Cardioscopic Detection of Left Ventricular Thrombi
– With Special Reference to a Comparison With Left Ventriculography and Echocardiography –
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Background: Thrombosis occurs in the left ventricle and causes ischemic cerebral attacks. However, differences in the incidence of left ventricular thrombi (LVT) among various categories of heart diseases are not known.

Methods and Results: From April 2000 to 31 March 2008, 258 patients (104 females and 154 males; age 63±6 years) with a heart disease underwent cardioscopy of the left ventricle. LVT were detected by cardioscopy in 78 of 258 patients; 12.5% of 57 patients with stable angina, 0% of 9 with unstable angina, 45.2% of 42 with acute myocardial infarction, 23.2% of 43 with old myocardial infarction, 61.9% of 21 with idiopathic acute myocarditis, 44.3% of 68 with idiopathic chronic myocardiitis, 33.3% of 6 with rheumatic valvular disease, 25.7% of 31 with idiopathic dilated cardiomyopathy and in 8.0% of 12 with idiopathic hypertrophic cardiomyopathy. Nine of 78 thrombi were globular and 69 were mural. The detection rate of LVT by cardioscopy, left ventriculography, non-contrast and contrast echocardiography was 30.2%, 2.7%, 1.9% and 7.0%, respectively.

Conclusions: LVT were frequently detected by cardioscopy in patients with heart diseases. Although invasive, cardioscopy was more sensitive in detecting LVT than left ventriculography, and non-contrast and contrast echocardiography. (Circ J 2011; 75: 1920–1926)

Key Words: Cardioscopy; Contrast echocardiography; Left ventricular thrombi; Non-contrast echocardiography; Ventriculography

It is well known that a fibrillating left atrium is the site of thrombus formation and acts as a major supply source of thromboemboli in cerebral ischemic attacks.\(^1\)\(^\text{-}\)\(^4\) It is also known that the left ventricle is the site of thrombus formation in a post-infarction state.\(^5\) There have been many case reports on left ventricular thrombi (LVT) in other categories of heart disease such as peripartal cardiomyopathy,\(^6\) idiopathic dilated cardiomyopathy (DCM),\(^7\) acute myocarditis (AM),\(^8\) and antiphospholipid syndrome,\(^9\) and they cause cerebral embolism.\(^10\)\(^\text{-}\)\(^11\) However, the exact incidence of LVT in various categories of heart disease is not well known due to the lack of systematic surveys.

Non-contrast echocardiography (UCG),\(^5\) contrast UCG,\(^5\)\(^,\)\(^12\) computed tomography,\(^13\) magnetic resonance imaging,\(^5\)\(^,\)\(^12\) and left ventriculography have been used for the detection of LVT in left atrial thrombi or pulmonary thromboemboli.\(^14\)\(^,\)\(^15\) Although large globular thrombi can be detected, small-sized mural thrombi are difficult to detect using these imaging modalities. Furthermore, because the shadows of the targets are imaged, definite determination of thrombi is beyond these imaging modalities. Therefore, thrombus characteristics, namely whether the thrombi are fresh or organized, or red blood cell-rich or platelet-rich, which might influence the selection of the therapeutic modality, are difficult to determine with these imaging modalities.

Cardioscopy, specially fiberoptic angioscopy of the heart, is a high resolution imaging modality that enables macroscopic pathological diagnosis of heart diseases. This technique was applied for observation of the cardiac chambers and valves and abnormal intracardiac structures, including LVT.\(^16\)\(^\text{-}\)\(^19\)

In the present study, percutaneous cardioscopy was performed to examine the incidence of LVT in patients with various types of heart diseases, and to compare the detection sensitivities among cardioscopy, left ventriculography, non-contrast UCG, and contrast UCG.
Methods

Subjects
From 1 April 2001 to 31 March 2008, 258 patients with heart diseases [104 females and 154 males; mean age ± SD, 63±6 years; 56 with stable angina (SA), 9 with unstable angina (UA), 42 with acute myocardial infarction (AMI), 43 with old myocardial infarction (OMI); 1 month or more since the onset of AMI] complicated with or without SA, 21 with AM and 38 with chronic myocarditis diagnosed based on Japanese Circulation Society criteria, 6 with rheumatic valvular disease, 31 with idiopathic DCM and 12 with idiopathic hypertrophic cardiomyopathy diagnosed by ventriculography and endomyocardial biopsy, underwent cardioscopy for detection of LVT (Table 1).

The present study was performed at Toho University Medical Center, Sakura Hospital and Funabashi-Futawa Hospital and was approved by their Institutional Review Boards. All the patients provided informed consent for the procedures.

