

Progression From Esophageal Thermal Asymptomatic Lesion to Perforation Complicating Atrial Fibrillation Ablation A Single-Center Registry

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Background—Up to 40% of patients demonstrate endoscopically detected asymptomatic esophageal lesions (EDEL) after atrial fibrillation ablation.

Methods and Results—Patients undergoing first atrial fibrillation ablation and postinterventional esophageal endoscopy were included in the study. Occurrence of esophageal perforating complications during follow-up was related to documented EDEL (category 1: erythema/erosion; category 2: ulcer). In total, 1802 patients underwent first atrial fibrillation ablation procedure between January 2013 and August 2016 at our institution. Out of this group, 832 patients (506 male patients, 61%; 64.0±10.0 years) with symptomatic paroxysmal (n=345; 42%) or persistent atrial fibrillation underwent postprocedural esophageal endoscopy. Patients were ablated using single-tip ablation with conventional or surround flow irrigation and circular ablation catheters with open irrigation (nMARQ). In 295 of 832 patients (35%), a temperature probe was used. EDEL occurred in 150 patients (18%; n=98 category 1 EDEL, n=52 category 2 EDEL). In 5 of 832 patients (0.6%), an esophageal perforation (n=3) or an esophagopericardial or atrioesophageal fistula (n=2) occurred 15 to 28 days (19±6 days) after ablation. Two patients (1 atrioesophageal fistula and 1 esophagopericardial fistula) died. Esophageal perforation occurred only in patients with category 2 lesions (absolute risk, 9.6%). In a logistic regression analysis, ulcers were identified to be a significant predictor for esophageal perforating complications.

Conclusions—Postablation endoscopy seems to identify patients at high risk of esophageal perforating complications only occurring in patients with category 2 EDEL. One out of 10 postablation esophageal ulcers progressed to perforation, and no patient without esophageal thermal ulcers showed the occurrence of perforating esophageal complications. (*Circ Arrhythm Electrophysiol.* 2017;10:e005233. DOI: 10.1161/CIRCEP.117.005233.)

Key Words: atrial fibrillation ■ atrioesophageal fistula ■ catheter ablation ■ endoscopy ■ esophageal fistula ■ esophageal perforation ■ thermal esophageal lesion

Major complications related to ablation of atrial fibrillation (AF) occur in ≤4.5% of patients. A large multicenter survey reports a procedure-related complication rate of 7.8%. One of the most fatal complications is atrioesophageal fistula (AEF) reported in ≤0.2% of AF ablation cases.^{1,2} A study comparing pulmonary vein isolation (PVI) using radiofrequency and cryoballoon ablation reported an overall complication rate of 12.8% in the radiofrequency ablation group without any perforating complication reported in this cohort.³ Whereas the exact mechanism of AEF is still unknown esophageal thermal lesions as a direct result of ablation within the left atrium (LA) have been proposed to be the starting point of the cascade leading to esophageal perforation and AEF.

Endoscopically detected asymptomatic esophageal lesions (EDEL) occur in ≤40% of asymptomatic patients after AF ablation.^{2,4-15} These asymptomatic complications have been used as a surrogate parameter for the risk of esophageal perforating complications related to AF ablation. To date, no study evaluated the relevance of EDEL in relation to the advent of esophageal perforation.

Aim of this study was to correlate postablation endoscopically detected thermal lesions to progression to esophageal perforating complications and potential risk factors.

Methods

Study Population

The study was approved by the local institutional review board. All patients with symptomatic paroxysmal and persistent AF who underwent their first LA radiofrequency catheter ablation, including PVI at our institution between January 2013 and October 2016,

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WHAT IS KNOWN

- Endoscopically detected asymptomatic esophageal lesions occur in $\leq 40\%$ of asymptomatic patients after atrial fibrillation ablation.
- Occurrence of atrioesophageal fistula is reported in $\leq 0.2\%$ of atrial fibrillation ablation procedures.

WHAT THE STUDY ADDS

- Endoscopically detected asymptomatic esophageal lesions seem to be a prerequisite for the occurrence of esophageal perforation or atrioesophageal fistula. Especially patients with procedure-related esophageal thermal ulcers seem to be at risk of progression toward esophageal perforation.
- Early application of esophageal stents in patients with esophageal perforation without esophageal fistula seems to be an effective treatment option.

were retrospectively enrolled. Patients were only included, if results of postprocedural esophagogastroduodenoscopy (EGD) performed within 7 days after ablation procedure were available.

AF Ablation Procedure

Transesophageal echocardiography was performed on the day before the ablation procedure to rule out LA thrombi in every patient. All procedures were performed either under continued oral anticoagulation using phenprocoumon with therapeutic international normalized ratio levels (2.0–2.5) or continued non-vitamin K antagonist oral anticoagulants. In patients not on oral anticoagulation on the day of admission before planned ablation procedure, an oral anticoagulation with a vitamin K antagonist or non-vitamin K antagonist oral anticoagulant was started directly after the ablation procedure. When beginning an oral anticoagulation with a vitamin K antagonist, a concomitant treatment with subcutaneous fractionated heparin or intravenous unfractionated heparin was started until an international normalized ratio level >2.0 was reached. Intravenous heparin was administered during the procedure to achieve a target activated clotting time of >300 s irrespective of the underlying oral anticoagulation regimen.

The procedure was performed using a 3-dimensional electroanatomic mapping system (CARTO; Biosense Webster, Diamond Bar, CA) in all patients. All LA ablation procedures were performed in deep sedation using continuous propofol infusion in conjunction with morphine derivatives as necessary according to our standard approach. In patients undergoing single-electrode radiofrequency catheter ablation, isolation of the ipsilateral PVs was performed en-block in a point-by-point fashion. In the group undergoing nMARQ catheter ablation, each PV was isolated itself whenever feasible or en bloc depending on the LA and PV anatomy.

The end point of the ablation procedure was exit and entrance block of each PV confirmed by the use of a lasso catheter (Biosense Webster) in single-electrode catheter ablation procedures or with the nMARQ circular ablation catheter (Biosense Webster), respectively. Maximum ablation energy, target temperature, contact force, and irrigation rate for each of the Ablation Catheters Used in the Study Cohort are listed in the section Ablation Catheters Used in the Study Cohort. PVI was performed by experienced operators, each having performed >500 AF ablation procedures before and experienced with each of the ablation catheter types used.

Ablation Catheters Used in the Study Cohort

Patients were ablated using single-electrode radiofrequency ablation catheters with conventional catheter tip irrigation (Group 1) or with modified surround flow irrigation (Group 2) or with a circular

irrigated ablation catheter—nMARQ—(Group 3). Posterior wall ablation was power limited (≤ 25 W for single-electrode ablation catheters; ≤ 15 W for circular irrigated catheters).

