The difference in autonomic denervation and its effect on atrial fibrillation recurrence between the standard segmental and circumferential pulmonary vein isolation techniques

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Aims
This study examined the difference in autonomic modification (AM) and its effect on paroxysmal atrial fibrillation (PAF) recurrence between segmental pulmonary vein isolation (S-PVI) and circumferential PVI (C-PVI).

Methods and results
Successful S-PVI or C-PVI with a basket catheter was achieved in 120 consecutive PAF patients. Serial 24 Holter-recordings were obtained before, immediately, and 1, 3, 6, 12 months after the PVI to analyse the heart rate variability (HRV). Nineteen patients were excluded from analysis because of additional ablation for recurrent PAF after successful PVI. Among the residual 101 patients, 33 had PAF recurrences (S-PVI = 44.0%, C-PVI = 21.6%) at 1 year of follow-up. The root mean square of successive differences and high-frequency power reflecting parasympathetic nervous activity were significantly lower in patients with and without PAF recurrences after C-PVI and patients without PAF recurrences after S-PVI than patients with PAF recurrences after S-PVI (p < 0.005–0.0001). However, there were no significant differences in any HRV parameters in the immediate aftermath of PVI among the patients without PAF recurrences after S-PVI and those with and without PAF recurrences after C-PVI.

Conclusion
Although additional radiofrequency ablation for AM may be recommended after S-PVI to reduce PAF recurrences, it should be carefully determined after C-PVI.

Keywords
Atrial fibrillation • Pulmonary vein isolation • Autonomic nervous system • Heart rate variability • Radiofrequency catheter ablation

Introduction
Two pulmonary vein isolation (PVI) techniques [segmental (S-PVI) and circumferential PVI (C-PVI)] have been clinically used for curing atrial fibrillation (AF).1–9 Several reports have suggested that the modification of the autonomic nervous function may prevent AF recurrences after PVI.10–12 Both S-PVI and C-PVI have been proven to induce an immediate decrease in the parasympathetic nervous function.13 However, the difference in autonomic denervation and its effect on AF recurrences between the two techniques remain unknown. This study was undertaken to investigate whether or not autonomic denervation can help prevent an AF recurrence after the two different PVI procedures.

Methods
Study population
The study population consisted of 120 consecutive patients (93 men, 59 ± 11 years; range 29–80 years old) with symptomatic paroxysmal AF (PAF) refractory to 3 ± 1 class I or III antiarrhythmic drugs (not including amiodarone). The mean PAF history was 4 ± 4 years (0–17). The mean echocardiographic dimension of
the left atrium (LA) was 35 ± 6 mm (25–46) and mean left ventricular ejection fraction 67 ± 9% (50–89). The exclusion criteria were sick sinus syndrome, diabetes mellitus, thyroid dysfunction, recent myocardial infarction (<6 months), history of a prior thoracotomy, β-blocker therapy, and a pacing rhythm. The first 60 patients underwent S-PVI and the second 60 C-PVI between September 2005 and August 2007. These patients were retrospectively examined. Each patient gave written, informed consent, and all antiarrhythmic drugs were discontinued for at least five half-lives prior to the study.

Electrophysiologic study

The patients were taken to the electrophysiologic laboratory in a fasting state and were given intravenous sedation with propofol and pentazocine. A 7-French decapolar catheter with 1.5-1-mm interelectrode spacing between each electrode pair (St Jude Medical, AF Division, Minneapolis, MN, USA) was deployed into the coronary sinus (CS) via the subclavian vein. The transseptal procedure was performed with intracardiac echocardiography guidance recorded with a 9-French transducer catheter (Boston Scientific, Natick, MA, USA) operating at 9 MHz. Catheterization into the LA was performed with a one puncture and two sheaths technique. A guidewire and ablation catheter were introduced into the LA through an 8.5-French sheath (Soft Tip EP Sheath™, EP Technologies, Boston Scientific corporation, San Jose, CA, USA) for a mapping catheter and an 8-French sheath (St Jude Medical), respectively, using a one puncture, double transseptal catheterization technique. Those two sheaths were then introduced into the LA over the guidewire and the ablation catheter, respectively. After the transseptal procedure, systemic anticoagulation was achieved with intravenous heparin to maintain an activated clotting time of >300 s. Selective angiography of the pulmonary veins (PVs) was performed in all patients.

