PULMONARY EMBOLISM AS A COMPLICATION OF TRANSFEMORAL ARTERIOGRAPHY

—Incidence, Symptoms, and Prevention—

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In order to evaluate the pulmonary embolism as a complication of transfemoral arteriography, we performed lung perfusion scintigrams before and after arteriography in consecutive 120 patients. Of the initial 60 patients who did not receive subcutaneous low-dose heparin, 19 (32%) demonstrated new pulmonary perfusion defects. There was no significant difference in regard to the incidence of new defects with or without right heart catheterization. On the other hand, in the latter 60 patients who received prophylactic heparin, the incidence of new defects decreased to 10%, without increasing clinically important bleeding. We believe that the source of emboli is from the leg vein thrombosis due to compression of the groin and subsequent bed rest. These data suggest that pulmonary embolism is a more common complication of transfemoral arteriography than previously appreciated and low-dose heparin is useful in reducing this complication.

PULMONARY embolism is one of the most common and most serious complication among hospitalized patients. It is also the most commonly missed clinical entity resulting in patient mortality. Several clinical states and a variety of diseases associated with the development of pulmonary emboli have been identified in these patients. They include immobilization, cardiac diseases, traumas, obesity, neoplasms, hematologic diseases etc! In addition to above mentioned conditions, transfemoral arteriography should be considered to be one of the predisposing factors for the development of pulmonary embolism, since this procedure often causes leg vein stasis due to compression of the groin and subsequent bed rest. In fact, we recently encountered two cases of symptomatic pulmonary embolism appeared on the next day of arteriography. Furthermore, the first patient was fatal because of extensive shock. Based on our experience with these two cases, asymptomatic pulmonary embolism as a complication of arteriography seemed to occur at a higher incidence than those expected, since pulmonary embolism is a commonly missed disorder?

In order to clarify this assumption, we performed lung perfusion scintigrams before and after arteriography, and by comparing both scintigrams we determined the incidence of pulmonary embolism after arteriography, the symptoms of pulmonary embolism, and the clinical features of patients who are most easily affected by pulmonary embolism. In the latter half of the patients, we studied the prophylactic effect of subcutaneous low-dose heparin against postarteriography pulmonary embolism.

Key Words:
Pulmonary embolism
Arteriography
Complication

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### TABLE 1 SUMMARY OF THE STUDY PATIENTS

<table>
<thead>
<tr>
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<th>Group 1</th>
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<th>Group 2</th>
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<tbody>
<tr>
<td></td>
<td>Total</td>
<td>PND (+)</td>
<td>PND (−)</td>
<td>Total</td>
</tr>
<tr>
<td>No. of patients</td>
<td>60</td>
<td>19</td>
<td>41</td>
<td>60</td>
</tr>
<tr>
<td>Median age (yr)</td>
<td>57 ± 12</td>
<td>59 ± 11</td>
<td>56 ± 12</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>Male (% of patients)</td>
<td>67</td>
<td>63</td>
<td>68</td>
<td>65</td>
</tr>
<tr>
<td>Obesity degree (%)</td>
<td>+7 ± 15</td>
<td>+8 ± 15</td>
<td>+6 ± 16</td>
<td>+8 ± 19</td>
</tr>
<tr>
<td>Red-cell (×10^6/mm³)</td>
<td>423 ± 66</td>
<td>419 ± 62</td>
<td>426 ± 68</td>
<td>418 ± 55</td>
</tr>
<tr>
<td>Platelet (×10^6/mm³)</td>
<td>27 ± 12</td>
<td>29 ± 15</td>
<td>25 ± 12</td>
<td>27 ± 11</td>
</tr>
<tr>
<td>Duration of catheterization (min.)</td>
<td>50 ± 12</td>
<td>45 ± 12</td>
<td>52 ± 12*</td>
<td>51 ± 14</td>
</tr>
</tbody>
</table>

Statistical significance: *p < 0.05; PND (+) vs PND (−). **p < 0.02; PND (+) vs PND (−)
Abbreviations: PND (+) = positive pulmonary new defects; PND (−) = negative pulmonary new defects.

