Death by a thousand delays

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The provision of cancer-related care in the United States involves coordination of multiple specialists, procedures, and resources. These complex intersections can be disrupted at any point, resulting in delays in care and progression of the underlying malignancy, which may translate into reduced overall survival. Some evidence suggests that delay of lung cancer care does not adversely affect patient outcomes, obfuscating conclusions about timeliness of care. These studies are retrospective and do not account for how patients are diagnosed, comorbidities, circumstances for delay, and stage. As a result, to date there are no consensus guidelines for timely lung cancer care. Figure 1 depicts the complexity of the interactive factors affecting access to care for patients with lung cancer.

DELAIS IN CARE AMONG PATIENTS WITH LUNG CANCER

Defining a delay in care is particularly challenging among patients with early-stage lung cancer. For example, should the start time for diagnosis be nodule identification, demonstration of growth, or tissue diagnosis? In addition, delay of care is not necessarily substandard care. Care of patient’s comorbidities, management of socioeconomic factors, and integration of patient choice may delay cancer treatment but are part of optimal cancer management. Furthermore, with the rapidly changing management of lung cancer screening, diagnosis, immunotherapy, and targeted therapy, standards of expected time from diagnosis to treatment are evolving. We must overcome these challenges in defining delay, as evidence overwhelmingly demonstrates increased mortality with delay of lung cancer treatment. The first step is to create a consensus on the definition of delay.

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CENTRAL MESSAGE

In patients with lung cancer, delays in care are common and negatively affect patients, providers, and the health care system. Efficient delivery models must be established.

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The harm of delay to surgery among patients with early-stage lung cancer has been comprehensively described in several large trials. Unfortunately, each study uses a different cut-off to define delay. Some studies find that a delay as short as 8 weeks causes harm, whereas other studies have found that a delay of greater than 12 weeks reduces survival. Despite this, a majority of studies agree that delay of lung cancer care beyond 90 days from the time of diagnosis negatively impacts survival. Kanarek and colleagues found that each week of delay confers a 4% risk of death. Although these studies defined delay using different time points, this should not detract from the shared conclusion that unintentional slowing to lung cancer treatment increases mortality. To set a benchmark against which future studies may compare, the lung cancer community should establish a consensus and standard of care: lung cancer treatment should commence within 90 days of diagnosis. If the lung cancer community can reach this consensus of 90 days as a maximum time to treatment, all future studies can be calibrated against this goal.

THE IMPACT OF DEFINING DELAY IN OTHER CANCER TYPES

Similar to lung cancer, delays of treatment for colon cancer and breast cancer adversely affect survival. When looking at all cancer types, colon cancer had the strongest association between time to treatment initiation
and increased mortality. With colon cancer, several groups and international organizations have proposed guidelines for surgical treatment within 4 to 6 weeks of diagnosis. Breast cancer care has analogous challenges to understanding delay, including difficulty in defining diagnosis and optimal timing to treatment. Breast cancer specialists have developed standards of timely care, specifically, diagnosis to surgery within 90 days, diagnosis to chemotherapy within 120 days, and diagnosis to radiation therapy within 360 days. The lung cancer community should learn from the success of establishing guidelines for time to treatment initiation. It may take time to develop a refined consensus to become clinically meaningful; however, this effort will assure improved outcomes in lung cancer treatment.

To improve timeliness of lung cancer treatment, mechanisms of care must be scrutinized for potential barriers and delays. Each process within the health care system—screening for cancer, the evaluation of cancer, and the treatment of cancer—introduces a chance for delay.

