Damage to the Esophagus After Atrial Fibrillation Ablation

Just the Tip of the Iceberg? High Prevalence of Mediastinal Changes Diagnosed by Endosonography

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Background—Radiofrequency catheter ablation is increasingly used in the treatment of atrial fibrillation. Esophageal wall changes varying from erythema to ulcers have been described by endoscopy in up to 47% of patients following pulmonary vein isolation (PVI). Although esophageal changes are frequently reported, the development of a left atrial (LA)-esophageal fistula is fortunately rare. Nevertheless, mucosal changes may just represent “the tip of the iceberg.” The aim of this study was, therefore, to investigate the more subtle changes of and injuries to the posterior wall of the LA, the periesophageal and mediastinal connective tissue, and the whole wall of the esophagus, including mucosal changes by esophagogastroendoscopy (EGD) combined with radial endosonography (EUS).

Methods and Results—Twenty-nine patients (7 females; mean age, 57.7 ± 10.5 years [range, 23–75 years]) underwent EGD and EUS before and after PVI within 48 hours. PVI was performed as a circumferential antral isolation of the septal and lateral pulmonary veins guided by a decapolar circular mapping catheter using a 3-dimensional mapping system with the integration of a preprocedurally acquired computed tomography scan of the left atrium. The maximum power applied was 30 W, with an open-irrigated catheter using a maximum flow rate of 30 mL/min. In all patients, the esophagus was reconstructed using the same computed tomography scan and displayed during the ablation procedure. In case of newly detected periesophageal changes, EGD and EUS were repeated 1 week after the PVI. In all patients, a regular contact area between the LA and the esophagus could be demonstrated before PVI. The mean vertical contact length was 4.4 ± 1.5 cm (range, 2–10 cm); and the mean distance between the anterior wall of the esophagus and the endocardium was 2.6 ± 0.8 mm (range, 1.4–4.0 mm). After PVI, morphological changes of the periesophageal connective tissue and the posterior wall of the LA were diagnosed by endosonography in 8 patients (27%; 95% confidence interval, 12.73–47.24). No mucosal changes of the esophagus in terms of erythema or ulcers were found. In all but one patient (who refused the control), all periesophageal and atrial changes had resolved within 1 week. No atrioesophageal fistula occurred during follow-up (mean follow-up, 294 ± 110 days [range, 36–431 days]).

Conclusions—Mucosal changes of the esophagus after PVI-like ulcers or erythema could not be demonstrated, yet structural changes of the mediastinum, which were only visible by endosonography, occurred in 27% of patients in the present study. This may indicate a higher than expected periesophageal injury because of PV ablation. Endosonography might prove to be a sensitive and reliable tool in the follow-up after PVI. (Circ Arrhythm Electrophysiol. 2010;3:155-159.)

Key Words: atrial fibrillation • catheter ablation • esophageal injury • mediastinal injury • fistula • endosonography

Radiofrequency (RF) catheter ablation has evolved to a possibly curative treatment of atrial fibrillation (AF) in recent years, giving rise to increasing procedural numbers throughout the world.1 Most procedures target the pulmonary veins by placing RF lesions around their ostia to isolate AF triggers from the left atrium.2 Collateral damage to adjacent structures3 has been described, in particular to the esophagus, caused by its vicinity to the posterior wall of the left atrium.4–6 In rare cases, this may lead to formation of left atrial (LA)-esophageal fistula, with disastrous consequences.7–9 Some studies investigated mucosal changes of the esophagus after AF ablation.10–12 However, these mucosal lesions may represent just “the tip of the iceberg,” as a dramatic swelling of the posterior LA wall caused by RF application has been described.13 The variability of the thickness of the posterior LA wall and the esophageal wall may play an important role in esophageal heating and development of thermal damages.

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Mediastinal and submucosal esophageal thermal injuries cannot be diagnosed by conventional esophago-gastro-duodenoscopy (EGD), whereas endosonography (EUS) may be useful to detect these mediastinal and submucosal esophageal changes after pulmonary vein isolation (PVI). EUS was developed as a diagnostic tool in diseases of the esophagus and the mediastinum, the gastric wall, and the pancreas. Furthermore, EUS enables aiming biopsies of mediastinal and pancreatic lesions and plays also a role as a therapeutic modality guiding drainage of pancreatic pseudocysts or abscesses.14,15 Compared with other imaging modalities such as computed tomography, EUS is superior in staging of esophageal tumors because of its higher spatial resolution, which allows to differentiate the esophageal wall layers.16,17 Using EUS, the aim of this study was to investigate the more subtle changes of and injuries to the posterior wall of the left atrium, the periesophageal connective tissue, and the whole wall of the esophagus including mucosal alterations.