### METHODS

**Patients**

The subject of this study included consecutive 120 patients who were admitted to the Division of Internal Medicine of our hospital from March to October, 1982, and underwent diagnostic transfemoral arteriography. These patients were divided into two groups, the initial 60 patients received routine arteriography without subcutaneous heparin administration (Group 1), while the latter 60 patients received subcutaneous heparin (Group 2). The clinical profile of the two groups are summarized in Table I. Unexpectedly, patients’ age, sex, obesity degree, red-cell count, and platelet count were not statistically different between the two groups. In Group 1, 24 patients underwent coronary arteriography, and remaining 36 underwent visceral or cerebral arteriography. In Group 2, 22 underwent coronary arteriography, and 38 underwent visceral or cerebral arteriography. The following patients were excluded from the study: (1) under the age of 30, (2) with recent history of deep vein thrombosis or pulmonary embolism, (3) on an anticoagulant therapy, (4) with active bleeding, and (5) patients who underwent arteriography on an emergency basis. The purpose and methods of our study were explained to all subjects before study and obtained their consent.

**Arteriography**

Intravenous 3,000 units heparin were administered at the beginning of coronary arteriography for preventing catheter-induced arterial embolization. Right heart catheterization was performed using a percutaneous femoral vein approach. Cardiac output was measured by a thermodilution method, and pressures were obtained using a Swan Ganz catheter. Coronary arteriography was performed by Judkins’ technique using #8F catheter. The left coronary artery was opacified from at least 6 directions including sagitally angulated views, the right coronary artery from two directions, and the left ventricle from two directions. Cerebral and visceral arteriographies were performed by Seldinger’s technique via the femoral artery. We used #6.5F or #7.3F Head-hunting or Simmons catheters for cerebral arteriography, and #6.5F or #7.3F preshaped catheters for selective and superselective visceral arteriographies. Intravenous heparin was not administered before cerebral or visceral arteriography but during the examination heparin was administered at a concentration of 1,000 units/100 ml in a flushing saline solution. About 1,000 to 3,000 units of heparin were administered during examination.

**Subcutaneous Heparin Administration**

In Group 2, subcutaneous heparin was administered in addition to the above mentioned procedures. Initial 5,000 units were injected one hour before arteriography, and another 5,000 units at ten hours later. Activated partial thromboplastin time was measured before and 2 to 3 hours after the first heparin injection, and 10 hours after the second heparin.
TABLE II INCIDENCE OF PULMONARY NEW DEFECTS

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>19/60 (32%)</td>
<td>6/60 (10%)</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>Coronary AG</td>
<td>7/24 (29%)</td>
<td>2/22 (9%)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Cerebral or visceral AG</td>
<td>12/36 (33%)</td>
<td>4/38 (11%)</td>
<td>&lt; 0.05</td>
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</table>

AG = arteriography

posterior tibial and dorsal arteries and the possible presence of venous congestion in the legs were frequently checked, and if any signs were observed the sandbag was immediately removed and the compression was relaxed. The sandbag was usually removed after 5 hours and each patient was then confined to complete bed rest with compression by gauze and Elatex until the following morning. Since all arteriographies are routinely performed in the afternoon in our hospital, such patients, usually maintain complete bed rest for about 15 to 19 hours.

Lung Perfusion Scintigraphy

Lung perfusion scintigraphy was performed the day before and the day after arteriography (within 16 to 20 hours after arteriography). After intravenous administration of 5 mCi of technetium-99m macroaggregated albumin, four images including anterior, posterior and both lateral projections were obtained. The information density for each image was 7,000 count/cm². The instrument used was a parallel hole and high resolution collimator by Hitachi Inc. The postarteriography scintigram was checked for any new lobar, segmental, or subsegmental defects which had not appeared on the prearteriography scintigram. All the scintigrams were interpreted by two observers, and they were only considered to be positive when both observers unerringly confirmed the presence of new defects. Thus, if one observer diagnosed the presence of new defects and the other observer judged the scintigram as "questionable", then this scintigram was not considered to be positive. When the scintigram was considered as showing new defects, the size of the defects was calculated as percentage of the total lung area.

Postarteriography Procedures

After removing the catheter, manual compression of the femoral artery was carried out for a minimum of 10 minutes, and after having confirmed that hemostasis completed, compression by gauze with Elatex (Tokyo Eizai Lab. Co.) was carried out at the puncture site and a 2 kg sandbag was placed on the groin. Pulsation of the

![Fig. 1. Lung scan in the anterior and left lateral views before (A) and after (B) arteriography. Arrows indicate new perfusion defects.](image)

