ORIGINAL ARTICLES

Influence of Delay of Surgery on the Survival of Patients With Bronchogenic Carcinoma

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OBJECTIVE: Bronchogenic carcinoma is the main cause of tumor-related deaths among men in Spain. The British Thoracic Society recommends that no longer than 4 weeks should pass from the moment a patient's name is placed on a waiting list until surgery takes place. We analyzed the influence of time until surgery on survival in patients with lung cancer.

PATIENTS AND METHODS: We operated on 108 patients diagnosed with bronchogenic carcinoma between January 1, 2001 and December 31, 2002. The time until surgery was defined by the date of application for care in our department until the moment of surgery.

RESULTS: The mean time on the waiting list was 56.87 days. No significant differences in mean wait-list times could be found in relation to tumor stage, type of surgery, patient age, or complete resection rate. The median survival in this patient series was 35 months. No significant differences in survival were found in relation to time until surgery in either the univariate or multivariate analysis. Pathologic stage, complete resection of the tumor, and patient age were prognostic factors.

CONCLUSIONS: We found no evidence that delaying surgery affects survival in lung cancer patients. However, efforts should be made to reduce surgical wait-list times to bring them into line with the recommendations of scientific societies.

Key words: *Bronchogenic carcinoma. Waiting lists: surgery. Tumor resection.*

Influencia de la demora quirúrgica en la supervivencia de los pacientes intervenidos por carcinoma broncogénico

OBJETIVO: La primera causa de muerte de origen neoplásico en varones en nuestro medio es el carcinoma broncogénico. La British Thoracic Society recomienda que el tiempo de demora quirúrgica desde el momento de inclusión en una lista de espera hasta la cirugía ha de ser menor de 4 semanas. Analizamos la influencia de la espera quirúrgica en la supervivencia de estos pacientes.

PACIENTES Y MÉTODOS: Entre el 1 de enero de 2001 y el 31 de diciembre de 2002 se intervino en nuestro servicio a 108 pacientes con el diagnóstico de carcinoma broncogénico. El tiempo de espera quirúrgica se consideró desde la fecha de solicitud de asistencia en nuestro servicio hasta el momento de la cirugía.

RESULTADOS: La media de los tiempos de espera fue de 56,87 días. No se hallaron diferencias significativas en las medias de los tiempos de espera según el estadio tumoral, el tipo de cirugía practicada, la edad del paciente o el índice de resección completa. La mediana de supervivencia de la serie fue de 35 meses. No se apreciaron diferencias significativas en la supervivencia en relación con la demora quirúrgica en el estudio univariante ni en el multivariante. El estadio patológico, la resección completa del tumor y la edad del paciente demostraron ser factores pronósticos.

CONCLUSIONES: No hemos encontrado evidencia de que nuestra demora quirúrgica influya en la supervivencia de estos pacientes. No obstante, nuestros esfuerzos deben dirigirse a la reducción de estos tiempos de espera quirúrgica hasta que se aproximen a las recomendaciones de las sociedades científicas.

Palabras clave: *Carcinoma broncogénico. Demora quirúrgica. Resección tumoral.*

Introduction

Bronchogenic carcinoma is the leading cause of death from tumor-related disease in men in the developed world.[1] Diagnosis usually comes at very advanced stages.[2] Although the delay between initial clinical suspicion and surgical treatment for patients who need it is recommended not to

