

PULMONARY EMBOLISM AND THROMBOSIS IN CHRONIC OBSTRUCTIVE EMPHYSEMA

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The course of chronic diffuse obstructive pulmonary emphysema is extremely variable. Certain cases manifest cyanosis, polycythemia and right ventricular cardiac failure relatively early, while others proceed to advanced pulmonary parenchymal destruction, hypoxia and hypercapnia, with right ventricular decompensation developing much later.¹ The disturbances in respiratory function which accompany these patterns have been studied.² Many cases in the former group are characterized by episodes of acute cardiopulmonary failure, superimposed upon chronic pulmonary insufficiency, in which the mortality rate is very high.³ These episodes of failure have been attributed by most investigators to acute bronchopulmonary infection although in many cases clinical and laboratory signs of infection are lacking.⁴

The role of pulmonary embolism or thrombosis has not been emphasized in these reports,⁴⁻⁷ although several cases of silent pulmonary emboli leading to chronic cor pulmonale in the absence of advanced pulmonary disease are recorded.^{8,9} This report studies the incidence of significant pulmonary embolism or thrombosis in long-standing, severe pulmonary emphysema and the possible influence of cardiac failure, polycythemia and immobilization.

PROCEDURE

Necropsy protocols at the Colorado General Hospital from 1946 through 1960 were reviewed. Clinical and necropsy records were examined for all patients in whom a postmortem diagnosis of pulmonary emphysema was made. Only patients who met the following criteria were placed in the series.

1. The patient must have had disabling dyspnea (i.e., dyspnea which prevented all but sedentary employment or activity) for at least 6 months prior to death.
2. Death must have been due to pulmonary emphysema either directly (respiratory failure) or indirectly (right ventricular failure, pneumonia, pneumothorax, peptic ulcer when duration was less than that of severe respiratory symptoms, and pulmonary thrombosis or embolism).
3. The presence of severe diffuse pulmonary emphysema must have been verified by microscopic examination of lung tissue.
4. The patient must have had no significant valvular or congenital heart disease and no additional chronic pulmonary disease, e.g., tuberculosis or silicosis.

Clinical records were reviewed and the course of the illness, history of pneumonia,

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chest pain, or hemoptysis, and the nature of the terminal episode were noted. The following specific information was recorded: clinical diagnosis; total duration of symptoms; duration of disabling symptoms; presence and duration of right ventricular failure; maximum hematocrit or hemoglobin level; and number of hospital days on final admission.

The following information was obtained from the necropsy protocol: anatomic diagnoses; gross and microscopic description of the lungs; weight of heart and thickness of the right ventricular myocardium; and presence or absence of mural thrombosis in the right cardiac chambers.

Among 5,302 necropsies performed during the years mentioned, the diagnosis of pulmonary emphysema was made in 201. Sixty-six met the criteria described. Table I indicates the reasons for rejecting the remaining cases. Microscopic sections of the lungs (an average of 5 for each case) were re-examined on each patient in the series; the presence, number and size of smaller emboli or thrombi were recorded and the severity of emphysema confirmed.

A control series was paired with those in the emphysema series with respect to age (within a 5-year span), sex and necropsy year. Patients in the control series were required to have had no significant emphysema or other chronic pulmonary disease and no valvular or congenital heart disease. Peripheral venous disease, neoplastic disease or cardiac failure did not exclude a case. The first case necropsied in the respective year which fit these criteria was placed in the control series. The number of hospital days and the cause of death were recorded in each case.

TABLE I
REJECTED PULMONARY EMPHYSEMA PATIENTS

Reasons for rejection	No. cases
1. "Senile" emphysema incidental at necropsy; minimal or no respiratory symptoms; cause of death entirely unrelated	26
2. Mild or moderate, obstructive, hypertrophic, bullous emphysema, incidental at necropsy; minimal or no respiratory symptoms; cause of death entirely unrelated	60
3. Sufficient respiratory disability; cardiorespiratory death but only mild obstructive or "senile" emphysema found at necropsy. Respiratory symptoms either unexplained or due to heart disease	6
4. Acute emphysema, focal or diffuse (usually pediatric cases) or purely focal chronic (isolated bullae)	11
5. Significant additional chronic pulmonary disease, e.g., tuberculosis, bronchiectasis, silicosis, valvular heart disease, or severe chronic left ventricular disease	22
6. Sufficient respiratory disability, severe emphysema at necropsy but cause of death entirely unrelated	8
7. Death from acute bronchial asthma although chronic emphysema of some degree present	2

RESULTS

Among the 66 patients in the emphysema series, 29 or 44 per cent were found to have significant pulmonary emboli or thrombi. Of these 29 patients, 26 or 39 per cent had large emboli (i.e., of arteries down to and including lobar arteries). In addition, 3 cases showed scattered small thrombi which could not be judged significant and 2 cases with

the necropsy diagnosis of multiple pulmonary emboli were rejected because the lesions could not be differentiated with certainty from severe medial sclerosis.