LUNG CANCER SCREENING

Many studies have found that despite patients receiving appropriate screening, follow-up is delayed. Delays in care following low-dose screening computed tomography (CT) scans appear to be common despite the presence of infrastructure dedicated for follow-up. In one study of 337 patients with abnormal CT findings, only 55% of the 184 patients requiring a follow-up had a timely follow-up, and only two-thirds of those patients diagnosed with cancer had an oncology visit within 30 days. Another study of 28,000 veterans found that 33% had delay in follow-up care after screening. Two recent multicenter retrospective reviews of Lung CT Screening Reporting and Data System (Lung-RADS) 3 or greater lesions found timely follow-up occurred between 40% and 47% of patients. Interestingly, both studies noted follow-up improved with a greater Lung-RADS score. Factors associated with delay include patients who had low income, patients who were an increased distance from health care facilities, and patients who identified as African American. Lung cancer screening has potential to avert lung cancer death, but only if those with concerning findings follow through with guideline-directed treatment. Resources for follow-up care after screening must be enhanced. Novel strategies, like mobile screening with nurse navigators, rapid reporting of results to patients, streamlined referrals to diagnose and treat cancer, and integration of clinical workflows with information technology are needed, especially for those at elevated risk for delay.

Patients with Lung RADS 1 and 2 results from screening pose challenges for cancer diagnosis because these patients are at particular risk of low adherence to annual screening. Evaluation of NELSON trial data identified <1% of patients had a subsolid nodule detected after baseline imaging and 6% were ultimately diagnosed with premalignancy during the course of the study. Despite these low numbers of cancer diagnoses in patients with Lung RADS 1 and 2, these patients are at high risk of treatment delay because these patients do not follow up. Low-dose CT can only avert lung cancer death through adherence to annual screening. Adherence rate to annual screening is between 20% and 30%, with especially low adherence among those who identified as Black and African American, Asian, Hispanic, currently smoking, and living in the Western and Southern states. Low annual adherence to lung cancer screening is a missed opportunity to diagnose early lung cancer and expedite lung cancer treatment. Just as navigation infrastructure and personnel should be bolstered for those with positive lung cancer screens, support for adherence to annual screening will improve early diagnosis and timely treatment.

EVALUATION OF LUNG CANCER

Evaluation of patients at risk of cancer and treatment of patients with cancer are sequential mechanisms of potential delay. A study from Denmark attributed the absence of
pulmonary symptoms, nonvisualized lesions on radiographs of the chest, and lack of explicit instructions for follow-up as mechanisms of evaluation delay. For patients presenting with symptoms of lung cancer, median time to the first medical visit was 44 days, evaluation by a specialist was 33 days, and time from specialist visit to diagnosis was 20 days. The impact of delays beyond these median times is unknown. Studies show no adverse clinical outcomes with delay of symptoms to diagnosis. However, these results may be confounded by the advanced stages, highly varying treatment options, and high mortality of people with symptomatic lung cancer.

The US Preventive Services Task Force provides guidelines for screening, and the National Comprehensive Cancer Network provides guidelines, once a nodule has been found, but the most current guidelines assisting physicians who do not specialize in lung cancer to distinguish lung cancer from other diagnoses are from the European Society of Medical Oncology. A Canadian group has added suggested timing for imaging, follow-up, and specialty referral. Specialists caring for patients with lung cancer should partner with family practice, internal medicine, and emergency/urgent care specialties to develop a single, national guideline for evaluating suspected lung cancer. This guideline would encompass evaluation after lung cancer screening, incidental nodules, and patients presenting with symptoms suspicious for lung cancer. Like the proposed Canadian guidelines, those for the American context should include recommendations for timing of imaging and specialty referral. Obtaining insurance authorization is another important source of delay which, for some patients, can also influence treatment plans.

In a survey of members of the American Society of Clinical Oncology, more than 90% of providers reported insurance delays in imaging or referral to specialists for their patients, and more than 30% indicated patients were harmed. The authors suggest that synchronizing the approval process with national guidelines may reduce delays.

Staging also offers multiple vulnerabilities for delay, particularly when endobronchial ultrasound or positron emission tomography imaging is needed. Finally, the culmination of all these efforts regularly results in a case presentation at a multidisciplinary tumor board. Recognizing the multiple, sometimes-unnecessary steps taken to reach the path to treatment, special care teams driven by advanced nursing practitioners have been used to expedite care. This model was shown to significantly reduce hospital and provider visits as well as the interval to treatment, improving efficiency.

