Increased ostial pulmonary vein diameter in congestive heart failure: a multi-slice computed tomography angiography evaluation

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Introduction
Congestive heart failure (CHF) is a major public health problem around the world. In the United States, approximately 5 million patients have CHF and nearly 500,000 patients are diagnosed for the first time each year. Of these, 30% to 40% will develop atrial fibrillation (AF) during the course of the disease.1 On the other hand, AF is often associated with heart failure. In China, approximately one-third of AF patients had a decreased left ventricular ejection fraction. About 6.4% of them had severe (ejection fraction<35%), and 22.4% had mild-to-moderate (ejection fraction 35–45%) cardiac systolic dysfunction.2 When AF develops in CHF patients, it is associated with increased morbidity and mortality.2,3

Many clinical and animal studies have demonstrated that atria electrophysiological and structural remodeling plays a role in the maintenance of AF.4,5 However, the PV morphological characteristics that predispose to AF in patients with CHF have not been determined. The pulmonary veins are known to play a major role in AF initiation as a prime source of atrial ectopic complex generation.6 There is also evidence that CHF can promote atrial ectopic impulse formation from the pulmonary vein regions.7 Lin et al., by means of selective PV angiography, demonstrated proximal dilatation of the superior PV ostia in patients with AF.8 Tsao et al. reported selective enlargement of superior PVs rather than inferior PVs by magnetic resonance angiography (MRA) in patients with paroxysmal AF compared with control patients.9 Another recent study with transesophageal echocardiographic (TEE) evaluation showed that AF was associated with a significant enlargement of the RSPV, LSPV, and LA.10 Herweg et al. found that PV ostia diameters were increased in patients with hypertension and hypertensive heart disease whether they had AF or not.11 These studies suggest that patients who have intrinsically larger pulmonary veins may be more likely to develop atrial fibrillation because stretch and dilation of the PVs might change the electrophysiological characteristics of the myocardial sleeve. The present study examined the morphological changes of the PVs and left atrium in patients with CHF.

Patients and methods

Patients
The study consisted of 51 patients who underwent MSCT...
scan for further diagnosis because of chest discomfort from March 2005 to November 2005. Patients were divided into two groups: CHF group, including 25 patients with symptomatic CHF; and control group, including 26 age-and gender-matched patients without CHF. CHF was defined by a left ventricular ejection fraction of < 35% associated with symptoms (New York Heart Association class II-IV). All patients with CHF were evaluated with transthoracic echocardiography. Patients were excluded if they had infiltrative cardiomyopathy, congenital pulmonary vein variation including common ostium of the left or right PVs and additional PVs, or atrial arrhythmias.

Scan protocol and image reconstruction

All patients were scanned on a 64-slice MSCT scanner (Sensation 64 Cardiac, Siemens Medical Systems, Forchheim, Germany). After an initial bolus-timing single-slice scan using 10 ml of contrast (Omnipaque, Amersham Health, Princeton, New Jersey, iodine content 370 mg/ml) followed by a 50-ml saline chaser, a contrast-enhanced scan was obtained using 100 ml of contrast injected through an antecubital vein at 5 ml/s followed by a 40-ml saline chaser. The scan parameters were: 32×0.6 mm collimation with dual focal spots per detector row; rotation time 330 ms; table feed 3.8 mm/rotation; tube voltage 120 kV; effective tube current 750 to 850 mA. Estimated effective radiation dose was 13 mSv for men and 18 mSv for women. The overall scan time was shorter than 12 sec. Electrocardiography gating was performed with a triggered delay set at 70% of the R-R interval to target the atrial end-diastolic phase. A processing workstation allowed for three-dimensional viewing of curved multiplanar reconstruction (MPR) images, maximal intensity projection (MIP) reconstruction, and volume rendering (VR) images.

