

Pulmonary embolism—a long-term follow-up

D. MACINTYRE
M.A., M.R.C.P.

S. W. BANHAM
M.B., M.R.C.P.

F. MORAN
M.B., F.R.C.P.

Centre for Respiratory Investigation, Glasgow Royal Infirmary, Glasgow G4 0SF

Summary

Fifty-three patients without pre-existing cardiac or pulmonary disease were reviewed 5 to 9 years after angiographically proved pulmonary embolism. Ten of the 42 (24%) with an initial predisposing factor for embolism had died, including 6 from a previously diagnosed medical condition. In this group there was no significant residual disability among survivors and no late recurrence of embolism. By comparison, there were 6 deaths among the 11 in whom no predisposing factor was identified (55%), including 3 from neoplasm and 2 from recurrent embolism with cardiac failure.

The identification of a predisposing factor at the time of embolism was associated with a significantly better long-term prognosis.

Introduction

Several reports have confirmed the rapid resolution of pulmonary embolism after commencing anticoagulant therapy (Tow and Wagner, 1967; Fred *et al.*, 1966). However, there is much less information on the long-term outcome after an acute embolic episode (Editorial, 1978) and in some cases the interpretation of such studies has been limited by uncertainty concerning the criteria for initial diagnosis (Davies and Golshetti, 1973; Phear, 1960). Clinical impression including the use of electrocardiogram (ECG) and chest X-ray is notoriously unreliable. Perfusion lung scanning, even accompanied by a ventilation scan, is a sensitive but at times non-specific investigation. Pulmonary angiography remains the most specific method of diagnosing pulmonary embolism. This study examined the outcome after several years in a group of patients without other cardiorespiratory disease in whom embolism was diagnosed by angiography.

Methods

Selection of patients

Patients were selected for follow-up from the

556 individuals who underwent single plane pulmonary angiography at the Centre for Respiratory Investigation, Glasgow Royal Infirmary, between January 1971 and December 1974. Pulmonary angiography had been available as a routine diagnostic service since 1969 and the great majority of angiograms were performed for suspected pulmonary embolism. One hundred and seventy-nine showed no abnormality of the pulmonary vasculature. In 227 cases non-diagnostic abnormalities, often consistent with pulmonary embolism, were demonstrated. A further 77 angiograms were confidently interpreted as showing pulmonary embolism on the basis of multiple minor defects, but without filling defects or vessel cut-offs in segmental arteries. The remaining 85 patients had angiograms which demonstrated filling defects or vessel cut-offs in segmental or larger arteries. In these, the diagnosis of pulmonary embolism could be accepted irrespective of the clinical history.

Follow-up

Twenty-six of the 85 patients were excluded because of pre-existing cardiac or respiratory disease which might affect prognosis or interfere with the assessment of symptoms at follow-up. Details of clinical features at presentation and some follow-up data were obtained from hospital records. Patients still alive were interviewed and examined by one of the authors (S.W.B. or D.M.). Routine pulmonary function tests and chest X-ray were obtained in the majority. For those who had died, full details were obtained from the general practitioner, relatives or hospital case records.

Results

Inadequate information was obtained on 6 patients of whom 3 were known to have died. The current analysis therefore relates to 53 people—32 men and 21 women with a mean age at the time of embolism of 52 years. The angiograms were not

graded according to the extent of involvement by embolism but in 12 the filling defect was in the main pulmonary artery and in a further 6 main branch arteries on both sides were obstructed. Of the remainder, 13 showed unilateral and 22 bilateral

TABLE 1. Pulmonary embolism—main presenting symptoms in 53 patients. Figures in parentheses are percentages

Dyspnoea	37	(70)
Pleuritic chest pain	34	(64)
Haemoptysis	16	(30)
Shock	9	(17)
Venous thrombosis	8	(15)

abnormalities. Table 1 gives the main presenting symptoms. Pleuritic chest pain, dyspnoea or shock was present in all patients. Of the 9 patients with shock, 6 were shown to have embolism involving the main pulmonary artery or major branch arteries on both sides. Table 2 lists the main predisposing

TABLE 2. Pulmonary embolism—predisposing factors in 53 patients. Figures in parentheses are percentages

Surgery	22	(41)
Leg injury	5	(9)
Bed rest	5	(9)
Longstanding venous pathology	3	(6)
Oral contraceptive	3	(6)
*Others	4	(8)
None	11	(21)

*: Diabetic ketosis; cerebral degeneration; hemiparesis; nephrotic syndrome.

