Intramural Coronary Vasculature Prevents Transmural Radiofrequency Lesion Formation
Implications for Linear Ablation

Ithiel A. Fuller, BA; Mark A. Wood, MD

Background—Blood flow near a radiofrequency (RF) lesion can reduce lesion size by convective cooling. It is unknown whether blood flow through small vasculature within an RF lesion can prevent transmural lesion formation.

Methods and Results—In 40 rabbit right ventricle preparations, 2 epicardial RF lesions were created straddling a selectively perfused (0 to 12 mL/min) marginal artery (diameter, 0.34±0.1 mm). RF lesions were created at either 60°C or 80°C and delivered either sequentially or simultaneously. Conduction through the lesion area was measured. The lesions were analyzed histologically. At a perfusion rate of 0 mL/min, all RF lesions were transmural and without conduction. As little as 1 mL of flow through the artery during RF delivery could prevent transmural lesion formation by preserving a cuff of tissue along the length of the vessel. High-energy delivery (45 W) and very high tissue temperatures (93°C) were needed to overcome the protective effect of vascular perfusion at 12 mL/min. The volume of preserved myocardium was related to arterial perfusion rate, artery diameter, and lesion temperature but not to the sequence of RF delivery (sequential versus simultaneous). Conduction persisted through the lesion in 20 experiments. Conduction through the lesion was related to the arterial perfusion rate and volume or cross-sectional area of preserved myocardium.

Conclusions—Flow through even small intramyocardial vessels can prevent transmural lesion formation and preserve conduction through an RF lesion. These findings may represent an unrecognized obstacle to the creation of linear RF lesions in the clinical setting. (Circulation. 2003;107:1797-1803.)

Key Words: catheter ablation ■ vasculature ■ conduction

The creation of linear radiofrequency (RF) ablation lesions is important in the treatment of cardiac arrhythmias. Linear lesions are used to treat isthmus-dependent and anatomically bounded atrial flutters. Linear atrial lesions emulating the surgical maze procedure or encircling the pulmonary veins can prevent recurrences of atrial fibrillation. Linear RF lesions connecting anatomic boundaries have been shown to prevent recurrences of drug-refractory ventricular tachycardia. The generation of long, continuous RF lesions with ablation catheters has been difficult, however. Discontinuities within linear lesions result from poor electrode-tissue contact, anatomic irregularities, or inaccurate catheter placement. In addition, an unexplored potential obstacle to linear RF lesion formation exists. Blood flow over the site of RF delivery cools the tissue and limits lesion size because of convective heat loss. It is unknown whether blood flow through vasculature within an RF lesion will alter the lesion morphology. The purpose of this study was to test the hypothesis that a small, perfused coronary vessel within tissue undergoing RF ablation will prevent transmural lesion formation because of convective heat loss. This surviving myocardium may allow for persistent conduction across the lesion. Methods of RF energy delivery that may overcome this phenomenon are tested.

Methods

Tissue Preparation
This preparation was designed to produce RF lesions in myocardial tissue that contained a small coronary artery branch that was perfused at controlled rates. New Zealand White rabbits (Blue and Gray Rabbitry, Unionville, Va) were anesthetized with xylazine (7 mg/kg) and ketamine (100 mg/kg) according to American Veterinary Association Panel on Euthanasia guidelines. The hearts were rapidly removed, and the aortic root was perfused under continuous pressure (80 cm H2O) with Krebs-Henseleit buffer. The atrioventricular junction was crushed to produce complete heart block. In a tissue bath, the right ventricle (RV) was cut free from the septum, leaving the right coronary artery intact. The RV flap was pinned to the floor of the bath with the epicardial surface upward. The bath and perfusate were maintained at 37°C (pH 7.38 to 7.42) under continuous monitoring. A right coronary artery marginal branch was cannulated near its origin for controlled perfusion with an adjustable pump (Figure 1). Selective perfusion of this vessel and the associated myocardium was confirmed by fluorescein injection of the cannula under ultraviolet light to illuminate the selected tissue. The tubing to the marginal artery perfusion cannula made redundant loops in the tissue to ensure perfusion to all areas.
tissue bath to ensure equilibrium of temperatures between the tissue and the perfusate.