Quantitative measurements

For MSCT, the pulmonary vein ostium was defined by the intersection of tangents extending from the surface of the pulmonary vein and the wall of the adjacent left atrium (Fig. 1). Measurements of the PV ostia in two directions were obtained: 1) the anterior-posterior direction, and 2) the superior-inferior direction. Multiplanar reformatting (MPR) was used to obtain these measurements in two perpendicular directions (Fig. 1). The ratio between these measurements and the venous ostium index were calculated to obtain information on the shape of the ostium. The more the venous ostium index deviates from the value 1, the more asymmetrical the shape of the ostium. LA diameters were obtained by measuring the maximal left-right diameter (LA1) of the LA on coronal section, the maximal anteroposterior diameter (LA2) of the LA on transverse section, and superoinferior diameter (LA3) of the LA on coronal section (Fig. 2). Quantitative measurements were performed using electronic three-dimensional digital calipers.

Another physician blinded to the patient diagnosis and
procedure was asked to assess measurements and characteristics of the PVs and LA.

**Statistical analysis**
Continuous variables are expressed as mean ± SD. Continuous variables were compared with the t test. Multivariate linear regression analysis was performed to determine the predictors of pulmonary vein size. \( P<0.05 \) was considered statistically significant. Statistical analysis was performed using SPSS version 11.0 for Windows (SPSS Inc., Chicago, IL, USA).

**Results**

**Patient Characteristics**

The underlying causes of CHF included coronary heart disease (n=16), cardiomyopathy (n=7) and valvular heart disease (n=2); CHF patients did not differ significantly from the controls in age, sex distribution, and cardiovascular diseases (Table 1). Patients with CHF had a lower mean LVEF (28.2±6.0% vs 65.6±9.0, \( P<0.01 \)), and a significantly larger left atrial diameter (43.9±6.3 mm vs 33.1±5.5 mm, \( P<0.01 \)) than the controls.

**MSCT findings**

**LSPV** The mean size of the LSPV ostia was significantly larger in patients with CHF than in controls (17.2±2.9 mm vs 12.7±1.4 mm in AP view, \( P<0.01 \), and significantly larger left atrial diameter (43.9±6.3 mm vs 33.1±5.5 mm, \( P<0.01 \)) than the controls.

**RSPV** In patients with CHF the mean size of the RSPV ostia assessed in the AP view was significantly larger than in controls (17.0±2.8 mm vs 13.9±2.7 mm, \( P<0.01 \)) (Table 2, Fig. 4).

**LIPV** In patients with CHF the mean size of the LIPV ostia assessed in both AP and SI views was not different compared to controls (Table 2, Fig. 4).

**RIPV** In patients with CHF, the mean size of the RIPV ostia was significantly increased compared to controls (15.3±2.6 mm vs 13.2±2.5 mm in AP view, \( P<0.01 \), 17.8±5.1 mm vs 15.4±2.0 mm in SI view, \( P<0.01 \)) (Table 2, Fig. 4).

**LA size** There were significant difference in the average diameters of LA1 (transverse) (42.0±6.6 mm vs 32.4±5.8 mm, \( P<0.01 \)), LA2 (anteroposterior) and LA3 (superoinferior) (56.2±6.1 mm vs 49.5±4.8 mm, \( P<0.01 \)) between the two groups (51.7±8.6 mm vs 40.4±7.8 mm, \( P<0.01 \)) (Table 3).

**PV ostium indexes** Calculations of the venous ostium indexes (ratios of measurements of PV ostia in the anterior-posterior and in the superior-inferior direction), as measured with MSCT, demonstrated that the venous ostium indexes of the LSPV and RSPV in the CHF group were significantly larger than those in the control group. There were no significant difference in the venous ostium indexes of the LIPV and RIPV between two groups, indicating a more round shape of superior PV ostia in the CHF group than the control group (Table 3).

**Multivariate predictors of pulmonary vein ostial size**
By multivariate analysis of several variables (age, gender, size of LA1, LA2, LA3, history of hypertension, and NYHA class of heart function), age and NYHA class of heart function were independent predictors of ostial diameter of the LSPV in the SI view (\( P<0.05 \)). Age and LA1, LA2 were independent predictors of ostial diameter of the RSPV in the AP view (\( P<0.05 \)). LA1 was an independent predictor of ostial diameter of the LSPV in the AP view (\( P<0.05 \)).