TREATMENT OF LUNG CANCER

Following surgery, initiation of adjuvant treatment can also be a point of delay. Risk factors for delay in adjuvant therapy include older age, non-White ethnicity, being underinsured, prolonged postoperative stay, and unplanned readmission. A recent report detailing the implementation of an Enhanced Recovery After Surgery (i.e., ERAS) protocol following resection identified a reduction in the interval to initiation and completion of adjuvant therapy. Interestingly, this group and others have reported that approach, that is, open or minimally invasive, did not significantly vary the interval to starting adjuvant treatment. Older age, more advanced resection, and declining functional status were predictors of not completing therapy in this study. Review of more than 12,000 patients in the National Cancer Database following resection for stages I-III lung cancer found a survival benefit if adjuvant chemotherapy was initiated within 4 months following surgery. An inflection point for initiating treatment within 50 days following surgery was associated with improved survival. Perhaps the time frame outlined in this large study may serve as an appropriate goal to start adjuvant treatment in patients with early-stage disease.

The addition of neoadjuvant immunotherapy in early-stage non–small cell lung cancer is a topic of interest to surgeons and medical oncologists, as there exists the theoretical advantages of a broader immune response with primary tumor exposure and therapeutic dissemination via intact lymphatics before surgery, the opportunity to treat micrometastatic disease, and better patient selection for surgery. The impact of the addition of neoadjuvant immunotherapy has been described in terms of pathologic response, given the lag time needed to generate overall survival estimates. However, the available data are promising, demonstrating robust pathologic response. In regard to delays in care with neoadjuvant immunotherapy, several things need to be considered. First, the potential for an inflammatory reaction in lymphoid tissue can be positron emission tomography–avid and may require reassessment in the form of repeated endobronchial ultrasound or mediastinoscopy to ensure the absence of advanced disease. In addition, expert multidisciplinary input and trial allocation may also represent opportunities for delay. Finally, increased risk of poor tolerance to systemic preoperative therapy may ultimately limit suitability to undergo resection. However, despite these potentials, the available data, although limited, suggest that the addition of neoadjuvant immunotherapy may not lead to delayed resection. Further study is needed to validate these findings.

Finally, among patients with advanced disease, the transition to a palliative focus is also often delayed. Overly optimistic survival estimates, rapid decline, and the perception that palliative care is analogous to giving up appear to be significant barriers to initiating palliative care. Engaging early in these difficult discussions may facilitate the transition to a palliative focus when clinically appropriate.
NEXT STEPS AFTER UNDERSTANDING THE MECHANISMS OF DELAY

With the evidence for timely lung cancer treatment established and potential mechanisms of delay known, the next steps fall upon practitioners, health care systems, and insurance agencies to take shared responsibility for expeditious lung cancer care. One of the first steps should be establishing a national standard for maximum time to treatment of 90 days. Individual practitioners or institutional may challenge themselves to achieve more rigorous standards. However, socioeconomic factors of the patient population and resources available to care for patients with lung cancer should be considered when setting achievable time to treatment goals. Next, algorithms for evaluation of suspicious symptoms or nodules should include standards for timing of imaging and specialty consultations. Similar to standards established by the breast cancer community, time to diagnosis, diagnosis to treatment, and adjuvant care should be defined. Further exploration of patient factors influencing timely care, ie, stage, comorbidities, access to care, and socioeconomic, may require adjustment of guidelines.

Standards of timely care will require continual evaluation and adjustment. In addition, health care providers, institutions, and payors must have steady commitment to identify and eliminate barriers to timely care. Similarly, proven facilitators of timely care should be replicated. The Lung Cancer Strategist Program uses an advance care practitioner to actively coordinate care for patients. Navigated and personalized care teams resulted in drastic decreases in times to diagnosis and treatment (shorter time from suspicious finding to work-up [3 vs 26 days], to surveillance decision [12.5 vs 39 days], and to diagnosis [30.5 vs 48 day]). The lung cancer community should prioritize timely care through evidence-based standards, research, collaboration, and dissemination of successful strategies.

