Clinical Significance of Collateral Superficial Vein Across Clavicle in Patients With Cardiovascular Implantable Electronic Device

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Background: Obstruction of the access vein is a well-known complication after cardiovascular implantable electronic device (CIED) implantation. In that case, well-developed collateral superficial veins are frequently observed on the skin surface around the CIED. The aim of this study was to clarify the relationship between venous obstruction and development of a superficial vein across the clavicle.

Methods and Results: A total of 107 patients scheduled for generator replacement, device upgrade, or lead extraction were enrolled. The skin surface around the device was photographed. A 20-ml bolus of contrast medium was injected into a peripheral arm vein on the side of CIED implantation, and contrast venography was performed. Venous obstruction was defined as luminal diameter narrowing >75%. Venography showed venous obstruction in 27 patients (25.2%). There were no statistically significant differences in patient characteristics between the venous obstruction and no venous obstruction group. Of 107 patients, 44 (41.1%) had a superficial vein across the clavicle on the side of CIED implantation. The sensitivity of the presence of a superficial vein across the clavicle in the diagnosis of venous obstruction was 96.3% and specificity was 77.5% (P<0.001).

Conclusions: The presence of a superficial vein across the clavicle is useful for the prediction of venous obstruction in patients with CIED. (Circ J 2014; 78: 1846–1850)

Key Words: Collateral circulation; Pacemaker; Stenosis; Vein

The number of cardiovascular implantable electronic devices (CIED) in use continues to grow worldwide because of their potency for the treatment of ventricular tachyarrhythmia and heart failure. There is controversy, however, regarding the implantation of permanent electrodes in relation to induction of obstruction of the access vein. Several investigators have shown that during the following period after implantation of pacing leads, venous obstruction was observed in 10–35% of CIED patients. Venous obstruction and thrombosis may impede lead extraction, increase the risk of pulmonary embolism, induce superior vena cava syndrome, or affect hemodialysis access patency. At present, venography is considered the gold standard for the diagnosis of venous obstruction, but venography requires use of an ioddinated contrast agent, which may cause allergic reaction or nephrotoxicity. Recently, venous Doppler ultrasonography has been utilized in some prospective studies, but has limitations in diagnosing innominate vein obstruction.

Well-developed superficial veins are frequently observed on the skin surface around the CIED during follow-up. In the case of venous obstruction in CIED-implanted patients, contrast venography shows that the main routes of collateral circulation frequently run toward the jugular vein. Therefore, we considered that collateral circulation close to the skin surface may run across the clavicle and reach the jugular vein. To the best of our knowledge, research on the collateral superficial vein correlating with venous obstruction has not yet been reported. Therefore, we investigated the collateral superficial vein across the clavicle as a non-invasive predictor of venous obstruction. The aim of the present study was to clarify the relationship between obstruction of the access vein and development of a superficial vein across the clavicle after CIED implantation.

Methods

A total of 107 patients scheduled for generator replacement, device upgrade, or lead extraction at Yokohama City University Hospital between 2010 and 2013 were enrolled. Patients with renal insufficiency (serum creatinine ≥2.0 mg/dl) or a history
of contrast medium hypersensitivity were excluded. The skin surface around the implanted device was photographed with a digital camera in all patients, and the development of superficial veins visible on the skin surface was carefully observed. This study was approved by the Yokohama City University Hospital Ethics Committee (approval number B080703013), and written informed consent was obtained from all patients.

Contrast venography was performed by placing a cannula in a peripheral arm vein on the side of CIED implantation, and a 20-ml bolus of contrast medium was injected through the cannula before generator replacement, device upgrade, or lead extraction. Contrast medium flow in the axillary vein, subclavian vein, innominate vein, and superior vena cava as well as collateral circulation was observed and recorded on cineangiography. Freeze-frame images with complete opacification of the lumen by contrast medium were selected for measurement. The narrowest and widest points of the target vessels were identified by visual inspection to obtain minimum and maximum venous diameters.

Statistical Analysis
Comparisons of quantitative and categorical variables between groups were done using Pearson chi-squared test or Student’s t-test. All continuous data are expressed as mean ± SD. For all tests, P<0.05 was considered statistically significant. All statistical analysis was carried out using SPSS.

Results
Baseline Characteristics
The mean subject age was 68.9±14.4 years, and 62% were men. The indication for original device implantation was sick sinus syndrome in 42%, atrioventricular block in 28%, ventricular tachycardia in 21%, and refractory heart failure in 7%. There were 76 patients with a pacemaker, 25 with an implantable cardioverter defibrillator (ICD), and 6 with a cardiac resynchronization therapy-defibrillator (CRT-D) or cardiac resynchronization therapy-pacemaker (CRT-P). The mean number of leads was 2.0±0.5. The underlying disease was hypertension in 41%, diabetes mellitus in 12%, atrial fibrillation in 31%, cerebral infarction in 7%, dilated cardiomyopathy in 10%, and coronary artery disease in 4%. The proportion of patients receiving warfarin was 27%, and that receiving antiplatelet drugs was 20%. Mean baseline serum creatinine was 1.05±1.14 mg/dl, and d-dimer was 1.18±2.69 mg/dl. Echocardiographic evaluation was performed before generator replacement, lead revision, or device upgrade. Mean left ventricular ejection fraction (LVEF) was 61.9±14.0%.

