

Lung Cancer in Lithuania



Vaida Gedvilaitė, MD,^{a,*} Edvardas Danila, PhD,^{b,c} Saulius Cicėnas, PhD,^{a,d}
Giedrė Smalytė, PhD^{e,f}

Introduction

Lithuania is a Northeastern European country (Fig. 1) the southernmost of the Baltic states. According to statistics in 2019, Lithuania had an estimated population of 2.79 million residents. In March 1990, Lithuania declared its independence from the Soviet Union and in 1991, became a member of the United Nations. Since then, there have been a series of reforms, both in the national economy and in the health system.

When the country was a part of the Soviet Union, the health care system was organized according to the Semashko system. The system was hierarchical, centrally-funded, and planned. Since 1990, extensive reforms have been undertaken in the health sector to renovate it and create a financially sustainable modern health care system that can provide high-quality services. A new system of health financing was introduced and administered by the National Health Insurance Fund (NHIF) on the basis of social health insurance. The health care system is also being decentralized, with management devolved to various government levels; these are, in descending order, the Ministry of Health, County Governors, Municipal Councils, and specialized supervisory institutions. The Lithuanian health system is a mixed system, predominantly funded from the NHIF through a compulsory health insurance scheme, supplemented by substantial state contributions on behalf of the economically inactive population amounting to about half of its budget. The state health care system is intended to serve the entire population, and the Health Insurance Law requires all permanent residents and legally employed nonpermanent residents to participate in the compulsory health insurance scheme without a choice to opt-out. About 60% of the total population is insured by the state. Compulsory health insurance provides standard benefits package for all beneficiaries.¹

Epidemiology

Lung cancer incidence rates in Lithuania in men are high compared with other Western and Northern European countries (world age-standardized rate 53.5 per

100,000), whereas rates in women are substantially lower than in the developed world (7.3 per 100,000). Trends in lung cancer incidence rates in Lithuanian men are similar to those reported in other developed countries: an initial peak followed by a sharp decrease (Fig. 2). In contrast to other western countries, incidence rates are stable in women.²

Tobacco is the principal established risk factor for lung cancer and trends in lung cancer largely correspond to changes in smoking prevalence. During the Soviet period, people in Lithuania consumed mainly domestic cigarettes and *papirosa* (nonfilter Russian cigarettes). The proportion of filter cigarettes increased from 1.1% in 1963 to 30% in 1982. However, the tar content in cigarettes was extremely high in about 90% of the cigarettes consumed (20 mg/cigarette and above).³ After the transition to an open market economy in the early 1990s, international tobacco brands became available and replaced the domestic products in Lithuania.

Only very limited data are available on smoking prevalence in Lithuania during the Soviet time. In the Soviet Union, the production of cigarettes and *papirosa* per capita increased substantially during the postwar period, reached its maximum in the year 1971 and then decreased thereafter. The highest per capita sales of

*Corresponding author.

^aDepartment of Thoracic Surgery and Oncology, National Cancer Institute, Vilnius, Lithuania, ^bCentre of Pulmonology and Allergology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania, ^cClinic of Chest Diseases, Immunology, and Allergology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania, ^dClinic of Internal Diseases, Family Medicine, and Oncology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania, ^eNational Cancer Institute, Laboratory of Cancer Epidemiology, Vilnius, Lithuania, and ^fDepartment of Public Health, Institute of Health Sciences, Vilnius University, Vilnius, Lithuania.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Vaida Gedvilaitė, MD, Department of Thoracic Surgery and Oncology, National Cancer Institute, Santariskiu g. 1, Vilnius, 08660 Lithuania. E-mail: vaidagedvilaite@yahoo.com

© 2020 International Association for the Study of Lung Cancer. Published by Elsevier Inc. All rights reserved.

