Experiences along the diagnostic pathway for patients with advanced lung cancer in the USA: a qualitative study

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ABSTRACT

Background  Most patients with lung cancer are diagnosed at advanced stages. However, the advent of oral targeted therapies has improved the prognosis of many patients with lung cancer.

Purpose  We aimed to understand the diagnostic experiences of patients with advanced lung cancer with oncogenic mutations.

Methods  Qualitative interviews were conducted with patients with advanced or metastatic non-small cell lung cancer with oncogenic alterations. Patients were recruited from online support groups within the USA. Interviews were conducted remotely or in person. Analysis used an iterative inductive and deductive process. Themes were mapped to the Model for Pathways to Treatment.

Results  40 patients (12 male and 28 female) with a median age of 48 were included. We identified nine distinct themes. During the ‘patient interval’, individuals became concerned about symptoms, but often attributed them to other causes. Prolonged or more severe symptoms prompted care-seeking. During the ‘primary care interval’, doctors initially treated for illnesses other than cancer. Discovery of an imaging abnormality was a turning point in diagnostic pathways. Occasionally, severity of symptoms prompted patients to seek emergency care. During the ‘secondary care interval’, obtaining tissue samples was pivotal in confirming diagnosis. Delays in accessing oncology care sometimes led to patient distress. Obtaining genetic testing was crucial in directing patients to receive targeted treatments.

Conclusions  Patients experienced multiple different routes to their diagnosis. Some patients perceived delays, inefficiencies and lack of coordination, which could be distressing. Shifting the stage of diagnosis of lung cancer to optimise the impact of targeted therapies will require concerted efforts in early detection.

BACKGROUND

Lung cancer is the leading cause of cancer death and the second most common cancer type in the USA.1 In 2016, the incidence of new lung cancer cases in the USA was 56 per 100 000 people and the rate of lung cancer death surpassed the rate of any other cancer death, with 38.5 per 100 000 people.2

Although screening for lung cancer using low-dose CT scanning has been recommended in the USA since 2013, the majority of individuals are diagnosed either after seeking clinical care with symptoms or as an incidental finding after imaging.3 The poor outcomes associated with lung cancer are at least partly the result of the length of time between a patient first experiencing bodily changes and being diagnosed.4–7 Based on a pooled analysis of 56 studies, the median time from symptom onset to diagnosis ranged from 41 to 143 days.8 Unfortunately, a significant proportion of individuals with lung cancer are at advanced stages at the time of diagnosis and have an overall survival rate measured in months.9

There has been surprisingly little US research on patients’ perceptions of the diagnostic pathways for lung cancer. Most research assessing time to diagnosis has been performed in European healthcare
systems and in smokers, making comparisons with the US population or with non-smokers difficult.\textsuperscript{10, 11} There has been almost no research on the diagnostic experiences of patients with advanced lung cancer who are receiving targeted therapies for oncogenic mutations such as c-ros oncogene 1 (\textit{ROS1}) mutations (1%), anaplastic lymphoma kinase (\textit{ALK}) rearrangements (3\%–7\%) and epidermal growth factor receptor (\textit{EGFR}) mutations (10\%–15\%).\textsuperscript{12} Targeted therapy has improved the outcomes of patients with these mutations, with median overall survival times of 52.1 months for \textit{ROS1}, 81 months for \textit{ALK} and 29.7 months for \textit{EGFR}. Thus, understanding the pathway to diagnosis is especially important in this population.\textsuperscript{13–16}

The purpose of this study was to explore the experience of the diagnostic process among patients with advanced lung cancer whose tumours tested positive for oncogenic driver mutations in order to identify potential areas to improve the efficiency and experience of the diagnostic pathway.

METHODS

Study design

This qualitative study used indepth individual patient interviews.

Study population

Participants met the following inclusion criteria: (1) histological or cytologically confirmed diagnosis of metastatic or advanced non-small cell lung cancer (NSCLC) with the presence of one oncogenic alteration (\textit{EGFR, ALK} or \textit{ROSI}); (2) physically and psychologically well enough to participate; (3) proficient in English; and (4) receiving care in the USA. We identified patients using online oncogene-focused lung cancer support groups. Detailed methods are included in a previous publication.\textsuperscript{17}

Study procedures

Participants were interviewed by phone, video conference or in person depending on location and preference. One author (MAA) conducted the interviews after receiving verbal consent. Interviews were audio-recorded and transcribed verbatim. Participants were asked to describe their diagnostic journey from the moment of first noticing symptoms to initial treatment. The interviewer asked follow-up questions for clarification. Participants were given a $50 gift card for participating. Interview questions and follow-up prompts are included in online supplemental appendix 1.