factor for thrombo-embolism in each patient. Recent surgery was the most common. In two patients, pre-existing varicose veins with associated thrombo-phlebitis were thought to be a separate predisposing factor rather than part of the thrombotic process. Similarly the presence of varicose veins with a history of previous venous thrombosis and pulmonary embolism during pregnancy in one patient was also regarded as a predisposing factor. In 4, underlying medical disorders were thought likely to increase the risk of venous thrombosis. In 11 (21%) no such factor was identified. The only previous medical history in this group was of mild peripheral vascular disease in one, and duodenal ulcer in another. There was no difference in the clinical presentation between those who did and those who did not have a predisposing factor.

Mortality

The mean follow-up period of those still alive was 6.5 years (4.5–8.5 years). Sixteen patients had died representing an overall mortality of 30%. Their mean age at presentation was 56.4 years compared with 49.6 years for those still alive. A difference in prognosis for those with and without an identified predisposing cause for embolism was apparent. Ten of the 42 with such a factor had died and 6 of these deaths were related to conditions present before the embolism. A substantially higher mortality, 6 of 11, occurred in those with no apparent predisposing factor (Table 3). Of the 6, two deaths were attributed to recurrent embolism, and three had developed neoplasm (bronchial carcinoma, renal carcinoma and myeloma). One of the patients who

TABLE 3. Major pulmonary embolism—mortality

Predisposing factor present	Age	Time after embolism	Cause
1	67	2.5 years	Stroke
2	77	3.5 years	Recurrence of carcinoma of bowel ¹
3	35	5 years	Nephrotic syndrome ²
4	67	1 month	Pulmonary embolism/carcinoma of oesophagus ¹
5	63	5 years	Bronchopneumonia/previous stroke ²
6	45	4 months	Extension of stroke ²
7	64	8 months	Stroke
8	55	3 years	Pancreatitis
9	53	5 years	Myocardial infarction
10	67	9 months	Carcinoma of ovary ¹
Predisposing factor absent			
11	66	7 years	Myeloma
12	66	5 years	Congestive cardiac failure/pulmonary thrombo-embolism
13	53	6 months	Carcinoma of bronchus
14	64	12 days	Retroperitoneal haemorrhage ³
15	27	4 years	Congestive cardiac failure/pulmonary thrombo-embolism
16	76	6 years	Bronchopneumonia

¹. Embolism followed surgery for known malignancy.

². Condition diagnosed before original embolism.

³. Renal carcinoma found at post-mortem.

died of recurrent embolism was a 24-year-old man with a history of possible previous embolism. He had significant pulmonary hypertension and dilated pulmonary arteries at angiography. He continued to suffer episodes of embolism diagnosed clinically and died 4 years after initial angiography in congestive cardiac failure. The second was a 61-year-old man who also had ischaemic heart disease. Later episodes of dyspnoea with gradual deterioration leading to congestive cardiac failure were thought clinically to be due to further embolism. He died suddenly 5 years after angiography. Post-mortem examination was not performed on either patient. No patient died of the initial embolism although one, following surgery for carcinoma of the oesophagus, died one month later following a further embolism.

The poor prognosis in the absence of an identified predisposing factor is highlighted by considering those under 65 years of age with no previously recognized chronic medical condition. The mortality in this group was 56% compared with 9% when a predisposing factor had been identified, a statistically significant difference ($P < 0.05$ by χ^2 test with Yates' correction) (Table 4).

Residual disability

All 37 survivors were questioned about respiratory symptoms. Eleven admitted exertional dyspnoea. In 10 of these, pulmonary function tests were performed showing airways obstruction in 5, a restrictive ventilatory defect in 4 and normal results in one. All those with measured airways obstruction and the patient with normal lung function had symptoms of chronic bronchitis. Two of the patients with restrictive defects had undergone thoracotomy and a third was an elderly man with mild congestive cardiac failure. Only two patients had persisting dyspnoea unexplained by factors other than the embolism. One further patient had angina and one described persisting episodes of pleuritic pain. Overall the striking impression at review 6.5 years after the embolism was of general well-being. No

patient had modified his lifestyle as a result of his illness.

