Earlier Diagnosis and Survival in Lung Cancer

G. Z. BRETT,* M.D.

British Medical Journal, 1969, **4**, 260–262

Summary: In a controlled investigation the survival prospects of lung cancer in a population of men aged 40 and over who had been offered six-monthly chest radiographs over a period of three years were compared with lung cancer in a similar population without such x-ray facilities. The five-year survival rate of lung cancer in the study series was 15%, and in cases discovered by six-monthly examination 23%, compared with 6% in the control series. The average expectation of life after diagnosis was 2·5 years for the test cases and 1·2 for the control cases. Survival declined with age. Of resected lung cancer, 32% survived five years in the test series and 23% in the control series. The five-year survival rate for squamous carcinoma and adenocarcinoma in the test series was 28% and 25% respectively, compared with 15% and nil in the control series.

On the basis of these results it is concluded that through earlier radiological detection a modest improvement in the prognosis of lung cancer can be achieved.

Introduction

In an earlier article an account was given of a controlled study carried out by the Mass Radiography Service of the North West Metropolitan Region in which the value of lung cancer detection by frequent chest radiographs of a population at risk was measured in terms of resectability and mortality (Brett, 1968). The present investigation evaluates early diagnosis of lung cancer on the basis of case survival.

To preserve the continuity of the study as a whole the following summary of its earlier results is submitted.

A test group of 29,723 men aged 40 and over, drawn mainly from large industrial establishments, was offered six-monthly chest radiographs over a period of three years, while a control group of 25,311 men of a similar age structure and with similar smoking habits was radiographed only at the beginning and the end of the study. To compare their lung cancer experience these populations were subsequently followed up by identical methods and 29,416 (98·9%) persons in the test group and 25,044 (99·0%) in the control were traced. Excluding those cases of lung cancer discovered at the first *x*-ray examinations, there were 101 cases in the test series and 76 in the control for analysis, giving an annual incidence of 1·1 and 1·0 per thousand, respectively. Of the 101 cases, 65 were discovered by six-monthly *x*-ray examination and 36 by other means, in between surveys. In the test group as a whole 43·6% of the patients underwent resection, compared with 29% in the control group, the difference being statistically significant. Of the 65 patients detected by six-monthly surveys 65% underwent resection. The annual mortality from lung cancer was 0·7 per thousand in the test population and 0·8 in the control; this difference was not statistically significant.

Had the improved resectability of lung cancer in the test population been reflected in a significantly lower lung cancer mortality compared with the controls, the case for early diagnosis by six-monthly examination would have been strong. In the event the difference in mortality rates was too small for definite conclusions to be drawn. The reasons for this equivocal result may only be surmised. It is possible that as the incidence of lung cancer was marginally higher in the test population the cause of death in this group was more accurately diagnosed than in the control. But it could also be argued that because of the relatively short duration of the study the number of deaths might have been too small for greater differences in mortality to emerge.

Hence it has been necessary to widen the scope of the original analysis and to explore the possibility that a comparison of the survival prospects in the two cancer series would provide a more positive criterion for the assessment of early diagnosis than a comparison of population mortality. Such a comparison was feasible because sufficient time had now elapsed from the final *x*-ray examination of the two population samples to allow for at least a five-year follow-up of each cancer case.

Method and Material

Survival has been related to age at the time of diagnosis, the histological type, and the resectability of the growth. The basic comparison was between the survival of 101 patients with lung cancer in the test series and 77† in the control series, but as the 65 cases detected by repeat chest radiographs were of special interest they were analysed separately. Though possibly some cases of lung cancer, alive or dead, have been overlooked, it is unlikely (since 99% of the two population samples have been traced) that their number would have been significantly greater in one series than in the other to affect the validity of the comparison.

Results

Survival in Both Series

By September 1968 a number of patients with lung cancer in the test series had survived for periods of up to eight years, whereas survivors in the control series, since they were, with one exception, diagnosed at the end of the three-year study, could only be followed up for five years. For this reason it was thought that the detailed comparison between the two series would be more profitable if confined to a five-year survival period.

Of the 101 patients in the study series, 15 (15%) survived five years and of the 77 in the control series 5 (6%) (Tables I and II). The average expectation of life from diagnosis, calculated by actuarial methods, is probably at least 2·5 years for the test patients compared with 1·2 years for the controls.

In the test series the prospects of survival declined with age (Table I), while in the control series the survival record was poor for all age groups (Table II). In age group 40–49 none of the eight cases survived even one year, and in age group 50–59 the five-year survival rate was less than half (8%) that of the test group. The distinct discrepancy between a nil five-year survival rate in age group 40–49 in the control series and the 33% in the test series was of interest. If it were thought that lung cancer in the younger man was of the fast-growing variety, it might well have been picked up early enough at six-monthly routine surveys, but too late by other methods in the

* Consultant Chest Physician and Director, Mass Radiography Service, North West Metropolitan Region.