1. Group 1: ThermoCool, Biosense Webster; irrigation rate 30 mL/min, maximum ablation energy of 35 W (maximum energy of 25 W at posterior wall); ThermoCool SmartTouch, Biosense Webster; irrigation rate 30 mL/min, maximum ablation energy of 35 W (maximum energy at posterior wall 25 W).
2. Group 2: ThermoCool SmartTouch SF, Biosense Webster; irrigation rate 17 mL/min, maximum ablation energy of 35 W (maximum energy at posterior wall 25 W).
3. Group 3: nMARQ, Biosense Webster; irrigation rate 60 mL/min, maximum ablation energy of 25 W (maximum energy at posterior wall 15 W).

Intraluminal Esophageal Temperature Measurement

In a subgroup of patients, esophageal endoluminal temperature (LET) probes (S-Cath; CIRCA Scientific, LLC, Englewood, CO or SensiTherm; St. Jude Medical, Palo Alto, CA) were used according to the operators choice, but not on a regular basis (Figure 1). According to our standard approach—when using LET measurement—ablation was interrupted when a cutoff intraluminal esophageal temperature of 40.5°C was documented. If necessary, posterior wall ablation sites for PVI were modified, and the maximum ablation energy was further reduced to achieve PVI without exceeding the cutoff esophageal temperature.

Postablation Esophageal Endoscopy

EGD was performed by experienced operators within 7 days after ablation to assess the presence and extent of endoscopically detected esophageal lesions (EDEL). EDEL was defined as any esophageal lesion in the region of the contact area between esophagus and LA (identified during EGD) and was classified as either erythema/erosion (category 1) or ulceration (category 2; Figure 2). On the basis of the visual aspect during endoscopy, erythema/erosion was defined as a thermal esophageal ablation-induced lesion with reddish discoloration or superficial disruption of the esophageal mucosa but without disruption of the lamina muscularis mucosae. An ulcer was defined as deep disruption of the esophageal mucosa extending into the sub-mucosal layers, including fibrinous coverage. The differentiation was performed based on operators estimation and visual aspect during initial endoscopy. Ulcerous lesions were considered more severe and deeper than category 1 lesions. Description and examples of EDEL from both categories were distributed to all endoscopy operators before performing EGD in post-AF ablation patients to ensure correct and uniform classification of esophageal findings.

All patients independent of EGD results received proton pump inhibitors (minimum 40 mg once daily) for 6 weeks after ablation. In case of EDEL, EGD was repeated within 14 days according to our standard protocol. Patients with esophageal ulcerations received a liquid diet in addition to proton pump inhibitors in double standard dose (80 mg per day) until repeat EGD indicated that esophageal injury was in remission (and would be categorized as category 1 lesion). Clinical follow-up (FU) was done after 6 weeks to 3 months after ablation procedure to identify any clinically relevant events related to esophageal injury. Perforating esophageal complications were defined as (1) any esophageal perforation occurring during FU based on computed tomographic (CT) imaging indicated by air and oral contrast medium extravasate after swallowing in the mediastinum or (2) pericardioesophageal or AEF based on CT imaging.

Parameters Evaluated

Sex, patient age, type of AF, CHA₂DS₂-VASc score, coronary artery disease, arterial hypertension, diabetes mellitus, left ventricular ejection fraction, LA diameter, body mass index, esophageal position in relation to LA according to CT scan, type of ablation catheter, use of esophageal temperature probe, type of temperature probe, total

ablation time, maximum ablation energy if applicable, maximum esophageal temperature $>40.5^{\circ}\text{C}$, and postprocedural proton pump inhibitor prescription were included in a logistic regression analysis to identify possible predictors of esophageal lesions or perforating esophageal complications.

Statistical Analysis

The data are expressed as mean \pm SD for continuous variables or as numbers and percentages for categorical variables. Continuous variables were evaluated by logistic regression; categorical variables were analyzed by contingency tables. Effect size Cramér's V and the results of the χ^2 test were given. For the analysis of possible risk factors for perforating complications, Fisher exact test was used because of the small number of events. For logistic regression, results were given as odds ratios and 95% confidence intervals and P values. Multivariable or bivariate regression analyses were used as appropriate (the type of regression analysis used is indicated within the table). P values <0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 24.

Results

Patient Characteristics

In total, 1802 patients underwent a first AF ablation procedure at our institution between January 2013 and August 2016. Out of this group, 832 patients (46%) underwent a postprocedural

esophageal endoscopy within 7 days after ablation and formed the study cohort. Patient characteristics are displayed in Table 1.

Procedural Parameters

Patients were ablated using different ablation technologies, including single-tip radiofrequency ablation catheters with and without contact force measurement, with conventional ($n=543$, 65%) and modified surround flow irrigation ($n=140$, 17%) and single-shot circular radiofrequency ablation catheters with open irrigation (nMARQ; $n=149$, 18%). In 295 patients (35%), a temperature probe was used. Total ablation time was 33.9 ± 13.4 minutes in the whole patient cohort, and mean maximum ablation energy was 34.3 ± 3.3 W in single-tip ablation catheters. A differentiation into ablation energy at posterior wall and at other ablation sites was not available for the whole cohort.

Use and Type of Temperature Probe and Maximum Temperature Rise in the Group With Temperature Measurement

In patients with LET monitoring, the SensiTherm (St. Jude Medical) probe was used in 232 cases and the S-Cath (CIRCA

