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Original Article

Impact of esophageal temperature monitoring guided atrial fibrillation ablation on preventing asymptomatic excessive transmural injury



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ABSTRACT

Background: Even with the use of a reduced energy setting (20–25 W), excessive transmural injury (ETI) following catheter ablation of atrial fibrillation (AF) is reported to develop in 10% of patients. However, the incidence of ETI depends on the pulmonary vein isolation (PVI) method and its esophageal temperature monitor setting. Data comparing the incidence of ETI following AF ablation with and without esophageal temperature monitoring (ETM) are still lacking.

Methods: This study was comprised of 160 patients with AF (54% paroxysmal, mean: $24.0 \pm 2.9 \text{ kg/m}^2$). Eighty patients underwent ablation accompanied by ETM. The primary endpoint was defined as the occurrence of ETI assessed by endoscopy within 5 d after the AF ablation. The secondary endpoint was defined as AF recurrence after a single procedure. If the esophageal temperature probe registered > 39 °C, the radiofrequency (RF) application was stopped immediately. RF applications could be performed in a point-by-point manner for a maximum of 20 s and 20 W. ETI was defined as any injury that resulted from AF ablation, including esophageal injury or periesophageal nerve injury (peri-ENI). *Results:* The incidence of esophageal injury was significantly lower in patients whose AF ablation

included ETM compared with patients without ETM (0 [0%] vs. 6 [7.5%], p=0.028), but not the incidence of peri-ENI (2 [2.5%] vs. 3 [3.8%], p=1.0). AF recurrence 12 months after the procedure was similar between the groups (20 [25%] in the ETM group vs. 19 [24%] in the non-ETM group, p=1.00).

Conclusions: Catheter ablation using ETM may reduce the incidence of esophageal injury without increasing the incidence of AF recurrence but not the incidence of peri-ENI.

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1. Introduction

Pulmonary vein isolation (PVI) has become a standard therapy in the management of atrial fibrillation (AF) [1,2]. Although AF ablation is

widely considered safe, serious esophageal complications, such as atrioesophageal fistulae, esophageal erythema, esophageal ulcerations, and periesophageal nerve injury (peri-ENI, e.g., acute pyloric spasms and gastric hypomotility), occasionally occur [3–8]. These serious esophageal complications may be caused by excessive damage beyond the left atrial (LA) posterior wall during radiofrequency (RF) energy deliveries. To avoid these complications, monitoring esophageal temperature is recommended during RF applications to the LA posterior

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wall [9]. Halm et al. reported that lesions occurred in patients with an esophageal temperature > 41 °C, and for every 1 °C increase in esophageal temperature, the odds of an esophageal lesion increased by a factor of 1.36 (95% confidence interval [CI] = 1.07 - 1.74; p = 0.012) [10]. Yamasaki et al. reported that body mass index (BMI) (kg/m²) was the only independent predictor of excessive transmural injury (ETI) (odds ratio [OR] = 0.76; 95% CI 0.59-0.97; p < 0.05) [5]. Most recently, we demonstrated that AF ablation with a lower-energy setting of 20 W strictly controlled by esophageal temperature monitoring (ETM) at 39 °C could reduce the esophageal injury even in patients with a $BMI < 24.9 \text{ kg/m}^2$ [11]. As for the incidence of peri-ENI. Mivazaki et al. reported that BMI was the only independent predictor for identifying patients who would develop peri-ENI during RF applications to the LA posterior wall with a relatively higher setting of 25-30 W and a duration of 30 s (OR=0.77; 95% CI=0.64-0.92; p=0.0045) [12]. However, data comparing the incidence of ETI (including esophageal injury and peri-ENI) following AF ablation with and without ETM are still lacking. In the current study, we sought to investigate the safety and effects of AF ablation strictly controlled by ETM in patients who underwent PVI with a lower energy setting of 20 W and a duration of 20 s for each RF application.

