



Challenging scenarios in the treatment of lung cancer

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Lung cancer continues to be a global health problem. Since the 1980s, it has been the leading cause of death from cancer, as well as accounting for approximately 13% of all new cases of cancer.⁽¹⁾ In Brazil, it is the most lethal type of cancer among males and the second most lethal among females, being responsible for a total of 28,717 deaths in 2018.⁽²⁾

Given that smoking is the main risk factor, lung cancer is one of the main avoidable causes of death. Due to a reduction in smoking rates, the lung cancer mortality rate began to decline in 2011. Nevertheless, nearly 75% of lung cancer patients are still diagnosed with either locally advanced or metastatic cancer. In the advanced disease scenario, fewer than 20% have a life expectancy of five years and systemic treatment is still the main therapeutic option available. In contrast, 50-90% of those diagnosed in the initial stages have survival rates of five years.^(1,2)

Access to diagnostic procedures to obtain tissue samples, which are linked to advances in surgical and systemic treatments, still differs between public and private institutions. In the public system, diagnostic procedures that are less invasive, such as imaging-guided percutaneous needle biopsy and bronchoscopy, are scarce and result in delays in the treatment timeline for patients with lung cancer.⁽³⁾

In the last ten years, thoracic surgery has evolved rapidly, with the development and assimilation of minimally invasive techniques in the management of lung cancer. According to the Brazilian Society of Thoracic Surgery database, 52% of patients diagnosed with lung cancer between August of 2015 and December of 2016 underwent anatomical lung resection. This number is higher than that reported by European societies.⁽⁴⁾ The use of robot-assisted thoracic surgery has also recently been adopted, although access to the technology is still very limited. Lobectomy continues to be the surgical procedure most commonly performed.⁽⁵⁾

Despite the advances in surgical techniques, only a small portion of lung cancer patients undergo surgery with curative intent. Data suggest that only a quarter of such patients undergo surgical treatment. Access to curative surgery is probably influenced by socioeconomic differences, performance status, comorbidities, geographic distribution, and advanced age.⁽⁶⁾ Data from the Brazilian National Cancer Institute indicate that more than 45% of lung cancer deaths occurring between 2010 and 2018 were in patients over 70 years of age.⁽²⁾ Studies that evaluate special populations are scarce. One retrospective study

conducted at a center in Portugal showed that, among patients over 70 years of age, the relapse and mortality rates were similar between those undergoing sublobar resection and those undergoing traditional lobectomy.⁽⁷⁾ Data from the São Paulo State Department of Health show that the probability of undergoing surgery is lower among individuals with a lower level of education.⁽⁸⁾

In another retrospective study, Younes et al.⁽⁹⁾ evaluated data collected from 2,673 patients with metastatic non-small cell lung cancer treated at two cancer treatment centers between 1990 and 2008. Only 10% of the patients had a Karnofsky performance status (KPS) score > 90, and half of the patients had a score of ≤ 70, reflecting the delayed access of these patients to cancer treatment centers. Although it is known that the KPS is influenced by multiple factors, anorexia and weight loss might be some of the main factors. Franceschini et al.⁽¹⁰⁾ addressed that theme, reporting that weight loss and anorexia are independent factors for mortality in patients with lung cancer, even before the initiation of treatment.

In one recent study,⁽¹¹⁾ real-life data were collected from 1,256 patients in seven countries, including 175 in Brazil. All the patients in the Brazilian cohort received at least first-line treatment. Only 58% of the patients were tested for the *EGFR* mutation (identified in 17% of those patients), and the *ALK* rearrangement test was applied in only 11% (no positive results). Most patients were treated with platinum doublet therapy. These results may reflect the fact that most patients diagnosed with advanced/metastatic non-small cell lung cancer in Brazil and showing a good KPS score are being treated with platinum doublet therapy because of their access to the public health care system.

The diagnosis of tumor-induced mutations is essential for the selection of the most appropriate treatment. Wider access to the genomic profiling of tumors and the respective corresponding molecularly targeted therapy is a high priority in Brazil. Restrictions and financial barriers are among the possible reasons why the clinical use of tyrosine kinase inhibitors and checkpoint inhibitors is so low in patients treated via the public health care system in the country.

Although anti-EGFR drugs have been incorporated into the Brazilian public health care system since 2015, neither the test for the *EGFR* mutation nor the medication is readily available or routinely provided to patients in the country. The first *ALK* inhibitor approved for use in Brazil was crizotinib, which was approved in February of

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2016. It is estimated that the delay in the approval of crizotinib resulted in the premature deaths of more than 700 patients due to a lack of access to the medication. Despite conflicting data on the cost-effectiveness of tyrosine kinase inhibitor use in Brazil, Aguiar et al.⁽¹²⁾ stated that there are different models for the analysis of these data in the Brazilian Unified Health Care System and showed that the use of anti-EGFR drugs can indeed be cost-effective.

The lack of local data in many sectors highlights the need for regional studies to help develop programs that are effective in the prevention, diagnosis, and

treatment of lung cancer, as well as fostering the creation of algorithms and guidelines for triage in Brazil.

Over the last decade, in addition to new drugs, technological innovations in treatment to allow the individualization of cancer treatment have appeared rapidly. However, the accessibility of such innovations has not kept pace with their evolution because of their cost. Because the population of patients with lung cancer is quite heterogeneous, it is essential that we be able to analyze the various scenarios and propose courses of treatment that can meet all of the challenges encountered in clinical practice.

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