, W... H. E. & Shick, R. M.:
temporal arteritis with adrenal corti-
ts of fifty-five cases in which lesions
iopsy. JAMA 163: 821, 1957.
gvold, O. & Øystese, B.: Temporal
myalgia rheumatica. Ann Intern Med

Shelley, W. M. & Tumulty, P. A.:
is: Including temporal arteritis and
matica. Medicine 50: 1, 1971.
ddy, W. J. & Thorn, G. W.: Studies
it corticosteroid dosage regimen. N
91, 1963.
V., Brown, J. R., Wagener, H. P. &
urologic aspects of temporal arteri-
: 490, 1960.
heps, S. G., Allen, G. L. & Joyce,
alternate-day corticosteroid regimen
iant cell arteritis. Comparison in a
. Ann Intern Med 82: 613, 1975.
: Treatment and prognosis in poly-
ca and temporal arteritis. A ten-year
nts. Acta Med Scand 205: 429, 1979.
Bengtsson, B. Å.: Giant cell arteri-
es and involvement of different or-
umatol 7: 154, 1978.
Bengtsson, B. Å., Alestig, K., Bojs,
: The clinical pictures of giant cell
l arteritis, polymyalgia rheumatica
own origin. Postgrad Med 67: 141,

Gi... ll arteritis and blindness.
835, 1967.
aly, J. R.: Corticosteroid and ACTH
les and problems. Arnold, London

ular crisis of the temporal arteritis
n). Acta Ophthalmol 36: 208, 1958.
Giant cell arteritis: A review of 35
: 471, 1959.
ggenstoss, A. H. & Polley, H. F.:
ne and A. C. T. H. on periarteritis
l arteritis. Preliminary report. Proc
Clin 25: 135, 1950.
n, P. & Lorentzen, I.: Giant cell
arteritis and polymyalgia rheuma-
and 201: 207, 1977.
V., Cooke, W. T., Jameson-Evans,
emporal arteritis and its treatment
A.C.T.H. Lancet 1: 408, 1953.

PE Dx
183/284 died

Acta Med Scand 209: 351–355, 1981

32

178 Fatal Cases of Pulmonary Embolism in a Medical Department

Hans Kræmmer Nielsen, Poul Bechgaard, Peter From Nielsen, Steen Elkjær Husted and Erling Geday

From the Medical University Departments, Aarhus Amtssygehus, Aarhus, Denmark

ABSTRACT. The diagnosis of pulmonary embolism was established during a 6-year period in 284 patients hospitalized in medical departments of a general hospital. Of the 183 patients who died, 178 were autopsied. A retrospective study was performed on the autopsy-verified fatal cases to correlate their clinical state to relevant postmortem findings. Two groups made thorough, independent evaluations of data from the medical and pathological records. In 95 % of the patients a confirmed fatal pulmonary embolism constituted only a slight modification of life expectancy, because of concomitant complicating, severe, terminal disease. Reflecting this poor clinical state, only 26 patients (15 %) had a diagnosis of pulmonary embolism premortally and of these patients, 13 died within 5 hours after onset of symptoms and 10 were treated with antithrombotic drugs. Our results seem to indicate an increase in the incidence of terminal diseases in the popultaion of elderly, hospitalized patients and change the concept of fatal pulmonary embolism into an agonal incident in a terminal-care medical patient.

Key words: fatal pulmonary embolism, premortal condition, clinical, pathological correlations, indication for treatment.

Acta Med Scand 209: 351, 1981.

Modern treatment of thromboembolic diseases was initiated more than 40 years ago, when active mobilization of patients was introduced (6, 10) almost simultaneously with clinical use of heparin (17) and peroral anticoagulants (17). Later, intravascular surgery (8), antiphlogistic drugs (19), and fibrinolytic therapy (11) have been added to the therapeutic arsenal.

During the subsequent four decades, indications for these treatments have been discussed in several hundreds of papers, and it is quite clear that prophylaxis with anticoagulant drugs has reduced the mortality from massive pulmonary embolism in surgical patients (12).

In contrast to these findings, the overall mortality from pulmonary embolism in the total hospitalized population has been rising for half a century (5, 19). For this reason we have analyzed all autopsy-verified cases of fatal pulmonary embolism in the medical departments of a general hospital over a six-year period. We have tried to correlate the clinical state of the patients to relevant postmortem findings.

STUDY POPULATION AND METHODS

Aarhus County Hospital is a general hospital with 200 surgical and 172 medical beds. During the period April 1, 1972 – Dec. 31, 1978 pulmonary embolism was diagnosed in 73 surgical and 284 medical patients.

