Clinical Studies

Cardiac Thrombus in Dilated Cardiomyopathy

Relationship between Left Ventricular Pathophysiology and Left Ventricular Thrombus

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SUMMARY

The relationship between left ventricular thrombus and left ventricular dynamics in dilated cardiomyopathy (DCM) was studied by echocardiography and postmortem examination.

The subjects were 57 patients with DCM, 40 were survival patients examined by echocardiography and 17 were autopsy patients. Systemic or pulmonary embolism occurred in 10 of 57 patients, 4 of 40 survival patients and 6 of 17 autopsy patients. Intracardiac thrombus was detected in 11 of 40 survival patients and was found in 8 of 17 autopsy patients.

Left ventricular segmental wall motion abnormalities were observed in all 40 patients examined by two-dimensional echocardiography and apical dyskinesis or akinesis was observed more frequently in patients with left ventricular thrombus than in patients without left ventricular thrombus. Of 33 patients examined by pulsed Doppler echocardiography, Doppler ejection flow signals in the apical long axis view were recorded in 9% at the apex, in 17% at the middle portion and in 57% at the portion near the interventricular septal center. The signals at the portion near the interventricular septal center were recorded in only 2 patients with left ventricular thrombus but in 66% of patients without left ventricular thrombus.

Systemic or pulmonary embolism and intracardiac thrombus occurred less frequently in patients treated with warfarin than in patients without warfarin.

These results indicate that endomyocardial and blood flow disorders of the left ventricle play important roles in the occurrence of left ventricular thrombus and that anticoagulant therapy is useful for the prevention of systemic or pulmonary embolism and cardiac thrombus.
Dilated cardiomyopathy (DCM) is a heart disease of poor prognosis, with congestive heart failure progressing due to a myocardial lesion of unknown cause. This disease frequently follows a downhill course ending in death from congestive heart failure, or results in sudden death due to arrhythmias. Cardiac thrombus occurs at a high incidence in association with DCM, causing embolism, which leads to death, or exacerbation of congestive heart failure and arrhythmia, in a considerable proportion of cases. The present study was aimed at elucidating the relationship between the left ventricular pathophysiological state and left ventricular thrombus.

**Methods**

*Patients:*

The subjects were 57 patients with DCM accompanied by marked left ventricular enlargement and impaired cardiac contractility without an apparent cause, such as valvular, hypertensive and ischemic heart disease. There were 46 male and 11 female patients ranging in age from 23 to 64 years (average, 44 years). The 57 patients consisted of 17 autopsy patients with a mean age of 34 years and 40 survival patients with a mean age of 48 years. All of survival patients were diagnosed by echocardiographic and angiographic examinations and none were found to have coronary artery stenosis by coronary angiography and none of the autopsy patients had any coronary lesion. Out of 57 patients 10 had a history of a systemic embolic episode since the time of initial manifestation of the disease.

*Echocardiography:*

An echocardiographic study was performed in the 40 survival patients using Toshiba’s ultrasonoscope SSH 11A and pulsed Doppler unit SDS 10A. M-mode echocardiogram and pulsed Doppler echocardiogram were recorded by stripchart recorder, and two-dimensional echocardiogram (2DE) on Polaroid film and video tape.

The presence or absence of a cardiac thrombus was determined by 2DE. Thrombus was defined as a consistent mass of refractile echoes that was detected with 2DE in more than two different views, was clearly seen throughout the cardiac cycle, projected into the left ventricular cavity, had a distinct border, and was contiguous with the endocardium.
In order to evaluate segmental wall motion of the left ventricle, the left ventricle was divided into 9 segments consisting of anterior (segments 1 and 5), lateral (segments 2 and 6), posterior wall (segments 3 and 7) and medial (segments 4 and 8) at the mitral valve level and papillary muscle level and the apex (segment 9) according to Heger et al’s segmentation as shown in the schematic diagram of Fig. 1. Segmental wall motion was rated by visual inspection on a scale of 4 grades (dyskinesis, akinesis, hypokinesis and normokinesis). If different wall motion abnormalities coexisted in a segment, the most extensive abnormality was used. In this study extent and grade of wall motion abnormality were evaluated independently by 2 observers without knowledge of other clinical findings such as the electrocardiogram, cineangiographic findings and so on. The correlation between evaluations of wall motion abnormalities in 440 segments was r=0.92 by each observer. When discrepancies occurred between the evaluations of 2 observers, the grade of wall motion abnormality was re-evaluated by consensus with a third observer.