2. Material and methods

2.1. Patient characteristics

Patients (N=160) with highly symptomatic, medically refractory AF who were treated with catheter ablation with or without ETM were retrospectively analyzed. Of these, 80 patients underwent AF ablation with ETM (the ETM group). During the same period, from a database of 312 patients who underwent AF ablation without ETM, a computer model created a control group of another 80 patients (controls; non-ETM group) matched to the ETM group according to age, sex, type of AF, and BMI. All procedures in both groups were performed in the following centers: Himeji Cardiovascular Center, Tsukuba University, and Kobe University. The baseline characteristics of the 2 groups are shown in Table 1. Ethical approval was obtained from the institutional review committees, and all patients in the ETM group gave their informed written consent before participation. Every researcher involved in this study acted in conformity with the Declaration of Helsinki (adopted by the 18th World Medical Association General Assembly, Helsinki, Finland in 1964).

2.2. Mapping and ablation procedure

Prior to the procedure, transesophageal echocardiography was performed to exclude any thrombus formation. Patients were studied under deep propofol sedation while breathing spontaneously. Standard electrode catheters were placed in the right ventricular apex

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Baseline characteristics of the 2 patient groups.

ETM group	Non-ETM group	p Value
60 (75)	65 (81)	0.45
60.7 ± 8.2	58.2 ± 10.6	0.10
45 (56)	41 (51)	0.63
36 (12; 72)	36 (12; 66)	0.78
44 (55)	31 (39)	0.06
11 (14)	19 (24)	0.16
8 (10)	11 (14)	0.63
41.3 ± 6.3	39.2 ± 6.7	0.05
61.7 ± 8.3	64.0 ± 8.6	0.09
$\textbf{23.9} \pm \textbf{3.1}$	23.9 ± 3.0	0.92
	$\begin{array}{c} \text{ETM group} \\ \hline 60 \ (75) \\ 60.7 \pm 8.2 \\ 45 \ (56) \\ 36 \ (12; \ 72) \\ 44 \ (55) \\ 11 \ (14) \\ 8 \ (10) \\ 41.3 \pm 6.3 \\ 61.7 \pm 8.3 \\ 23.9 \pm 3.1 \end{array}$	ETM groupNon-ETM group $60 (75)$ $65 (81)$ 60.7 ± 8.2 58.2 ± 10.6 $45 (56)$ $41 (51)$ $36 (12; 72)$ $36 (12; 66)$ $44 (55)$ $31 (39)$ $11 (14)$ $19 (24)$ $8 (10)$ $11 (14)$ 41.3 ± 6.3 39.2 ± 6.7 61.7 ± 8.3 64.0 ± 8.6 23.9 ± 3.1 23.9 ± 3.0

 $\label{eq:expectation} ETM = esophageal temperature monitoring, AF = atrial fibrillation, LVEF = left ventricular ejection fraction, BMI = body mass index.$

and coronary sinus, after which a single transseptal puncture was performed. Unfractionated heparin was administered in a bolus form before the transseptal puncture to maintain an activated clotting time of > 300 s. If AF occurred, internal electrical cardioversion was performed to restore sinus rhythm. Selective angiography of the pulmonary veins and barium esophagography were performed.

After integration of a 3-dimensional (3D) model of the anatomy of the LA and pulmonary veins (PVs) obtained from preinterventional computed tomography (CT) or magnetic resonance imaging (MRI), mapping and ablation were performed using the CARTO3 (Biosense Webster Inc., Diamond Bar, CA, USA) or NavX (St. Jude Medical, Inc., St. Paul, MN) system as a guide. Prior to the ablation, the circular mapping catheter (Lasso, Biosense Webster, Diamond Bar, CA; Optima, St. Jude Medical Inc., St. Paul, MN, USA) and ablation catheter–reconstructed LA posterior anatomies were aligned with the CT or MRI image [13–15]. Image integration was finely adjusted using 3 additional landmarks (top of the left superior PV [LSPV], right superior PV [RSPV], and bottom of the left inferior PV [LIPV]), and the tip of the ablation catheter (ThermoCool, Biosense Webster; IBI Therapy Cool Flex, St. Jude Medical, Inc.) was positioned at the landmarks based on fluoroscopic and electrographic information.