Methods

Patient Characteristics and PV Isolation

Twenty-nine patients (7 women; mean age, 57.7±10.5 years; range, 23 to 75 years) underwent PVI for paroxysmal (n=12) or persistent (n=17) symptomatic AF refractory to antiarrhythmic drugs. The clinical demographics of the study are shown in Table 1. All patients received intravenous piritramide and midazolam to achieve consciousness. After venous access, a decapolar catheter was placed into the coronary sinus via the left femoral vein. Double transseptal puncture was accomplished by using fluoroscopic imaging and pressure monitoring. Ablation was performed as a circumferential antral isolation of the septal and lateral pulmonary veins guided by a decapolar circular mapping catheter (Inquiry Optima, St Jude Medical, St Paul, Minn) using a 3D mapping system (CARTO XP, Biosense Webster, Diamond Bar, Calif) or 4.0-mm (ThermoCool, Biosense Webster, Diamond Bar, Calif) or 4.0-mm (Therapy CoolPath, St Jude Medical, St Paul, Minn) open-irrigated tip catheter, using a maximum irrigation rate of 30 mL/min. The ablation catheter was moved around the pulmonary veins in a dragging fashion rather than a point-by-point ablation, with 48°C maximum catheter tip temperature. Energy delivery was adjusted to 20 W when ablation was performed in close proximity to the esophagus, and ablation was prematurely stopped in response to pain. The end point of the PVI technique was the local elimination of all the pulmonary vein potentials with an electric disconnection between the LA and the pulmonary veins. No additional lines in the left or right atrium were drawn. PVI and endoscopic examinations were only performed after extensive information of the patient and after receiving written informed consent regarding the PVI itself as well as the endoscopic examinations.

Table 1. Clinical Demographics

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>29</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
</tr>
<tr>
<td>Age, y</td>
<td>57.7±10.5</td>
</tr>
<tr>
<td>AF type</td>
<td></td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>12</td>
</tr>
<tr>
<td>Persistent</td>
<td>17</td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>3</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>History of stroke</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21</td>
</tr>
</tbody>
</table>

EGD and EUS

Endoscopic examinations were performed by 2 highly experienced EUS endoscopists (H.U. and T.M.). All examinations were done in a standardized way. Patient preparation consisted of a fasting period of at least 6 hours before the examination. Sedation was performed by intravenous administration of 50 mg pethidine once and propofol in a dosage as needed for adequate sedation. Patients were monitored by continuous measurement of oxygen saturation and pulse rate as well as intermittent measurement of blood pressure.

EGD and EUS were performed before and after PVI within 48 hours. Because of the stiffness of EUS endoscopes, the fundic region of the stomach could not precisely be evaluated in retroflexion. Therefore, we performed EGD with a standard video-gastroscope (GIF-Q160 or GIF-Q160Z, Olympus, Tokyo, Japan) previous to EUS to detect endoluminal changes of the esophagus and stomach. EUS was performed with a 7.5-MHz radial scanner (EUB 8500, Hitachi, Tokyo, Japan). With the deflated EUS balloon, the minimal distance between the esophageal lumen and the endocardium of the left atrium as well as the vertical contact length between the left atrium and the esophagus were determined. Careful examination of the mediastinum and the esophageal wall was performed using a moderately inflated EUS balloon before ablation to document preexisting esophageal and mediastinal alterations. Within 48 hours after ablation, a follow-up endoscopic examination was performed assessing mucosal and peri-esophageal/mediastinal lesions. In cases of newly detected structural changes, a second follow-up examination including EGD and EUS was performed 1 week after PVI.

Statistical Analysis

Categorical variables were compared using the Fisher exact test. Continuous variables are presented as mean±1 SD and were compared using an unpaired Student t test. Statistical significance was reached at P≤0.05.

Results

Topographical Anatomy

In all patients, a regular contact area between the LA and the esophagus could be demonstrated before PVI. The mean vertical contact length was 4.4±1.5 cm (range, 2 to 10 cm); the mean distance between the anterior wall of the esophagus and the endocardium was 2.6±0.8 mm (range, 1.4 to 4.0 mm).

