Original Article

Delays in the diagnosis of lung cancer

Peter M Ellis, Rachel Vandermeer

Juravinski Cancer Centre, Hamilton, Ontario, Canada

ABSTRACT

Background Many patients with lung cancer report delays in diagnosing their disease. This may contribute to advanced stage at diagnosis and poor long term survival. This study explores the delays experienced by patients referred to a regional cancer centre with lung cancer.

Methods A prospective cohort of patients referred with newly diagnosed lung cancer were surveyed over a 3 month period to assess delays in diagnosis. Patients were asked when they first experienced symptoms, saw their doctor, what tests were done, when they saw a specialist and when they started treatment. Descriptive statistics were used to summarize the different time intervals.

Results 56 of 73 patients consented (RR 77%). However only 52 patients (30M, 22F) were interviewed as 2 died before being interviewed and two could not be contacted. The mean age was 68yrs. Stage distribution was as follows (IB/IIA 10%, stage IIIA 20%, IIIB/IV 70%). Patients waited a median of 21 days (iqr 7-51d) before seeing a doctor and a further 22d (iqr 0-38d) to complete any investigations. The median time from presentation to specialist referral was 27d (iqr 12-49d) and a further 23.5d (iqr 10-56d) to complete investigations. The median wait to start treatment once patients were seen at the cancer centre was 10d (iqr 2-28d). The overall time from development of first symptoms to starting treatment was 138d (iqr 79-175d).

Conclusions Lung cancer patients experience substantial delays from development of symptoms to first initiating treatment. There is a need to promote awareness of lung cancer symptoms and develop and evaluate rapid assessment clinics for patients with suspected lung cancers.

KEY WORDS non-small cell lung cancer; symptoms; diagnostic delay; outcomes

Introduction

Lung cancer represents a major health burden in most developed countries. Within Canada in 2007, there were 23,300 cases and 19,900 deaths from lung cancer (1). The majority of patients present with either locally advanced or metastatic disease and only 20-30% of patients have potentially operable, early stage disease at presentation. As a result the five year survival is only around 15%.

There is concern that delays in diagnosis may be a contributing factor in the high frequency of advanced disease at presentation (2). Common symptoms at the time of presentation of lung cancer include cough, dyspnea, chest pain, fatigue, chest infection, hemoptysis and weight loss (3-5). Significant overlap occurs between these symptoms and symptoms of other chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD). Such overlap in symptoms might lead to delay in recognition of a lung cancer diagnosis.

Several authors have investigated the time taken to initiate diagnosis and treatment of patients with lung cancer (3,6-10). Koyi et al (10) prospectively evaluated the time from onset of first symptoms until commencing treatment. They reported that the median time from patients' first report of symptoms until the start of treatment was around six months (189 days). They observed delays in presentation to a family doctor (median 21 days), referral to a specialist (median 56 days) and time taken for subsequent investigations (median 33 days). Additionally the type of symptoms at presentation appears to influence the time to delay. Bjerager et al reported that patients with typical lung cancer symptoms such as cough, dyspnea and hemoptysis waited a median 29 days for referral for investigation (3). However, patients with atypical symptoms such as bone and joint pain, or fatigue waited a median of 104 days for referral. A retrospective audit of cancer cases in Scottish family practices demonstrated that lung cancer patients waited longer for specialist referral than patients with most other cancers (7). Missed opportunities to

Ellis and Vandermeer. Delays in the diagnosis of lung cancer

184

establish a lung cancer diagnosis might be a contributing factor to this. A review of 587 new lung cancer cases at two tertiary institutions reported that 38% of cases had missed opportunities to establish a diagnosis of lung cancer (6). This group of patients had a substantially longer time to diagnosis than patients without missed opportunities (132 vs 19 days).

Other than surgical wait times (11) there are little data examining the time course from onset of first symptoms to commencement of treatment for Canadian lung cancer patients. Therefore we conducted a prospective study to examine the trajectory of patients from onset of symptoms, initial presentation, diagnostic work up and referral to a regional cancer centre. Our objective was to establish the time delays in each phase to help inform strategies to reduce overall diagnostic delays.

