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SHORT COMMUNICATION

Structural relation between the superior vena cava and pulmonary veins in patients with atrial fibrillation

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Abstract

The superior vena cava (SVC) is a main source of non-pulmonary vein (PV) ectopies that initiate atrial fibrillation (AF). Although the critical role of structural remodeling of the left atrium (LA) in the occurrence of AF was extensively investigated by atrial voltage mapping, that of PVs and the SVC has been less explored. Study subjects comprised 47 patients undergoing catheter ablation of lone AF. During sinus rhythm, PV, SVC, and atrial voltage maps were acquired, and sleeve length of each PV and SVC was determined by an electroanatomical mapping system. The sleeves of the superior PVs were significantly longer than those of the inferior PVs (left superior PV (LSPV): 21 ± 5, left inferior PV: 14 ± 4, right superior PV (RSPV): 19 ± 5, right inferior PV: 15 ± 5, and SVC: 23 ± 10 mm, $p < 0.0001$). The LSPV sleeve was longer in men than in women (22 ± 6 vs. 19 ± 4 mm, $p < 0.05$). The sleeve length in the LSPV correlated positively with the body surface area (BSA) ($p = 0.003$, $R = 0.42$). Of note, there was a significant correlation in sleeve length between the RSPV and SVC ($p < 0.0001$, $R = 0.64$). In conclusion, not right- but left-sided PV sleeves were associated with the BSA of the patients, whereas a structural relation between the right-sided PVs and the SVC was implied based on sleeve mapping. This novel finding may provide mechanistic implications for the development of AF in future studies.

Keywords Catheter ablation · Atrial fibrillation · Pulmonary vein · Superior vena cava · Sleeve · Remodeling

Introduction

The superior vena cava (SVC) is a main source of non-pulmonary vein (PV) ectopies that initiate atrial fibrillation (AF). During catheter ablation, SVC ectopies and tachycardias are commonly observed, and isolation of the SVC is an effective approach to abolishing these arrhythmogenic activities. Empiric or semi-empiric SVC isolation is also recommended in prior studies [1–5]. Although a critical role of structural remodeling of the left atrium (LA) in the occurrence of AF was extensively investigated by atrial voltage mapping, that of PVs and SVC has been less explored [6]. In the present study, we focused on the sleeve length of the SVC and PVs on 3D voltage maps depicted by an electroanatomical mapping system to investigate structural relation between the veins in patients with AF.

Akihiko Nogami and Masaki Ieda contributed equally to this work.

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Methods

Study subjects

Forty-seven consecutive patients (65 ± 10 years, 16 women) referred to our hospital for initial catheter ablation of AF were included in this study (Table 1). Patients who had structural heart disease (hypertrophic cardiomyopathy and ischemic heart disease) and/or presented to the laboratory in AF were excluded from the study. The mean LA volume index was 28 ± 7 mL/m^2. There was a negative correlation between the body surface area (BSA) and age ($p < 0.0001$,

Table 1 Patient characteristics

Variable	$N = 47$
Female	16 (34%)
Age (years)	65 ± 10
Body mass index (kg/m^2)	24 ± 3
Body surface area (m^2)	1.68 ± 0.19
Systemic hypertension	26 (55%)
Diabetes mellitus	10 (21%)
Sick sinus syndrome	6 (13%)
Type of AF (paroxysmal)	41 (87%)
Duration of AF history (months)	12 [6–48]
eGFR (mL/min/1.73 m^2)	70 ± 12
BNP (pg/mL)	35 [12–71]
LV ejection fraction (%)	69 ± 6
LA volume index (mL/m^2)	28 ± 7

AF atrial fibrillation, *BNP* brain natriuretic peptide, *eGFR* estimated glomerular filtration rate, *LA* left atrium, *LV* left ventricular

$R = -0.66$). The study protocol was approved by the hospital's institutional review board.

Ostial diameter of the PVs and SVC

ECG-gated 256-slice CT imaging of the heart was performed within 7 days before the ablation procedure (SOMATOM Definition Flash, Siemens, Erlangen, Germany). The LA and PVs were reconstructed with 3-D segmentation software using a CARTO 3 system (Biosense Webster Inc., Diamond Bar, CA, USA). The details of the measurements were described previously [7]. The longitudinal (superoinferior) diameter of each PV ostium was measured on the 3D-CT image. SVC ostial diameter was defined as the major axis at the level of the SVC proximal limit.

