

Lung Cancer in Georgia



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Introduction

According to Global Cancer Incidence, Mortality and Prevalence or GLOBOCAN, in 2018, lung cancer (LC) was the most common malignancy and deaths from LC exceeded those from any other malignancy worldwide.¹ Approximately 58% of all occurrences and 70% of cancer deaths are reported in low- and middle-income countries.² Despite being an easily preventable disease (given that more than 85% of the cases in developing countries are caused by smoking), the incidence of LC is increasing drastically owing to the increased use of tobacco products.³ In recent years, several publications have addressed the specifics of LC diagnostics and treatment in various parts of the world, but none have addressed the needs of the Georgian population.³⁻⁵ We decided to conduct the first study in Georgia to not only evaluate the current LC clinical practice and its flaws but also to delineate future strategies for improving the care of patients with cancer in the country. We convened LC specialists from all over the country to discuss the situation on access to diagnostics and treatment. A survey was done to collect information about pretreatment and treatment aspects and existing challenges on a national level. The survey questionnaire was distributed among 12 main cancer hospitals across four cities in Georgia.

Demographics and the Health care System

Georgia is a country in the Caucasus region of Eurasia located at the crossroads of Western Asia and Eastern Europe with a population of 3.7 million and classified as a lower-middle-income country (Fig. 1). In 2019, the country's classification was changed to an upper-middle-income country on the basis of per capita gross national income by the World Bank.⁶ In the recent 15 years, there were changes in Georgia's health care system, and about 80% of the hospitals were sold to the private sector for redevelopment, with most of them now being multiprofile hospitals. Nearly all health care providers are private entities, independent of the state.⁷ Nevertheless, all patients, irrespective of the insurance

type (private or government), have an opportunity to choose their hospital for treatment.

According to GLOBOCAN 2018, in Georgia, LC alone accounted for 1217 incidences (13%) in both sexes, with a male-to-female ratio of 5.9:1 (Figs. 2 and 3). In men, the number of new LC cases was 1041 (incidence 32.4/100,000), which accounted for 20% of all cancers; there were 1103 deaths reported, which was 18% of the general mortality.⁸

Despite noticeable improvements since 2000, the country still faces multiple health challenges.

Smoking Epidemiology

The estimated age-standardized prevalence of tobacco use in Georgia is 58.5% for men, one of the highest in the European Region (wherein the average rate is 38.5%) and higher than the average for the Commonwealth of Independent States (51.8%).

According to the 2016 results of the non-communicable disease risk factors STEPwise approach to surveillance (STEPS), almost one-third of Georgia's population (31.1%) smokes. Among current smokers, 57.1% of men reported smoking tobacco products daily compared with 7.1% of women.⁹

The government has recently developed a tobacco control strategy to bring in tobacco control measures similar to international and national efforts.

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Figure 1. Map of Georgia.

Screening, Prevention, and Early Detection

There is currently no active LC public screening program for high-risk populations.

In Georgia, patients with stage I to II LC are rare, and 90% of the patients are diagnosed with late-stage disease (stage III or IV).¹⁰

The National Center for Disease Control and Public Health data from 2018 revealed the median age of diagnosis as 63.3 years. The youngest patient was diagnosed at the age of 20 years and the oldest at 86 years. Possible reasons for this include difficult access to the health care system, socioeconomic problems, and lack of education.

