Journal of Cardiology 60 (2012) 119–125

Contents lists available at SciVerse ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Effectiveness of esophagus detection by three-dimensional electroanatomical mapping to avoid esophageal injury during ablation of atrial fibrillation

Ryuichi Maenosono (MT)[a,b], Naoya Oketani (MD)[c,*], Sanemasa Ishida (MD)[c], Yasuhisa Iriki (MD)[c], Hitoshi Ichiki (MD)[c], Hideki Okui (MD)[c], Yuichi Ninomiya (MD)[c], Shuichi Hamasaki (MD, FJCC)[c], Fuminori Namino (MT)[a], Masakaze Matsushita (MT)[a], Chuwa Tei (MD, FJCC)[c], Teruto Hashiguchi (MD)[a,b]

[a] Clinical Laboratory Unit, Kagoshima University Hospital, Kagoshima, Japan
[b] Department of Laboratory and Vascular Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan
[c] Department of Cardiovascular, Respiratory, and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Kagoshima, Japan

ARTICLE INFO

Article history:
Received 13 January 2012
Received in revised form 27 February 2012
Accepted 29 February 2012
Available online 21 April 2012

Keywords:
Atrial fibrillation
Ablation
Complex fractionated atrial electrogram
Esophageal temperature

ABSTRACT

Aims: Esophageal-left atrial (LA) fistula during atrial fibrillation (AF) ablation is a fatal event. We explored the relation of the esophagus-to-ablated point distance and esophageal temperature rise.
Methods: Consecutive patients ($n = 106$) underwent complex fractionated atrial electrogram-guided AF ablation using CartoMerge; the pulmonary veins were isolated in 23 patients. Maximum radiofrequency (RF) power near the esophagus was 15 W. Ablated points with esophageal temperature rise (monitored with a probe) to ≥38.0 °C were tagged; if ≥39.0 °C, RF was discontinued.
Results: Of 1647 ablated points near the esophagus, 274 were associated with a temperature rise to 38.0–38.9 °C and 241 points to ≥39.0 °C. Distances (mm) from points to esophagus were 5.1 ± 0.6 (no rise), 4.2 ± 3.1 (38.0–38.9 °C), 2.9 ± 2.5 (≥39.0 °C). Altogether, 15.5% of points in the upper LA posterior wall, 41.5% in the middle, and 30.2% in the lower caused rises to ≥38.0 °C; 8.7%, 24.6%, and 11.0% caused rises to ≥39.0 °C. The middle wall was most affected ($p < 0.01$), as shown by multiple logistic regression analysis (both temperatures). Points causing a rise increased significantly as distance decreased ($p < 0.001$). The odds ratio for rise to ≥38.0 °C compared with <4.0 to >5.0 mm distance was 2.28 ($p = 0.004$). The longest distance for ≥38.0 °C rise was 18.5 mm.
Conclusion: Distance is an important predictor of esophageal temperature rise. The middle LA posterior wall is most vulnerable. A dose of 15 W is too high for ablation, especially <4.0 mm from the esophagus. Points >20.0 mm away are relatively safe.
© 2012 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

Introduction

It has been widely reported that the prevalence of atrial fibrillation (AF) increases with age and is associated with high mortality and morbidity [1–3]. Catheter ablation is an effective approach to its management [4–10]. Pulmonary vein isolation (PVI) is one of the most common strategies for ablation of paroxysmal AF, but the outcome of PVI alone for patients with persistent AF is poor [11–13]. Additional approaches, such as linear ablation after PVI, have also been reported [14–17]. Nademanee et al. described a different approach for AF ablation. The strategy involved identifying the target "substrate" sites using electroanatomical mapping on complex fractionated atrial electrograms (CFAEs) [10,18]. PVI is not required with this approach, and AF ablation guided solely by CFAE resulted in a high rate of success in maintaining the sinus rhythm in patients with paroxysmal or persistent AF. The results of their study could not be replicated by others [9,19,20], however, so the role of CFAE-guided ablation in treating AF patients remains controversial.

It is necessary to consider the complications associated with catheter ablation of AF. An esophageal-left atrial (LA) fistula is a rare but fatal complication [21,22]. Cury et al. [23] reported that the anterior esophagus was in direct contact with the posterior wall of the LA in all patients, as seen with multidetector computed tomography (CT). Esophageal ulcerations have been reported as potential precursors of an esophageal-LA fistula, and endoscopy has revealed similar esophageal damage after AF ablation [24–27]. These

* Corresponding author at: Department of Cardiovascular, Respiratory, and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan. Tel.: +81 99 275 5318; fax: +81 99 265 8447.
E-mail address: oketani@m.kufm.kagoshima-u.ac.jp (N. Oketani).

0914-5087/$ – see front matter © 2012 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jjcc.2012.02.009

Table 1
Patients' characteristics.

	Mean ± SD
Number	106
Sex (men/women)	88/18
Age (years)	61.3 ± 10.0
BMI (kg/m^2)	24.1 ± 2.8
LAV (ml)	69.0 ± 23.2
LAD (mm)	40.9 ± 6.1
EF (%)	64.6 ± 11.0
Types of AF (paroxysmal/persistent)	59/47

Data are presented as mean ± SD or number. BMI, body mass index; LAV, left atrial volume; LAD, left atrial dimension; EF, ejection fraction; AF, atrial fibrillation.

complications have been reported to be induced by radiofrequency (RF) delivery at the LA posterior wall, with the esophageal injury being caused by conductive heating [21,24–27].