Sleeve length of the PVs and SVC

Electrophysiological study and catheter ablation proceeded under conscious sedation. A 6F 20-pole dual-site mapping catheter (BeeAT; Japan Lifeline Co., Ltd., Tokyo, Japan) was inserted through the subclavian vein and positioned in the coronary sinus, right atrium (RA), and SVC throughout the procedure. After transseptal puncture, the PVs, LA, SVC, and RA were mapped with a duo-decapolar mapping catheter (Pentaray, Biosense Webster, Inc.) during sinus rhythm [8]. The BeeAT catheter allowed us to simultaneously record electrograms of the right superior PV (RSPV) and SVC and to exclude farfield electrograms between the two veins. Points were acquired using the CARTO CONFIDENSE module in the auto-freeze mode (Biosense Webster, Inc.) [8]. We mapped the SVC and each PV as distally as possible to determine the distal edge of the sleeve. For safety reasons, the cutoff value of the distal edge of the sleeve was set at 0.2 mV in this study. PV sleeve length for superior PVs was defined as the length at the roof side between the venoatrial junction and the distal edge with its amplitude of 0.2 mV, whereas that for the inferior PVs was defined as the length at the bottom side between the venoatrial junction and the distal edge. In accordance with a prior study [9], we defined the proximal limit of the SVC sleeve by the presence of merged SVC and local right atrial potentials. All measurements were performed by the same reviewer (M.E.) who was blinded to the study protocol. Fifteen patients were selected at random for the assessments of the interobserver reproducibilities of the PV and SVC sleeve measurements (by M.E. and M.B.).

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD). Differences between groups were tested using

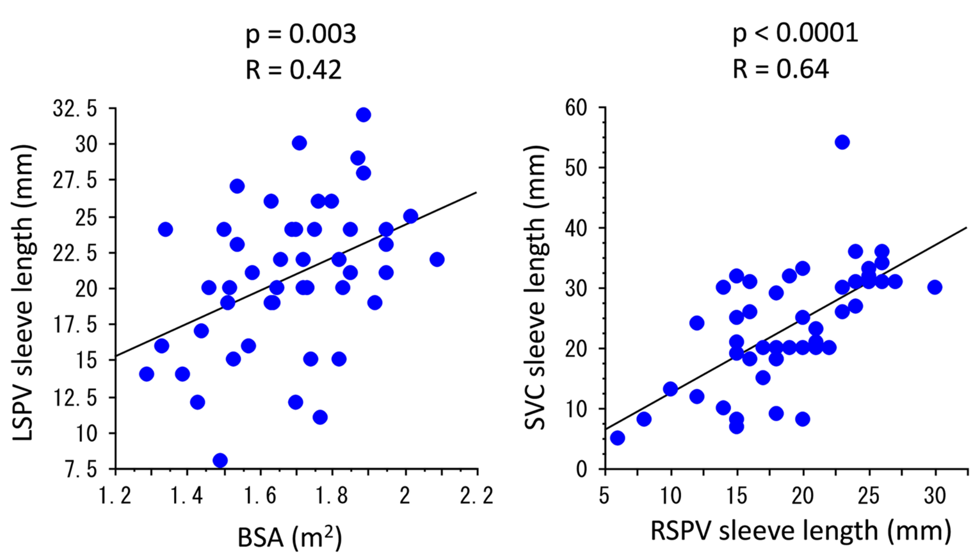

Fig. 1 Correlations between LSPV sleeve length and BSA and between RSPV sleeve length and SVC sleeve length are shown. *BSA* body surface area, *LS* left superior, *PV* pulmonary vein, *RS* right superior, *SVC* superior vena cava

the unpaired Student t test. A two-tailed p value of <0.05 indicated statistical significance. Correlation analysis was calculated using the Pearson correlation test. Multiple regression analysis was applied to determine variables contributing to the prediction of the left superior PV (LSPV) sleeve length. Data with statistical significance ($p < 0.05$) was presented in bold in Tables 2, 3, 4, 5. All statistical analyses were carried out using JMP version 12.0 (SAS Institute Inc., Cary, NC).

