International Journal of Community Medicine and Public Health
Jamal AD et al. Int J Community Med Public Health. 2023 Oct;10(10):3875-3879
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20232854

Review Article

The use of low-dose computed tomography for lung cancer screening

Doha Jamal Ahmad[1]*, Abdullah Ali Alasmari[2], Sahar Ali Alasmari[3], Mohammed Mufadhi Alanazi[4], Bashayer Ahmed Qirati[5], Aeshah Abdullah Hassani[6], Sultan Nasser Hezam[7], Shatha Magboul Alzaidi[8], Naif Ali Domari[5], Layla Masoud Sawa[5], Waad Saleh Alqahtani[9]

[1]Department of Radiology, Al Aziziyah Children Hospital, Jeddah, Saudi Arabia
[2]Department of Radiology and Applied Services, King Abdullah Hospital, Bisha, Saudi Arabia
[3]Department of Radiology, Maternity and Children Hospital, Abha, Saudi Arabia
[4]Department of Radiology, Hail General Hospital, Hail, Saudi Arabia
[5]Department of Radiology, King Fahad Central Hospital, Jazan, Saudi Arabia
[6]Department of Radiology, Prince Saud bin Jalawi Hospital, Al-Ahsa, Saudi Arabia
[7]Department of Radiology, Prince Mohammed bin Nasser Hospital, Jazan, Saudi Arabia
[8]Department of Radiology, King Faisal Medical Complex, Taif, Saudi Arabia
[9]Department of Radiology, Ahad Rafidah General Hospital, Abha, Saudi Arabi

Received: 26 August 2023
Accepted: 11 September 2023

***Correspondence:**
Dr. Doha Jamal Ahmad,
E-mail: dohajamal86@gmail.com

ABSTRACT

Around the globe, lung cancer is among the most prevalent cancers, accounting for significant morbidity and mortality. Compared to breast, cervical, and colorectal cancers combined, lung cancer is the leading cause of mortality. Higher survival rates are achieved with an early lung cancer diagnosis. The aggressiveness and heterogeneity of lung cancer have impeded endeavours to use screening to lower mortality from the disease. Due to studies showing that low-dose computed tomography may identify many tumors in their early stages, the development of low-dose computed tomography has significantly changed the landscape of lung cancer screening. Long-term research studies have demonstrated that low-dose computed tomography for the secondary prevention of lung cancer considerably lowers lung cancer mortality in high-risk populations. Screening with low-dose computed tomography reduces the mortality associated with it by 20-30%. Low-dose computed tomography is a fast and simple chest exam that does not involve the use of a contrast agent. Based on the current recommendations, eligible individuals with a history of heavy smoking will benefit from yearly low-dose computed tomography, but because of the risks involved, such as false-positive results, radiation exposure, and overdiagnosis, joint decision-making consultation is necessary. The purpose of this research is to review the use of low-dose computed tomography for lung cancer screening.

Keywords: Lung, Cancer, Screening, Low-dose, Computed tomography

INTRODUCTION

Lung cancer is an aggressive and diverse condition. Despite improvements in surgical, radiotherapeutic, and chemotherapeutic methods, the long-term survival rate is still dismal.[1] With an estimated 2 million diagnoses and 1.8 million deaths, lung cancer is the primary cause of cancer incidence and mortality worldwide. Lung neoplasms are the second most frequent cancer diagnosis in both men and women after prostate and breast cancer, respectively. Lung cancer incidence is rising internationally due to increased tobacco access and industrialization in developing countries.[2] The prognosis relates directly to the stage of the disease at the time of diagnosis, and the overall survival rate at 5 years is less than 16%. Early disease diagnosis is crucial if mortality is to be decreased, even with this primary prevention and recent therapeutic advances.[3] Small-cell carcinoma and non-small/large-cell carcinoma are the two classifications for lung cancer that are used for determining treatment modalities and forecasting prognosis. Depending on the type of tumour and the number of metastases, different signs and symptoms may be present.[4]

