

Delays to surgery in non-small-cell lung cancer

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Background: In Canada, waiting times for referral and surgery exist for both benign and malignant disease. We attempted to evaluate the length of various waiting times for surgery as well as their association with surgical stage in patients with non-small-cell lung cancer (NSCLC). **Methods:** This observational study consisted of a retrospective review of data for all patients who underwent an operation with the intent to cure NSCLC between Jan. 1, 1993, and Dec. 31, 2002, at the Montreal General Hospital, McGill University Health Centre, Montréal, Que. Time intervals between multiple preoperative points and surgery were calculated. The patients were then linked via universal health care insurance numbers with data from the centralized provincial inclusive health care database. This allowed the calculation of the precise interval between the patients' first contact with a physician for symptoms related to their malignancy and surgery. Mean time intervals were then compared with surgical stage. **Results:** We found adequate data for time interval analysis over 10 years for 256 patients who had undergone surgery with intent to cure. The distribution of patients by TNM stage was as follows: stage I, 144 patients (56.3%); stage II, 47 patients (18.4%); stage III, 41 patients (16.0%); and stage IV, 24 patients (9.4%). Mean and median time intervals between initial contact with physician or first onset of symptoms relating to lung cancer and surgery were 208 (standard deviation [SD] 313) days and 109 days, respectively. Mean and median time intervals between initial contact with the thoracic surgeon and surgery were 104 (SD 99) days and 82 days, respectively. No detrimental effect was observed between time to surgery and surgical stage in patients with NSCLC. **Conclusions:** Excessive preoperative waiting times before attempts at curative surgical resection for NSCLC exist in our centre. These intervals are exceptionally long, multifactorial and cause for concern.

Contexte : Au Canada, il existe des temps d'attente pour la référence et l'intervention chirurgicale à la fois pour les maladies bénignes et pour les cancers. Nous avons tenté d'évaluer la durée de divers temps d'attente pour une intervention chirurgicale, ainsi que les liens avec le stade chirurgical chez les patients atteints de cancer du poumon non à petites cellules (CPNPC). **Méthodes :** Cette étude d'observation a consisté en une analyse rétrospective de données portant sur tous les patients qui ont subi une intervention visant à guérir un CPNPC entre le 1^{er} janvier 1993 et le 31 décembre 2002 à l'Hôpital général de Montréal, Centre universitaire de santé McGill, Montréal, Que. On a calculé des intervalles entre de multiples points préopératoires et l'intervention chirurgicale. On a ensuite établi un lien entre les patients en utilisant les statistiques de l'assurance-maladie universelle et des données provenant de la base de données provinciale centralisée qui comprend les soins de santé. Ces liens ont permis de calculer avec précision le temps qui s'est écoulé entre le premier contact entre le patient et un médecin au sujet des symptômes reliés à la tumeur maligne et l'intervention chirurgicale. On a ensuite comparé les intervalles moyens au stade de la chirurgie. **Résultats :** Nous avons trouvé, pour l'analyse des intervalles, des données adéquates sur 10 ans portant sur 256 patients qui avaient subi une intervention chirurgicale visant à les guérir. La répartition des patients selon le stade TNM était la suivante : stade I, 144 patients (56,3 %); stade II, 47 patients (18,4 %); stade III, 41 patients (16,0 %) et stade IV, 24 patients (9,4 %). Les intervalles moyen et médian entre le premier contact avec le médecin ou la première manifestation

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des symptômes du cancer du poumon et la chirurgie se sont établis à 208 (écart type [ET], 313) jours et 109 jours respectivement. Les intervalles moyens et médians entre le premier contact avec le chirurgien thoracique et la chirurgie se sont établis à 104 (ET 99) jours et 82 jours respectivement. On n'a observé aucun lien nuisible entre le temps qui s'est écoulé avant la chirurgie et le stade chirurgical chez les patients atteints d'un CPNPC. **Conclusions** : Dans notre centre, on attend trop longtemps avant d'essayer de procéder à une résection chirurgicale curative du CPNPC. Ces intervalles sont d'une longueur exceptionnelle, d'origine multifactorielle et une cause de préoccupation.

Lung cancer is the leading cause of deaths from cancer in both men and women. In 2005, it was estimated that lung cancer would be diagnosed in about 22 200 Canadians and 19 000 would die from it.¹ These numbers have increased compared with 21 000 and 18 800, respectively, in 2003.^{2,3} Lung cancer is extremely virulent and is associated with an overall 5-year survival rate of 10%–15%.⁴ Non-small-cell lung cancer (NSCLC) can be treated and cured with surgical resection, if the intervention is performed at an early stage. Therefore, early diagnosis and treatment are essential in order to improve prognosis and increase the likelihood of a cure.