Pulsed Doppler echocardiograms of the apical long axis view were obtained from 35 of 40 survival patients and 10 normal healthy subjects. The depth of the sample volume with this instrument is variable to a maximum of 16 cm from the transducer and the sample volume length is adjustable from 2 to 10 mm. As we previously reported, intra-left ventricular flows in 3 regions, left ventricular apex (A), left ventricular center (B) and a left ventricular region near the interventricular septal center (D), were obtained for examination of the presence or absence of ejection flow in each area (Fig. 2). The Doppler sampling direction of flow in each area was adjusted to within less than 20 degrees. Absence of systolic ejection flow in each region was defined as a flow velocity of less than 16 cm/sec.

M-mode echocardiogram, spatially oriented from the 2DE long axis
image from the parasternal approach, was used to obtain end-diastolic and end-systolic dimensions (LVDd and LVDs) and % fractional shortening \( \left( \% FS = \frac{LVDd - LVDs}{LVDd} \times 100 \right) \).

**Cineangiography:**

All 40 survival patients underwent coronary arteriography and left ventriculography using an area length method.\(^{14} \) No coronary lesion was revealed in any of them and left ventricular ejection fraction (EF) was obtained by left ventriculography.
Autopsy study:
In all the autopsy patients cardiac weight and presence or absence of cardiac thrombus in each cardiac chamber were determined from autopsy records. All autopsy patients were grossly free of atherosclerotic plaques in the extramural coronary artery.

Anticoagulant therapy:
Out of 57 patients with DCM, 21, consisting of 7 of 17 autopsy patients and 14 of 40 survival patients, were treated with warfarin. The presence of warfarin treatment was defined as warfarin administration at echocardiographic examination in survival patients or just before death in autopsy patients, respectively.

Statistical analysis:
Average values are presented as mean±SD. Comparison of M mode echocardiographic and histopathologic parameters was done with Student's unpaired t-test. Nonparametric values were compared by Fisher's exact test. A p value <0.05 was considered statistically significant.

RESULTS

1. Incidences of embolism and cardiac thrombus (Table I)

Emboli occurred in 10 of the 57 DCM patients, and these 10 patients included 6 of the 17 autopsy patients and 4 of the 40 survival patients. The embolic site was the lung in 6 patients, kidney in 4, brain in 3 and intestine in 1. Cardiac thrombus was observed in 19 of the 57 patients, and these 19 included 11 of the 40 survival patients. Of the survival patients, the thrombus was detected in the left ventricle in 11 patients and right ventricle in 1, being located at the cardiac apex in all patients. Of the 17 autopsy patients, thrombus was observed in 8, being present in the left ventricle, right ventricle and right atrium in 6 patients each and in the left atrium in 2 patients.

2. Cardiac weight, left ventricular size and left ventricular function (Table II)

Although there was no significant difference in heart weight in autopsy patients and left ventricular end-diastolic dimension in survival patients be-

Table I. The Incidences of Embolic Episode and Intracardiac Thrombus in Patients with Dilated Cardiomyopathy

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<thead>
<tr>
<th></th>
<th>embolic episode</th>
<th>cardiac thrombus</th>
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<tbody>
<tr>
<td>autopsy 17 cases</td>
<td>6 (35%)</td>
<td>7 (41%)</td>
</tr>
<tr>
<td>survival 40 cases</td>
<td>4 (10%)</td>
<td>11 (28%)</td>
</tr>
<tr>
<td>total 57 cases</td>
<td>10 (18%)</td>
<td>18 (32%)</td>
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between the patients with and without cardiac thrombus, the patients with cardiac thrombus had lower %FS and lower EF than those without thrombus (\( %\text{FS} : 13.1 \pm 4.5 \) vs \( 17.9 \pm 7.9 \), \( p < 0.001 \); \( \text{EF} \): \( 24.8 \pm 14.8 \) vs \( 38.6 \pm 9.3 \), \( p < 0.001 \)).

