Ablation of atrial fibrillation and esophageal injury: Effects of energy source and ablation technique

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Objective: The aim of this study was the evaluation of histologic changes induced on the esophagus by surgical ablation therapy for atrial fibrillation.

Methods: Experiments were performed on 39 sheep. Circular lesions were created endocardially or epicardially in the left atrium and at the pulmonary veins by using different energy sources: cryoablation, microwave, laser, and unipolar or bipolar radiofrequency. Temperatures inside the esophagus were measured, and esophageal tissue was investigated macroscopically and histopathologically.

Results: Esophageal damage was seen histologically in 24 of 39 cases. The epithelium was intact in all cases. Unipolar radiofrequency induced the most intensive esophageal lesions in 4 of 6 cases. The affected areas were small (1.56-3.01 mm) but reached deep into the tissue. Endocardial cryoablation resulted in wider lesions (2.01-8.54 mm), which were intensive in only 2 of 6 cases. Epicardial cryoablation and bipolar radiofrequency induced wide (1.11-6.8 mm) but mainly mild alterations. Endocardial and epicardial microwave energy affected the esophagus in single cases, and lesions were small (0.97-2.81 mm). Only in 1 case did laser energy induce a moderate alteration (5.30 mm) of the esophageal wall.

Conclusions: Esophageal alterations were found in numerous cases. However, marked lesions were especially induced by endocardial unipolar radiofrequency and cryoablation.

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Atrial fibrillation is the most common cause of arrhythmia in humans. It contributes significantly to morbidity and mortality, particularly in elderly patients.¹ The aim of surgical ablation therapy for atrial fibrillation is to create transmural lesions to eliminate focal triggers or macro reentry circuits. A milestone was set by the maze procedure, which applies a cut-and-sew technique of atrial tissues.^{2,3}

In recent years, several alternative surgical approaches have been developed. Transmural lesions have been created by different energy sources (unipolar and bipolar radiofrequency [RF], cryoablation, laser, ultrasonography, and microwave energy).⁴

Numerous reports have emphasized various levels of success for different treatments. The incidences of postoperative complications, including the thromboembolic events,⁴ pulmonary vein stenosis,⁴ and coronary artery stenosis,⁵ seem variable.⁶

Furthermore, some cases of perforation of the esophagus after surgical or transcatheter atrial ablation by unipolar RF have been reported.⁷⁻¹² In those cases, clinical symptoms of esophageal perforations after atrial ablation were observed 4

Abbreviations and Acronyms

RF = radiofrequency

to 10 days after surgery. Neurologic symptoms, dyspnea, thoracic pain, leucocytosis, sepsis, and fever were reported. Transmural esophageal lesions were seen approximately 30 cm after the incision. Because of the small number of cases, no predisposing factors could be identified.⁹ The lack of protective isolating fatty tissue in the presence of cachexia may be one factor.⁷ The aim of this study was to evaluate the presence of esophageal lesions after ablation therapy by using different energy sources and techniques.

Materials and Methods

From an ethical point of view, this study could not be performed in human beings, because intraoperative resection of atrial tissue involves a great risk of postoperative hemorrhage and would prolong surgical procedures unacceptably. Magnetic resonance tomographic scans of the thorax of sheep were performed (Figure 1). The results showed that sheep are a suitable species for this study, because the main pulmonary vein is located close to the esophagus, comparable to the anatomic situation in human beings.¹³ Sheep are relatively easy to handle, tolerating off-pump as well as on-pump surgical interventions to guarantee a good success rate for the study.

Thirty-nine female Merino sheep (7.3 ± 1.6 months old; body weight, 59.2 ± 6.7 kg) were included in this experiment. All animals received humane care in compliance with standard guidelines.¹⁴ The study was approved by local governmental offices.

A routine anesthesia was induced, and monitoring consisted of jugular central venous catheter measurements, femoral artery line pressures, continuous electrocardiogram, and routine blood gas analyses. A standard median sternotomy was performed, the heart was exposed by opening the pericardium, and the pulmonary veins were dissected.

Procedure for Electrophysiological Measurements

For pacing and threshold measurements, bipolar electrodes were placed on the left atrial appendage and pulmonary veins. Pacing thresholds were determined from the pulmonary veins and left atrial appendage before ablation and immediately after and 2 hours after ablation to confirm electrical isolation. Insulation was defined as the inability to capture the heart with a frequency of 140 beats/min and a maximum stimulus strength of 25 mA at 5.0 ms. The energy sources and technical equipment used for endocardial or epicardial ablation are listed in Table 1.

