

Relation between Lung Cancer, Chronic Bronchitis, and Airways Obstruction

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Summary

Since cigarette smoking is an important cause of lung cancer and chronic bronchitis both conditions should occur together more often in cigarette smokers than would result from chance. If they do commonly occur together then severe airways obstruction, which is often associated with chronic bronchitis, should also be often associated with lung cancer. To discover whether this were so three groups of patients were studied at the London Chest Hospital. Two hundred men and 43 women who presented with lung cancer provided information on the prevalence of defined chronic bronchitis and airways obstruction in those suffering from lung cancer. The third group consisted of 233 men presenting with defined chronic bronchitis who were kept under observation to discover how many would die from lung cancer.

The results suggested that simple bronchitis and lung cancer often occur together but that obstructive bronchitis and lung cancer do not often occur together. The lack of association between lung cancer and severe airways obstruction requires an explanation.

Introduction

The evidence that cigarette smoking is associated significantly with both lung cancer and chronic bronchitis is beyond doubt.¹ Hence in cigarette smokers both diseases should occur together more often than would result from chance. Such an increased association has been reported in several clinical studies,²⁻⁶ though studies based on mortality statistics have suggested that bronchitis may protect from lung cancer.^{7, 8}

Severe airways obstruction is often associated with chronic bronchitis. If chronic bronchitis and lung cancer commonly occur together then severe airways obstruction should also be often associated with lung cancer. It was our impression, however, that such is not the case. To test the validity of this clinical impression we established a survey at the London Chest Hospital to determine the prevalence of chronic bronchitis and airways obstruction in patients presenting with lung cancer, and the incidence of lung cancer during observation of patients presenting with chronic bronchitis.

Patients and Methods

The following groups of patients were studied at the chest clinic, London Chest Hospital, which serves the east London boroughs of Hackney and Tower Hamlets: all men presenting with lung cancer (200 such patients were seen between 1966 and 1973); all women presenting with lung cancer (43 patients were seen during the same period); and 233 men referred to the bronchitis registry, which was established in January 1963 at the chest clinic at the suggestion of

the Chest and Heart Association. The function of the registry was to collaborate with local general practitioners in the diagnosis, treatment, prevention, and aftercare of chronic bronchitis.⁹ Selected general practitioners referred to the bronchitis registry all male patients aged 40 to 67 years to whom they had just given a sickness benefit certificate bearing a diagnosis of bronchitis.

All referrals in the three groups had standard clinical and radiological examination and simple ventilatory studies. The forced expiratory ratio (FER; forced expiratory volume in one second (FEV₁) as a percentage of the forced vital capacity) was recorded on the first attendance or admission and used as an index of the degree of airways obstruction. A FER of less than 50% was taken to indicate severe airways obstruction. All referrals in the three groups completed the Medical Research Council's questionnaire on respiratory symptoms.¹⁰ To reduce errors due to observer variability nearly all the interviews were conducted by either of two doctors with experience of the questionnaire. On the basis of their replies the patients could be separated into those who had had cough or phlegm or both on most days for as much as three months each year for more than two years and those who had not. Those who had were included in this study as suffering from chronic bronchitis.

Results

Men Presenting with Lung Cancer.—The 200 men presenting with lung cancer were aged 42 to 86 years (mean 63 years), and all except one had been smokers. On the basis of their replies to the questionnaire 157 men (79%) had chronic bronchitis as well. The mean length of their history of cough or phlegm was 24 years. Thirty-two (16%) of the men had severe airways obstruction. The degree of airways obstruction in the 157 men suffering from both lung cancer and chronic bronchitis was not significantly different from that in the remaining 43 men suffering from lung cancer only (table I).

Women Presenting with Lung Cancer.—The 43 women presenting with lung cancer were aged 40 to 76 years (mean 59 years), and eight (19%) had never smoked. On the basis of their replies to the questionnaire 24 women (56%) had chronic bronchitis as well. The mean length of their history of cough and phlegm was 12 years five months. Only one out of 43 women presenting with lung cancer had severe airways obstruction. The degree of airways obstruction in the 24 women suffering from both lung cancer and chronic bronchitis was similar to that found in the 19 women suffering from lung cancer without chronic bronchitis (table I). The numbers involved were too small to permit of any definitive conclusion, but there seemed to be no statistical difference between the two groups.

Men Presenting with Chronic Bronchitis.—There were 233 men aged 40 to 67 years (mean 56 years) who had had a recent sickness absence certified by their general practitioners owing to bronchitis and who on referral to the bronchitis registry fulfilled the criteria for the diagnosis of chronic bronchitis. These patients are called registry bronchitics in the tables. Of these 233 patients 228 (98%) had been smokers and the mean length of their history of cough or phlegm was 17 years.

Airways Obstruction in Men with Bronchitis.—The degree of airways obstruction in patients registered as having bronchitis was compared with that in 107 of the 200 men presenting with lung cancer who were also suffering from chronic bronchitis and were of similar ages (table II). Severe airways obstruction was twice as common among the former group (33%) than among the men with lung cancer and chronic bronchitis (15%). The difference was highly significant (0.1% level).