Based on these findings, AF ablation guided by monitoring the esophageal temperature and limiting the power and duration of RF application may reduce the complication risk [24,26]. The reported data, however, were based on ablation applied to the pulmonary vein antrum, so it was not clear if the results could be transposed to ablated points in all areas of the LA posterior wall. The areas where CFAE exists are more anterior than posterior, but all of the posterior wall areas eventually require ablation. The aim of this study was to evaluate the relations between the ablated points on parts of the LA posterior wall, the distance from the esophagus, and the esophageal temperature rise during CFAE-guided ablation using the CartoMerge system (Biosense Webster, Diamond Bar, CA, USA).

Methods

Study population and protocol

We studied 106 consecutive patients (59 with paroxysmal AF, 47 with persistent AF including 13 patients whose AF lasted >1 year). From September 2009 to March 2011, we enrolled 18 women and 88 men (mean age 61.3 ± 10.0 years) who underwent CFAE-guided AF ablation using CT image integration into an electroanatomical map with the CARTO mapping system (CartoMerge). PVI was combined with CFAE-guided ablation in 23 patients. The patients' characteristics are shown in Table 1.

All antiarrhythmia drugs were discontinued at least five half-lives before the study, with the exception of amiodarone, which was discontinued at least 3 months before the study. All patients provided written informed consent for the procedure. The study protocol was approved by the Institutional Ethics Committee. AF was defined in accordance with the 2007 Heart Rhythm Society Expert Consensus Statement [28].

Paroxysmal AF was defined as recurrent AF (two or more episodes) that terminates spontaneously within 7 days. Persistent AF was defined as AF that is sustained for more than 7 days or as AF lasting <7 days but necessitating pharmacological or electrical cardioversion.

Computed tomography imaging

Each patient underwent CT imaging within 1 week prior to the ablation using a 64-slice CT scanner (Aquillon; Toshiba Medical Systems, Tochigi, Japan). Scanning was performed during a single breath-hold in the craniocaudal direction. A nonionic contrast agent (370 mg I/ml) (Iopamiron 370; Bayer, Osaka, Japan) was injected via a cubital vein at an infusion rate of 1 ml/kg/s for 15 s. It was immediately followed by injection of a mixture of nonionic contrast and physiological saline at a rate of 0.5 ml/kg/s for 15 s. Digital Imaging and Communications in Medicine data converted with a soft tissue algorithm were imported to a CD-ROM to use the images on the CartoMerge system.

Mapping and ablation

The following AF ablation technique, described by Nademanee et al. [10,18] was modified and utilized for this study as reported before [29,30]. In brief, after the coronary sinus (CS) was cannulated with a decapolar catheter (Inquiry Luma-Cath; St. Jude Medical, Irvine, CA, USA) for recording and induction, patients underwent nonfluoroscopic electroanatomical mapping with the CARTO mapping system. A 3.5-mm NaviStar ThermoCool catheter (Biosense Webster) was used for mapping and ablation in all patients. Heparin (3000 IU initial bolus, 1000–2000 IU subsequent boluses, as needed to keep the activated clotting time at >250 s) was administered for anticoagulation.

All electroanatomical maps were created for patients who were in AF that was occurring spontaneously or by induction. Burst pacing utilizing a CS catheter to a lower limit of 1:1 capture or up to 150 ms was used to induce AF occasionally with an infusion of isoproterenol (0.01–0.02 μg/kg/min). When AF terminated during the ablation procedure in paroxysmal AF patients, it was reinduced until it was no longer inducible.

Electroanatomical maps were created and displayed as a shortest complex interval map. The areas of CFAE were identified manually, tagged, and associated with the atrial anatomy created by CARTO. This enabled the operator to associate areas of CFAE with the LA, CS, and occasionally the right atrium, thereby identifying target sites for ablation.

Bipolar recordings were filtered at 30–500 Hz, and the CFAE was defined as follows: (1) fractionated electrograms with two or more deflections and/or perturbation of the baseline with continuous deflection of a prolonged activation complex; and (2) atrial electrograms with a very short cycle length (≤120 ms).

After acquiring the shortest complex interval maps associated with CFAE, we searched the areas of CFAE that had the tagged points because CFAE areas have temporal spatial stability. RF applications using a 3.5-mm NaviStar ThermoCool catheter were delivered with the following conditions: maximum temperature 43.0 °C; 15 W of energy delivered to the posterior wall, which was supposed to be close to the esophagus, 15 W to the CS, 35 W to all other locations; irrigation flow rate 17–30 ml/min; RF time ≤40 s at each point.

The primary endpoints during RF ablation were either complete elimination of areas of CFAE or conversion of AF to sinus rhythm (SR) with or without an intravenous injection of nifekalant (0.3 mg/kg over 10 min, once or at most twice). Nifekalant is a class III antiarrhythmia drug similar to ibutilide, which is not available in Japan. If the arrhythmias were not successfully terminated, internal cardioversion was performed.

PVI was performed to encircle the left- and right-side PVs in pairs 1–2 cm from their ostia, as defined by fluoroscopy and a three-dimensional map [31]. At the anterior aspect of the left PV, ablation was performed along the ridge between the left atrial appendage and the PV ostia.

Pulmonary vein potentials were recorded using a circular catheter (Inquiry Optima; St. Jude Medical) before and after ablation to confirm the success of PVI. The electrograms were collected and measured with the Prucka (GE Medical Systems, Milwaukee, WI, USA) and CARTO mapping system.