RF alternating current was delivered in unipolar mode between the irrigated-tip electrode of the ablation catheter and an external backplate electrode. The initial RF generator setting consisted of an upper catheter tip temperature of 43 °C, maximal RF power of 30 W, and irrigation flow rate of 17 or 13 mL/min using the CARTO3 and NavX systems, respectively. In patients requiring RF applications to the posterior wall, the initial RF generator setting consisted of a maximal RF power of 20 W. All patients underwent extensive encircling pulmonary vein isolation [16]. RF applications were performed in a point-by-point manner. The maximum time spent at the anterior and posterior walls was 40 s and 20 s. respectively. The encircling ablation line was created approximately 0.5–1 cm from the PV ostia. In the ETM group, the RF energy was routinely reduced by 10 W when ablating the posterior wall, based on the esophageal temperature measured with an esophageal temperature probe (SensiTherm, St. Jude Medical) [17]. If the esophageal temperature rose to > 39 °C, the ablation was stopped immediately and the energy was further reduced. After the esophageal temperature decreased to the normal range (37 °C), the RF application was resumed. If ablation could not be performed with 20-W energy, the line placement was performed either more antral or closer to the PV, depending on the patient's anatomical characteristics (Fig. 1) [18]. The RF energy setting for the posterior wall far from the esophagus was 25 W for a duration of 30 s. In the non-ETM group, the RF energy for the LA posterior wall was titrated to 20 W with an RF duration of 20 s at the Himeji Cardiovascular Center and Kobe University, and to 20 W for 30 s at Tsukuba University. Furthermore, a > 50-s break was applied between each RF energy application at Tsukuba University. Catheter navigation was performed with a nonsteerable sheath (Preface[®], Biosense Webster) or a steerable sheath (Agilis, St. Jude Medical Inc.).

The procedural endpoint was electrophysiologically proven bidirectional block of the PV-encircling ablation lines, confirmed with a circular mapping catheter. After proving bidirectional block of the PVs, we performed a stimulation protocol (burst pacing from the coronary sinus at 300 ms, 250 ms, and 200 ms for 10 s each) to test the inducibility of AF. When AF was induced, additional ablation consisting of linear ablation at the LA roof and/or a bottom line connecting the bottom of the inferior PVs was performed. A pharmacological test consisting of high-dose isoproterenol infusion ($20 \mu g/min$) was performed to identify non-PV triggers. Ablation of the cavotricuspid isthmus was performed only if typical right atrial flutter was either documented previously or induced by burst pacing at the end of the procedure. Patients were started on proton pump inhibitors on admission and continued for 4 weeks at the Himeji Cardiovascular Center and Kobe University, and for 2 weeks



Fig. 1. Radiofrequency applications to the LAPW strictly controlled by ETM. (A) Esophageal temperature monitoring during RF applications. The 3D yellow and red tags indicate ablation points with and without an esophageal temperature rise of > 39 °C, respectively (left panel). The 3D green tags indicate the ablation points achieving bidirectional block between the LA and PV. Of note, the esophageal temperature increased to 40.7 °C even though the RF applications were terminated immediately after esophageal temperature rose to > 39 °C (right panel). (B) A representative case of esophageal temperature rise. Even with RF applications delivered with a reduced energy of 20 W, esophageal temperature increased to 39 °C nine seconds after RF application. Despite the cessation of the RF application, the esophageal temperature continued to increase to 41.3 °C. LAPW=left atrial posterior wall, RF=radiofrequency, LA=left atrium, PV=pulmonary vein.



PV-LA angiography

Esophagography

Fig. 2. PV–LA angiography and esophagography during the procedure. (A) PV–LA angiography during high-rate right ventricular pacing (anteroposterior view). We classified the LAPW into 3 segments: left-sided area, right-sided area, and middle area. (B) Esophagography in the same patient. Of note, the esophagus was located in the left-sided area of the LAPW (anteroposterior view). PV=pulmonary vein, LA=left atrium, LAPW=left atrial posterior wall.

at Tsukuba University. Esophagoscopy was repeated after 3-4 d if mucosal ulcerations > 10 mm were observed initially [10].

2.3. Assessment of the esophageal course

Before the RF applications to the LA posterior wall, PV and left atrium (PV–LA) angiography and esophagography were performed during high-rate right ventricular pacing of 200 ppm and sinus rhythm, respectively (Fig. 2). The course of the esophagus was categorized into 3 columns: column 1 indicated the left-sided area of the posterior wall from the left antral portion, column 3 indicated the right-sided area of the posterior wall from the right antral portion, and column 2 indicated the middle area between columns 1 and 3 (Fig. 2A).