RF Lesion Formation

RF lesions were created using an Atakr generator and Mariner 7F temperature-monitoring RF catheters (Medtronic CardioRhythm Inc). The catheter tip was held perpendicular to the epicardial surface under 40 g of pressure. RF lesions were delivered in temperature-controlled mode for 30 seconds between the catheter tip and an indifferent electrode. Power and related parameters are reported as average instantaneous values.

Pacing and Recording Electrodes

A silver pacing wire electrode was placed adjacent to the marginal artery both proximal and distal to the site of lesion formation for unipolar pacing to an indifferent electrode. Transmembrane action potentials were recorded with 2 glass microelectrodes filled with 3 mol/L KCl solution (10 to 20 MΩ). One electrode each was positioned near each pacing electrode proximal and distal to the site of lesion formation (Figure 1). Conduction time through the site of lesion formation was defined as the time interval separating phase 0 of the action potential recordings from the 2 sites during pacing from the proximal electrode.

Experimental Protocol

Each heart was allowed to equilibrate in the bath for 20 minutes. Pacing (2 times diastolic threshold) was then performed from the proximal electrode at 200- and 600-ms cycle lengths to determine the conduction time between the microelectrodes. All measurements before and after lesion formation were made during perfusion of the artery at 6 mL/min. This value approximated the flow through this segment of RV flap under constant pressure perfusion (80 mm Hg) in preliminary work. In each heart, 2 RF lesions were created, 1 on either side of the midportion of the marginal artery with lesion centers 4 mm apart (Figure 1). In preliminary work, this spacing consistently resulted in dense overlapping transmural RF lesions. Three variables were altered among experiments: (1) the sequence of lesion formation, (2) lesion temperature, and (3) perfusion rate of the marginal artery. The target temperature for lesion delivery was either 60°C or 80°C. The 2 lesions delivered in an experiment were always at the same temperature. All lesions were delivered during perfusion of the RV marginal artery at 0, 2, 4, 6, 8, 10, or 12 mL/min. Fifteen minutes after lesion formation, the tissue was incised from the edges of the RV flap to the edges of the RF lesions to prevent conduction around the RF lesions (Figure 1). Pacing was performed proximal and distal to RF lesions at 200- and 600-ms cycle lengths, and conduction was assessed.

Three separate protocols were followed.

**Protocol 1:** To demonstrate the reproducibility of flow-related tissue protection, 2 sequential lesions at 60°C were formed in hearts undergoing marginal artery perfusion at either 0 mL/min (n=4) or 12 mL/min (n=4).

**Protocol 2:** To examine the effect of perfusion rate on lesion formation, lesions were created starting at 12-mL/min flow rates,
and in subsequent experiments, the flow rate was reduced to 10, 8, 6, 4, 2, and 0 mL/min until a transmural lesion was created. This procedure was repeated for a series of hearts using 60°C sequential lesions, 60°C simultaneous lesions, 80°C sequential lesions, and 80°C simultaneous lesions.

Protocol 3: To compare the effects of temperature and sequence of lesion volumes: (1) Total lesion volume

**Statistics**

All values are expressed as mean±SD. Student’s *t* test was used for comparisons between 2 independent groups. ANOVA was used for comparisons between more than 2 groups. The Mann-Whitney *U* test was used for nonparametric comparisons in protocol 2. Nonstepwise linear regression was used for the relationships of experimental variables to the amount of preserved myocardium. Nonstepwise logistic regression with the likelihood-ratio test was used for relationships of continuous variables to persistent conduction through the lesion. Pearson correlation coefficients were determined for correlations between continuous variables. A probability value of *P*<0.05 was considered significant for all analyses, including entry of variables into the regression models.

**Results**

A total of 40 hearts were studied in the 3 protocols.