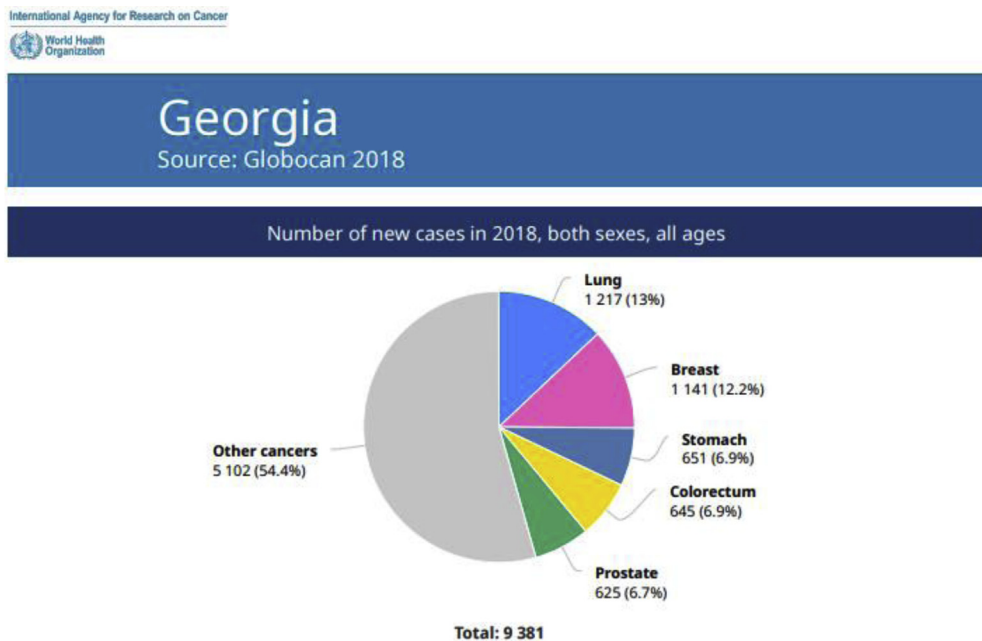


Figure 2. Number of new cases.

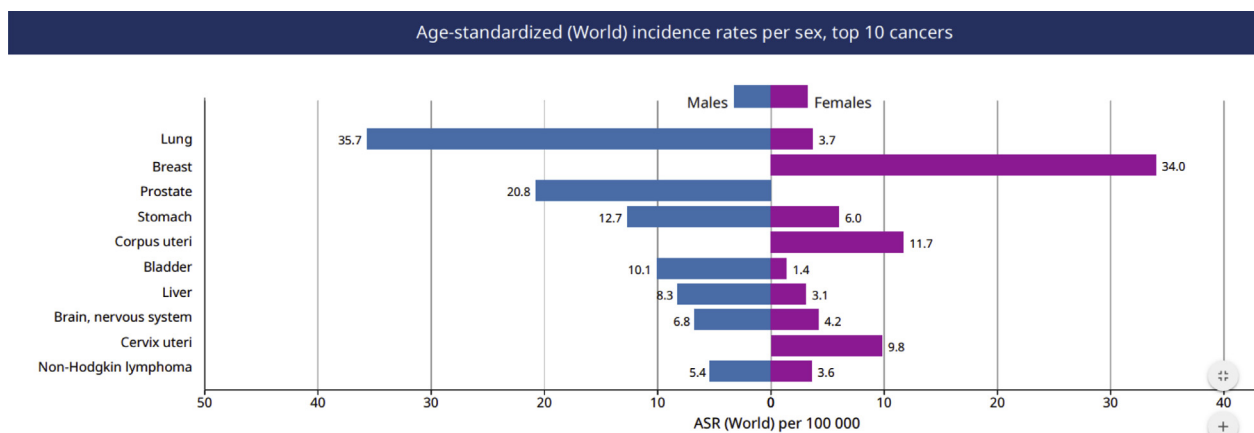


Figure 3. Age-standardized (world) incidence rates per sex, top 10 cancers.

Diagnosis and Staging

Staging is usually done using computed tomography (CT) scanning, which is available in all tertiary centers. All patients who have access to CT without delay are mainly covered by private insurance whereas patients with government insurance get financial support from various programs with a waiting period of 2 to 3 weeks. On the other hand, positron emission tomography–CT (PET-CT) is not reimbursed, and there is no cyclotron in the country. Nevertheless, there are opportunities to get financial support for diagnostics from Tbilisi City Hall and programs of the Ministry of Health Care. In addition, the facility to perform endobronchial ultrasound-transbronchial needle aspiration is limited in the country. Only one hospital provides this service for diagnostic purposes and this negatively affects adequate assessment of newly diagnosed patients.