Delays to definitive treatment exist in all areas of medicine. These delays are often long in Canada and even more so in the province of Quebec. Long waiting times or a large number of patients waiting for definitive care, or both, are exclusively the result of a lack of available resources creating an imbalance between the demand for health care and the supply. This phenomenon is observed today in the Canadian universal health care system that has been subjected to increased cost containment in the presence of an aging population that demands and requires increased levels of health care. Long delays are even more apparent for surgical treatment because of limited operating room availability and a lack of qualified surgeons. In our university hospital centre, thoracic surgeons have recorded delays to surgical consultation and to surgery. The purpose of this study was to describe and identify preoperative factors that are significantly associated with the length of preoperative delays in the treatment of NSCLC.

Methods

This study consisted of a retrospective chart review with linking to the Quebec provincial insurance claims database: the Régie de l'assurance maladie du Québec (RAMQ). The patients included in the study had undergone surgical resection or biopsy for lung cancer between Jan. 1, 1993, and Dec. 31, 2002, and were identified from the pathology tumour registry at the Montreal General Hospital, McGill University Health Centre, Montréal, Que. Medical charts for all patients were then extracted from medical archives. Exclusion criteria consisted of the following: not having undergone surgical resection or lung biopsy (open or thoracoscopic) for lung cancer (i.e., patients in the tumour registry who had received bronchoscopic biopsy, transthoracic needle biopsy, lymph node biopsy, mediastinoscopy), having a tumour pathology that was not consistent with NSCLC, and having incomplete files or the lack of a Quebec unique provincial health care identifier (out of province or out of country residents). Patients who underwent mediastinoscopy without subsequent attempts at primary tumour resection were also excluded.

Various preoperative staging techniques, including bronchoscopy, transthoracic needle aspiration (TTNA), computed tomography (CT) scan (chest, abdomen, head), positron emission tomography (PET), CT–PET, bone scan, mediastinoscopy, thoracoscopy and peripheral lymph node biopsy, were used in the workup of patients before surgery. Patients with stage III and IV disease were those who underwent preopera-

tive testing that did not show any signs of an unresectable lesion or for whom a preoperative diagnosis could not be made without operation (by thoracotomy or thoracoscopy). These patients were taken to the operating room for an attempt at resection or biopsy and the disease (1) was found to be unresectable (unresectable lesion invading unresectable mediastinal structures or malignant pleural or pericardial effusion) (T4, stage IIIB); (2) had metastasized to ipsilateral mediastinal lymph nodes (N2, stage IIIA) or contralateral lymph nodes (N3, stage IIIB); or (3) had metastasized to distant organs discovered on pre-hospital or in-hospital workup and lung biopsy was the method chosen to achieve tissue diagnosis (M1, stage IV).

The population served at our centre is diverse and includes patients from Montréal and the surrounding area referral base. There are a number of different centres in the city and surrounding region that provide lung resection for NSCLC. Four surgeons completed all procedures over the study period. The data were not analyzed based on treatment protocols and/or adjuvant or neoadjuvant chemoradiotherapy, because the treatment strategies in North America for NSCLC changed over the long study period.

Inpatient hospital charts and outpatient clinic charts for all patients were reviewed manually by 2 of the investigators. Patient age at surgery, sex, tumour subtype, initial symptom, surgical procedure and pathological TNM stage (based on pathology report) were recorded in a database. The date of initial symptoms related to the cancer, initial visit with a physician, initial visit with the patient's

own general practitioner (GP), initial clinic visit with a respirologist, initial radiological diagnosis of lung mass (based on chest radiograph, CT scan, PET or magnetic resonance imaging report), first bronchoscopy, TTNA, mediastinoscopy, diagnosis of lung cancer, referral to thoracic surgeon, placement on an operating room waiting list and operation date were also abstracted and recorded.

The unique health insurance numbers of all patients were used to retrieve their information from the provincial health insurance database of the RAMQ. The RAMQ database includes information regarding all health care utilization claims including those for admissions to hospital, physician visits, prescription medications and other paramedical services. Dates of all physician visits (in-hospital and clinic visits) were obtained for all patients. The initial visit for symptoms relating to lung cancer was used to determine the precise time interval between first contact with the health care system and surgery for lung cancer.