Esophageal, Mediastinal, and Atrial Findings

The course of the esophagus was left-sided in the majority of patients (n=17), a right-sided and middle course could be demonstrated by CT in 1 and 10 patients, respectively. One patient with a history of achalasia and myotomy presented with a dilated esophagus covering the whole posterior wall of the left atrium. After PVI, morphological changes in the periesophageal connective tissue and the posterior wall of the LA were diagnosed by endosonography in 8 patients (27%; 95% CI, 12.73 to 47.24), including abolition of the regular esophageal mucosal layer pattern with edema and peri-esophageal accumulation of liquid, swelling of the posterior wall of the LA also beyond the site of ablation, and mediastinal adenopathy (Table 2 and the Figure). The observed changes did not correlate with the vertical contact length or with the distance between the
anterior wall of the esophagus and the endocardium. No mucosal changes of the esophagus in terms of erythema or ulcers were found. The patient with achalasia presented no lesions detectable by EGD/EUS. Two of the 8 patients (25%) with documented lesions reported mild chest pain, yet 3 of the remaining 21 patients without esophageal and mediastinal alterations also reported such symptoms (14%). Clinical characteristics of the 2 groups were not different (Table 3).

Follow-Up
In all but 1 patient (who refused the control), the above-mentioned changes were checked again 1 week after the first post-PVI endoscopy: All changes had resolved within this period of time. No atrioesophageal fistula occurred during follow-up (mean follow-up, 294 ± 110 days; range, 36 to 431 days).

Discussion
Thermal injury is likely to play the crucial role in the development of atrioesophageal fistula. Consequently, limiting the magnitude of power (20 to 30 W) and duration of RF application is used in the clinical setting to avoid esophageal

<table>
<thead>
<tr>
<th>Type of Lesion/Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tr>
<td>Pericardial effusion</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Alteration of the interface between LA and esophagus</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinal edema</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinal adenopathy</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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</table>

Table 3. Characteristics of Patients With and Without Newly Detected Lesions After PVI

<table>
<thead>
<tr>
<th></th>
<th>Patients With Lesions (n=8)</th>
<th>Patients Without Lesions (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>56±6</td>
<td>58±12</td>
</tr>
<tr>
<td>Sex</td>
<td>2 women, 6 men</td>
<td>5 women, 16 men</td>
</tr>
<tr>
<td>LA diameter, cm</td>
<td>4.5±0.6</td>
<td>4.7±0.7</td>
</tr>
<tr>
<td>Distance LA-esophageal fistula, mm</td>
<td>2.7±0.7</td>
<td>2.5±0.8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29±3.7</td>
<td>28±4.7</td>
</tr>
<tr>
<td>Total RF duration, min</td>
<td>44±15</td>
<td>49±15</td>
</tr>
</tbody>
</table>

P=NS for all variables.

Figure. A and B, EUS showing periesophageal edema and swelling of the posterior wall of the left atrium; C, EUS showing preserved esophageal, mediastinal, and LA anatomy in another patient. PV indicates pulmonary vein; AV, azygos vein.
damage. Additionally, the course of the esophagus in relation to the left atrium is monitored by numerous investigators.\textsuperscript{18–20} The exact position of the esophagus and its relation to the posterior wall may be different at the time of the ablation procedure compared with the preprocedurally acquired CT scan, perhaps because of the fasting state and resulting fluid changes. Yet, Piorkowski et al\textsuperscript{21} showed a high concordance between the esophageal-LA relationship on an electroanatomic reconstruction and a CT-scan in a similar setting. The mobility of the esophagus, however, cannot be monitored by this approach. Apart from a probe inside the esophagus and tagging its course in the 3D mapping system, this may be accomplished by ingestion of barium paste at the beginning of the ablation.\textsuperscript{22,23} However, there are conflicting data concerning the mobility of the esophagus in the segments relevant to the ablation procedure. Piorkowski et al\textsuperscript{21} described a degree of mobility of the esophagus toward the roof of the LA using an in vivo 3D tagging of the esophagus and a stable anatomic relationship at the midportion and the inferior LA. In contrast to this, Good et al\textsuperscript{24} demonstrated a significant mobility of the esophagus also in these segments, visualizing the esophagus by a barium swallow. A significant discord between CT-defined and esophagram-defined borders of the esophagus was also reported by Daoud et al.\textsuperscript{24} Luminal esophageal temperature monitoring during ablation at the posterior LA wall is used to guide the ablation procedure and possibly reduce esophageal injury.\textsuperscript{25–27} All periesophageal and mediastinal lesions described here are directly related to the ablation procedure, given the regular index examination before ablation. The absence of mucosal changes in the present study is possibly due to a different ablation strategy and the use of conscious sedation rather than general anesthesia or deep sedation. Schmidt et al\textsuperscript{11} reported esophageal wall changes in 47% of their patients using either an 8-mm solid-tip ablation catheter or a 3.5-mm tip open irrigated catheter with a maximum power setting of 50 W. This high power, compared with our study, may lead to deeper ablation lesions affecting also the esophageal mucosa. Medial-wall changes were not investigated in that study. Recently, a US-wide survey reported 6 fistulae in 20,425 patients undergoing AF ablation.\textsuperscript{28} The development of an atrioesophageal fistula was associated with the use of 8-mm-tip catheters and high power settings, further supporting the above hypothesis. Recently, an increased risk of esophageal damage caused by ablation of AF in patients undergoing general anesthesia has been described.\textsuperscript{12} Mucosal lesions of the esophagus occurred in a much higher proportion in this subgroup than in patients undergoing conscious sedation. Several mechanisms may explain the higher incidence of esophageal lesions in the general anesthesia group. The esophageal motility may be reduced, leading to a prolonged exposure of the same area of the esophagus to thermal energy during ablation. Moreover, the lack of swallowing might reduce the physiological cooling effect and lead to thermal injury. In general, ischemia by thermal damage to the anterior esophageal arteries is likely to play a crucial role in the development of esophageal lesions. Whether a reduced or changed perfusion under general anesthesia might aggravate this during PVI is not known. Stopping ablation secondary to pain may not be specific concerning esophageal injuries. Yet, Aryana et al\textsuperscript{29} found an association with pain and esophageal temperature rise and a lack of pain with an absence of temperature rise in patients undergoing PVI during monitoring the esophageal temperature with a probe. Hence, not being able to detect pain during ablation under general anesthesia as a surrogate for imminent tissue injury might also add to the likelihood of esophageal injury. In the study by di Biase et al.,\textsuperscript{12} endoscopic evaluation was performed using capsule video endoscopy, which is unable to provide information concerning esophageal wall and mediastinal changes. Moreover, cost-efficiency strongly favors standard endoscopic evaluation.