Contrast Venography
Mean follow-up period after initial implantation was 119.9±70.8 months. Contrast medium-associated complications were not seen in any patients during the acute period or at follow-up. Venous obstruction was defined as luminal diameter narrowing >75%. Contrast venography showed venous obstruction in 27 (25.2%) of 107 patients. Each patient had well-developed venous collateral circulation. Of 27 patients with venous obstruction, 18 had total occlusion. The site of venous obstruction was the left subclavian vein in 17 of 27 patients, right subclavian vein in 1 patient, and left innominate vein in 9 patients.

Risk Factors for Venous Obstruction
The patients were divided into 2 groups: a venous obstruction group (n=27) and a no venous obstruction group (n=80). Clinical characteristics were compared between the 2 groups, and risk factors for venous obstruction were investigated (Table). There were no statistically significant differences in age, sex, diabetes mellitus, atrial fibrillation, or follow-up period after initial implantation between the 2 groups. There were also no statistically significant differences in number of leads, LVEF, or use of warfarin or antiplatelet drugs.

### Table. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Venous obstruction (n=27)</th>
<th>No venous obstruction (n=80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69.4±13.5</td>
<td>68.8±14.8</td>
<td>0.857</td>
</tr>
<tr>
<td>Male</td>
<td>15 (55.6)</td>
<td>51 (63.8)</td>
<td>0.454</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>17 (63.0)</td>
<td>59 (73.8)</td>
<td>0.290</td>
</tr>
<tr>
<td>ICD</td>
<td>8 (29.6)</td>
<td>17 (21.3)</td>
<td>0.378</td>
</tr>
<tr>
<td>CRT-D(P)</td>
<td>2 (7.4)</td>
<td>4 (5.0)</td>
<td>0.642</td>
</tr>
<tr>
<td>Period after implantation (months)</td>
<td>102.6±72.7</td>
<td>125.9±69.5</td>
<td>0.140</td>
</tr>
<tr>
<td>No. leads</td>
<td>2.07±0.39</td>
<td>1.98±0.55</td>
<td>0.389</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (40.7)</td>
<td>33 (41.2)</td>
<td>0.963</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2 (7.4)</td>
<td>11 (13.8)</td>
<td>0.388</td>
</tr>
<tr>
<td>Smoke</td>
<td>11 (40.7)</td>
<td>33 (41.3)</td>
<td>0.963</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>9 (33.3)</td>
<td>24 (30.0)</td>
<td>0.749</td>
</tr>
<tr>
<td>EF (%)</td>
<td>58.7±18.0</td>
<td>63.0±12.4</td>
<td>0.227</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.17±1.65</td>
<td>1.01±0.91</td>
<td>0.534</td>
</tr>
<tr>
<td>D-dimer &gt;1μg/ml</td>
<td>10 (37.0)</td>
<td>21 (26.3)</td>
<td>0.246</td>
</tr>
<tr>
<td>Warfarin</td>
<td>10 (37.0)</td>
<td>19 (23.8)</td>
<td>0.183</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>6 (22.2)</td>
<td>15 (18.8)</td>
<td>0.698</td>
</tr>
<tr>
<td>ACEI or ARB</td>
<td>13 (48.1)</td>
<td>26 (32.5)</td>
<td>0.147</td>
</tr>
<tr>
<td>β-blocker</td>
<td>8 (29.6)</td>
<td>13 (16.3)</td>
<td>0.133</td>
</tr>
</tbody>
</table>

Data given as mean±SD or n (%). ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRT-D(P), cardiac resynchronization therapy-defibrillator/pacemaker; EF, ejection fraction; ICD, implantable cardioverter defibrillator.
Significance of Collateral Superficial Vein Across Clavicle
We focused on the presence of a collateral superficial vein across the clavicle visible on the skin surface. Of 107 patients, 44 (41.1%) had a superficial vein across the clavicle on the side of CIED implantation. Among these patients, we describe the case of a typical patient who had a superficial vein across the clavicle together with vein obstruction, as follows. Patient 1 was a 67-year-old man, in whom a pacemaker had been implanted 6 years previously, and who was referred for pacemaker replacement because of battery depletion. Collateral superficial veins across the left clavicle were clearly observed on the skin surface (Figure 1). Contrast venography just before pacemaker replacement showed total occlusion of the left innominate vein with collateral circulation toward the jugular vein (Figure 2). Patient 2 (a 59-year-old woman in whom an ICD was implanted 6 months previously) is shown in Figures 3, 4. This patient was referred for left ventricular pacing lead implantation and device upgrade to CRT-D. Superficial veins across the clavicle were seen on the skin surface (Figure 3). Contrast venography showed total occlusion of the left subclavian vein with collateral circulation toward the jugular vein (Figure 4).