Of the 29 patients with significant emboli, 23 or 79 per cent had intermittent right ventricular failure for an average duration of 3 years. Of the 37 patients who had no emboli, 30 or 81 per cent had intermittent right ventricular failure for an average duration of 2.8 years. Mural thrombi in the right side of the heart were found in 7 or 24 per cent of the 29 patients with significant emboli.

Polycythemia was defined as a single hemoglobin or hematocrit determination above 20 gm. per 100 cc. or 58 per cent respectively during any hospitalization for respiratory disease. Of the 29 patients with emboli, 10 or 34 per cent had polycythemia. Sixteen or 43 per cent of the 37 patients without emboli had polycythemia. Table II summarizes these data.

TABLE II
SIXTY-SIX EMPHYSEMA PATIENTS

	With pulmonary emboli 29 patients (44%)		Without pulmonary emboli 37 patients (56%)	
	(No.)	(%)	(No.)	(%)
Right ventricular failure	23	79	30	81
Mural thrombi	7	24	2	5
Polycythemia	10	34	16	43

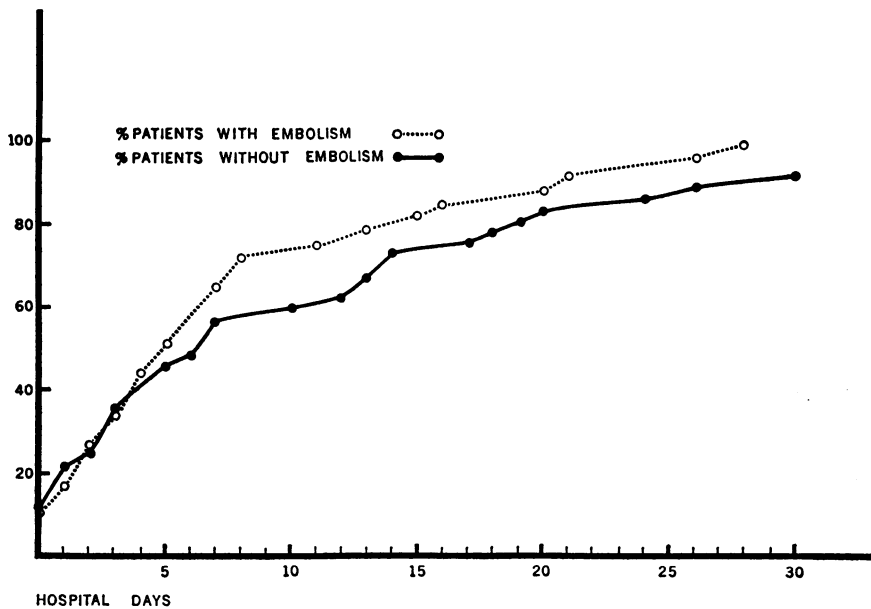
In the control series the incidence of pulmonary embolism was 15 per cent; 70 per cent of these emboli were large. The incidence in this group falls outside the 99 per cent confidence interval (26 to 63)¹⁰ of the incidence in the emphysema group ($P = < 0.001$).

The average number of hospital days was 15.3 in the emphysema group and 26.6 in the control group. The median number of hospital days was 6 in the emphysema group and 12 in the control group. Text-figure 1 compares the number of hospital days on the terminal admission in the emphysema group with pulmonary emboli (29 patients) with those in the emphysema group without pulmonary emboli (37 patients). Three patients with hospital stays of 123, 169, and 192 days are excluded from this figure. None of these patients had pulmonary emboli.