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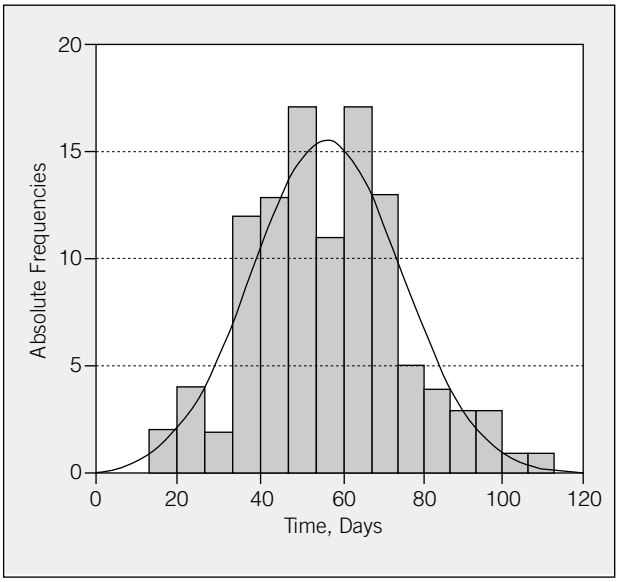

Figure 1. Distribution of surgical waiting times and the curve of normal distribution.

exceed 8 weeks,[3] the waiting period is longer in most patient series in the literature. Surgery is delayed for many reasons (related to diagnosis, patient referral, type of surgery); nonetheless, the social impact of lung cancer calls for an analysis of the situation in our practice setting. The aim of this study was to analyze the impact of surgical delay on survival in patients with lung cancer.

Patients and Methods

Between January 1, 2001 and December 31, 2002, 141 patients newly diagnosed with bronchogenic carcinoma were consecutively placed on the waiting list of the thoracic surgery department of our hospital after assessment of operability and resectability. While the patients waited for surgery, laboratory, radiologic and echocardiographic studies were carried out and a preanesthetic assessment was performed. Other examinations, imaging or function studies, or consultations with other specialists were also ordered to complement the preoperative assessment as necessary. Patients who were undergoing any type of neoadjuvant treatment (9 cases) or who refused surgery after being placed on the waiting list (11 cases) were excluded from the study. Operations were canceled for 8 patients due to disease progression during the waiting period. Also excluded from statistical analysis was 1 patient who waited 177 days while recovering from myocardial infarction and 4 patients who died within 30 days of surgery and whose deaths were attributed to the operation.

The remaining 108 patients underwent surgery. Complete resection was performed in 96 patients and exploratory thoracotomy or incomplete resection in 12. Resection was considered complete if margins were free of tumor. Stages on the pathology reports were as follows: 15 patients (13.9%) were in stage Ia, 38 (35.2%) in stage Ib, 18 (16.7%) in stage IIb, 20 (18.5%) in stage IIIa, 11 (10.2%) in stage IIIb, and 6 (5.6%) in stage IV. Atypical segmentectomy was performed in 7 patients (6.5%), lobectomy or bilobectomy in 47 (43.5%), and pneumonectomy in 43 (39.8%). Mediastinal nodes were sampled systematically in all cases except those in whom no adenopathy was visible in regions that were accessible during surgery. The mean (SD) was 64.46 (9.14) years at the moment of surgery (range, 42-80 years). Patients were followed for at least 36 months.

The following variables were studied retrospectively: waiting list time, tumor stage, age (analyzed categorically as younger and older than 70 years), surgical technique, tumor resectability, and survival. The period of time on the waiting list was considered to start when a request for care was received by the thoracic surgery outpatient clinic and to end at the moment of surgery; thus, delay was the time attributable to outpatient care until the operation. The series was divided into 2 groups for statistical analysis: group A patients who waited 56 days or fewer, and who made up half the series, and group B patients who waited longer than 56 days.

Statistical Analysis

Overall results were expressed as absolute and relative frequencies for qualitative variables and means (SD) for quantitative variables, except for survival, which was expressed as the median and 95% confidence interval (CI). The Student *t* test was used for univariate analysis, and analysis of variance was used to compare means between each group. A χ^2 was used for categorical variables. The Kaplan–Meier method and log-rank test were used to compare survival. Multivariate analysis was carried out by binary logistic regression for categorical variables, and survival was further analyzed by forward conditional stepwise Cox regression. A value of *P* less than .05 was considered to indicate a statistically significant result. Data were analyzed with the Statistical Package for the Social Sciences, version 12.0 for Windows (SPSS, Chicago, Illinois, USA).