Analysis

NVivo V.11 was used to organise the data and conduct the analysis. Inductive and deductive thematic analysis was applied. As outlined by Carspecken,\textsuperscript{18} the transcripts were read by the lead author (MAA) and low-level codes were developed. The codes were then collated by topic. Codes were mapped following the Model for Pathways to Treatment (\textit{figure 1}).\textsuperscript{8, 19, 20} Themes and subthemes emerged through an iterative process, and all authors engaged in peer debriefings as groups and

![Figure 1](Image)

\textit{Figure 1} The conceptual Model for Pathway to Treatment. HCP, healthcare provider. Reproduced with permission of SAGE Publications Ltd., London, Los Angles, New Delhi, Singapore and washington DC, from Walter FM et al.\textsuperscript{19}
dyads reviewing aspects of the work, including coding and analysis, theme development, and description of findings. Themes were organised based on the *Aarhus statement on cancer diagnostic research* stages: patient interval, primary care interval and secondary care interval.\textsuperscript{21, 22} Transcripts and themes were reviewed and synthesised to characterise the different types of diagnostic pathways experienced by patients.

MAA is a patient with stage IV, ALK-positive lung cancer, a family doctor and a qualitative researcher. MZS is a researcher with experience in qualitative research. MT is a family physician in the USA with extensive research experience on disease diagnosis. BHG is an oncologist and health service researcher. FMW and RDN are primary care lung cancer researchers from the UK. MAA performed the main analysis and engaged in peer debriefing with coauthors as dyads and groups. The coauthors reviewed aspects of the work, such as analysis and coding, theme development, and writing the results.

**Patient and public involvement**

The main author is a patient with stage IV lung cancer and a member of one lung cancer support group. The research questions were informed by conversations with lung cancer communities. Patient gatekeepers helped in recruiting participants by sharing about the study in their support groups. The study will be shared with cancer communities on social media and specifically in support group venues.

**RESULTS**

A total of 40 patients were interviewed. Their mean age was 48 (range 30–75); 12 were male and 28 were female. Interviews were conducted for a median of 19.5 months (range 3–152) after diagnosis (table 1). All participants had a primary diagnosis of metastatic or advanced NSCLC with one driver oncogenic alteration. We noted seven different diagnostic pathways experienced by patients, rather than a single course. These pathways varied primarily by the initial presentation site (primary care, emergency room (ER) and so on) due to the perceived urgency of symptoms (figure 2).

**The experience of lung cancer diagnosis**

Emergent themes within the diagnostic intervals (patient, primary care and secondary care) are detailed in the following sections.

**Patient interval**

*Initial concerns about symptoms despite low perception of risk*

Prior to diagnosis, lung cancer did not come to mind for most participants, especially as most were younger and non-smokers. Many believed their healthy lifestyle protected them against such illnesses. In contrast, those who smoked suspected lung cancer from the onset of symptoms. The participants recalled experiencing various new symptoms or a change in persisting symptoms that concerned them. Most reported non-specific symptoms; some were respiratory in nature, while others related to organs and systems due to metastatic spread (eg, bone pain) or were constitutional (eg, fatigue, weight loss). Some recalled the symptoms being present up to a few months prior to diagnosis. A minority did not recall any symptoms. Diagnosis occurred after imaging for other reasons, such as an injury or trauma (box 1).

**Attribution of symptoms to other causes and not always seeking care immediately**

Participants initially attributed their symptoms to reasons other than lung cancer. Coughing, for example, was explained by forest fire smoke in the air; back pain was attributed to muscle spasm; fatigue was blamed on depression; and shortness of breath with activities on excessive weight. Even haemoptysis raised concern for tuberculosis as a more likely cause. Many participants did not worry initially because the symptoms were perceived as mild or they felt others had similar symptoms, such as

| Table 1 Participant characteristics | Median (range)/count |
|-----------------------------------|---------------------|
| **Participant characteristics**    |                     |
| Age                               | 49 (30–75) years    |
| Gender                            |                     |
| Male                              | 12                  |
| Female                            | 28                  |
| Race                              |                     |
| White                             | 34                  |
| Others (Asian, Hispanic, biracial (Asian and Hispanic)) | 6                  |
| **Region in the USA**             |                     |
| West                              | 18                  |
| Northeast                         | 8                   |
| Midwest                           | 7                   |
| South                             | 6                   |
| **Insurance**                     |                     |
| Private                           | 34                  |
| Medicare                          | 4                   |
| Medicaid                          | 2                   |
| **Time since diagnosis**          | 19.5 (3–152) months |
| **Cancer stage at time of interview** |                   |
| IV                                | 38                  |
| Illb                              | 2                   |
| **Mutation**                      |                     |
| ALK                               | 20                  |
| EGFR                              | 14                  |
| ROS1                              | 6                   |

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; ROS1, c-ros oncogene 1.
dismissing a cough during influenza season. Finally, some people did not have health insurance at the time of early symptoms and the potential cost of healthcare services deterred them from seeking help.