Treatment during the period consisted of intermittent i.v. heparin for three days, combined with peroral anticoagulants for 3–6 months. Phenylbutazone, 200 mg twice a day, was given to a minority of patients for a concomitant thrombophlebitis. Two patients were transferred to the adjacent Thoracosurgical Department. One of them died during operation, while the other responded successfully to treatment with streptokinase. Of the 73 surgical patients, 37 (50 %) died from massive pulmonary embolism, while 183 medical patients (64 %) died from this disease.

We have studied the medical patients with fatal, autopsy-verified pulmonary embolism. Autopsy was performed in 178 patients (97 %), representing 9 % of the total number of autopsies at the medical departments during the period investigated. Thus, our material comprises 90 females and 88 males with a mean age of 74 years (range 46–94).

A standard sheet, containing information on patient data, premortal condition, diagnoses, medical treatment, and important pathological findings, was compiled for each patient from pathological and medical records. To reduce bias, estimation of the indication for surgical or medical intervention—if the diagnosis of pulmonary embolism had been known—was done from the standard sheets and independently from this by renewed study of pathological and medical case reports. In 8 cases the two groups of investigators agreed that they would have

Table I. *Premortal condition in 168 patients with fatal pulmonary embolism and a concomitant complicating, severe, terminal disease*

	No. of pats.
Acute fulminant disease	
Extensive acute myocardial infarction with pronounced arrhythmias	8
Fulminant pneumococcal septicaemia admitted in terminal state	1
Cerebral thrombosis or haemorrhage	3
Pulmonary embolism with fatal outcome within 5 h	16
Severe, chronic disease with hopeless prognosis	
Cerebral thrombosis or haemorrhage	
Comatose for more than 4 days at death	6
Fed by tube	11
Debilitated, completely immobilized and helpless patients	40
Cardiovascular diseases	
Intractable cardial decompensation	27
Universal severe arteriosclerosis	11
Terminal pulmonary disease	6
Diabetes mellitus with severe organic damage	2
Malignant haematological diseases	6
Other malignant diseases	27
Terminal hepatic and/or renal insufficiency	4

started treatment, if the diagnosis had been known, while disagreement was found in two cases described below.

Case 1

A 68-year-old male with a pronounced angina pectoris for 5 years and a subendocardial infarction 6 months prior to admission for severe retrosternal pain and dyspnoea. Suddenly, after 6 days in hospital, he went into shock and died. Premortal diagnosis was myocardial infarction, in spite of negative ECG findings and atypical changes in serum transferases. Autopsy demonstrated massive pulmonary embolism and no recent myocardial infarction. The possibility of earlier pulmonary infarction could not be ruled out in the autopsy report.

Case 2

An 83-year-old man with three earlier myocardial infarctions. The last admission was occasioned by severe dyspnoea. The patient was treated for cardiac failure and pneumonia. After 12 days he developed irreversible ventricular fibrillation. Autopsy showed multiple, bilateral pulmonary infarctions of varying age and scarring after several earlier myocardial infarctions.

RESULTS

Table I shows the clinical state before death in 168 patients (95% of the total series) in whom the authors agreed that the final outcome was little influenced by pulmonary embolism. Dominating findings were severe cerebral and cardiovascular diseases (64%). Malignant diseases were found in 19%. Sixteen patients died within 4 hours after admission, and a further ten within 24 hours.

Table II. *Essential clinical diagnoses in 178 patients with autopsy-verified fatal pulmonary embolism*

	No. of pats.
Cardiovascular	
Acute or recent myocardial infarction	55
Cerebral arteriosclerosis	29
Arterial hypertension	18
Universal severe arteriosclerosis	8
Cardial decompensation	65
Atrial fibrillation	13
Acute or recent cerebral thrombosis or haemorrhage	49
Venous thrombosis of the lower limbs	27
Pulmonary	
Pulmonary embolism	26
Pulmonary insufficiency	6
Bronchopneumonia or lobar pneumonia	32
Metabolic	
Diabetes mellitus	21
Cancer	24
Renal insufficiency	7
Anaemia or dehydration	12
Various[a]	64
No. of diagnoses per patient	2.6

[a] Only diagnoses present in more than five patients are grouped.

The predominant premortal diagnoses are listed in Table II. Forty-nine patients (30%) had had a recent or earlier cerebral insult, 26 (15%) had been suspected of pulmonary embolism, 27 (15%) had had clinical signs of venous thrombosis.