**TABLE III ACTIVATED PARTIAL THROMBOPLASTIN TIME (SEC.) IN GROUP 2**

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 60)</th>
<th>PND (+) (n = 6)</th>
<th>PND (-) (n = 54)</th>
</tr>
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<tbody>
<tr>
<td>Before heparin</td>
<td>30.8 ± 5.0</td>
<td>32.1 ± 3.2</td>
<td>30.6 ± 5.3</td>
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<tr>
<td>2 to 3 hours after the first heparin</td>
<td>40.3 ± 12.5</td>
<td>40.0 ± 11.2</td>
<td>40.4 ± 13.0</td>
</tr>
<tr>
<td></td>
<td>* ns</td>
<td>* ns</td>
<td>* ns</td>
</tr>
<tr>
<td>10 hours after the second heparin</td>
<td>31.7 ± 4.1</td>
<td>31.3 ± 4.0</td>
<td>31.8 ± 4.3</td>
</tr>
</tbody>
</table>

Statistical significance: *p < 0.01; ns = not significant. Abbreviations as in TABLE I.

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and unpaired t tests and Chi square test with or without Yates' correction were used where appropriate. Probability (p) values are listed for each comparison and a probability of less than 0.05 was considered statistically significant.

RESULTS

Of 60 patients in Group 1, 19 (32%) demonstrated new pulmonary perfusion defects on the day following arteriography that had not been observed in the scintigram on the day before arteriography. These 19 patients consisted of 7 out of 24 patients (29%) underwent coronary arteriography with right heart catheterization and 12 out of 36 patients (33%) underwent cerebral or visceral arteriography. No statistically significant difference was observed between these two types of arteriography in regard to the incidence of new perfusion defects (Table II). In respect to the rate of affected area against total lung area, it was 20% or less in 16 patients, and from 20% to 40% in the remaining 3. Fig. 1 shows a typical example of pulmonary new perfusion defects which occurred on the next day of cerebral arteriography for the preoperative estimation of transient cerebral ischemic attack in a 66-year-old man.

On the other hand, among 60 patients received prophylactic heparin (Group 2), only 6 (10%) demonstrated new perfusion defects. This value was significantly lower than that in Group 1. There were no cases with excessive bleeding during catheterization, or extended wound hematoma or recurrence of bleeding after arteriography in Group 2. The mean activated partial thromboplastin time was slightly, but significantly, prolonged within two to three hours after the first subcutaneous heparin injection, and returned to the pretreatment level ten hours after the second injection (Table III).

The underlying diseases of patients in both groups are shown in Table IV. Although statistical analysis could not be employed because of small number of patients included in individual subgroup, it is notable that no patients with chronic liver disease had new perfusion defects in both groups. Patients with malignant neoplasms in Group 2 seem to remain to be relatively high incidence of new perfusion defects. Patients with and without new defects were compared in regard to age, sex, obesity degree, red-cell count, platelet count, and the duration of catheterization in Group 1 (Table I). The only significant difference found was that the duration of catheterization was shorter in patients who developed new defects. Only one of 25 patients who developed new defects complained of apprehension but no patients complained of chest pain or dyspnea. No anomaly was also detected in the physical examination, chest X-rays, or electrocardiogram. Only arterial PO$_2$ showed a slight but significant decline after arteriography in patients who developed new defects (from 89.5 ± 7.8 to 79.0 ± 11.1 mmHg; p < 0.001).

DISCUSSION

Lung perfusion scintigram is highly sensitive for detecting pulmonary embolism and is therefore an excellent screening test. However, such a defect per se is somewhat nonspecific. Besides pulmonary embolism, other conditions having a chance to produce such defects include obstructive lung diseases, inflammations, tumors, pleural effusion, cardiomegaly, etc. Thus, in order to attribute these defects definitely to pulmonary embolism, it is necessary to rule out these other conditions as possible causes, and combination of ventilation-perfusion scanning may lessen the problem of interpretation. Although we did not perform ventilation lung scintigram, we believe that most of the new perfusion defects observed in our study can be attributed to pulmonary embolism for the following reasons. First, we obtained two scintigrams within 48 hours before and after arteriography and considered as positive only those cases in which new defects appeared. During this 48
hours period, no interventions that could affect the lungs were carried out, and we confirmed by chest X-rays that no new infiltration of the lungs or accumulation of pleural effusion occurred. Thus, the possibility that other conditions except for pulmonary embolism caused these new perfusion defects must be very low. Second, in Group 2 patients who had received prophylactic low-dose heparin had a significantly low incidence of pulmonary new perfusion defects. This finding strongly suggests that new defects are due to thromboembolism.

