Long-term Effects of Percutaneous Laser Balloon Ablation From the Canine Coronary Sinus

Claudio D. Schuger, MD; Linda McMath, MS; Gerald Abrams, MD; Hong Zhan, MD; J. Richard Spears, MD; Russell T. Steinman, MD; and Michael H. Lehmann, MD

Background. Radiofrequency catheter ablation of left-sided accessory pathways is becoming the first line of therapy for patients with symptomatic Wolff-Parkinson-White syndrome. Nevertheless, alternative ablation techniques merit development, at least as supplementary modalities for cases in which conventional ablation approaches may prove unsuccessful. We recently reported the short-term results with transcatheter laser balloon ablation from the coronary sinus in a canine model, proving that the procedure is feasible for the potential ablation of left-sided accessory pathways. We now report the effects of percutaneous transcatheter laser balloon ablation in a chronic canine model.

Methods and Results. Twenty adult mongrel dogs were studied. After baseline coronary arteriography, left ventriculography, and coronary sinus angiography were obtained, 15 dogs received two or three consecutive laser doses from the coronary sinus of 30–40 W for 15–30 seconds, for a total cumulative energy of 1,200–2,400 J. The five remaining animals underwent a procedure consisting of balloon shamm inflation without laser exposure and served as controls. After a mean follow-up of 6 weeks, the angiographic procedures were repeated, and the animals were killed. The mean extent of the fibrotic lesion was 15 mm long, 6 mm wide, and 4.5 mm deep and involved the coronary sinus wall, atrium, and, frequently, the summit of the posterior left ventricular wall. Six animals (four in the study group and two in the control group) showed asymptotic narrowing of the coronary sinus lumen but always with total angiographic reconstititution due to extensive collateral circulation. The circumflex artery and mitral valve were intact angiographically and histologically in all animals.

Conclusions. Percutaneous transcatheter laser balloon ablation via the coronary sinus produces a lesion that may be anatomically well suited for left-sided accessory pathway ablation. Although coronary sinus narrowing may occur, adverse physiological effects are unlikely due to the development of extensive collateral circulation. Systematic clinical studies of this new approach to catheter ablation appear warranted. (Circulation 1992;86:947–954)

KEY WORDS: ablation • balloons • lasers

Based on the close proximity of left-sided accessory atrophicventricular pathways to the coronary sinus, it was initially suggested1–5 that this anatomic relation might be exploited to create localized lesions involving the accessory pathway by delivering energy from the coronary sinus. Unfortunately, when delivered from the lumen of the distal coronary sinus, DC electrical shocks frequently resulted in rupture and cardiac tamponade due to the generated barotrauma,6–9 whereas radiofrequency energy delivered from the coronary sinus was often ineffective, probably due to the lack of adequate tissue penetration and/or contact.10,11

Since its recent introduction, percutaneous radiofrequency catheter ablation of accessory pathways performed from the left ventricular cavity12,13 instead of the coronary sinus has established itself as a highly effective and safe alternative to surgery in patients with symptomatic Wolff-Parkinson-White syndrome. Success with this technique, however, often requires precise pathway localization and good tissue–catheter contact, which can be time consuming and has the potential to expose both operators and patients to long fluoroscopy times.

Despite the impressive results with the radiofrequency-ventricular approach for left-sided accessory pathway ablation, energy delivery via the coronary sinus may still be clinically useful if a safe and effective technique can be identified. Nd:YAG laser radiation is an appealing energy source for ablation of left-sided pathways from the coronary sinus because of the following considerations: 1) tissue coagulation is achieved by direct absorption of laser light by chromophores in the tissue, so the depth of damage is dependent on the optical properties of the constituents in the atrophicventricular groove in addition to heat conduction; 2) theoretically, more energy will be deposited at the desired location due to relatively less absorption of radiation by adipose tissue (representing the bulk of tissue in the atrophicventricular groove); and 3) laser light can be delivered via
balloon catheters that emit a cylindrical pattern of radiation, resulting in thermal coagulation of a significant area of the atrioventricular groove and thereby enhancing the chances of successful ablation.

