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Original Article

Vagal response in cryoballoon ablation of atrial fibrillation and autonomic nervous system: Utility of epicardial adipose tissue location

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ABSTRACT

Background: Mechanism and effects of vagal response (VR) during cryoballoon ablation procedure on the cardiac autonomic nervous system (ANS) are unclear. The present study aimed to evaluate the relationship between VR during cryoballoon catheter ablation for atrial fibrillation and ANS modulation by evaluating epicardial adipose tissue (EAT) locations and heart rate variability (HRV) analysis.
Methods: Forty-one patients with paroxysmal atrial fibrillation (11 with VR during the procedure and 30 without VR) who underwent second-generation cryoballoon ablation were included. EAT locations and changes in HRV parameters were compared between the VR and non-VR groups, using Holter monitoring before ablation, immediately after ablation and one month after ablation.
Results: The total EAT volume surrounding the left atrium (LA) in the VR and non-VR groups was 29.0 ± 18.4 cm^3 vs 27.7 ± 19.7 cm^3, respectively ($p=0.847$). The VR group exhibited greater EAT volume overlaying the LA-left superior pulmonary vein (PV) junction (6.1 ± 3.6 cm^3 vs 3.6 ± 3.3 cm^3, $p=0.039$) than the non-VR group. HRV parameters similarly changed following ablation in both the groups. EAT volume overlaying LA-right superior PV junction was significantly correlated with the relative changes in root-mean-square successive differences ($r=-0.317$, $p=0.043$) and high frequency ($r=-0.331$, $p=0.034$), immediately after the ablation.
Conclusions: Changes in HRV parameters following ablation were similarly observed in both the groups. EAT volume on the LA-PV junction is helpful for interpretation of VR occurrence and ANS modulation.

1. Introduction

Cryoballoon-based catheter ablation is a recently developed therapeutic device for treating atrial fibrillation (AF), and has demonstrated efficacy and prognosis similar to that of radiofrequency catheter ablation for paroxysmal AF patients [1,2]. With a unique combination of balloon occlusion of the pulmonary vein (PV) and cooling of the attached surface, PV triggers can be eliminated, and substrate modification of the left antrum (LA) obtained. During cryoballoon catheter ablation of AF, vagal responses (VRs) such as bradycardia, asystole, and atrioventricular block, occasionally occur [3–6]. Recent reports have shown that these responses may be associated with intrinsic cardiac autonomic nervous system (ANS) expression. However, the underlying mechanism and association between VR during cryoballoon ablation procedure and the cardiac ANS remain unclear.

In discussing the cardiac ANS for catheter ablation, the ganglionated plexi (GP) located between the LA and PV junction, which are part of the ANS, may have an important role in the initiation and maintenance of AF [7,8]. The GP are located on the epicardial surface of the atria, and are involved in the epicardial adipose tissue (EAT) surrounding the LA. As the GP are unable to attach directly to the LA surface, the surrounding EAT may play an accessory role in receiving neural activity associated with the GP, and in producing pro-inflammatory adipokines [9]. Several studies have demonstrated the precise location of EAT through imaging modalities, and have suggested the presence of potential overlap between the EAT and GP areas during radiofrequency catheter ablation [10,11]. Therefore, EAT volume on the LA-PV junction area could represent an area of interconnected cardiac ANS tissue.

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This study investigated the relationship between the VR during cryoballoon ablation and the effects of the cardiac ANS, using both, visual imaging modalities and autonomic nerve function assessment. We compared the EAT volume surrounding the LA and changes in pre- and post-procedural heart rate variability (HRV) parameters between the VR and non-VR groups.

2. Material and methods

2.1. Study population

Subjects were recruited retrospectively from a catheter ablation database at Nagoya University Hospital in Japan. This ablation database was approved by our institutional ethics committee. Total 148 patients who underwent second-generation cryoballoon catheter ablation for paroxysmal AF for the first time between July 2014 and December 2015 were firstly evaluated. We excluded patients who were lost to follow-up within three months after the ablation, and those who received intravenous atropine administration prior to the procedure. For the HRV assessment, we additionally excluded patients who were administered beta-blocker, digoxin, amiodarone, and/or bepridil agents during the procedure; those who presented with structural heart diseases, diabetes mellitus, stroke and/or unusual pacing rhythms; and those who had an inadequate HRV assessment. Finally, 41 patients (11 in whom VRs, such as sinus bradycardia, asystole, and atrioventricular block occurred during the procedure, and 30 patients in whom VR did not occur) were included in the present study. The indications for catheter ablation of AF complied with the latest guidelines [12]. Before the procedure, informed consent was obtained from all patients, according to our hospital guidelines.