Pulmonary vein mapping

All four PVs were targeted for two PVI techniques, S-PVI and C-PVI. Both PVI techniques were performed with the guidance of a basket catheter. A 31 mm multielectrode basket catheter (MBC) (Constellation™, EP Technologies, Boston Scientific corporation, San Jose, CA, USA), which consisted of eight splines (A–H) with eight 1-mm electrodes and 2-mm spacing, was deployed within three to four PVs via the atrial septum. An MBC was introduced towards the distal PV and then pulled back as proximally as possible without dislodgement with fluoroscopic guidance until its most proximal electrodes were positioned at the PV ostium or antrum, which was identified by a selective angiogram. A total of 56 bipolar electrograms were recorded by the MBC during sinus rhythm (right PVs) or distal CS pacing (left PVs). When AF persisted during the electrophysiologic study, internal cardioversion was used to restore sinus rhythm and an MBC recording of at least one beat was obtained during the appropriate rhythm above. If an MBC could not be deployed in the right inferior PVs, a 20-electrode circular catheter (Lasso™, Biosense Webster, Diamond Bar, CA, USA) was used for mapping those PVs.

Catheter ablation

S-PVI targeting a preferential electrical connection between the PVs and LA was performed as we previously described.5 For the PV potential mapping using a computerized three-dimensional mapping system with an MBC, the onset of a longitudinal activation pattern towards the distal PVs with the earliest activation at the circumference of the LA-PV junction was identified as a prior electrical connection. Radiofrequency (RF) energy was delivered with a target temperature of 55°C and maximum power output of 40 W for 60 s (EPT-1000TC generator™, EP Technologies, Boston Scientific corporation, San Jose, CA, USA), using an 8-mm tip catheter (Blazer II 5770™, EP Technologies, Boston Scientific corporation, San Jose, CA, USA). C-PVI targeting the PV antrum potentials was performed as we previously described.6 RF energy was delivered in the same manner as in the S-PVI. If a residual conduction gap was detected after the PV antrum ablation, additional RF applications to the PV side just next to the previous RF lesions were delivered only at the site of a residual conduction gap. The final end-point of those two PVI techniques was defined as either the abolition or dissociation of the distal PV potentials independent of the elimination of vagal reflexes. After successful PVI, the presence of non-PV AF foci was examined. When sinus rhythm persisted after the PVI, we first tried to record any spontaneous AF occurrences during the baseline state for at least 30 min. If no spontaneous AF was observed during that period, it was attempted to be induced by intermittent atrial pacing, from 10 to 15 beats at a cycle length between 200 and 300 ms from the distal CS during an isoproterenol infusion (up to 2 μg/min for 5 min). Following the pause after terminating the atrial pacing, if no spontaneous AF appeared, burst pacing from the distal CS was performed until AF was induced. If the AF was sustained even after the PVI or for more than 5 min after the induction, it was converted to sinus rhythm using internal cardioversion, and then we monitored for the spontaneous reoccurrence of AF. When non-PV AF foci were found, isolation of the superior vena cava (SVC) for the SVC triggers, or focal ablation targeting the other triggers was performed as we previously reported.9 Those procedures above were repeated until it was confirmed that no further spontaneous AF occurred.

Analysis of the heart rate variability

Serial 24-h Holter recordings were obtained at baseline, immediately, and 1, 3, 6, 12 months after the PVI to analyse the heart rate variability (HRV). After an automatic analysis, the data file was visually reviewed and edited by an experienced technician. The heart rate and time- and frequency-domain HRV were analysed from the Holter recordings using an analysis programme (Philips Zymed Holter 2010 Plus). Supraventricular pre-mature beats, AF, ventricular pre-mature beats, electrical noise, and other aberrant ECG signals were excluded from the HRV analysis. The underlying rhythm was carefully analysed, and only artifact-free episodes of sinus rhythm were included in the further analyses. The HRV was used as an indicator of the autonomic activity in accordance with the guidelines for standardization.17 The time-domain measures of the HRV included the standard deviation (SD) of all NN intervals (SDNN), SD of the averages of the NN intervals in all 5-min segments (SDANN), mean of the SD of all NN intervals for all 5-min segments (SD250N), and root mean square square successive differences (rMSSD). The frequency-domain measures of the HRV included the low-frequency (LF; 0.04–0.15 Hz) power, high-frequency (HF; 0.15–0.40 Hz) power, and ratio of the low-frequency to high-frequency powers (LF/HF). The frequency-domain HRV was calculated by a fast Fourier transform for each 5-min segment of data. All values of the frequency-domain HRV were expressed as the average of all 5-min segments of the 24-h recordings and were log-arithmically transformed to avoid the undue influence of extreme values. The rMSSD and HF have been used to reflect the parasympathetic nervous activity, and the LF/HF has been used to reflect the sympathetic nervous activity.
Follow-up
The patients remained hospitalized under continuous rhythm monitoring for at least 3 days. During the follow-up period, no antiarrhythmic drugs were administered in any of the patients. The clinical follow up was performed at 2 weeks, 1 month, and every month until 12 months after the procedure, using the cardiac recordings. A 24-h Holter recording was performed at 1 month, 3 months, and every 3 months thereafter until 12 months after the procedure. All patients who reported symptoms were given an event monitor to document the cause of the symptoms. Multi slice computed tomography was performed 3 and 6 months after the procedure for the detection of PV stenosis in all the patients.

