



Determination of the effects of cryoablation for atrial fibrillation on esophageal functions

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ABSTRACT

Objective: Periesophageal vagal plexus injury is a complication of cryoablation for atrial fibrillation (AF). The aim of this study is to investigate the effect of cryoablation on esophageal functions and to determine the relationship between esophageal temperature and esophageal motility. **Methods:** Twenty patients with symptomatic paroxysmal AF who underwent cryoablation were included in this study. The lowest cryoballoon temperature for each pulmonary vein (PV) was recorded. Esophageal temperature was measured using an esophageal probe during each cryo-application. Esophageal manometry was performed before the procedure and one day after the procedure for each patient in order to assess the esophageal functions.

Results: During the procedure, the highest esophageal temperature change was found in the left-side PVs in 13 patients (65%) and in the right-side PVs in seven patients (35%). No correlation was found between the lowest cryoballoon temperature and esophageal temperature change ($r=0.22$, $p=0.05$). It was detected that the lower esophageal sphincter pressure and esophageal contraction amplitude pressure decreased after the procedure (before: 19.7 ± 9.3 mm Hg, after: 14.3 ± 4.9 mm Hg, $p=0.001$; before: 84.5 ± 28.3 mm Hg, after: 72.7 ± 34.3 mm Hg, $p=0.005$, respectively). Five patients (25%) developed gastrointestinal symptoms after the procedure.

Conclusion: During cryoablation, esophageal temperature measurement can be performed to reduce the probability of esophageal injury. Cryoablation affects esophageal motility, and esophageal manometry can be performed to detect esophageal motility impairments in patients with gastrointestinal symptoms. (*Anatol J Cardiol* 2020; 23: 223-7)

Keywords: atrial fibrillation, cryoablation, esophagus, esophageal manometry

Introduction

Atrial fibrillation (AF) is one of the most common types of cardiac arrhythmia, with a prevalence ranging from 1% to 3% (1, 2). Antiarrhythmic agents and catheter ablation are commonly used for rhythm control of AF. The use of catheter ablation has been on the rise because of the low efficacy and long-term side effects of antiarrhythmic agents. Pulmonary vein isolation (PVI) is accepted as the fundamental treatment modality for the ablation of AF. Cryoablation and radiofrequency (RF) ablation are also effectively and commonly used for PVI. However, cryoablation may

cause some serious complications, such as possible damage to the esophagus, bronchi, and phrenic nerve. The esophageal temperature decreases during the procedure. It has been demonstrated in various studies that the rate of esophageal damage due to cryoablation is 12% (3). Vagal plexus damage around the esophagus has been demonstrated to be associated with gastroparesis (4). However, the effect of this damage on the esophageal functions is so far unknown.

The aim of this study was to investigate the effect of cryoablation on the esophageal functions and to determine the relationship between esophageal temperature change and esophageal motility.

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Methods

Patient selection and study protocol

Twenty patients who were admitted to the Department of Cardiology, Faculty of Medicine, Çukurova University, with symptomatic paroxysmal AF, despite taking at least one class I or III antiarrhythmic agent, undergoing cryoablation, were included in this prospective study. A detailed assessment including medical history, physical examination, electrocardiogram and transthoracic echocardiography was performed and recorded before the procedure. The lowest cryoballoon temperature was recorded for each pulmonary vein (PV) during the procedure. Esophageal temperature was measured and recorded using an esophageal probe for each PV during the procedure. An esophageal manometry test was performed before and on the day after the procedure to evaluate the esophageal functions. The patients were queried for symptoms of gastrointestinal complications before and 72 h after the procedure via telephone calls. This study was conducted according to the principles of the Declaration of Helsinki and was approved by the Çukurova University Faculty of Medicine Ethics Committee (TTU-10.02.2017-61/59). Informed consent was obtained from all the patients included in the study.

Exclusion criteria

- Patients in whom a thrombus was detected by transesophageal echocardiography.
- Patients with a left ventricular ejection fraction of <50%.
- Patients with a left atrial size of >55 mm.
- Patients who were New York Heart Association class III/IV.
- Patients with persistent, long-standing persistent, permanent AF.
- Patients with a previous history of AF ablation.
- Patients with gastroesophageal reflux.
- Patients with a previous history of abdominal surgery.
- Patients who use drugs that affect gastrointestinal motility.
- Patients who disagreed and/or refused to use an oral anticoagulant.