**Protocol 1**

Sequential lesions at 60°C were created in 4 hearts at 0-mL/min perfusion rate and in 4 hearts at 12-mL/min perfusion rate to assess the reproducibility of the model. The epidermal lesion area was greater than the endocardial lesion area (Figure 2), supporting the use of the trapezoidal model for lesion volume calculations. The diameter of the marginal artery in this and subsequent protocols was quite small, 0.34±0.1 mm (Table 1). No experiments at the 0-mL/min flow rate showed any preserved tissue within the lesion, whereas all experiments at 12 mL/min had well-demarcated areas of preserved myocardium within the area of necrosis that extended along the entire length of the vessel within the lesion. There was no difference between the groups of perfused and nonperfused experiments in the overall lesion volume, total lesion cross-sectional area, RF power, temperature, current, or impedance (all *P*>0.05; Table 1). All experiments at 12 mL/min had preserved conduction through the lesion, but no experiment at 0 mL/min had conduction through the lesion (*P*=0.029).

**Protocol 2**

Twenty experiments were performed at flow rates from 0 to 12 mL/min during simultaneous or sequential lesion formation at 60°C or 80°C. Experiments performed in protocol 1 that fulfilled the conditions for experiments in protocol 2 were not repeated. The results of all experiments are shown in Figure 3. Preserved myocardium was present with perfusion rates as low as 2 mL/min with 60°C simultaneously created lesions (Figure 4). The volumes of preserved myocardium for 60°C sequential lesions across the range of perfusion rates were greater than those for lesions created at 80°C either sequentially or simultaneously (both *P*=0.038 but were similar to those for lesions created at 60°C simultaneously (*P*=0.12). For lesions created at 60°C simultaneously, the volumes of preserved myocardium were similar to those created at 80°C either sequentially or simultaneously (both *P*=0.70). The volumes of preserved myocardium were similar for the 2 sets of experiments performed at 80°C (*P*=0.88). For the 60°C sequential lesions, the distribution of data points fit a linear curve-fitting model (*P*=0.025). This protocol suggested that a higher perfusion rate produced a greater volume of preserved myocardium.

### Table 1. 60°C Sequential Lesions

<table>
<thead>
<tr>
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<th>Perfusion at 0 mL/min</th>
<th>Perfusion at 12 mL/min</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Marginal artery diameter, mm</td>
<td>0.28±0.06</td>
<td>0.36±0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Total lesion cross-sectional area, mm²</td>
<td>20±4</td>
<td>20±3</td>
<td>NS</td>
</tr>
<tr>
<td>Total lesion volume, mm³</td>
<td>66±21</td>
<td>59±32</td>
<td>NS</td>
</tr>
<tr>
<td>Cross-sectional area preserved myocardium, mm²</td>
<td>0</td>
<td>2.4±0.2</td>
<td>0.003</td>
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<tr>
<td>Volume preserved myocardium, mm³</td>
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<td>10±0.6</td>
<td>0.001</td>
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<td>Delivered power, W</td>
<td>3.6±2.8</td>
<td>2.0±1.6</td>
<td>NS</td>
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<td>Temperature, °C</td>
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<td>59±0.8</td>
<td>NS</td>
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<td>Delivered current, mA</td>
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<td>148±46</td>
<td>NS</td>
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<td>Impedance, Ω</td>
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<td>111±10</td>
<td>NS</td>
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<td>Transmural lesion</td>
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<td>0/4</td>
<td>0.029</td>
</tr>
<tr>
<td>Conduction through lesion</td>
<td>0/4</td>
<td>4/4</td>
<td>0.029</td>
</tr>
</tbody>
</table>

**Notes:**

- NS indicates *P*>0.05.