Changes in severity or nature of symptoms prompting care-seeking actions
Participants expressed experiencing a change in their level of concern prompting them to seek medical attention. Reasons included symptoms getting worse, especially after initially improving; not responding to treatments for other suspected illnesses; symptoms lingering; disruptive pain; symptoms developing in combination; alarming symptoms appearing, such as haemoptysis or significant weight loss; and symptoms affecting quality of life or affecting sleep. Sometimes family members or friends had advised the person to seek care after noticing symptoms.

Most individuals initially visited their primary care providers (PCPs) to get help with their symptoms or to determine the reason for the symptoms that had become concerning. Some first visited urgent care, especially when they encountered delays in accessing a PCP. Some patients who had established relationships with specialists consulted with them first; some complained to their ear, nose and throat doctor about their haemoptysis, while others complained to their gastroenterologist about their shortness of breath.

Primary care interval

Doctors initially treated for illnesses other than lung cancer
Participants described that providers were not alarmed by, or sometimes dismissed, their initial symptoms. For many, the initial course of management was the investigation and treatment of benign aetiologies. In some cases, initial investigations supported other diagnoses, such as a respiratory infection from chest X-ray (CXR) or acid reflux confirmed on endoscopy. In other cases, initial tests were normal. Some patients’ symptoms were attributed to and treated as other diseases, for example, a shortness of breath was attributed to underlying asthma and treated with inhalers and steroids. Some patients were referred to specialists, such as physical therapy or orthopaedics for musculoskeletal complaints. The wait for specialist appointments sometimes took several weeks. Not infrequently, providers used ‘safety netting’, or contingency plans, such as scheduling return visits, follow-up CXR and trying other treatment plans (box 2).

Discovery of imaging abnormality, often on CXR and/or chest CT, leading to diagnosis
A major turning point identified by some participants was getting a CXR, either at their request or prompted by their PCP, intended to identify the cause of symptoms. Imaging studies were also ordered when treatment failed or to assess whether previously noted radiological findings had been resolved. Occasionally, imaging tests
were used to evaluate incidental conditions such as injuries, while other patients received CXR to follow up on nodules seen on previous imaging. Other imaging tests used to evaluate symptoms elsewhere in the body identified lung cancer as an incidental or unexpected finding, such as MRI for back pain or breast-screening MRIs identifying lung lesions.

For many patients, a diagnosis of lung cancer was supported by a chest CT done after an abnormal CXR or to discover the primary site after a metastasis was found. Scheduling the CT scan was often rushed. Sometimes PCPs pushed for this to happen or, when scheduling was delayed, advised patients to go to the ER.

Severity of symptoms prompting need for emergency care

Some patients went directly to the ER with distressing symptoms such as severe shortness of breath. Others sought care in the ER for symptoms such as headache and back pain as they had no PCP. At times, the patient’s condition deteriorated quickly, requiring admission due to hypoxia or losing consciousness with brain tumours causing seizures. Occasionally, delays in diagnostics or the delay, advised patients to go to the ER.
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Patients were referred to an oncologist once diagnosed. 
The pivotal nature of tissue sample collection. 

⇒ “I was scheduled for a CT scan but the next opening wasn’t for like 2 or 3 weeks. I was having so much coughing that I couldn’t speak or breathe properly. So I called my healthcare provider’s office. She advised that I should go to the ER and get a CT scan.” (2007) 
⇒ “We scheduled the biopsy for Thursday. Tuesday morning before I could go for the biopsy, I woke up coughing up blood, a considerable amount of blood which was new that it never happened. So I drove myself to the ER.” (2008) 
⇒ “The second I went in the pulmonologist office, he checked my ox- ygen and it was 85%. I took his advise and went to the hospital.” (1014) 

CXR, chest X-ray; ER, emergency room; PET, positron emission tomography.

Box 2 Continued

Severity of symptoms prompting need for emergency care.
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perception that their PCP could not offer much besides office testing prompted the patient to go to the ER. Other patients were advised to go to the ER after findings such as a pulmonary embolism or massive brain metastasis. At the ER, it was not uncommon for the patient to be admitted. Some patients demanded urgent consultations from specialists and to be admitted to complete the cancer work-up and start treatment.