In order to further examine preoperative delays for the majority of patients, 2 time intervals were additionally examined. The first was the interval between the first onset of symptoms or physician visit relating to the lung cancer diagnosis and surgery. This interval was defined as the first available date in the chart or in the RAMQ database for each patient for any of the following until the date of surgery: onset of symptoms, physician visit, GP visit or contact with health care relating to the diagnosis of lung cancer. The second time interval was calculated based on the time from the patient's first contact with the surgeon until surgery. These intervals were compared in order to examine whether patients with advanced disease were triaged to longer waiting times compared with those with more favourable results on preoperative workups.

Mean times (and a standard deviation [SD]) were calculated between

all preoperative points and the date of attempts at surgical resection for NSCLC. Time intervals were compared between groups (stage I and II v. III and IV) using the 1-way analysis of variance (ANOVA) test. Logistic regression modelling was used to look at the effect of preoperative delays on stage of lung cancer. Ethical approval for the study was obtained from the Montreal General Hospital, McGill University Health Centre, as well as from the Commission d'accès à l'information du Québec.

Results

Between 1993 and 2003, 283 patients had surgical pathology biopsy specimens coded as lung cancer in the pathology database at the Montreal General Hospital. Of these patients, 256 fulfilled the study inclusion and exclusion criteria and had undergone attempts at surgical resection for NSCLC. The patients consisted of 155 (60.5%) men and 101 (39.5%) women. The mean age of the study sample was 65.3 (SD 10.2) years. Demographic characteristics of the study sample, including presenting symptom, procedure, tumour pathology and TNM stage, are presented in Table 1.

Time intervals between defined preoperative points and surgery are outlined in Table 2. Table 3 shows the preoperative delays between 2 important preoperative time points and surgery: (a) interval between symptom onset or first physician visit and surgery; (b) interval between first contact with the thoracic surgeon and surgery. Mean and median times between initial contact with physician or first onset of symptoms relating to lung cancer and surgery were 208 (SD 313) days and 109 days, respectively. Mean and median time intervals between initial contact with the thoracic surgeon and surgery were 104 (SD 99) days and 82 days, respectively.

Table 4 outlines the association between waiting times for surgery and surgical stage. No significant differ-

ences were observed between preoperative points and surgery and TNM stages. Logistic regression modelling for surgical stage did not show any effect of preoperative delays on surgical stage for the 2 primary time intervals (Table 5).

Discussion

Significant delays to attempts at surgical resection for NSCLC occurred for patients referred to thoracic surgeons at the Montreal General Hospital. Mean times between contact with the health care system for symptoms related to lung cancer and surgery were surprisingly long (254 [SD 649] d). Even more surprising were the excessively long time intervals between radiological diagnosis and surgery (mean 135, SD 195, median 80 d).

The median time interval between the date the patient was placed on the operating room list and surgery was about 3 weeks (23 d) and the mean time interval between first contact with a thoracic surgeon and surgery was 3½ months (104 d). The large difference between the 2 points is secondary to the excess times it takes in our current system to acquire important diagnostic (PET scans, CT scans, TTNA, bronchoscopy, etc.) and preoperative consultations and procedures. Although the appropriate time interval between the patient being ready for the operating room (diagnosis made, preoperative evaluation done, deemed medically fit) has not been defined in the literature, the earlier the operation occurs, the better. Earlier resection is not only advantageous in terms of the risk of tumour metastasis but also in terms of the patient's psychological status.

These results differ significantly from the Fraser Institute's figures for waiting times between appointment with a specialist and treatment for lung cancer in 1999.⁵ They report median waiting times of 1.0 week in Quebec. In the 2004 Fraser Institute report on waiting times, the median wait between appointment with a

surgeon and surgery for lung cancer (operations on the bronchus and lung) rose to 3.0 weeks.⁶ The Fraser Institute report estimates waiting times based on surveys of specialists across the provinces of Canada. These estimates are therefore not objective measures of waiting times but, rather, are based on the subjective opinions of a cross-section of physicians. The Institute admits that in comparison with “academic research, the Institute’s measurements may be biased downward, understating actual waiting times.”

Patients operated on for stage I tumours have significantly better survival than those with higher stage

tumours.⁷ This highlights the importance of prompt and early referral of patients with lung lesions on radiographs by primary care physicians to respirologists and by respirologists to thoracic surgeons. Delays to definitive care need to be minimized, and it is inappropriate for patients with suspected lung carcinoma to experience delays of more than 6 months (mean 196 d) between contact with the health care system for symptoms relating to lung cancer and referral to a thoracic surgeon.