Three-dimensional mapping with CT integration

The CT images were imported into the CARTO mapping system using custom-designed software (CartoMerge). It was used to separate the LA and PVs from the surrounding cardiac structures when

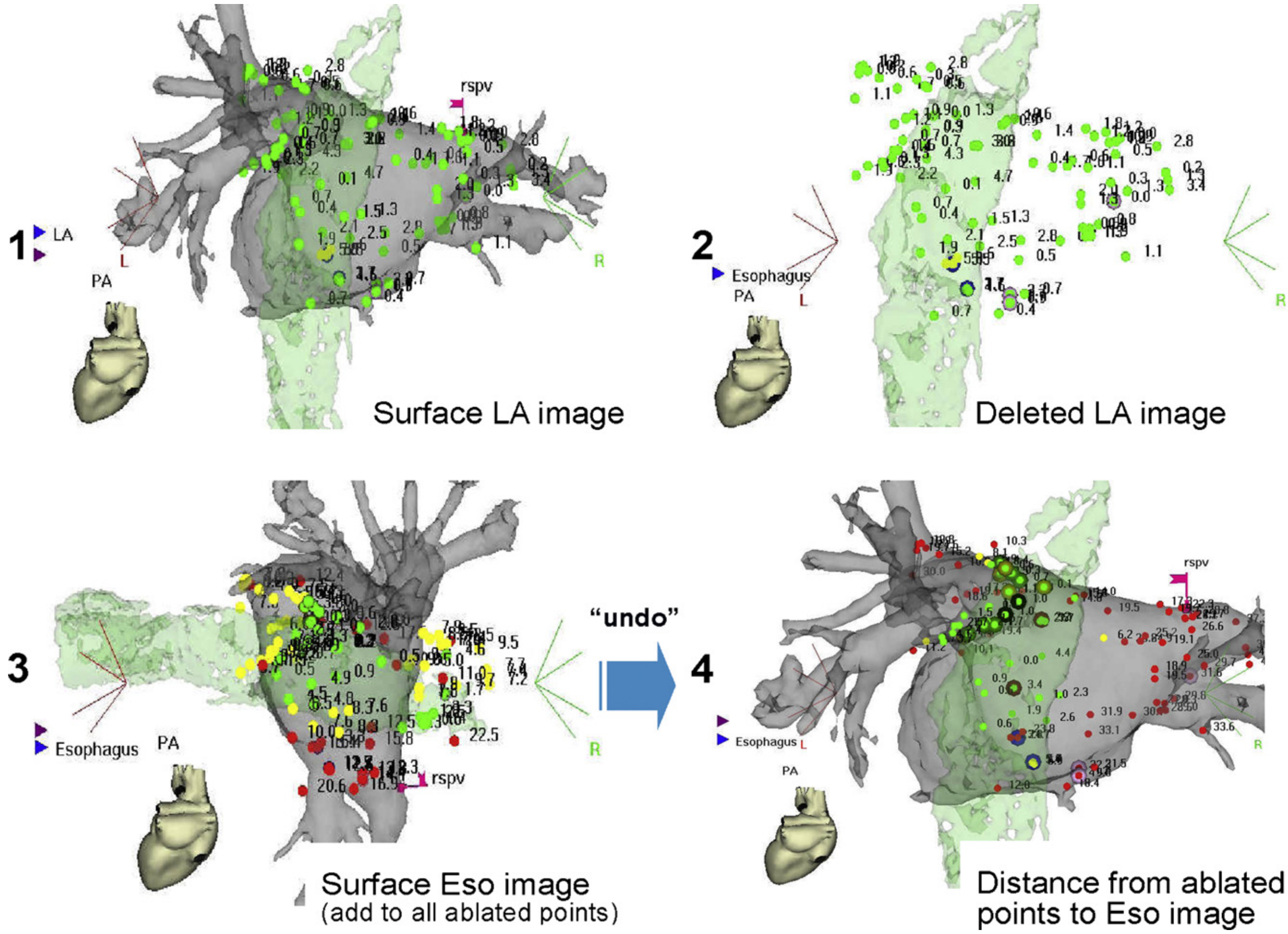

Fig. 1. Calculating the distance from ablated points to the esophagus using computed tomography (CT) images. First, registration of the CT images was performed using landmark and surface mapping. Second, the CT images were deleted except for an esophageal image. Third, all of the ablated points were registered in regard to the esophageal image, and then the registration was "undone." Finally, the distances from all of the ablated points to the esophagus were measured automatically by the Registration Match View. LA, left atrium; Eso, esophagus.

using proprietary software tools. The LA image including the PVs was merged with real-time electroanatomical maps for registration. Registration of the CT images was performed using landmark and surface mapping.

Monitoring esophageal temperature

Esophageal temperature was monitored using a 7 French esophageal temperature probe (Esotherm; FIAB SpA, Florence, Italy). The probe has five electrodes, the middle three of which monitored the esophageal temperature. A temperature probe was inserted nasally and with fluoroscopic guidance was advanced into the esophagus to a position close to the LA. The position of the temperature probe was adjusted (referring to the fluoroscopic images) as close as possible to the RF ablation catheter tip each time an RF application was delivered to the LA posterior wall close to the esophagus. The esophageal temperature was monitored continuously in real time throughout the procedure [26].

