Preferrential Conduction Properties Along The Left Lateral Ridge And The Arrhythmogenicity Of The Left Pulmonary Veins In Patients With Atrial Fibrillation

Toshiya Kurotobi, MD PhD, Yoshihisa Shimada, MD PhD, Naoto Kino, MD, Kazato Ito, MD, Kosuke Takehara, MD, Daisuke Tonomura, MD, Tomohiro Nakashoji MD, Kentaro Yano, MD, Chiharu Tanaka, MD, Masataka Yoshida, MD, PhD, Takao Tsuchida, MD PhD, Hitoshi Fukumoto, MD PhD

Abstract

Purpose: In this study, we examined the hypothesis that the preferential conduction property along left lateral ridge (LLR) might affect the arrhythmogenicity of left pulmonary veins (LPVs).

Methods: The study population included 40 consecutive AF patients. Radiofrequency energy (RF) was sequentially delivered along the LLR from a lower to upper manner during postero-lateral CS pacing during an isoproterenol infusion.

Results: The conduction time during pacing from the CS was significantly prolonged during radiofrequency (RF) deliveries (before vs. after, upper; 91±26ms vs. 127±38ms, p<0.001, lower; 86±21ms vs. 103±22ms, p<0.001). Remarkable prolongation of more than 30ms was observed in 19 of 40 patients (48%) (both LPVs, 6; only the upper LPVs, 12; and only the lower LPV, 1). Sites with a remarkable prolongation were observed at the carina between the LPVs, anterior site of the upper LPV carina, anterior wall of the lower LPV, and bottom of the lower LPVs.

Conclusion: The LLR includes the preferential conduction properties between the CS and LPVs, and the observation of the serial changes during the RF delivery could provide us information about the LPVs arrhythmogenicity.

Introduction

The Left lateral ridge (LLR) between left atrial appendage and left pulmonary veins (LPVs) showed a fiber orientation perpendicular to LPVs ostium, and it includes the ligament and vein of Marshall with the ganglia and fibers of the autonomic nervous system. The ligament and vein of Marshall containing the Marshall bundle (MB) with richly innervates the sympathetic and parasympathetic nerves can serve as a source of triggers and the substrate of reentry of atrial fibrillation (AF). Histological studies indicated that the proximal portion of the MB directly connects to the muscular sleeve of the CS, and the distal portion connects to the left atrial wall along the LLR and LPVs with wide variations. Because the dominant electrical connections and the conduction of the MB could serve as substrates for reentry as well arrhythmogenicity, the change of activation pattern along the LLR during radiofrequency application (RF) may be associated with the arrhythmogenicity of the LPVs. Actually, our previous study confirmed that the sites of AF initiation can be identified by using the angiographic vein of Marshall with balloon-occluded venography of CS during isoproterenol infusion. In this study, we examined the relationship between the conduction properties along LLR and the arrhythmogenicity of the LPVs.

Methods

The study population consisted of 40 out of 47 consecutive patients with drug-refractory AF episodes who underwent radiofrequency catheter ablation (CA). Seven patients were excluded because sinus rhythm could not be maintained during the RF ablation. Exclusion criteria for the patient characteristics were as follows, 1) a left atrial diameter (LAD) of more than 50mm, 2) significant valvular disease requiring surgery, 3) an ejection fraction of less than 40%, 4) hypertrophic obstructive cardiomyopathy, and 5) long lasting AF of more than 5 years. The patients’ mean age was 63 years, 29
(73%) were male, and 8 (20%) had persistent AF. Persistent AF was defined as that lasting longer than 7 days, not self-terminating and usually requiring medical intervention. Structural heart disease consisted of 10 patients (25%). The mean period of suffering from an AF episode was 55 months. The mean left atrial diameter was 39.6±5.6 mm, and left ventricular ejection fraction was 60.1±13.0%. All antiarrhythmic drugs were generally discontinued for at least 3 days before the CA. All patients provided written informed consent for the electrophysiological study and CA.