Therapy and recurrence

All patients received heparin for 2–10 days. This was followed in most cases by warfarin given for a period varying from several months to several years. Embolectomy was performed in one case. Five patients had recurrent embolism, all diagnosed clinically. In three cases the recurrence was within 4 weeks. Two patients, already described, eventually died following recurrent thrombo-embolism over a period of years. One, the 24-year-old man, had marked pulmonary hypertension at angiography and had almost certainly suffered recurrent embolic episodes before angiographic diagnosis. Neither of these (and one other) had an initial predisposing factor for embolism. Both had been maintained continuously on warfarin. Two of the forty-two patients with an identified risk factor had recurrences.

Complications of anticoagulant therapy occurred in 14 patients (26%). Two were fatal. Three patients with cerebrovascular accidents were presumed to have had intracerebral haemorrhage and were therefore included. There were two cases each of retroperitoneal, gastrointestinal and urinary haemorrhage and five of bruising. Three bleeding episodes occurred on heparin and the remainder on warfarin.

Discussion

Although a number of angiographic signs of pulmonary embolism are recognized, only constant filling defects and cut-off points in major vessels give definitive diagnosis (Dalen *et al.*, 1971). Other features such as small vessel loss and asynchronous filling, commonly seen as residual angiographic evidence of major embolism when investigation has been delayed, may also occur in other pulmonary disorders. Limiting the present study to these absolute criteria will have excluded many patients with pulmonary embolism but does allow confident identification of a group with recent embolism. The group was further selected by excluding those with

TABLE 4. Long-term mortality following pulmonary embolism—significance of initial predisposing factor

		Predisposing factor	No predisposing factor	
All patients	Alive	32	5	n.s.
	Dead	10	6	
*Under 65 years, previously fit	Alive	28	4	$P < 0.05$
	Dead	4	5	

*Excludes patients with pre-existing chronic medical illness.

significant pre-existing cardio-respiratory disease whose subsequent symptoms may have proved difficult to evaluate. Co-existing cardiac disease has been shown to worsen significantly the prognosis following pulmonary embolism (Hall, Sutton and Kerr, 1977).

These patients have thus been selected as having pulmonary embolism rapidly diagnosed after the event, having no complicating cardiac or respiratory disease and having been treated promptly. Several general conclusions emerge. Firstly, in this group a specific risk factor can usually be identified, a finding which is in agreement with other reports (Hall *et al.*, 1977; Bell, Simon and De Mets, 1977). Secondly, those patients still alive some years later note few residual symptoms despite compromising probably a third or more of the pulmonary vasculature at the time of embolism. Only two patients in the present study went on to develop chronic recurrent thrombo-embolism with pulmonary hypertension and in one the condition was almost certainly established some time before the initial angiogram. Previous studies of survival based on firm diagnostic criteria have reported a generally favourable long-term prognosis following both massive and minor pulmonary embolism in the absence of co-existing cardiac disease (Hall *et al.*, 1977; Sutton, Hall and Kerr, 1977; Paraskos *et al.*, 1973). A report by Hall *et al.* (1977) found that of 51 such patients who survived the initial embolism, only 5 had died during a follow-up period varying from one to 9 years; in the remainder any residual symptoms were mild and only one had suffered possible late recurrence of embolism. The greater overall mortality in the present study may be in part due to a longer mean follow-up period and a slightly older population but may also be influenced by the greater proportion of patients with no identified pre-disposing factor for embolism (21% compared with 14%). These patients appear to have an appreciably poorer prognosis with a greater likelihood of recurrent embolism and with the possibility of occult neoplasm. By contrast, the otherwise fit patient in whom a risk factor can be identified and removed is likely to have no persisting disability following initial recovery and has no significant risk of recurrence.

A common feature of studies of angiographically proved pulmonary embolism is relatively prompt diagnosis followed by anticoagulant therapy. It is not known whether a patient undiagnosed or un-

treated following a major pulmonary embolism will go on to develop recurrent thrombo-embolic disease. Oral anticoagulation for a few months following acute pulmonary embolism is generally accepted clinical practice. The duration of therapy varied considerably in the present study. However, only one episode of recurrent embolism, 2 weeks after the initial event, occurred after stopping anticoagulants, although in 50% of the patients, treatment was for less than 6 months. Prolonged anticoagulation following acute pulmonary embolism occurring in the context of a clear and removable predisposing factor is generally thought unnecessary. This view is supported by the absence of late recurrence in the present patients and is further reinforced by the high incidence of side effects from therapy. However, some doubt arises when pulmonary embolism occurs in the absence of a predisposing factor. Of the 5 survivors in this group, one remains on warfarin after 5 years. It is not clear what duration of anticoagulation should be recommended in such patients.

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