Predictors of Non-Pulmonary Vein Ectopic Beats Initiating Paroxysmal Atrial Fibrillation — Implication for Catheter Ablation

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Non-pulmonary vein (PV) ectopic beats have been proven to initiate paroxysmal atrial fibrillation (PAF) in some patients, and the presence of non-PV ectopic beats might play an important role in the recurrence of PAF after PV isolation. This review article discusses the differential diagnosis, ablation strategy, anatomical substrate and clinical predictors in patients with non-PV ectopic beats initiating AF. In general, P wave morphology of surface ECG and intracardiac recordings are important in making an accurate diagnosis of non-PV AF. In clinical practice, left atrial enlargement could predict the presence of left atrial posterior free wall (LAPFW) ectopic beats initiating PAF; increased automaticity and increased trigger activity from the LAPFW might occur in patients with left atrial enlargement. Furthermore, female gender could predict the presence of superior vena cava (SVC) ectopic beats initiating AF; the gender difference in the incidence of SVC ectopic beats initiating PAF might be explained by the gender difference in female hormones and/or autonomic activities. Further studies are needed to define the exact effects of female hormones and autonomic tone on the SVC ectopic beats initiating PAF.

Key Words: Atrial fibrillation • Pulmonary vein • Superior vena cava • Catheter ablation

INTRODUCTION

Several studies have demonstrated that pulmonary veins (PVs) are the major site of ectopic beats initiating paroxysmal atrial fibrillation (PAF), and isolation of the PVs from the atrial tissue can cure 65% to 85% of patients with PAF.¹,² Non-PV ectopic beats have been proven to initiate PAF in some patients, and the presence of non-PV ectopic beats might play an important role in the recurrence of PAF after PV isolation.³,⁴ (Figure 1).

Diagnosis of Non-PV Ectopic Beats Initiating PAF

Mapping of the PVs is guided by selective PV an-
giography or the venous phase of selective pulmonary artery angiography, with the first pair of electrodes straddling the ostium. The catheters are first put into the superior PVs and then the inferior PVs if the ectopic focus was suspected to be from the inferior PVs. We use two multipolar catheters to perform simultaneous mapping of the PVs and left atrial posterior free wall (LAPFW), if necessary. If the initiating focus of PAF is considered to be from the right atrium, we put one duodecapolar catheter (1-mm electrode width and 2-mm interelectrode spacing) along the crista terminalis (CT) to reach the top of the superior vena cava (SVC) for simultaneous mapping of the PVs, SVC and right atrial free wall. In clinical practice, it is useful to use the P wave morphology of surface ECG and intracardiac recordings to make an accurate diagnosis of non-PV ectopic beats initiating AF. The differential diagnosis between SVC ectopic beats initiating AF and right superior pulmonary vein (RSPV) ectopic beats initiating AF is important because the SVC and RSPV are very close. First, the time interval between high right atrial and His-bundle atrial activation obtained during the sinus beats and atrial premature beats can differentiate SVC and PV ectopic beats initiating PAF. In SVC ectopic beats, the time interval between high right atrial and His-bundle atrial activation is longer in the atrial premature beats than that of the sinus beats. On the contrary, in PV ectopic beats, the time interval between high right atrial and His-bundle atrial activation is longer in the sinus beats than that of the atrial premature beats. Kuo et al. also showed that P waves polarities were negative in 47%, positive in 47% and isoelectric in 6% of SVC ectopic beats but positive in all the RSPV ectopies (Figure 2). Thus, a biphasic or isoelectric P wave polarity in lead V1 favors SVC ectopy rather than RSPV ectopy.