2.2. Examination course

Patients scheduled for catheter ablation treatment were admitted the day before the procedure. At admission, baseline blood testing, echocardiography, electrocardiography and Holter examination were performed. Antiarrhythmic agents were discontinued five half-lives before ablation. Transesophageal echocardiography was performed in all patients to confirm the absence of atrial thrombus. All patients underwent three-dimensional (3D) computed tomography (Aquilion ONE™, TSX-301C, Toshiba Medical Systems, Japan) using contrast medium (OMINIPAQUE™ 350 mgL/mL) for the visualizing LA and PV. Anticoagulant drugs, including direct oral anticoagulants, were continued during the procedure [13].

2.3. Ablation procedure

For the cryoballoon ablation procedure, the entire technique was performed with the patient conscious, using a minimal sedation strategy. Boluses of hydroxyzine pamoate 25 mg and buprenorphine 0.1 mg were administered intravenously before vascular puncture. After administration of an 80–100 IU/kg bolus of heparin, a transseptal puncture was performed using a radiofrequency needle (Baylis Medical, Inc., Montreal, QC, Canada) and an 8-French (Fr) sheath under intracardiac echocardiography monitoring. A 15-Fr steerable sheath (Flexcath Advance, Medtronic, Minneapolis, MN, USA) was introduced into the LA. Following all PV venography during rapid ventricular pacing, a second-generation 28-mm cryoballoon system (Arctic Front Advance, Medtronic, Minneapolis, MN, USA) was advanced and placed on the ostium of each PV using an inner circular mapping catheter (Achieve, Medtronic, Minneapolis, MN, USA). Following confirmation of PV ostium occlusion with the cryoballoon using contrast medium, a 180-second cycle freeze ablation was repeated until electrical isolation of the PV was achieved using the mapping catheter. During the freeze ablation of the right PV, pacing phrenic nerve stimulation was performed with compound motor action potential monitoring to avoid phrenic nerve injury [14]. During the procedure, we systematically began with isolation of the left superior PV (LSPV), followed by the left inferior PV (LIPV), right inferior PV (RIPV) and right superior PV (RSPV), respectively. An 8-mm tip cryocatheter (Freezor MAX, Medtronic, Minneapolis, MN, USA) was also available for additional touch-up freeze applications. All procedures were performed using a 3D electroanatomical mapping system (EnSite™, NavX™, St. Jude Medical, Inc., St Paul, MN, USA). After confirmation of PV isolation, a bipolar voltage amplitude map of the LA was generated with the aforementioned EnSite™ NavX system. Using a post-ablation voltage map, the level of ablation scar was quantitatively assessed by measuring post-ablation low-voltage areas (<0.5 mV). The ablation area was defined as a low-voltage area surrounded by the voltage borderline of the left atrial side and ipsilateral PV ostia [15].

VR was defined as sinus bradycardia (<40 bpm), asystole and/or atrioventricular block at any time during the procedure, from the time of balloon occlusion to deflation following the thawing period. Temporal ventricular pacing and intravenous atropine administration were applied in cases in which VR occurred.

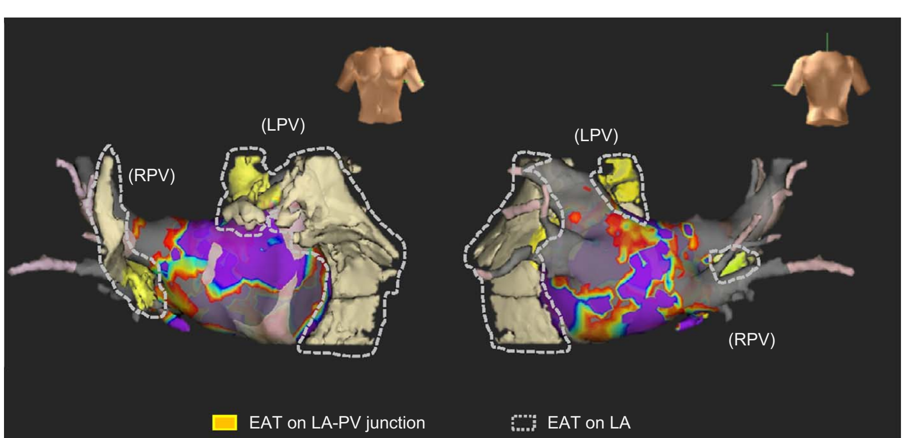

Fig. 1. Representative case showing the distribution of EAT on the LA. Fusion between the EAT image and voltage mapping in sinus rhythm after cryoballoon ablation was performed. In the voltage map, areas under 0.05 V were mapped to gray, between 0.05 and 0.5 V to colors between red and purple, and above 0.5 V to purple.

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