Molecular Testing and Access

In general, molecular testing (EGFR, ALK, ROS1, BRAF, and programmed death-ligand 1) is available in three to four pathology centers for patients with NSCLC. It is mostly done in a metastatic setting. Genetic testing to identify *EGFR* oncogenic mutations is available, and it is free in cases of adenocarcinoma, which is fully covered by the pharmaceutical industry.

This testing is not covered for squamous cell carcinomas. The identification of genetic mutation of *EGFR* is performed predominantly using methods that are reverse transcription polymerase chain reaction–based. The prevalence of *EGFR* mutation in the country is about 16% (22 of 138). In most cases, ALK testing is performed after a recommendation from the oncologist responsible, and fluorescence in situ hybridization technology is largely used. *ROS1* mutation testing is mostly done in *EGFR* wild type and *ALK*-negative cases on the recommendation of the treating oncologist, and it is not

reimbursed. Testing for *BRAF* mutations is rarely performed in NSCLC. Testing for programmed death-ligand 1 is done in the country by immunohistochemistry using clone CAL 10 (Zytomed Systems), but it is not covered by insurance and is not routinely used. All these tests are available in a clinical trial setting, in which many patients throughout the country are enrolled. Next-generation sequencing was introduced in Georgia in 2019 and is used on a very limited basis for selected patients. In 2019, about 40% to 50% of the patients with LC underwent genetic testing (mostly within clinical trials).

Surgical Approaches

The percentage of surgical patients remains very low because of late diagnosis, and most patients are treated with radiotherapy or drug therapy. There are only a few trained consultant thoracic surgeons to manage LC in tertiary hospitals. Most surgeons are involved in obtaining diagnostic specimens, mediastinal staging, metastasectomy, and early stage LC curative-intent operation. Most surgical procedures are performed using open surgical approaches. Only few hospitals provide video-assisted thoracic surgery procedures.

In most centers, surgical indications are not discussed in a multidisciplinary consultation meeting.

Radiation Therapy

There are seven centers performing radiotherapy for LC, five of which are located in the capital, Tbilisi. The first modern radiotherapy machine (linear accelerator) was introduced in daily clinical practice in 2009. Six centers house modern megavoltage linear accelerators (one has CyberKnife) with capabilities for intensity-modulated radiation therapy, volumetric-modulated arc therapy, stereotactic radiosurgery, stereotactic body radiation therapy, and 4D radiotherapy. All centers have

accompanying equipment such as a dedicated CT scan for treatment planning and full medical physics for dosimetry and planning. Two centers have access to PET-CT for treatment planning purposes. Owing to the availability of these technological advances, more patients are now treated with either high-dose radiation therapy alone or with chemotherapy in the non-metastatic setting; whereas in the oligometastatic NSCLC setting, these metastases are treated more aggressively.

Systemic Therapy

Oncologists in Georgia usually refer to the National Comprehensive Cancer Network and European Society for medical oncology guidelines. In some institutions, various professional guidelines (National Institute for Health and Care Excellence, American College of Clinical Pharmacy, American Society of Clinical Oncology, American Society for Radiation Oncology, and European Society for Radiation Oncology) are used, as most hospitals do not have country-adopted LC guidelines or protocols.

Patients have access to tyrosine kinase inhibitors (TKIs) within the public health system (with copayments) in certain settings; for example, patients with *EGFR* mutations may receive first-line TKIs (erlotinib), whereas some government programs cover third-generation TKIs (osimertinib). In contrast, patients

with ALK-rearrangements have no access to crizotinib in the first-line setting. Most patients who have advanced-stage LC in Georgia receive treatment with platinum-based chemotherapy (Fig. 4).

There is limited access to immunotherapy (IO) drugs; only a minority of patients receive IO and they bear the expenses themselves. Nevertheless, there are many clinical trials in the country for IO using immune checkpoint inhibitors and patients are encouraged and motivated to enroll themselves. Participation in clinical trials is the only way for patients with LC to receive immune checkpoint inhibitors. Some government programs (by City Hall or Ministry of Health) reimburse expensive novel agents but with a copayment of 25% to 50%. This still results in a large payment that most Georgian citizens cannot afford.