Distance from ablated points to esophagus

The ablated points near the esophagus were defined as posterior ablated points that overlapped with the esophagus CT from the PA view. The distance from the ablated points to the esophagus was calculated using the method that evaluates the discrepancy of the CT image and the real-time mapping image (registration matched view). The minimum distance from all of the ablated points to the esophagus CT were measured automatically (Fig. 1). The points where the ablation caused the esophageal temperature rise to 38.0–38.9 °C were assigned brown tags. When the esophageal temperature rose to ≥39.0 °C, the RF applications were discontinued and the points were assigned black tags (Fig. 2).

Statistical analysis

Data are presented as the mean ± SD. Categorical data were evaluated using the χ^2 test. The two-sample *t*-test, Mann–Whitney tests, and analysis of variance were used to compare proportions among groups. A multiple logistic regression model was used to assess the relative odds of each temperature rise factor. The results were compared with the distance >5.0 mm from the ablated points to the esophageal images. $p < 0.05$ indicated a significant difference. All statistical analyses were conducted with SPSS software (version 11.5 for Windows; SPSS Japan, Tokyo, Japan).

Results

Incidence of AF termination during CFAE-guided ablation

The AF was converted to SR in 59 (100%) patients with paroxysmal AF [30 (51%) with nifekalant] and in 39 (83%) patients

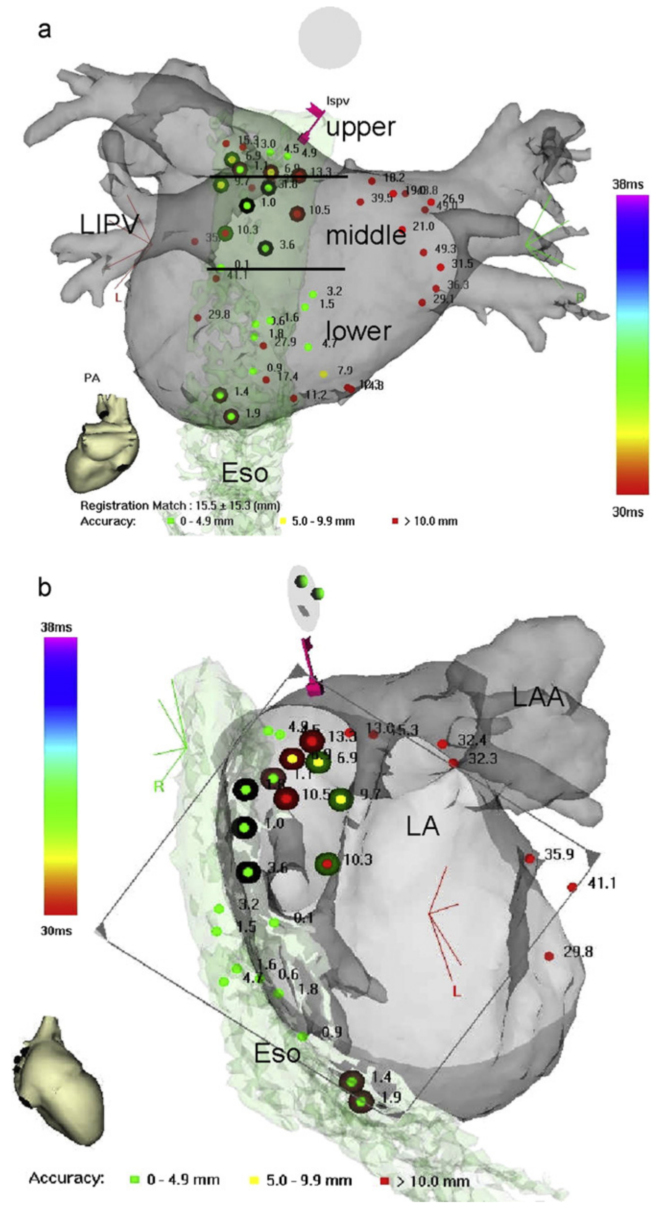

Fig. 2. Computed tomography images of the left atrium (LA) and pulmonary veins merged with real-time electroanatomical maps by surface registration. Posteroanterior view (a) and inner view (b) of the merged image of the LA and the esophagus. The LA was divided into three areas based on the boundary of the left inferior pulmonary vein (LIPV). Ablated points were measured at the shortest distance from the esophagus and are shown by three colors: green 0–4.9 mm, yellow 5.0–9.9 mm, red ≥10.0 mm. LAA, left atrial appendage; Eso, esophagus. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

with persistent AF [29 (74%) with nifekalant]. When the AF was "organized" or changed to atrial tachycardia or flutter, we ablated the points that showed more organized fractionated potential to convert to SR. The points were usually found in areas previously ablated. We did not perform linear ablation in this study, except PVI. The remaining patients required cardioversion to maintain the SR.

The common areas of the CFAE were at the anterior aspect of the right PV antrums, the posterior aspect of the left PV antrums, the ridge of the LA appendage, the proximal CS, and the posterior septum of the right atrium. The mean RF time, procedure time, and fluoroscopic time are shown in Table 2.