A total of 107 patients were subdivided into 4 groups: venous obstruction with superficial vein across clavicle (subgroup A); venous obstruction without superficial vein across clavicle (subgroup B); no venous obstruction with superficial vein across clavicle (subgroup C); and no venous obstruction without superficial vein across clavicle (subgroup D); and the numbers in subgroups A, B, C, and D were 26, 1, 18, and 62, respectively. Accordingly, the sensitivity of the presence of a superficial vein across the clavicle in the diagnosis of venous obstruction was 96.3% and specificity was 77.5% (P<0.001).

Discussion
The present study suggests that the presence of a superficial vein across the clavicle is useful for the prediction of venous obstruction in patients with CIED.

There are several reports about venous obstruction after CIED implantation. The first large study reported by Goto et al evaluated 100 consecutive patients undergoing elective replacement of a pacemaker.² Twenty-one venograms (21%) showed moderate-severe venous stenosis, defined as luminal diameter narrowing >50% in 9 patients and total occlusion in 12 patients. Oginosawa et al noted venous obstruction >60% in 26 (32.9%) of 79 patients after implantation of pacing leads.³ Da Costa et al evaluated a large sample of 202 patients 6 months after pacemaker implantation and reported that venography showed severe stenosis (70–99% narrowing) in 31 patients (15%) and total occlusion in 12 patients (6%).⁴ Recently, widening of the indications and technological advances have resulted in a marked increase in ICD and CRT-D (-P) implantation.¹⁷,¹⁸ Follow-up procedures such as generator replacement and lead extraction are also expected to rapidly increase. Lickfett et al reported that contrast venography performed prior to the first elective ICD generator replacement showed complete occlusion in 9% and severe stenosis (>75%) in 6% of 105 patients.¹⁹ In the present study, a total of 107 patients scheduled for pacemaker or ICD or CRT-D (-P) generator replacement, device upgrade, or lead extraction were enrolled. Contrast venography showed venous obstruction, which was defined as luminal...
Superficial Vein Across Clavicle in CIED Patients

In 107 patients, 44 (41.1%) had a superficial vein across the clavicle on the side of CIED implantation. As already noted, 27 patients developed venous obstruction, of whom 26 were found to have a superficial vein across the clavicle. In contrast, of 80 patients with no venous obstruction, 62 did not have a superficial vein across the clavicle. Accordingly, the sensitivity of the presence of a superficial vein across the clavicle in the diagnosis of venous obstruction was calculated to be 96.3% and specificity was 77.5% (P<0.001). These results, especially the high sensitivity, suggest that the presence of a superficial vein across the clavicle can be useful for the prediction of venous obstruction in patients with CIED. The specificity, however, was not relatively high because 18 patients with no venous obstruction had a superficial vein across the clavicle.

Well-developed superficial veins were frequently observed on the skin surface around the CIED during follow-up. In cases of obstruction of the access vein after CIED implantation, contrast venography showed that the main routes of collateral circulation frequently ran toward the internal or external jugular vein. Therefore, we considered that newly developed collateral circulation close to the skin surface may run across the clavicle and reach the jugular vein, and conducted a study to test the hypothesis that a collateral superficial vein across a clavicle visible on the skin surface might be a valuable predictor of venous obstruction. In 107 patients, 44 (41.1%) had a superficial vein across the clavicle on the side of CIED implantation. As already noted, 27 patients developed venous obstruction, of whom 26 were found to have a superficial vein across the clavicle. In contrast, of 80 patients with no venous obstruction, 62 did not have a superficial vein across the clavicle.

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most of them had some collateral circulation toward the jugular vein in spite of having no venous obstruction. Considering that collateral circulation toward the jugular vein generally reflects the existence of some disorder of blood flow, these patients might have had some risk of development of venous obstruction caused by blood flow disturbance due to the pacing lead itself in the future, which needs further investigation.

Another non-invasive method of detecting venous obstruction is ultrasonography. According to Nishino et al, ultrasonography can accurately show severe access vein stenosis due to thrombosis after CIED implantation. It was difficult, however, to visually detect the proximal or distal innominate vein and superior vena cava precisely on ultrasonography. We first focused on the superficial veins on the skin surface around the CIED, and found a collateral superficial vein across the clavicle to be a simple and non-invasive marker to predict venous obstruction without difficulty compared with ultrasonography. This suggests that most patients without a superficial vein across a clavicle do not have obstruction of the access vein, and contrast venography might be unnecessary. In contrast, in patients with a superficial vein across a clavicle, the present findings underline the importance of contrast venography, especially when adding or extracting a CIED lead.

In order to confirm this result, however, we have to consider the following study limitations. One possible limitation is that this study was a small-sample-size, single-center analysis. Venous obstruction in some patients with de novo CIED implantation is a significant issue. In the present study, however, contrast venography was not performed and the development of superficial veins visible on the skin surface was not assessed before CIED implantation, which are other limitations. Further study with a larger sample size is needed to confirm the present results.

Conclusions

The presence of a collateral superficial vein on the skin surface around the CIED during follow-up is very closely correlated with obstruction of the access vein. Especially, the presence of a superficial vein across the clavicle is useful for the prediction of venous obstruction in patients with CIED.

References