ISSN: 1556-0864

<https://doi.org/10.1016/j.jtho.2020.02.029>



Figure 1. Map of Lithuania and surrounding countries.

smoking materials were reported from 1976 to 1980; they have declined slightly since then.³ Systematic collection of health behavior information started in Lithuania in the 1990s. In the past two decades, the overall smoking prevalence in Lithuania declined; however, the trends were sex-specific. Smoking among men declined from 44% in 1994 to 33% in 2012, whereas it increased from 7% to 13% in women. Smoking prevalence increased among both sex groups until 2000; then, the prevalence of male smokers started to decrease, whereas the rate of female smokers remained quite constant.⁴ A downtrend in smoking prevalence could be related to active positive policy developments in Lithuania. In 1996, the law on tobacco control in the Republic of Lithuania was adopted, and it was then followed with additional improvements: a ban on advertising (2000), ratification of the WHO Framework Convention on tobacco control (2004), a public smoking ban in restaurants, bars, and cafes (2007), tobacco excise tax increases (2004, 2007–2010, 2012–2015), a ban on smoking in cars with children under 18 and pregnant women (2015), ratification of the protocol to eliminate illicit trade in tobacco products (2016), and complete

ban on all forms of sponsorship from the tobacco industry (2017).⁵

Lung Cancer Screening

European chest specialists' societies recommend lung cancer screening in the setting of comprehensive, quality-assured, longitudinal programs within a clinical trial or in routine clinical practice at certified multidisciplinary medical centers⁶ and started preparations for national screening programs in European countries⁷; or both.

Not one Lithuanian national chest specialists' society has formally recommended national lung cancer screening; thus far, no lung cancer screening has been implemented. Nevertheless, very preliminary discussions for the implementation of such a program have recently begun with the National health care system and NHIF authorities.

Diagnosis

Lung cancer is suspected and diagnosed in particular patients in Lithuania in several scenarios. These scenarios are the following: (1) patients seeking medical

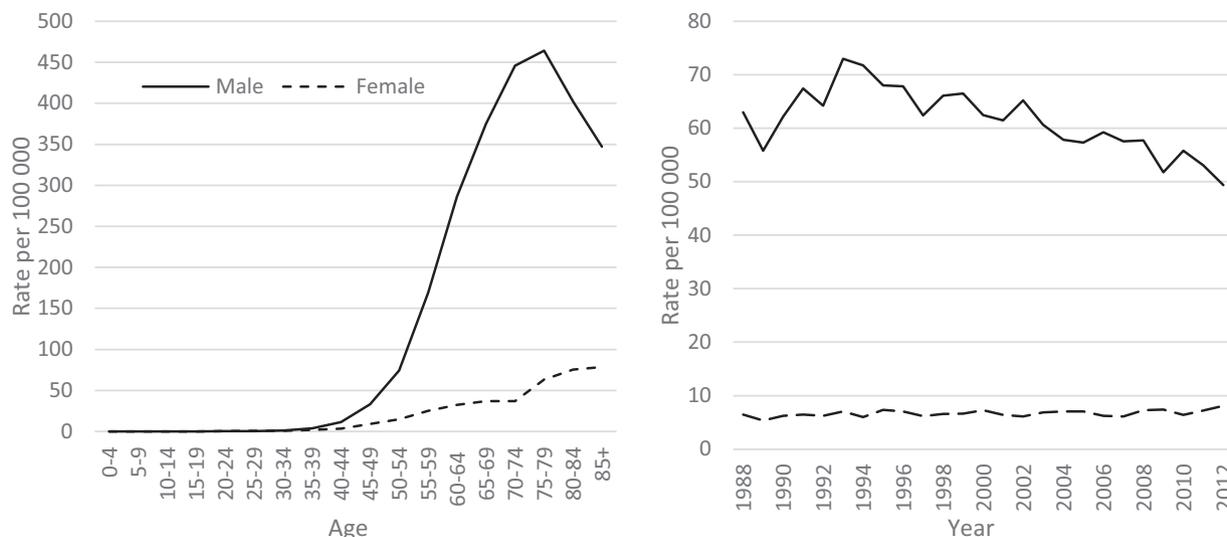


Figure 2. Age-specific (2008-2012) and age-standardized (world standard) incidence rates per 100,000 for lung cancer in Lithuania from 1988 to 2012.

