Impact of the origin of sinus node artery on recurrence after pulmonary vein isolation in patients with paroxysmal atrial fibrillation

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Keywords: atrial fibrillation; catheter ablation; coronary angiography; recurrence; sinus node artery

Background Major atrial coronary arteries, including the sinus node artery (SNA), were commonly found in the areas involved in atrial fibrillation (AF) ablation and could cause difficulties in achieving linear block at the left atrial (LA) roof. The SNA is a major atrial coronary artery of the atrial coronary circulation. This study aimed to determine impact of the origin of SNA on recurrence of AF after pulmonary vein isolation (PVI) in patients with paroxysmal AF.

Methods Seventy-eight patients underwent coronary angiography for suspected coronary heart disease, followed by catheter ablation for paroxysmal AF. According to the origin of SNA from angiographic findings, they were divided into right SNA group (SNA originating from the right coronary artery) and left SNA group (SNA originating from the left circumflex artery). Guided by an electroanatomic mapping system, circumferential pulmonary vein ablation (CPVA) was performed in both groups and PVI was the procedural endpoint. All patients were followed up at 1, 3, 6, 9 and 12 months post-ablation. Recurrence was defined as any episode of atrial tachyarrhythmias (ATAs), including AF, atrial flutter or atrial tachycardia, that lasted longer than 30 seconds after a blanking period of 3 months.

Results The SNA originated from the right coronary artery in 34 patients (43.6%) and the left circumflex artery in 44 patients (56.4%). Freedom from AF and antiarrhythmic drugs (AADs) at 1 year was 67.9% (53/78) for all patients. After 1 year follow-up, 79.4% (27/34) in right SNA group and 59.1% (26/44) in left SNA group ($P=0.042$) were in sinus rhythm.

On multivariate analysis, left atrium size ($HR=1.451, 95\% CI: 1.240–1.697, P<0.001$) and a left SNA ($HR=6.22, 95\% CI: 2.01–19.25, P=0.002$) were the independent predictors of AF recurrence.

Conclusions The left SNA is more frequent in the patients with paroxysmal AF. After one year follow-up, the presence of a left SNA was identified as an independent predictor of AF recurrence after CPVA in paroxysmal AF.

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice and a major risk factor for ischemic stroke.1,2 Pulmonary vein isolation (PVI) has become the mainstream catheter ablation of AF, demonstrating high procedural success rates of 70%–80% in paroxysmal AF for the first time during a 6 to 20 months follow-up period.3,5 However, approximately half of these patients will have to undergo a second procedure to achieve this, usually as a result of pulmonary vein (PV) reconnection.6-8

Previous studies have described the role of atrial coronary perfusion in AF initiation and maintenance.9,10 Atrial ischemia could create a substrate for AF by causing fibrosis and scarring of the atrial wall.11 Major atrial coronary arteries, including the sinus node artery (SNA), are commonly found in the areas involved in AF ablation12 and could cause difficulties in achieving linear block at the left atrial (LA) roof.13 The SNA is a major atrial coronary artery of the atrial coronary circulation. This study was to determine the prognostic value of the origin of SNA in relation to AF recurrence in patients with paroxysmal AF undergoing PV isolation (PVI).

METHODS

Study population Consecutive 1066 patients with drug-refractory paroxysmal AF referred for invasive treatment were screened for eligibility from March 2009 to October 2011 in our hospital. Prior to AF ablation, coronary angiography had been performed in some patients to rule
out of coronary artery disease. Patients were excluded from the study if they did not have an assessment of coronary anatomy by angiography during hospitalization. In total, 78 patients suffering from drug-refractory paroxysmal AF were consecutively enrolled into this study. All patients (mean age of \((60.8 \pm 9.3)\) years, 55 men) were referred to Beijing Anzhen Hospital, Capital Medical University for sequential coronary angiography for suspected coronary heart disease and then first-time AF ablation during the same hospitalization.

