Importance of the relative epicardial connection locations and right-sided pulmonary vein isolation line for successful pulmonary vein isolation

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Abstract

Background: The presence of an epicardial connection (EC) decreases the success rate of pulmonary vein isolation (PVI); however, the effect of designing isolation lines has not been evaluated. **Objective:** We sought to clarify the effects of designing an anterior line for right-sided PVI considering the presence and location of the EC. **Methods:** Seventy-four consecutive patients who underwent initial catheter ablation for atrial fibrillation were retrospectively included in this study. The presence of the EC was determined by the left atrial (LA) activation map during right atrial pacing, and patients were divided into EC-positive (n=23, 31%) and EC-negative (n=51, 69%) groups. EC-positive patients were further subdivided based on the EC location: on-the-line group, (EC on the PVI line, n=11); inside-line group (EC on the pulmonary vein [PV] side, n=10); and outside-line group (EC on the LA side, n=2). The PVI parameters were compared among the three groups. **Results:** The success rates of the first-pass isolation were comparable between the EC-negative and EC-positive groups (70.6% vs. 60.9%, ns), but the success rate was significantly higher in the on-the-line group than in the inside-line group (91% vs. 20%, p=0.002). First-pass isolation was successful in both patients in the outside-line group. Additional carina ablation was required only in the inside-line group. **Conclusions:** The association between the EC site and the right-sided PV anterior isolation line affected the success rate of first-pass isolation. For successful right-sided PVI, it is important to consider the EC site when designing the PVI line.

Introduction

Circumferential pulmonary vein isolation (PVI) is an effective therapy for atrial fibrillation (AF). Recently, the impact of first-pass isolation has become the focus of research. The success of first-pass isolation has been reported to result in less AF recurrence and a lower rate of PV reconnection during the second procedure.[1-2] Advances in catheter technology and ablation strategies have reduced the residual gaps in isolation lines and increased the success rate of first-pass isolation.[3] Specifically, 3D mapping systems reduce interlesion gaps. Moreover, advances in contact-force sensing and irrigation catheters have reduced transmural gaps.

However, a wide antral approach has been shown to be more effective than ostial PVI for AF.[4] Yet, wide area first-pass isolation can be difficult and sometimes requires additional carina ablation, especially in right-sided PV.[5-6] The presence of epicardial connections (ECs) imposes additional difficulty in PVI.[5-10] Barrio-Lopez et al. reported an association between the presence of ECs and a lower success rate of PVI, leading to AF reccurence.[7]Thus, ECs may be one of the remaining therapeutic targets for successful first-pass isolation. However, these two studies did not evaluate the relative locations of the PVI line and ECs, and the effects of the positional relationship between the EC and right-sided PV anterior isolation line on the success rate of first-pass PVI remain unclear. The objective of this study was to examine the importance of designing an anterior line for right-sided PVI, considering the EC site.

Methods

Study patients

Consecutive patients who underwent initial radiofrequency catheter ablation for AF between February 2020 and October 2021, and who had a left atrial (LA) activation map obtained during right atrium (RA) pacing were enrolled. The study was approved by the Institutional Review Board of Kobe City Medical Center General Hospital, and an opt-out system was used to obtain patient consent for the use of their clinical data for research purposes. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Electrophysiological study and catheter ablation

The electrophysiological study (EPS) and ablation procedures were performed as previously described.[11] Catheter ablation was performed under conscious sedation using dexmedetomidine, thiopental, and fentanyl. A multipolar catheter with internal cardioversion (BeeAT, Japan-Life-Line, Tokyo, Japan) was placed in the coronary sinus through the internal jugular vein, and a deflectable multipolar catheter was placed in the right ventricle or RA through the right femoral vein. Transseptal puncture was performed with a radiofrequency needle (Baylis Medical, Montreal, QC, Canada) under intracardiac echocardiography guidance, and two sheaths were introduced into the LA. A deflectable sheath (Agilis, Abbott, St. Paul, MN, USA, or Vizigo, Biosense Webster Inc., Irvine, CA, USA) and a long sheath (Swartz SL0 introducer, Abbott) were inserted into the LA. If AF persisted, defibrillation was performed. During RA pacing (from the high or lateral RA), a high-resolution LA activation map was created using a mapping catheter (Pentaray, Biosense Webster). Points were acquired using the CARTO ConfiDENSE module (Biosense Webster). The preprocedural computed tomography image of the LA was integrated with a 3D electroanatomical map. After LA activation mapping was created, bilateral extensive PVI was performed using a contact force-sensing radiofrequency catheter (TermoCool SmartTouch SF, Biosense Webster) with a high-power short-duration (50 w) protocol. The contact force was controlled at 10–20 g, and the application time was titrated using the lesion formation index (Ablation Index (AI), Biosense Webster). The ablation lesions were tagged in a contiguous fashion within a 6-mm interval (VISITAG, 6-mm diameter setting). The AI was targeted to 500–550 except for 400 along esophageal lesions on the posterior wall with the limitation of maintaining an esophageal temperature of <41 °C. The PVI lines were designed by operators without considering the ECs site. To confirm the completion of PVI, the bidirectional block of paced or self-activated PV electrograms was assessed using a 10 or 20 multipolar circular catheter after ablation of all PVs. If PVI could not be achieved using the originally designed isolation line, the earliest activation sites inside the isolation line were ablated. If acute PV reconnections were observed during the waiting period, the earliest activation sites inside the isolation line were ablated.