Challenges

Georgian patients with LC still suffer from shortcomings when considering several aspects of their health care. The lack of screening programs present as the first obstacle, likely leading to underdiagnosis and missing of early stage patients with expected prolonged survival.

As data from the United States revealed, screening programs have a substantial impact on the fate of patients with LC, with significant marked improvement in the overall results. Perhaps reintroducing the place and

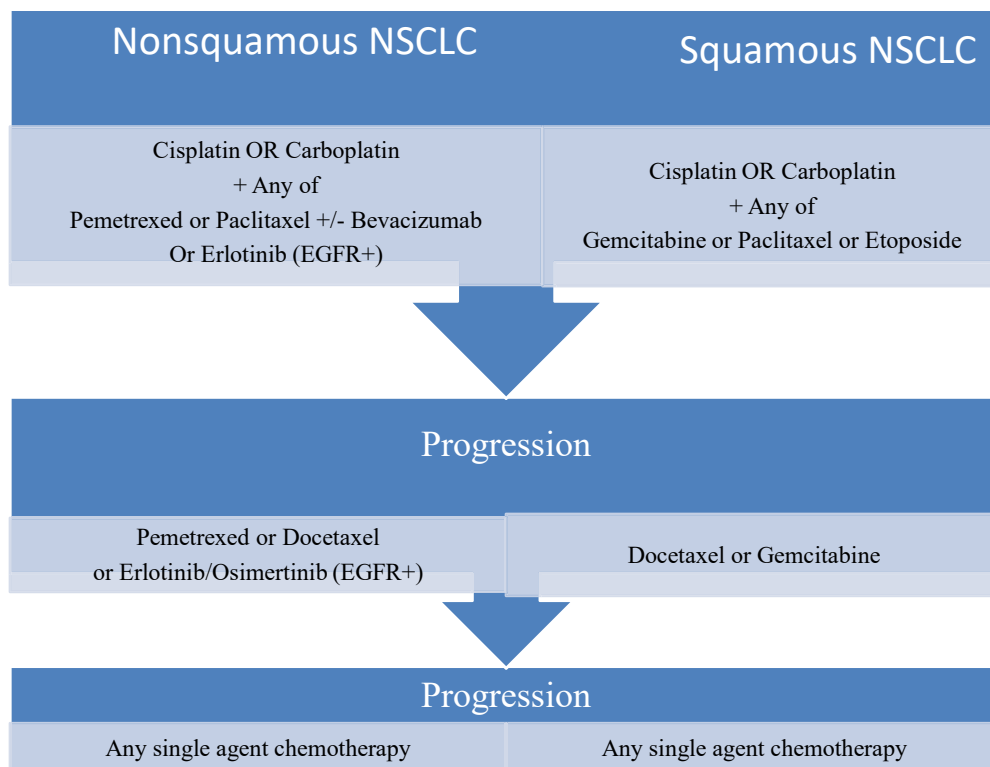


Figure 4. Treatment algorithm for advance NSCLC.

role of general practitioners in this scenario would be of additional help. Although state-controlled programs exist to address the nationwide problem of smoking, the situation is still far from satisfactory; hence, results are still lacking.

With respect to diagnostics, although PET-CTs exist in the country, there are no fully provided services covering the entire Georgian population. Furthermore, there are only two such imaging facilities in Tbilisi, and there is no cyclotron in the country; therefore, fluorodeoxyglucose needs to be imported, thereby limiting access.

In the treatment domain, surgery as an important treatment modality is largely underutilized. Although, worldwide, detection of LC in the advanced stages limits the use of surgery to 20% to 25% of all cases, the situation in Georgia is much worse, with 90% of all patients being inoperable. It is hoped that, with the establishment of screening programs coupled with widespread and better diagnostics, the number of surgical candidates will rise in the future. Consequently, the predicted rise in patient numbers calls for timely preparation by the thoracic surgery community for implementing modern surgical procedures such as video-assisted thoracoscopic surgery.