Table 2 Relation of BSA to PVs and SVC

	LSPV		LIPV		RSPV		RIPV		SVC	
	Sleeve length	Ostial diameter	Sleeve length	Ostial diameter	Sleeve length	Ostial diameter	Sleeve length	Ostial diameter	Sleeve length	Ostial diameter
BSA	**$p=0.003$ $R=0.42$**	$p=0.36$ $R=0.14$	$p=0.07$ $R=0.27$	$p=0.76$ $R=0.05$	$p=0.07$ $R=0.26$	$p=0.36$ $R=0.14$	$p=0.08$ $R=0.26$	$p=0.29$ $R=0.16$	$p=0.48$ $R=0.11$	$p=0.94$ $R=0.11$

BSA body surface area, *LIPV* left inferior pulmonary vein, *LSPV* left superior PV, *RIPV* right inferior PV, *RSPV* right superior PV, *SVC* superior vena cava

Results

Sleeve length

Interobserver variability had an acceptable degree of reproducibility as reflected by a correlation coefficient of 0.88 for the sleeve length measurements between the two investigators. The sleeves of the superior PVs were significantly longer than those of the inferior PVs (LSPV: 21 ± 5, left inferior PV: 14 ± 4, RSPV: 19 ± 5, right inferior PV: 15 ± 5, and SVC: 23 ± 10 mm, $p < 0.0001$). The LSPV sleeve was longer in the men than in the women (22 ± 6 vs. 19 ± 4 mm, $p < 0.05$). The sleeve length in the LSPV correlated positively with the BSA ($p = 0.003$, $R = 0.42$) (Fig. 1 and Table 2) and correlated negatively with age ($p = 0.008$, $R = -0.39$). In multiple regression analysis using a stepwise method for the LSPV sleeve length, the inclusion of only the BSA resulted in the best model (beta coefficient = 11.35, 95% confidence interval 4.01–18.69). As shown in Table 3, there was a significant relation in sleeve length between the ipsilateral superior and inferior PVs, whereas there was no relation in the length between the right- and left-sided PVs. Of note, there was a significant correlation in sleeve length between the RSPV and SVC ($p < 0.0001$, $R = 0.64$) (Table 3 and Fig. 1). A patient with long sleeves of both the RSPV and SVC, a patient with short sleeves of these two veins, and a patient in whom the sleeve limits (0.2 mV) of these two veins were continuously observed are presented in Fig. 2. The ostial diameters of the PVs and SVC and the relations between them are shown in Table 4. There were weak correlations between the ipsilateral superior and inferior PVs and between the LSPV and RSPV. Also, relations between the ostial diameter and sleeve length in each vein are shown in Table 5. There was a weak correlation only in the right inferior PV.

Table 3 Relation of sleeve length between the PVs and SVC

	LSPV (21 ± 5)	LIPV (14 ± 4)	RSPV (19 ± 5)	RIPV (15 ± 5)	SVC (23 ± 10)
LSPV	–	**$p < 0.0001$ $R = 0.56$**	$p = 0.18$ $R = 0.20$	$p = 0.09$ $R = 0.25$	$p = 0.38$ $R = 0.13$
LIPV	–	–	$p = 0.43$ $R = 0.12$	$p = 0.09$ $R = 0.25$	$p = 0.20$ $R = 0.19$
RSPV	–	–	–	**$p = 0.009$ $R = 0.38$**	**$p < 0.0001$ $R = 0.64$**
RIPV	–	–	–	–	**$p = 0.003$ $R = 0.43$**
SVC	–	–	–	–	–

The numbers in the parentheses indicate sleeve length (mm) of each vein

LIPV left inferior pulmonary vein, *LSPV* left superior PV, *RIPV* right inferior PV, *RSPV* right superior PV, *SVC* superior vena cava

Discussion

PVs and SVC

The sleeve length of the LSPV was related to the BSA, whereas right-sided PVs appeared to be independent from physiological factors and were structurally related to the SVC instead. A previous study recently reported an electrophysiological relation between the RSPV and SVC [3]. Arrhythmogenic RSPVs were more prevalent in patients with an arrhythmogenic SVC during catheter ablation than in those without, whereas these prevalences in the other three PVs were not associated with the arrhythmogenicity of the SVC [3]. Although the mechanisms for the both the electrical and structural relation between the RSPV and SVC are not clear, one possible contributing factor is epicardial adipose tissue (EAT) around the heart. EAT is known to promote substrate maintaining AF through the release of inflammatory cytokines and adipokines into adjacent myocardium. A previous study showed that the presence of adjacent EAT was associated with reduced bipolar voltage, electrogram fractionation, and widening of electrograms [10]. Interestingly, EAT was unevenly distributed around the LA [11, 12]. Predominant distribution was observed in the region surrounded by the SVC, RSPV, and right-sided roof of the LA (~29.8% of the total amount), in contrast to that around the LSPV (~8.3%) [12]. Calò et al. also showed that the superior part of the EAT containing the so-called posterior RA ganglionated plexus lies between the RSPV and SVC [13]. This may account for the lower impact of EAT on LSPV remodeling than on RSPV and SVC remodeling and for the preserved association of LSPV sleeve length with physiological factors such as the BSA.

