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The Use of Low-Dose Chest Computer Tomography in Screening of Lung Cancer in Georgia

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ABSTRACT

Background: Lung cancer is one of the leading causes of cancer-related mortality worldwide, including in our country, Georgia. Lung cancer is associated with smoking. Almost one-third of Georgia's population smokes. Several countries have implemented lung cancer screening programs with low-dose chest computed tomography (LDCT) with promising results.

Objectives: Our study aimed to evaluate the role of low-dose chest CT in screening lung cancer in high-risk individuals.

Methods: A pilot study was launched, and between June 1, 2021, and June 30, 2021, our institution, Todua Clinic, offered the Georgian population LDCT for screening of lung cancer in high-risk populations. The eligibility criteria included risk factors: tobacco smoking (>20 pack-years), former heavy smoking, and age>55 years. The images were interpreted and categorized according to LUNG RADS version 1.1. The multidisciplinary team was involved in further stratification and decision-making. Our institution's ethics committee approved the study.

Results: Five of the screened individuals were diagnosed with lung cancer, and three patients had suspicious findings, needing closer follow-up (3 months) or PET/CT. In conclusion, important findings were reported in 27 individuals (11.2%); most were males (88.9%).

Conclusions: The preliminary data from our pilot study show that low-dose chest CT can be used for screening lung cancer in an asymptomatic high-risk population group. Further results and better population recruitment are needed to prove this approach's mortality reduction and cost-effectiveness in Georgia.

Keywords: Low-dose chest CT; lung cancer; screening.

BACKGROUND

Lung cancer is one of the most commonly diagnosed cancers worldwide, accounting for 11.4% of all cancer diagnoses, and remains the leading cause of cancer-related mortality, accounting for 18.0% of overall cancer mortality (1.8 million cases).[1,2] Lung cancer is the second most frequent malignancy in Georgia.[3] 1347 deaths from lung cancer were reported in 2020, which was 16.4% of the general mortality from all cancer types.[3] According to 2015-2021 data from the Cancer Population Registry of Georgia, the incidence range of lung cancer in men was 31.6-40.7/100 000, the incidence being 35.7 in 2021. 637 new cases were registered 2021, constituting 13 % of all new malignancies registered in Georgia among men. In 2021, more than 55% of cases were diagnosed with stage IV.[4,5]

There have been significant improvements in the treatment of advanced-stage lung cancer in the past years, such as the introduction of molecularly targeted agents and immune-checkpoint inhibitors with systemic chemotherapeutic regimens.[6] This has led to improved outcomes. However, stage IV lung cancer remains the leading cause of cancer-related mortality worldwide. On the contrary, patients with early-stage disease have a >75% chance of survival over 5 years.[7] Several trials throughout the world have shown that the main strategy to reduce lung cancer-related mortality over a more extended time period is based on early detection of lung cancer by screening asymptomatic individuals with low-dose CT (LDCT). Two large randomized controlled trials of low-dose CT (LDCT)-based lung cancer screening in high-risk populations have shown a statistically significant mortality reduction in patients: the US National Lung Screening Trial (NLST) and the Dutch–Belgian lung-cancer screening trial NELSON.[8-10] Lung cancer is a smoking-related disease: in high-income countries, ~10–20% of current and former heavy smokers will be diagnosed with lung cancer during their lifetime compared with 1–2% of never-smokers.[8,11,12] Thus, high-risk individuals with a history of smoking are likely to have more benefit from screening.

To our knowledge, no lung cancer screening studies have been conducted, nor have screening programs been implemented in Georgia. The majority of lung cancer cases are associated with smoking.[1] The estimated age-standardized prevalence of tobacco use in Georgia is 58.5% for men, one of the highest in the European Region and higher than the average for the Commonwealth of Independent States (51.8%).[13] According to the results of the survey STEPS 2016, almost one-third of Georgia's population (33.7%) smokes, and the smoking rate

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has increased since 2010 (30.3% in 2010).[13] Among current smokers, 57.1% of men reported smoking tobacco products daily compared with 7.1% of women.[13,14] We decided to launch the pilot study of lung cancer screening with low-dose chest CT in high-risk populations. Our study aimed to recruit high-risk individuals and evaluate the efficacy of LDCT in the early detection of lung cancer. Our institution's ethics committee approved the entire study.