We recently reported our observations of the acute effects of percutaneous transcatheter laser balloon ablation from the coronary sinus.\textsuperscript{14} The present study was undertaken to investigate the chronic effects of this procedure in a group of 20 dogs followed for as long as 11 weeks.

**Methods**

**Laser Balloon Catheter**

The laser balloon catheter used in this study is a modified angioplasty catheter\textsuperscript{15} that has an optical fiber terminating in a 2-cm-long diffusing tip wrapped around the shaft in the center of the balloon (Figure 1). This cylindrical diffusing tip is capable of delivering diffuse continuous-wave Nd:YAG laser radiation (0.06 μm), which is relatively uniform both axially and circumferentially (Figure 2). The polyethylene terephthalate balloon and central shaft material are transparent to the laser radiation, so tissue heating results solely from absorption of the radiation by the adjacent tissues. The balloon is inflated with a combination of deuterium oxide (D\textsubscript{2}O), a nontoxic, nonradioactive isotope of water (50–80% less absorbent than water), and metrizamide, a contrast material that has negligible absorption of the Nd:YAG wavelength (1,064 nm) used in this study.

**Study Protocol**

Twenty adult mongrel dogs weighing 18–33 kg (mean, 25±4 kg) were studied. Using a protocol approved by the Wayne State University Animal Investigation Committee, each dog was anesthetized with intravenous sodium pentobarbital (25–30 mg/kg) and then intubated and mechanically ventilated. An 8F sheath was placed via a cutdown in the right femoral artery, and baseline coronary arteriography and left ventriculography were obtained with the aid of a 7F left Judkins catheter and a 7F pigtail catheter, respectively (Cordis, Miami, Fla.). An 8F guiding catheter was then inserted into the right external jugular vein via a 9F sheath. Under fluoroscopic guidance, this catheter was placed into the coronary sinus os, and the position was confirmed by a coronary sinus angiogram. Surface ECG lead II and arterial blood pressure were recorded throughout the procedure with a Gould two-channel physiological recorder (Gould-Statham, Cleveland, Ohio). Intravenous heparin (100 units/kg) was given to all animals. Baseline angiograms and ventriculograms were recorded on videotape for later comparison.

Once the baseline angiograms were obtained, the laser balloon catheter was introduced into the coronary sinus via the guiding catheter as follows. Under fluoroscopic guidance, a 0.014-in. flexible wire was advanced in the coronary sinus up to the point where the great cardiac vein becomes anterior. The laser balloon catheter was advanced over the wire to within ±1 cm of the wire tip.

During active flushing with normal saline via the guiding catheter (to dilute highly absorbent deoxygenated blood), the 5-mm balloon was inflated to 4 atm with the D\textsubscript{2}O metrizamide mixture. Once the balloon was inflated, flushing via the guiding catheter was stopped, and laser exposure was initiated. During lasing, flushing via the central lumen of the catheter was performed to prevent thermal bonding of the guide wire to the central shaft.

**FIGURE 1.** The 5-mm-diameter, gold-coated laser balloon catheter prototype used in the study. Note the optical fiber wrapped around the catheter central shaft.

**FIGURE 2.** Relative intensity of infrared radiation along the 2-cm length of the diffusing tip. Four profiles were generated by rotating the balloon catheter 90° for each scan. An infrared detector with a pinhole was placed 2 mm from the balloon surface and scanned the length of the balloon at 100 μm/sec.
TABLE 1. Chronic Atrioventricular Groove Lesions Resulting From Laser Balloon Ablation via the Canine Coronary Sinus