Non-Invasive Examinations Before Cardiac Catheterization
On admission, chest X-rays, electrocardiograms, blood sampling, and transthoracic non-contrast UCG followed by contrast-UCG were carried out. Contrast-UCG was not performed in hemodynamically unstable patients, so they were excluded from the analyses.

Cardioscopy System
The cardioscopy system was composed of a light source, 4.5-F fiberscope, 9-F guiding balloon catheter, intensified chilled coupled device camera, camera controller, DVD recorder and television monitor.

The fiberscope (AF 14; Olympus Corporation, Tokyo) was composed of a 4.5-F fiberscope containing 3,000 glass fibers for image guidance and 300 glass fibers for light guidance. The fiberscope could be passed through the 9-F guiding balloon catheter (Clinical Supply Co, Gifu, Japan). The balloon was inflatable with CO₂. The catheter had a Y connector at the proximal end; 1 channel for fiberscope insertion and another for saline solution flush. The fiberscope and guiding balloon catheter have been approved for clinical use by the Japanese Ministry of Health, Labor and Welfare.

Table 1. Background of Patients With Heart Diseases

<table>
<thead>
<tr>
<th>Heart diseases</th>
<th>n</th>
<th>Gender (F/M)</th>
<th>Age (years)</th>
<th>Time from onset*</th>
<th>LVG EDVI (ml/m²)</th>
<th>EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA</td>
<td>56</td>
<td>18/38</td>
<td>62±7</td>
<td>4.7±2.3 m</td>
<td>76±5</td>
<td>64±9</td>
</tr>
<tr>
<td>UA</td>
<td>9</td>
<td>3/6</td>
<td>64±3</td>
<td>1.3±0.5 d</td>
<td>85±10</td>
<td>53±11</td>
</tr>
<tr>
<td>AMI</td>
<td>42</td>
<td>14/28</td>
<td>63±5</td>
<td>1.6±0.8 d</td>
<td>78±8</td>
<td>50±8</td>
</tr>
<tr>
<td>OMI</td>
<td>43</td>
<td>21/22</td>
<td>63±6</td>
<td>8.2±7.8 m</td>
<td>81±11</td>
<td>54±7</td>
</tr>
<tr>
<td>AM</td>
<td>21</td>
<td>13/8</td>
<td>48±9</td>
<td>5.2±3 d</td>
<td>78±9</td>
<td>47±9</td>
</tr>
<tr>
<td>CM</td>
<td>38</td>
<td>26/12</td>
<td>52±9</td>
<td>4.1±3 m</td>
<td>91±15</td>
<td>51±10</td>
</tr>
<tr>
<td>RVD</td>
<td>8</td>
<td>4/2</td>
<td>42±4</td>
<td>16.9±8 m</td>
<td>88±12</td>
<td>56±6</td>
</tr>
<tr>
<td>DCM</td>
<td>31</td>
<td>14/17</td>
<td>46±5</td>
<td>4.2±2.7 m</td>
<td>113±15</td>
<td>45±8</td>
</tr>
<tr>
<td>HCM</td>
<td>12</td>
<td>3/9</td>
<td>52±8</td>
<td>8.3±4.2 m</td>
<td>67±15</td>
<td>74±7</td>
</tr>
</tbody>
</table>

*Time from onset of subjective symptoms or clinical diagnosis to cardioscopy.

n, number of patients; F, female; M, male; LVG, left ventriculography; EDVI, left ventricular enddiastolic volume index; EF, ejection fraction; SA, stable angina; m, months; UA, unstable angina; d, days; AMI, acute myocardial infarction; OMI, old myocardial infarction; AM, acute idiopathic myocarditis; CM, chronic idiopathic myocarditis; RVD, rheumatic valvular disease; DCM, idiopathic dilated cardiomyopathy; HCM, idiopathic hypertrophic cardiomyopathy.

Observation of the LVT by Cardioscopy
In a preliminary experimental cardioscopic study, it was confirmed that the thrombi that had formed on the endocardial surface of the infarcted portion were not detached by saline solution infusion using a power injector toward the thrombi. 16