Cryoablation procedure

Cryoablation was performed as commonly described in the literature. A Medtronic Achieve 15 mm catheter was used to record the PV potentials. Then, a Medtronic Arctic Front Advance 2AF283 balloon (diameter: 28 mm) was engaged to each PV. After inflating the balloon, a contrast agent was administered to check whether complete occlusion was achieved. We routinely applied 240 s of freezing. In case of delayed PV isolation time (>90 s), we prolonged the time up to 300 s.

During the cryoablation procedure, a temperature probe with a single sensor (PEF 401/701; Nihon Kohden, Irvine, CA, USA) was introduced into the esophagus. The baseline temperature of the esophagus was recorded for each patient. During the application of cryotherapy to each PV, the cryoballoon and the

esophageal temperature probe were fluoroscopically aligned so as to bring the temperature sensor and the cryoballoon as close as possible, and the change in the esophageal temperature was recorded during freezing. The distance between the cryoballoon and the esophagus is thought to have an impact on esophageal functions. In case the esophageal probe is at the same side as the cryoballoon with respect to the midline in the anteroposterior position, the esophagus is stated to be close to the cryoballoon; otherwise, it is stated to be away from the cryoballoon. There may be an anatomical variability in the distance between the esophagus and the PVs between individuals; therefore, the fluoroscopic location of the esophageal temperature probe in the anteroposterior view and the distance between the temperature probe and the balloon were evaluated visually by the operators (Fig. 1). The temperature cut-off of the cryoballoon for the termination of freezing was -60° , and the esophageal temperature cut-off was accepted as 10° (5).

Esophageal manometry

A water perfusion esophageal manometry (Latitude esophageal motility catheter, Minneapolis, USA) test was performed before and 24 h after the procedure to evaluate the esophageal function and motility. The patients were fasted for 6 h before the manometry test. This test was performed via the transnasal route in each patient. During the procedure, the upper and lower esophageal sphincters and esophageal body functions [lower esophageal sphincter (LES) pressure, esophageal body resting pressure, amplitude of contractions occurring in the esophagus during swallowing, relaxation, and peristalsism] were examined and recorded.

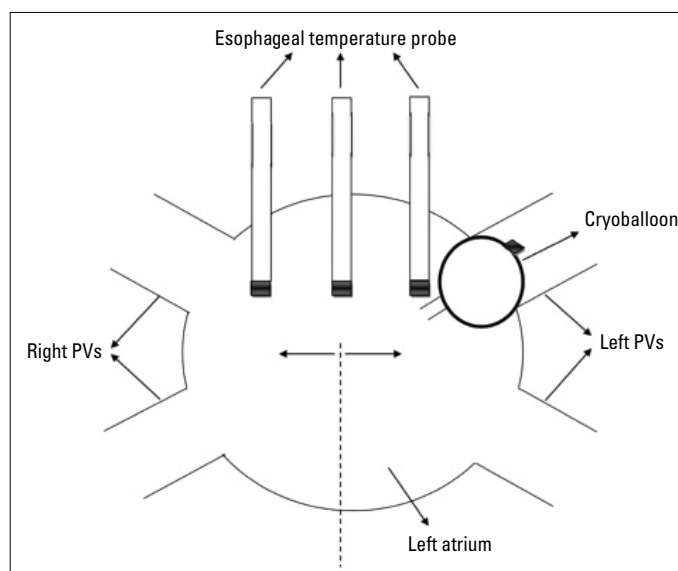


Figure 1. The location of the esophageal temperature probe is determined by the position of the esophagus relative to the left atrium. In case the esophageal probe is at the same side as the cryoballoon with respect to the midline in the anteroposterior position, the esophagus is stated to be close to the cryoballoon; otherwise, it is stated to be away from the cryoballoon

Statistical analysis

SPSS Statistics Version 20.0 (IBM Corp., Armonk, NY, USA) software package was used to statistically analyze the data. Categorical measurements were summarized as a number and percentage, whereas continuous measurements were summarized as the mean and standard deviation [median (Q1–Q3) when necessary]. The Wilcoxon signed-rank test was used to compare two dependent numerical measurements that did not show normal distribution. The correlation between these continuous measurements was examined using Spearman’s correlation coefficient as some numerical measurements did not meet the normal distribution assumption. Evaluations using partial correlation were also included. The statistical significance level was taken as <0.05 for all tests.