Endocardial Ablation Procedure

For endocardial procedures, the extracorporeal circulation was always used. Arterial cannulation (18F) of the supra-aortic truncus and venous cannulation (28F) of the right atrium were performed.

The extracorporeal circulation system consisted of a centrifugal pump and a pressure-controlled, biocompatible, heparin-coated polypropylene oxygenator and a heat exchanger. The procedures were executed in mild hypothermia (32°C).

Figure 1. Magnetic resonance tomography of the thorax from a sheep to demonstrate the anatomic position of the heart and the pulmonary veins entering the left atrium (arrow) and the esophagus (dotted arrow).

The aorta was crossclamped. Myocardial protection was achieved by using antegrade cold blood cardioplegia (16 mmol/L potassium) delivered over 3 minutes.

A small left atriotomy was performed through an incision parallel to the interatrial groove and anterior to the right pulmonary veins. This enabled direct access to the ostia of the pulmonary veins and the mitral valve annulus.

A continuous lesion line was created around the common pulmonary vein and the ostium of the left atrial appendage (Figure 2). Application times and energies are listed in Table 1. After the endocardial ablation procedure, the left atrial incision was closed, the heart was deaired, the aorta was declamped, and the sheep was weaned from cardiopulmonary bypass.

Epicardial Ablation Procedure

Epicardial ablation was performed off pump as described previously.¹⁶ Circular atrial lesions (Figure 3) were created around the pacing electrodes with sufficient space between the electrodes to prevent direct contact. Application times and energies are listed in Table 1.

Temperature Measurement in the Esophagus Lumen

A 16-mm-diameter tube was positioned within the esophagus lumen for online temperature measurements during ablation. Inside the tube, 8 infrared temperature probes were placed in a zigzag pattern in a 2.5-cm circular area. The probes were palpable through the esophagus, thus allowing optimal positioning. The area of potential esophageal damage was marked.

Pathologic Investigations

Sheep were killed 2 hours after the ablation procedure, and thoracic organs were explanted. The heart and esophagus were fixed

TABLE 1. Technical equipment, energy sources, and approaches used in atrial ablation in this sheep model

Energy source	Approach	Technical equipment	Technical data
Cryoablation	Epicardial (n = 6) Endocardial (n = 6)	SurgiFrost, CryoCath, Endocare Inc, Irvine, Calif	Argon, maximum −160°C, endocardial 60 s, epicardial 120 s
Microwave	Epicardial (n = 3) Endocardial (n = 6)	Flex 4, Fa. AFX, Fremont, Calif	90 s, 65 W
Laser	Endocardial (n = 6)	Optimize, Edwards Surgical Ablation System, Edwards Lifesciences, Irvine, Calif	36 s, 21.5 W, 980-nm wavelength
Unipolar radiofrequency	Endocardial (n = 6)	Cardioblate, Medtronic Inc, Minneapolis, Minn	10-20 s, 25 W
Bipolar radiofrequency	Epicardial (n = 6)	Cobra Bipolar, Boston Scientific, Natick, Mass	30 s, 50 W, maximum 80°C

in 4% formalin, and lesions were investigated macroscopically. Representative specimens (0.4-mm-thick cross sections) of the esophagus at the region of risk were embedded in Paraplast (Vogel GmbH & CoKG, Giessen, Germany), cut in three 50-μm steps, and stained with hematoxylin and eosin.

The degree of the alteration in the esophageal tissue was histopathologically graded as follows: mild alteration, single myocytes of the muscular layer with eosinophilic degeneration and mild intercellular edema; moderate alteration, numerous myocytes

with eosinophilic degeneration or necrosis and mild to moderate intercellular edema; and severe alteration, complete focal destruction of the muscular layer with necrotic myocytes at the borders and mild to moderate intercellular edema.

The diameter of the esophageal lumen and the thickness of the esophageal wall were measured macroscopically on the slides. The extension of the altered area was measured by light microscopy by using an interactive digital camera system (DP-Soft; Olympus Optical Co, Ltd, Tokyo, Japan).