**Discussion**

**Major Findings**

Our study with 64-slice MSCT showed significant dilation of LSPV, RSPV, RIPV and LA in patients with CHF however, similar findings could not be demonstrated in LIPV.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of CHF and control group</th>
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<tr>
<td><strong>CHF patients</strong> (n=25)</td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>Hypertension, n(%)</td>
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<tr>
<td>Coronary heart disease, n (%)</td>
</tr>
<tr>
<td>Cardiomyopathy, n (%)</td>
</tr>
<tr>
<td>Valvular heart disease, n (%)</td>
</tr>
<tr>
<td>LVEF (%)</td>
</tr>
<tr>
<td>LA diameter (mm)</td>
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<tr>
<td>NYHA class</td>
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LVEF: left ventricular ejection fraction; LA: left atrial; NYHA: New York Heart Association.
Table 2. Diameters of the pulmonary vein ostia in CHF and control groups (mm)

<table>
<thead>
<tr>
<th></th>
<th>CHF (n=25)</th>
<th></th>
<th>Control (n=26)</th>
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<tr>
<td></td>
<td>AP</td>
<td>SI</td>
<td>AP/SI</td>
</tr>
<tr>
<td>LSPV</td>
<td>17.2±2.9**</td>
<td>20.1±3.1**</td>
<td>0.87±0.15**</td>
</tr>
<tr>
<td>LIPV</td>
<td>11.9±3.1</td>
<td>16.6±2.3</td>
<td>0.72±0.18</td>
</tr>
<tr>
<td>RSPV</td>
<td>17.0±2.8**</td>
<td>17.0±2.5</td>
<td>1.01±0.17*</td>
</tr>
<tr>
<td>RIPV</td>
<td>15.3±2.6**</td>
<td>17.8±3.1**</td>
<td>0.87±0.16</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation. **P<0.01, *P<0.05 compared with control subjects. CHF: congestive heart failure; LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein; RSPV: right superior pulmonary vein; RIPV: right inferior pulmonary vein; SI/AP: ratio of supero-inferior diameter to antero-posterior diameter.

Fig. 3. Comparison of left superior pulmonary vein (LSPV) between the congestive heart failure (CHF) group and control group. A: Measurements of LSPV in the AP direction in a patient with CHF; B: Measurements of LSPV in the AP direction in a patient without CHF.

Fig. 4. A: Mean ostial diameter of the pulmonary veins in the AP direction in patients with CHF and in control subjects. B: Mean ostial diameter of the pulmonary veins in the SI direction in patients with CHF and in control subjects. **P<0.01 vs control subjects. LSPV: left superior pulmonary vein; LIPV: left inferior pulmonary vein; RSPV: right superior pulmonary vein; RIPV: right inferior pulmonary vein; CON: control group; CHF: congestive heart failure.
In addition, a more round shape of superior PV ostia could be found in the CHF group. Age, heart function, and size of LA were independent predictors of ostial diameter of PVs. These anatomic changes may play an important role in the development of AF in CHF patients.

Dilation of LA and PVs in CHF patients without the history of atrial arrhythmias

The relationship between LA structural remodeling and development of AF in CHF patients has been studied extensively. Sanders et al. demonstrates that patients with CHF and no prior atrial arrhythmias have significant atrial remodeling characterized by anatomic and structural changes, including atrial enlargement, regions of low voltage, and scarring; abnormalities of conduction, including widespread conduction slowing and anatomically determined conduction delay and block; increased refractoriness. These abnormalities are associated with an increased inducibility and sustainability of AF in patients with CHF. In the present study, not only size of LA but PVs are found to be enlarged in the CHF patients, which demonstrates that PVs morphological changes of CHF patients may also play a role in the development of AF. From ICE measurements, Chen et al. also found that patients with impaired LV systolic function had significantly larger PV ostia (average of all four veins = 2.2 cm), as compared with patients with normal LV systolic function (average of all four veins = 1.4 cm) (P<0.05).