2.4. Esophageal and gastric endoscopy after AF ablation

Esophageal and gastric endoscopy was performed 1–5 d after ablation for AF in all patients. ETI was defined as any esophageal

injury resulting from RF energy applications, including esophageal erythema, necrotic ulcerations, atrioesophageal fistulae, acute pyloric spasms, or peri-ENI [5,12]. Patients were diagnosed as having peri-ENI if they exhibited the following symptoms and findings after AF ablation: acute onset of characteristic prolonged symptoms of gastric delayed emptying, such as nausea, vomiting, postprandial fullness, bloating, constipation, or epigastric pain and the finding of gastric hypomotility assessed by abdominal X-ray and CT. ETI was assessed and diagnosed by independent, experienced gastroenterologists blinded to the patients' characteristics and ablation procedures [12].

2.5. Follow-up

Antiarrhythmia treatment was discontinued postinterventionally, and beta-blockers were administered to all patients. After treatment, patients were administered oral anticoagulants for ≥ 6 months (target international normalized ratio: 2.0–3.0), depending on their individual stroke risk based on the CHADS₂ score. In all patients, 24-h Holter electrocardiography (SCM-6600, Fukuda Denshi, Tokyo, Japan) was performed after 3 and 6 months. If symptoms occurred outside of the recording period, patients were requested to contact our center or the referring physician to obtain electrocardiographic documentation. AF and/or macroreentrant atrial tachycardia episodes lasting > 30 s were considered recurrences [19].

2.6. Statistics

Data assessed using the Kolmogorov–Smirnov test are presented as the mean \pm standard deviation for normally distributed variables. Median and quartile values are given for nonnormally distributed variables. Categorical variables are expressed as the number and percentage of patients. Continuous and categorical variables between the 2 groups were analyzed using Student's *t* test and Fisher's exact test, respectively. If the distribution was skewed, the data were compared using the Mann–Whitney *U* test. Differences were considered statistically significant if p < 0.05. All statistical analyses were performed with IBM SPSS Statistics version 17.0 (IBM Inc., Chicago, IL, USA).

3. Results

3.1. Patient characteristics

Patient characteristics are displayed in Table 1. The 2 groups were electronically matched in a 1-to-1 ratio according to age, sex, type of AF, and BMI. There were no significant differences in AF history and left ventricular ejection fraction (LVEF) between the 2 groups (AF history (months)=56 [12;72] vs. 56 [12;66]; p=0.78; LVEF (%)=61.7 ± 8.3 vs. 64.0 ± 8.6; p=0.09). The groups were comparable with the exception of the left atrial diameter (41.3 ± 6.3 mm vs. 39.2 ± 6.7 mm in the ETM and non-ETM groups, respectively, p=0.05).

3.2. Course of the esophagus and procedural parameters

In the majority of patients, the esophageal course assessed by esophagography was in the left-sided LA posterior wall (LAPW). Esophageal course was in the left-sided area, middle area, and right-sided LAPW in 61 (76%), 10 (13%), and 9 (11%) patients in the ETM group, and in 69 (86%), 8 (10%), and 3(4%) patients in the non-ETM group respectively. The distribution of esophageal courses did not differ between the 2 groups (p=0.16) (Table 2).

The procedural parameters included procedure time, additional ablation with or without a superior vena cava isolation, linear ablation, and complex fractionated atrial electrogram ablation. In all these parameters, the groups were comparable, with the exception of the use of a steerable sheath (49 [61%] vs. 4 [5%] in the ETM and non-ETM groups, respectively; p < 0.001) (Table 2). In the ETM group, esophageal temperature reached 39 °C during a mean number of 3.2 ± 2.2 RF applications; the mean duration of RF applications when esophageal temperature reached > 39 °C was 13 ± 3 s, and the maximal esophageal temperature was 40.5 ± 0.6 °C.

3.3. Incidence of ETI and AF recurrence in the ETM and non-ETM groups

The incidence of ETI was lower in the ETM than in the non-ETM group (2 [3%] vs. 9 [11%] patients, respectively; p=0.06). Compared with catheter ablation without using ETM, catheter ablation with ETM significantly reduced the incidence of esophageal injury from 7.5% to 0% (p=0.03). However, the incidence of peri-ENI was comparable between the 2 groups (2 [2.5%] in the ETM group vs. 3 [3.8%] in the non-ETM group; p=1.00) (Table 3). AF recurrence at

Table 2

Esophageal course and procedural parameters in the 2 patient groups.