Results

Twenty patients were included in our study, whose baseline characteristics are presented in Table 1. The mean follow-up period was 14.55±10.15 months. The mean procedure time and fluoroscopy time were 65.25±11.61 min and 23.30±6.57 min, respectively, and the mean fluoroscopic radiation exposure was 28.60±14.65 cGyxm².

In total, 74 PVs were isolated by 136 cryoapplications (1.84 freezes per vein) in the 20 patients. The lowest temperature value of the cryoballoon was recorded for each PV. Before initiating the procedure, the baseline esophageal temperature value for each patient was recorded. The median baseline esophageal temperature value was 36.9°C (36.4–37.2°). The minimal esophageal temperature value was measured using an esophageal probe for each PV during the procedure. We did not encounter excessive cooling of the esophagus (<10°) necessitating premature termination of freezing. The cryoballoon and esophageal temperatures for each PV are tabulated in Table 2.

Changes in the esophageal temperatures of the patients were evaluated during the procedure. The highest esophageal temperature change occurred in the left-side PVs in 13 patients (65%) and in the right-side PVs in seven patients (35%). It was found that, out of the 13 patients in whom the highest esophageal temperature change was in the left-side PVs, the esophagus was close to the left PVs in six (46.2%), equidistant to both PVs in five (38.5%), and close to the right PVs in two (15.4%) patients fluoroscopically in the anteroposterior position. Of the seven patients in whom the highest esophageal temperature change was in the right-side PVs, the esophagus was equidistant to both PVs in five (71.4%) and close to the left PVs in two (28.6%) patients fluoroscopically in the anteroposterior position.

Table 1. Distribution of the demographic and clinical characteristics of the patients

Variable	
Age (years) ^a	52.10±14.75 54.00 (25.00-84.00)
Sex (Male/Female) ^b	11 (55)/9 (45)
Body mass index (kg/m ²) ^a	29.51±4.76 29.05 (23.39-44.98)
Hypertension ^b	10 (50)
Coronary artery disease ^b	8 (40)
Diabetes mellitus ^b	3 (15)
Smoking ^b	5 (25)
Left atrial diameter (mm) ^a	37.30±5.47 37.00 (27.00-48.00)
Ejection fraction (%) ^a	62.75±5.21 64.50 (50.00-74.00)

^aMean±standard deviation (median, interquartile). ^bn (%).

Table 2. Balloon and esophageal temperatures for each pulmonary vein

	Upper-left PV	Lower-left PV	Left common PV	Upper-right PV	Lower-right PV	Right common PV
Number of PVs	15	15	5	19	19	1
Isolated PV ^a	15/15 (100)	15/15 (100)	5/5 (100)	19/19 (100)	19/19 (100)	1/1 (100)
Lowest temperature value of the cryoballoon (°C) ^b	-45 (-48 to -41)	-44 (-45 to -38)	-48 (-56 to -46.5)	-48 (-53 to -45)	-44 (-47 to -41)	-42
Minimal esophageal temperature value (°C) ^b	35.0 (31.6-35.9)	35.3 (31.2-35.8)	36.3 (35.4-36.6)	36.0 (35.4-36.3)	35.4 (32.6-36.2)	34.0
Lowest esophageal temperature value (°C)	30.5	24	34.6	27.2	27.6	32
Number of veins with an esophageal temperature of <32° ^a	5 (33)	5 (33)	0	1 (5)	4 (21)	0

^an (%). ^bMedian (Q₁-Q₃). PV - pulmonary vein

The relationship between the lowest cryoballoon temperature and the esophageal temperature change was evaluated for each PV (74 PVs). No relationship was found between the lowest cryoballoon temperature and the esophageal temperature change ($r=0.22$, $p=0.05$).