Statistical analysis
Continuous variables are expressed as the group mean ± 1SD. The frequency-domain measurements of the HRV (LF and HF) were expressed in squared milliseconds. The comparisons of the continuous variables between the two groups were analysed with the use of the paired or unpaired t-test as appropriate. When comparisons involved >2 groups, an analysis of variance (ANOVA) was used. When group differences were found, a one-way ANOVA was followed by the Fisher’s LSD method to test the significance of the difference among the means in all groups. The categorical variables expressed as numbers and percentages in the different groups were compared with a χ² test and the Yates correction if necessary. An overall χ² test for a 2 × n table was constructed when comparisons involved >2 groups. Statistical significance was selected at a value of P < 0.05.

Results
There were no significant differences in the age, sex, duration of PAF, number of ineffective antiarrhythmic drugs, incidence of structural heart disease, echocardiographic LA dimension, or left ventricular ejection fraction between the patients undergoing S-PVI and C-PVI.

Catheter ablation
In 12 and 10 RIPVs in the patients with S-PVI and C-PVI (no significant differences), respectively, the deployment of the MBC was impossible and PV mapping was performed with a circular catheter. MBC mapping was successfully performed in all the other PVs. In all the study patients, successful isolation of all four PVs could be achieved. During the S-PVI and C-PVI, vagal reflexes such as transient AV block, sinus bradycardia, and hypotension were elicited in five and seven patients, respectively. In 19 patients (S-PVI = 10, C-PVI = 9), spontaneous AF was observed after successful PVI and additional SVC isolation and/or focal ablation targeting the triggers was performed. All 19 cases were excluded from the analysis because additional ablation after the PVI might have had additional effects on the autonomic nervous function. There were still no significant differences in the clinical characteristics between the remaining 50 patients with S-PVI and 51 patients with C-PVI.

Among the 101 patients, 68 (28 with S-PVI and 40 with C-PVI; Group-I) were free from symptomatic PAF without any antiarrhythmic drugs and 33 (22 with S-PVI and 11 with C-PVI; Group-II) had a PAF recurrence at 1 year of follow-up. In 10 (45.4%) and 18 (81.8%) of the 22 Group II patients with an S-PVI, PAF recurred within 1 and 3 months after the PVI, whereas PAF did not recur in any of the Group II patients with a C-PVI within 3 months after the PVI. The PAF recurrence rate was significantly higher in the patients with the S-PVI than in those with the C-PVI (44.0% vs. 21.6%, P < 0.05). There were no significant differences in the clinical characteristics among those patients undergoing S-PVI or C-PVI and those with or without a PAF recurrence (Table 1). There were no significant differences in the extent of the RF lesions in the circumference of the LA–PV junction or total duration or amount of RF energy delivery between the patients with and without a PAF recurrence after the S-PVI (70.0 ± 16.9 vs. 70.4 ± 21.6%, 66.1 ± 16.1 vs. 66.9 ± 20.5 min, and 81 520 ± 33 030 vs. 76 310 ± 38 800 J, respectively). No critical complications such as PV stenosis, cerebrovascular attacks, or atrio-esophageal fistulae occurred in either PVI technique.