The patients had been in the department on average for 15 days (range 0–98) at the time of death. Altogether 107 had been immobilized by severe incapacitating illness for 17 days (range 2–102) before death.

Essential autopsy findings are given in Table III. In 17 patients (9%) pulmonary embolism was the predominant finding. Most of the remaining cases were dominated by severe arteriosclerotic, pulmonary and neoplastic diseases.

Medication of these elderly patients is composite. Digitalis derivatives and/or diuretics were given to the majority, chemotherapy to 23%, and 59 (33%) received drugs with a major effect on the central

...d fatal pulmonary em-

	No. of pats.
...cardial infarction	55
...osis	29
...n	18
...eriosclerosis	8
...tion	65
	13
...bral thrombosis or	49
...of the lower limbs	27
	26
...ncy	6
...or lobar pneumonia	32
	21
	24
	7
...ion	12
	64
...patient	2.6

...sent in more than five patients are

...erebral and cardiovascular dis-...gnant diseases were found in ...nts died within 4 hours after ...rther ten within 24 hours.

premortal diagnoses are listed ...nine patients (30%) had had a ...ebral insult, 26 (15%) had been ...nary embolism, 27 (15%) had venous thrombosis.

...been in the department on aver-...age 0–98) at the time of death. ...been immobilized by severe in-...or 17 days (range 2–102) before

findings are given in Table III. pulmonary embolism was the .... Most of the remaining cases severe arteriosclerotic, pulmo-diseases.

...e elderly patients is composite. and/or diuretics were given to ...therapy to 23%, and 59 (33%) a major effect on the central

...fatal pulmonary embolism

	No. of pats.
Cardiovascular	
Universal severe arteriosclerosis	68
Chronic congestion of organs	91
Recent or old myocardial infarction	44
Recent or old cerebral emollitio	59
Aneurysm of abdominal aorta	7
Pulmonary	
Pulmonary embolism (without other essential findings)	17
Pulmonary insufficiency	13
Bronchopneumonia	23
Cancer	
Inoperable	27
Cerebral	
Diffuse cortical atrophy	23
Chronic pyelonephritis	9
Gastric ulcer	6
Other	42
No. of diagnoses per patient	2.4

nervous system. Nine patients were treated with heparin and phenprocoumon, and 9 with phenylbutazone (Table V). This level of antithrombotic treatment reflects a low incidence of premortal diagnosis (Table II), a high frequency of contraindications to medical intervention (Table IV), a short time of survival (13% died within 24 hours), and the premortal condition (Table I).

DISCUSSION

Venous thrombosis complicated by pulmonary embolism was a major problem after operations in the days before early mobilization (6, 10) and anticoagulant treatment (12, 17).

However, overall mortality from pulmonary embolism has not been reduced (5, 19) (Fig. 1). Several explanations of this phenomenon have been offered: 1) An increasing number of medical patients in a poor clinical state. 2) Persistence of rapidly progressing, fulminant cases. 3) Failure to diagnose pulmonary embolism (15, 18). 4) Insufficient effect of antithrombotic treatment (16, 17, 21).

Premortal condition

The average age of patients in this report, 74 years, is consistent with earlier findings (2, 4, 9). A certain

...therapy

	No. of pats.
Cerebral haemorrhage	13
Malignant arterial hypertension	0
Haemorrhagic diathesis	2
Gastric or duodenal ulcer	14
Bleeding from gastrointestinal tract, respiratory organs or genitourinary tract	6
Operation on central nervous system	2
Cooperation not possible	30
Hepatic insufficiency	3
Renal insufficiency	4
Total no. of pats. with contraindications	74
Fatal outcome within 24 h of hospital stay	26
Total no. of pats.	100

dominance of younger females has been observed by Havig (9). We found no sex difference, but this series includes no fertile females or females on peroral anticonceptive treatment.

It is noteworthy that for 95% of our patients a confirmed fatal pulmonary embolism constituted only a slight modification of life expectancy because of concomitant complicating, severe, terminal disease. Intensive medical treatment of severe diseases may extend life expectancy for very ill patients, but the price may be protracted immobilization (9). This shift from surgical to medical ward for patients in the terminal stage of the disease may reflect the finding that the frequency of pulmonary embolism is four times as high in medical as in surgical patients (1, 2, 14).

A high incidence of severe conditions has been noted earlier (5, 18, 22) but definitely lower percentages have also been given. Thus, Towbin (22) found terminal disease in about 40% of patients with fatal pulmonary embolism; Pallesen and Nørregaard (18) reported 43%, and Coon (5) estimated that pulmonary embolism influenced life expectancy in only half of his patients.