Definitions and grouping

After the procedures, the presence of an EC was verified based on a centrifugal conduction pattern near the right-sided PV, which was differed from the early activation site of Bachman bundle. We confirmed the electrical conduction pattern using Ripple mapping and Coherent mapping. The EC site was determined on the basis of the earliest activation points.

The patients were divided into two groups according to the presence or absence of an EC (EC-positive and EC-negative groups). Patients in the EC-positive group were further subdivided into three groups according to the relative locations of the EC site and the originally designed isolation line: on-the-line group (EC site on the isolation line); inside-line group (EC on the PV side of the isolation line); and outside-line group (EC on the LA side of the isolation line) (Figure 1).

Follow-up

Scheduled follow-up visits, including a physical examination, 12-lead electrocardiogram (ECG), and blood examinations, were performed at 1, 3, 6, 9, 12, and 24 months after ablation. Daily pulse self-checks or ambulatory ECG monitoring was mandatory, and an extra-visit ECG was required in the case of abnormal pulse detection. In addition, 24-h Holter recordings were performed at 6, 12, and 24 months after the procedure. AF recurrence was defined as any documented episode of AF lasting at least 30 seconds.

Statistical analysis

Continuous variables were analyzed using the t-test and are presented as means and standard deviations. Fisher's exact test was used to compare categorical variables. Time-to-event analysis was performed using Kaplan–Meier curves, and the log-rank test was used to compare the differences between the groups. For all analyses, p values were two-sided, and statistical significance was set at $p < 0.05$. JMP version 13 (SAS Institute Inc., Cary, NC, USA) was used for all the statistical analyses.

Results:

Patient background characteristics

A total of 74 patients were matched and enrolled in this study. An EC between the right-sided PV and RA was observed in 23 patients (31%, EC-positive group) but not in the remaining 51 patients (69%, EC-negative group) (Figure 2). There were no differences in patient characteristics between the groups, except the EC-positive group had a smaller LA diameter, lower CHADS2 score, and smaller body mass index than that in the EC-negative group (Table 1).

Relative locations of ECs and isolation lines and their association with first-pass isolation success rate

The success rate of first-pass isolation was similar between the EC-negative and EC-positive groups (36/51, 70.6% vs. 14/23, 60.9%; ns) (Table 2).

In the EC-positive group, patients were also divided into three groups according to the relative location of the EC site and the originally designed isolation line (on-the-line group, 11 patients; inside-line group, 10 patients; outside-line group, 2 patients). The ECs were located on the anterior to the carina segment of the right-sided PV (10 patients in the on-the-line group and 9 patients in the inside-line group) and anterior segment of the right inferior PV (1 patient in the on-the-line group, 1 patient in the inside-line group, and 2 patients in the outside-line group). The distance from the EC site to the center of the carina segment was not significantly different among the three groups (Table 3). The success rate of first-pass isolation in the on-the-line group was significantly higher than that in the inside-line group (10/11, 91% vs. 2/10, 20%; p=0.0019) (Figure3).

Additional ablation for first PVI and acute reconnection

In total, 15/51 (29.4%) and 9/23 (39.1%) of the patients in the EC-negative and EC-positive groups, respectively, failed first-pass isolation. Of these patients, the most common success site of PVI was the anterior carina, observed in 7/15(46.7%) of the patients in the EC-negative group and in 7/9 (77.8%) of the patients in the EC-positive group. In the EC-positive group, the concordance rate between success and EC sites was higher in the inside-line group than that in the online group (7/8, 88% vs. 0/1, 0%; p=0.0472).