Results

The mean number of days on the waiting list in this series was 56.87 (18.557) days (range, 18-112 days) (Figure 1). Table 1 shows the distribution of stages on the pathology reports.

Further testing was considered necessary for 33 patients (30.6%) after the first visit to the outpatient thoracic surgery service. The mean time on the waiting list for this group of patients was 58.58 (18.283) days, in comparison with 56.12 (18.749) days for the remaining patients. The differences were not statistically significant (*P*=.526). Nor were there significant differences in waiting list times in function of tumor stage (*P*=.437).

Type of surgery (*P*=.754) and patient age (*P*=.488) also had no significant influence on waiting list time (Table 1). Nor were significant differences found in the distribution of complete resections, surgical techniques, and tumor stage in the surgery or pathology reports in groups A and B.

The median survival was 35 months (95% CI, 28-42 months). Other variables were also analyzed for a correlation with survival in order to study the effect surgical delay might have had on prognosis for these patients undergoing lung cancer operations. Statistically significant correlations with survival were found for complete resection of the tumor *P*<.005), surgical technique (*P*<.005), and tumor stage stated on the surgery or pathology report (*P*<.005). No significant correlations were found for patient age (*P*=.100) or time on the waiting list (*P*=.803) (Figure 2).

The median survival was 38 months (95% CI, 29-47 months) in group A and 35 months (95% CI, 22-48 months) in group B (Table 2). No significant differences in survival were found between patients who underwent further preoperative testing and those who did not (*P*=.448).

However, the multivariate Cox regression analysis revealed the following variables to be independently associated with patient survival: tumor stage on the reports from surgery or pathology, complete resection of the tumor, and age 70 years or older (Table 2). Surgical delay was not a significant variable in that analysis (*P*>.05).

To rule out the influence of tumor stage on prognosis, the analysis was repeated for patients in tumor stage Ia or Ib (n=53) according to the surgery or pathology report. The median survival for this group was 54 months. Only age 70 years or older proved to be an independent risk factor in these patients both in the univariate (*P*=.0425) and multivariate (*P*=.051) analyses. In these cases, the influence of complete resection was not assessed, given that all patients were in stage I.

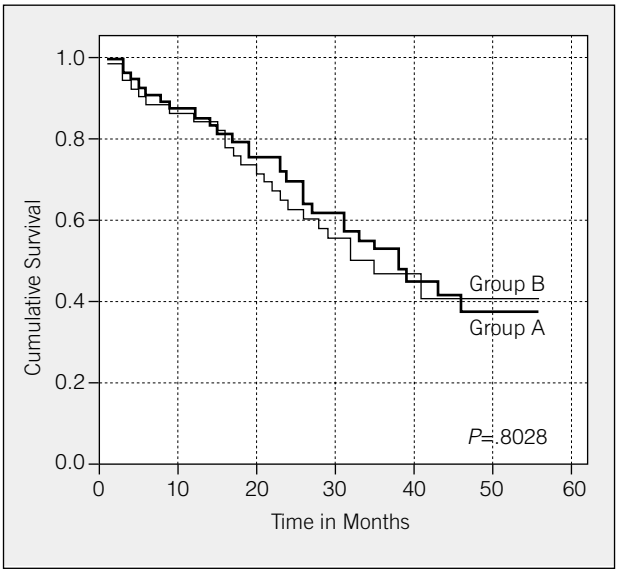

Figure 2. Survival of patients with bronchogenic carcinoma receiving surgical treatment, by surgical delay (group A, ≤ 56 days; group B, >56 days).

Discussion

In 1998, the British Thoracic Society (BTS) published recommendations for the management of lung cancer in which maximum acceptable therapeutic and diagnostic delays were set.[3] The BTS considered that the delay between a first visit to a pneumologist and thoracotomy should be 8 weeks at the most in uncomplicated cases. Surgical delay, understood to be the time a patient remains on a waiting list should not exceed 4 weeks.