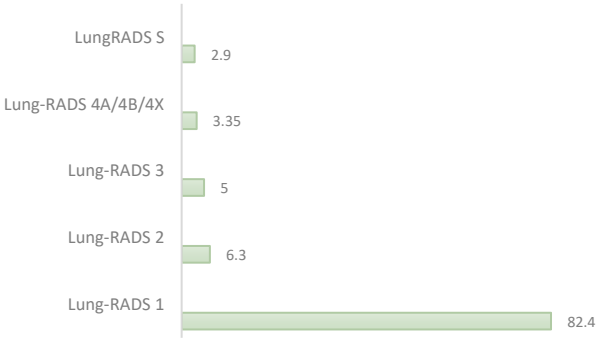
METHODS

Between June 1, 2021, and June 30, 2021, our institution, Todua Clinic, offered the Georgian population LDCT of the chest for lung cancer screening in high-risk populations. The eligibility/inclusion criteria included risk factors: tobacco smoking (>20 pack-years), former heavy smoking, and age>55 years. The patients applied online and filled in the online questionnaire. A total of 241 individuals were registered; two were excluded due to a history of malignancy (one with breast cancer (female) and one with lung cancer (male)). 239 individuals were screened: 62.34 % of screened individuals were males (N=149), and 37.66 % were females (N=91). The low-dose chest CT was performed on the state-of-the-art scanner, with contiguous thin (1 mm thickness) sections and a high spatial frequency (sharp) filter displayed in the lung window. Axial sections were reconstructed using coronal and sagittal series. The low dose technique was applied according to the body habitus. The longest diameter of lung nodules was measured manually. The images were interpreted by five radiologists with more than 5 years of experience (5-25 years). The results were interpreted and categorized according to Lung Imaging Reporting and Data System (Lung-RADS) screening guidelines, version 1.1 (2019). The multidisciplinary team made further stratification and decisions about screening frequency.

RESULTS AND DISCUSSION

The majority of individuals (82.4%) fell in Category 1, with no lung nodules, and four of them with specific benign calcifications, while 15 (6.3 %) fell in Category 2 (Fig.1). Biennial screening was suggested for these groups (Fig.2). Category 3 nodules were discovered in 12 individuals (5.0 %) and 6-12 months interval CT was suggested, depending on their risk factors, such as tobacco smoking, age, sex and family history (12 of them were males) (Fig.3). Eight individuals (3.35%) had findings categorized as 4A/4B/4X. 3 of these individuals had suspicious findings, categorized as 4A, needing closer follow-up (3 months) or PET-CT (all of them were males) (Fig.4). Five participants (all males) were diagnosed with lung cancer: three cases were stage IV disease (two with metastasis to the contralateral lung and one with unsuspected metastasis to the lumbar vertebra), they proceeded to systemic treatment, two patients were diagnosed with clinical stage I-II disease with radical treatment intentions (surgical treatment was planned) (Fig.5). Seven of the screened individuals (2.9%) were identified with pathology other than lung cancer needing further workup (two of them were females).

FIGURE 1. Categorization of screened individuals (%) according to Lung-RADS v.1.1



Abbreviations: Lung-RADS, lung imaging reporting and data system.

FIGURE 2. Perifissural nodule - category two nodule according to Lung-RADS v.1.1

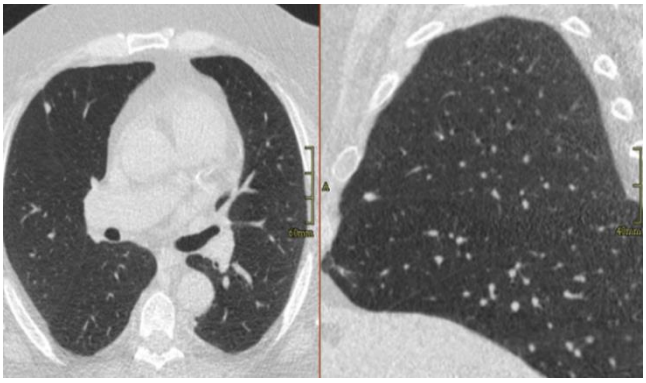


FIGURE 3. Part-solid nodule, >6 mm total diameter, with solid component <6 mm, category three nodule according to Lung Rads v.1.1