Asymmetry is a distinct characteristic of the human heart. Since the systemic venous system including the SVC and the pulmonary venous system including the PVs develop independent of each other from the early fetal period, it may be difficult to account for the mechanisms behind the structural relation from an embryological point of view. However, a recent embryological study showed that the PV and SVC myocardium derives from the same cardiomyocyte progenitors of the cardiac inflow tract [14], implying a congenital or genetic relation between the veins.

Clinical relevance

The strong association of AF with aging, sex (male), and large body size was clearly revealed in previous cohort studies [15, 16]. The close association of the BSA and LSPV sleeve length in the present study, in part, may account for such characteristic distribution of patients with AF. Although we commonly consider an ectopic beat from the PVs as a critical trigger of AF, the role of PVs as substrate to perpetuate AF is also important [6]. If structural remodeling associated with EAT is dominantly present around the RSPV and SVC, performance of SVC isolation as recommended by several previous studies [1–3] may be further supported and may have the potential to improve clinical outcomes of catheter ablation.

Limitations

This study has several limitations. First, the study volume was small. However, we believe that the prospective design of this study was an advantage by allowing us to perform high-density mapping of the PVs and SVC. Second, the present study did not provide mechanistic insights into the development of AF although the results observed were novel. Also, a longitudinal analysis in each patient would be needed to validate the interpretation regarding structural remodeling of the PVs and SVC. Third, the sleeve length was determined based on the cutoff value of 0.2 mV in an indirect fashion. Different cutoff values might affect the