Specialty care interval
The pivotal nature of tissue sample collection
Once imaging raised the alarm for cancer, interventional radiologists, pulmonologists or thoracic surgeons obtained tissue samples. While some patients saw a specialist fairly quickly, others experienced significant delays. Bronchoscopy, needle biopsies, sampling of pleural effusions and occasionally surgical biopsies were used to clarify if the lesions seen on imaging were cancer, to identify the type of cancer and to obtain tumour tissue for genetic testing. Results were delivered within a few days. While a bronchoscopy was often uneventful, it sometimes led to major bleeding, collapsed lungs or the patient requiring resuscitation. Occasionally, concerns over the procedure led to delays in this diagnostic step. When decisions were made to forego biopsy, patients felt they were provided false reassurance based on less reliable information, such as the appearance on images and their overall assumed low risk for cancer (box 3).

Access to oncologists determined staging but perceived delays led to distress.

Patients were referred to an oncologist once diagnosed. The referral was made urgently, often by the PCP or pulmonologist based on imaging findings or following pathology results. It was not uncommon for patients to perceive a delay in making appointments, causing frustration. To identify the right specialist and overcome delays, patients often leveraged personal connections or sought help from family and the cancer community. First meet- 

ings with oncologists often involved reviewing the results and setting treatment plans. These were usually short, especially if molecular results were not back. Oncologists...
often completed the diagnostic work-up by ordering additional imaging such as positron emission tomography (PET) scans or brain MRIs. Since our participants had advanced diseases, PET scans often showed metastasis outside the lungs.

**Genetic testing was crucial in directing patients to targeted treatments**

For our participants, molecular testing on tissue or blood samples was obviously an instrumental part of their diagnosis. Realisation of a positive mutation was met with relief, as patients were fortunate to be a candidate for targeted therapy. However, molecular testing results sometimes took several weeks or were overlooked by providers. Looking back, some patients described frustration at being given chemotherapy instead of waiting for molecular testing results. Some, however, needed emergency chemotherapy, radiation or surgery to relieve symptoms.

**DISCUSSION**

As the first on the subject, this study contributes to the literature on pathways to diagnosis and the intervals of diagnosis among patients with advanced lung cancer on targeted therapy. The participants were mostly young, non-smokers, unlike those in previous research in this area. We used a well-established model to map participants’ experiences from their initial realisation of symptoms, through contact with healthcare, and diagnostic workup.

Previous studies on this ‘patient interval’ suggested that atypical or vague symptoms caused delays in knowing when to seek care. Previous research (with participants who were predominantly smokers) noted reluctance among patients to visit their healthcare provider when symptoms emerge, but this pattern was not reported by the majority of our study participants. Because they were younger than the average age at presentation of lung cancer and/or presented with non-specific symptoms, their concerns were typically attributed initially to benign diseases. Recognising the symptoms and making a diagnosis can be particularly challenging when a patient has comorbid conditions with symptoms similar to those of lung cancer.

Many patients perceived inefficiency and delays in the primary care interval. However, these perceptions were made retrospectively, bringing into question whether an actual delay took place. Some patients felt they had to advocate for themselves to obtain initial diagnostic testing and push for more advanced testing when initial tests were inconclusive. This finding is consistent with the role of self-advocacy in improving the quality of care for patients with cancer.

Previous studies suggested dismissive responses from PCPs may impact patients’ decisions to consult care again. In contrast, our participants reported persistence and at times sought other providers. Some providers clearly had contingency and follow-up plans, but patients commonly felt they were dismissed without clear ‘safety netting’. Previous US studies of patients with lung cancer have suggested delays occur mainly in the primary care interval through misdiagnosis (and from monitoring nodules) rather than in the specialty care interval. In contrast, difficulty in accessing secondary care is a major cause for delays in the UK. Our study found that patients’ sense of urgency and perception of unnecessary waiting intensified after receiving imaging diagnosing possible cancer. Many complained about delays in accessing pulmonologists, oncologists or in results from molecular testing. While these waits were fairly short and probably had little impact on the overall prognosis, they did appear to intensify patient emotion.

This study has many strengths. It is the first to explore the perspectives of a relatively new group of lung cancer survivors: those on targeted therapies who experience significantly superior outcomes. Interviewees may have been better able to reflect on their diagnostic journey in the absence of side effects from chemotherapy or radiation therapy. Our findings were developed within an existing framework used in research on early diagnosis of cancer by many other countries. Our study also has a few limitations. Only a small proportion of our participants experienced barriers to accessing care due to financial concerns, which may have limited our ability to determine the impact of these factors. Our sampling relied on individuals identified from lung cancer survivor...
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