There were no significant differences in the rate of acute reconnection during the procedure between the groups. The acute reconnection sites were widely distributed, including an EC site in the inside-line group. Despite achieving first-pass isolation in the inside-line group, one of the two patients required additional ablation at the EC site because of acute reconnection.

The need for additional carina ablation for the first PVI and acute reconnection was not significantly different between the EC-negative and EC-positive groups (9/51,17.7% vs. 8/23, 34.8%; p=0.1377). However, among the patients in EC-positive group, additional carina ablation was required significantly more frequently in the inside-line group than in the online or outside-line groups (8/10, 80% vs. 0/11, 0% vs. 0/2, 0%; p<0.001).

Finally, all the right-sided PVs were successfully isolated. No major complications, such as cardiac tamponade or stroke, occurred.

Clinical outcome

Six patients (3 in the EC-negative group and 3 in the EC-positive group) had AF recurrence after the blanking period, and one patient underwent a repeat procedure due to AF recurrence. The patients who underwent repeat procedures were in the on-the-line group and had no PV reconnection. The rate of freedom from AF recurrence was similar between the two groups during the follow-up period of 312.5±137 days (94.1% in the EC-negative group vs. 87.0% in the EC-positive group, p=0.2582).

Discussion

Main findings

This is the first study to show the significance of the positional relationship between the EC site and right-sided anterior PVI line in successful PVI. We report the following findings: (1) In high-density LA mapping before ablation, an EC between the right-sided PV and RA was observed in 23/74 patients (31%); (2) In the on-the-line and outside-line groups, the success rate of first-pass isolation was high (91% and 100%, respectively), while it was low in the inside-line group (20%); and (3) Even in the presence of an EC, PVI could be successfully achieved without additional carina ablation by intentionally setting isolation lines.

Prevalence of the EC

Previous studies have reported an inconsistent prevalence of an EC between right-sided PV and the RA in patients undergoing PVI: 18% by Yoshida et al. and 51% by Hanaki et al.[6,12] The prevalence of an EC in the current study fell between that of those studies of Japanese patients, at 31%. In contrast, Barrio-Lopez et al. reported a much lower prevalence (6.8%).[7] This may be due to differences in races and the method of ECs verification. They confirmed the presence of ECs after PV antrum ablation, which might have led to underestimation because of the elimination of ECs. Contrary to their study, three other studies, including the current study, evaluated ECs before PV antrum ablation using the LA activation map.

As for the LA activation map, the mean number of LA mapping points in the current study was much larger than that in the reports by Yoshida and Hanaki (2532 vs. 679 vs. 1479, respectively). Further, those other reports did not mention specific methods for visualizing the activation pattern of LA in detail. We confirmed the existence of the EC before ablation with Ripple mapping and Coherent mapping, which are useful for atrial tachycardia and other reentrant tachycardia ablations as well as for detecting the presence of ECs by visualizing activation patterns.

In accordance with previous reports, most EC sites were located anterior to the carina segment of the right-sided PV. However, we must recognize that the EC is composed of multiple myofibers.[9] The EC site was defined as the earliest activation site near the right-sided PV except for Bachman bundle. However, the "EC site" in our study was only the earliest conduction site on the PV side of the myofibers. In previous anatomical studies, the muscle fibers were also widely attached elsewhere in the craniocaudal direction and transverse to the epicardial fat of the interatrial groove.[9] In Figure4A, we depict the figure of epicardial fiber connected between the RA and LA speculated in a previous study. The attachment of epicardial fibers in the LA might be a variable location that would influence PVI success.

Association of ECs and the location with PVI success

The presence of an EC did not influence the success rate of first-pass isolation (36/51, 70.6% in the EC-negative group vs. 14/23, 60.9% in the EC-positive group, p=0.4321). However, in patients with an EC, the relative locations of the EC site and the anterior isolation line of the right-sided PV affected the success rate of first-pass isolation. The relationship between the PVI line and the presence of ECs has not yet been fully elucidated. Our results suggest that the PVI line should be designed on the EC site (on-the-line) or closer to the PV than the EC site (outside-line) for successful first-pass isolation in patients with ECs.