<table>
<thead>
<tr>
<th>Dog</th>
<th>Dose</th>
<th>Cumulative energy (J)</th>
<th>Count (mm)</th>
<th>Lesion size</th>
<th>Narrowing of coronary sinus (%)</th>
<th>Death (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ablation group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>30 W×20 sec×2</td>
<td>1,200</td>
<td>10</td>
<td>7</td>
<td>2</td>
<td>...</td>
</tr>
<tr>
<td>2</td>
<td>35 W×30 sec×1</td>
<td>1,575</td>
<td>10</td>
<td>4</td>
<td>3.5</td>
<td>...</td>
</tr>
<tr>
<td>3</td>
<td>35 W×15 sec×1</td>
<td>2,100</td>
<td>15</td>
<td>9</td>
<td>2.5</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>20</td>
<td>8</td>
<td>6.5</td>
<td>...</td>
</tr>
<tr>
<td>5</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>15</td>
<td>6</td>
<td>5</td>
<td>...</td>
</tr>
<tr>
<td>6</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>20</td>
<td>9</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>7</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>20</td>
<td>6</td>
<td>5.5</td>
<td>70</td>
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<tr>
<td>8</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>15</td>
<td>5</td>
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<td>9</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
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<td>35 W×30 sec×2</td>
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<td>15</td>
<td>7</td>
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<tr>
<td>11</td>
<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>15</td>
<td>9</td>
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<td>35 W×30 sec×2</td>
<td>2,100</td>
<td>15</td>
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<td>2,100</td>
<td>15</td>
<td>7.5</td>
<td>6.5</td>
<td>...</td>
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<tr>
<td>14</td>
<td>40 W×20 sec×2</td>
<td>2,200</td>
<td>15</td>
<td>6.5</td>
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<td>15</td>
<td>30 W×20 sec×1</td>
<td>2,100</td>
<td>20</td>
<td>9</td>
<td>6</td>
<td>100</td>
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<tr>
<td>Control (balloon inflation) group</td>
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<tr>
<td>16</td>
<td>0 W×60 sec×1</td>
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<td>...</td>
<td>...</td>
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<td>17</td>
<td>0 W×60 sec×1</td>
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<td>...</td>
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<tr>
<td>18</td>
<td>0 W×60 sec×2</td>
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<td>...</td>
<td>...</td>
<td>70</td>
</tr>
<tr>
<td>19</td>
<td>0 W×60 sec×2</td>
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<td>...</td>
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Dosimetry

In our previous study with 3-mm-diameter balloon catheters, we empirically chose 30 W of power for 20 seconds of exposure (600 J) as a starting dose (proven to be safe in human coronary arteries); this was repeated two or three times at the same location. With these doses, we showed the lack of immediate, major complications.

In the present study, 5-mm balloon catheters were used, a size more appropriate for filling the lumen of the distal human coronary sinus. Accordingly, we increased the dose to compensate for the loss of power density in all except one dog. Doses of 30–40 W for 20–30 seconds (repeated two or three times at the same location) representing cumulative energies of 1,200–2,400 J were used (Table 1). A 50-W continuous-wave 1,064-nm Nd:YAG laser (Quantronix, Smithtown, N.Y.) was used for this study. The continuous-wave Nd:YAG laser was chosen as the energy source because 1,064-nm radiation penetrates deeper into myocardial tissue (based on absorption coefficients) than the wavelengths of other commonly used clinical lasers (488/514 and 1,320 nm).

Control Study

To assess the effects of balloon inflation alone on the wall of the coronary sinus, five dogs underwent a sham procedure that consisted of balloon inflation (4 atm) for a period of 60 seconds but without laser exposure. This procedure was repeated twice in three of the five animals (Table 1).

Follow-up

After the procedure, all dogs received 125 mg/day aspirin for the entire follow-up period. Before death, all 15 dogs again underwent coronary sinus and coronary artery angiography and left ventriculography. The animals were killed with 20 mg/kg pentobarbital and potassium chloride. The chest was opened, the pericardial space was inspected carefully for the presence of fluid or blood, and the heart was excised.