3. Abnormality of regional left ventricular wall motion (Fig. 3)

2DE revealed wall motion abnormalities in all 9 segments of the left

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>autopsy heart weight (g)</th>
<th>autopsy patient</th>
<th>No. of cases</th>
<th>echo</th>
<th>survival patient</th>
<th>LVG</th>
</tr>
</thead>
<tbody>
<tr>
<td>cardiac (+)</td>
<td>8</td>
<td>555 \pm 86</td>
<td>(11)</td>
<td>71.8 \pm 13.7</td>
<td>13.1 \pm 4.5*</td>
<td>24.8 \pm 14.8*</td>
</tr>
<tr>
<td>thrombus (-)</td>
<td>9</td>
<td>601 \pm 129</td>
<td>(29)</td>
<td>68.7 \pm 6.7</td>
<td>17.9 \pm 7.9</td>
<td>38.6 \pm 9.3</td>
</tr>
<tr>
<td>total</td>
<td>17</td>
<td>580 \pm 113</td>
<td>(40)</td>
<td>60.2 \pm 7.0</td>
<td>15.6 \pm 6.4</td>
<td>32.1 \pm 10.4</td>
</tr>
</tbody>
</table>

* \( p < 0.001 \)

\((+)\)=patients with cardiac thrombus; \((-)\)=patients without cardiac thrombus; \(Dd\)=end-diastolic left ventricular dimension; \(\%FS\)=percent fractional shortening; \(\text{EF}\)=ejection fraction; \(\text{echo}\)=echocardiography; \(\text{LVG}\)=left ventriculography.

The patients with intracardiac thrombus had more reduced \% fractional shortening and ejection fraction than those without thrombus.

**Table II. Comparison of Heart Weight, Left Ventricular Size and Contractility between Patients with Dilated Cardiomyopathy with or without Cardiac Thrombus**

**Fig. 3.** Incidences of wall motion abnormality in each segment of left ventricle in patients with dilated cardiomyopathy. Upper panel shows incidences of akinetic or dyskinetic segments in patients with or without left ventricular thrombus. Lower panel shows incidences of segments with any degree of wall motion abnormality in patients with or without left ventricular thrombus.
ventricular wall in 26 of the 40 survival patients. Abnormality of wall motion in the apex was noted in all 40 survival patients, with akinesis or dyskinesis being observed in 19 patients (48%). As shown in Fig. 3, the frequency of these severe wall motion abnormalities in the apex was definitely higher in the group showing thrombus in the left ventricle than in the thrombus-free group (9 of 11 vs 12 of 29 segments, p<0.05). Furthermore, wall motion at the site of thrombus attachment showed a higher degree of abnormality than did the remaining area within the same segment, and this abnormality was akinesis or dyskinesis in all patients.

4. Left ventricular ejection flow (Fig. 4)

Figure 4 shows the incidences of left ventricular ejection flows detected by the pulsed Doppler method in 35 patients of DCM. Ejection flow was detected in the A, B and D regions in all 10 normal subjects. Of the 35 patients with DCM, ejection flow was detected at the A region (apex) in 3 patients (9%), B region (left ventricular center) in 6 (17%) and D region (a left ventricular region near the interventricular septal center) in 20 patients. In the group with left ventricular thrombus, A and B regions were completely devoid of ejection flow, and the flow at the D region was present only in 2 patients.

<table>
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<tr>
<th>sampling site</th>
<th>A</th>
<th>B</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mural thrombus (+)</td>
<td>8 cases</td>
<td>0</td>
<td>2 (25)</td>
</tr>
<tr>
<td>(-)</td>
<td>25 cases (12)</td>
<td>3</td>
<td>16 (64)</td>
</tr>
<tr>
<td>total</td>
<td>33 cases (9)</td>
<td>6</td>
<td>18 (55)</td>
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Fig. 4. Incidences of ejection flow signal recorded at 3 portions (A, B and D) of the left ventricle in patients with dilated cardiomyopathy. Abbreviations are same as in Fig. 2.
thus showing differences from the thrombus-free group.

5. Incidences of embolic episode and cardiac thrombus in patients with DCM with and without warfarin treatment (Tables III, IV)

Systemic or pulmonary embolism occurred in 3 of 21 patients treated with warfarin and 7 of 36 untreated patients. The incidence of embolism was not different between patients with and without warfarin. However, the incidence in the survival patients was lower in the warfarin treated group than in the untreated group (none of 14 vs 4 of 26 patients).

Cardiac thrombus was observed in 18 (32%) of 57 patients by echocardiography or autopsy. The incidence of cardiac thrombus in the warfarin treated group was significantly lower than that in the untreated group (3 of 21 patients vs 15 of 36, p<0.05). Each investigation in the survival and autopsy groups also revealed that the incidence was lower in the warfarin treated group than in the untreated group (survival group: 2 of 14 vs 9 of 26 patients, autopsy group: 1 of 7 vs 6 of 10 patients).