Practice organization guidelines from the American College of Chest Physicians admit that there is no direct evidence that accelerated diagnostic

testing or resection reduce mortality.⁸ They do, however, recommend that North American physicians approximately follow arbitrary guidelines put forth by the British Thoracic Society (BTS) for a timetable to workup and treatment for lung cancer.⁹ The BTS recommends that all patients should be seen for an initial evaluation by a respirologist within 1 week of referral from their primary care physician. Diagnostic testing should be performed within 2 weeks of the decision to undergo the test. There should be a maximum of 8 weeks between the first consultation with a respirologist in an uncomplicated operable case and surgery, and surgery should be per-

Table 1

Demographic characteristics of the study sample (n = 256)

Characteristic	No. (and %) of study subjects
Male sex	155 (60.5)
Presenting symptom	
Cough	38 (14.8)
Hemoptysis	34 (13.3)
Pain	21 (8.2)
Pneumonia	5 (2.0)
Dyspnea	6 (2.3)
Incidental lesion found on chest radiograph	113 (44.1)
Unknown	39 (15.3)
Procedure	
Biopsy	4 (1.6)
Lobectomy	175 (68.4)
Pneumonectomy	40 (15.6)
Wedge resection	37 (14.5)
Tumour pathology	
Adenocarcinoma	88 (34.4)
Squamous cell	79 (30.9)
Bronchoalveolar	37 (14.5)
Clear cell	3 (1.2)
Large cell	38 (14.8)
Mixed	10 (3.9)
Poorly differentiated	1 (0.4)
TNM surgical stage	
IA	69 (27.0)
IB	75 (29.3)
IIA	17 (6.6)
IIB	30 (11.7)
IIIA	36 (14.1)
IIIB	5 (2.0)
IV	24 (9.4)

Table 2

Preoperative delays (time interval between preoperative points and surgery)

Preoperative point	No. of patients	Median interval, d	Mean interval, d	SD
Symptom onset	163	122	174.9	221.1
Physician visit	152	30	50.9	83.4
GP visit	27	84	112.3	84.3
Contact with health care system	216	64	253.5	649.0
Respirologist visit	13	68	122.1	205.2
Radiological diagnosis	184	80	135.3	194.6
Bronchoscopy	61	55	62.6	44.2
TTNA	52	57	75.6	102.9
Diagnosis	115	52	75.4	98.7
Referral to surgeon	107	38	57.2	81.4
Placed on OR list	146	23	36.9	61.6

GP = general practitioner; OR = operating room; SD = standard deviation; TTNA = transthoracic needle aspiration.

Table 3

Preoperative delays (time interval between 2 primary preoperative points and surgery)

Preoperative delay	No. of patients	Median interval, d	Mean interval, d	SD
From first onset of symptoms or physician visit to surgery	250	109.0	207.7	313.1
From first contact with surgeon to surgery	252	81.5	103.7	99.1

SD = standard deviation.

formed within 4 weeks of surgical evaluation, unless the patient is sent for neoadjuvant therapy. Lee and colleagues¹⁰ compared the waiting periods in the workup and evaluation of patients with lung cancer at the Royal Brompton Hospital, London, UK, and the BTS recommendations. They found that most patients were treated within the recommended time frames; however, there were a number of patients with very long and unacceptable delays before they received definitive care.

Delays within our centre were mostly attributed to multiple appointments for patients requiring frequent hospital visits and delays between appointments. It was not uncommon for patients to return to hospital multiple times on different occasions for visits with respirologists and surgeons, radiology (chest radiograph, CT scan), bronchoscopy, TTNA, preoperative evaluation, mediastinoscopy and, finally, surgery. These multiple visits that not only cause significant delays to surgery are also extremely inconvenient for patients. A solution

to this would be a comprehensive lung cancer clinic, similar to breast cancer centres, where patients could be seen by respirologists, radiologists and surgeons in one clinic and undergo diagnostic imaging and testing with minimal delay and inconvenience. These multidisciplinary clinics have been shown to be feasible and effective in the diagnosis and treatment of lung cancer.¹¹

Inadequately funded public health care systems result in waiting lists for services and delays to care due to inadequate supply for existing demand. Waiting times for surgery have been shown to significantly increase the risk of death in patients waiting for coronary artery bypass surgery in both Ontario^{12,13} and Quebec.¹⁴ Preoperative delays are also associated with decreased survival in patients with breast cancer.¹⁵ These waiting times have become a reality in Canada and exist not only in the preoperative setting^{16,17} but also postoperatively for patients requiring both radiotherapy and chemotherapy.¹⁸

Billings and Wells¹⁹ studied delays

in the diagnosis and surgical treatment of lung cancer in Cambridge, UK, and found the mean time from presentation to surgery to be 109 days among 39 patients undergoing resection for lung cancer. Delays were also observed in time between referral to a respirologist (32 d) and between surgical referral and operation (24 d).