Histopathology

After macroscopic inspection of the posterior atrioventricular groove and surrounding tissues, the heart was fixed in 10% formalin. Sections were stained with hematoxylin-eosin and/or Masson's trichrome. The resulting lesion was described based on the following parameters. Length was measured as the number of sections in...
which the lesion was evident microscopically (each section being approximately 5 mm long). Width was measured from the most cranial to the most caudal border of the microscopically defined lesion. Depth was measured from the most posterior to the most anterior border of the lesion.

Results

All 20 dogs (15 laser-treated dogs and five controls) tolerated the procedure without complications. No significant changes in blood pressure or heart rate were recorded during laser use or immediately thereafter. As seen in Table 1, doses of 35 W for 30 seconds were repeated twice in 11 of the 15 dogs, for a cumulative energy of 2,100 J. The remaining four dogs were irradiated as follows: two applications of 30 W for 20 seconds (1,200 J); three applications of 40 W for 20 seconds (2,400 J); one application each of 35 W for 30 seconds followed by 35 W for 15 seconds (1,575 J); and, finally, two applications of 40 W for 20 seconds followed by one application of 30 W for 20 seconds (2,200 J).

Coronary sinus angiograms immediately after the procedure failed to show any evidence of narrowing or perforation. Coronary artery angiograms as well as left ventriculograms were also unchanged compared with those obtained before the procedure.

The animals were followed for a mean of 5±2 weeks (range, 4–11 weeks). No complications or unexpected deaths were documented. As shown in Table 1, coronary sinus angiograms before death showed 40–100% coronary sinus luminal narrowing in six of the 15 ablation protocol dogs and in 70% and 100%, respectively, in two of the five controls (Figure 3). There always was total reconstitution of the coronary sinus proximal to the narrowed or obstructed area via multiple collaterals. There was no correlation between the presence or degree of the narrowing and the lesion size in the irradiated dogs (Table 1). There also was no correlation between animal weight, number of inflations, or follow-up time and the presence of coronary sinus narrowing in either the irradiated or the control dogs. Coronary artery angiograms revealed no luminal pathology, and in no case was there any evidence of mitral regurgitation.

Macroscopic and Microscopic Findings

No evidence of pericardial fluid or blood in the pericardial space was found in any of the 20 dogs. Small punctate hemorrhagic petechiae were present in the epicardial aspect of the atrioventricular groove at the site of balloon inflation in both irradiated and control dogs. After opening the left atrium, the endocardial aspect of the atrioventricular groove and the posterior leaflet of the mitral valve were visualized. White discoloration, sometimes associated with old, spotty hemorrhagic lesions, was present in the endocardial atrial surface in most of the irradiated dogs but not in the control dogs. In all cases, the mitral valve leaflet appeared morphologically normal.
Microscopic examination revealed a zone of tissue injury surrounding the coronary sinus, extensively involving the adipose tissue in the atrioventricular groove. Fat necrosis with associated chronic inflammation and scarring was evident in this adipose tissue, and cellular, vascular scar tissue extended variably from the atrial myocardium to the epicardium and into the summit of the left ventricle (Figure 4). The mean lesion length was 16 mm (range, 10–20 mm). The mean lesion width was 7 mm (range, 3.5–10 mm), and the mean depth 5 mm (range, 2–6.5 mm). In several animals from both the irradiated and the control group, the distal coronary sinus was occluded to some degree by thrombus in various states of organization (Figures 5A and 5B). In both groups, even when the coronary sinus was widely patent, there was patchy internal fibrous thickening and focal scarring of the wall that was confluent with the scarring in the adipose tissue of the atrioventricular groove. The coronary arteries were invariably patent in all animals. A common finding in both groups (presumably related to the age of the animals) was focal fraying and splitting or reduplication of the internal elastic lamina. The coronary artery of a single dog (dog 15) had a focal inflammatory cellular infiltrate in the wall beneath an apparently intact endothelium. The mitral valve was found to be histologically unremarkable in animals of both groups.