We defined paroxysmal AF as lasting seven days or less with spontaneous termination according to published guidelines.\(^1^4\) The exclusion criteria of PVI included: left atrial antero-posterior diameter (LAD) >55 mm, left ventricular ejection fraction (LVEF) <35\%, New York Heart Association functional classes III and IV, contraindications for anticoagulation, valvular heart disease, previous AF ablation or the presence of LA thrombus. This study was approved by the Institutional Review Board of the Beijing Anzhen Hospital, Capital Medical University. All patients gave a written informed consent.

**Coronary angiography image analysis**

Coronary anatomy of all the patients was assessed by invasive angiography for suspected coronary heart disease before catheter ablation. Selective catheterization of the right and left coronary arteries was carried out followed by hand injection of the contrast agent with a standard radial or femoral approach using 5-F coronary catheters. Coronary angiography image analysis was performed by a single investigator blinded to the rest of the patients’ clinical data using a computerized quantitative analysis system. Coronary anatomy and coronary vessel dominance were assessed in a standardized manner by dividing the coronary artery tree into 17 segments according to the guidelines of the American Heart Association.\(^1^5\) The SNA was assessed from the angiogram and mainly determined from anterior posterior or 30° right anterior oblique projections.

SNAs were identified from their origins, and followed to their destinations by coronary angiography.\(^1^6\) The SNA is a major atrial coronary artery of the atrial coronary circulation and was defined as the artery that supplies the sinoatrial node, located at the cavoatrial junction. Two major groups of SNA were distinguished based on the origin of the artery, from right coronary artery or left circumflex coronary artery.\(^1^7\) If the SNA originated from the proximal portion of the right coronary artery, it was termed as a right SNA (Figure 1). If the artery originated from the proximal portion of the left circumflex coronary artery, it was designated as a left SNA (Figure 2).\(^1^2\)

In total, seventy-eight consecutive patients with paroxysmal AF in whom coronary anatomy was assessed by invasive angiography for suspected coronary heart disease were divided into right SNA group \((n=34)\) and left SNA group \((n=44)\). Then guided by an electroanatomic mapping system, circumferential pulmonary vein ablation (CPVA) was performed in both groups.

**Electrophysiological study**

The catheter ablation procedure consisted of a wide-area linear antrum ablation with documented PVI with decapolar circular mapping catheter as the end point. Transthoracic echocardiography was obtained prior to ablation in order to measure LAD, left ventricular end diastolic diameter (LVEDD), and LVEF. The presence of intra-atrial thrombus was excluded by transesophageal echocardiography. Prior to ablation, all antiarrhythmic drugs (AADs) except amiodarone were discontinued for at least 5 half-lives. Low molecular weight heparin was administered subcutaneously until ablation procedure. The electrophysiological study and ablation procedure were performed in a fasting state under conscious sedation.\(^1^8\) A quadripolar catheter was positioned within the coronary sinus for atrial pacing and signal reference. One or two 8-F long sheaths (SL1, St Jude Medical, USA) were delivered into the LA using a modified Brockenbrough technique. The transseptal sheaths were flushed continuously with heparinized saline (20 ml/h) in order to prevent thrombus formation and air embolism. Heparin was administered to maintain an activated clotting time (ACT) of 300–350 seconds. After transseptal puncture, a 3.5 mm cool saline-irrigated ablation catheter (Navi-Star Thermo-Cool\(^\text{TM},\)
Biosense-Webster Inc., USA) was applied for mapping and ablation using the CARTO system. A continuous irrigated radiofrequency ablation was performed along each PV antrum in order to encircle the ipsilateral PVs (target temperature 45°C, maximum power 35 W, and infusion rate 17 ml/min). Procedural end-points were completeness of continuous circular lesions and electrical isolation of all PVs (defined as entrance block) identified by a decapolar circumferential mapping catheter (Biosense-Webster Inc.). Immediately after PVI, programmed atrial stimulation and burst pacing were performed in all patients. If a typical atrial flutter (AFL) had been documented before the procedure or was induced during the procedure the tricuspid isthmus was targeted to achieve a bidirectional block. In the repeat procedure, the ablation strategy was described previously targeted to achieve a bidirectional block. In the repeat procedure, the ablation strategy was described previously in detail with the endpoint of PVI.19

**Postablation management and follow-up**

After the procedure, amiodarone was administered to all the patients if there were no contraindications or intolerance. If no recurrent atrial tachyarrhythmia occurred after two or three months, amiodarone was discontinued. All patients received warfarin anticoagulation, which was bridged with low molecular weight heparin. Warfarin was discontinued after 3 months if no AF and/or AT was detected.

