protocols were not assessed in the same heart, but in different animals. Nevertheless, changes in RF energy parameters, microbubbles formation, and detection of char formation were consistent in all five animals in each group. These data were initiated using a 4-mm tip ablation catheter. Results from an 8-mm tip or cooled-tip catheter may have demonstrated different outcomes. In order to unify the catheter orientation in every ablation attempt, we made an effort to keep the ablation catheter tip perpendicular to the endocardial surface. The results presented in this study might have been different if we targeted a parallel orientation of the catheter tip to the endocardial surface. In group 3, no impedance cutoff was used, and a 60°C target temperature was defined. Using an impedance cutoff and a 50°C target temperature might have revealed a different outcome.

**Conclusion**

RF energy delivery with power titration to avoid microbubbles seems to be superior to temperature-guided RF ablation and continuous microbubble-formation ablation in terms of the safety and efficiency during RF ablation in the PV antrum. This ablation technique is shown to be more appropriate for creating transmural lesions, and to reduce the risk of procedural complications like char/thrombus formation and perforation during RF energy delivery. Therefore microbubbles monitoring could be proposed as a reliable method to guide safe and effective RF ablation procedure.

**References**