Discussion

The present study demonstrates the lesion-generating capability and absence of adverse physiological effects of percutaneous laser balloon ablation from the coronary sinus in a canine model. We found that laser balloon ablation resulted in significant coagulation necrosis in the atrioventricular groove that involved the atrial wall adjacent to the coronary sinus, most of the fat
FIGURE 5. Top panel: Photomicrograph of coronary sinus of control dog 18 killed 4 weeks after balloon inflation. Polypoid masses of connective tissue representing organized thrombus project into the lumen (Hematoxylin-eosin stain; original magnification, ×60). Bottom panel: Photomicrograph of coronary sinus of dog 6 killed 3 weeks after irradiation. The vessel is occluded by thrombus, which is partly organized (left half) (Hematoxylin-eosin stain; original magnification, ×60).
in the atrioventricular groove, and parts of the summit of the posterior ventricular wall. Such lesions are appropriately located for possible extrapolation to the clinical setting of left-sided accessory atrioventricular connections. Predictions regarding the relation between lesion size parameters and total energy delivered, however, cannot be made based on our study because we concentrated our efforts in defining the effects and safety of a narrow range of doses.

Importantly, we observed that the circumflex coronary artery and the mitral valve apparatus were remarkably spared. The coronary arterial wall is probably protected from injury because of the rapid blood flow that acts as a "heat sink" by cooling the arterial wall transmurally. In the case of the mitral valve and annulus, the optically reflective nature of the tissue and possibly the constant leaflet motion within the blood pool minimize the possibility of thermal injury.

In contrast, the coronary sinus exhibited luminal narrowing in six of the 15 irradiated dogs and in two of the five controls. This suggests that mechanical injury caused by balloon inflation, independent of the thermal damage, was the main contributing factor for the luminal strictures. These narrowings were the result of organized thrombus attached to the coronary sinus wall, with advanced degrees of recanalization in some cases. We can only speculate as to the chain of events that ultimately resulted in coronary sinus thrombosis, but it is reasonable to assume that the mechanical damage caused by balloon inflation resulted in endothelial denudation and some degree of medial disruption that, in turn, triggered platelet aggregation and activation with the formation of mural thrombosis. In a few cases, this small mural thrombus evolved into significant coronary sinus thrombosis, resulting in varying degrees of coronary sinus occlusion. The number of dogs as well as the narrow range of laser doses studied were insufficient to evaluate the role of laser-induced injury alone in this process. It must be stressed, however, that the clinical effects of coronary sinus thrombosis, when it develops gradually, are, and if any, minimal. Although this represents an adverse anatomic effect of the procedure, the apparent lack of clinical significance will have to be considered against the potential ability of percutaneous laser balloon ablation to achieve a rapid ablation of left-sided accessory pathways. As with all new invasive techniques, longer follow-up periods will be necessary to establish the complete safety of the procedure.

Implications

Among currently available methods for catheter ablation of left-sided accessory pathways, delivery of radiofrequency energy from the left ventricle (or left atrium) is becoming the treatment of choice. Although recent reports have shown that this technique can be abbreviated significantly, it still can be a tedious and lengthy procedure, exposing both patients and operators to relatively prolonged fluoroscopic time. The use of laser balloon catheters in the coronary sinus to ablate accessory pathways could result in the abbreviation of the ablation effort unlike other energy sources, although only a clinical trial can definitely demonstrate this point. The lesion size and distribution are determined mainly by the optical properties of the atrioventricular groove tissues, not solely by heat conduction (as is the case with radiofrequency). Also, the use of laser balloon catheters to coagulate tissue over a length of 1–1.5 cm will theoretically eliminate the importance of extremely precise pathway–catheter contact. Except for the possible occurrence of coronary sinus thrombosis in a distal location, which is unlikely to be clinically significant, the procedure appears to be safe based on our chronic canine studies.

Percutaneous laser balloon ablation of left-sided accessory pathways merits further investigation as a complementary approach to the radiofrequency technique. Because of the complexity of the equipment involved, the laser catheter approach—if clinically validated—might be most meaningfully used in patients who fail conventional ablation procedures.

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