The parameters of the esophageal manometry performed before and 24 h after the cryoablation procedure were compared. It was found that there was a significant decrease in the LES pressure after the procedure [before: 19.70 ± 9.33 , 17.00 (6.00–45.00) mm Hg, after: 14.25 ± 4.92 , 14.00 (6.00–26.00) mm Hg; $p=0.001$; Fig. 2].

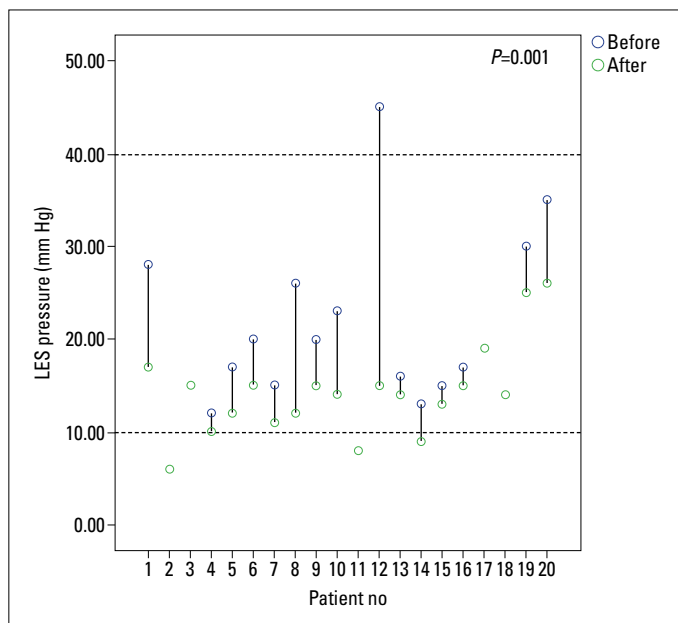


Figure 2. Lower esophageal sphincter pressure before and after the procedure for each patient (normal range: 10–40 mm Hg)

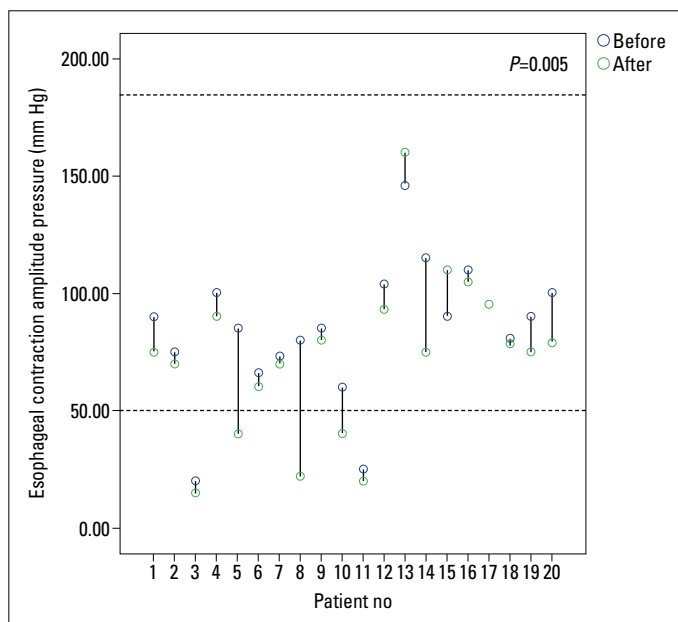


Figure 3. Esophageal contraction amplitude pressure before and after the procedure for each patient (normal range: 50–180 mm Hg)

There was no significant difference between the esophageal body resting pressure values measured before and after the procedure [before: 0.10 ± 1.74 , 0.00 (from –2.00 to 7.00) mm Hg, after: 2.10 ± 6.60 , 0.00 (from –2.00 to 28.00) mm Hg; $p=0.131$]. The esophageal contraction amplitude decreased after the procedure [before: 84.5 ± 28.3 mm Hg, after: 72.65 ± 34.33 , 75.00 (15.00–160.00) mm Hg; $p=0.005$; Fig. 3].