consultation because of subacute or chronic clinical (mostly respiratory) symptoms; (2) accidental findings on chest X-ray examination, which is strongly recommended once a year or every 2 years (depending on the employee's job or before starting any new job); (3) accidental findings on chest X-ray or computed tomography (CT) scanning performed because of acute illnesses (e.g., nonresolving pneumonia, acute viral respiratory infection); and (4) individual seeking a prophylactic laboratory and instrumental examination. No formal study was performed to analyze which of the scenarios occurred most often. All of this leads to the conclusion that in Lithuania, most of the newly diagnosed lung cancer cases are in advanced stages.⁸

Various diagnostic techniques, including bronchoscopy, endobronchial ultrasound bronchoscopy, trans-thoracic needle aspiration, CT scan (chest, abdomen, and head), magnetic resonance imaging (chest and head), positron emission tomography-CT scan, isotope bone scan, mediastinoscopy, thoracoscopy, and peripheral lymph node biopsy are available and are being used in lung cancer diagnosis and staging.

A comprehensive pathologic examination, including testing for *EGFR*, *ALK*, and programmed ligand 1 immunohistochemistry, is available in three major medical centers. NSCLC is tested for *ALK*. Adenocarcinoma cases are tested for *EGFR*. A liquid biopsy is used to detect *T790M* resistance mutation in patients who progress on *EGFR* tyrosine kinase inhibitor therapy.

Management

In Lithuania, lung cancer is treated according to the national guidelines, which are updated regularly. All

patients with lung cancer are discussed among multidisciplinary teams. Generally, multidisciplinary teams include, at the minimum, respiratory physicians (pulmonologists), thoracic surgeons, radiologists, and nuclear medicine physicians.

Surgical Procedure

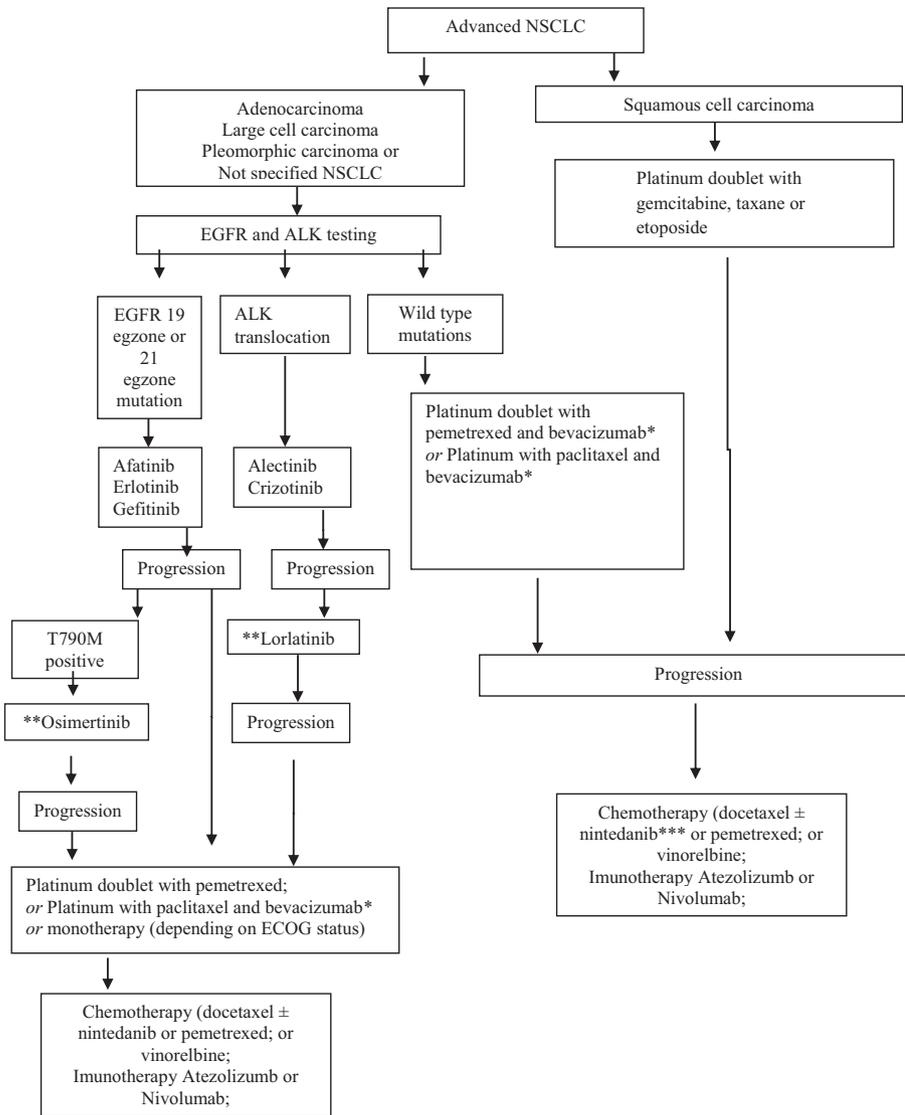
Surgical procedure remains the main treatment modality for early NSCLC. However, less than 25% of all lung cancers are surgically managed.