Figure 2. Endocardial ablation lines. RAA, Right atrial appendage; RV, right ventricle; LV, left ventricle; SVC, superior vena cava; PV, pulmonary vein. Pacing leads are shown by arrows, and endocardial ablation lines are shown by continuous lines. (Schematic illustration modified from Nickel R, Schumacher A, Seiferle E. Lehrbuch der Anatomie der Haustiere. Vol. 3. 2nd ed. Berlin: Paul Parey; 1984. p. 63.)

Figure 3. Epicardial ablation lines. RAA, Right atrial appendage; RV, right ventricle; LAA, left atrial appendage; LV, left ventricle; SVC, superior vena cava; PV, pulmonary vein. Pacing leads are shown by arrows, and epicardial ablation lines are shown by continuous lines. (Schematic illustration modified from Nickel R, Schumacher A, Seiferle E. *Lehrbuch der Anatomie der Haustiere*. Vol. 3. 2nd ed. Berlin: Paul Parey; 1984. p. 63.)

Results

Temperature Measurements Inside the Esophagus

In sheep with endocardial ablation, the temperature inside the esophagus was decreased (approximately 32°C) during the entire operation because of the extracorporeal circulation system. During the ablation procedure, variations of the temperature measured in the esophagus lumen were not found in any case of endocardial or epicardial ablation.

Macroscopic Findings

The diameter of the cross-sectioned esophagus was approximately 2.5 cm. The muscular layers were approximately 1 mm thick, and the submucosal and mucosal layers together were approximately 2 mm thick. The area of risk at the esophagus was macroscopically intact. Only in 1 sheep treated with laser energy was a thin rim (5 × 10 mm) of pale, mildly edematous swelling seen in the periesophageal tissue and esophageal wall.

Histopathologic Findings

Histopathologic lesions of the esophagus were found in the area of risk in 24 of 39 cases (Table 2). The size of the lesions in the slides (width) varied from 0.97 to 8.54 mm. In general, the lesions were found in all slides (3 steps) of a case to a similar degree. The most intensive alterations were

seen in periesophageal connective tissue and in the outer muscular layers of the esophagus. Affected periesophageal tissue, muscular layers, and vessels showed signs of degeneration and necrosis. Myocyte degeneration was characterized by increased eosinophilia of the sarcoplasm, loss of cross-striation, and hyperchromatic shrunken nuclei, but intact sarcolemma. Necrosis was characterized by discoid coagulation of the sarcoplasm, ruptured sarcolemma, and pyknotic nuclei.

In the muscular layer, eosinophilic degeneration of single scattered myocytes and mild to moderate interstitial edema (15 cases; mild lesions) or groups of numerous degenerated myocytes occurred in the muscular layer and reached the submucosal layer (9 cases; moderate lesions). In 5 animals, the muscular layer was disrupted, and necrotic myocytes were seen at the border of the lesion (severe lesions; Figure 4).

In 2 animals, there was an acute focal mild infiltration of a few lymphocytes and polymorphonuclear granulocytes in the muscular layer. The submucosal interstitium showed a mild to moderate edema in the area of risk, and some fibrocytes seemed necrotic. The epithelial layer was focally separated from underlying connective tissue by edema, but epithelial lesions were not seen.

TABLE 2. Histopathologic findings at the esophagus after application of different energy sources and approaches in this sheep model (number of cases and size of histologic lesions)

Variable	Degree of esophageal damage			
	None	Mild	Moderate	Severe
Cryoablation epicardial	2/6	3/6	1/6	—
Size of histologic lesion (mm)	—	1.11–4.21	3.4	—
Bipolar RF epicardial	3/6	3/6	—	—
Size of histologic lesion (mm)	—	2.4–6.8	—	—
Microwave epicardial	1/3	1/3	—	1/3
Size of histologic lesion (mm)	—	1.08	—	2.81
Cryoablation endocardial	2/6	2/6	1/6	1/6
Size of histologic lesion (mm)	—	2.01–3.415	5.23	8.54
Unipolar RF endocardial	2/6	—	1/6	3/6
Size of histologic lesion (mm)	—	—	1.80	1.56–3.01
Microwave endocardial	5/6	1/6	—	—
Size of histologic lesion (mm)	—	0.97	—	—
Laser endocardial	—	5/6	1/6	—
Size of histologic lesion (mm)	—	1.70–1.80	5.30	—

RF, Radiofrequency.