The largest patient series published to date seems to be that of Aragoneses et al,[4] for the Bronchogenic Carcinoma Cooperative Group of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR). In that study, the mean time between diagnostic confirmation and surgery was 35 days (range, 1-154 days) for 1082 patients with clinical stage I and II tumors. López Encuentra et al[5] described a mean waiting period of 45.2 (34.7) days. Other authors have reported mean delays of 24 to 47 days, with actual figures ranging from 4 to 172 days.[2,6,7] Liberman et al,[8] however, described a series of 252 patients for whom the mean time between first contact with the surgeon and the operation was 104 (99) days (median delay, 82 days). The mean waiting period for our series, from first visit to our service until thoracotomy, was 56.87 (18.557) days. However, as the moment for starting the waiting list time in our study (date of applying to the thoracic surgery department) was different from the moment usually used (date of diagnosis), we are not fully able to compare our data with the findings of other investigators listed in Table 3.

TABLE 1
Wait Times According to Studied Variables (ANOVA and Student *t* Test)

	No. of Patients	Mean Wait Time Until Surgery, d	Statistical Significance
Surgical-pathologic study of the tumor			
I	53	54.32 (17.291)	No differences (*P*=.437)
II	18	60.17 (20.477)	
III	31	60.06 (20.481)	
IV	6	53 (11.314)	
Resection			
Complete	96	56.69 (18.532)	No differences *P*=.786)
Incomplete/exploratory thoracotomy	12	58.33 (19.523)	
Surgical procedure performed			
Exploratory thoracotomy	11	61.82 (16.092)	No differences (*P*=.754)
Segmentectomy	7	52.43 (11.297)	
Lobectomy	47	56.36 (19.352)	
Pneumonectomy	43	56.88 (19.423)	
Preparatory studies			
No	75	56.12 (18.749)	No differences (*P*=.526)
Yes	33	58.58 (18.283)	
Age, y			
<70	71	55.97 (20.055)	No differences (*P*=.488)
≥70	37	58.59 (15.388)	

TABLE 2
Patient Survival by the Studied Variables*

	No. of Patients	Median, mo	95% CI	Logarithmic Ranges	Cox Regression		
					P	OR	95% CI
Tumor stage, surgery, or pathology				<.005			
I	53	–	–				
II	18	26	14-38		.005	3.368	1.450-7.824
III	31	23	17-29		.001	3.364	1.687-6.708
IV	6	19	3-35		.009	5.392	1.511-19.247
Resection				<.005			
Complete	96	41	34-42				
Incomplete/exploratory thoracotomy	12	15	4-26		.002	3.612	1.609-8.108
Surgery performed				<.005			
Exploratory thoracotomy	11	15	0-33				
Segmentectomy	7	39	6-72				
Lobectomy	47	43	29-57				
Pneumonectomy	43	41	28-54				
Age, y				0.1			
<70	71	43	–				
≥70	37	31	21-41		.022	1.949	1.103-3.444
Waiting list time, d				0.803			
≤56	55	38	29-47				
>56	53	35	22-48		>.05	1.001	0.988-1.015
Further preoperative testing†				.448			
No	75	35	28-42				
Yes	33	–	–				

*CI indicates confidence interval; OR, odds ratio.
†Preoperative tests other than the usual ones.

TABLA 3
Therapeutic Delay From Diagnosis of Bronchogenic Carcinoma: Analysis of Series in the Literature

	Aragoneses et al[4,*]	López Encuentra et al[5]	Montero et al[2]	Lee et al[7]	Billing et al[6]	Liberman et al[8,†]	Cañizares et al‡
No. of patients	1082	49	64	59	39	252	108
Mean or median delay, d	35§	53.3	47.2	32.5	24	103.7	56.87
SD	–	22	–	–	–	99.1	18.557
Range	1-154	–	4-172	–	–	–	18-112

*Patients in stages I and II.
†Delay, from the moment of first contact with the thoracic surgeon.
‡Delay, from application for evaluation by the external thoracic surgery outpatient clinic. §Median delay.