Our study, like earlier reports on the subject, is retrospective. We tried to minimize bias, the data on each patient being studied independently by two groups. Thus our results should reflect a real increase in the incidence of terminal diseases in elderly, hospitalized, medical patients.

Fulminant cases

Death after pulmonary embolism is rapid in a

Fig. 1. Frequency of autopsy-verified, fatal pulmonary embolism during 1890–1974 in the Department of Pathology, Vienna (quoted from Sigg (19) with the author's permission).

majority of cases. Thus Pallesen and Nørregaard (18) found that 70% of their patients with autopsy-verified pulmonary embolism died within 24 hours after the onset of symptoms. Havig (9) reports that 30% of patients with fatal pulmonary embolism died within 10 min, and MacIntyre (14) that 50% died within one hour.

Of our patients, 16 (9%) died within 5 hours after admission to the department and 26 during the first 24 hours in hospital.

Further analysis of the 26 patients with a premortal diagnosis of pulmonary embolism (Table V) and of the registered exact time of the onset of symptoms revealed that 13 of these patients died within 5 hours after the onset of symptoms.

Table V. *Antithrombotic treatment and premortal diagnosis of pulmonary embolism and/or venous thrombosis*

	Premortal diagnosis of pulmonary embolism (n=26)	Premortal indication of anti-thrombotic treatment (n=8)
No. of pats. treated with		
Anticoagulants	6	1
Phenylbutazone	4	0
Embolectomy	1	1
Premortal condition		
Death within 5 h of onset of symptoms	13	
Terminal cardiovascular diagnoses	2	
No premortal diagnosis		4
Failure of therapeutic consequence of diagnosis		2

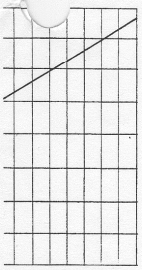
Failure to diagnose pulmonary embolism

Pulmonary embolism may be difficult to diagnose, as may venous thrombosis, and there is a definite discrepancy between clinical features and the result of different diagnostic procedures. Thus, the clinical diagnosis of venous thrombosis can be confirmed only by phlebography in 30% of cases (20), and vice versa, only 1/3 of phlebography-positive cases reflect clinical manifestations (9). Likewise, Goodall (7) confirmed clinical suspicion of pulmonary embolism in only 29% by pulmonary angiography.

Most studies report a premortal diagnosis in 10–27% of cases with fatal pulmonary embolism. We found that 11% of our cases had clinical signs of venous thrombosis, 10% of pulmonary embolism, and 4% of both diseases, totalling to 25% of the patients. This agreement between different reports probably reflects a poor clinical state of the patients, making the clinician hesitate to diagnose and treat.

Insufficient effect of antithrombotic treatment

Prospective, controlled clinical trials have clearly demonstrated the effect of a low-dose heparin regime in reducing thromboembolic incidences in risk-patients without involving severe bleeding episodes (12). However, there is still no convincing documentation for the postulated therapeutic effect of heparin (16).



ɔm Sigg (19) with the author's

ıat 13 of these patients died
e onset of symptoms.

lmonary embolism

may be difficult to diagnose,
bosis, and there is a definite
:linical features and the result
procedures. Thus, the clini-
ous embosis can be con-
graphy in 30% of cases (20),
1/3 of phlebography-positive
nanifestations (9). Likewise,
clinical suspicion of pulmo-
y 29% by pulmonary angio-

a premortal diagnosis in 10–
al pulmonary embolism. We
r cases had clinical signs of
)% of pulmonary embolism,
ses, totalling to 25% of the
:nt between different reports
ɔor clinical state of the pa-
cian hesitate to diagnose and

ıtithrombotic treatment

ł clinical trials have clearly
:t of a low-dose heparin re-
ɔmboembolic incidences in
ıvolving severe bleeding epi-
there is still no convincing
postulated therapeutic effect

Presenting a prospective, controlled clinical trial, Barrit and Jordan (3) reported a marked effect of antithrombotic therapy with heparin and oral anticoagulants in patients with pulmonary embolism. The set-up of this study has been criticized (16, 17, 21), and their results still await confirmation by other workers. Earlier reports could not use modern statistical tools and definite conclusions cannot be drawn (16).

A few patients may benefit from thoracosurgical intervention, but mortality in this procedure is very high (8), although recent reports are more promising (1). Fibrinolytic treatment may be a future answer to venous thrombosis and pulmonary infarction, but side-effects are still too serious for a more general application (11). Antiphlogistic therapy has a place in the treatment of venous thrombosis and may assist in preventing pulmonary embolism. However, clinical trials are still needed (19).