Heart rate and heart rate variability changes
There were no significant differences in the heart rate, percentage of pre-mature atrial contractions (PACs) out of the total beats in the Holter recordings (%PACs), and HRV parameters before the

<table>
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<tr>
<th>Table 1 Patient characteristics</th>
<th>S-PVI</th>
<th>C-PVI</th>
<th>P-value</th>
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<tr>
<td></td>
<td>Late recurrence</td>
<td>Late recurrence</td>
<td></td>
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<tr>
<td></td>
<td>No (n = 28)</td>
<td>Yes (n = 22)</td>
<td>No (n = 40)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>58 ± 12</td>
<td>59 ± 12</td>
<td>58 ± 10</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>22/6</td>
<td>16/6</td>
<td>33/7</td>
</tr>
<tr>
<td>Duration of PAF (year)</td>
<td>4 ± 4</td>
<td>4 ± 3</td>
<td>5 ± 4</td>
</tr>
<tr>
<td>Ineffective AADs (n)</td>
<td>2 ± 1</td>
<td>2 ± 1</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>Structural heart disease (n)</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>34 ± 4</td>
<td>35 ± 6</td>
<td>35 ± 5</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>68 ± 9</td>
<td>68 ± 9</td>
<td>67 ± 8</td>
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AAD, antiarrhythmic drug; LAD, left atrial dimension; LVEF, left ventricular ejection fraction; M/F, male/female; PAF, paroxysmal atrial fibrillation.
PVI among the patients undergoing S-PVI or C-PVI and with or without PAF recurrences (Tables 2 and 3). The results of the heart rate, %PACs, and HRV parameters in the patients without any PAF recurrences after the PVI are shown in Figure 1 and Tables 2 and 3. In those patients, the minimum and average heart rate increased immediately after either PVI and remained elevated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months. The time- and frequency-domain HRV parameters including the SDNN, rMSSD, and HF decreased immediately after either PVI technique and remained attenuated for 3–12 months. The LF/HF did not change significantly after either PVI technique during the entire follow-up. The %PACs had an acute reduction immediately after either PVI technique and remained attenuated for 6–12 months.
Figure 1  Serial changes in the heart rate, percentages of premature atrial contractions, and heart rate variability before, immediately (1 day), 1 month (1M), 3 months (3M), 6 months (6M), and 12 months (12M) after the pulmonary vein isolation in the patients without any recurrences of atrial fibrillation. The solid lines indicate the segmental pulmonary vein isolation group data and dotted lines the circumferential pulmonary vein isolation group data. The other abbreviations are as in Table 2.
Table 4 Comparisons of the heart rate and heart rate variability in the immediate aftermath of the pulmonary vein isolation in the two groups

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<tr>
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<th>S-PVI</th>
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<th>C-PVI</th>
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<tr>
<td></td>
<td>Late recurrence</td>
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<td>Late recurrence</td>
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<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>P-value</td>
<td>No</td>
</tr>
<tr>
<td>Minimum HR (bpm)</td>
<td>58.0 ± 10.1</td>
<td>55.8 ± 7.4</td>
<td>0.34</td>
<td>58.8 ± 9.4</td>
</tr>
<tr>
<td>Average HR (bpm)</td>
<td>76.9 ± 7.7</td>
<td>80.4 ± 5.8</td>
<td>0.10</td>
<td>76.5 ± 9.8</td>
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<tr>
<td>Maximum HR (bpm)</td>
<td>119.5 ± 15.8</td>
<td>123.2 ± 17.2</td>
<td>0.36</td>
<td>116.6 ± 14.3</td>
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<tr>
<td>PACs (%)</td>
<td>1.1 ± 1.6</td>
<td>2.5 ± 3.2</td>
<td>0.001</td>
<td>0.4 ± 0.6</td>
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<tr>
<td>ASDNN (ms)</td>
<td>37.0 ± 19.7</td>
<td>50.9 ± 26.1</td>
<td>0.003</td>
<td>30.1 ± 14.5</td>
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<td>SDANN (ms)</td>
<td>78.3 ± 28.3</td>
<td>81.2 ± 18.3</td>
<td>0.63</td>
<td>72.6 ± 24.9</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>94.8 ± 36.9</td>
<td>112.0 ± 38.6</td>
<td>0.034</td>
<td>82.2 ± 26.7</td>
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<td>ln LF (ms²)</td>
<td>8.33 ± 0.86</td>
<td>8.63 ± 0.87</td>
<td>0.13</td>
<td>8.49 ± 0.80</td>
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<td>Parasympathetic nervous activity</td>
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<tr>
<td>rMSSD (ms)</td>
<td>34.7 ± 23.3</td>
<td>72.1 ± 30.8</td>
<td>0.0001</td>
<td>34.5 ± 16.5</td>
</tr>
<tr>
<td>ln HF (ms²)</td>
<td>8.68 ± 0.79</td>
<td>9.28 ± 0.93</td>
<td>0.002</td>
<td>8.80 ± 0.68</td>
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<tr>
<td>Sympathetic nervous activity</td>
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<tr>
<td>LF/HF</td>
<td>0.74 ± 0.28</td>
<td>0.61 ± 0.23</td>
<td>0.07</td>
<td>0.75 ± 0.30</td>
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</table>

