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Delay in the diagnosis and surgical treatment of lung cancer

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ABSTRACT

BACKGROUND: Lung cancer is the leading cause of cancer-related death worldwide.
OBJECTIVE: To determine the time spent diagnosing, staging and surgically treating lung cancer in a university hospital.
METHODS: Between January 1990 and December 1998, 69 (53 male, 16 female) patients were diagnosed with lung cancer and underwent surgery. The hospital records of these patients were reviewed to evaluate clinical and histological data, dates of outpatient visits, hospital admission, tests and procedures, as well as to determine if the patients were examined as inpatients or as outpatients.
RESULTS: The 15 patients examined as outpatients were designated as Group 1, the 28 examined as both inpatients and outpatients as Group 2, and the 26 examined only as inpatients as Group 3. Ages ranged from 43 to 79 years (mean ± SD; 61 ± 10). Of the 69 patients, 43 were smokers and 23 were ex-smokers. The mean time from onset of symptoms to the first outpatient visit was 110 days and 33 days from the first outpatient visit until diagnosis. There was a lapse of 25 days between diagnosis and surgery. The mean total elapsed time between the first outpatient visit and surgery was 58 days. The mean total time was 72 days for Group 1, 72 days for Group 2, and 35 days for Group 3 ($p < 0.01$). There was no significant difference regarding total time in relation to the different stages of the disease ($p = 0.16$).
CONCLUSIONS: The results show that patients waited too long before seeking medical assistance and that medical treatment of lung cancer was further delayed when patients were examined in an outpatient setting.

Key words: *Lung neoplasm/surgery. Disease progression.*

Acronyms and abbreviations used in this work
AP – Anatomo-pathological
CP – Cytopathological
GI – Group I – Patients evaluated at the day-care unit
GII – Group II – Patients evaluated at day-care unit and in-hospital admission
GIII – Group III – Patients evaluated during in-hospital stay
HCPA – Hospital de Clínicas de Porto Alegre
OP – Obstructive pneumonia
CT – Computerized tomography

INTRODUCTION

Lung cancer, or pulmonary epithelial neoplasm, represents about 90% of all tumors that beset this organ. According to the Brazilian Health Ministry, there will be 22,085 new cases of lung cancer across the nation in 2003.[1] It is estimated that lung cancer was responsible for approximately one million deaths worldwide in 2001 and that its incidence has been increasing by 0.5% per year.[2] For many years, this type of cancer has been the leading cause of cancer death in males. In recent decades, it has become the primary cause of cancer-related death among women in developed countries, surpassing even breast cancer.[3] In Brazil, the main cause of cancer-related death among women continues to be breast cancer.[1] Nevertheless, over the past few years, the number of lung-cancer deaths among Brazilian women has been increasing.[4]

Lung cancer may be divided into two major groups: small-cell carcinoma and non-small-cell carcinoma. This division is used for therapeutic and prognostic purposes. Amid the main histological types of the non-small-cell group are adenocarcinoma, squamous-cell (epidermoid) carcinoma and large-cell carcinoma. Tumor resection is the treatment of choice in the early stages of the of non-small-cell lung cancer. However, most cases are diagnosed at a later stage, when patients present symptoms related to the tumor itself or secondary to metastasis or paraneoplastic syndromes.

It is commonly accepted that, in the evolution of a neoplasm, diagnosis must be made and therapy initiated as soon as possible. Delay in treatment may be attributed to patient delay in seeking medical attention or by a healthcare system that does not function properly. Various studies have evaluated the time expended for investigation and treatment of lung cancer and have found that excessive delay may be related to patient behavior[5 11] or to the efficiency of the healthcare system to which the patient is referred.[12-17] According to the Standing Medical Advisory Committee of Great Britain, the time from entry into the healthcare system to tumor resection should be from six to eight weeks.[18] However, the effect that delaying lung cancer treatment has on patient survival rates is still under debate.[19]

The objective of this study is to evaluate the time required for diagnosis and surgical treatment of lung cancer in a general university hospital, distinguishing between and among patients who were treated as inpatients, outpatients or both.

METHODS

This was a prospective study of 69 patients submitted to curative surgical treatment of lung cancer at the Hospital das Clínicas de Porto Alegre (HCPA) from January 1990 to December of 1998. All lung cancer patients submitted to surgery during this period were included.

The following data: age, gender, smoking history, time of symptoms onset, presence of obstructive pneumonia (OP), place of investigation, dates of consultations and procedures, methods of tumor diagnosis, tests carried out and histological tumor type were collected from the medical charts. All patients produced or underwent chest X-ray upon being enrolled in this study.