Delays are not only introduced through each step of lung cancer care; looking at the coronavirus disease 2019 (COVID-19) pandemic, as well as care received by disparate populations, we see that delays are multifactorial and dynamic.

LEARNING FROM COVID-19

The COVID-19 pandemic demonstrated the harmful effects of delaying lung cancer care. A single center evaluated their experience navigating these unprecedented disruptions and noted reduction in lung cancer screening and a simultaneous increase in the number of suspicious nodules identified when patients ultimately accessed care. Predictably, this resulted in a backlog of patients needing follow-up, putting pressure on providers and institutions to accommodate demand. Another study showed the trend of reduced patient visits during COVID-19 and increased proportions of patients with advanced disease. Although COVID-19 provided examples of exacerbated delays, each mechanism of delay still inherently exists in our health care system. However, COVID-19 necessitated a revolution in telemedicine technology and widespread acceptance among patients, providers, health care systems, and payors. Integrating telemedicine into lung cancer screening resulted in similar follow-up rates and similar detection of early-stage lung cancer compared with prepandemic lung cancer screening.

Hopefully, COVID-19 has resulted in greater awareness of how socioeconomic factors can impact delay of care, but also that we are capable of developing innovations to improve access and adherence to lung cancer care.

DISPARATE POPULATIONS

Delays in lung cancer care among minorities and patients facing health disparities have been previously documented. In a study of 1600 patients with incidental pulmonary nodules, Black patients had delays in each step of follow-up, including ordering tests, scheduling appointments, and timely adherence, when compared with White patients. Large database studies have examined the potential impact on delay on care, but fewer data are available to explore why care is delayed. Thus far, factors including non-White ethnicity, lower income, urban location, and academic medical center appear to be significant predictors that may extend the interval from diagnosis to treatment.

Furthermore, the Lung Cancer Strategist Program identified the additional following factors to increase delays: psychiatric disorder, >80 years old, language barrier, physical disability, transportation limitation, polysubstance abuse, and caregiver responsibilities. Understanding why an individual’s care is being delayed is paramount to implementing steps to reduce the delay. Care appears to be delayed due to issues with care coordination, communication between patients and providers, and access to specialists.

The recent Accountability for Cancer Care throughUndoing Racism and Equity (ACCURE) trial aimed to improve care delivery by employing several interventions aimed at identifying high-risk patients, tracking treatment completion, and reducing barriers for patients to access care. The trial showed improved survival rates for patients with breast and lung cancer. Key components of intervention included a real-time registry with automation alerts for delays, a specialized nurse and physician trained in anti-racism who can increase accountability, and as a system to audit the progress of the intervention for enhanced transparency. The results improved care delivery for all patients, including the underserved. Interventions designed to identify impediments to timely care can improve care delivery and will require participation from multiple providers. New strategies, such as that modeled in the ACCURE trial, will be needed to help reduce the barriers encountered by minority groups as they access treatment for cancer. There are several
implications, including placing unachievable standards on lung cancer clinicians who work with health disparities. However, these challenges should not be a barrier to at least setting a goal of timely care.

CONCLUSIONS

Although no specific definition of delay to treatment has been established in patients with lung cancer, it is important that providers try to optimize efficiency and reduce gaps in care. Delays are common in lung cancer, and the impact on survival outcomes is imprecise, although the negative impact of delay is experienced by patients, providers, and the health care system. The path from diagnosis to treatment is complex and subject to numerous opportunities for delay. The impact of these treatment lags is magnified in disparate populations, and additional focus is needed to improve outcomes for these patients. A common definition of delay of greater than 90 days from diagnosis to treatment should be established to further investigate the many factors at play. Each mechanism of delay needs to be thoroughly investigated, and lastly, patient factors need to be considered for each individual case. Establishing benchmarks for timely care may have to be an individual or institutional initiative but is the starting point to build a program that can expedite care, reduce excess, and allow for provider assessment aimed at improving efficiency and access.

Conflict of Interest Statement

The authors reported no conflicts of interest. The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have disclosed conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest.

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