Electrophysiological Study And Catheter Ablation

A single 3000 IU bolus of heparin was administered and then an activated clotting time of >300 seconds was maintained after the transseptal puncture. A 20-pole diagnostic catheter was positioned in the CS for pacing and recording. A 20-pole catheter was placed in the right atrium to cover the area along the crista terminalis or superior vena cava (SVC). The LA and PVs were accessed by a transseptal approach. We introduced 3 steerable catheters, including two spiral curve catheters, into the left atrium through a single transseptal puncture site. The upper and lower LPVs were simultaneously mapped with two adjustable 20-pole catheters (OPTIMA, Irvine, USA) (Figure 1).

Coronary angiography was performed to evaluate the junction of the CS and great cardiac vein to identify the orifice of Marshall vein and ligament. The features of the CS were determined by a subsequent filling and staining with contrast and/or by noting the location of the multipolar electrodes of the catheter within the CS. The 3D constructed geometry of the entire left atrium including the LPVs and LLR was created by using a NavX system (St. Jude Medical, St. Paul, Minnesota, USA). At first RF energy during CS pacing was delivered along the LLR as a part of the LPV ablation (Figure 2), and each ablation site and the conduction pattern during the RF delivery were monitored and recorded by fluoroscopy and a 3D electroanatomical system. The surface ECG and intracardiac electrograms filtered between 30 to 500 Hz were recorded simultaneously with a polygraph (Cardiolab; GE, USA or EP workmate; SJM, USA).

Radiofrequency (RF) energy was delivered for 30 to 60 seconds at each site using a dumbbell shaped 8 mm tip (Japan Life Line, Fantasista, Tokyo, Japan) or 3.5-mm irrigation tip catheter (St. Jude Medical, Minneapolis, Minnesota, USA). The RF energy was delivered with a power of 35 W with 8-mm-tip catheters, and 30 W with 3.5-mm-tip catheters.

The Detection Of Arrhythmogenic FOCI

An isoproterenol (ISP) infusion (0.5-2μg/min) was administered to determine the arrhythmogenicity of the LPVs during the left PV ablation. If AF persisted or spontaneously occurred under the ISP infusion, we attempted to cardiovert the AF up to 3 times. The DC energy was delivered with an external biphasic wave form of up to 270 J.

Arrhythmogenic foci (AMF) were detected using our previously reported methods. In summary, we simultaneously used five multipolar catheters to record the electrograms from the LPVs to search for any AMF. A 20-pole catheter (2 mm inter-electrode spacing) covered the area from the SVC to the crista terminalis, and the coronary sinus in addition to the ostium of the left PVs. AMF were defined as direct AF triggers or spontaneous reproducible atrial premature beats with coupling intervals of < 350ms or frequent repetitive firings. The earliest activated sites were determined according to the sequence and time difference recoded by multipolar catheters. The early activated double potentials of the AMF from the PVs and SVC were reversed, and we considered that those AMF originated from each site. If the AMF were suspected to have originated from a non-PV area uncovered by the catheters, we attempted to search the location with a roving catheter around the early centrifugal activated sites.

Statistical Analysis

The continuous variables are expressed as the mean±SD. The variables were compared by a t-paired test or chi-square test. The data without a normal distribution were compared by a Mann–Whitney U test, which was used for the non-parametric analysis. A P<0.05 was considered statistically significant. All analyses were performed using SPSS 10.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

The change in the conduction properties during ablation along the left lateral ridge

The earliest activated site of the upper LPV during CS pacing was
observed at the carina lesion in 32 of 40 patients (80%), anterior wall in 4 of 40 (10%), and posterior wall in 4 of 40 (10%). The earliest activated site was at the upper LPV in 34 of 40 (85%), bottom of the lower LPV in 4 of 40 (10%), and posterior site in 2 of 40 (5%).

After the RF delivery along the LLR, the PV potentials of the upper LPV completely disappeared in one patient and that of the lower LPV in 2 patients. The conduction time between the LPVs and CS stimulus site was significantly prolonged during the RF delivery (before vs. after, upper, 91±26 ms vs. 127±38 ms, p<0.001, lower; 86±21 ms vs. 103±22 ms, p<0.001). A remarkable prolongation of more than 30 ms was observed in 19 of 40 patients (48%) (both LPVs; 6, only the upper LPVs; 12, and only the lower LPV; 1). The sites of the remarkable prolongation during the RF delivery were observed at the carina between the LPVs, anterior site of the upper LPV carina, anterior wall of the lower LPV, and bottom of the lower LPVs (Figure 3).