**TABLE 1. 60°C Sequential Lesions**
Protocol 3
Experiments performed in protocols 1 or 2 that fulfilled the conditions for protocol 3 were not repeated. Twelve experiments were performed with lesions created at 60°C sequentially, 60°C simultaneously, 80°C sequentially, and 80°C simultaneously (n=4 for each group) all at the same perfusion rate of 6 mL/min. The resulting total lesion volumes and volumes of preserved myocardium are shown in Figure 5. The total lesion volumes created at 80°C temperatures were greater than for 60°C (n=8 for each group; 91.2±24.0 versus 61.2±14.7 mm³, P=0.013). The average power (19.9±9.2 versus 6.7±3.7 W) and temperature (75.1±2.7°C versus 60.6±6.6°C) were each greater for the 80°C experiments than for those performed at 60°C (all P≤0.002). The volume of preserved myocardium was

Figure 3. Graph showing relationships between arterial perfusion rate and volume of preserved myocardium for 4 methods of lesion formation. Each data point represents a single experiment. *P<0.05 for distribution of values vs sequential lesions at 60°C.

Figure 4. Top, Cross section of 2 sequential lesions at 60°C temperature during perfusion at 2 mL/min. Area of preserved myocardium is 0.4 mm², and volume is 1.8 mm³. Bottom, Cross section of 2 sequential lesions at 60°C temperature during perfusion at 6 mL/min. Area of preserved myocardium is considerably larger, at 1.75 mm² and volume of 7.3 mm³.

Figure 5. Graph showing total RF lesion volume (top) and volume of preserved myocardium (bottom) for 4 methods of lesion formation, all at 6 mL/min perfusion rate: 60=60°C, 80=80°C, sequential (SEQ), simultaneous (SIM). *P<0.05 vs 60°C sequential, +P<0.05 vs 60°C simultaneous.
similar for the 60°C sequential and 60°C simultaneous lesions (11.1±3.8 versus 10.0±2.8 mm³, P=0.56). Both of these values were greater than the volume of preserved myocardium for either 80°C sequentially created (4.8±1.9 mm³) or 80°C simultaneously created (4.0±2.2 mm³) lesions (all P≤0.022). There was no difference in the volume of preserved myocardium between the lesions created sequentially or simultaneously at 80°C (P=0.72). The average total power for all lesions created simultaneously (8.0±4.5 W) and all lesions created sequentially (8.1±9.6 W) was similar (P=0.98). This protocol demonstrated that the volume of preserved myocardium was related to lesion temperature but not the sequence of RF delivery.

**Determinants of Preserved Myocardium**

By linear regression analysis of all 40 experiments, the volume of preserved myocardium was related only to arterial perfusion rate, lesion temperature, and arterial diameter (all P<0.001). The same results were found for area of preserved myocardium, which was very highly correlated to volume of preserved myocardium (Pearson correlation=0.975, P<0.001). The range of arterial diameters was 0.15 to 0.57 mm (average, 0.34±0.1 mm). The volume of preserved myocardium was correlated with perfusion rate (r=0.57, P<0.001) and vascular diameter (r=0.48, P=0.002) (Figure 6). The volume of preserved myocardium was not related to total lesion volume, power, voltage, current, depth of the marginal artery from the epicardial surface, or sequence of lesion delivery (all P>0.05).

**Conduction Through Lesions**

Conduction was present after lesion formation in 20 of 40 experiments. Conduction through the lesions was bidirectional in the relationship between conduction through the lesion and study variables is shown in Table 2. By logistic regression, conduction through the lesion was related to the arterial perfusion rate and the volume or cross-sectional area of preserved myocardium (all P≤0.03) (Table 2). Conduction was preserved with as little as 0.81 mm² preserved myocardium cross-sectional area or 4.4 mm³ preserved myocardial volume. At a 600-ms paced cycle length, conduction time increased from 39.9±8.3 ms at baseline to 51±18.6 ms after lesion formation (P=0.014). Conduction time increased from 49.7±14.7 ms at baseline to 65.9±25.2 ms after lesion formation at a 200-ms paced cycle length. The increase in conduction time through the lesions was inversely correlated with the cross-sectional area of preserved myocardium (r=-0.62, P=0.006 for 200-ms cycle length; r=-0.045, P=0.045 for 600-ms cycle length) but was not related to the length of the preserved myocardium (both P≥0.53).