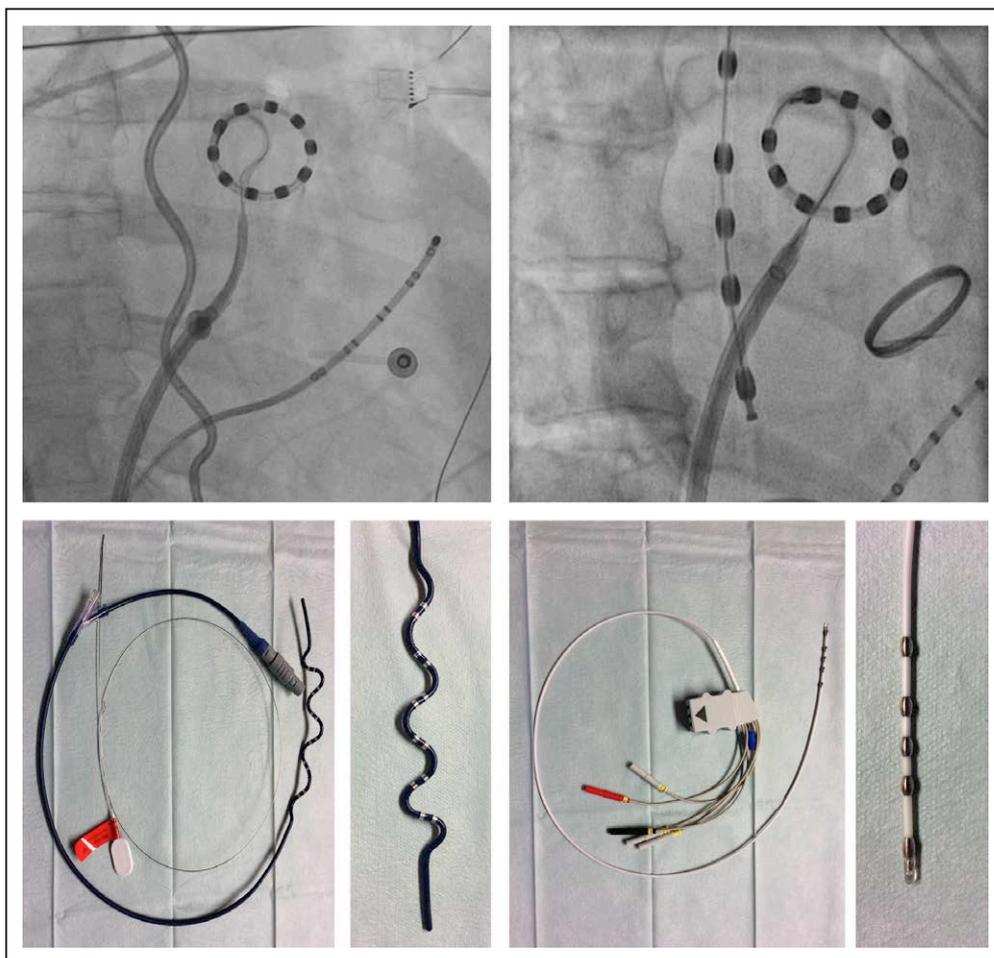


Figure 1. S-Cath temperature probe within the esophagus during an ablation procedure with nMARQ ablation catheter (fluoroscopy; **left top**); S-Cath probe without mandrine—12 insulated thermocouples in pairs on a flexible shaft (with an S shape when mandrine pulled out; **left bottom**); SensiTherm temperature probe during ablation with nMARQ ablation catheter (fluoroscopy; **right top**); SensiTherm probe with 3 olive-shaped thermocouples on a flexible shaft (**right bottom**).

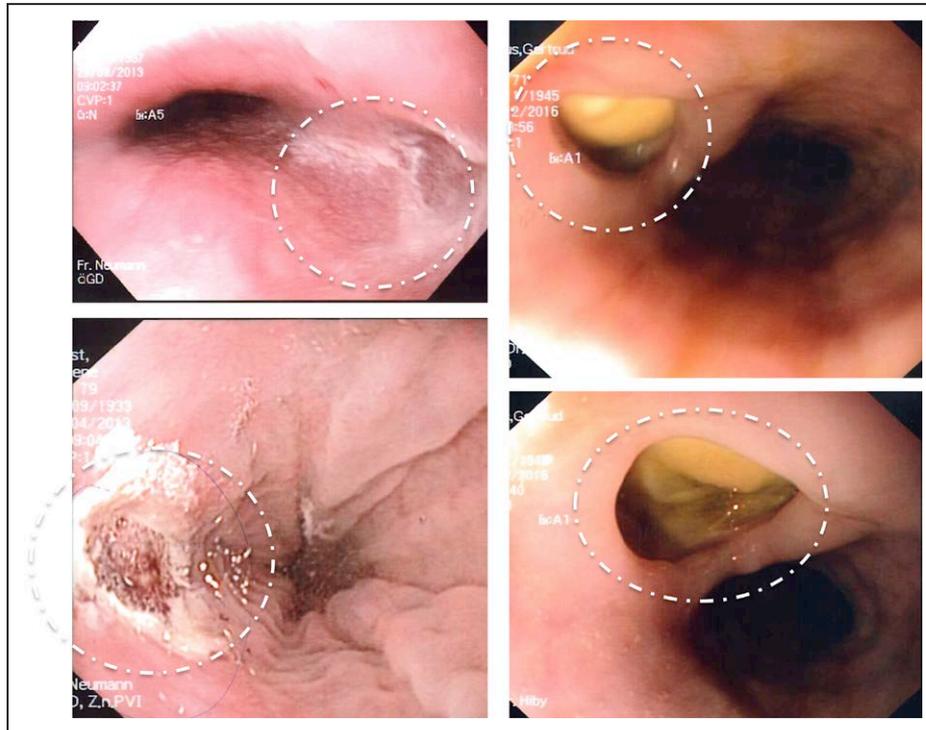


Figure 2. Examples of esophageal endoscopy findings. Esophageal erosion at typical location within the esophagus (**left top**); esophageal ulceration (**left bottom**); perforation confirmed by contrast dye computed tomographic scan, this patient was treated with a covered stent in the same procedure (**right top and bottom**).

Scientific) probe in 63. One-hundred fifty-seven of the 295 patients (53.2%) demonstrated at least 1 intraluminal temperature rise $>40.5^{\circ}\text{C}$ with a mean peak temperature of $40.9 \pm 1.2^{\circ}\text{C}$ (highest esophageal temperature 45.0°C).

Incidence of EDEL and Esophageal Perforation After AF Ablation

One-hundred fifty patients (18%) demonstrated EDEL in postprocedural endoscopy ($n=98$ erythema or erosion, $n=52$

Table 1. Patient Characteristics

	Patients With EDEL in Postprocedural Endoscopy ($n=150$), 18%	Patients Without EDEL in Postprocedural Endoscopy ($n=682$), 82%	<i>P</i> Value	All Patients Included in the Study ($n=832$)	Patients Not Included in the Study ($n=970$)	<i>P</i> Value
Age, y	64.1 ± 10.5	63.9 ± 9.9	0.79	63.9 ± 10.0	63.7 ± 10.4	0.70
Sex: female, n (%)	68 (45)	258 (38)	0.09	326 (39)	359 (37)	0.36
BMI	29.3 ± 5.3	29.9 ± 5.6	0.40	29.8 ± 5.6	29.8 ± 6.4	0.95
LA area, mm^2	23.7 ± 5.7	24.0 ± 5.0	0.52	24.0 ± 5.2	23.9 ± 4.8	0.79
Persistent AF, n (%)	91 (61)	396 (58)	0.80	487 (59)	603 (62)	0.12
LVEF (%)	58.8 ± 10.2	59.5 ± 9.5	0.39	59.4 ± 9.6	58.9 ± 10.6	0.28
CHA ₂ DS ₂ -VASc score	2.4 ± 1.4	2.3 ± 1.4	0.35	2.3 ± 1.4	2.4 ± 1.4	0.35
Hypertension, n (%)	123 (82)	574 (84)	0.52	697 (84)	832 (86)	0.26
CAD, n (%)	41 (27)	171 (25)	0.57	212 (26)	238 (25)	0.66
Diabetes mellitus, n (%)	16 (11)	86 (13)	0.51	102 (12)	129 (13)	0.53
Stroke/TIA, n (%)	11 (7)	30 (4)	0.13	41 (5)	67 (7)	0.09
Esoph. position (in CT)			0.09	
Left to LA, n (%)	76/141 (54)	300/676 (44)		376/817 (46)		
In the middle, n (%)	64/141 (45)	363/676 (54)		427/817 (52)		
Right to LA, n (%)	1/141 (1)	13/676 (2)		14/817 (2)		

Values are presented as mean \pm SD and as numbers and percentages. AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CT, computed tomography; EDEL, endoscopically detected esophageal lesion; Esoph., esophageal; LA, left atrium; LVEF, left ventricular ejection fraction; and TIA, transient ischemic attack.