The attending physician diagnosed OP when the overall condition, laboratory tests and chest radiography were consistent with such.

For assessment of the delay in diagnosis, we took into account dates of consultations, exams and surgery, designating the date of the first (outpatient or inpatient) visit to the institution as day 1. The time elapsed between the onset of symptoms and initial examination and between initial examination and diagnosis, as well as between diagnosis and surgery, was assessed. The total time encompasses time from the initial examination to surgery. These times were compared for two sequential periods of four and a half years: from 1990 to 1994 and from

1994 to 1998. Patients were divided into three groups according to admission status: those treated as outpatients were designated as group 1 (G1), those treated as both out- and inpatients as group 2 (G2) and those treated only as inpatients as group 3 (G3).

Tumor-node-metastasis (TNM) staging for each patient was carried out based upon preoperative tests, intraoperative findings and postoperative histology and pathology. Staging was carried out according to hospital and departmental norms. Chest X-rays, fiberoptic bronchoscopy, spirometry, linear or computed tomography (CT) of the chest, echography or abdominal CT scan and bone scintigraphy were recommended for all patients. Cranial CT scan and mediastinoscopy were performed in cases of specific indication. All cases were classified according to the international guidelines for the staging of lung cancer, revised in 1997.[21]

Information collected was stored in a data bank (Epi-Info 6.1) and submitted to statistical analysis. To compare the time expended from the first consultation to surgery according to patient admission status (groups G1, G2 and G3) and according to the surgical staging of the disease, the Kruskal-Wallis test was used. A further distinction was made by separating patients diagnosed with OP from those not presenting with symptoms of OP at the time of initial examination, since this could be a factor in treatment delay. The Mann-Whitney test was utilized to assess overall time from onset of symptoms to surgery during the two time frames, time from admission to surgery and overall time for patients treated as inpatients or outpatients with or without PO. Data are expressed as simple frequency and percentage, mean ± standard deviation (SD) or median and confidence interval. For statistical significance, a value of $p<0.05$ was set.

The study was approved by the Ethics Committee for Research of the Research and Post-Graduation Group of the HCPA.

RESULTS

Sixty-nine patients were submitted to surgery for lung cancer between January 1990 and December 1998. The study group comprised 53 men and 16 women, and the mean age was 61.4 ± 7.1 (median, 62). Of the 69 patients, 15 were outpatients (G1), 28 had been both outpatients and inpatients (G2) and 26 were only inpatients (G3).

Sixty-six patients (96%) reported a history of smoking. In 51 medical charts, the time interval between the onset of symptoms and the first visit was recorded. The mean time between onset of symptoms and first visit was of 110.0 ± 72.5 days. After the onset of symptoms, 10 patients sought specialized medical attention within 30 days, 9 patients after 30 to 60 days, 11 patients after 60 to 120 days and the remaining 39 after 120 days.

Table 1 shows the delay in diagnosis at each stage of the process as median and inter-quartile ranges of time waited until performance of the exams. In 42% of patients, the diagnostic method was postoperative anatomical and pathological (AP) analysis, and in 40.6% it was biopsy or cytopathology of specimens collected by fiberoptic bronchoscopy (Table 2). Adenocarcinoma was found in 38 patients (55%), squamous-cell carcinoma in 26 (38%), adenosquamous carcinoma in 1, small-cell carcinoma (diagnosed postoperatively) in 3 and large-cell carcinoma in 1. The TNM staging showed 27 patients (39%) with stage I tumors; 18 (26%) with stage II; and 24 (35%) with stage III. Histological types and staging of cases are detailed in Table 3.

Table 1
Delay in the diagnosis of 69 lung cancer patients who eventually underwent surgery

Exam	Number of patients	Median (days)	25-75% range (days)
Fiber bronchoscopy	54	8	3-23
Sputum CP	27	9	4-31
Spirometry	67	12	7-29
Bone scintigraphy	63	17	5-42
Cranium CT	29	17	11-30
Abdominal echography	46	18	6-35
Thorax CT	48	22	10-41
Mediastinoscopy	33	32	20-68

CP = cytopathology; CT = computerized tomography

TABLE 2
Diagnostic* methods applied in 69 patients undergoing surgical treatment for lung cancer

Method	Number of patients	Percentage (%)
Postoperative AP	29	42
Biopsy AP	19	27.6
CP of washing and brushing	9	13
Sputum CP	8	11.6
AP of mediastinoscopy	2	2.9
Transcutaneous lung biopsy	2	2.9