Figure 2. Twelve-lead ECG shows one major pattern of P wave polarities in paroxysmal atrial fibrillation (PAF) from the superior vena cava (SVC). A: An arrowhead indicates P wave polarities of the premature atrial beat. B: Intracardiac tracing of panel A. Long arrow indicates the atrial activation sequence of the ectopic beat that initiated PAF from the SVC. DCS = distal coronary sinus; HIS = His-bundle recording; MCS = middle coronary sinus; PCS = coronary sinus ostium; RSPV-D = distal right superior pulmonary vein; RSPV-P = proximal RSPV; SVC-D = distal SVC; SVC-P = proximal SVC. (reproduced with permission from reference 9)
Catheter Ablation of Non-PV Ectopic Beats Initiating PAF

For the ectopy from the LAPFW and CT, a unipolar QS pattern indicates the presumed ablation site. Furthermore, if the ectopic beat is located at the LAPFW nearby the PV ostium, we usually extend the ablation lesion from the ostium to encircle part to the posterior wall with a square-shaped (around 1.5 to 2.0 cm on each side) linear lesion to ablate or isolate the ectopy.3,10 In patients with ectopy from the SVC, the atriocaval junction is confirmed by an SVC venogram, intracardiac ultrasound and the electrical signals. SVC isolation is performed at a level about 5 mm below the atriocaval junction.3,5,10 The SVC-right atrial junction exhibits an eccentric shape, not a round shape, thus the ablation catheter may not contact the wall well. Application of radiofrequency (RF) energy at the level of SVC more easily interrupts the right atrium-SVC myocardial sleeve, however, it may result in a higher risk of SVC narrowing or stenosis.7,10 For cases with a high risk of sinus node injury (acceleration of the sinus rate during SVC isolation), we use 3-dimensional non-contact mapping to identify the origin and exit sites of the sinus node activation, and to avoid the application of any energy around that area.

SVC Substrate for PAF

In general, the PVs have myocardial sleeve extension from the left atrium. The SVC also has myocardial sleeve extension from the right atrium. Therefore, the myocardial sleeves in the SVC may be the arrhythmogenic origin of atrial fibrillation. Laza et al. showed that the mean length of SVC myocardial sleeve extension in human hearts was more than 16 mm.11 Huang et al. performed an MRA study of the SVC morphology.12 We found that patients with SVC ectopic beats initiating AF had a more eccentric morphology at the middle portion of the SVC compared with those without AF. Furthermore, all the ectopic beats initiating PAF came from the middle portion of the SVC. Thus, the eccentricity of the SVC might play an important role in arrhythmogenesis.

Predictors of Non-PV PAF

Non-PV ectopic beats may play an important role in the initiation of PAF. However, whether there are predictors of non-PV ectopic beats initiating PAF was unknown. Awareness of this information may be useful in planning the ablation strategy. Therefore, we performed a study to investigate the predictors of non-PV ectopic beats initiating PAF.10

This study included 293 patients (215 men) with a mean age of sixty years. The analyzed variables included sex, age (≥ 65 or < 65 years), prior history of documented PAF (≥ 5 or < 5 years), presence of other cardiovascular disease (e.g., hypertensive cardiovascular disease, coronary artery disease, congestive heart failure, hypertrophic cardiomyopathy, valvular heart disease), the presence of related arrhythmias (e.g., atrial flutter, atrial tachycardia, atrioventricular nodal reentrant tachycardia, right atrial enlargement, left atrial enlargement), and concurrent drug usage (e.g., beta-receptor blocker, calcium channel blocker, digitalis, angiotensin-converting enzyme inhibitor).

In our study, 68% of patients had pure PV, 20% of patients had both PV and non-PV and 12% of the patients had pure non-PV ectopic beats initiating PAF. Among the 94 patients with non-PV ectopic beats, 40% of patients had SVC and 34% of the patients had LAPFW ectopic beats initiating PAF.

In a univariate analysis, only female gender was related to the presence of non-PV (p = 0.016) and SVC ectopic beats (p = 0.012) (Figure 3). Right atrial enlargement (p = 0.005) and left atrial enlargement (p < 0.001) were related to the presence of LAPFW ectopic beats (Figure 4). In a multivariate analysis, female gender (p = 0.043; odds ratio 2.00, 95% CI 1.02 to 3.92) and left atrial enlargement (p = 0.007; odds ratio 2.34, 95% CI 1.27 to 4.32) could predict the presence of non-PV ectopic beats. Subgroup analysis showed that female gender could predict the presence of SVC ectopic beats (p = 0.039; odds ratio 2.14, 95% CI 1.04 to 4.43); in contrast, left atrial enlargement could predict the presence of LAPFW ectopic beats (p = 0.002, odds ratio 3.89; 95% CI 1.62 to 9.38).