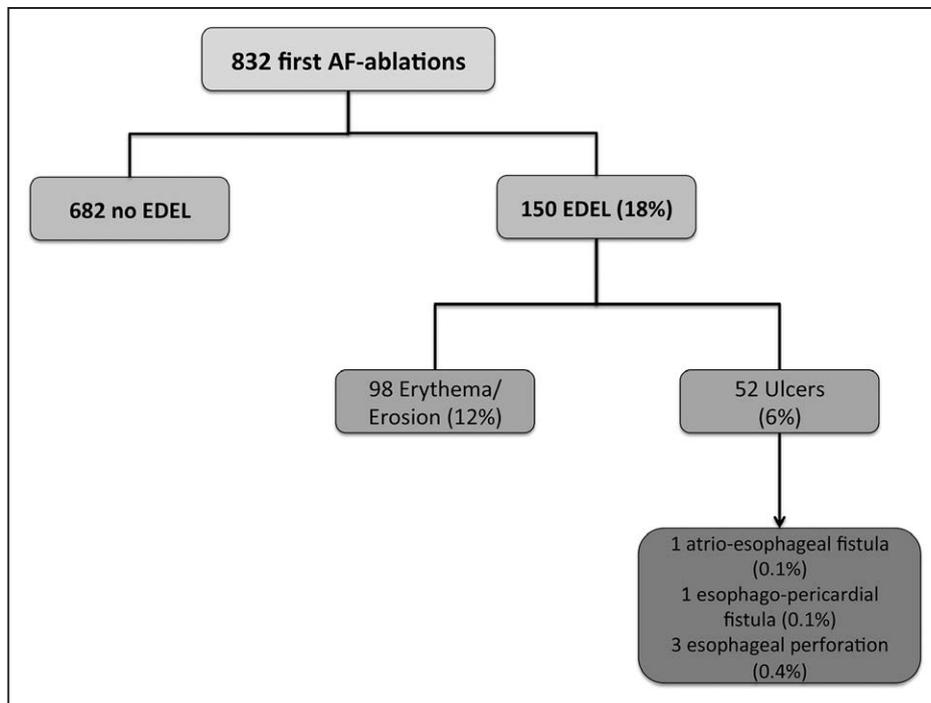


Figure 3. Flow chart of patient cohort that was analyzed and included in the study. AF indicates atrial fibrillation; and EDEL, endoscopically detected asymptomatic esophageal lesions.

ulcers; Figure 3). EDEL occurred in 103 patients (34.9%) with esophageal temperature probe use (ulcers $n=29$; erythema/erosion $n=74$).

The incidence of EDEL in relation to the used ablation catheter was radiofrequency irrigated ablation catheters 95 EDEL, 17.5% (66 category 1; 29 category 2); radiofrequency surround flow irrigation catheters 29 EDEL, 20.7% (16 category 1; 13 category 2); and nMARQ ablation catheter 26 EDEL, 17.4% (16 category 1, 10 category 2). During a median FU of 8.8 months, 5 of 832 patients (0.60%) demonstrated esophageal perforation (15–28 days after ablation; a median of 16 days). Two of 5 patients (0.2%) died because of AEF ($n=1$) and esophagopericardial fistula ($n=1$). All 5 patients had category 2 EDEL (ulcer) on postablation endoscopy. Out of 52 ulcerous EDEL, 5 progressed to perforation (9.6%). No esophageal perforating complication was seen in patients with category 1 EDEL (erythema/erosion) or no EDEL on postablation endoscopy. Category 2 thermal lesions (ulcer) demonstrated to be a prerequisite for the occurrence of an esophageal perforation or AEF ($P=0.001$). During FU, no other patients out of the study cohort showed esophageal perforation or died.

Treatment of Esophageal Perforating Complications

Three patients with documented esophageal perforation in CT were treated with covered esophageal stents tacked to the esophageal wall for 4 to 6 weeks until remission. All of these patients recovered completely, and the stent could be retrieved after 4 to 6 weeks (Figure 4).

One patient with esophagopericardial fistula underwent surgery (15 days after ablation) but died because of septic shock 4 days after surgical repair. One patient with esophageal perforation documented by CT scan died after assumed

progression to AEF suddenly 5 days after CT scan after admission to an external hospital (Table 2).

Predictors of EDEL and Esophageal Perforation After AF Ablation

The only risk factor associated with the occurrence of EDEL according to the multivariable logistic regression analysis was maximum intraesophageal temperature rise $>40.5^{\circ}\text{C}$ in the group of patients monitored with luminal esophageal temperature probes (about maximum temperature rise $>40.5^{\circ}\text{C}$: odds ratio, 4.044; 2.049–7.984; $P<0.001$). The relative risk for the incidence of a category 2 EDEL was 2.76 if esophageal temperature exceeded 40.5°C in patients with luminal esophageal temperature monitoring. The mean maximum esophageal temperature was $40.9\pm 1.2^{\circ}\text{C}$. The optimal cutoff value predicting EDEL in postprocedural endoscopy was identified between 40.55°C and 41.45°C . Using a cutoff value of 40.55°C maximum esophageal temperature, 76% of patients with EDEL would have been identified, whereas 52.5% with negative endoscopy results would have been falsely assumed as EDEL positive. When using a cutoff value of 41.45°C , 47.9% of all patients with positive endoscopy results (EDEL positive) would have been identified, whereas 18.1% would have been falsely declared as EDEL positive. The Youden's Index identified an optimal cutoff value of 41.15°C (61.5% correctly identified as EDEL positive and 26.2% patients with negative endoscopy falsely identified as EDEL positive).