Liberman et al[8] detected no significant relationship between waiting list time and tumor stage in either univariate or multivariate analysis. However, Christensen et al[9] found that the median time between start of symptoms until surgery was significantly less for patients with stage I and II tumors than for those with stage III and IV disease, in a study of 172 patients. We found no statistically significant differences related to tumor staging.

The rate of complete resection in our study (88.9%) was within the range reported in the medical literature,[10-13] where rates vary from 89.6% to 94.7%. We did not find that mean times spent on the surgical waiting lists were different for patients who underwent complete resection of the tumor and those whose resection was incomplete, even taking into account tumor stage in the multivariate analysis.

However, a persistent question remains to be answered: What effect does surgical delay have on the survival of patients with lung cancer? The literature does not seem to support a relationship. Aragoneses et al[4] found no significant effect of surgical delay on survival in patients with stage I and II tumors. Other authors have confirmed that finding, both for initial stages[14] and for all stages together.[15,16] In our series, tumor stage, complete tumor resection, and age 70 years or older were prognostic factors determining survival. However, delay does not appear to differ by tumor stage. In fact, when only patients in stage I were analyzed, the results were comparable and only

age proved to be a prognostic factor. In any case, it must be remembered that surgery was ruled out in a small number of patients because of disease progression during the waiting period (n=8) and as a result the data should be interpreted cautiously.

The American College of Chest Physicians (ACCP) has admitted that there is no evidence that early surgery increases survival[18]; however, patients in stage I have a significantly better prognosis than those in more advanced stages, justifying diagnosis and treatment in initial stages of the disease.[8,17] Nonetheless, the ACCP recommends following the periods stipulated by the BTS[3] in managing these patients.

The societal and cultural impact of delay and the fear engendered by reports in the lay press must also be considered. This aspect of the problem obliges us to analyze the situation deeply, with a critical spirit. Furthermore, the legal implications of the question cannot be downplayed. Between 1985 and 1990, 50 claims related to diagnostic and treatment delays in lung cancer were filed in the United States of America; they accounted for 15% of claims for tumor-related diseases during that period.[19] However, most cases of delay between 1 and 3 months were not counted, as it was waiting periods exceeding 6 months that received large settlements.

In any case, delay in providing treatment for a patient with lung cancer must be viewed in a larger context, as part of a continuous process from the moment a primary care physician suspects the diagnosis,[20] through the diagnostic studies ordered by a pneumologist, until appropriate treatment takes place, whether it is surgical or not. Various authors have analyzed diagnostic delay in lung cancer in this way.[2,5,6,21,22] Therefore, all these components should be remembered in managing this disease and future studies should cover the entire process of diagnosis and treatment. Efforts to reduce waiting times should continue, for even though a clear association with survival has not been found, there is still a small group of patients who have potentially treatable disease whose prognosis might change because of delay.[23] This is particularly relevant for those whose tumors are borderline between resectable and nonresectable. An interdisciplinary, integrated approach to the process would help to curtail delays.[24] Increasing resources directed toward diagnosing and treating lung cancer would also help.[23]

Given that it would be unethical to propose a prospective, randomized trial to assess the effect of surgical delay, we must settle for retrospective analyses. In any case, the lack of an association between surgical delay and tumor stage does not rule out the possibility that stage progression will occur during the waiting period, as associations are being observed, not causes and effects.[8]

In conclusion, we cannot state that survival in patients with lung cancer is influenced by surgical delay, supposing waiting time is kept with the range in this study. Therapeutic delays in our study and in the literature exceed the 4 weeks recommended by international scientific societies, although our findings and those reported in the literature are not completely comparable. Efforts should be made to decrease surgical and diagnostic delay as much as possible until the recommended times are achieved. Furthermore, other factors such as the societal and cultural impact of disease should be borne in mind when assessing the problems of surgical waiting lists. Anxiety and the consequent deterioration in quality of life of these patients alone would justify decreasing delay in providing surgical treatment of lung cancer.

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