Unipolar RF induced most intensive esophageal lesions in 4 of 6 cases. The affected areas were small (1.56-3.01 mm) but reached deep into the tissue. Endocardial cryoablation resulted in wider lesions (2.01-8.54 mm), which were intensive in only 2 of 6 cases (Table 2).

Epicardial cryoablation and bipolar RF mainly induced wide (1.11-6.8 mm) but mainly mild alterations of the esophagus. Endocardial and epicardial microwave energy affected the esophagus only in 3 cases, and lesions were small (0.97-2.81 mm).

In 1 case with macroscopically obvious lesions induced by laser energy, a moderate alteration (5.30 mm) of the esophageal wall was detected. In the other cases, small (1.70-1.80 mm) mild lesions were induced by laser energy (Table 2).

Discussion

Atrial fibrillation is of significant social and individual clinical importance. New techniques have been developed over the last 10 years, and several modifications were proposed to improve success rates while minimizing surgical trauma and operative risks during ablation therapy. Varying results have been described for different modifications using RF, cryoablation, and microwave energy.⁶

This study was designed to perform a detailed comparison of esophageal alterations induced by different energy sources and approaches. To reach that goal, a standard experimental model had to be applied.

Alterations of the esophagus were found histopathologically in 24 of 38 cases in our experiment. However, mild macroscopical lesions were observed in only 1 case. Esophageal injury was most pronounced after the endocardial approach, especially after unipolar RF. In most cases (n =

15), only a few peripheral myocytes of the muscular layer showed signs of degeneration. However, in 8 animals, moderate or severe necroses of the periesophageal connective tissue, of muscular layers, and of the submucosa were seen. Lesions of the epithelial layer were not found in any case.

This was confirmed by the finding that no increase of the temperature was measured inside the esophagus lumen.

Figure 4. Necrosis of the muscular layer of the esophagus induced by unipolar radiofrequency. The periesophageal connective tissue (*p*) is disrupted, and inner and outer muscular layers are destroyed (*arrow*). Myocytes show signs of coagulation necrosis (*n*); in the periphery of the lesion, the muscular layer is intact (*i*). The submucosal layer (*sm*) and the vessels (*v*) are also damaged (hematoxylin-eosin stain).

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Connective tissue and muscular layers probably absorbed the energy. Other authors reported that RF with a temperature of approximately 80°C on 1 side of the atrium led to a temperature of approximately 50°C on the other side.¹⁷⁻¹⁹ This supports the thesis that not too much heat is reaching the esophagus. It can be hypothesized that the muscular layer of the esophagus is probably more sensitive to heat energy than the myocardium.

Previously we reported that resected esophagus segments of patients with esophagus perforation after left atrial ablation induced by unipolar RF showed an extended inflammation of the muscular layer but had only focal mucosal ulceration.⁹ Relying on the findings in this study, it can be concluded that inflammatory reactions and subsequent granulation tissue will appear in the necrotic muscular layer. This site of decreased resistance may lead to increased rigidity and diminished contractility and elasticity of the wall of the esophagus. Additionally, vascular damage may induce ischemic alterations of the epithelial layer and may increase the risk of perforation. This pathogenetic model would be an explanation for the delayed occurrence (approximately 5 days after surgery) of clinical symptoms and esophageal perforation in humans.^{7,9}

Furthermore, esophageal strictures, diverticula, disturbed motility due to muscular fibrosis, or neural alterations may be long-term complications. Experimental studies have revealed that during percutaneous RF ablation, damage can occur in the lungs, phrenic nerves, and pulmonary venous tissue.²⁰

With this study, we showed that different energy sources and approaches can be correlated with varying risks of esophageal alteration. The results of this study are limited because only acute lesions were investigated. The clinical relevance of the diameter and depth of the lesions should be confirmed in a long-term study. However, to us it seems important to realize that the lesions were not obvious macroscopically, and, therefore, it would be difficult to recognize esophageal injury during surgery.

In summary, comparing the techniques used in this study, unipolar RF and endocardial cryoablation induced the most intensive esophageal lesions. Bipolar RF, laser, and microwave energy resulted in milder esophageal lesions. Some modifications and further long-term studies are necessary to confirm the clinical relevance and to minimize the complications described in our study. Combination with clinical data will be needed to determine the potential advantages and risks of different energy sources in practice.¹⁵

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