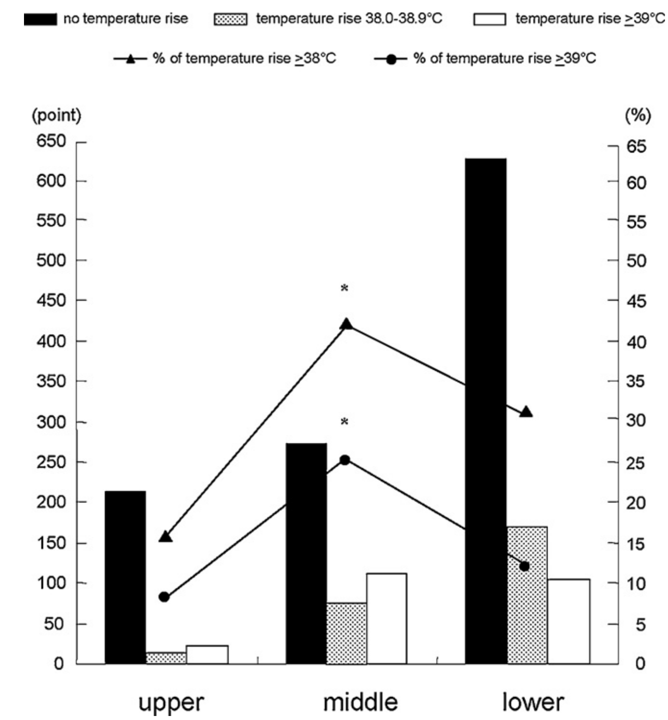

Fig. 3. Frequency of the temperature rise in each area of the left atrial posterior wall. Black bars = number of no-temperature-rise points; dotted bars = number with a temperature rise to 38.0–38.9 °C; white bars = temperature rise to ≥39.0 °C; line graphs = percentage of temperature rise points for a rise to ≥38.0 °C and to ≥39.0 °C. *Significantly higher compared with other parts of the left atrial posterior wall ($p < 0.01$).

Differences between SR and AF in the CT images

All of the real-time electroanatomical maps were created during AF, either spontaneous or induced during the procedure. In all, 50 paroxysmal AF and 19 persistent AF patients during CT scanning had SR. A total of 12 patients with persistent AF underwent cardioversion until CT showed that the SR was maintained. Differences in the accuracy of the CT images compared with the real-time CARTO map for SR and AF are shown in Table 3.

Relation between the distance from ablated points to the esophagus and the temperature rise

We excluded 5 of the 106 patients for two reasons: RF applications caused a temperature rise in the CS ($n = 1$); and the esophageal location was obviously different between the CT and fluoroscopic images ($n = 4$).

There were 1647 ablated points that were judged close to the esophagus in 101 patients. We divided the ablated points according to their location on the LA posterior wall and the maximum temperature of the esophagus. The LA posterior wall was classified into three parts: upper, middle, lower. The middle part was defined as the area from the bottom of the left superior PV to the bottom of the left inferior PV. There were 252 ablated points in the upper part (no temperature rise for 213 ablated points; rise to 38.0–38.9 °C for 17 points; rise to ≥39.0 °C for 22 points). There were 479 ablated points in the middle part (no temperature rise for 280 ablated points; rise to 38.0–38.9 °C for 81 points; rise to ≥39.0 °C for 118 points). There were 916 ablated points in the lower part (no temperature rise for 639 ablated points; rise to 38.0–38.9 °C for 176 points; rise to ≥39.0 °C for 101 points) (Fig. 3). The percentages of ablated points for which a temperature rise to ≥38.0 °C occurred were 15.5% in the upper, 41.5% in the middle, and 30.2% in the lower posterior

Table 2
Comparison of various parameters of ablation procedures.

	Total	CFAE	PVI + CFAE23	p value
Number	106	83	23	
Radio-frequency time (min)	89.1 ± 28.1	88.8 ± 28.5	90.2 ± 27.1	0.832
Fluoroscopic time (min)	22.8 ± 12.3	19.2 ± 10.5	35.8 ± 8.9	<0.001*
Procedure duration (min)	223.8 ± 47.1	218.8 ± 46.2	242.0 ± 46.9	0.035*

Data are presented as mean ± SD. min, minutes; CFAE, complex fractionated atrial electrogram; PVI, pulmonary veins isolation.
* $p < 0.05$ vs solely guided by CFAE group.

Table 3
Differences on CT images: sinus rhythm versus atrial fibrillation.

	Total	CT in sinus rhythm	CT in atrial fibrillation	p value
Number	106	69	34	
CT and ablation				
Procedure interval (days)	2.2 ± 1.4	2.3 ± 1.4	2.0 ± 1.5	0.185
Total surface points	102 ± 22	103 ± 24	99 ± 16	0.290
Surface registration				
Average (mm)	2.1 ± 0.4	2.0 ± 0.4	2.2 ± 0.4	0.005*
Standard deviation (mm)	1.6 ± 0.3	1.5 ± 0.3	1.7 ± 0.3	0.003*
Minimum (mm)	0.038 ± 0.041	0.038 ± 0.041	0.036 ± 0.041	0.752
Maximum (mm)	8.3 ± 2.5	7.9 ± 2.4	9.1 ± 2.5	0.009*

Two patients had unknown rhythm and one patient had a pacing rhythm at the time of CT. CT, computed tomography; SR, sinus rhythm; AF, atrial fibrillation.
* $p < 0.01$ vs CT in AF group.

LA; the corresponding percentages for a rise to ≥39.0 °C were 8.7%, 24.6%, and 11.0%, respectively. The percentage of ablated points that caused a rise to ≥38.0 °C was significantly higher in the middle portion of the LA posterior wall than in the other parts; this was true for both temperature parameters—38.0–38.9 °C and ≥39.0 °C ($p < 0.01$).