Methods

We conducted a prospective study at a regional cancer centre in Ontario covering a population of approximately 2 million people. Eligible patients were all lung cancer cases referred to a medical or radiation oncologist at the Juravinski Cancer Centre over a three month period. Eligible patients were within six weeks of referral, and needed to be able to read and understand English, or have a family member or friend present to interpret. Patients with brain metastases were included. Patients who had systemic therapy at another institution, or who had a previous lung cancer diagnosis were not eligible for participation.

Data were collected over a three month period. Consecutive patients meeting the eligibility criteria were approached by a research assistant at their initial or second visit. Information was provided about the purpose of the study and patients were invited to participate. Arrangements were made with consenting patients, to conduct a telephone interview with the research assistant in the near future. Informed consent was obtained from all study participants and the study was approved by the Hamilton Health Sciences Research Ethics Board.

Structured telephone interviews were conducted with consenting patients using a standardized data collection form. Information was collected on patient demographics, stage and type of cancer, date and type of presenting symptoms, initial presentation and management by a family doctor, date of specialist referral, diagnostic tests ordered by both the family doctor and specialists, plus date of referral to cancer centre. The dates of physician appointments and diagnostic tests were verified by way of the family doctor or patient chart. Participants were also asked to describe their own delay in presentation to a family doctor, as well as perceptions of a delay by their family doctor, respirologist, thoracic surgeon, medical oncologist and radiation oncologist. Reasons for delays were recorded and categorized after data collection.

The sample size was based on the number of patients seen during the time period rather than a priori calculations. The data analysis was primarily descriptive. Categorical variables were summarized using proportions and continuous variable with median and standard deviation or interquartile range (IQR). The primary outcome of the study was the time taken from initial onset of patients' symptoms to commencement of treatment. The data was used to calculate the following time intervals:

•T1: time from initial symptoms to first presentation to a family doctor or emergency department

•T2: time from initial presentation to the last date of diagnostic testing ordered by the family physician

•T3: time from initial presentation to the first appointment with a specialist, either directly to the JCC or to a respirologist or thoracic surgeon

•T4: time between the initial appointment with the specialist and the last date of additional diagnostic testing

•T5. Time from JCC referral to initial consultation

•T6: time from initial contact with a medical or radiation oncologist to the starting date of treatment, defined as chemotherapy, radiation therapy, or the decision not to pursue treatment

•T7: Overall time from onset of symptoms to commencement of definitive therapy was also calculated as a global delay

Results

There were 73 patients seen during the study period of whom 52 were interviewed (Fig 1). Patient demographics are summarized in table 1. The median age was 70 years (sd 9.8 yrs) and there were approximately equal number of male and female patients. Most patients (77%) had non small cell lung cancer (NSCLC) and the majority of patients seen, had advanced disease. Almost all patients reported symptoms prior to diagnosis (94%). Common symptoms at presentation are summarized in table 2. The most common symptoms at presentation were cough, shortness of breath, chest pain and hemoptysis. The initial management for patients was as follows: antibiotics (40%), inhalers (16%), cough syrup (4%), and referral to hospital (17%). Investigations were ordered following the initial presentation in 48 patients (92%). These investigations included: CXR (98%), CT (56%), bone scan (6%), brain scan (2%), abdominal US (13%), and blood tests (36%).