† One additional case has come to light since the report in 1968.

control series. This is supported by the fact that on average 78% of the cases in this age group were resectable in the test series and only 13% in the control series.

Correlation between survival of the patient and the resectability and histological type of lung cancer is better substantiated in the test series than in the control. This may be attributed to the fact that the numerically larger test series could more easily support the fragmentation necessary for the analysis of these variables than the control series. To the disadvantage of the control series was also its higher proportion of cases of unverified histology. Since this is probably an indication of the advanced stage of the disease at diagnosis it has to be accepted in a study of this kind.

In the test series 44% of lung cancer cases were resected, and 32% of these survived five years. There was one unresected survivor. In the control series 29% of the cases were operable and 23% of these survived five years.

The five-year survival rate of 28% for squamous carcinoma and 25% for adenocarcinoma in the test series compares favourably with a 15% and nil survival rate respectively in the control series. Survival of undifferentiated cancer was equally poor in both series (11%).

Thus at almost every point of the comparison lung cancer in the test series did better than in the control.

Cases Detected by Six-monthly Examination

The 65 cases in this group were extracted from the total of 101 in the test series for separate analysis (Table III). It may be seen that 23% survived five years after diagnosis. This is considerably better than the 15% survival for the test series as a whole (Table I) and more than three times as good as the 6% in the control series (Table II). Squamous carcinoma and adenocarcinoma had the best prognosis; 30% and 40% respectively survived five years, compared with 16% of the undifferentiated type. Both resectability and survival worsened with age, but the gradient was less pronounced than in the test series as a whole. Of the cases of resected lung cancer 33% survived five years.

The five-year survival rate of 23% in these 65 cases compares with a 30% five-year survival rate observed in an earlier investigation for cases picked up by mass radiography conducted at three-yearly or longer intervals (Brett, 1959). This poses the interesting question whether the length of the interval between routine surveys leading to the detection of lung cancer is relevant to an improved prognosis of the disease. To try to answer this question the survival prospects of all (51) lung cancer cases discovered at the first (three-yearly) examination of both test and control populations were investigated. Table IV shows that of these 51 cases 61% were resected and 31% survived five years. These figures are broadly comparable to those observed in cases detected by six-monthly surveys (Table III).

TABLE IV.—*Survival of* 51 *Cases of Lung Cancer Detected at the First X-ray Examination of Test and Control Populations*

Histology	No.	Percentage Resected	Percentage of 5-Year Survivors
Squamous	23	70	48
Undifferentiated ..	19	58	26
Adenocarcinoma ..	4	100	0
Not established ..	5	0	0
Total	51	61	31

Discussion and Conclusions

Results of statistical calculations based on relatively small numbers have to be assessed with caution. Thus, although the

TABLE I.—*Survival of* 101 *Cases of Lung Cancer in Test Series Irrespective of the Source of Detection*

Histology	Age 40–49 Years					Age 50–59 Years					Age 60+ Years					Total				
	No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors	
		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
Squamous	3	3	100	2	67	17	14	82	6	35	12	8	67	1	8	32	25	78	9	28
Undifferentiated ..	5	4	80	1	20	19	7	37	2	11	12	3	25	1	8	36	14	39	4	11
Adenocarcinoma ..	—	—	—	—	—	6	5	83	2	33	2	0	0	0	0	8	5	62	2	25
Not established ..	1	0	0	0	0	11	0	0	0	0	13	0	0	0	0	25	0	0	0	0
Total ..	9	7	78	3	33	53	26	49	10	19	39	11	28	2	5	101	44	44	15	15

TABLE II.—*Survival of* 77 *Cases of Lung Cancer in Control Series*

Histology	Age 40–49 Years					Age 50–59 Years					Age 60+ Years					Total				
	No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors	
		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
Squamous	1	1	100	0	0	11	7	64	1	9	8	3	38	2	25	20	11	55	3	15
Undifferentiated ..	1	0	0	0	0	10	5	50	2	20	7	3	43	0	0	18	8	44	2	11
Adenocarcinoma ..	1	0	0	0	0	4	2	50	0	0	1	0	0	0	0	6	2	33	0	0
Not established ..	5	0	0	0	0	12	1	8	0	0	16	0	0	0	0	33	1	3	0	0
Total ..	8	1	13	0	0	37	15	41	3	8	32	6	19	2	6	77	22	29	5	6

TABLE III.—*Survival of* 65 *Cases of Lung Cancer Detected in Test Series by Six-monthly X-ray Examinations*