None of the patients who were treated with warfarin had major hemorrhagic complications.

DISCUSSION

Numerous reports have demonstrated that cardiac thrombus and peripheral or pulmonary embolism were frequently observed in DCM. The incidence of embolism varies from 13 to 38% depending on the individual report,1),6),15) and the incidence of cardiac thrombus in autopsy study6),7),15) varies from 20 to 67%. But there is only 1 report8) concerning the incidence

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<th>Table III. The Incidence of Embolic Episode in Patients with Dilated Cardiomyopathy Treated with or without Warfarin</th>
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<tr>
<td>warfarin (+)</td>
</tr>
<tr>
<td>survival</td>
</tr>
<tr>
<td>autopsy</td>
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<tr>
<td>total</td>
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<th>Table IV. The Incidence of Intracardiac Thrombus in Patients with Dilated Cardiomyopathy Treated with or without Warfarin</th>
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<tr>
<td>warfarin (+)</td>
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<tr>
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<tr>
<td>autopsy</td>
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<tr>
<td>total</td>
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of cardiac thrombus in survival patients with DCM to our knowledge.

Cardiac thrombus frequently occurs not only in the left ventricle but also in other cavities. Robert and Ferrans\(^7\) reported in their pathological study of 60 patients with DCM that 32 patients had cardiac thrombus. The left ventricle contained a thrombus in 27 patients, the right ventricle in 15, the right atrium in 12 and the left atrium in 5. Our autopsy study also revealed that cardiac thrombus was frequently observed in any of the 4 chambers. However, echocardiographic study in survival patients showed that the incidence of cardiac thrombus was lower than that in the autopsy study and the location is most commonly the left ventricle (11 patients) and infrequent in other cardiac chambers (only 1 in the right ventricle). These differences between autopsy and survival studies might have occurred because echocardiography was limited in detecting cardiac thrombus and the myocardial disorder was more advanced in autopsy patients than that in survival patients. DCM shows an increase in cardiac weight, left ventricular enlargement and a decrease in left ventricular contractility. In this study it was found that cardiac thrombus occurred more frequently in patients with more reduced left ventricular contractility, although the incidence was not related to cardiac weight and left ventricular size.

Although regional wall motion abnormalities had been thought to be uncommon\(^16\) in patients with DCM, recent reports\(^17\) to \(^19\) of studies using angiography, radionuclide and echocardiography have frequently shown regional wall motion abnormalities in patients with DCM. Our study of regional left ventricular wall motion using echocardiography has also revealed that the myocardial lesions in patients with DCM advanced nonuniformly and the left ventricular apex is the most likely site for the onset of advanced myocardial lesions. Furthermore, investigation of the left ventricular blood flow by the pulsed Doppler method has disclosed marked intra left ventricular blood flow disorders in patients with DCM. This marked blood flow disorder was observed not only in the ventricular apex, but also in the center of the left ventricle and the left ventricular portion near the interventricular septal center. The group with left ventricular thrombus showed greater disorders in left ventricular blood flow and contractility than did the thrombus-free group, and the former group also showed higher degrees of wall motion abnormality and blood flow disorder in the left ventricular apex, where thrombus occurred frequently. These findings suggest that myocardial disorders and left ventricular blood flow disorders are greatly involved in the development of thrombus in the left ventricle in patients with DCM.

Fuster et al\(^1\) demonstrated that systemic embolism occurred in 18% of patients without anticoagulant treatment but in none with it. Our study in
autopsy patients did not show a lower incidence of embolic episodes in the warfarin-treated group than that in the untreated group. The reason might be that the presence of warfarin treatment was defined as warfarin administration just before death in this study. In some of the autopsy patients with warfarin treatment, embolism had occurred before treatment. On the other hand, systemic or pulmonary embolism did not occur in any of the survival patients with warfarin treatment but did in 3 of those without warfarin treatment. The incidence of cardiac thrombus was significantly lower in the warfarin-treated group than in the untreated group.

Thus, endomyocardial and blood flow disorders of the left ventricle play important roles in the occurrence of left ventricular thrombus and anticoagulant therapy is useful and necessary for the prevention of peripheral or pulmonary embolism and cardiac thrombus in patients with DCM.

REFERENCES