Early rate of resolution of major pulmonary embolism

A study of angiographic and haemodynamic changes occurring in the first 24 to 48 hours

I. G. McDonald, J. Hirsh, and G. S. Hale
From the Cardiovascular Unit and Department of Medicine, University of Melbourne, St. Vincent's Hospital, Melbourne, Victoria, Australia

Nine patients with major pulmonary embolism who were free of serious cardiopulmonary disease were studied by pulmonary angiography with measurement of pulmonary arterial pressure and cardiac output. The pulmonary angiogram was initially performed 20-0 hours (range 5 to 48 hours) after the first symptoms of the most recent episode of embolism and then repeated after 26.5 hours (range 17 to 48 hours) of heparin therapy. Six patients showed no change, slight improvement, and deterioration. The reductions in the average values of both the total pulmonary resistance and the mean pulmonary arterial pressure were slight. It was concluded that little resolution of major pulmonary embolism occurs during the first 24 to 48 hours of heparin therapy.

Most of the patients who die from pulmonary embolism do so within the first few hours (Donaldson et al., 1963; Soloff and Rodman, 1967), but some survive this early period only to die during the subsequent few days (Stoney, Jacobs, and Collins, 1963; Rosenberg, Pearce, and McNulty, 1964). Some of these later deaths are a direct consequence of severe pulmonary vascular obstruction which leads to sustained shock refractory to treatment. Other deaths are due to recurrent pulmonary embolism or to other complications in patients who are vulnerable because the initial embolus has abolished the normally large reserve capacity of their pulmonary circulation to tolerate obstruction. The rate of resolution of the pulmonary embolus is the factor that determines how long these patients will be exposed to the risks associated with persistent severe pulmonary vascular obstruction. Knowledge of this rate of spontaneous resolution of major pulmonary embolism during the critical first few days would also clarify the indications for pulmonary embolectomy (Beall and Cooley, 1965) and for thrombolytic therapy (Hirsh et al., 1967, 1968; Tow, Wagner, and Holmes, 1967; Sasahara et al., 1967; Sautter et al., 1967a; Genton and Wolf, 1968; Miller, 1969; Walsh, Stengle, and Sherry, 1969).

Sequential pulmonary angiography and radioisotope scanning have demonstrated partial resolution of major pulmonary embolism during the first week or two in some patients (Dalen et al., 1969; Sautter et al., 1964, 1967b; Emanuel, Sautter, and Wenzel, 1966; Simon and Sasahara, 1965; Fred et al., 1966; Chait et al., 1967; Tow and Wagner, 1967; Murphy and Bulloch, 1968; Secker-Walker, 1968), but the extent and incidence of spontaneous resolution occurring during the first few days are not yet known. The study of Dalen et al. (1969) provided valuable data and included a group of patients with severe pulmonary embolism in whom pulmonary angiography was repeated after intervals of 1 to 7 days. In the present study angiographic and haemodynamic progress has been followed during the first 24 to 48 hours after major pulmonary embolism in order to determine the early rate of resolution.

Patients and methods

Patient selection  The diagnosis of major pulmonary embolism required the demonstration of both pulmonary hypertension (mean pulmonary arterial pressure > 15 mmHg) and of bilateral filling defects consistent with pulmonary embolism.
in the pulmonary angiogram. There were 9 patients who fulfilled these criteria and in whom cardiac catheterization and pulmonary angiography were repeated. Their average age was 54.4 years (23 to 73 years) and there were 5 men and 4 women. Seven of these patients had clinical evidence of minor pulmonary embolism within the preceding two weeks. In 3 this had been recognized and treated with anticoagulant therapy. None had previously been in heart failure nor had pulmonary disease of clinical significance. Six patients presented postoperatively; the other significant predisposing factors have been summarized in the Table.

Investigations Right heart and percutaneous brachial arterial catheterization were performed immediately after the initial clinical assessment. The pulmonary arterial and brachial arterial pressures were measured with reference to a point 5 cm posterior to the sternal angle and the cardiac output was measured by the indicator dilution method.