*First positive test; AP = Anatomical and pathological analysis; CP = cytopathology

TABLE 3
Histological type and staging of tumors in 69 surgically treated patients

Histological type	Number of patients	Stage
Squamous-cell	1	IA
	11	IB
	5	IIB
	6	IIIA
	3	IIIB
Adenocarcinoma	5	IA
	9	IB
	1	IIA
	12	IIB
	11	IIIA
Adenosquamous	1	IIIA
Small-cell	1	IA
	2	IIIA
Large-cell	1	IIIA

The mean delay between the first visit and diagnosis was 33.4 ± 4.2 days (median, 18 days). This time period was less than 15 days for 31 patients (45%) and ranged from 16 to 30 days in another 15 patients (22%). In the remaining 23 cases (33%), diagnosis was delayed by more than 30 days (Table 4).

TABLE 4
Time elapsed from first visit to diagnostic confirmation in 69 surgically treated lung cancer patients

Delay	Number of patients	Percentage (%)
1-15 days	31	45
16-30 days	15	22
31-60 days	9	13
61-90 days	9	13
Over 90 days	5	7
Total	69	100

Mean time between diagnosis and surgery was 25.0 ± 30.8 days (median, 20 days) (Table 5). Twenty-two patients (32%) were submitted to surgery within the 30 days following diagnosis and 18 patients (26%) more than 30 days after diagnosis. In the remaining 29 patients (42%), diagnosis was made from specimens collected during surgery.

TABLE 5
Delay in diagnosis and surgical treatment of lung cancer in 69 surgically treated patients

Interval	Wait time (days)		
	Mean	Median	25-75% range
From onset of symptoms to 1st visit	110	90	60-180
From 1st visit to diagnosis	33	18	7-57
From diagnosis to surgery	25	20	0-36
From 1st visit to surgery:			
Group I	72	63	42-93
Group II	72	53	30-89
Group III	35	30	20-43
Stage I	54	39	27-74
Stage II	71	63	42-93
Stage III	53	35	29-65

G1 – outpatients; G2 – outpatients and inpatients; G3 – inpatients

The mean overall time from the first visit until surgery was of 58.2 ± 44.7 days, varying by patient admission status (Table 5). In G1, the mean was 72.4 ± 31.3 days (median, 63 days), in G2 it was 72.3 ± 57.4 days (median, 53 days) and in G3 it was significantly less than in the other groups (34.9 ± 20.7 days; median, 30 days; $p < 0.01$). The overall mean time from the first visit to surgery did not differ between the first four-and-a-half-year period (32 patients, 57.8 ± 45.9 days) and the second (37 patients, 58.7 ± 44.3 days) ($p = 0.87$). No significant difference in the overall delay was detected when comparing patients with different stages of the disease ($p = 0.16$). Furthermore, there was no significant difference in staging when the three groups of patients were compared according to the admission status ($p > 0.05$).

Eighteen patients (26%) presented with OP, 7 of them investigated as outpatients and inpatients and 11 as inpatients only, and 51 (74%) presented no signs of OP. The mean overall time from the first visit until surgery was 51.4 ± 23.3 days for patients with OP and 60.6 ± 50.2 days for those without ($p = 0.79$). However the mean time from hospitalization until surgery was significantly lower in the group of patients without OP (16.8 ± 15.7 days) when compared to the group with OP (34.8 ± 21.1 days) ($p < 0.01$). In patients without OP, mean overall time from first visit until surgery was 26.0 ± 16.0 days for inpatients ($n = 15$), and 75.0 ± 52.6 days for those patients ($n = 36$) who were examined as outpatients only or as both inpatients and outpatients ($p < 0.01$).

DISCUSSION

Surgical resection continues to be the treatment of choice for non-small cell lung cancer in the initial stages of the disease. However, the success of this surgical procedure depends upon patient status and tumor disposition (size and location). Diagnosis and intervention during the early stages, while the tumor is still restricted, is crucial in determining whether a tumor will be operable or inoperable. In stage I non-small-cell lung cancer, the 5-year survival rate is 70 to 80%,(22) whereas, at the more advanced stages (III and IV), the rate is less than 10%.[(23,24)]

The present study showed that hospital admittance for investigation of symptoms consistent with lung cancer is usually delayed due to patient reluctance to seek medical attention; 58% of the patients sought medical care only after being symptomatic for at least 60 days. Recently, in a series of 90 English patients, Lee et al.(9) reported a delay of 39 days between onset of

symptoms and referral to a surgeon. More et al.(10) reported that 25% of patients waited over 3 months before seeking care, and Hackett et al.(7) reported a similar delay in 39% of patients. A protracted length of time, ranging from 2.4 to 20.8 months, from onset of symptoms to medical consultation has also been related by other authors.(5,6,8,11)