	ETM group	Non-ETM group	p Value
Esophageal course			0.16
Left-sided area (n, %)	61 (76)	69 (86)	
Middle area (n, %)	10 (13)	8 (10)	
Right-sided area (n, %)	9 (11)	3 (4)	
Procedural parameters			
Procedure time (min)	264 ± 59	242 ± 91	0.14
Usage of a steerable sheath (<i>n</i> , %)	49 (61)	4 (5)	< 0.001
SVC isolation (n, %)	8 (10)	4 (5)	0.37
Box lesion (n, %)	6 (8)	9 (11)	0.59
Mitral isthmus ablation (n, %)	3 (6)	5 (6)	0.72
CFAE ablation (<i>n</i> , %)	8 (10)	8 (10)	1.00

ETM=esophageal temperature monitoring, SVC=superior vena cava, CFAE=complex fractionated atrial electrogram.

Table 3

Incidence of ETI and AF recurrence in the 2 patient groups.

	ETM group	Non-ETM group	p Value
ETI (n, %)	2 (3)	9 (11)	0.06
Esophageal injury (n, %)	0 (0)	6 (7,5)	0.03
Periesophageal nerve injury (n, %)	2 (3)	3 (4)	1.00
AF recurrence (n, %)	20 (25)	19 (24)	1.00

ETI=excessive thermal injury, AF=atrial fibrillation.

12 months after a single ablation procedure was also comparable for both groups (20 [25%] in the ETM group vs. 19 [24%] in the non-ETM group; p=1.00) (Table 3). A second AF ablation session was performed in 15 (75%) of 20 patients with AF recurrence in the ETM group. A total of 33 reconduction sites were detected. Of those, only 6 sites were located on the esophageal course: 1 in the posterior wall of LSPV, 3 in the carina posterior, and 2 in the posterior wall of the LIPV. The remaining 27 sites were as follows: 5 in the roof at the LSPV, 5 in the carina between the LSPV and LIPV, 4 in the anterior ridge of the LSPV, 3 in the bottom of the LIPV, 5 in the roof at the RSPV, 3 in the carina between the RSPV and RIPV, and 2 in the bottom of the RIPV. The reconduction sites were likely distributed equally around the PV circular lesion. A multivariable logistic regression analysis model was applied to define predictors of the incidence of peri-ENI. After performing this analysis, BMI was associated with a higher risk of peri-ENI (OR=0.56; 95% CI=0.52-0.98; p=0.04). Patient age, sex, type of AF, AF history, left atrial diameter (LAD), LVEF, and use of a steerable sheath were not associated with peri-ENI (Table 4). However, the maximal esophageal temperature and number of times esophageal temperature reached $> 39 \degree C$ were probably higher in 2 patients with peri-ENI in the ETM group (patient 1: 41.6 °C, $6 \times RF$ applications with temperature rise to > 39 °C; patient 2: 41.9 °C, $9 \times RF$ applications with temperature rise to > 39 °C). Of interest, frequent RF applications at the posterior wall of the LIPV were performed in such patients.

4. Discussion

4.1. Main findings

The results of this study demonstrated that ETM-guided AF ablation at a 39 °C setting significantly reduced the incidence of esophageal injury without elevating the risk of AF recurrence. However, the incidence of peri-ENI could not be reduced by using ETM. A lower BMI was associated with a higher incidence of peri-

Table 4

Predictors of the incidence of peri-ENI based on a multivariable logistic regression analysis.

	Adjusted HR	95% CI	p Value
Age	0.98	0.86-1.12	0.77
Female sex	1.73	0.12-24.8	0.69
BMI (kg/m ²)	0.56	0.32-0.98	0.04
Type of AF	6.70	0.58-77.4	0.13
AF history, months	1.01	0.99-1.03	0.27
LAD, mm	1.20	0.99-1.16	0.63
LVEF, %	1.03	0.92-1.14	0.63
Use of a steerable sheath	1.67	0.16-18.1	0.67

HR=hazard ratio, BMI=body mass index, AF=atrial fibrillation, LAD=left atrial diameter, LVEF=left ventricular ejection fraction.