All asymptomatic patients were followed up with a 12-lead electrocardiogram and 24-hour Holter recordings before discharge and at the 1st, 3rd, 6th and 12th month after the ablation procedure. If the patient was symptomatic, a new electrocardiogram was obtained. In addition, telephone interviews were conducted monthly for all patients by a physician. Recurrence was defined as any episode of atrial tachyarrhythmias (ATAs), including AF, atrial flutter or atrial tachycardia, that lasted longer than 30 seconds after a blanking period of 3 months.

**Statistical analysis**

All analyses were performed with the SPSS software version 18.0 (SPSS Inc., USA). Continuous data are presented as mean ± standard deviation (SD). Univariate analysis was computed using the unpaired independent samples t test for continuous variables between two groups and the chi-square test or Fisher’s exact test was performed if necessary for categorical variables. Multivariate stepwise Cox-regression analyses were used to estimate contributors to AF recurrence. All probability values were 2-sided, and a P value ≤0.05 was considered statistically significant.

**RESULTS**

**Patients’ clinical characteristics**

Of the 78 patients eligible for inclusion, they were divided into right SNA group (n=34) and left SNA group (n=44) according to the origin of SNA from angiographic findings. The clinical characteristics of the patients are presented in Table 1. Patients of the two groups had similar baseline characteristics including age, gender, body mass index (BMI), left atrial size, ejection fraction, LVEDD, history of hypertension, coronary heart disease, diabetes mellitus, and duration of AF.

### Table 1. Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Left SNA group (n=44)</th>
<th>Right SNA group (n=34)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.3±8.9</td>
<td>58.9±9.4</td>
<td>0.100</td>
</tr>
<tr>
<td>Male (n (%))</td>
<td>30 (68)</td>
<td>25 (74)</td>
<td>0.608</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2±2.5</td>
<td>27.0±2.5</td>
<td>0.168</td>
</tr>
<tr>
<td>AF history (months)</td>
<td>37.0±24.8</td>
<td>42.3±27.3</td>
<td>0.371</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
<td>39.3±5.2</td>
<td>39.0±6.3</td>
<td>0.831</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>46.0±4.6</td>
<td>47.0±4.7</td>
<td>0.357</td>
</tr>
<tr>
<td>LVH (%)</td>
<td>65.0±6.3</td>
<td>63.9±8.5</td>
<td>0.516</td>
</tr>
<tr>
<td>Hypertension (n (%))</td>
<td>35 (79.5)</td>
<td>27 (79.4)</td>
<td>0.988</td>
</tr>
<tr>
<td>DM (n (%))</td>
<td>8 (18.2)</td>
<td>7 (20.6)</td>
<td>0.789</td>
</tr>
<tr>
<td>CAD (n (%))</td>
<td>21 (47.7)</td>
<td>11 (32.4)</td>
<td>0.171</td>
</tr>
</tbody>
</table>

SNA: sinus node artery; BMI: body mass index; AF: atrial fibrillation; LA: left atrial; LVEDD: left ventricular end diastolic diameter; LVH: left ventricular ejection fraction; DM: diabetes mellitus; CAD: coronary artery disease.