Patients spent a significant time waiting in each time period (Table 3). Patients waited a median of 21 days (IQR 5-51d) from the onset of initial symptoms until first presentation to a doctor. An additional 22 days (IQR 0-38d) were taken to complete initial investigations by the family physician and a median of 27 days (IQR 12-49d) from presentation to family doctor until specialist referral. The median time from specialist referral to referral to JCC was 23.5 days (IQR 10-58d) and an additional 12
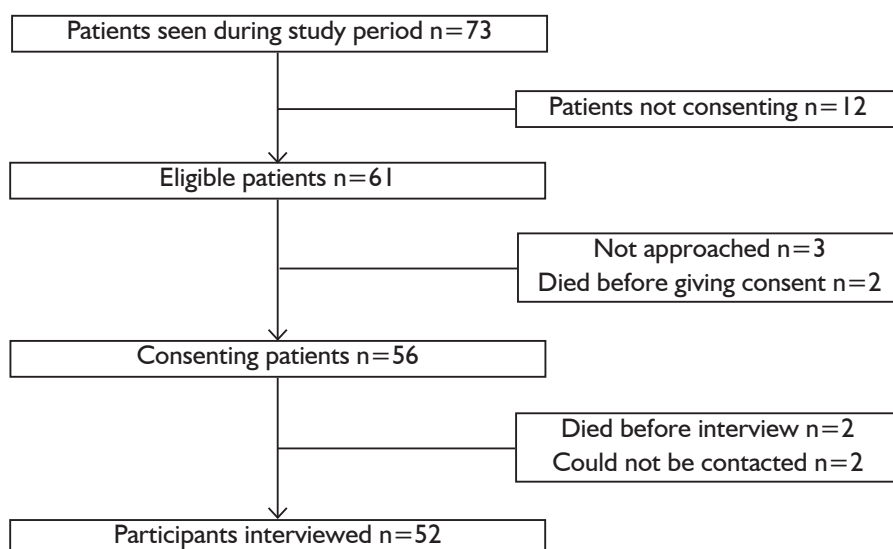
Fig 1. Patient participation

Table 1. Patient demographics

Variable	N	%
Age	52	Median 70 years (sd 9.8)
Gender		
Male	30	58
Female	22	42
Type of Lung Cancer		
NSCLC	40	77
SCLC	12	23
Stage		
Stage I	3	6
Stage II	1	2
Stage IIIA	8	16
Stage IIIB	13	25
Stage IV	15	29
LS SCLC	6	11
ES SCLC	6	11
Symptoms at presentation		
Yes	49	94
No	3	6

Table 2. Frequency of symptoms at initial presentation

Symptom	N	%
Cough	21	40
Short of breath	20	40
Chest pain	12	23
Hemoptysis	11	21
Head cold	6	11
Malaise	6	11
Pain	5	10
Fatigue	5	10
Loss appetite	4	8
Back pain	3	6
Nausea	3	6
Weight loss	3	6
Edema	3	6
Headache	2	4
Hoarse voice	1	2

days (IQR 6-18d) occurred from referral to initial consultation. The median time from consultation to commencement of treatment was 10 days (IQR 2-28d). In total, patients spent a median of 138 days (IQR 19-174d) waiting from the initial onset of symptoms to commencement of treatment.

Patients' perception of delays varied according to the time period. Twenty four patients (46%) perceived that delays occurred from the onset of symptoms to presentation to the family doctor. The most common reason was the patients' perception that the symptoms were not serious (n=11). On the other hand only 12 patients (23%) believed there was a delay in initial investigations by their family doctor. A larger proportion of patients (n=19, 37%) perceived delays in waiting for tests arranged by a specialist. These delays were primarily perceived to

Table 3. Summary of time delays for each time period

Time period	Median delay (days)	Interquartile range
T1: time from initial symptoms to first presentation to a doctor	21	7-51
T2: time from initial presentation to the last date of diagnostic testing ordered by the family physician	22	0-38
T3: time from initial presentation to the first appointment with a specialist, either directly to the JCC or to a respirologist or thoracic surgeon	27	12-49
T4: time between the initial appointment with the specialist and the last date of additional diagnostic testing	23.5	10-56
T5. Time from JCC referral to initial consultation	12	6-18
T6: time from initial contact with a medical or radiation oncologist to the starting date of treatment, defined as chemotherapy, radiation therapy, or the decision not to pursue treatment	10	2.5-28
T7: Overall time from onset of symptoms to commencement of definitive therapy was also calculated as a global delay	138	79-175

be waiting for tests. Interestingly, the actual wait times in each of these time periods were similar. Patients were asked to rate their satisfaction on a scale of 1-5 (Fig 2). Thirty one patients (61%) were satisfied with the amount of time spent waiting for tests, as well as their overall satisfaction.