Video-assisted thoracoscopic surgery (VATS) lobectomy is the standard treatment of early lung cancer stages in Lithuania. The percentage of microinvasive VATS operations increased from 10% in 1990 to 54% in 2018 for all lung cancer surgeries. Nowadays, more than 50% of all lung resections performed are VATS.

The number of pneumonectomies decreased tremendously from 100 cases in 1990 to 10 to 15 cases in 2018. Robotic surgery was started for early stages in one hospital at the beginning of 2019.

Adjuvant (postoperative) chemotherapy is provided to patients with stages IB to IIIA. Postoperative radiotherapy (RT) without chemotherapy is provided very rarely. For patients with accidental N2 lymph node involvement, postoperative radiotherapy is recommended to improve local control but is given sequentially after adjuvant chemotherapy.

Neoadjuvant (preoperative) chemotherapy or chemoradiotherapy (rarely) is done before an operation is performed for N2 disease in NSCLC; restaging of mediastinum lymph nodes is then provided. Surgical procedure for SCLC is used only in small peripheral lesions less than 2 cm after negative positron emission



*Bevacizumab reimbursed only for adenocarcinoma. **Lorlatinib and osimertinib only in the Early Access program provided by pharmaceutical companies. ***Nintedanib reimbursed only for adenocarcinoma.

Figure 3. Advanced NSCLC treatment algorithm. ECOG, Eastern Cooperative Oncology Group.

tomography-CT of the mediastinum (limited lung resections).

Radiotherapy

RT is recommended for patients with early-stage NSCLC who are medically inoperable or who refuse to have an operation after surgical evaluation. Such treatments include [brachytherapy](#) and [stereotactic body radiotherapy](#).

In Lithuania, concurrent or sequential chemoradiotherapy is the standard treatment for patients with inoperable stage II (node-positive) and stage III NSCLC. Sequential chemoradiotherapy or radiotherapy

alone is appropriate for frail patients unable to tolerate concurrent therapy. Induction chemotherapy with carboplatin and etoposide is followed by thoracic RT at a dose of 66 Gy in 33 fractions (2 Gy per fraction and five fractions per week). Patients with a good performance status often receive concurrent chemotherapy and radiation (from two to four courses with cisplatin and etoposide). The same RT starts on day 1 with two concurrent cycles of cisplatin and etoposide.

Other treatment techniques for early-stage NSCLC are radiofrequency ablation, [microwave ablation](#), percutaneous [cryoablation](#), and [photodynamic therapy](#).