As shown in Figure4B, the distance from the endocardium to the EC varied according to the relative location between the EC attachment site and ablation line. Therefore, the distance from the endocardium to the EC may affect the success rate of first-pass isolation in patients with an EC. Because the EC gets closer to the endocardium toward the right-sided PV attachment site, it could be eliminated in the on-the-line group. However, a longer distance from the endocardium to the EC might result in failure to eliminate the EC. A longer distance might also cause incomplete elimination and hinder the long-term success of PVI if the procedure shows an acute effect. Hasebe et al. reported a similar case of temporal elimination of an EC by ablation right-sided PVI.[13] If the PVI line was designed on the EC lesion, the EC could have been eliminated, as was the case in our on-the-line group. Previous reports have concluded that an EC cannot be eliminated by circumferential ablation.[5,6,12,13] However, the results of the current study suggest that an EC can be eliminated by intentionally designing an isolation line. Advances in mapping systems have contributed to the precise detection and localization of ECs.

In this study, the distances from the EC site to the center of the carina segment were not significantly different among the three groups (on-the-line, inside-line, and outside-line), which suggests that the PVI line can be designed on the EC site in many cases. However, in cases where the EC site is very close to the carina, designing a PVI line on the EC lesion is difficult, and the isolation area becomes too small. In such cases, a strategy for designing a PVI line regardless of the EC lesion and adding carina ablation may be considered.

In addition, in this study, we did not verify the earliest activation site of the RA by PV or LA pacing and performed ablation from the RA side. Barrio-Lopez et al. reported an insufficient success rate of ablating the EC from the RA.[7]

Limitations

First, because this was a retrospective observational study with a relatively small number of patients, biases common to non-randomized studies could not be eliminated. Second, we excluded patients who could not return or maintain sinus rhythm before PVI. Therefore, the prevalence of an EC in the total AF ablation cohort remains unknown. In addition, we confirmed the presence of an EC during RA pacing by Ripple mapping and Coherent mapping. If we had changed the pacing site in each case, we might have detected more or lesser ECs. In the EC-negative group, eight patients required additional carina ablation. In these cases, an EC might have been overlooked. This may partly explain the low success rate of first-pass isolation in the EC-negative group. Third, the duration of follow-up was relatively short, and there were only two cases in which the second procedure was performed. We could not evaluate long-term outcomes and PVI durability in this study.

Conclusions

A considerable percentage of patients undergoing PVI have an EC between the right-sided PV and RA. In patients with an EC, designing a right-sided PVI anterior line considering the presence and location of the EC lesion may achieve a higher success rate of first-pass isolation without additional carina ablation.

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Figure legends

Figure 1. Determination and relative location of the EC site and the ablation line

Coherent mapping of three EC-positive groups: On-the-line group, the EC located on PVI line; Inside-line group, the EC located on PV side; Outside-line group, the EC located on LA side. Star symbol with dashed line shows the earliest activation point in the EC site. Bachman bundle was shown in earlier activation site in the anterior wall of LA (square symbol). EC, epicardial connection; LA, left atrium; PV, pulmonary vein

Figure 2. Grouping of patients

Patients were divided into two groups according to the presence or absence of the EC (EC-positive group and EC-negative group). Patients in the EC-positive group were further divided into two groups according to the relative location of the EC. EC, epicardial connection; PV, pulmonary vein; RA, right atrium.

Figure 3. First-pass isolation

In EC-positive group, the success rate of first-pass isolation in the On-the-line group was significantly higher than that in the inside-line group (10/11, 91% vs. 2/10, 20%; p=0.0019).

Figure 4. Speculative schema of association of epicardial connection and ablation site

A. The green line indicates the EC between right-sided PV and RA. The EC transverses the epicardial fat of the interatrial groove.

B. a.) Since the ablation lesion is close to the attachment site, the EC can be eliminated. b.) Since the EC runs farther from the endocardium, the ablation lesion cannot sufficiently reach the EC. c.) Since the EC site is on the LA side of the isolation line, it does not affect the pulmonary vein isolation.