It is apparent that some patients are seen by multiple specialists before having a treatment decision finalised (Table 4). All patients saw at least two specialists including a medical or radiation oncologist. However, 24 (46%) saw four specialists including at least one medical or radiation oncologist. All patients had multiple investigations performed. These were ordered by multiple physicians (Table 5). The investigations ordered most frequently by specialists include bronchoscopy (90%), CT scan (65%) and bone scan (65%).

In an exploratory analysis, patients' initial symptoms were classified as respiratory (cough, shortness of breath, head cold, chest pain, hemoptysis, or hoarse voice), or non-respiratory (all other symptoms). Forty three patients (83%) had at least one respiratory symptom, whereas 9 (17%) presented with non-respiratory symptoms. Interestingly, the median wait time in patients presenting with non-respiratory symptoms was significantly shorter than patients presenting with respiratory symptoms (median 74 vs 145 days, P=0.047).

Discussion

It is apparent from our survey that patients with suspected lung cancer take a considerable amount of time to present to a doctor, undergo investigations and then commence treatment. In our study, the median total wait time was approximately 4.5 months. This time appears excessive in comparison to recommendations from professional organizations. The Canadian Strategy for Cancer Control recommends that the maximum time to

diagnose most cancers should not exceed four weeks (12). In the UK, standards implemented by the National Health Service (NHS) state that all patients with a suspected cancer diagnosis should be seen within two weeks (13,14).

However, recommendations about wait times are largely empirically based. It is unclear what, if any impact delays in diagnosing and treating lung cancer might have on treatment outcomes. There are some data examining outcomes of patients with stage I and II NSCLC waiting for surgery (15). Patients waiting longer for surgery did not have any detriment in their survival. It is possible though, that patients with more advanced disease might progress during these wait times and no longer be eligible for aggressive treatment options. Additionally, delays in diagnosis can result in psychosocial morbidity (16,17).

Our data would suggest that delays in the diagnosis occur at each step in the process. However, it is apparent that two major themes occur. The first issue is that there appears to be a lack of recognition of the presenting symptoms from lung cancer. Many patients delay presenting to their doctor because they initially think the symptoms are not serious. Once they do present to a doctor they often receive treatments such as antibiotics, inhalers or cough syrup that would be more appropriate treatments for infection. This issue is highlighted by the observation that patients presenting with respiratory symptoms had a significantly longer time from initial presentation to commencement of treatment than those with atypical symptoms. The presence of such typical symptoms may result in more uncertainty about the initial diagnosis and longer time to diagnosis. However, these findings though are opposite to those observed by Bjerager, who found that patients with atypical symptoms had a much longer time to diagnosis (3).

The other significant issue contributing to the delay in starting treatment is the time taken to complete diagnostic investigations.
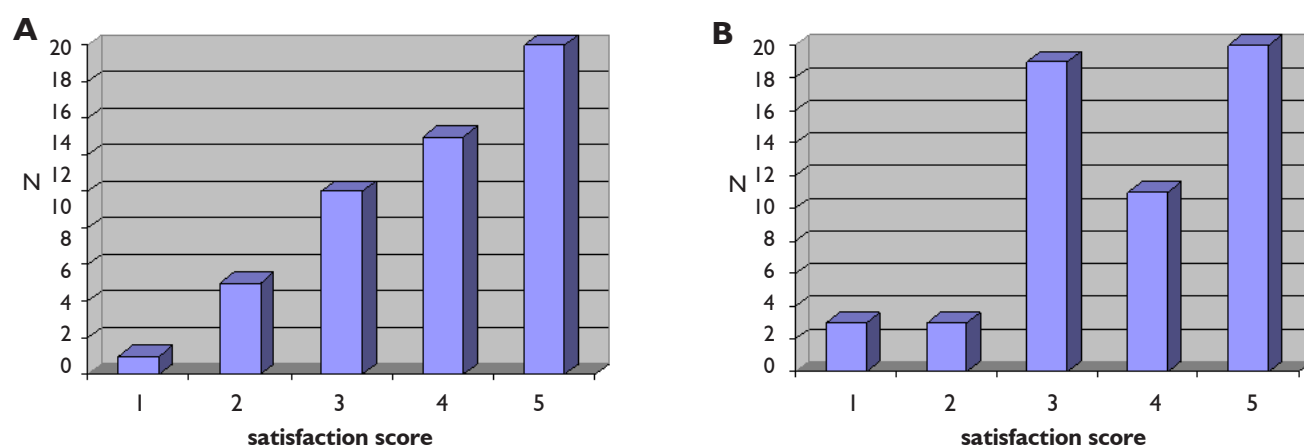
A