### Table 2. Procedural characteristics of the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Left SNA group (n=44)</th>
<th>Right SNA group (n=34)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure time (minutes)</td>
<td>140.5±18.6</td>
<td>133.4±22.1</td>
<td>0.125</td>
</tr>
<tr>
<td>Fluoroscopy time (minutes)</td>
<td>35.4±23.0</td>
<td>33.5±18.5</td>
<td>0.693</td>
</tr>
<tr>
<td>Ablation time (minutes)</td>
<td>33.7±5.9</td>
<td>31.8±5.7</td>
<td>0.134</td>
</tr>
</tbody>
</table>

**Adverse events**

| Stroke/TIA (n) | 0 | 0 |
| Tampenade (n)  | 0 | 0 |
| Groin hematoma/bleed (n (%)) | 2 (4.5) | 1 (2.9) |

SNA: sinus node artery, TIA: transient ischemic attack.

**Arrhythmia recurrence**

Freedom from AF and AADs at 1 year was 67.9 % (53/78) for all patients. After 1 year follow-up, 79.4 % (27/34) in the right SNA group and 59.1% (26/44) in the left SNA group (P=0.042) were in sinus rhythm (Figure 3). The prevalence of a left SNA and right SNA among patients with AF recurrence was 72.0% (18/25) and 28.0% (7/25), respectively. On multivariate analysis, left atrium size (HR=1.451, 95% CI: 1.240–1.697, P<0.001) and a left SNA (HR=6.22, 95% CI: 2.01–19.25, P=0.002) were the independent predictors of recurrence after catheter ablation of paroxysmal AF. A repeat CA procedure was performed in 5 patients among the 25
Figure 3. Kaplan-Meier curves depicted atrial tachyarrhythmias (ATa) free period of different origin of the SNA groups after AF ablation. The ATa free rates were 79.4% in right SNA group and 59.1% in left SNA group, respectively ($P=0.042$ by log-rank test).

recurrence patients during one year follow up, including 3 of the left SNA group (2 for AF and 1 for AF and AFL) and 2 of the right SNA group (1 for AF and 1 for AFL). There were 6 gaps in 3 patients of the left SNA group and 2 gaps in 2 patients of the right SNA group. The sites of PV reconnection were as follows: 3 at the ridge between the left atrial appendage and pulmonary vein (PV-LAA ridge), 1 at inferior area of left inferior pulmonary vein (LIPV) and 2 at the inferior area of right inferior pulmonary vein (RIPV) in the left SNA group and 2 gaps in the right SNA group were located at the roof of RIPV.

DISCUSSION

Previous studies have described the role of atrial coronary perfusion in AF initiation and maintenance. Some studies demonstrated that chronic atrial ischemia or an atrial infarction can provide the triggers and substrate needed to develop AF. Coronary artery disease affecting the atrial branches, possibly due to atrial ischemia, was associated with promotion of AF genesis, regardless of whether it originated from the left or right coronary system. Atrial ischemia could create a substrate for AF by causing fibrosis and scarring of the atrial wall. Regional irrigation of ethanol in some atrial coronary arteries could enable ablation of high-frequency sites during AF.

Coronary circulation to the atria was considered to be important in patients with AF. The largest atrial coronary artery in man was the SNA that supplies the sinoatrial node region. Coronary angiography and postmortem studies have shown that the SNA originates from the right coronary artery in the majority (51%–61%) of the patients, and the remaining from the left circumflex artery (35%–42%). In those studies, the origin of SNA was evaluated in only structurally normal hearts, which may differ from those patients with AF. Our work demonstrated a higher percentage (56.4%) of the SNA arising from the circumflex artery, probably because of our smaller sample or due to the kind of our study population made up of paroxysmal AF. The left SNA may be more frequent in patients with paroxysmal AF.

The SNA was defined as the artery that supplies the sinoatrial node, located at the cavoatrial junction. It is the major atrial coronary artery of the atrial coronary circulation and could cause difficulties in achieving linear block at the LA roof. The SNA was also frequently found on the anterior and anterolateral areas of mitral isthmus lines. The SNA originates from the right or left coronary arteries. The diameters of SNA originating from right coronary artery were reported to be 0.28–2.70 mm, with a mean of 1.09 mm, while those originating from the left circumflex artery were reported to be 0.33–1.90 mm, with a mean of 1.03 mm. A prior experimental study showed that flow through arteries as small as about 0.3 mm can prevent transmural lesion formation. The diameters of SNA could exert a significant heat-sink effect and hinder linear ablation at the pulmonary vein antrum during catheter ablation.