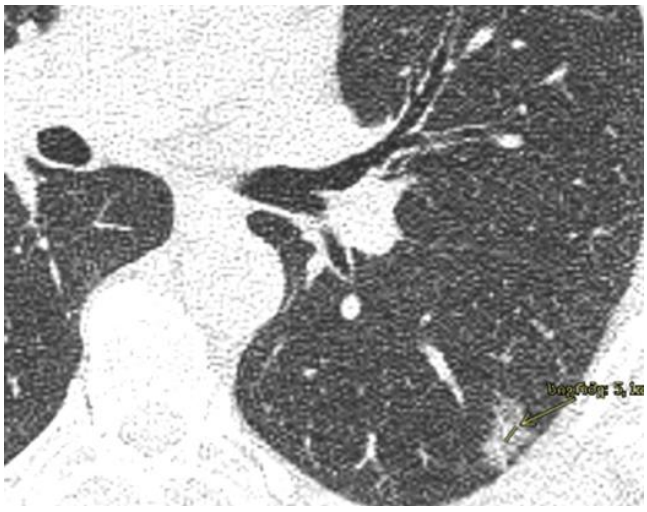


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FIGURE 4. Part-solid nodule, >6 mm total diameter, with solid component <6 mm, category three nodule according to Lung Rads v.1.1

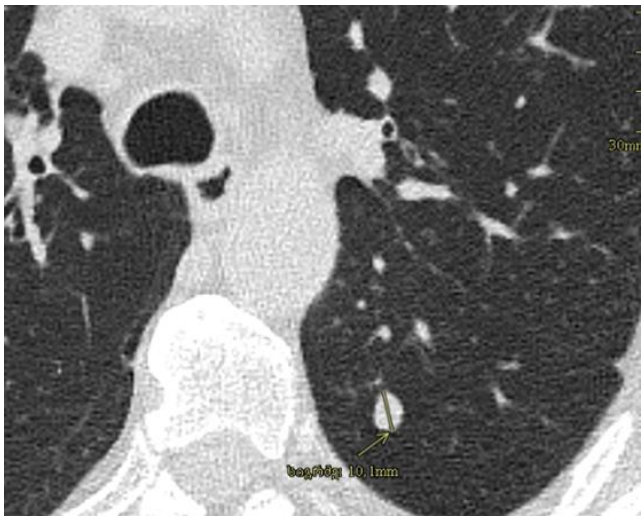
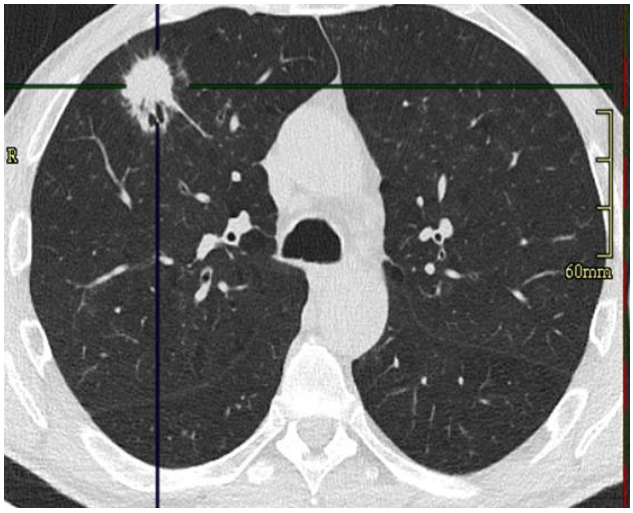