B

Fig 2. (A) Satisfaction with waiting times; (B) Overall satisfaction

Table 4. Pattern of specialist referral prior to treatment decision

Specialist	Referral 1 (n=52)	Referral 2 (n=52)	Referral 3 (n=41)	Referral 4 (n=24)
Internal medicine	3 (6%)	2 (4%)	-	
Emergency physician	1 (2%)	1 (2%)	-	
Respirologist	28 (54%)	4 (8%)	2 (4%)	
Thoracic surgeon	16 (31%)	18 (35%)	3 (6%)	
Other	2 (4%)		4 (8%)	
Medical oncologist	2 (4%)	11 (21%)	16 (31%)	13 (25%)
Radiation oncologist		15 (29%)	13 (25%)	11 (21%)
Second opinion		1 (2%)	3 (6%)	

Our patient sample saw up to four specialists before commencing treatment, and had investigations ordered by multiple physicians. This complex diagnostic process adds considerable time to the entire process.

There is a strong need to simplify the diagnostic process for patients with lung cancer. Our data would suggest that physicians and people in the community require education about the common presentations of lung cancer patients. This might raise awareness of lung cancer and help in part to overcome the initial belief that patients' symptoms are not serious. Nihilism still exists about treatment options for lung cancer. There is little research though, on knowledge transfer strategies to increase community physician knowledge and awareness of treatment options. However, the largest benefit in shortening the time taken to diagnose and commence treatment would appear to be in simplifying the diagnostic process. Delays in completing diagnostic tests are only compounded by the fact that tests are often ordered sequentially by multiple physicians. One solution would be the establishment of diagnostic assessment units (DAUs). DAUs offer a number of advantages including ease of access, access to multidisciplinary teams, and offer the potential of collaborative research, provider training opportunities

and may enhance quality improvement and performance measurement. A systematic review of DAUs has shown that they reduce the time required to access diagnostic services, reduce patient short term anxiety and increase patient satisfaction, although most data exists in breast cancer diagnostic assessment units (18). There is a paucity of data though, on longer term disease outcomes.

Currently the majority of patients present with advanced stages of lung cancer. While attempts are needed to reduce the time spent moving through the diagnostic process, this is likely to have modest gains in patient outcomes at best. The real potential to reduce the burden of lung cancer in our community comes from smoking cessation programs. However, lung cancer remains the largest cause of cancer death in western countries and there is a need for effective early detection programs. Up to now this has been hampered by the lack of effective proven screening methods (19). The recent announcement from the US National Cancer Institute that the National Lung Screening trial comparing screening for lung cancer with spiral CT versus CXR reduces the relative risk of death from lung cancer by 20%, offers real hope to impact on the burden of lung cancer in our society (20).

Table 5. Summary of patient investigations according to ordering physician

Investigation	Respirologist	Thoracic Surgeon	Medical Oncologist	Radiation Oncologist	Not ordered
Bronchoscopy	21 (40%)	24 (46%)	1 (2%)	-	5 (10%)
Fine Needle biopsy	10 (20%)	12 (23%)	1 (2%)	1 (2%)	28 (54%)
Mediastinoscopy	-	10 (20%)	-	-	42 (80%)
CXR	17 (33%)	10 (19%)	3 (6%)	3 (6%)	25 (48%)
CT	17 (33%)	10 (20%)	3 (6%)	3 (6%)	18 (35%)
Bone scan	6 (11%)	5 (10%)	8 (15%)	15 (29%)	18 (35%)
Brain MRI / CT	3 (6%)	2 (4%)	5 (10%)	11 (21%)	31 (60%)
Abdominal US	4 (8%)	1 (2%)	4 (8%)	2 (4%)	41 (79%)
PET	3 (6%)	3 (6%)	-	1 (2%)	45 (86%)