None of the tested variables except overall EDEL and category 2 EDEL in postprocedural endoscopy demonstrated a significant association with occurrence of esophageal perforating complications—effect size Cramér's V : 0.166 and 0.255 for overall EDEL and category 2 EDEL, respectively; $P<0.001$ and $P=0.004$, (Tables 3 and 4). The absolute risk for

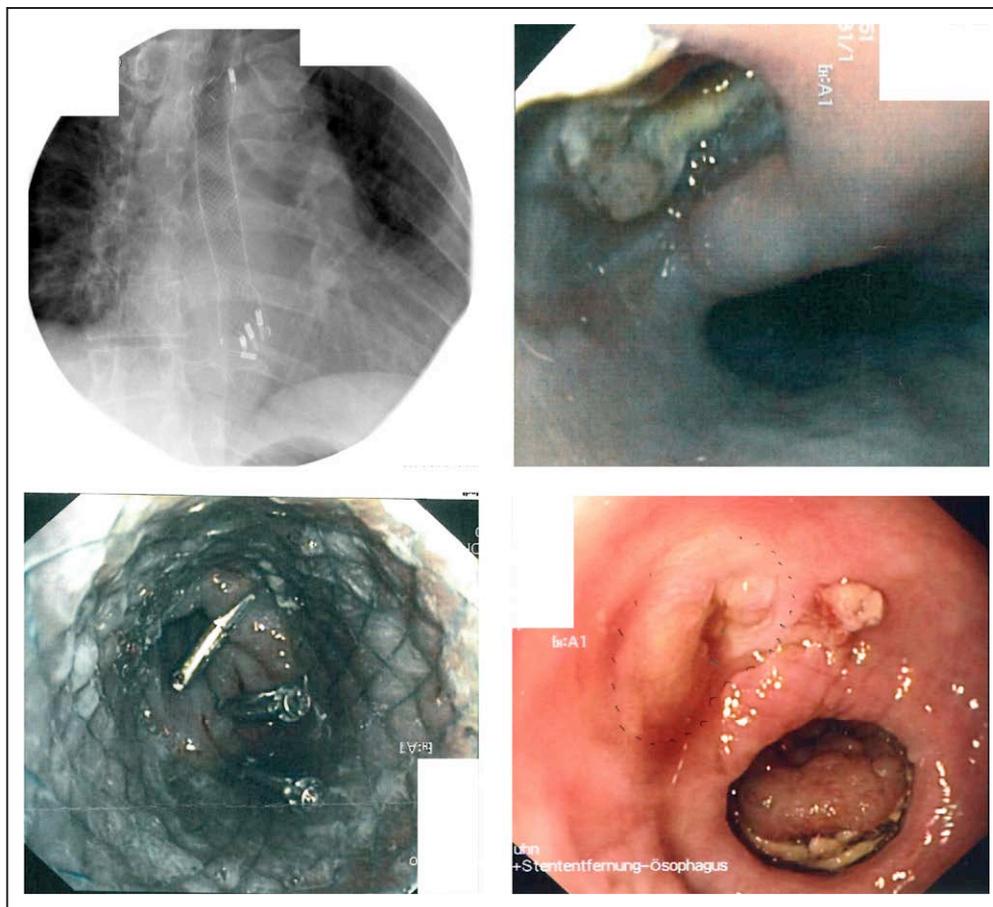


Figure 4. Patient with esophageal perforation detected in computed tomographic scan: fluoroscopy of esophageal stent in correct position (left top) and in endoscopic control fixed by the use of clips (left bottom). Esophageal perforation before placement of the stent (right top) and after retraction of the stent in endoscopy (right bottom).

the incidence of esophageal perforation or fistula in patients demonstrating category 2 EDEL in postinterventional EGD was 9.6% (5 of 52 patients with an ulcer diagnosed in EGD).

EDEL in Control EGD and Progression to Perforating Complications

All patients with documented EDEL underwent a control EGD after a mean of 12.3 ± 8.9 days. Results of control EGD

were available in 47 patients: in 24 of 47 (51%) patients, lesions regressed but the lesion site was still detectable on EGD, and 23 of 47 patients (49%) showed no detectable residual lesions in control EGD. In patients with category 1 EDEL in 5 of 24 patients, lesion site was still visible in control EGD (21%), whereas in patients with category 2 EDEL 19 of 23 patients (83%) still demonstrated a visible lesion residuum.

Table 2. Summary of Patients With Perforating Esophageal Complications, Including Surgical and Nonsurgical Treatment Strategy Used

Patient	Age (y)	Sex	CHA ₂ DS ₂ -VASc	LVEF (%)	LAD (mm)	Ablation Catheter	Temperature Probe	Max. Temperature (°C)	Les. Type	Days After Ablation	Surg. Stent	Fatal
Patient 1, fistula	67	F	3	50	50	nMARQ	SensiTherm	40.4	Ulcer	15	Surg.	Yes
Patient 2, fistula	57	F	2	65	40	Non-SF	SensiTherm	41.7	Ulcer	15	Surg.	Yes
Patient 3, perforation	70	M	1	65	36	SF	SensiTherm	42.4	Ulcer	16	Stent	No
Patient 4, perforation	67	M	3	45	50	nMARQ	None	n/a	Ulcer	28	Stent	No
Patient 5, perforation	68	F	3	65	40	Non-SF	None	n/a	Ulcer	19	Stent	No

F indicates female; LAD, left atrial diameter; Les., lesion; LVEF, left ventricular ejection fraction; M, male; n/a, not applicable; SF, surround flow; and Surg., surgery.

Table 3. Logistic Multivariable Regression Analysis of Variables Potentially Influencing EDEL (Dependent Variable)

	Odds Ratio (95% CI)	P Value
Female sex	1.433 (0.967–2.124)	0.073
Age	0.999 (0.979–1.019)	0.893
BMI	0.972 (0.932–1.015)	0.202
Paroxysmal AF	1.183 (0.800–1.750)	0.400
CHA ₂ DS ₂ -VASc score	1.078 (0.391–2.971)	0.885
LA area, mm ²	0.986 (0.948–1.025)	0.466
LVEF	0.988 (0.969–1.007)	0.203
CAD	1.259 (0.277–1.509)	0.312
Previous cardiac surgery	0.647 (0.312–1.603)	0.314
Arterial hypertension	0.767 (0.460–1.279)	0.309
Diabetes mellitus	0.789 (0.439–1.418)	0.428
Previous stroke	1.892 (0.908–3.943)	0.089
Ablation method (RF vs nMARQ)	0.956 (0.588–1.552)	0.663
Ablation method (RF-SF vs nMARQ)	1.167 (0.642–2.120)	0.203
In patients with esophageal temperature measurement		
Max. esoph. temperature >40.5°C	4.044 (2.049–7.984)	<0.001

AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; EDEL, endoscopically detected asymptomatic esophageal lesions; LA, left atrial; LVEF, left ventricular ejection fraction; RF, radiofrequency; and SF, surround flow.

Discussion

Main Findings

For the first time, a direct relation between postablation endoscopically detected esophageal thermal lesion and esophageal perforation was demonstrated. Eighteen percent of patients undergoing a first AF ablation using radiofrequency technology showed EDEL, including one third being category 2 (ulcerous) lesions. Almost 10% of category 2 lesions but none of category 1 lesions progressed to esophageal perforation or fistula. None of the patients without EDEL demonstrated an esophageal perforating complication during FU. An overall incidence of EDEL of 18% was documented using current standard radiofrequency ablation technology. This is well in line with previous published reports of smaller patient cohorts.