The pulmonary veins and pulmonary vein antra have been shown to play a major role in the initiation and the maintenance of AF. PVI has become the mainstream catheter ablation of AF, demonstrating a high procedural success rate of 70%–80% in paroxysmal AF (PAF) for the first time during a 6 to 20 month follow-up period. Recovery of PV conduction has been demonstrated as the main cause of AF recurrence after PVI procedure. Additionally, PV reconnection was found more commonly in left superior pulmonary vein (LSPV), which is covered by thicker and broader muscular sleeves. The return of PV conduction was associated with histopathologic evidence of nontransmural lesions along the ablation line.

Major atrial coronary arteries, including the SNA, were commonly found in the areas involved in AF ablation and could cause difficulties in obtaining transmural lesions and electric isolation or even lead to ischemic sinus node or atrial dysfunction. Previous studies have reported that the heat-sink effect of blood flow in the SNA may prevent adequate heating of the atrial myocardium at the LA roof during radiofrequency ablation. Major arteries (≥1 mm in external diameter) were found in the mitral isthmus in 54%, at the LA roof in 54%, at the LA anterior wall in 29%, around the left PV ostia in 37% (at the roof and inferior segments) and around the right PV ostia in up to 29% (at the roof segment). Another study showed that atrial coronary arteries including the SNA, crosses the ablation line in about 69% of subjects overall by angiographic analysis, mainly at the mitral isthmus in 45% and at the LAA-LSPV region in 35%.
The left SNA usually branches off the left circumflex artery, passes along the anterior surface of the left atrium toward the border of the left and right atrium, crosses the posterior interatrial sulcus and encircles the superior vena cava (SVC) from the left side. The right SNA usually passes along the anterior surface of the right atrium toward the orifice of the SVC and then encircles the SVC from the right side. The left SNA has more distribution than the right SNA in the left atrium. It is interesting to acknowledge that in a study evaluating acute and chronic PV reconnection after AF ablation, Rajappan et al identified that besides the intervenous ridge (between ipsilateral PVs), the preferential site of acute reconnection is the PV-LAA ridge, and the preferential sites of chronic reconnections were at the PV-LAA ridge, the roof of the right superior PV, and the floor of the right inferior PV. Atrial arteries were prevalent at the areas described as sites of frequent reconnection.

Such interactions could be expressed as a protective effect on the atrial myocardium because of convective heat loss to the blood flowing through the vessels, creating difficulties in obtaining transmural lesions and electric isolation and leading to gaps in the isolation lines or possibly to late reconnection. The left SNA has more distribution than the right SNA in the left atrium, the presence of a left SNA had been proven to be associated with unsuccessful linear ablation at the LA roof. There was maybe more PV reconnection in the left SNA than the right SNA, leading to AF recurrence. For safe and effective procedures, it might be important to identify the origin and course of the SNA performed before the ablation. It may influence the operator’s ablation strategy at some special sites and the damage of SNA can also be avoided.

The limitations of this study include: First, the relatively small sample size. Second, angiographic method cannot identify all atrial arteries and appropriate anatomic and spatial relationships, but the sensitivity of the computed tomographic imaging is not sufficient to detect small arteries because of the difficulty in identifying small arteries. Third, we did not perform any coronary angiography after the ablation and, therefore, coronary injury due to ablation could not be fully evaluated. Fourth, the relationship between origin of SNA and pulmonary vein reconnection sites need to be clarified hence further investigation is still be needed.

In conclusion, the left SNA may be more frequent in patients with paroxysmal AF. After one year follow-up period, the presence of a left SNA was identified as an independent predictor of AF recurrence after CPVA in paroxysmal AF.

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(Received December 8, 2012)