From daily clinical experiences, it is generally recognized that symptomatic pulmonary embolism as a complication of arteriography is extremely rare. In studies concerning complications of transfemoral arteriography, pulmonary embolism has not been reported at all5-9 or if reported only at very low incidences10,11 Primm et al12 and Iuchi et al13 performed a prospective study on both symptomatic and asymptomatic pulmonary embolism by comparing lung scintigrams before and after cardiac catheterization, and reported that pulmonary embolism was observed in 12% and 23%, respectively. However, it still remains unclear from these studies whether or not pulmonary embolism would also develop at a relatively high incidence in other types of arteriography without right heart catheterization. It is well known that right heart catheters can cause thrombophlebitis or pulmonary embolism.14-16 However, such problems usually occur with indwelling catheters for a prolonged time such as days, and the possibility that right heart catheterization caused pulmonary new defects in our study is unlikely because of its very short time of procedures employed. Furthermore, we demonstrated that there was no significant difference between the incidence of pulmonary embolism with and without right heart catheterization. This finding strongly suggests that right heart catheterization per se has no important role in the development of pulmonary embolism, and arteriography itself must cause leg vein thrombosis and pulmonary embolism. The possible cause of leg vein thrombosis and subsequent pulmonary embolism is considered that the femoral vein is compressed by a local hematoma or a pseudoaneurysm as indicated by Lang.10,11 In addition, manual compression of the femoral region, compression due to a sandbag and gauze with Elatex, and/or prolonged bed rest after arteriography are also potentially important factors. Rather strict compression with gauze and Elatex after arteriography in our study may explain our higher incidence of pulmonary embolism (32% in Group 1) compared with previous studies.12,13

Of our 25 patients with pulmonary embolism, 24 patients were completely asymptomatic and only one patient complained of apprehension. Even this one patient may have been overlooked unless our earnest questioning was made. It is not surprising that pulmonary embolism remains asymptomatic in the majority of cases. Even when pulmonary embolism is massive, the symptoms remain quite frequently nonspecific and often overlooked.17,18 Changes in chest X-rays, serum chemistry analysis, and electrocardiograms are often of no diagnostic value, thus providing a failure of accurate diagnosis.19,20 Pleuritic pain was reported at a relatively high incidence in patients with submassive or less severe pulmonary embolism,18,21 but this high incidence is mostly based on a retrospective viewpoint after the clinical diagnosis of pulmonary embolism had already made. In some clinicopathological correlative studies, pulmonary embolism is often overlooked22-24 and, especially, in the case of small emboli, about 80% remain asymptomatic.22 Therefore, most cases of pulmonary embolism as a complication of transfemoral arteriography are considered to have been overlooked.

The efficacy of low-dose heparin in preventing postoperative deep vein thrombosis and pulmonary embolism has been established.25-27 The use of low-dose heparin is based on the identification that trace amounts of heparin, which cannot block fibrinogen conversion to fibrin, can profoundly augment antithrombin III and subsequently decrease thrombogenicity.1 Thus, the use of small doses of heparin (for practical purposes 5,000 units heparin every 8 to 12 hours) does not induce a hypocoagulable state and therefore should not be associated with increasing bleeding. In our study, low-dose heparin could decrease the incidence of pulmonary embolism after arteriography to about one-third of that in the control group, although it was less effective in patients with malignant neoplasm. The mean activated partial thromboplastin time was slightly, but significantly, prolonged within two to three hours after the first heparin injection as compared to the pretreatment level, and there were no cases with extended wound hematoma or rebleeding after arteriography in the heparin-treated group. Therefore, low-dose heparin in preventing pulmonary embolism after
arteriography can be administered with no need of extensive and costly laboratory monitoring, and no troublesome bleeding during and after arteriography.

Recent improvement in catheter design have led to the development of thinner, more controllable catheters with better radiopacity. Since such new style catheters have become used more extensively, the risk of leg vein thrombosis as mentioned above seems to be declining. Further studies are necessary to assess the risk of pulmonary embolism under these new conditions. However, the risk of leg vein thrombosis and pulmonary embolism should be considered to be high in some cases such as patients having a widened punctured pore of the femoral artery due to the use of larger-sized catheters or introducers, or those affected by atherosclerosis or hypertension, since hematoma at the puncture site may develop more often and compression with a sandbag and complete bed rest may become necessary. In these cases low-dose heparin administration is useful in reducing the occurrence of pulmonary embolism after arteriography without increasing clinically important bleeding.

REFERENCES


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