LA, left atrium; EC, epicardial connection; PV, pulmonary vein; RA, right atrium

Table 1. Patients characteristics

Variable	EC-negative group (n=51)	EC-positive group (n=23)	P value
Age (y)	70.7 ± 9.6	66.1 ± 10.5	0.0715
Sex: male	31 (60.8)	16 (69.6)	0.6036
BMI	24.5 ± 4.0	22.2 ± 2.6	0.0162
AF type: PAF	28 (54.9)	15 (65.2)	0.4544
LVEF (%)	60.5 ± 7.0	58.7 ± 10.5	0.7959
LAD (mm)	41.3 ± 8.4	36.2 ± 7.8	0.0163
LAVI (mL/m^2)	48.5 ± 15.1	41.4 ± 16.5	0.0737
Hypertension	32 (62.8)	9 (39.1)	0.0783
Diabetes mellitus	6 (11.8)	2 (8.7)	1
Stroke	6 (11.8)	0 (0)	0.168
Heart failure	9 (17.7)	4 (19.4)	1
Valvular disease	5 (9.8)	0 (0)	0.3161
CHADS2 SCORE	1.5 ± 1.1	0.83 ± 0.8	0.009
HAS-BLED SCORE	1.6 ± 0.9	1.3 ± 0.9	0.31
Sleep Apnea Syndrome	1 (2.0)	1 (4.4)	0.528
Hemodialysis	1 (2.0)	1 (4.3)	0.528

Values are presented as mean ± SD and as n (%). AF, atrial fibrillation; BMI, body mass index; CHADS2, congestive heart failure, hypertension, age, diabetes mellitus, stroke; EC, epicardial connection; HAS-BLED, hypertension, abnormal renal/liver function, bleeding, labile international normalized ratio; elderly, drugs/alcohol; LAD, left anterior descending; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; PAF, paroxysmal AF

Table 2. Ablation data

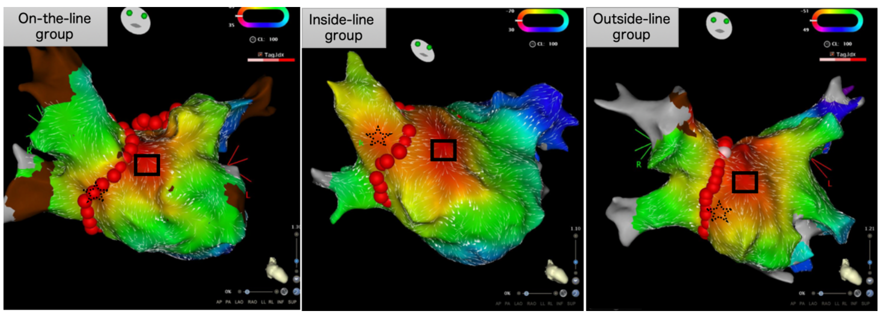
Variable	EC-negative group (n=51)	EC-positive group (n=23)	P value
First-pass-isolation	36 (70.6)	14 (60.9)	0.4321
First isolation time (min)	26.0 ± 14.7	20.9 ± 9.3	0.1311
Total number of energy applications	32.2 ± 9.2	33.2 ± 9.2	0.6455
Total duration of energy applications (sec)	648.2 ± 187.1	660.0 ± 191.0	0.8045
PV reconnection	9 (17.7)	6 (26.0)	0.5331
Additional carina ablation	9 (17.7)	8 (34.8)	0.1377
Posterior wall isolation	27 (52.9)	13 (56.5)	0.8062
Number of mapping points	2693 ± 782.7	2173 ± 737.7	0.0087
Pacing rate cycle length	608 ± 39.8	628 ± 61.4	0.0904
Bachman breakthrough	51 (100)	22 (95.7)	0.3108

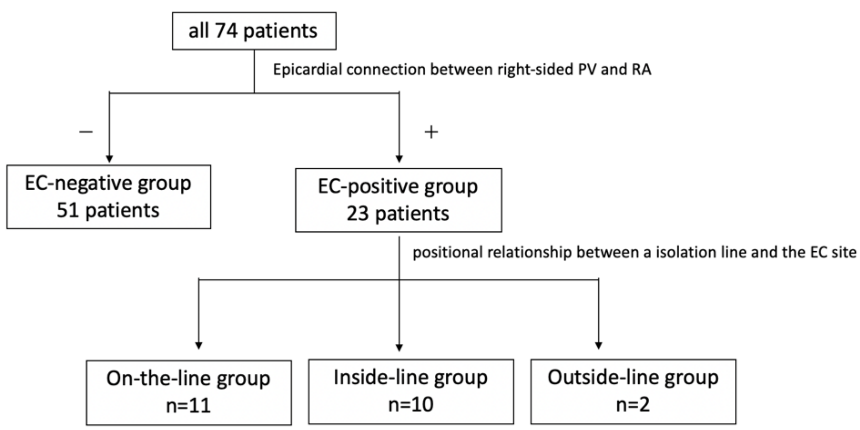
Values are presented as mean ± SD and as n (%). EC, epicardial connection; PV, pulmonary vein