Incidence of Perforating Esophageal Complications

Perforating esophageal complications of AF ablation have been estimated to be as high as 0.2%, but reliable data are missing as there are an estimated number of undetected cases.^{2,15–20} In our cohort, the incidence of esophageal perforation after AF ablation was 0.6% and 0.2% for fatal outcome esophageal perforation. Dagues et al²⁰ reported an incidence of 0.2% fatal AEF. However, 2 patients in their study (0.2%) died suddenly within weeks after ablation with unknown cause of death. All of the patients included in our study were followed for at least 6 weeks or until death, and therefore no dropout or missed cases of esophageal perforation are expected. Our

Table 4. Bivariate Logistic Regression Analyses of Variables Potentially Influencing Perforating Esophageal Complications (Dependent Variable)

	Odds Ratio (95% CI)	Effect Size Cramér's V	P Value
Female sex	2.341 (0.389–14.084)		0.353
Age	1.018 (0.928–1.116)		0.708
BMI	1.039 (0.849–1.271)		0.713
Paroxysmal AF	0.168 (0.019–1.510)		0.111
CHA ₂ DS ₂ -VASc score	1.047 (0.559–1.962)		0.885
LA area, mm ²	0.994 (0.835–1.183)		0.945
LVEF	0.987 (0.910–1.069)		0.743
CAD		0.045	0.337
Previous cardiac surgery		0.020	1.0
Arterial hypertension	0.773 (0.086–6.974)		0.819
Diabetes mellitus	1.797 (0.199–16.237)		0.602
Previous stroke		0.018	1.0
Ablation method (RF/RF-SF/nMARQ)		0.048	0.516
EDEL in EGD		0.166	<0.001
Category 2 vs category 1 lesion		0.255	0.004
In patients with esophageal temperature measurement			
Esoph. temperature >40.5°C	1.768 (0.159–19.710)		0.643

AF indicates atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; EGD, esophagogastroduodenoscopy; LA, left atrial; LVEF, left ventricular ejection fraction; RF, radiofrequency; and SF, surround flow.

study indicates, that the real incidence of perforating complications after first AF ablation procedures when using different radiofrequency technologies might be higher as assumed on the basis of preexisting data.

Relation Between Category 2 EDEL and Esophageal Perforation

For the first time, this study was able to document a direct relation between EDEL and esophageal perforating complications. All 5 patients experiencing a perforating esophageal complication demonstrated a category 2 thermal esophageal lesion at postablation endoscopy. Postablation endoscopy allowed to identify patients at high risk for the development of esophageal perforation. No patient without EDEL or with category 1 EDEL developed esophageal perforation, whereas 10% of category 2 EDEL progressed to perforation. In a canine model of AEF, different mechanisms leading to AEF were identified, including initial thermal damage to the esophageal wall plus damage to periesophageal autonomic nerves and vasculature. Increased gastric reflux seems to be a crucial factor leading to esophageal wall inflammation with locus minoris resistentiae at sites with severe thermal wall damage. Our study documents that an initial thermal esophageal lesion seems to be

a prerequisite as a starting point of a cascade leading to AEF. Patients without EDEL seem to have a much lower or even no tendency of progression toward esophageal perforation. In our opinion, the clinical consequence of these findings is that—if not routinely performed after every postprocedural endoscopy with a positive finding of an EDEL—surveillance for asymptomatic esophageal thermal lesions should be performed after AF ablation. In our experience, endoscopy is sensitive in identifying patients with category 2 EDEL (ulcer). In these high-risk patients, an in-hospital monitoring and additional treatment and diagnostic measurements should be discussed.

Standardized Operating Procedures for the Management of High-Risk Patients

In our study, operating procedures as a consequence to the detection of EDEL changed during the study period. On the basis of our initial experience, patients with category 2 EDEL routinely underwent early control endoscopy and in case of progression were put on nonsolid food or intravenous feeding plus antibiotics. After applying this strategy, 3 patients with esophageal perforation were identified and controlled using covered esophageal stenting early after the perforation seemed to have occurred. It seems feasible to have close surveillance of patients with category 2 lesions and most appropriate standard operating procedures need to be established in future registries and studies. In contrast to our experience, other studies have identified nonsurgical treatment of AEF to be related to higher mortality. In our cohort, only patients with early detection of esophageal perforation were treated using esophageal stenting, and patients eligible for this therapy need to be carefully identified.

In our study, only patients undergoing their first AF ablation procedure, including PVI and with a postprocedural EGD, were included as a recent analysis revealed EDEL to be relevantly less common in redo procedures because of the lesser incidence of ablations performed at the posterior LA wall.

In case of suspected esophageal perforation, fast diagnosis using emergency CT chest scan, including intravenous and per-os contrast (oral) dye, is needed. This strategy might have contributed to the favorable outcome of the 3 patients after esophageal stenting.

Immediate CT chest scan (using intravenous and per-os contrast dye) to avoid air embolism seems to be the ideal emergency test in case of suspicion of perforating esophageal complications.

The Role of Esophageal Temperature Monitoring as a Predictor of EDEL and a Risk Factor Itself and Other Predictors of EDEL

Preexisting studies showed a lower body mass index, the use of general anesthesia, maximum energy at the posterior LA wall, maximum esophageal temperature during ablation, and type of ablation performed to influence the incidence of thermal esophageal injury after AF ablation.⁴⁻¹³ In our cohort, using luminal esophageal temperature monitoring (LET) in only a minor number of patients increased esophageal temperatures were associated with higher incidences of EDEL. However, a substantial number of patients with LETs below the cutoff temperature of 40.5°C demonstrated category 1 and

2 EDEL indicating the insufficiency of current LET probes to precisely detect maximum esophageal temperatures (30 of 103 patients, 29%). In our study, LETs >40.5°C were associated with a 2.1-fold increased risk for any thermal esophageal lesion, but no temperature increase can rule out the occurrence of EDEL. Of note, as demonstrated by a receiver operating characteristic analysis because of a relatively small area under the curve, the optimal cutoff temperature is not able to reliably separate between patients with true positive and true negative endoscopy findings in this study.

Temperature probes with uncoated thermocouples may paradoxically contribute to an increase of EDEL by inductive heating during radiofrequency ablation.¹⁴ This hypothesis was supported by a study of Nguyen et al²¹ and clinical findings from our study group. Whereas noninsulated metal thermistor LET probes have been associated with increased incidences of EDEL in patients undergoing AF ablation, different probe designs may be of value if accurate and fast temperature control can be achieved.¹³ Recently, a probe using infrared thermography has been evaluated allowing complete monitoring of the esophageal luminal surface and identification of local accurate temperature measures.²²

According to logistic regression analysis, no further risk factors for EDEL apart from higher maximum esophageal temperature could be identified. Nonetheless, female sex showed a mild tendency for a higher incidence of EDEL. However, this was not significant ($P=0.088$), and the effect size was rather low. A larger patient cohort may possibly demonstrate a significant association of female sex and postinterventional EDEL.