ENI. Other preprocedural and procedural parameters, including age, sex, type of AF, AF history, LAD, LVEF, and use of a steerable sheath were not associated with peri-ENI.

4.2. Impact of ETM-guided AF ablation on reducing the incidence of esophageal injury

We previously reported on the prevalence and characteristics of asymptomatic ETI after AF ablation that used lower-energy application of 20 W to the LAPW, but without ETM. Yamasaki et al. demonstrated that ETI occurred in 10 (9.6%) of 104 patients, all of whom were asymptomatic: esophageal injury occurred in 4 patients, and peri-ENI occurred in 6. All patients who developed ETI were below normal weight (BMI $< 24.9 \text{ kg/m}^2$). In our multivariable logistic analysis, we demonstrated that the only independent predictor of ETI was BMI (OR=0.76; 95% CI=0.59-0.97; p < 0.05) [5]. Furthermore, we reported the incidence of esophageal injury after ETMguided AF ablation in patients with a small BMI [11]. No esophageal injury was observed in any patients in that study. Halm et al. reported that the maximal temperature in the esophagus was significantly higher in patients with esophageal injury than in patients without injury [10]. Of interest, esophageal injury did not occur below an intraluminal esophageal temperature of 41 °C. As for the ETM, Kuwahara et al. reported gradual increases in esophageal temperatures after the cessation of RF energy applications and found that increases of 1–3 °C within 10–20 s of RF energy cessation were common before temperatures returned to control levels [20]. Therefore, we considered that ceasing RF energy at 39 °C should be ideal to prevent reaching the maximum esophageal temperature of 41 °C. In our study, the maximal esophageal temperatures of $> 41 \degree C$ and > 41.5 °C were documented in 8 (10%) and 1 (1.3%) patients in the ETM and non-ETM groups, respectively. Fortunately, no esophageal injury was documented in those patients. We speculated that RF application, even with a reduced power setting of 20 W, could increase esophageal temperature to >41 °C in patients with a lower BMI.

4.3. Limitations of ETM-guided AF ablation for reducing the incidence of peri-ENI

In contrast to esophageal injury, the incidence of peri-ENI was not reduced by using ETM-guided AF ablation. Kuwahara et al. reported that the clinical course and severity of peri-ENI vary, but most patients ultimately recover with conservative treatment. In their study, peri-ENI occurred in 4 of 157 (2.5%) patients whose ablation procedure did not use ETM, and 7 of 3538 (0.2%) patients who did have ETM during ablation [21]. Furthermore, Kuwahara et al. suggested the possibility of reducing both the incidence and severity of peri-ENI by applying RF under ETM guidance [22]. Recently, Miyazaki et al. reported on factors associated with peri-

ENI after AF ablation. They demonstrated that peri-ENI was a more common form of collateral damage than direct esophageal injury, and that BMI was an independent periprocedural predictor of the incidence of peri-ENI after AF ablation. Of note, Miyazaki et al. suggested that no peri-ENI was observed after AF ablation, regardless of patient BMI, under a power titration regimen in a specific, small area of the posterior LA where the ablation line transversed the esophagus. They emphasized both the need to recognize this unnoticeable complication and the importance of titrating energy at that specific area while taking BMI into account in AF ablation procedures [12]. In the current study, peri-ENI occurred in 2 (2.5%) patients in the ETM group and 3 (3.8%) patients in the non-ETM. The current power setting of RF applications to the LAPW was reduced to 20 W in all patients in both the ETM and non-ETM groups. Therefore, we speculated that discrepancies in outcomes were caused by the following: (1) patients with a significantly lower BMI, (2) the use of steerable sheaths, and (3) an additional ablation line. The mean BMI in patients with peri-ENI was 22 ± 0.1 kg/m². RF applications to the LAPW with a steerable sheath were performed in 49 (61%) patients in the ETM group. Of interest, additional ablation with a roof line including a box lesion was performed in 4 (80%) of 5 patients with peri-ENI. The vagus nerve bifurcates the anterior and posterior portions of the periesophageal nerve at the roof level of the left atrium and forms the plexus. The plexus was widely located on the anterior and posterior wall of the esophagus and converged with the anterior and posterior vagal trunks, which control gastric peristalsis, the pyloric sphincter, and gastric motility, at the bottom level of the LA. Considering this anatomical localization of the vagal nerve, including the periesophageal nerve, a single RF application at the vagal trunk, which was located at the roof and/ or bottom line near the esophagus, could have caused peri-ENI, even with a maximum esophageal temperature of $< 41 \,^{\circ}$ C. This theory is consistent with our results in patients in the ETM group who developed peri-ENI.