Mechanism of PVs Dilation in CHF

The mechanism of increased PV diameter in patients with CHF is unclear. PV dilation may be the result of chronically elevated LA and/or left ventricular end-diastolic pressure. In addition, the structural changes that the atria undergo with increasing duration of CHF, like interstitial fibrosis may also occur in the PVs. Okayama et al. demonstrates that the percentage of fibrosis in PVs was significantly greater in CHF dogs than in control dogs. Neurohormonal activation of the renin, angiotensin, and aldosterone systems occurs in CHF, which may play an important role in this kind of structural remodeling. Excessive fibrosis in PVs during CHF may also increase passive dilation of PVs. Therefore it would be reasonable to hypothesize that any process that involves structural changes in the atria will also affect atrial tissue within the PVs thereby possibly contributing to PV dilatation. Moreover, if the atrial volume increases, the PV ostia may be passively stretched which also might partially account for the increased PV diameters observed in CHF patients.

Relationship between PVs dilation and development of AF

Information on the association of PVs dilation and AF is not limited. By means of selective PV angiography, MRA, and TEE, many authors have described PV morphology related to AF. These results suggest that patients who have intrinsically larger pulmonary veins may be more likely to develop atrial fibrillation because stretch and dilation of the PVs might change the electrophysiologic characteristics of the myocardial sleeve. Yamane et al. reported that the diameters of arrhythmogenic PVs were significantly larger than those of nonarrhythmogenic PVs, irrespective of the specific PV. Mechano-electrical feedback due to stretch might impact on the triggering substrate and on the atrial myocardial remodeling processes leading to perpetuation of AF. A decrease of the local refractory period of myocardial sleeves within the PV was observed during PV dilatation in a rabbit Langendorff model. A short PV refractory period may facilitate rapid conduction of ectopic foci from the PV to the left atrium.

Evaluation of PVs morphology by 64 slice MSCT imaging

Based on our experience, each PV and LA could be seen by 64 slice MSCT without technical difficulty in every subject. Clinically, several imaging modalities, such as pulmonary PV angiography, TEE, intracardiac echocardiography(ICE), MSCT and MRA, are available for visualization of PVs. Although it must be recognized that a standardized measurement of the PV ostia has not been developed, studies have showed that MSCT allows accurate and reproducible assessment of PVs and provides optimal delineation of PVs and their connection with the LA through 3D reconstruction. MSCT examination is noninvasive, relatively independent of operator skill, and has a wide field of view. With the three-dimensional multiple-plane reconstruction method, the four PVs and their junction with the LA can be seen clearly. In addition, the present study evaluated the diameters of PV ostia in the AP and SI views, which had been applied in previous studies. It might supply more information about PVs ostia morphology from different directions. 64 slice MSCT, with its improved spatial and temporal resolution, provides high quality image and facilitates the assessment of PVs. Moreover, the scanning time may be shortened, allowing a decreased breath-hold time, a better exploitation of contrast media with less enhancement of adjacent structures, and a lower dose of applied contrast media.

Study limitations

Whether the PVs ostia dilation observed in patients with CHF in the present study is responsible for the increased incidence of clinical AF seen in patients with CHF remains speculative, we need continuous follow-up to investigate the incidence of AF in those patients with CHF and PVs dilation. On the other hand, the relationship between PVs dilation and their electrophysiological characteristics triggering or initiat-

Table 3. Diameters of the left atria in CHF and control groups (mm)

<table>
<thead>
<tr>
<th></th>
<th>CHF (n=25)</th>
<th>Control (n=26)</th>
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<tbody>
<tr>
<td>LA1</td>
<td>51.7±8.6**</td>
<td>40.4±7.8</td>
</tr>
<tr>
<td>LA2</td>
<td>42.0±6.6**</td>
<td>32.4±5.8</td>
</tr>
<tr>
<td>LA3</td>
<td>56.2±6.1**</td>
<td>49.5±4.8</td>
</tr>
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</table>

Values are mean ± standard deviation. **P<0.01 compared with control subjects. LA1: the maximal left-right diameter of the LA on coronal section; LA2: the maximal anteroposterior diameter of the LA on transverse section; LA3: the maximal superoinferior diameter of the LA on sagittal section.
Conclusions

This study demonstrated that ostial PV diameter and LA size in patients with CHF were increased and involved most PVs ostia. These anatomic changes may supply a kind of arrhythmia substrate for the development of AF in CHF patients.

References