Abbreviations are as in the previous tables.

had a subsequent gradual decrease throughout the entire observation period. The results of the heart rate, %PACs, and HRV parameters in the patients with a PAF recurrence after the PVI are shown in Tables 2 and 3. In those patients, the minimum and average heart rate increased and the SDANN, SDNN, and LF/HF decreased immediately after either PVI. The other time- and frequency-domain HRV parameters did not change significantly after either PVI technique. Because 27 of 33 (81.8%) patients with a PAF recurrence underwent another ablation procedure (n = 23) and/or took antiarrhythmic drugs or β-blockers (n = 13) due to PAF recurrences, subsequent Holter recordings after those interventions were excluded from the HRV analyses in those patients.

Comparisons of the heart rate, %PACs, and HRV in the immediate aftermath of the PVI among the patients undergoing S-PVI or C-PVI and with or without a PAF recurrence are shown in Table 4. In the patients undergoing S-PVI, the rMSSD and HF which reflected the parasympathetic nervous activity and %PACs were significantly lower in the patients without any PAF recurrences than in those with a PAF recurrence (rMSSD, 34.7 ± 23.3 vs. 72.1 ± 30.8 ms, P < 0.0001; ln HF, 8.68 ± 0.79 vs. 9.28 ± 0.93 ms², P = 0.002; and %PACs, 1.1 ± 1.6 vs. 2.5 ± 3.2%, P = 0.001). On the other hand, there were no significant differences in the heart rate, %PACs, or HRV parameters in the immediate aftermath of the PVI among the patients without any PAF recurrences after the S-PVI and those with and without PAF recurrences after the C-PVI.

Discussion

This study revealed that in PVI procedures of which the end point was not the elimination of the vagal reflexes but was PV electrical disconnection, the autonomic modification (AM) significantly differed between the patients with and without PAF recurrences after the S-PVI, whereas it did not between the patients with and without PAF recurrences after the C-PVI. Anatomical studies demonstrated that the adrenergic and cholinergic nerve densities were not homogeneous around the PV ostium and they had no relation to the distribution of the musculature connections between the LA and PVs. As a result, an S-PVI targeting those musculature connections alone may not cause uniform damage to the autonomic nervous activities although C-PVI may cause a uniform AM despite the heterogeneity in the autonomic nerve distribution. Therefore, it may be difficult to control the amount of the AM by monitoring the parameters of the catheter ablation during the S-PVI.

This study also revealed that AM was significantly greater in the patients with the C-PVI and the patients without PAF recurrences after the S-PVI than in the patients with PAF recurrences after the S-PVI. Considering the significantly lower PAF recurrence rate in the patients with the C-PVI than in those with the S-PVI in this study, further AM and HRV attenuation might have resulted in a greater suppression of the PAF recurrence after the PVI. It still seems controversial which is superior for preventing a PAF recurrence, S-PVI, or C-PVI. This study suggests that in terms of the AM that may reduce a PAF recurrence, C-PVI may be superior to S-PVI.