4.4. AF recurrence and procedure time in ETM-guided AF ablation

In this study, AF recurrence at 12 months after the single ablation procedure did not differ between the 2 groups. ETM-guided AF ablation was able to reduce the incidence of esophageal injury without increasing the risk of AF recurrence. To prevent esophageal injury, prolonging the procedure time $\leq 10\%$ is considered acceptable. AF ablation with a steerable sheath is reported to improve the quality of the PVI and rhythm outcome owing to improved contact force. Although many studies have reported on the incidence of esophageal injury in ablation procedures, the ablation strategy used (e.g., with or without a steerable sheath, temperature setting guided by ETM or not, and RF power settings) varied among reports. A previous study that used an ablation style similar to ours (using a steerable sheath and ETM) demonstrated that the incidence of esophageal injury and peri-ENI was 11%, much higher than our results [15–17,23]. Considering the details of the ablation settings, a difference in ETM setting could have caused these differences. An ETM setting of 39 °C was considered acceptable for preventing a maximal esophageal temperature of > 41 °C and for providing safe RF application with a steerable sheath, especially in patients with a lower BMI.

4.5. Study limitations

Our study had 3 major limitations. First, the sample size was relatively small. Second, the control cases were recruited from 2 different centers, between which the operator's experience and ablation technique may have varied. However, the concept of an ablation strategy including extensive encircling pulmonary vein isolation was the same, and the RF power settings for the LAPW and esophagography for preventing esophageal injury were performed in the same manner. Third, this study was a nonrandomized, case-control study with many inherent drawbacks. Its retrospective design makes it prone to bias. The patients in the ETM group were enrolled from the Himeji Cardiovascular Center and Kobe University. Patients in the non-ETM group were enrolled from Tsukuba University. Therefore, the use of steerable sheaths differed between the groups. As for the efficacy of RF applications, the use of steerable sheaths was reported to provide more contact force and durable RF lesions without gaps, thereby reducing AF recurrence. As for the safety of RF applications, AF ablation using steerable sheaths made it easier to control the contact force and the ablation site compared with AF ablation without steerable sheaths. Therefore, the use of steerable sheaths may have affected the impact of ETM.

Esophageal and gastric endoscopy both before and after AF ablation could not be performed. Therefore, we could not confirm whether the esophageal erythema was caused by transesophageal echocardiography before AF ablation or RF energy application. However, the impact of ETM in reducing the incidence of esophageal injury was evident. Ethically, it may be difficult to verify our findings in a randomized prospective study.

5. Conclusion

Catheter ablation using ETM may be able to reduce the incidence of esophageal injury without elevating the risk of AF recurrence, but it did not reduce the incidence of peri-ENI. To completely prevent ETI, a more careful ablation procedure should be performed in patients with a small BMI, even if ETM is used for guidance.

Disclosure

All authors declare no conflict of interest related to this study. Institutional review board information for this clinical study is as follows: approval was obtained on June 10, 2012 (approval number 12), and written informed consent was obtained from participants.

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References

- Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.
- [2] Takahashi A, Iesaka Y, Takahashi Y, et al. Electrical connections between pulmonary veins: implication for ostial ablation of pulmonary veins in patients with paroxysmal atrial fibrillation. Circulation 2002;105:2998–3003.
- [3] Pappone C, Oral H, Santinelli V, et al. Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. Circulation 2004;109:2724–6.
- [4] Kumar S, Ling LH, Halloran K, et al. Esophageal hematoma after atrial fibrillation ablation: incidence, clinical features, and sequelae of esophageal injury of a different sort. Circ Arrhythm Electrophysiol 2012;5:701–5.
- [5] Yamasaki H, Tada H, Sekiguchi Y, et al. Prevalence and characteristics of asymptomatic excessive transmural injury after radiofrequency catheter ablation of atrial fibrillation. Heart Rhythm 2011;8:826–32.