References

1. http://www.cancer.ca [Internet]. Toronto: Canadian Cancer Society; c2010 [updated 2010 November 04]. Available from: http://www.cancer.ca/canada-wide/about%20cancer/cancer%20statistics/~/media/CCS/Canada%20wide/Files%20List/English%20files%20heading/pdf%20not%20in%20publications%20section/2007%20Canadian%20Cancer%20Statistics%20%20PDF%20English_1816216925.ashx.

2. Mackillop WJ. Killing time: the consequences of delays in radiotherapy. Radiother Oncol 2007;84:1-4.

3. Bjerager M, Palshof T, Dahl R, Vedsted P, Olesen F. Delay in diagnosis of lung cancer in general practice. Br J Gen Pract 2006;56:863-8.

4. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. Thorax 2005;60:1059-65.

5. Buccheri G, Ferrigno D. Lung cancer: clinical presentation and specialist referral time. Eur Respir J 2004;24:898-904.

6. Singh H, Hirani K, Kadiyala H, Rudomiotov O, Davis T, Khan MM, et al. Characteristics and predictors of missed opportunities in lung cancer diagnosis: an electronic health record-based study. J Clin Oncol 2010;28:3307-15.

7. Baughan P, O'Neill B, Fletcher E. Auditing the diagnosis of cancer in primary care: the experience in Scotland. Br J Cancer 2009;101:S87-91.

8. Hall SE, Holman CD, Threlfall T, Sheiner H, Phillips M, Katriss P, et al. Lung cancer: an exploration of patient and general practitioner perspectives on the realities of care in rural Western Australia. Aust J Rural Health 2008;16:355-62.

9. Barrett J, Hamilton W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. BMC Fam Pract 2008;9:31.

10. Koyi H, Hillerdal G, Brandén E. Patient's and doctors' delays in the diagnosis of chest tumors. Lung Cancer 2002;35:53-7.

11. Bardell T, Belliveau P, Kong W, Mackillop WJ. Waiting times for cancer surgery in Ontario: 1984-2000. Clin Oncol (R Coll Radiol) 2006;18:401-9.

12. Canadian Strategy for Cancer Control; 2001 Jan 18. Available from: www.hc-sc.gc.ca/hppb/cscc/work_reports.html.

13. Hanna SJ, Muneer A, Khalil KH. The 2-week wait for suspected cancer: time for a rethink? Int J Clin Pract 2005;59:1334-9.

14. Dodds W, Morgan M, Wolfe C, Raju KS. Implementing the 2-week wait rule for cancer referral in the UK: general practitioners' views and practices. Eur J Cancer Care (Engl) 2004;13:82-7.

15. Quarterman RL, McMillan A, Ratcliffe MB, Block MI. Effect of preoperative delay on prognosis for patients with early stage non-small cell lung cancer. J Thorac Cardiovasc Surg 2003;125:108-13.

16. Gray RE, Fitch MI, Phillips C, Labrecque M, Klotz L. Presurgery experiences of prostate cancer patients and their spouses. Cancer Pract 1999;7:130-5.

17. Risberg T, Sørbye SW, Norum J, Wist EA. Diagnostic delay causes more psychological distress in female than in male cancer patients. Anticancer Res 1996;16:995-9.

18. Gagliardi A, Grunfeld E, Evans WK. Evaluation of diagnostic assessment units in oncology: a systematic review. J Clin Oncol 2004;22:1126-35.

19. Flehinger BJ, Kimmel M, Polyak T, Melamed MR. Screening for lung cancer. The Mayo Lung Project revisited. Cancer 1993;72:1573-80.

20. US National Cancer Institute. National lung screening trial: Questions and answers. [updated 2002 Sep 18; cited 2010 Nov 23]. Available from: http://www.cancer.gov/newscenter/qa/2002/nlstqaQA.