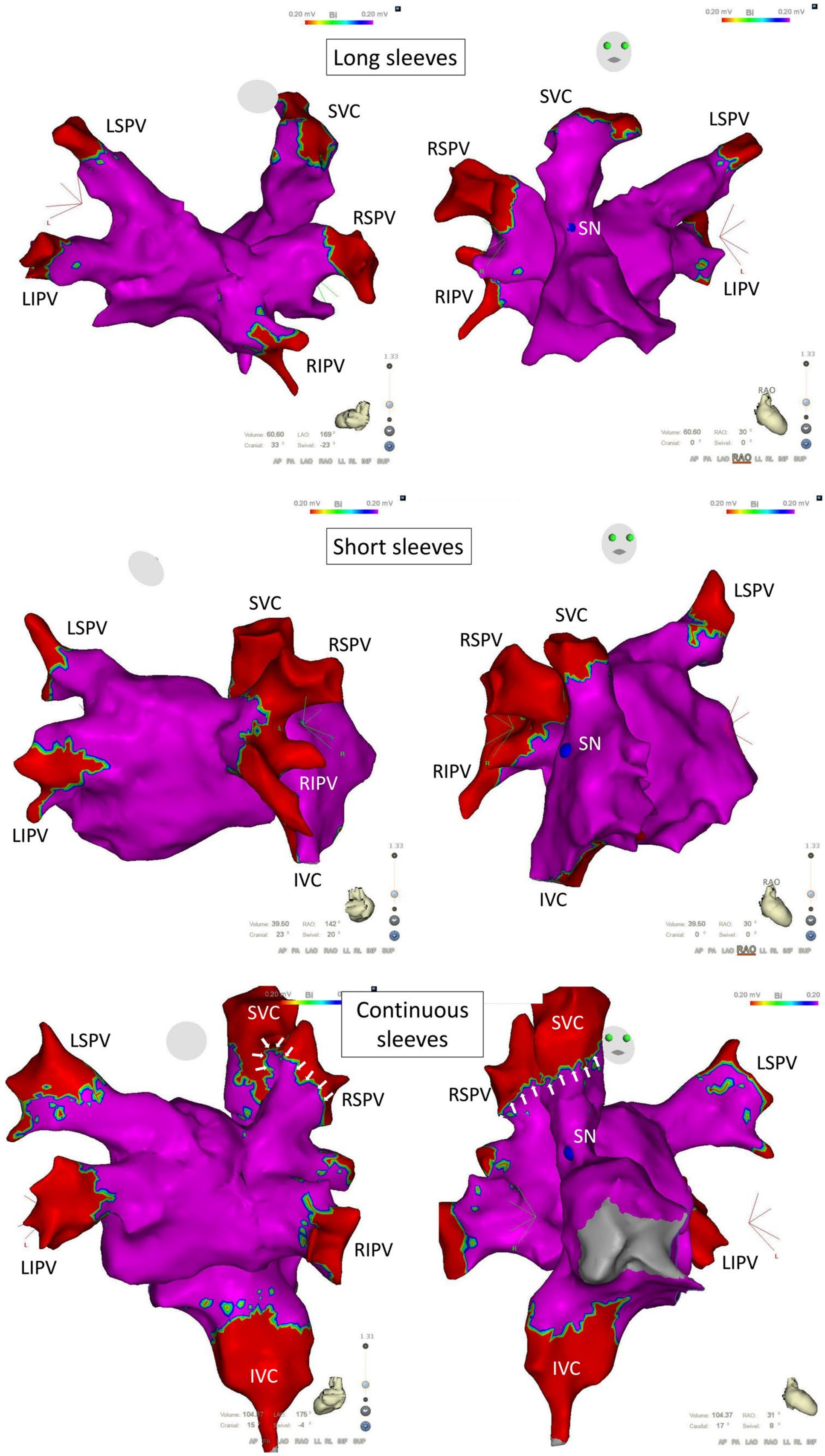

Fig. 2 Representative cases with long sleeves, short sleeves, and sleeves continuously distributed over the RSPV and SVC junction. In the three-dimensional voltage maps, the cutoff voltage was set as 0.2 mV. White arrows in the continuous sleeves case indicate the distal edges of the RSPV and SVC sleeves in which their continuity is clearly shown. *IVC* inferior vena cava, *LI* left inferior, *LS* left superior, *PV* pulmonary vein, *RI* right inferior, *RS* right superior, *SN* sinus node, *SVC* superior vena cava

Table 4 Relation of ostial diameter between the PVs and SVC

	LSPV (21 ± 3)	LIPV (18 ± 3)	RSPV (21 ± 4)	RIPV (17 ± 3)	SVC (21 ± 3)
LSPV	–	**$p = 0.04$ $R = 0.30$**	**$p = 0.006$ $R = 0.40$**	**$p = 0.04$ $R = 0.30$**	$p = 0.06$ $R = 0.27$
LIPV	–	–	$p = 0.65$ $R = 0.07$	$p = 0.18$ $R = 0.20$	$p = 0.71$ $R = 0.06$
RSPV	–	–	–	**$p = 0.01$ $R = 0.37$**	$p = 0.13$ $R = 0.23$
RIPV	–	–	–	–	$p = 0.72$ $R = 0.05$
SVC	–	–	–	–	–

The numbers in the parentheses indicate sleeve length (mm) of each vein

LIPV left inferior pulmonary vein, *LSPV* left superior PV, *RIPV* right inferior PV, *RSPV* right superior PV, *SVC* superior vena cava

Table 5 Relation of sleeve length and ostial diameter in each vein

	LSPV sleeve	LIPV sleeve	RSPV sleeve	RIPV sleeve	SVC sleeve
LSPV ostium	$p = 0.44$ $R = 0.12$	–	–	–	–
LIPV ostium	–	$P = 0.46$ $R = 0.11$	–	–	–
RSPV ostium	–	–	$P = 0.77$ $R = 0.04$	–	–
RIPV ostium	–	–	–	**$P = 0.04$ $R = 0.30$**	–
SVC ostium	–	–	–	–	$P = 0.51$ $R = 0.10$

LIPV left inferior pulmonary vein, *LSPV* left superior PV, *RIPV* right inferior PV, *RSPV* right superior PV, *SVC* superior vena cava

present results. However, more distal mapping of the PVs with a Pentaray catheter may risk venous injury and the inappropriate detection of farfield electrograms with their low voltage.

Conclusions

Not right- but left-sided PV sleeve was associated with the BSA of the patients, whereas a structural relation between the right-sided PVs and the SVC was implied based on sleeve mapping. Clinical relevance and therapeutic implications of this novel finding remain to be evaluated in future studies.

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Compliance with ethical standards

Conflict of interest Dr. Nogami has received honoraria from Abbott and an endowment from Medtronic and Johnson and Johnson. The other authors report no conflicts.

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