Measurements Capable to Reduce the Risk of EDEL

As a consequence of our study results in light of preexisting literature esophageal temperature monitoring should be used at least in patients with a substantial amount of ablation at the posterior wall. No ideal temperature cutoff value has been identified yet, and it might be <40.5°C as used in our analysis. In cases of radiofrequency ablations at least probes with insulated thermocouples should be considered. Of note, an analysis of the impact of probes with insulated versus uncoated thermocouples was not the focus of this study. To date, no study identified a reduced incidence of EDEL when using intraluminal esophageal temperature probes of different models. Drawbacks of currently available probes are thermal latency and incomplete temperature surveillance coverage of the esophagus.

Other measures like limiting power, ablation time per lesion, and contact force (in case of contact force measuring catheters) when ablating at the posterior wall have been shown to reduce the incidence of EDEL. However, power reduction at posterior wall in this patient cohort was done routinely, and thereby, its effect cannot be evaluated in comparison to a control group.

Future Scientific Approaches to Better Identify and Avoid Esophageal Perforating Complications

Improved esophageal temperature monitoring technologies may have the ability to overcome the limitations of the existing temperature probes in near future.

EDEL may serve as surrogate parameter of risk of esophageal perforation as only severe—category 2—EDEL seem to progress. Future studies may focus on effects on EDEL incidences when evaluating strategies to decrease collateral esophageal damage.

Study Limitations

The study is of observational retrospective character, and patients were only included if postablation endoscopy was available. At our center, postablation endoscopy has evolved as part of the standard testing after AF ablation. In this study, we demonstrated that postablation category 2 EDEL identifies patients at high risk for esophageal perforation, and these patients need close surveillance and decisive management protocols, including control endoscopy, high-dose proton pump inhibitor, and early reevaluation in case of clinical signs for esophageal perforation using CT.

Most important, the results of a patient cohort treated at our institution according to our standard protocol may not be transferrable to other patient cohorts and other institutions using different protocols (eg, other sedation protocols) and different ablation catheters with different ablation settings.

There is a selection bias concerning patients with use of temperature probes. In the initial phase of our experience, patients only underwent endoscopy, if luminal temperature increased $\geq 40.5^{\circ}\text{C}$. Therefore, patients with lower intraluminal temperatures have only been included in the later phase of the study. As higher LET is related to EDEL, the incidence of thermal lesions is expectedly higher in the LET group. Recent studies on radiofrequency AF ablation have documented a higher incidence of EDEL when using noninsulated LET probes compared with control groups not using LET monitoring, whereas incidences of EDEL were similar when using insulated LET probes versus no LET monitoring.^{13,14} The effects of LET monitoring on incidences of EDEL remains unclear, and future probes using high-density luminal temperature mapping and appropriate and fast temperature response are needed.

Of note, on prediction of EDEL by intraprocedural esophageal temperature measurement, the optimal cutoff temperature calculated by a receiver operating characteristic analysis was not able to reliably separate between patients with true positive and true negative endoscopy findings because of a relatively small area under the curve.

The incidence of a perforating esophageal complication was low in our study cohort. Therefore, analysis of predictors of this event is restricted by limited statistical power. However, incidence of EDEL and specifically category 2 EDEL—considered as surrogate parameter for the risk of this complication—was much higher and therefore statistically evaluable. EDEL may be used in future studies to evaluate risk (and risk factors) of perforating esophageal injuries after LA ablations.

A limitation of our study is incomplete FU data in the group of patients not undergoing postablation esophageal endoscopy. This cohort was not included in the final analysis, and, therefore, the value of postablation endoscopy and detecting asymptomatic esophageal lesions cannot be directly

assessed. In our study, we consequently adopted our FU strategy for patients with esophageal thermal lesions detected on endoscopy, and this impacted our approach to these patients. We feel that monitoring for esophageal damage is important for adequate patient FU. And finally, as a limitation of procedural data acquisition, we were not able to document total ablation time, contact force, force-time integral, and impedance drop at LA posterior wall at the time of the study. It would have been interesting to identify potential differences comparing patients with and without the occurrence of esophageal lesions or perforating esophageal complications.

Conclusions

EDEL seem to be a prerequisite for the occurrence of esophageal perforating complications related to AF ablation. In our series, 18% of asymptomatic patients had endoscopically detected EDEL, and one third was categorized as ulcers (category 2). Only patients with esophageal thermal ulcers (category 2 EDEL) showed progression toward esophageal perforation during FU (9.6% of esophageal ulcers progressed to esophageal perforation). Thereby, postablation endoscopy may identify patients at high risk for developing esophageal perforation, and close surveillance and alertness during FU of these patients is warranted. Whether specific management strategies may prevent progression needs further evaluation, but early detection of esophageal perforation may be beneficial (potential for treatment strategies using nonsurgical interventions). Preventing EDEL may help to reduce the incidence of severe esophagus-related AF ablation complications.

Further larger prospective trials have to clarify the impact of the type of ablation catheter and temperature probe on the incidence of EDEL. Patient education on symptoms related to esophageal perforating complications is important for early admission and detection.

Disclosures

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References

- Arbello E, Brugada J, Lundqvist CB, Laroche C, Kautzner J, Pokushalov E, Raatikainen P, Efremidis M, Hindricks G, Barrera A, Maggioni A, Tavazzi L, Dagres N. Contemporary management of patients undergoing atrial fibrillation ablation: in-hospital and 1-year follow-up findings from the ESC-EHRA atrial fibrillation ablation long-term registry. *Eur Heart J*. 2017;38:1302–1316. doi: 10.1093/eurheartj/ehw564.
- Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A, Ambrogi F, Biganzoli E. Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circ Arrhythm Electrophysiol*. 2010;3:32–38. doi: 10.1161/CIRCEP.109.859116.
- Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KR, Elvan A, Arentz T, Bestehorn K, Pocock SJ, Albenque JP, Tondo C; FIRE AND ICE Investigators. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. *N Engl J Med*. 2016;374:2235–2245. doi: 10.1056/NEJMoa1602014.
- Deneke T, Bünz K, Bastian A, Päsler M, Anders H, Lehmann R, Meuser W, de Groot JR, Horlitz M, Haberkorn R, Mügge A, Shin DI. Utility of esophageal temperature monitoring during pulmonary vein isolation for atrial fibrillation using duty-cycled phased