Why could the AM after the PVI prevent the PAF recurrences? The occurrence of PAF greatly depends on the variations in the autonomic tone according to studies using HRV. A shift towards vagal predominance was observed essentially in the patients with PAF triggered by PV foci. AF is easily initiated in normal hearts and transvascular atrial parasympathetic nervous system modification by RF catheter ablation abolishes vagally mediated AF in mongrel dogs. Parasympathetic stimulation...
dramatically shortens the atrial effective refractory period and decreases the wavelength of atrial re-entrant circuits that play an important role in the initiation and perpetuation of AF.\textsuperscript{25–27} Therefore, vagal denervation may suppress the initiation and perpetuation of AF whether the mechanism of AF is mediated via the PVs or not. Although in this study, it was in fact unclear whether or not the PACs originated from the PVs with the conduction recovery, suppression of the PACs after the PVI was significantly greater in the patients with greater autonomic denervation such as those without any PAF recurrences after the S-PVI or C-PVI and in the patients with a PAF recurrence after the C-PVI as compared with the patients with a PAF recurrence after the S-PVI. On the other hand, most PAF recurrences after the S-PVI occurred within the first 3 months after the PVI, whereas all PAF recurrences after the C-PVI occurred after the first 3 months after the PVI. Previous reports\textsuperscript{10,28} as well as this study suggest that autonomic denervation after the catheter ablation may be a transient phenomenon. Pappone et al.\textsuperscript{10} proposed that the transient autonomic denervation effects might contribute to the prevention of AF recurrence by reversing the AF-induced atrial electroanatomic remodelling. In a clinical phase, it may be challenging to demonstrate atrial electroanatomic reverse remodelling after the PVI by the signal averaged ECG or echocardiography because healing of the LA tissue damaged by the RF ablation may occur simultaneously. However, their proposal seems to be the most reasonable explanation of the mechanism so far. Therefore, we think that suppression of the PAF triggers early after the PVI by the autonomic denervation might have allowed for not only the suppression of the early PAF recurrences but also the atrial reverse remodelling, resulting in the long-term prevention of PAF recurrences.

Previous studies have suggested that adding an ablation to the PV ablation aimed at autonomic denervation is adequate to eliminate the vagal reflexes,\textsuperscript{10} or targeting ganglionated plexi in the LA\textsuperscript{11} may reduce the AF recurrence by modifying the autonomic nerve function. The present study suggests that additional RF applications for autonomic denervation after the S-PVI may reduce a PAF recurrence because in this study, the S-PVI caused some AM, which could be helpful for preventing a PAF recurrence. When AM after the S-PVI is limited in the patients with a PAF recurrence, adjunctive autonomic denervation may be recommended to prevent a PAF recurrence in the redo-session. Although the degree of AM did not differ significantly between the patients with and without PAF recurrences after the C-PVI in this study, that result would neither suggest that adjunctive autonomic denervation may not reduce a PAF recurrence nor deny the previous reports.\textsuperscript{10,11} However, it should be noted that the same degree of AM as in the patients without any PAF recurrences after the S-PVI or C-PVI occurred in the patients with a PAF recurrence after the C-PVI. Considering the risk of critical complications during PV ablation,\textsuperscript{29–31} additional RF ablation for autonomic denervation may be carefully determined after the C-PVI.

In a recent report, the deceleration capacity and acceleration capacity which are believed to mainly reflect the vagal and sympathetic aspect of the autonomic function, respectively, were assessed using a novel signal-processing technology in Holter recordings.\textsuperscript{13} That report demonstrated that standard S-PVI and C-PVI led to significant impairment of both the deceleration capacity and acceleration capacity. However, in that report, there were no significant differences in the rMSSD or HF, which are standard parameters for assessing the parasympathetic nervous activity, before and after the PVI. No association between the extent of the autonomic denervation and success in terms of freedom from atrial tachyarrhythmias could be found. The discrepancy between the new and standard parameters may have been a reason to explain why that study could not elicit such an association.

**Study limitations**

In the recent reports, a detailed follow-up using transtelephonic and long-term Holter monitoring has revealed that freedom from AF after an AF ablation may be overestimated because of missing asymptomatic AF recurrences.\textsuperscript{19,20} In this study, the cure rate of AF might have been a little overestimated because intermittent Holter recordings alone were performed for the clinical follow up.

**Conclusions**

The PAF recurrence rate was significantly lower in the patients with the standard C-PVI than in those with the standard S-PVI. The AM was significantly greater in the patients with and without PAF recurrences after the standard C-PVI and the patients without PAF recurrences after the standard S-PVI than in the patients with PAF recurrences after the S-PVI. However, there were no significant differences in the AM among the patients without PAF recurrences after the standard S-PVI and those with and without PAF recurrences after the standard C-PVI. Although additional RF ablation for autonomic denervation may be recommended after the S-PVI in order to reduce a PAF recurrence, it should be carefully determined after the C-PVI.

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**References**

The effect of vagal denervation on AF recurrence after PVI