- [6] Knopp H, Halm U, Lamberts R, et al. 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;11:574–8.
- [7] Eitel C, Rolf S, Zachaus M, et al. Successful non-surgical treatment of esophagopericardial fistulas following atrial fibrillation catheter ablation: a case series. Circ Arrhythm Electrophysiol 2013;6(4):675–81.
- [8] Tancevski I, Hintringer F, Stuehlinger M, et al. Atrioesophageal fistula after percutaneous transcatheter ablation of atrial fibrillation. Circulation 2012;125:966.
- [9] Furnkranz A, Bordignon S, Bohmig M, et al. Reduced incidence of esophageal lesions by luminal esophageal temperature-guided second-generation cryoballoon ablation. Heart Rhythm 2015;12:268–74.
- [10] Halm U, Gaspar T, Zachaus M, et al. Thermal esophageal lesions after radiofrequency catheter ablation of left atrial arrhythmias. Am J Gastroenterol 2010;105:551–6.
- [11] Kiuchi K, Okajima K, Shimane A, et al. Incidence of esophageal injury after pulmonary vein isolation in patients with a low body mass index and esophageal temperature monitoring at a 39 °C setting. J Arrhythm 2014;31 (1):12–7.
- [12] Miyazaki S, Taniguchi H, Kusa S, et al. Factors associated with periesophageal vagal nerve injury after pulmonary vein antrum isolation. J Am Heart Assoc 2014;3:e001209.
- [13] Itoh T, Sasaki S, Kimura M, et al. Three-dimensional cardiac image integration of electroanatomical mapping of only left atrial posterior wall with CT image to guide circumferential pulmonary vein ablation. J Interv Card Electrophysiol 2010;29:167–73.
- [14] Ouyang F, Bansch D, Ernst S, et al. Complete isolation of left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. Circulation 2004;110:2090–6.
- [15] Piorkowski C, Eitel C, Rolf S, et al. Steerable versus nonsteerable sheath technology in atrial fibrillation ablation: a prospective, randomized study. Circ Arrhythm Electrophysiol 2011;4:157–65.
- [16] Takigawa M, Takahashi A, Kuwahara T, et al. Long-term follow-up after catheter ablation of paroxysmal atrial fibrillation: the incidence of recurrence and progression of atrial fibrillation. Circ Arrhythm Electrophysiol 2014;7:267–73.
- [17] Kiuchi K, Kircher S, Watanabe N, et al. Quantitative analysis of isolation area and rhythm outcome in patients with paroxysmal atrial fibrillation after circumferential pulmonary vein antrum isolation using the pace-and-ablate technique. Circ Arrhythm Electrophysiol 2012;5:667–75.
- [18] Kottkamp H, Piorkowski C, Tanner H, et al. Topographic variability of the esophageal left atrial relation influencing ablation lines in patients with atrial fibrillation. J Cardiovasc Electrophysiol 2005;16:146–50.
- [19] Calkins H, Kuck KH, Cappato R, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration (AHA), the Asia Pacific Heart Rhythm Society (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the Suropean Cardiac Arrhythmia Society, the European Heart Rhythm Society, and the Heart Rhythm Society. 2012. Heart Rhythm Society, and the Heart Rhythm Society. 2012. Heart Rhythm Society, and the Heart Rhythm Society.
- [20] Kuwahara T, Takahashi A, Takahashi Y, et al. Incidences of esophageal injury during esophageal temperature monitoring: a comparative study of a multi-thermocouple temperature probe and a deflectable temperature probe in atrial fibrillation ablation. J Interv Card Electrophysiol 2014;39:251–7.
- [21] Kuwahara T, Takahashi A, Takahashi Y, et al. Clinical characteristics and management of periesophageal vagal nerve injury complicating left atrial ablation of atrial fibrillation: lessons from eleven cases. J Cardiovasc Electrophysiol 2013;24:847–51.
- [22] Kuwahara T, Takahashi A, Kobori A, et al. Safe and effective ablation of atrial fibrillation: importance of esophageal temperature monitoring to avoid periesophageal nerve injury as a complication of pulmonary vein isolation. J Cardiovasc Electrophysiol 2009;20:1–6.
- [23] Rolf S, Kircher S, Arya A, et al. Tailored atrial substrate modification based on low-voltage areas in catheter ablation of atrial fibrillation. Circ Arrhythm Electrophysiol 2014;7:825–33.