The Features Of The Arrhythmogenic Foci And Their Relationship To The Conduction Properties

Thirty-three AMF from LPVs (upper; 22, lower; 11) were observed in 23/40 patients 56%. Fifteen of the detected AMF directly shifted to AF, and 16 of them exhibited premature atrial contractions and/or transient frequent repetitive firings.

The patient characteristics in the patients with AMF and without AMF are shown in Table 1. There were no significant differences in the gender, age, AF period, hypertension, diabetes mellitus, history of heart failure, history of cerebral artery disease, left atrial parameters, and left ventricular ejection fraction, between the two groups.

The earliest activated site of the AMF from the upper LPV was found at the carina region in 12 of 22 [55%], anterior wall in 3 of 22 [14%], roof site in 3 of 22 [14%], and posterior wall in 4 of 22. The earliest activated site of the AMF from the lower LPV was found at the carina region in 6 of 11 [55%] anterior wall in 2 of 11 [18%] bottom in 1 of 11 [9%], and posterior wall in 2 of 11 [18%].

The conduction time from the CS to the earliest activated upper PV after the RF delivery was significantly longer in the patients with AMF from the upper LPV than in those patients without (107±36 ms vs. 146±40 ms, p<0.01), and the conduction time from the CS pacing site to the earliest activation site of the upper LPV was significantly prolonged in the patients with AMF than in those without during the RF delivery (44±22 ms vs. 17±11 ms, p<0.01). The following AF after AMF was spontaneously terminated in 2 of 15 AF episodes during RF along LLR, and the prolonged conduction time after RF along LLR were 47 ms and 44 ms, respectively. The premature atrial contractions and/or transient frequent repetitive firings were no more observed after RF along LLR in 11 of 16 [69%].

Discussion

In this study, the dominant conduction from the CS to the upper LPV was commonly observed in the carina region with its increased arrhythmogenicity. The conduction time between those was significantly prolonged during the RF deliveries along the LLR, and a remarkable jump prolongation of more than 30 ms in those was observed in approximately half of the patients. The extent of the prolongation was significantly higher in the patients with AMF, as compared to the patients without AMF. Thus, these findings could imply that the LLR containing the MB includes the preferential conduction properties between the CS and LPVs, and has an association with the increased arrhythmogenicity of the upper LPV.

The observation of the change in the conduction properties during the RF delivery could provide us with useful information about the potential upper LPVs arrhythmogenicity.

Anatomical Myocardial Structure Of The Left Lateral Ridge

The LLR showed a fiber orientation perpendicular to the blood flow, and the LPVs and left atrial musculature are likely to be disconnected or was only connected via a narrow isthmus because of the bulging ridge structure. There are abrupt changes in the fiber orientation in the middle portion of the LPVs.

The VOM, or LOM as the MB including the density of the ganglia and fibers of the autonomic nervous system, can be traced on the epicardial aspect of the LLR with a close proximity to the endocardial surface, and they course obliquely and superficially in the ridge at variable distances from the endocardial surface of the LLR within 3 mm from the endocardium. The other most dominant fiber of the LLR is Bachmann's bundle, which runs leftward to the neck of the left atrial appendage on the epicardial aspect of the LLR with a close relationship to the vein of Marshall or its ligament. Deeper than Bachmann's bundle is another subepicardial fiber, which is the septopulmonary bundle that covers the orifices of the left PVs. Futhermore, the subendocardial septoatrial bundle forms a broad flat bundle towards the orifices of the left PVs.