Next, we measured the minimum distance from the esophagus to all the ablated points. The distance from the esophagus to each part of the LA posterior wall, according to the temperature rise caused by the ablation is shown. The longest distance from the ablated point causing a rise to ≥38.0 °C was 18.5 mm in the lower posterior LA. The average distance from the esophagus to all the RF-treated points was 4.8 ± 4.0 mm in the upper, 4.3 ± 3.3 mm in the middle, and 4.6 ± 3.2 mm in the lower parts.

The distance from the esophagus to the middle part of the LA posterior wall was significantly shorter for a temperature rise to ≥39.0 °C (2.9 ± 2.2 mm) than for no temperature rise (4.9 ± 3.7 mm) ($p < 0.01$). The distance from the esophagus to the lower part of the LA posterior wall was significantly shorter for a rise to 38.0–38.9 °C (4.1 ± 3.1 mm) and to ≥39.0 °C (2.8 ± 2.5 mm) than for no temperature rise (5.1 ± 3.3 mm) ($p < 0.01$). There were no significant differences between the ablated points that caused an esophageal temperature rise and those that caused no temperature rise in the upper part of the LA posterior wall (data not shown).

Multiple analysis

In age-, sex-, and body mass index (BMI)-adjusted models, multiple logistic regression analysis demonstrated that the distance from the esophagus significantly correlated with the esophageal temperature rise caused by RF applications to the LA posterior wall. The upper part of the LA posterior wall had a significantly lower probability of esophageal temperature rise than its other parts—for ≥38.0 °C, the odds ratio (OR) = 0.36, 95% confidence interval (CI) = 0.22–0.57, $p < 0.001$; for ≥39.0 °C, the OR = 0.51, 95% CI = 0.28–0.93, $p = 0.027$. The middle part of the LA posterior wall had a significantly higher probability of esophageal temperature rise than other parts of the LA posterior wall—for ≥38.0 °C, the OR = 1.66, 95% CI = 1.21–2.27, $p = 0.002$; for ≥39.0 °C, the OR = 2.24, 95% CI = 1.51–3.33, $p < 0.001$.

The OR for rise to ≥38.0 °C compared with <4.0 to >5.0 mm distance was 2.28 ($p = 0.004$). The esophageal temperature rise was significantly increased as the distance from the esophagus decreased ($p < 0.001$).

Discussion

This study is the first to evaluate the relation between the distance from ablated points to the esophagus and the esophageal temperature rise during CFAE-guided AF ablation. The findings from this study are as follows.

First, the distance from the esophagus to the ablated points was the most important predictor of an esophageal temperature rise during CFAE-guided ablation of the LA posterior wall. The distance was 5.1 ± 3.6 mm when there was no temperature rise, 4.2 ± 3.1 mm for a rise to 38.0–38.9 °C, and 2.9 ± 2.5 mm for a rise to ≥39 °C; i.e. the shorter the distance, the greater is the rise.

Second, of the three LA posterior wall portions, the middle one had the highest possibility of esophageal temperature rise. This finding was supported by a multiple logistic regression analysis, which showed that the percentage points associated with a temperature rise were greater in the middle part than in other parts of the LA posterior wall ($p < 0.01$). The distance between esophagus and left atrial posterior wall in antero-posterior direction was 3.6 ± 3.1 mm in the upper, 2.2 ± 2.2 mm in the middle, 2.5 ± 2.1 mm in the lower parts, then the middle was the shortest ($p < 0.01$). The possible impact of this factor on the difference of thermal effects of RF energy applications in each portion may be big.

CFAE-guided AF ablation has been reported to produce good outcomes in patients with paroxysmal or persistent AF [10,32]. Although the distribution of CFAE areas were more abundant in the anterior than the posterior part of the LA, the posterior aspect of the left PV is one of the most common CFAE areas [10,33]; and all of the LA, except the left atrial appendage, has the possibility of showing fractionated potentials. PVI is the most common strategy for treating paroxysmal AF, but the outcomes after treating patients with persistent AF by PVI alone are not guaranteed. Additional treatment using linear ablation and/or CFAE-guided ablation have been reported [34,35]. Our data may contribute data not only for CFAE-guided ablation but also other AF ablations.

Radiofrequency delivery to the LA posterior wall and the resultant conductive heating caused esophageal injury. This study seems to support the findings of Martinek et al. [27], who also found that the esophageal-LA distance is a risk factor for esophageal ulceration. Our multivariate analysis clearly showed that a shorter distance caused the greater temperature rise.

Study limitations

Our study has several limitations. First, the position of the esophagus may not be exactly the same on the day of CT as on the day of ablation. Second, the distance from the esophagus to ablated points was measured at the closest esophageal lesion based on CT images, but the position of the esophageal temperature probe may not be the closest to the RF points in the esophagus because the esophageal temperature probe was adjusted only in the vertical position based on fluoroscopic images. Therefore, it should be emphasized that at the side edge of esophagus, temperature monitoring might not detect any excessive temperature rise if temperature monitoring electrode is far away from the ablation point in the horizontal direction. Third, it is not possible to assess the presence of an esophageal ulcer because it was not investigated by endoscopy.

Conclusion

The distance from the esophagus to ablated points is the most important predictor of esophageal temperature rise, and the middle of the LA posterior wall is the most prevalent location. A dose of 15 W is too high to ablate the points, especially within 4.0 mm of the esophagus. Points >20.0 mm from esophageal images are relatively safe.