At first, the right femoral artery was cannulated and left ventriculography and coronary angiography were performed. Cardioscopy was performed in the patients based on this result. In brief, after left ventriculography, a guiding balloon catheter was introduced into the left ventricle so its distal tip was in a location that did not touch the endocardium, usually in the middle portion of the ventricle, and the balloon was inflated with CO₂ to make a dead space between the fiberscope and the target. Next, a fiberscope was introduced into the guiding catheter to place the fiberscope tip at the distal most end of the guiding catheter. Thereafter, the guiding balloon catheter was slowly advanced while infusing heparinized (10 U/ml) saline solution at a rate of 5–10 ml/s for 5 s to displace the blood between the target and the fiberscope. When a thrombus was detected, the catheter was stopped so it did not touch the thrombus. The anterior, apical, lateral and inferior wall segments of the left ventricle were surveyed in each patient. When a thrombus was detected in a segment, the other segments were not surveyed. The guiding balloon catheter tip was pre-shaped into a “S”-configuration for observation of the anterior, apical and inferior wall segments, and in a “J”-configuration for the lateral wall segment observation. 18

Cardioscopic measurement of thrombus size was difficult because the images obtained by cardioscopy were fish-eye images. 18

Cardioscopic images were displayed on a television monitor simultaneously with the fluoroscopic images and electrocardiogram. The details of the cardioscopic procedures are reported elsewhere and are shown in Figure 1. 17–19

Classification of LVT
The LVT were classified by their configuration into globular (a large thrombus protruding into the cardiac chamber occupying the entire visual field of a cardioscope) and mural (a small sized thrombus attached to the left ventricular luminal surface, not protruded, and not occupying the entire visual field of the cardioscope).

The color of the thrombi was classified into red, cotton...
candy-like white, red-and-white in a mosaic pattern, yellow, and red-and-yellow in a mosaic pattern. Intraobserver and interobserver agreements on red, cotton candy-like white, red-and-white in a mosaic pattern, yellow, and red-and-yellow in a mosaic pattern LVT were 96%, 88%, 81%, 100%, and 100%, respectively, and 91%, 88%, 81%, 97%, and 100%, respectively.

**Statistical Analysis**
The data obtained were tested by Fischer’s exact test. A $P<0.05$ was considered significant.

**Results**

**Representative Examples**

Figure 2 shows a globular thrombus that was red-and-white in a mosaic pattern and was attached to the luminal surface of the infarcted apical wall segment of the left ventricle in a patient with OMI.

Figure 3 shows demonstrable examples of mural LVT with different colors, namely red, white, yellow, and red-and-yellow in a mosaic pattern.
Incidence of LVT by Cardioscopy

The incidence of LVT in AMI was 45.2%, which was higher than in the SA group, but was not different to that of the OMI group. The incidence of LVT in the AM group was 61.9% and it was higher than that of the CM group. Although lower in incidence, LVT were observed in all other categories of heart disease except UA (Table 2).

Morphology and Color of LVT

Globular and mural thrombi were detected in 9 and 69 patients, respectively. Globular thrombi were observed in patients with AMI, OMI and AM. All globular LVT were located in the apical portion. LVT were mural in the other types of heart diseases (Table 2). The relationship between regional wall motion and presence or absence of LVT was not examined because left ventriculograms were obtained only in 2 directions and therefore to quantitatively measure regional wall motion at the site of LVT was difficult.

Red, cotton candy-like white, red-and-white in a mosaic pattern, yellow, and red-and-yellow in a mosaic pattern LVT were observed in 24, 8, 11, 27 and 2 patients, respectively. The incidence of red thrombi was higher than cotton candy-like white and red-and-white in a mosaic pattern LVT. The incidence of yellow thrombi was higher (P<0.05) than cot-

Table 2. LVT Detected by Cardioscopy, Left Ventriculography and UCG in Patients With Heart Diseases

<table>
<thead>
<tr>
<th>Heart diseases</th>
<th>n</th>
<th>Cardioscopy</th>
<th>UCG</th>
<th>LVG</th>
<th>Cont</th>
<th>Non-cont</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Thrombus present (%)</td>
<td>Thrombus globular/mural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SA</td>
<td>56</td>
<td>7 (12.5)</td>
<td>0/7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UA</td>
<td>9</td>
<td>0 (0.0)</td>
<td>0/0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AMI</td>
<td>42</td>
<td>20 (45.2)**</td>
<td>5/15</td>
<td>4</td>
<td>5 (2*)</td>
<td>6 (1*)</td>
</tr>
<tr>
<td>OMI</td>
<td>43</td>
<td>10 (23.2)</td>
<td>2/8</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>AM</td>
<td>21</td>
<td>13 (61.9)†</td>
<td>2/11</td>
<td>2</td>
<td>3 (1*)</td>
<td>5</td>
</tr>
<tr>
<td>CM</td>
<td>38</td>
<td>17 (44.3)</td>
<td>0/17</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>RVD</td>
<td>6</td>
<td>2 (33.3)</td>
<td>0/2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DCM</td>
<td>31</td>
<td>8 (25.7)</td>
<td>0/8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HCM</td>
<td>12</td>
<td>1 (8.0)</td>
<td>0/1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>258</td>
<td>78 (30.2)**</td>
<td>9/69</td>
<td>8 (2.7)</td>
<td>10 (1.9)</td>
<td>18 (7.0)</td>
</tr>
</tbody>
</table>

LVT, left ventricular thrombi; UCG, echocardiography; Non-cont, non-contrast UCG; Cont, contrast UCG. Other abbreviations are as per Table 1.