Systemic Treatment

In Lithuania, the systemic treatment approaches closely resemble the currently available international guidelines (Fig. 3).^{7,9} Management of NSCLC has changed considerably over the past two decades with the development of numerous systemic treatments including targeted therapies and immunotherapy. Reflex testing of *EGFR* and *ALK* have improved the time to optimal systemic therapy (targeted therapy) for patients with advanced NSCLC.

Other treatment options include clinical trial involvement as a good alternative for patients to access newer and more effective therapies.

Patients with limited-stage SCLC receive concurrent chemoradiotherapy with platinum and etoposide. Patients receive prophylactic cranial irradiation if the disease is stable or if a partial response is seen after initial treatment.

The standard first-line treatment of advanced SCLC is etoposide-platinum-based chemotherapy.

Topotecan (either oral or intravenous) or a combination of cyclophosphamide, doxorubicin, and vincristine is used as a second-line chemotherapy for metastatic or recurrent SCLC (<6 mo). Chemotherapy with platinum-based treatment is used for patients with SCLC who progress after the completion of first-line chemotherapy (when the time to relapse is >6 mo).

Prophylactic cranial irradiation for patients with metastasis is not usually used.

Challenges

Unfortunately, the survival of patients with lung cancer in Lithuania has remained poor despite better diagnostic and treatment approaches. As in other countries, most patients are often diagnosed in an advanced stage of lung cancer when the perspectives for curative treatment are rather limited. Despite new treatments in Europe, the processes involving drug reimbursement decision-making systems in Lithuania take too long (at times, it lasts a couple of years from applying to authorities to the final decision). In addition, drug expenditure as a proportion of overall cancer-related health care costs is low compared with other European Union countries.¹⁰ Thus, the best option for some patients is

participating in a clinical trial. Fortunately, the situation is getting better. Appropriate lung cancer staging and comprehensive examination of patients with lung cancer, including molecular diagnostic testing, has become increasingly sophisticated. New treatment options are becoming regularly available for patients with lung cancer.

References

1. Murauskienė L, Janonienė R, Veniute M, van Ginneken E, Karanikolos M. Lithuania: health system review. *Health Syst Transit*. 2013;15:1-150.
2. Ferlay J, Colombet M, Bray F. *Cancer incidence in five continents, CI5plus: IARC CancerBase No. 9*. Lyon, France: International Agency for Research on Cancer; 2018.
3. Zaridze DG, Dvoirin VV, Kobljakov VA, Pisklov VP. Smoking patterns in the USSR. *IARC Sci Publ*. 1986;74:75-86.
4. Grabauskas V, Klumbienė J, Petkevičienė J, et al. Suaugusių Lietuvos žmonių gyvenimo tyrimas. Vol. 139; 2012. <https://publications.lsmuni.lt/object/elaba:15365482/15365482.pdf>. Accessed October 6, 2019.
5. Klumbienė J, Sakyte E, Petkevičienė J, Prattala R, Kunst AE. The effect of tobacco control policy on smoking cessation in relation to gender, age, and education in Lithuania, 1994-2010. *BMC Public Health*. 2015;15:181.
6. Kauczor HU, Bonomo L, Gaga M, et al. ESR/ERS white paper on lung cancer screening. *Eur Radiol*. 2015;25:2519-2531.
7. Pedersen JH, Rzyman W, Veronesi G, et al. Recommendations from the European Society of Thoracic Surgeons (ESTS) regarding computed tomography screening for lung cancer in Europe. *Eur J Cardiothorac Surg*. 2017;51:411-420.
8. Gedvilaitė V, Danila E, Cicėnas S, Smailytė G. Lung cancer survival in Lithuania: changes by histology, age, and sex from 2003-2007 to 2008-2012. *Cancer Control*. 2019;26:1-7.
9. Planchard D, Popat S, Kerr K, et al. Metastatic non-small cell lung cancer: ESMO clinical practice guidelines for diagnosis, treatment, and follow-up. *Ann Oncol*. 2018;29(suppl 4):iv192-iv237.
10. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol*. 2013;14:1165-1174.