The results of studies of the effect of delays to surgery on outcome in lung cancer are conflicting. Bozcuk and Martin²⁰ found that preoperative delays did not affect survival in a hospital in Norfolk, UK. The association between a delayed diagnosis of lung cancer and the surgical stage was also studied in a group of 172 patients who had undergone surgery in Denmark.²¹ Significantly shorter median delays between the appearance of the first symptom and surgery were associated with stage I and II tumours at operation compared with stage III and IV tumours. In terms of delays between first contact with the health care system and operation, similar results were observed.

Simunovic and colleagues²² looked

Table 4

Relation between surgical TNM stage and preoperative delays

Preoperative delay	TNM stage	No. of patients	No. of days			p value*
			Mean	SD	SE	
From first onset of symptoms or physician visit to surgery	I-II	186	201.1	292.1	21.4	0.57
	III-IV	64	227.1	369.3	46.2	
	Total	250	207.7	313.1	19.8	
From first contact with surgeon to surgery	I-II	187	104.9	99.9	7.3	0.75
	III-IV	65	100.3	97.6	12.1	
	Total	252	103.7	99.1	6.2	

SD = standard deviation; SE = standard error.
*Analysis of variance was used to compare differences between means. Significance was set at $p < 0.05$.

Table 5

Logistic regression model for surgical TNM stage and preoperative delays

Preoperative delay	Parameter estimate (β)	p value	Odds ratio		
			Estimate	95% confidence limits	
From first onset of symptoms or physician visit to surgery	0.000	0.57	1.000	0.999	1.001
From first contact with surgeon to surgery	0.000	0.74	1.000	0.997	1.002

at waiting times for cancer surgery in a group of patients with diverse malignancies in Ontario. They found that in patients with thoracic malignancies median time between referral to a surgeon and surgery was 36.0 days.²² These results do not differ from our results, because median time between referral to a thoracic surgeon and surgery was 38 days in our study. The median number of days between treatment decision for all cancers and surgery were also similar in both studies (20 d in the study by Simunovic and colleagues and 23 d in the current study).

The strengths of the current study include our ability to precisely and objectively assess the initial contact of the patient with the health care system because of the linkage of patients through a universal provincial health care database (single payer system), as well as the inclusion of consecutive patients over a 10-year period. Limitations include the retrospective nature of the data, the fact that not all preoperative time points were available for all patients and the inability to differentiate higher stage tumours preoperatively.

Acceptable waiting times for lung cancer surgery have not been established. Most people would agree that the shorter the waiting period, the better the chance of resectability and, therefore, improved outcome; however, this has not been proven. Prospective, randomized studies evaluating delays to surgery are unethical and we therefore must rely on retrospective studies to evaluate waiting times for cancer surgery. The lack of association between preoperative delays and surgical stage does not rule out the possibility that delays may upstage tumours. This observation is an association and not an identification of cause and effect. Without the ability to control for the stage of the tumour at presentation, we cannot conclude that delays do not affect surgical stage. We excluded all patients who were deemed to have unresectable tumours and were not taken to the operating room for attempts at surgical resection. This removed a large num-

ber of stage III and IV tumours. Patients with stage III and IV tumours who were not deemed suitable for operation may have experienced long delays before presentation.

A further limitation of the study is the fact that all patients were treated in an academic medical centre, which may limit the generalization of the results of this study to nonacademic hospitals performing lung cancer surgery.

Conclusions

We have observed significantly long delays between the onset of symptoms, first contact with the health care system, diagnosis and referral to both respirologist and surgeon and surgery in patients with NSCLC who underwent operations with intent to cure at a single academic hospital in Montréal. Swifter referral between primary physician and specialist, as well as the creation of comprehensive, multidisciplinary lung cancer clinics, may decrease these delays.

Competing interests: None declared.

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