*P<0.01 vs. SA. †P<0.05 vs. CM. ‡‡P<0.0001 vs. LVG Non-cont and Cont. ‡Thrombus suspected but inconclusive.
Table 3. Color of LVT

<table>
<thead>
<tr>
<th>Heart diseases</th>
<th>Red</th>
<th>White</th>
<th>Red-and-white</th>
<th>Yellow</th>
<th>Red-and-yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AMI</td>
<td>11</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>OMI</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>AM</td>
<td>8</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CM</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>12†</td>
<td>2</td>
</tr>
<tr>
<td>RVD</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>DCM</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>HCM</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>24†</td>
<td>8</td>
<td>11</td>
<td>27§</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations as per Tables 1, 2.
*P<0.05 vs. CM. †P<0.01 vs. AM. ‡P<0.05 vs. White, Red-and-white and Red-and-yellow. §P<0.05 vs. White, Red-and-white, and Red-and-yellow.

Discussion

Incidence of LVT

In the present study, LVT were observed by cardioscopy, on average, in approximately 30% of patients with heart diseases, suggesting that LVT was prevalent in patients with heart diseases.

LVT was observed in AMI and AM more frequently than in other heart diseases. It is known that LVT are formed more frequently in a left ventricle with contraction disturbance or deformation, which causes stagnation and turbulence of blood flow. The left ventricular contraction (ejection fraction) was reduced in patients with AMI and AM. This might be the reason why LVT was frequent in these 2 diseases. Although left ventricular contraction was also decreased in patients with DCM, the incidence of LVT was less than that in AMI and AM. Loss of antithrombolytic activity of the endocardial cells due to ischemia or inflammation might also have contributed to the higher incidence of LVT in AMI and AM. Occurrence of LVT in patients with SA might have also been due to ischemia-induced endocardial cell damages.18

Fibrillating atrium is a major supplying source of thromboemboli in patients with ischemic cerebral attacks. In the present follow-up study, ischemic cerebral attacks occurred in 4 patients without atrial fibrillation. Although definite evidence is lacking, there is a possibility that LVT was the mother thrombus.

Determination of Composition and Age of LVT by Color

It is well known that a thrombus (in any vessel or cardiac chamber) forms a red color within a few days; a dark-red color at around 1 week; and a yellow color at around 1 month. When red blood cells are washed out from the surface of a recently formed thrombus, the thrombus appears soft and exhibits a white color due to exposed platelets and fibrin.24 Therefore, the red, cotton candy-like white, red-and-white in a mosaic pattern, yellow, and red-and-yellow in a mosaic pattern LVT were considered to be fresh, fresh, fresh, old, and fresh-and-old in mixture, respectively, and, red, white and cotton-candy-like white, red-and-white in a mosaic pattern were considered to be red blood-rich, fibrin and/or platelet-rich, and both red blood cell- and fibrin and/or platelet-rich, respectively.

LVT exhibiting red, cotton candy-like white, red-and-white in a mosaic pattern, and red-and-yellow in a mosaic pattern were observed in chronic diseases, suggesting repeated formation of fresh thrombi even in chronic diseases. In addition to the anatomical and functional properties of the left ventricle, the loss of anti-thrombotic action of the endocardial cells and changes in humoral mechanisms such as the thrombotic, thrombolytic and fibrinolytic actions of the blood might have contributed to the repeated LVT formation.

Comparison With Other Imaging Modalities

The rate of detection of LVT by cardioscopy was significantly higher than that by non-contrast and contrast UCG in the present study, indicating that cardioscopy is a more sensitive method for detecting LVT.

Siebenlink observed LVT by contrast UCG in 9.0% (conclusive) of 156 patients with post-infarction.5 Weinsaft observed LVT by non-contrast UCG in 6% and by contrast UCG in 12% of 121 patients with post-infarction.12 In the present study, the patients with myocardial infarction were observed by non-contrast UCG in 5.8% and by contrast UCG...
Disclosures

There are no conflicts of interest to disclose. Relationships With Industry: No relationships. Funds: This study was performed without financial support.

References