Histology	Age 40–49 Years					Age 50–59 Years					Age 60+ Years					Total				
	No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors		No.	Resected		5 Year Survivors	
		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%		No.	%	No.	%
Squamous	3	3	100	2	67	16	14	88	6	38	11	7	64	1	9	30	24	80	9	30
Undifferentiated ..	5	4	80	1	20	15	7	47	2	13	5	3	60	1	20	25	14	56	4	16
Adenocarcinoma ..	—	—	—	—	—	5	4	80	2	40	—	—	—	—	—	5	4	80	2	40
Not established ..	1	0	0	0	0	—	—	—	—	—	4	0	0	0	0	5	0	0	0	0
Total ..	9	7	78	3	33	36	25	69	10	28	20	10	50	2	10	65	42	65	15	23

five-year survival prospects for lung cancer patients in a test population subjected to frequent examination have been more than twice as good as in a control population without such facilities, this improvement, measured by the number of long-term survivors, has been of modest proportions. It provides suggestive but not conclusive evidence of the value of earlier diagnosis of lung cancer, the difference in survival ($\chi^2=2{\cdot}28$) not being statistically significant at the 5% level. This may be attributed to the many imponderable factors affecting the individual case and more particularly to the fact that only 65% of all cases in the test series were actually detected by six-monthly chest radiographs. As in this group of patients the five-year survival is significantly better than in the controls ($P<0{\cdot}01$), using the χ^2 test, it is conceivable that, had more lung cancer been discovered by six-monthly *x*-ray examination than has been the case, the observed survival rate of 15% for the test series as a whole might have been substantially higher and its significance greater.

The question arises whether the improved survival prospects observed in the test series were simply due to survival being measured from an earlier period in the duration of the disease (because the diagnosis was made earlier), while the course of the disease remained the same. If this were so, the distribution of deaths from lung cancer at six-monthly intervals from diagnosis would just show that its peak in the test series had shifted slightly to the right compared with the control series. In fact, the mortality curves of both cancer series are almost identical over a period of at least four years ; thereafter a number of long-term survivors can be found in the test series. There are therefore no grounds for assuming that the improvement in survival of lung cancer in the test series was an artifact.

The failure of early detection to reduce lung cancer mortality in a population at risk (Brett, 1968) has not precluded an improvement in the long-term survival of individual cancer patients in the same population, as the present investigation has shown. This reflects the difference between the two approaches to the problem—in which death rates are concerned with whether people die and survival rates with when they die. The possible reasons why lung cancer mortality in the test population was not significantly reduced by earlier diagnosis are discussed in the introduction to this paper. That it is now possible to show that the survival prospects of lung cancer patients in the test series were more favourable than in the control series suggests that in a short-term study of this kind survival rates may be more suitable for an appraisal of early diagnosis than mortality rates. For a complete assessment both lines of investigation had to be explored.

The worsening survival prospects with advancing age of the patients in this study are at variance with results reported by Nash, Morgan, and Tomkins (1968), who found an opposite trend in their series. This is difficult to explain. Apart from this discrepancy, and if the different design of their study as well as the slightly shorter follow-up are considered, the four-year survival rates of 27% in lung cancer picked up by six-monthly examination of 67,400 men aged 45 and over and of 18% in lung cancer, irrespective of its source of detection reported by these authors, are comparable to the 23% and 15% five-year survival rates respectively in this series. In the absence of a control group Nash *et al.* compared the number of their four-year survivors with that expected on the basis of records from the South Metropolitan Cancer Registry. They found that the expected number of four-year survivors was only half that actually observed in their mass radiography series. This result is similar to the 15% and 6% survival rates obtained from a direct comparison between the test and control groups in the present study.

The finding that, so far as survival prospects are concerned, there is little to choose between lung cancer detection by six-monthly examination and more widely spaced out routine surveys merits attention. Johnston and Smith (1968) reported in a different context that the two-year survival in lung cancer discovered by "normal" mass radiography was practically the same as in special yearly cancer surveys. If the essential feature of routine mass radiography is considered to be an absence of significant symptoms in its examinees, the diagnosis of lung cancer by this method will be "early" whatever the interval between *x*-ray examinations, as symptom cases will have been discovered in the interim period by other means. For this reason the similarity of the survival figures between cases detected by frequent and infrequent routine surveys is not surprising. It suggests that it is the presymptomatic aspect of mass radiography detection and not the timing of examinations that influences prognosis.

Six-monthly surveys have, however, the additional value that in a population at risk they will discover more lung cancer earlier than surveys conducted at three-yearly or longer intervals, thus giving the chance of a better prognosis to more patients. On this basis there is a case for directing mass radiography towards earlier detection of lung cancer in high-risk population groups, provided this could be done economically and would not, because of limited resources, restrict the still necessary search for tuberculosis.

I am grateful to Dr. B. Benjamin for his help in calculating the survival rates, and to Professor R. Doll for his valuable advice.

REFERENCES

Brett, G. Z. (1959). *Tubercle*, **40**, 192.
Brett, G. Z. (1968). *Thorax*, **23**, 414.
Johnston, R. N., and Smith, D. H. (1968). *Lancet*, **2**, 588.
Nash, F. A., Morgan, J. M., and Tomkins, J. G. (1968). *British Medical Journal*, **2**, 715.