**High-Power Lesion Creation**

High-power delivery may overwhelm the effects of arterial perfusion. Attempts to deliver >30 W power to the right ventricular preparation, even with an irrigated cooled-tip catheter and high epicardial superfusate flow, failed because of catheter tip temperatures consistently exceeding 100°C. The model of perfused intramyocardial vasculature was simulated by passing a 0.95-mm (internal diameter) plastic catheter 1 mm deep beneath the left ventricular epicardial surface and perfusing this cannula at 12 mL/min. In 1 experiment, 2 overlapping 40-W lesions (average temperature, 82°C; 62 Ω) were delivered over the cannula. Despite the creation of a large, deep RF lesion (43.2 mm² cross-sectional area), a 0.9-mm² area of preserved myocardium remained around the cannula. Conduction could not be assessed in this preparation. In a second preparation, 2 45-W lesions (average temperature, 93°C; 62 Ω) were delivered over the cannula, and no preserved myocardium remained.

**Discussion**

The major findings of this study are that (1) flow through very small intramural coronary arteries can prevent transmural RF lesion formation; (2) the amount of protected myocardium around the perfused vessel is related to arterial flow rate,
The remaining volume of an RF lesion results from conductive heating of adjacent myocardium. Blood flow over the surface of myocardium undergoing RF ablation reduces the lesion size by convective heat loss to the blood. Convection is defined as the amount of heat transferred per unit time over a defined surface area. The possibility that intramyocardial vasculature can alter RF lesion morphology through convective heat loss has not been explored previously. This concept differs from the work of Nath et al., who demonstrated impaired circulation at the microscopic level immediately around RF lesions.

In our study, flow through an intramural coronary artery resulted in preserved myocardium around the vessel that traversed the RF lesion. Consistent with the determinants of convective heat transfer, the volume of preserved myocardium was directly correlated with arterial flow rate through the lesion. With higher flow rates, more heat is carried away from the myocardium. In this model, transmural lesion formation was prevented by as little as 1 mL of perfusate passing through the tissue during RF delivery (Figure 3). Also consistent with convective heat loss, the volume of preserved myocardium was directly related to the diameter of the vessel within the RF lesion. A larger vessel diameter would provide a greater surface area for heat transfer to occur between the tissue and perfusate.

The failure of simultaneous RF delivery to significantly reduce the volume of preserved myocardium compared with sequential RF delivery at the same temperature is an interesting finding. Given the instantaneous heating of a larger volume of myocardium with simultaneous energy delivery, a smaller volume of preserved myocardium might be expected. This may result from similar total energy deliveries to create simultaneous and sequential lesions. The protective effect of intramyocardial perfusion even at high flow rates can be overwhelmed by high energy deliveries and very high tissue temperatures.

Conduction was preserved through the lesions with as little as 0.8-mm² cross-sectional area of preserved myocardium around the vessel. Our study and others have demonstrated that conduction through intentional transmural gaps in linear lesions is related to the width of the gap. Our study also demonstrated slowing of conduction through the lesion that was related to the cross-sectional area of preserved tissue.

**Limitations**

The relevance of this animal model to clinical ablation procedures can be questioned. Nonphysiologically high flow rates for the vascular diameters studied may exaggerate the cooling effects. Nonpulsatile flow was used, which may differ from in vivo flow patterns. Nitro blue tetrazolium staining may underestimate the true border of tissue viability. This finding has not yet been described in vivo in animal models of linear ablation; therefore, its occurrence remains speculative.

**Clinical Significance**

Intramural arteries up to 1 mm in diameter are present in human atrial myocardium. Flow through these vessels that cross lines of RF delivery could prevent complete conduction block, and the slowed conduction may form the substrate for reentry. Results of this study suggest that high tissue temperatures are needed to overcome the effect of intramural vascular cooling. Simultaneous energy delivery, as from multipolar linear catheters, does not appear to offer any advantage in this model.

**References**


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