Selective pulmonary angiography was performed by injecting contrast material (Urografin 76%) under pressure into the main pulmonary artery and recording its passage through the pulmonary circulation with a rapid film changer (Elera-Schonander) in the anteroposterior projection. The timing of the exposure of these radiographs was adjusted according to the anticipated rate of pulmonary blood flow as predicted from the patient's clinical condition. The pulmonary angiogram was subsequently analysed by three observers who made an independent estimate of the degree of pulmonary vascular occlusion. The decision on the presence and degree of changes between initial and follow-up angiograms was made by comparing the entire series of radiographs taken on each occasion, allowing for any slight technical differences. The radiographs reproduced in Fig. 1, 2, 3, and 4 are representative of each series in 4 patients. The average time lapse between the last clinical episode of pulmonary embolism and the initial pulmonary angiogram was 20±0 hours (5 to 48 hours) and the angiogram was repeated on average 26±5 hours (17 to 48 hours) later. The pulmonary arterial pressure was measured in all of the follow-up studies and the cardiac output in 5 of them. The total pulmonary resistance was calculated when possible by dividing the mean pulmonary arterial pressure by the cardiac output.

Treatment When the clinical diagnosis of pulmonary embolism had been made heparin 10,000 units was administered intravenously and continued by intravenous infusion in the dose necessary to maintain the activated partial thromboplastin time between 2 and 3 times normal. After the initial angiogram had been performed the heparin was infused via the angiographic catheter, which was left in the pulmonary artery until the second angiogram had been performed.

Results Angiography The results are summarized in the Table. The average degree of pulmon-

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Predisposition</th>
<th>Previous pulmonary embolism</th>
<th>Degree of obstruction (%)</th>
<th>Time after embolism (hr)</th>
<th>Mean pulmonary arterial pressure (mmHg)</th>
<th>Cardiac output (l/min)</th>
<th>Total pulmonary resistance (units)</th>
<th>Change in pulmonary angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 36 M Postoperative, gastrectomy</td>
<td>No 70</td>
<td>5</td>
<td>25</td>
<td>5.4</td>
<td>4.6</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 70 F Lymphosarcoma</td>
<td>No 60</td>
<td>5</td>
<td>25</td>
<td>5.5</td>
<td>4.5</td>
<td>Slight improvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3 57 M Postoperative, gastrectomy</td>
<td>Yes 50</td>
<td>42</td>
<td>31</td>
<td>5.4</td>
<td>5.7</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 73 M Carcinoma of prostate</td>
<td>Yes 65</td>
<td>12</td>
<td>35</td>
<td>2.8</td>
<td>12.5</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 23 F Postoperative, choledochectomy</td>
<td>Yes 45</td>
<td>36</td>
<td>19</td>
<td>—</td>
<td>—</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>6 65 M Postoperative, endarterectomy</td>
<td>Yes 35</td>
<td>48</td>
<td>21</td>
<td>3.8</td>
<td>5.6</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 35 M Nil</td>
<td>Yes 45</td>
<td>12</td>
<td>28</td>
<td>3.7</td>
<td>7.6</td>
<td>Slight improvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 64 F Postoperative, repair of hiatus hernia</td>
<td>Yes 50</td>
<td>18</td>
<td>27</td>
<td>—</td>
<td>—</td>
<td>Moderate deterioration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 67 F Postoperative, arthroplasty</td>
<td>Yes 35</td>
<td>15</td>
<td>30</td>
<td>5.5</td>
<td>5.5</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean values</td>
<td>54.4</td>
<td>50.6</td>
<td>20.0</td>
<td>27.4</td>
<td>5.76*</td>
<td>(0.2 &gt; P &gt; 0.1)</td>
<td>3.72*</td>
<td>(0.2 &gt; P &gt; 0.1)</td>
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</table>

* Mean values for 5 patients in whom total pulmonary resistance was measured in both studies.
ary vascular obstruction shown in the initial pulmonary angiogram was 50-6 per cent (35 to 75%). When pulmonary angiography was repeated within 48 hours no change had occurred in 6 patients, further vascular occlusion had occurred in 1 patient, and slight improvement in the remaining 2 patients. Examples are shown in Fig. 1-4. In the patient who showed angiographic deterioration the initial pulmonary angiogram showed a filling defect which indicated that an embolus had lodged at the bifurcation of the short upper lobe artery, partially obstructing both the medial and lateral branches (Fig. 3a). After 24 hours of heparin therapy the embolus seemed to have moved into the lateral branch and completely occluded it, but had left the medial branch apparently free of obstruction (Fig. 3b).

**Haemodynamics** The total pulmonary resistance could be calculated for the initial study in the 8 patients in whom both pulmonary arterial pressure and cardiac output were measured. The mean value in these patients was 6.6 units (3.1 to 9.0 units). In 5 patients the total pulmonary resistance could be calculated for both the initial and follow-up studies. The observed change from 5.8 to 3.7 units was not statistically significant. The pulmonary arterial pressure was measured during both initial and follow-up studies in all patients. The change from 27.4 to 24.0 mmHg was not significant.