In the nonsurgical treatment domain as well, much needs to be done. Now there are six radiation therapy centers with modern megavolt linear accelerators with capabilities for intensity-modulated radiation therapy, volumetric-modulated arc therapy, stereotactic radiosurgery, stereotactic body radiation therapy, and 4D radiotherapy as compared with zero in 2008. However, radiation therapy facilities are largely concentrated in the capital Tbilisi and are available only in two other large cities (Kutaisi and Batumi). Some regions have no radiotherapy facilities and discussions are going on to address this issue. Furthermore, although most of the existing radiotherapy facilities offer contemporary planning and execution treatments, room for improvement still exists. For instance, most patients with locally advanced NSCLC and limited disease SCLC experience significant adverse effects during concurrent radiochemotherapy, requiring adequate symptomatic care and frequent hospital admissions, an issue not addressed in these hospitals. Apart from this, there is a clearly identified lack of psychological and social support during treatment. Only one center has devoted a palliative care unit to address this issue; however, this is not exclusive to patients with cancer.

Research in the domain of LC is limited to a clinical trial settings and is completely dominated by drug industry-sponsored trials. There are no current investigator-initiated trials, and much needs to be done in this domain given the ever-increasing number of

cancer specialists. Unfortunately, there are no LC-specific charities, and LC-specific philanthropy is virtually nonexistent.

In the past 10 to 15 years, changes in the country's health care system have dramatically improved many aspects of LC treatment. Compared with previous years, there are many more well-equipped hospitals with staff trained from overseas high-quality cancer centers.

Most oncologists usually refer to international guidelines, which makes treatment in the country more modernized and standardized. Many hospitals implement multidisciplinary team meetings in daily practice. With the help of international oncology societies, many young oncologists in the country regularly participate in fellowship programs. In recent years, high-quality international oncology conferences have been organized in Georgia, with an increasing number of fellowships and training programs available abroad and helping oncologists improve their knowledge and skills. Some programs sponsored by the Tbilisi City Hall and Ministry of Health Care are implemented to cover the costs of expensive drugs that are not reimbursed by the government or private insurance companies. A country like Georgia, with limited resources and many socioeconomic challenges, needs more orchestrated efforts in the field of LC. In addition to the further expansion and enrichment of diagnostic and treatment capabilities, the activation of preventive programs and implementation of LC screening for early detection of LC should lead to further reduction of national LC mortality rates.

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References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018;68:394-424.
2. The International Agency for Research on Cancer (IARC). <https://www.iarc.fr/>. Accessed September 12, 2018.
3. Jazieh AR, Algwaiz G, Errihani H, et al. Lung cancer in the Middle East and North Africa region. *J Thorac Oncol.* 2019;14:1884-1891.
4. Zwitter M, Čufer T, Vrankar M, et al. Lung cancer in Slovenia. *J Thorac Oncol.* 2019;14:1327-1331.

5. van Eeden R, Tunmer M, Geldenhuys A, Nayler S, Rapoport BL. Lung cancer in South Africa. *J Thorac Oncol*. 2020;15:22-28.
6. The World Bank. <http://povertydata.worldbank.org/poverty/category/UMC>. Accessed April 1, 2019.
7. WHO Georgia. Profile of Health and well-being. http://www.euro.who.int/__data/assets/pdf_file/0020/351731/20170818-Georgia-Profile-of-Health_EN.pdf?ua=1. Accessed August 18, 2017.
8. Global Cancer Observatory, IARC. <https://gco.iarc.fr/today/data/factsheets/populations/268-georgia-factsheets.pdf>. Accessed May 1, 2019.
9. Sturua L, Maglakelidze N, Gamkrelidze A. Smoking prevalence in Georgian adults: results of non-communicable disease risk factors STEPS 2016 survey. *Tob Prev Cess*. 2018;4(suppl):A166.
10. NCDC. Cancer statistics. <https://www.ncdc.ge/Pages/User/News.aspx?ID=bec659c0-56a2-4190-9c0c-e47a63bcca4f>. Accessed January 1, 2019.