FIGURE 5. Part-solid nodule, >6 mm total diameter, with solid component <6 mm, category three nodule according to Lung Rads v. 1.1



Besides age (>60 years), smoking status has the greatest influence on the probability of lung cancer.[15] However, other factors, such as a family history of lung cancer, an individual history of respiratory diseases, other malignancies, and exposure to asbestos, can also contribute to the risk of developing lung cancer.[8,15] Thus, out of several multivariable risk-prediction models, Liverpool Lung Project - LLPv2 has been used to select high-risk individuals for cancer screening in clinical trials and projects.[16] The US National Lung Screening Trial (NLST) used risk factors such as current and former heavy smoking (≥30 or more pack-years of cigarette smoking; former smokers if they quit smoking <15 years before) aged between 55 and 74 years.[8] NELSON involved current and former heavy smokers (≥30 pack-years) aged 55–75 years.[8] The recruitment of high-risk individuals is a challenging process and may differ among regions. However, screening should only be implemented for high-risk individuals, and the potential benefits and risks should be presented to the participants appropriately.[8]

Radiation dose from a chest LDCT is ~1.5 mSv, 15-fold higher than a conventional chest X-ray but <25% of the dose delivered from conventional chest CT.[8,17] LDCT-based lung cancer screening is the only approach that has shown a statistically significant reduction in lung cancer-related mortality.[9,10]

The assessment of nodule size is essential for managing detected lung nodules. Manual measurement of the longest diameter has been routinely used.[18,19] However, volumetric measurement is more reliable as pulmonary nodules are not perfectly geometrically shaped.[20,21] European position statement on lung cancer screening (EUPS) recommends the use of semi-automatically measured volume and volume-doubling time for the management of detected nodules,[22] as well as clinical practice guidelines from the British Thoracic Society suggest the use of volumetry, whenever available.[23] Volume standards have been added to the 2019 Lung Imaging Reporting and Data System (Lung-RADS) screening guidelines as a more reproducible measurement method when appropriate software is available.[24] The nodule-based risk-prediction models, which had perfect predictive accuracy, were published in 2013 in the Pan-Canadian Early Detection of Lung Cancer Study (PanCan), referred to as the Brock parsimonious model (PanCan-1b), and the comprehensive model (PanCan-2).[25] Female sex, larger size of the nodule, location of the nodule in the upper lung, and nodule speculation were associated with lung cancer, while the so-called “full models” additionally included older age, a family history of lung cancer, emphysema, lower nodule count and part-solid nodules as compared with solid nodules. These models became management tools recommended by EUPS and the British Thoracic Society.[8,22,23]

In the USA, annual screening is performed based on the frequency of NLST criteria.[26] All countries recommend an annual screening interval. The results of the NELSON study suggest that a sex-specific interval can be used in the future, as nodules tend to have a slower growth rate in women than in men.[10] The Analysis of the results of the Multicentric Italian Lung Detection (MILD) trial shows that individuals with a negative baseline result could benefit from undergoing biennial instead of annual screening.[27] In the NELSON study, annual LDCT after a negative baseline CT might not be necessary for some patients, while a screening interval of >24 months might be too long.[8,28] The Analysis of these studies shows the added value of patient stratification based on the results from the baseline LDCT scan.

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CONCLUSIONS

In our pilot study, using low-dose chest CT for lung cancer screening, we reported significant findings in 27 individuals (11.2%); most were males (88.9%). The preliminary data suggest that low-dose chest CT can be used for screening for lung cancer in asymptomatic high-risk individuals. However, more extensive population studies and better population recruitment are needed to prove the statistically significant reduction of lung cancer-related mortality and the cost-effectiveness of this approach in Georgia. Challenges and future perspectives must be addressed, such as optimal strategy for recruiting high-risk individuals and improving screening procedures using AI (artificial intelligence)-based strategies to detect and classify pulmonary nodules. Personalized screening intervals using baseline LDCT scan, assessing the sex differences in lung cancer screening programs and beneficial effects in women than in men, integrating smoking cessation within lung cancer screening programs, and estimating the long-term health outcomes, including benefits and harms.

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