Mortality Among Registered Patients.—The patients who were registered as having bronchitis were observed from January 1963 to December 1970, and none were lost to the survey. By the end of that period 60 of the 233 had died; their mean survival time was two years 10 months (range one month to seven years). The mean period of

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TABLE 1—Airways Obstruction in 200 Men and 43 Women Presenting with Lung Cancer

	Men			Women		
	All Patients	Lung Cancer with Chronic Bronchitis	Lung Cancer without Chronic Bronchitis	All Patients	Lung Cancer with Chronic Bronchitis	Lung Cancer without Chronic Bronchitis
No. of patients	200	157	43	43	24	19
Mean age (range)	63 (42-86)	64 (42-86)	63 (49-84)	59 (40-76)	59 (40-76)	59 (46-74)
Mean FER (%)	61	60	64	70	69	71
No. (%) in each FER range:						
<40%	11 (6)	10 (6)	1 (2)	0	0	0
40-49%	21 (11)	17 (11)	4 (9)	1 (2)	1 (4)	0
50-59%	44 (22)	36 (23)	8 (19)	7 (16)	4 (17)	3 (16)
60-69%	66 (33)	52 (33)	14 (33)	15 (35)	10 (42)	5 (26)
≥70%	58 (29)	42 (27)	16 (37)	20 (47)	9 (38)	11 (58)
<50%	32 (16)	27 (17)	5 (12)	1 (2)	1 (4)	0
≥50%	168 (84)	130 (83)	38 (88)	42 (98)	23 (96)	19 (100)

TABLE 2—Airways Obstruction in Registry Bronchitics and in Men with both Lung Cancer and Chronic Bronchitis

	Registry Bronchitics	Patients with Lung Cancer and Chronic Bronchitis
No. of patients	233	107
Mean age (range)	56 (40-67)	60 (42-67)
Mean FER (%)	58	62
No. (%) in each FER range:		
<40%	33 (14)	7 (7)
40-49%	43 (18)	9 (8)
50-59%	44 (19)	24 (22)
60-69%	55 (24)	31 (29)
≥70%	58 (25)	36 (34)
<50%	76 (33)	16 (15)
≥50%	157 (67)	91 (85)

observation of the 173 patients who survived was five years nine months (range two to eight years). The causes of death were divided into four groups: lung cancer, respiratory diseases (excluding lung cancer), cardiovascular diseases (including cerebrovascular diseases), and all other causes. Table III shows how these causes were related to the severity of airways obstruction on first attendance. Of the 76 registry bronchitics who had severe airways obstruction on first attendance 31 (41%) died. None died from lung cancer. Of the 29 registry bronchitics without severe airways obstruction who died 11 died from lung cancer. The lack of deaths from lung cancer among those with severe airways obstruction compared with 11 out of 29 (38%) deaths from lung cancer among those without severe airways obstruction was highly significant (0.1% level). In table IV deaths in registry bronchitics are shown by mean age at death, FER on first attendance, and cause. There was no statistical difference between the mean ages at death for the different causes. The mean FER of those who died from all causes was 50%. The difference between that and the mean FER for those who died from lung cancer (68%) was significant (1% level).

TABLE 3—Cause of Death in Registry Bronchitics related to Severity of Airways Obstruction

Cause of Death	All Registry Bronchitics (n = 233)	Patients with Severe Airways Obstruction (n = 76)	Patients without Severe Airways Obstruction (n = 157)
Lung cancer	11 (18%)	0	11 (38%)
Respiratory	22 (37%)	18 (58%)	4 (14%)
Cardiovascular	18 (30%)	9 (29%)	9 (31%)
Other causes	9 (15%)	4 (13%)	5 (17%)
Total	60 (100%)	31 (100%)	29 (100%)

TABLE 4—Cause of Death in Registry Bronchitics related to Initial FER and Age at Death

Cause of Death	No. (%) of Deaths	Mean Age at Death (Years)	Mean FER (%)
Lung cancer	11 (18)	64	68
Respiratory	22 (37)	62	39
Cardiovascular	18 (30)	62	52
Other causes	9 (15)	61	51
Total	60 (100)	62	50

Discussion

Our results show, firstly, that lung cancer and chronic bronchitis often occur together; secondly, that when they do severe airways obstruction is uncommon; and, finally, that death from lung cancer is uncommon in patients suffering from chronic bronchitis with severe airways obstruction even though they survive to lung cancer age.

The prevalence of chronic bronchitis among our patients presenting with lung cancer was 79% for men and 56% for women. Since the mean length of history of cough or phlegm was 24 years for men and over 12 years for women it was unlikely that these symptoms resulted from their lung cancer. These patients were therefore chronic bronchitics who had subsequently developed lung cancer. This supports the finding of an increased association between these two conditions in an Australian survey,⁴ in which chronic bronchitis, similarly defined, was found in 74% of ex-servicemen suffering from lung cancer.