In contrast, a study involving 300 patients and conducted by Silva et al.(17) from 1988 to 1991, showed that the majority of patients (69.6%) sought medical care within 30 days after onset of the symptoms. Similar data was observed in 134 Swiss patients who sought medical attention within 43 days (median, 21 days) after the onset of symptoms.(25) The shortest interval from onset of symptoms to medical visit (a median of 7 days) was reported in Italy. (26)

In the present study, we observed that fiberoptic bronchoscopy was the first procedure used (median, 8 days). This finding is similar to that of Lopez Encuentra et al.(27), who observed that, on average, patients were submitted to bronchoscopy 9.5 days after the first visit, with a shorter time of 3.1 days in the group of inpatients. In our series, only 39.1% of patients performed the sputum cytopathology exam. This is a non-invasive test whose positivity varies depending on tumor size and site. In large and centralized tumors, positivity of multiple samples may reach 85%.(28). Furthermore, CT scans of the chest (CT scan data may be useful during fiberoptic bronchoscopy) were, in many cases, performed later (median, 22 days). In our institution, sputum cytopathology testing and chest CT scans were delayed, whereas bronchoscopies were carried out quickly and with ease. This may be explained by the fact that bronchoscopy is part of the staging for lung cancer surgery.

Delay between the first visit and confirmation of the neoplasm exceeded 30 days in one-third of our patients (mean, 33 days). In the study conducted by Silva et al.,(17) this delay was in excess of 90 days in 56% of the patients. The Italian Interdisciplinary Group for Cancer Evaluation(26) found the wait time from symptom onset to final diagnosis to be 50 days on average. One of the factors that may have contributed decisively to increasing the time between the first visit and diagnosis in our hospital is that, in 42% of cases, diagnosis was made through postoperative anatomical and pathological analysis. This means that, in those patients, all earlier exams had come back negative.

In this study, the mean lag time between diagnosis and surgery (therapeutic delay) was 25 days, and more than 70% of the patients underwent surgery more than 30 days after diagnosis. This finding coincides with that of Ringbaek et al.,(14) who demonstrated a mean therapeutic delay of 26 days, where 95% of the 83 patients with resectable lung tumors underwent surgery within 60 days. Billing and Wells,(12) who evaluated 38 patients with lung cancer being treated in a British hospital, observed a mean delay between referral for surgical treatment and lung resection of 24 days. Other authors reported means of 45 and 54 days in two groups of patients in Spain.(27)

Our study showed that inpatients were, on average, submitted to tumor resection in half the time of those completely or partially treated as outpatients (35 vs. 72 days). Such results suggest that outpatient treatment is one of the delaying factors in surgical treatment of lung cancer. Furthermore, when patients with OP (a factor which could skew the data regarding overall time from first consultation to surgery) were excluded, the mean overall time was 26 days for inpatients and 75 days for outpatients. However, the time between the first medical consultation and lung cancer resection of resectable tumors should not exceed 8 weeks.(18)

In the present study, wait time was not associated with tumor stage at the time of surgery. A similar result has been reported by other authors who found no correlation of delayed diagnosis or treatment with tumor stage and patient survival rate.(19,12,15,29) In contrast, Chirstensen et al.,(13) in a study of patients in Denmark that involved 172 patients with lung cancer, reported that the delays from onset of the symptoms until surgery and from the first visit to the health system until surgery were shorter in patients with better prognoses (stages I and II). In another study, 6 out of 29 patients became incurable (stage IV) while waiting for radiotherapy.(16)

Excessive delay in diagnosing or staging lung cancer cases contributes to patient suffering. This in itself justifies a review of the efficiency and timeliness of the diagnostic and therapeutic processes. In our facilities, diverse factors may create inefficiency in outpatient care of lung cancer patients: difficulty of access to specialized medical care, problems of referral and counter-referral of patients within the health system, overload of the diagnostic and treatment centers and lack of a specific treatment regimen. Early identification of patients at higher risk of developing cancer is crucial. Therefore, outpatient care within the public health system must be restructured so as to prioritize and accelerate scheduling of consultations and requests for diagnostic exams, thereby reducing delays in tumor detection and treatment.

In conclusion, we suggest that lung cancer patients may suffer significant delays, both on the part of the patients themselves in seeking medical attention and on the part of the healthcare system in diagnosing and treating lung cancer outpatients.

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