More Questions about Non-PV PAF

A question is how to explain female gender as a predictor of SVC ectopic beats initiating PAF. Some studies have consistently shown that men had higher sympathetic activity and women had higher parasympathetic activity.13-14 Schauerte et al. also showed that high-frequency stimulation of cardiac autonomic nerves in the vicinity of the canine SVC could induce SVC ectopy ini-
Figure 3. This figure shows that 45% of the patients with superior vena cava (SVC) ectopic beats and 24% of those without SVC ectopic beats initiating paroxysmal atrial fibrillation (PAF) were female. Thus, in univariate analysis, female gender was related to the presence of SVC ($p = 0.012$) and non-pulmonary vein (PV) ectopic ($p = 0.016$) beats initiating PAF. In multivariate analysis, female gender could predict the presence of SVC and non-PV ectopic beats initiating PAF. LAPFW = left atrial posterior free wall. (data from reference 10)

Figure 4. This figure shows that 72% of the patients with left atrial posterior free wall (LAPFW) ectopic beats and 35% of those without LAPFW ectopic beats initiating paroxysmal atrial fibrillation (PAF) had left atrial enlargement. Thus, in univariate analysis, left atrial enlargement was related to the presence of LAPFW ectopic beats initiating PAF ($P < 0.001$). In multivariate analysis, left atrial enlargement could predict the presence of LAPFW and non-pulmonary vein (PV) ectopic beats initiating PAF. SVC = superior vena cava. (data from reference 10)
tiating PAF, and that this phenomenon could be abolished by atropine.\textsuperscript{15} Tai et al. also demonstrated that an increase in vagal tone induced by phenylephrine was effective in suppressing focal PAF originating from the PVs but not the SVC.\textsuperscript{16} These findings suggested that women with higher parasympathetic activity might be associated with a higher incidence of SVC ectopic beats initiating AF. Furthermore, female hormones might play a role in the higher incidence of SVC ectopic beats in women. However, the effects of female hormones on automaticity were not reported.

And why was left atrial enlargement a predictor of LAPFW ectopic beats initiating PAF? Increased automaticity and increased trigger activity might occur in diseased atrial fibers.\textsuperscript{17-18} Thus, it is possible that LAPFW could be the site of spontaneous ectopy in patients with left atrial enlargement. Furthermore, based on the theory of multiple reentrant wavelets, AF could be more easily induced and maintained in larger atrial size.\textsuperscript{19}

**CONCLUSION**

Female gender can predict the presence of SVC ectopic beats. Thus, provoking SVC ectopic beats initiating AF during the electrophysiological study is important in women. Furthermore, left atrial enlargement can predict the presence of LAPFW ectopic beats initiating PAF. Thus, left atrial substrate ablation might be considered in those patients with left atrial enlargement if the LAPFW ectopic beats are difficult to map.

**REFERENCES**


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非肺靜脈異位發電所引發陣發性心房顫動的預測因子
— 導管灼燒術的應用

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非肺靜脈的異位發電已證實會在某些病人引發陣發性心房顫動，而且非肺靜脈的異位發電在陣發性心房顫動病人接受肺靜脈隔絕電燒術後復發心房顫動扮演重要的角色。這篇回顧文章討論非肺靜脈電位發電所引發心房顫動病人的鑑別診斷，電燒策略，解剖基礎和臨床預測因子。通常要正確診斷非肺靜脈心房顫動，體表心電圖的 P 波和心內電氣紀錄是很重要的，在臨床工作時，左心房擴大可以預測左心房後壁異位發電所引發的陣發性心房顫動，在左心房擴大的病人左心房後壁自動去極化可能有增加的情形，女性性別可以預測上腔靜脈的異位發電，上腔靜脈異位發電引發陣發性心房顫動發生率的性別差異可能是由於男性和女性有不同的心房編動和自主神經功能，未來的研究應探討女性荷爾蒙和自主神經在上腔靜脈異位發電所扮演的角色。

關鍵詞：心房顫動、肺靜脈、上腔靜脈、導管電燒。