**FIG. 1** Case 1. No significant improvement in pulmonary angiographic appearance between initial angiogram (a) and follow-up angiogram (b) performed 17 hours later.

**FIG. 2** Case 4. No significant improvement in pulmonary angiographic appearance after 24 hours.
Correlation of angiography and haemodynamics The small reductions observed in the average values of both the total pulmonary resistance and pulmonary arterial pressure correlated well with the finding of little or no change in the pulmonary angiograms. In individual patients, however, there was sometimes haemodynamic improvement with no change or even deterioration in the pulmonary angiogram, and, conversely, there was sometimes angiographic improvement with little haemodynamic change. Thus of the 5 patients in whom the total pulmonary resistance could be calculated for both initial and follow-up studies, a reduction was observed in 3, no change in 1, and a slight increase in 1 patient. The pulmonary angiogram showed no improvement in 2 of the 3 patients with haemodynamic improvement and showed deterioration in the third. Slight angiographic improvement was noted in the 2 patients in whom the total pulmonary resistance showed no change and a slight increase, respectively. Of the 4 patients in whom only the pulmonary arterial pressure was measured in both initial and follow-up studies, 1 showed a substantial reduction, 2 a slight reduction, and the fourth a slight increase. No angiographic improvement was observed in any of these patients.
Discussion

Our observation that little or no resolution was demonstrable by angiography over a period of 24 to 48 hours after major pulmonary embolism is consistent with the findings of the only other systematic study of early resolution in this condition. Thus Dalen et al. (1969) found no resolution in 1 patient and minimal resolution in 6 patients with severe pulmonary embolism when pulmonary angiography was repeated after intervals ranging from 1 to 7 days. Episodes of minor pulmonary embolism commonly preceded a major episode, and this was the case in 7 of our patients. Hence some of the pulmonary vascular obstruction demonstrated by the initial angiograms could have represented residual changes from an earlier episode. However, this does not vitiates our conclusions, since all of our patients presented with typical major pulmonary embolism so that our results are representative of this group of patients.

In the present study the severity of pulmonary embolism has been expressed in terms of two indices, the total pulmonary resistance calculated from the haemodynamic measurements, and the degree of pulmonary vascular occlusion estimated from the pulmonary angiogram. The correlation between the average changes in each was good, but in individual patients a reduction in the total pulmonary resistance was not always accompanied by improvement in the pulmonary angiogram and vice versa. This is not surprising, because there are important differences in what is actually measured by these two indices. Thus the total pulmonary resistance is an acceptable index of pulmonary vascular resistance (Fishman and Cournand, 1953) and therefore a reflection of the overall degree of obstruction to blood flow through the lungs. On the other hand, the pulmonary angiogram provides an approximate measure of the amount of embolus in the proximal pulmonary arteries, of the degree of occlusion of individual arteries, and of regional differences in pulmonary blood flow. However, the angiogram is of limited value as an indicator of changes in the pulmonary vascular resistance and hence of the severity of obstruction to pulmonary blood flow, since vascular occlusion must be extensive before there is any increase in resistance (Fishman, 1963). In addition, the angiogram does not detect obstruction in smaller peripheral arteries, nor can it detect subtle changes in the degree of obstruction of individual vessels which may cause substantial changes in vascular resistance. Nevertheless, the pulmonary angiogram is important in evaluating the severity of pulmonary embolism because it does provide a useful assessment of the 'reserve capacity' of the pulmonary circulation to tolerate further vascular occlusion. Thus, even when there is little or no haemodynamic abnormality, a severe degree of occlusion in the pulmonary angiogram serves as a warning that further embolism may be poorly tolerated.

Implications for therapy

Previous reports and our own study clearly indicate that substantial early resolution of major pulmonary embolism cannot be expected even in patients who are young and who have previously been in good health. This conclusion justifies attempts to obtain therapeutic relief of pulmonary vascular obstruction in selected patients. A compelling case has already been made for early pulmonary embolectomy in those patients with sustained shock who do not respond adequately to vasopressor therapy (Beall and Cooley, 1965; Moulder et al., 1967). The place of thrombolytic therapy is less clear. Nevertheless, the early rate of resolution of pulmonary embolism reported in patients treated with thrombolytic agents (Hirsh et al., 1967, 1968; Tow et al., 1967; Sasahara et al., 1967; Sautter et al., 1967a; Genton and Wolf, 1968; Miller, 1969) appears to be considerably more rapid than that found in our patients and in those of Dalen et al. (1969). The efficacy of thrombolytic therapy in major pulmonary embolism is currently being investigated in a collaborative controlled trial and should provide a more definitive answer (Walsh et al., 1969).

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References