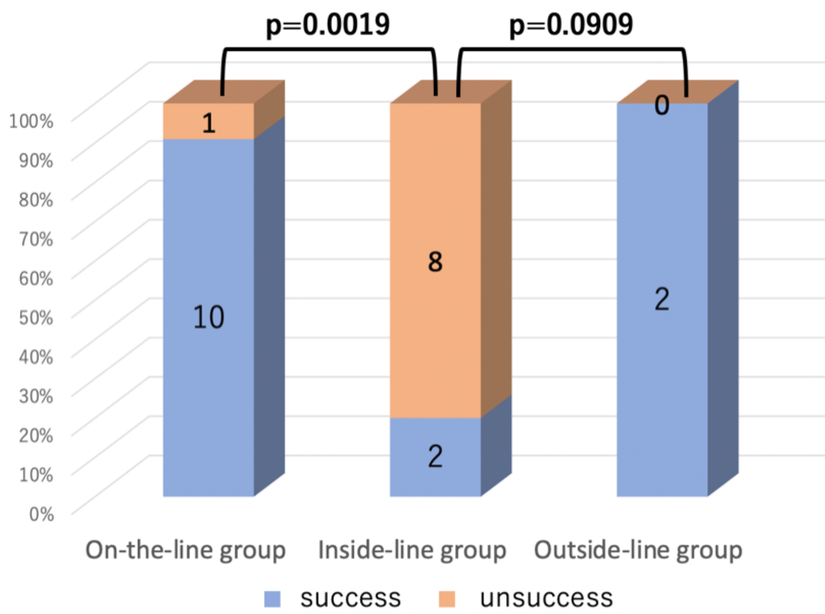
Table 3. Ablation data

Variable	On-the-line group (n=11)	Inside-line-group (n=10)	Outside-l
First-pass-isolation	10(90.9)	2(20.0)	2(100)
First isolation time (min)	17.5 ± 8.5	24.9 ± 9.9	19.5 ± 4.
Total number of energy applications	32.7 ± 11.0	34.5 ± 8.2	29.5 ± 3.
Total duration of energy applications (sec)	643.9 ± 231.4	691.8 ±163.3	589.5 ±
PV reconnection	3 (27.3)	3 (30)	0 (0)
Posterior wall isolation	6 (54.6)	3 (30)	1 (50)
Additional carina ablation	0 (0)	8 (80)	0 (0)
Number of mapping points	2434.5 ± 761.8	1857.2 ± 675.2	2314.5 ±
Pacing rate cycle length	600 ± 0	659 ± 83.2	635 ± 49
Bachman breakthrough	11 (100)	10 (100)	1 (50)
Distance from an EC site to anterior isolation line (mm)	0.8 ± 1.2	11.2 ± 3.6	7.1 ± 0.7
Distance from an EC site to carina (mm)	21.0 ± 7.2	14.9 ± 6.9	25.3 ± 3.

Values are presented as mean ± SD and as n (%). PV, pulmonary vein



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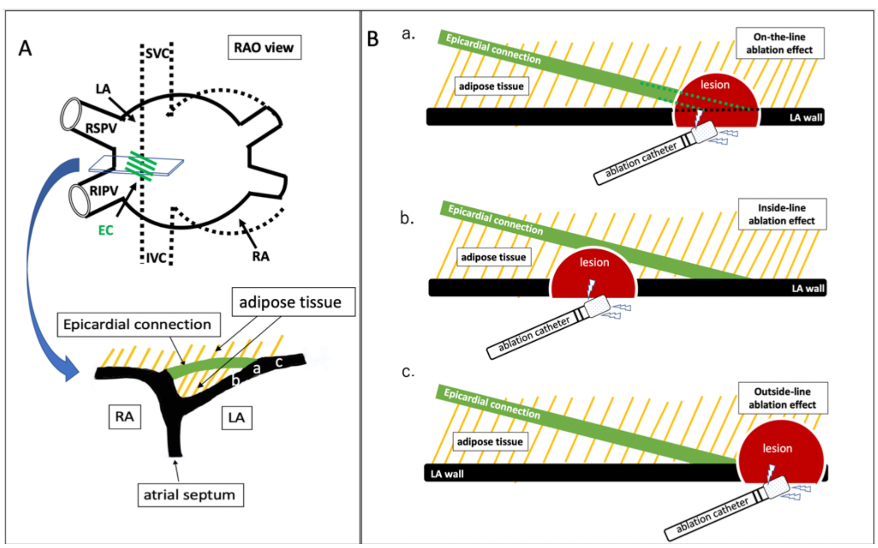
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