DISCUSSION

The frequency and significance of pulmonary embolism or thrombosis in advanced emphysema has not been emphasized. Liebow¹¹ has stated that pulmonary thromboembolism is common in emphysema but emphasized the importance of capillary destruction and muscular obliteration of pulmonary arteries in the genesis of cor pulmonale. Baum and Fisher¹²

reported a series in which 12 of 33 patients with the necropsy diagnosis of pulmonary emphysema were found to have multiple small pulmonary emboli associated with cor pulmonale. However, Kernen, O'Neal and Edwards¹⁸ in a series of 125 necropsies in patients with moderate to severe chronic emphysema found no increased incidence of pulmonary



TEXT-FIG. 1. Duration of terminal hospitalization in emphysema patients.

emboli over a control series without significant lung disease. Furthermore, the patients who had had pulmonary hypertension and cor pulmonale had no higher incidence of pulmonary emboli than those without this complication. That series comprised necropsied patients with moderate or severe emphysema without respect to clinical severity, duration or cause of death.

In the present group of cases the incidence of pulmonary embolism or thrombosis was significantly higher in patients with long-standing severe emphysema than in a series representing essentially a general hospital population of similar age without pulmonary disease.

The difficulty in assessment of clinical severity of emphysema from routine necropsy material is well known. In the present report only those cases with prolonged disability and death due to emphysema were studied. In cases of this kind, actual severity of the process is more certain. Most (90 per cent) of the occlusions were large and many led directly to death. Many of the cases in which the occurrence of the occlusion was clinically evident were in the process of digitalization and vigorous diuresis. Most were completely unsuspected clinically, and repeated epi-

sodes of fever, hemoptysis, pleuritic pain and pulmonary infiltrates by radiograph were attributed to infection.

Heart disease, particularly if associated with chronic congestive heart failure has long been known to predispose to thromboembolism.¹⁴⁻¹⁷ From 10^{18,19} to 48 per cent²⁰ of patients with congestive failure have been found to have this complication. In the present series, congestive failure was no more frequent in patients with thrombosis or embolism (79 per cent) than in those without it (81 per cent) and the average duration of failure was similar (3 and 2.8 years respectively). Stated conversely, pulmonary embolism or thrombosis occurred no more frequently in patients with right ventricular failure (43 per cent) than in those without it (46 per cent). Since most (80 per cent) of the patients manifested cardiac failure and only a small group (13 patients) were free of this complication, statistically certain conclusions cannot be drawn from the above figures. They do suggest, however, that other factors may be significant.

The similarity between the duration of cardiac failure in the groups with and without thrombosis or embolism should not be interpreted as indicating that this complication did not shorten the course in the former group. The relative severity of the airway disease in the two groups may have been quite different.

The role of polycythemia in thrombosis has also been stressed.^{21,22} In this series 34 per cent of the patients with thrombosis or embolism had polycythemia, while 43 per cent of them without emboli had polycythemia. Conversely, 38 per cent of the patients with polycythemia had thrombosis or embolism but 48 per cent of the patients without polycythemia had this complication. The numbers of patients with and without polycythemia were similar in the groups with and without pulmonary thrombosis or embolism, and an exclusive predisposing influence of polycythemia was not demonstrated.

It is possible that both polycythemia and congestive heart failure are predisposing factors which act independently of one another. For this possibility to fit the facts, congestive heart failure would have to be much more common in patients without polycythemia than in patients with it. As might be expected, this was not the case; 49 per cent of the patients with failure had polycythemia and the remaining 51 per cent did not. Nineteen per cent of the emphysema patients with thrombosis or embolism had neither cardiac failure nor polycythemia.

In the present series no attempt was made to distinguish embolic from autochthonous phenomena, and in most cases a source of embolism was not found. Of the 7 cases in which right-sided mural thrombi were found, 6 had been in right ventricular failure.

Prolonged bed rest and immobility are well recognized contributing influences in the formation of venous thrombosis and subsequent pulmonary embolization.^{23,24} The influence of such factors in patients with advanced respiratory disease is difficult to study. Duration of terminal hospitalization did not appear to play a significant role since the distribution of hospital days was similar between the groups with and without thrombosis or embolism (Text-fig. 1). The much longer average and median hospital stay in the control group had similar significance.

Pulmonary embolism has been noted in from 5 to 14 per cent of various necropsy series.^{15,17,25-27} The high incidence in our control group could probably be attributed to the age and to the high percentage (40 per cent) of cases with malignant neoplastic disease, a factor emphasized by Zimmerman, Miller and Marshall.²⁷

SUMMARY

The incidence of significant pulmonary thrombosis or embolism was higher in a group of patients with advanced pulmonary emphysema than in a similar group of patients without pulmonary disease. Most of the occlusions were large. Right ventricular cardiac failure, polycythemia and prolonged immobilization may not be the only factors which predispose to the occurrence of pulmonary embolism or thrombosis in emphysema patients.

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