CONCLUSION

We conclude that the persistently high frequency of fatal pulmonary embolism in hopitalized patients has a multifactorial origin. The predominant premortal finding is a poor clinical state of the patients, with an incidence of 95% fulminant diseases and chronic illnesses with a hopeless prognosis.

A rapidly progressing fatal pulmonary embolism precluded intervention in about 10% of our patients, even if otherwise indicated. On the other hand, fatal pulmonary embolism in younger as well as elderly patients with no concomitant diseases has become very rare.

Sensitive diagnostic procedures are available for definite confirmation of manifest pulmonary embolism. However, very often the condition is clinically silent or the symptoms are misleading. In patients in a poor clinical state, diagnosis and treatment of pulmonary embolism has no influence on life expectancy. These two factors explain the low frequency of antithrombotic treatment in patients with fatal pulmonary embolism.

The number of very old and weak patients in medical wards will no doubt increase further in the years to come. This will certainly change the concept of fatal pulmonary embolism from "the dread of clinicians" (13) into an agonal incident in a terminal-care medical patient.

REFERENCES

1. Axelsen, F., Albrechtsen, O. & Fasting, H.: Behandling af massiv lungeemboli. Ugeskr Laeger 141: 1680, 1979.
2. Bang, N., Iversen, K. & Schmidt, H.: Thromboemboliske lungesygdomme belyst ved klinik og sektionsfund på et større hospitalsmateriale. Nord Med 60: 1413, 1958.
3. Barrit, D. W. & Jordan, S. C.: Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet 1: 1309, 1960.
4. Björnberg, Ö.: Dödande lungemboli hos gamla patienter med internmedicinska sjukdomar. Nord Med 68: 1548, 1962.
5. Coon, W. W.: The spectrum of pulmonary embolism. Arch Surg 111: 393, 1976.
6. Fabricius-Møller, J.: Thrombosebehandling i praksis. Månedsskr Prakt Lægegern 26: 489, 1948.
7. Goodall, R. J. R. & Greenfield, L. J.: Clinical correlations in the diagnosis of pulmonary embolism. Ann Surg 191: 219, 1980.
8. Greenfield, L. J.: Pulmonary embolism: Diagnosis and management. Curr Probl Surg 13: 4, 1976.
9. Havig, Ö.: Deep vein thrombosis and pulmonary embolism. Acta Chir Scand (Suppl) 478, 1977.
10. Heckscher, H.: Om rörelsebehandlingen vid thrombophlebitis i de nedre extremiteterna. Nord Med 22: 1094, 1944.
11. Kakkar, V. V. & Scully, M. F.: Thrombolytic therapy. Br Med Bull 34: 191, 1978.
12. Kiil, J., Kiil, J. & Axelsen, F.: Lavdosis-heparin som profylakse mod postoperativ lungeemboli og dyb venøs trombose. Ugeskr Laeger 140: 1224, 1978.
13. Leading article: Treatment of deep-vein thrombosis. Lancet 2: 593, 1962.
14. MacIntyre, I. M. C. & Ruckley, C. V.: Pulmonary emoblism—A clinical and autopsy study. Scott Med J 19: 20, 1074.
15. Marks, J., Truscott, B. M. & Withycombe, J. F. R.: Treatment of venous thrombosis with anticoagulant. Review of 1 135 cases. Lancet 2: 787, 1954.
16. McNicol, G. P.: Conventional uses of heparin. Thromb Diathes Haemorrh 33: 97, 1974.
17. Morris, G. K. & Mitchell, J. R. A.: Clinical management of venous thromboembolism. Br Med Bull 34: 169, 1978.
18. Pallesen, A. E. & Nørregaard, S.: Trombo-embolisk lungesygdom i en medicinsk afdeling. Ugeskr Laeger 127: 1493, 1965.
19. Sigg, K.: Varicen, Ulcus cruris und Thrombosen. Springer-Verlag, Berlin, Heidelberg and New York 1976.
20. Simpson, F. G., Robinson, P. J., Back, M. & Losowsky, M. S.: Prospective study of thrombophlebitis and "pseudothrombophlebitis". Lancet 1: 331, 1980.
21. Thomas, D. P.: Heparin in the prophylaxis and treatment of venous thromboembolism. Semin Hematol 15: 1, 1978.
22. Towbin, A.: Pulmonary embolism. Incidence and significance. JAMA 156: 209, 1954.