Conflict of interest

There are no conflicts of interest for this study.

References

[1] Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991;22:983–8.

[2] Wolf PA, Dawber TR, Thomas Jr HE, Kannel WB. Epidemiologic assessment of chronic atrial fibrillation and risk of stroke: the Framingham study. Neurology 1978;28:973–7.

[3] Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino Sr RB, Newton-Cheh C, Yamamoto JF, Magnani JW, Tadros TM, Kannel WB, Wang TJ, Ellinor PT, Wolf PA, Vasan RS, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. Lancet 2009;373:739–45.

[4] Haïssaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.

[5] Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, Bash D, Schweikert R, Brachmann J, Gunther J, Gutleben K, Pisano E, Potenza D, Fanelli R, Raviele A, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. JAMA 2005;293:2634–40.

[6] Pappone C, Rosanio S, Augello G, Gallus G, Vicedomini G, Mazzone P, Gulletta S, Gugliotta F, Pappone A, Santinelli V, Tortoriello V, Sala S, Zangrillo A, Crescenzi G, Benussi S, et al. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation: outcomes from a controlled nonrandomized long-term study. J Am Coll Cardiol 2003;42:185–97.

[7] Cappato R, Calkins H, Chen SA, Davies W, Iesaka Y, Kalman J, Kim YH, Klein G, Packer D, Skanes A. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circulation 2005;111:1100–5.

[8] Stabile G, Bertaglia E, Senatore G, De Simone A, Zoppo F, Donnici G, Turco P, Pascotto P, Fazzari M, Vitale DF. Catheter ablation treatment in patients with drug-refractory atrial fibrillation: a prospective, multi-centre, randomized, controlled study (catheter ablation for the cure of atrial fibrillation study). Eur Heart J 2006;27:216–21.

[9] Oral H, Chugh A, Good E, Wimmer A, Dey S, Gadeela N, Sankaran S, Crawford T, Sarrazin JF, Kuhne M, Chalfoun N, Wells D, Frederick M, Fortino J, Benloucif-Moore S, et al. Radiofrequency catheter ablation of chronic atrial fibrillation guided by complex electrograms. Circulation 2007;115:2606–12.

[10] Nademanee K, McKenzie J, Kosar E, Schwab M, Sunsaneewitayakul B, Vasavakul T, Khunnawat C, Ngarmukos T. A new approach for catheter ablation of atrial fibrillation: mapping of electrophysiologic substrate. J Am Coll Cardiol 2004;43:2044–53.

[11] Kanagaratnam L, Tomassoni G, Schweikert R, Pavia S, Bash D, Beheiry S, Lesh M, Niebauer M, Saliba W, Chung M, Tchou P, Natale A. Empirical pulmonary vein isolation in patients with chronic atrial fibrillation using a three-dimensional nonfluoroscopic mapping system: long-term follow-up. Pacing Clin Electrophysiol 2001;24:1774–9.

[12] Oral H, Knight BP, Tada H, Ozaydin M, Chugh A, Hassan S, Scharf C, Lai SW, Greenstein R, Pelosi Jr F, Strickberger SA, Morady F. Pulmonary vein isolation for paroxysmal and persistent atrial fibrillation. Circulation 2002;105:1077–81.

[13] Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, Risius T, Lutomsky B, Meinertz T. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. Eur Heart J 2006;27:2871–8.

[14] Pappone C, Oreto G, Rosanio S, Vicedomini G, Tocchi M, Gugliotta F, Salvati A, Dicandia C, Calabrò MP, Mazzone P, Ficarra E, Di Gioia C, Gulletta S, Nardi S, Santinelli V, et al. Atrial electroanatomic remodeling after circumferential radiofrequency pulmonary vein ablation: efficacy of an anatomic approach in a large cohort of patients with atrial fibrillation. Circulation 2001;104:2539–44.

[15] Stabile G, Turco P, La Rocca V, Nocerino P, Stabile E, De Simone A. Is pulmonary vein isolation necessary for curing atrial fibrillation? Circulation 2003;108:657–60.

[16] Haïssaguerre M, Sanders P, Hocini M, Takahashi Y, Rotter M, Sacher F, Rostock T, Hsu LF, Bordachar P, Reuter S, Roudaut R, Clémenty J, Jaïs P. Catheter ablation of long-lasting persistent atrial fibrillation: critical structures for termination. J Cardiovasc Electrophysiol 2005;16:1125–37.

[17] Oral H, Chugh A, Good E, Sankaran S, Reich SS, Igic P, Elmouchi D, Tschopp D, Crawford T, Dey S, Wimmer A, Lemola K, Jongnarangsin K, Bogun F, Pelosi Jr F, et al. A tailored approach to catheter ablation of paroxysmal atrial fibrillation. Circulation 2006;113:1824–31.

[18] Nademanee K, Schwab MC, Kosar EM, Karwecki M, Moran MD, Visessook N, Michael AD, Ngarmukos T. Clinical outcomes of catheter substrate ablation for high-risk patients with atrial fibrillation. J Am Coll Cardiol 2008;51:843–9.

[19] Estner HL, Hessling G, Ndrepepa G, Wu J, Reents T, Fichtner S, Schmitt C, Bary CV, Kolb C, Karch M, Zrenner B, Deisenhofer I. Electrogram-guided substrate ablation with or without pulmonary vein isolation in patients with persistent atrial fibrillation. Europace 2008;10:1281–7.