- radiofrequency ablation. *J Cardiovasc Electrophysiol.* 2011;22:255–261. doi: 10.1111/j.1540-8167.2010.01916.x.
5. Rillig A, Meyerfeldt U, Birkemeyer R, Wiest S, Sauer BM, Staritz M, Jung W. Oesophageal temperature monitoring and incidence of oesophageal lesions after pulmonary vein isolation using a remote robotic navigation system. *Europace.* 2010;12:655–661. doi: 10.1093/europace/euq061.
 6. Knopp H, Halm U, Lamberts R, Knigge I, Zachäus M, Sommer P, Richter S, Bollmann A, Hindricks G, Husser D. Incidental and ablation-induced findings during upper gastrointestinal endoscopy in patients after ablation of atrial fibrillation: a retrospective study of 425 patients. *Heart Rhythm.* 2014;11:574–578. doi: 10.1016/j.hrthm.2014.01.010.
 7. Sohara H, Satake S, Takeda H, Yamaguchi Y, Nagasu N. Prevalence of esophageal ulceration after atrial fibrillation ablation with the hot balloon ablation catheter: what is the value of esophageal cooling? *J Cardiovasc Electrophysiol.* 2014;25:686–692. doi: 10.1111/jce.12394.
 8. Halm U, Gaspar T, Zachäus M, Sack S, Arya A, Piorkowski C, Knigge I, Hindricks G, Husser D. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias. *Am J Gastroenterol.* 2010;105:551–556. doi: 10.1038/ajg.2009.625.
 9. Di Biase L, Saenz LC, Burkhardt DJ, Vacca M, Elayi CS, Barrett CD, Horton R, Bai R, Siu A, Fahmy TS, Patel D, Armaganjian L, Wu CT, Kai S, Ching CK, Phillips K, Schweikert RA, Cummings JE, Arruda M, Saliba WI, Dodig M, Natale A. Esophageal capsule endoscopy after radiofrequency catheter ablation for atrial fibrillation: documented higher risk of luminal esophageal damage with general anesthesia as compared with conscious sedation. *Circ Arrhythm Electrophysiol.* 2009;2:108–112. doi: 10.1161/CIRCEP.108.815266.
 10. Martinek M, Bencsik G, Aichinger J, Hassanein S, Schoeffl R, Kuchinka P, Nesser HJ, Purerfellner H. Esophageal damage during radiofrequency ablation of atrial fibrillation: impact of energy settings, lesion sets, and esophageal visualization. *J Cardiovasc Electrophysiol.* 2009;20:726–733. doi: 10.1111/j.1540-8167.2008.01426.x.
 11. Deneke T, Müller P, Halbfass P, Szöllösi A, Roos M, Krug J, Fochler F, Schade A, Schmitt R, Christopoulos G, Mügge A, Nentwich K. Effect of different ablation settings on acute complications using the novel irrigated multipolar radiofrequency ablation catheter (nMARQ). *J Cardiovasc Electrophysiol.* 2015;26:1063–1068. doi: 10.1111/jce.12736.
 12. Halbfass P, Nentwich K, Krug J, Roos M, Sonne K, Ene E, Hamm K, Barth S, Szöllösi A, Fochler F, Mügge A, Lüsebrink U, Deneke T. Impact of surround flow catheter tip irrigation in contact force ablation on the incidence of asymptomatic oesophageal lesions after atrial fibrillation ablation: a prospective comparative study [published online ahead of print June 27, 2016]. *Europace.* doi: 10.1093/europace/euw119. <https://doi.org/10.1093/europace/euw119>.
 13. Halbfass P, Müller P, Nentwich K, Krug J, Roos M, Hamm K, Barth S, Szöllösi A, Mügge A, Schieffer B, Deneke T. Incidence of asymptomatic oesophageal lesions after atrial fibrillation ablation using an oesophageal temperature probe with insulated thermocouples: a comparative controlled study. *Europace.* 2016;19:385–391.
 14. Müller P, Dietrich JW, Halbfass P, Abouarab A, Fochler F, Szöllösi A, Nentwich K, Roos M, Krug J, Schade A, Mügge A, Deneke T. Higher incidence of esophageal lesions after ablation of atrial fibrillation related to the use of esophageal temperature probes. *Heart Rhythm.* 2015;12:1464–1469. doi: 10.1016/j.hrthm.2015.04.005.
 15. Mohanty S, Santangeli P, Mohanty P, Di Biase L, Trivedi C, Bai R, Horton R, Burkhardt JD, Sanchez JE, Zagrodzky J, Bailey S, Gallinghouse JG, Hranitzky PM, Sun AY, Hongo R, Beheiry S, Natale A. Outcomes of atrioesophageal fistula following catheter ablation of atrial fibrillation treated with surgical repair versus esophageal stenting. *J Cardiovasc Electrophysiol.* 2014;25:579–584.
 16. Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Natale A, Packer D, Skanes A. Prevalence and causes of fatal outcome in catheter ablation of atrial fibrillation. *J Am Coll Cardiol.* 2009;53:1798–1803. doi: 10.1016/j.jacc.2009.02.022.
 17. Nair KK, Shurrab M, Skanes A, Danon A, Birnie D, Morillo C, Chauhan V, Mangat I, Ayala-Paredes F, Champagne J, Nault I, Tang A, Verma A, Lashevsky I, Singh SM, Crystal E. The prevalence and risk factors for atrioesophageal fistula after percutaneous radiofrequency catheter ablation for atrial fibrillation: the Canadian experience. *J Interv Card Electrophysiol.* 2014;39:139–144. doi: 10.1007/s10840-013-9853-z.
 18. Ghia KK, Chugh A, Good E, Pelosi F, Jongnarangsin K, Bogun F, Morady F, Oral H. A nationwide survey on the prevalence of atrioesophageal fistula after left atrial radiofrequency catheter ablation. *J Interv Card Electrophysiol.* 2009;24:33–36. doi: 10.1007/s10840-008-9307-1.
 19. Dagues N, Kottkamp H, Piorkowski C, Doll N, Mohr F, Horlitz M, Kremastinos DT, Hindricks G. Rapid detection and successful treatment of esophageal perforation after radiofrequency ablation of atrial fibrillation: lessons from five cases. *J Cardiovasc Electrophysiol.* 2006;17:1213–1215. doi: 10.1111/j.1540-8167.2006.00611.x.
 20. Dagues N, Hindricks G, Kottkamp H, Sommer P, Gaspar T, Bode K, Arya A, Husser D, Rallidis LS, Kremastinos DT, Piorkowski C. Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: still cause for concern? *J Cardiovasc Electrophysiol.* 2009;20:1014–1019. doi: 10.1111/j.1540-8167.2009.01493.x.
 21. Nguyen DT, Barham W, Zheng L, Dinegar S, Tzou WS, Sauer WH. Effect of radiofrequency energy delivery in proximity to metallic medical device components. *Heart Rhythm.* 2015;12:2162–2169. doi: 10.1016/j.hrthm.2015.05.011.
 22. Crozier I, Daly M, Lim G, Roper G. Esophageal infrared thermography during atrial fibrillation ablation. *Heart Rhythm.* 2015;12:2362–2363. doi: 10.1016/j.hrthm.2015.07.037.

Progression From Esophageal Thermal Asymptomatic Lesion to Perforation Complicating Atrial Fibrillation Ablation: A Single-Center Registry

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