The esophageal relaxation values of all 20 patients were normal before the procedure, and no esophageal relaxation impairment was found in any patient after the procedure. Two patients were found to have peristalsis impairment before the procedure. Although a newly developed peristalsis impairment was found in two patients (10%) after the procedure, it was statistically nonsignificant ($p=0.157$).

Newly developed gastrointestinal symptoms were observed after the procedure in five patients (25%) (epigastric pain, epigastric fullness, reflux, and indigestion). Both of the patients who developed peristalsis impairment after the procedure exhibited the symptoms of epigastric fullness and indigestion.

Discussion

The main finding of this study was the demonstration of the effect of cryoablation on esophageal functions possibly due to periesophageal vagal nerve damage. The structures adjacent to the left atrium are known to be affected by cryoablation (6). The esophagus and the periesophageal vagal plexus surrounding the esophagus are among the affected structures (7). There are cases of direct esophageal damage following cryoablation in the literature (8, 9). It has been stated that the symptoms of gastroparesis develop after cryoablation (4). Previous studies evaluated the effects of cryoablation on the esophagus using endoscopic methods. In our study, the effects of cryoablation on esophageal functions were evaluated and investigated using the esophageal manometric parameters.

Esophageal manometry shows the functions and motility of the esophagus. This technique helps examine the LES pressure, esophageal body resting pressure, esophageal contraction amplitude, relaxation, and peristalsis. It has been demonstrated that, in patients whose esophageal vagal plexus is affected, gastric emptying may decrease and gastroparesis may develop, thereby causing gastrointestinal symptoms (10). In our study, the LES pressure and esophageal contraction amplitude values were shown to decrease after cryoablation, although they remained within the normal limits. Cryoablation may also have some effects on esophageal peristalsis, and both patients who newly developed peristalsis impairment had gastrointestinal complaints after the procedure.

John et al. (11) conducted a study demonstrating that developing atrioesophageal fistulas is more common in the left-sided PVs. In addition, in our study, the highest esophageal temperature change was observed in the left-sided PVs in 13 patients (65%). In a study conducted by Jang et al. (12), it was demon-

strated that the esophagus is located closer to the left-sided PVs. Our study demonstrated that 10 out of the 15 PVs (66%) in which the esophageal temperature decreased below 32°C were seen while isolation was being applied to the left-sided PVs. Therefore, we think that the duration of cryoablation application to the left-sided PVs should not be unnecessarily long and that unnecessary and bonus applications should be avoided. We earlier supposed that the closer the PV is to the esophagus, the more the esophagus is affected; however, the results showed no such relationship.

Another complication seen following cryoablation is phrenic nerve paralysis. Recent studies showed a rate ranging from 4% to 14% for phrenic nerve paralysis following cryoablation (13). We observed phrenic nerve paralysis in one patient, which is consistent with the literature (5%).

Study limitations

Only 20 patients were included in this study. Studies on a larger number of patients will allow determining the relationship between the reduction in the esophageal temperature and the esophageal motility during cryoablation more clearly. A single source of energy (i.e., cryoablation technique) was used for AF ablation in our study. No comparison or evaluation was made with other sources of energy (especially RF ablation). The manometric parameters were assessed using water perfusion manometry. Using high-resolution manometry will provide more precise and correct measurement results. Visually evaluating the distance between the esophagus and the cryoballoon was a crude type of evaluation and might be considered as a limitation. Symptom queries were a subjective evaluation method; therefore, it was not easy to demonstrate the association between cryoablation and gastrointestinal symptoms. However, preablation and postablation questioning of symptoms show only a probable association between cryoablation and gastrointestinal symptoms. According to our study, we cannot comment on the durability of the effects of cryogenics on esophageal functions. For long-term effects, late manometric evaluations should be performed.

Conclusion

It was found that esophageal functions, including LES pressure, esophageal contraction amplitude, and peristalsis, may be affected following cryoablation. Therefore, we suggest that the duration of ablation should not be unnecessarily long and that bonus applications should be avoided. Further studies are needed to understand the role of esophageal manometry in a larger patient series of cryoablation and the relationship between functional impairments of the esophagus and postprocedural gastrointestinal symptoms.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

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