Arrhythmogenicity Of The Marshall Bundle

The Vein of Marshall or its ligament containing the MB is a remnant of the left superior vena cava, and is accompanied with richly innervated sympathetic and parasympathetic nerves, and its arrhythmogenicity could be revealed during an ISP infusion. In this study, AMF were highly observed from both LPVs under an ISP infusion, and the earliest site of those from the LPVs was often determined to be around the carina region. These observations are likely to be consistent with the previous report. In addition, the complex crossing of the muscular connections, bridges, neural inputs, and the adjoining muscle sleeves, possibly related to the MB conduction in the inter-PV carina, might promote electrical arrhythmogenicity including spontaneous ectopies of AF. From those observations, intensified RF applications targeting the carina...
LPV Arrhythmogenicity And Prolonged Conduction

The electrical connections and the conduction of the MB could serve as substrates for reentry as well as arrhythmogenicity. The MB runs along the LLR between the LAA and anterior wall of the LPVs. The proximal portion of the MB directly connects to the muscle sleeve of the CS, and the distal end of that connects to the left atrial wall and LPVs. Our recent case report confirmed that the epicardial MB conduction could include a preferential conduction to the LPVs.

In this study, the RF application along the LLR suddenly and remarkably prolonged the conduction time between the CS and LPVs in approximately half of the patients, and these observations might reflect the presence of a dominant longitudinal conduction along the LLR. And then, the earliest activated site of the upper LPVs during CS pacing was highly observed around the carina region, and also a remarkable prolongation jump during the RF delivery was highly observed around the carina and/or adjacent anterior area. A previous report suggested that the distal exit of the MB into the upper LPV is commonly located around the inter-PV junction, possibly bypassing the LPV junction to the left atrium. These specific muscle orientations and the dominant MB conduction toward the carina region could promote the preferential conduction properties.

Recent studies demonstrated that the carina region should be the target site to achieve complete LPV-LA disconnection whether using circumferential or wide encirclement ablation strategies, and the additional ablation at the PV carina region may be sometimes associated with the improved outcome of AF ablation. These reports consistently imply that the carina region can be a favorable target for an AF ablation strategy. In the meantime, we have to keep in mind that an excessive multiple RF energy toward carina may increase the risk of PV stenosis, and the careless catheter manipulation along LLR from LAA side may be prone to increase the risk of cardiac perforation, because the LAA has a very thin wall structure.

Table 1:

<table>
<thead>
<tr>
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<th>AMF (+) (N=23)</th>
<th>AMF (-) (n=17)</th>
<th>p value</th>
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<tr>
<td>Male (%)</td>
<td>67</td>
<td>65</td>
<td>0.624</td>
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<tr>
<td>Age (years)</td>
<td>68±10</td>
<td>68±10</td>
<td>0.985</td>
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<tr>
<td>AF periods (months)</td>
<td>5.5±5.4</td>
<td>6.4±8.4</td>
<td>0.596</td>
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<tr>
<td>Hypertension (%)</td>
<td>57</td>
<td>65</td>
<td>0.436</td>
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<tr>
<td>Diabetes Mellitus (%)</td>
<td>17</td>
<td>12</td>
<td>0.452</td>
</tr>
<tr>
<td>History of HF (%)</td>
<td>13</td>
<td>18</td>
<td>0.624</td>
</tr>
<tr>
<td>History of CI (%)</td>
<td>11</td>
<td>12</td>
<td>0.774</td>
</tr>
<tr>
<td>Left atrial diameter (mm)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>A-P</td>
<td>35.4±4.7</td>
<td>35.9±6.2</td>
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<tr>
<td>PV-MV</td>
<td>47.4±6.8</td>
<td>48.4±6.7</td>
<td>0.854</td>
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<tr>
<td>LVER(%)</td>
<td>66.3±7.2</td>
<td>67.2±6.3</td>
<td>0.846</td>
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Conduction Properties Of The Marshall Bundle

The electrical connections and the conduction of the MB should be required to delineate the arrhythmogenicity of the MB because of its epicardial location.

Limitations

CS pacing could not only capture the MB, but also atrial muscle. In addition, we could not directly record the MB potentials. When the rapid conduction endocardially traveled through atrium muscle, the interpretation of MB conduction could be limited. A previous study reported that the PV muscle covers a large extent of the PV perimeter, and there are specific breakthroughs from the left atrium. If the continuous MB conduction is present, careful 3D mapping system should be required to assess the preferential conduction properties via the MB.

Conclusions

MB predominant conduction properties during the RF delivery could provide us with useful information about the potential upper LPV arrhythmogenicity. These findings imply the necessity for intensified RF applications in the carina region and entire LLR.

References