Our definition of chronic bronchitis took no account of breathlessness or chest illness and therefore covered both the simple and disabling forms of chronic bronchitis. The index of severe airways obstruction was a FER of less than 50%. This figure was chosen after a hunt for a value which would produce the most statistically significant differences. No advantage was found using the FEV₁ instead of the FER.

Only 17% of the men with lung cancer who also had chronic bronchitis had severe airways obstruction. Among women suffering from lung cancer and chronic bronchitis only one out of 24 had severe airways obstruction. The prevalence and severity of airways obstruction in patients presenting with lung cancer was the same whether or not they had chronic bronchitis as well.

Severe airways obstruction was only half as common in the men presenting with lung cancer as in those registered as having bronchitis. The registered patients with bronchitis came from the same area and were in the same age range as the men presenting with lung cancer. They were selected because they had defined chronic bronchitis plus a recent sickness absence on account of it. Severe airways obstruction would obviously be common in such a group. If cigarette smoking is related to the development of both lung cancer and airways obstruction then it is surprising that the airways obstruction in the men with lung cancer was significantly less than in those referred to the bronchitis registry.

If airways obstruction is not common in patients suffering from lung cancer thoracotomy should not be frequently precluded on this account. Out of 260 men and women suffering from bronchial carcinoma without metastatic spread 35 (13%) were considered unfit for thoracotomy, mainly on clinical grounds.¹¹ Pulmonary function tests in those rejected for thoracotomy showed evidence of significantly worse airways obstruction and lung hyperinflation and a greater reduction in transfer factor and arterial oxygen pressure than in those accepted for surgery. If cigarette smoking is associated with both lung cancer and airways obstruction it is again surprising that the rejection figure was not higher.

The close liaison between the bronchitis registry, local general practitioners, chest clinic social workers, and health visitors made it possible to follow up all 233 registered patients with bronchitis from January 1963 to December 1970. Eleven (18%) of the 60 deaths in this group were due to lung cancer, and all eleven deaths were in patients who did not have severe airways obstruction. This suggests that people with chronic bronchitis who do not have severe airways obstruction are more likely to die from lung cancer than those with bronchitis with severe airways obstruction.

The lack of deaths from lung cancer in registered bronchitic patients with severe airways obstruction was not due to failure to survive to lung cancer age because of earlier death from another cause: the mean age at death from all causes was 62 years, compared with 64 years for those who died from lung cancer, and this difference is not significant.

A study of mortality from bronchitis and lung cancer in England and Wales⁸ showed that death from bronchitis tended to occur later than death from lung cancer. Furthermore, more deaths from bronchitis and fewer deaths from lung cancer were found in coal-mining and textile-producing towns, and it was suggested that "bronchitis may have a protective effect on the lungs, and that the patient who has this chronic inflammatory and degenerative process at work may be at a relative advantage vis-à-vis his fellow with more normal lungs."

Our findings suggest that simple bronchitis and lung cancer often occur together and that obstructive bronchitis and lung cancer do not often occur together. This raises several questions. Is severe airways obstruction unfavourable to the development of lung cancer or is it associated with the same factor which protects against lung cancer? Does the patient with severe airways obstruction give up smoking and so reduce his chances of developing lung cancer? Do repeated episodes of lung infection, which are commonly associated with obstructive bronchitis, enhance immunological defence against the malignant cell? Does the

severe airways obstruction of asthma also show a lack of association with lung cancer, as suggested in a report from Australia in which only one man among 13 000 people with asthma observed over 12 years developed lung cancer?¹²

Our findings pose but do not answer any of these questions. Further study of the lack of association between lung cancer and the severe airways obstruction of chronic bronchitis may provide a better understanding of both conditions.

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Hyperparathyroidism after Renal Transplantation

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Summary

Renal transplantation reduced circulating parathyroid hormone in recipients of renal allografts. Nevertheless, biochemical and histological evidence of mild hyperparathyroidism persisted up to eight years after renal transplantation despite good graft function.

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Introduction

The effects of renal transplantation on secondary hyperparathyroidism have been well documented.¹⁻⁷ In most patients the radiological and biochemical changes of hyperparathyroidism regress after transplantation so that parathyroidectomy is rarely needed,⁸ but there are conflicting reports⁵⁻⁷ on the rate and extent of this regression.

Hence we investigated parathyroid function in 71 recipients of cadaveric renal allografts with biochemical, radioimmuno-logical, and histological techniques. This is the first paper in which skeletal histology has been systematically studied in renal allograft recipients with good graft function.

Patients and Methods

Two groups of renal allograft recipients were investigated. The first group consisted of 11 patients (four men and seven women) who were studied before transplantation and during the subsequent three months. The second group consisted of 60 patients (30 men and 30 women) who had received renal transplants from six and a half to 95 months (median 46 months) before this study, after haemodialysis ranging from a few days to two years (mean 7.2 months). In 40 of