More recently, Badger et al\textsuperscript{30} demonstrated the feasibility of using delayed-enhancement MRI to assess the extent and progression of esophageal wall injury after PVI in 41 patients. Endoscopic evaluation, however, was performed in only 3 of the 5 patients exhibiting esophageal delayed hemorrhage after ablation. In these patients, mucosal lesions in terms of erosions and erythema were observed. However, in contrast to our study, EUS was not performed routinely but only in 1 patient. This patient was reported to have a preserved esophageal wall architecture with no mediastinal or periesophageal adenopathy, despite a more aggressive ablation strategy, which also targeted the posterior wall of the LA. Thus, it is tempting to speculate that MRI is less sensitive than EUS in detecting periesophageal lesions after PVI.

The present study clearly shows that endosonographic evaluation is a safe and reliable method to identify mediastinal changes after catheter ablation of AF. This tool might prove to be a valuable diagnostic option in symptomatic patients after pulmonary vein isolation concerning the possible development of LA-esophageal fistula. Patients with mediastinal lesions identified by endosonography might be selected for a closer clinical and endosonographic follow-up than those with no lesions. In our patients, all mediastinal changes resolved completely within 1 week after PVI. Persisting mediastinal changes might herald the later development of an LA-esophageal fistula and should be monitored even more closely.

**Limitations**

An esophageal temperature probe was not routinely used in all patients to detect temperature rise during power delivery with RF energy applications, therefore a possible beneficial effect on esophageal damage as described elsewhere\textsuperscript{27} was not evaluated.

**Conclusion**

Mucosal changes of the esophagus after PVI, such as ulcers or erythema, as recently published, could not be demonstrated in this study, yet structural changes in the mediastinum, which were only visible by endosonography, occurred in 27% of patients in the present investigation. This may indicate a higher-than-expected periesophageal injury rate caused by PV ablation. Endosonography might extend the range of tools at hand in the follow-up of patients after PVI, considering the presumably higher sensitivity of EUS compared with MRI.

**Disclosures**

None.

**References**


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Clinical Perspective

Atrial-esophageal fistula is a rare but usually fatal complication of atrial fibrillation ablation. A reliable method for early detection of esophageal tissue injury after catheter ablation is of interest. Our study demonstrates that structural changes in the mediastinum are of patients with atrial fibrillation.

CLINICAL PERSPECTIVE

Atrial-esophageal fistula is a rare but usually fatal complication of atrial fibrillation ablation. A reliable method for early detection of esophageal tissue injury after catheter ablation is of interest. Our study demonstrates that structural changes in the mediastinum are detectable by endosonography in a large proportion of patients early after atrial fibrillation ablation. Evidence of injury was present, despite the absence of visible abnormalities with conventional endoscopy. These findings suggest that injury to periesophageal tissues may be relatively common. Its relation to atrial-esophageal fistula is not known. Endosonography might help further define the prevalence of injury, which could assist in developing methods to reduce the risk of esophageal injury.

Zellerhoff et al

Esophageal and Mediastinal Changes After PVI


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Supplemental figure 1: Normal endosonography prior to ablation

Supplemental video 1: Endosonography in the same patient showing mediastinal and esophageal changes after ablation