[20] Deisenhofer I, Estner H, Reents T, Fichtner S, Bauer A, Wu J, Kolb C, Zrenner B, Schmitt C, Hessling G. Does electrogram guided substrate ablation add to the success of pulmonary vein isolation in patients with paroxysmal atrial fibrillation? A prospective, randomized study. J Cardiovasc Electrophysiol 2009;20:514–21.

[21] Pappone C, Oral H, Santinelli V, Vicedomini G, Lang CC, Manguso F, Torracca L, Benussi S, Alfieri O, Hong R, Lau W, Hirata K, Shikuma N, Hall B, Morady F. Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. Circulation 2004;109:2724–6.

[22] Dagres 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;17:1213–5.

[23] Cury RC, Abbara S, Schmidt S, Malchano ZJ, Neuzil P, Weichet J, Ferencik M, Hoffmann U, Ruskin JN, Brady TJ, Reddy VY. Relationship of the esophagus and aorta to the left atrium and pulmonary veins: implications for catheter ablation of atrial fibrillation. Heart Rhythm 2005;2:1317–23.

[24] Cummings JE, Schweikert RA, Saliba WI, Burkhardt JD, Brachmann J, Gunther J, Schibgilla V, Verma A, Dery M, Drago JL, Kilicaslan F, Natale A. Assessment of temperature, proximity, and course of the esophagus during radiofrequency ablation within the left atrium. Circulation 2005;112:459–64.

[25] Schmidt M, Nölker G, Marschang H, Gutleben KJ, Schibgilla V, Rittger H, Sinha AM, Ritscher G, Mayer D, Brachmann J, Marrouche NF. Incidence of oesophageal wall injury post-pulmonary vein antrum isolation for treatment of patients with atrial fibrillation. Europace 2008;10:205–9.

[26] Singh SM, d'Avila A, Doshi SK, Brugge WR, Bedford RA, Mela T, Ruskin JN, Reddy VY. Esophageal injury and temperature monitoring during atrial fibrillation ablation. Circ Arrhythm Electrophysiol 2008;1:162–8.

[27] Martinek M, Meyer C, Hassanein S, Aichinger J, Bencsik G, Schoefl R, Boehm G, Nesser HJ, Purerfellner H. Identification of a high-risk population for esophageal injury during radiofrequency catheter ablation of atrial fibrillation: procedural and anatomical considerations. Heart Rhythm 2010;9:1224–30.

[28] European Heart Rhythm Association (EHRA), European Cardiac Arrhythmia Society (ECAS), American College of Cardiology (ACC), American Heart Association (AHA), Society of Thoracic Surgeons (STS), Calkins H, Brugada J, Packer DL, Cappato R, Chen SA, Crijns HJ, Damiano Jr RJ, Davies DW, Haines DE, Haissaguerre M, et al. HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) task force on catheter and surgical ablation of atrial fibrillation. Heart Rhythm 2007;4:816–61.

[29] Iriki Y, Ishida S, Oketani N, Ichiki H, Okui H, Ninomiya Y, Maenosono R, Matsushita T, Miyata M, Hamasaki S, Tei C. Relationship between clinical outcomes and unintentional pulmonary vein isolation during substrate ablation of atrial

fibrillation guided solely by complex fractionated atrial electrogram mapping. J Cardiol 2011;58:278–86.

[30] Ichiki H, Oketani N, Ishida S, Iriki Y, Okui H, Ninomiya Y, Maenosono R, Matsushita T, Miyata M, Hamasaki S, Tei C. Incidence of asymptomatic cerebral micro-thromboembolism after atrial fibrillation ablation guided by complex fractionated atrial electrogram. J Cardiovasc Electrophysiol 2012;February, http://dx.doi.org/10.1111/j.1540-8167.2011.02259.x.

[31] Oral H, Scharf C, Chugh A, Hall B, Cheung P, Good E, Veerareddy S, Pelosi Jr F, Morady F. Catheter ablation for paroxysmal atrial fibrillation: segmental pulmonary vein ostial ablation versus left atrial ablation. Circulation 2003;108:2355–60.

[32] Nademanee K, Lockwood E, Oketani N, Gidney B. Catheter ablation of atrial fibrillation guided by complex fractionated atrial electrogram mapping of atrial fibrillation substrate. J Cardiol 2010;55:1–12.

[33] Oketani N, Lockwood E, Nademanee K. Incidence and mode of AF termination during substrate ablation of AF guided solely by complex fractionated atrial electrogram mapping. Circulation 2008;118(Suppl.):S925.

[34] Haïssaguerre M, Hocini M, Sanders P, Sacher F, Rotter M, Takahashi Y, Rostock T, Hsu LF, Bordachar P, Reuter S, Roudaut R, Clémenty J, Jaïs P. Catheter ablation of long-lasting persistent atrial fibrillation: clinical outcome and mechanisms of subsequent arrhythmias. J Cardiovasc Electrophysiol 2005;16:1138–47.

[35] Verma A, Patel D, Famy T, Martin DO, Burkhardt JD, Elayi SC, Lakkireddy D, Wazni O, Cummings J, Schweikert RA, Saliba W, Tchou PJ, Natale A. Efficacy of adjuvant anterior left atrial ablation during intracardiac echocardiography-guided pulmonary vein antrum isolation for atrial fibrillation. J Cardiovasc Electrophysiol 2007;18:151–6.