Early detection is favourable in the case of lung cancer due to certain factors, including the presence of a high-risk population, the relative asymptomatic nature of the disease during its early phase, and a generally improved prognosis. Sputum cytology, computed tomography (CT), and chest radiography are among the diagnostic techniques employed for the diagnosis of lung cancer. Numerous observational studies and clinical trials have investigated the use of chest X-ray and sputum cytology for screening; the results have not indicated a decrease in disease-specific mortality, and the excess of lung malignancies in the intervention group has been attributed to overdiagnosis. Advancements in radiological and CT techniques have lowered radiation exposure through the application of low-dose CT, which is demonstrated to have almost the same radiation dose as mammography.[5]

The primary strategy for secondary lung cancer prevention is screening with low-dose CT, which reduces mortality associated with it by 20-30%, notably in women. The screening low-dose CT is a fast and simple chest exam that does not involve using a contrast agent. A volume capture from the apex to the bases of the lungs is performed after a bidimensional scout scan of the chest. The tube configuration for volume capture is low current, usually under 40 mAs, and 120 kVp or 140 voltages. The radiation exposure for a screening chest low-dose CT varies according to the subject's anthropometric characteristics, including height and weight. The American College of Radiology has determined a 2.0 mGy upper limit as the optimal volume CT dose index criterion. For the classification of results from low-dose CT for lung cancer screening, the Lung-RADS 1.1 system is advocated.[6] Based on the current recommendations, eligible individuals with a history of heavy smoking will benefit from yearly low-dose CT, but because of the risks involved, such as false-positive results, radiation exposure, and overdiagnosis, a joint decision-making consultation is necessary.[7] The purpose of this research is to review the use of low-dose CT for lung cancer screening.

LITERATURE SEARCH

This study is based on a comprehensive literature search conducted on August 22, 2023, in the PubMed, Web of Science, Science Direct, and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the use of low-dose CT for lung cancer screening. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

The aggressiveness and heterogeneity of lung cancer have impeded endeavours to use screening to lower mortality from the disease. Due to studies showing that low-dose CT may identify many tumors in their early stages, the development of low-dose CT has significantly changed the landscape of lung cancer screening.[1] Studies utilizing sputum cytology and chest radiography in the past have been insufficient to indicate any decrease in lung cancer mortality due to screening. The relatively low sensitivity of both of these investigations in early tumors is possibly one of the causes. Small pulmonary nodules, thought to be the most typical manifestation of early lung cancer, have been demonstrated to have a substantially better sensitivity for low-dose CT. To appropriately categorize the identified lesions and prevent intrusive procedures in benign nodules, non-invasive diagnostic methods are needed since small pulmonary nodules are prevalent and the majority of them are benign. Nodule density, size, and the presence of growth during follow-up have been found to be helpful in this regard, and contrast-enhanced CT and positron emission tomography may be added as a supplement. Preliminary low-dose CT investigations in heavy smokers have shown a large number of asymptomatic, early, treatable malignancies with favourable survival rates based on these diagnostic algorithms. However, given that a number of biases could account for these results in the absence of cancer screening's ultimate purpose, namely mortality reduction, most researchers agree that randomized controlled trials involving significant or large population numbers (at least 10,000) are necessary to show a potential mortality reduction.[8]

Evidence from literature

So far, many of the randomized clinical trials that have been conducted to assess the efficacy of low-dose CT lung cancer screening in the United States and Europe have presented promising outcomes. Both the national lung screening trial and the Nederlands-Leuvens Longkanker screenings Onderzoek (NELSON) trial demonstrated that low-dose CT screening could considerably lower lung cancer mortality in a high-risk population. These trials had sufficient power to assess the reduction in lung cancer mortality.[9] The National Lung Screening Trial started in 2002 and enrolled 53,454 participants, aged 55 to 74, who were either current or former smokers with a smoking history of at least 30 packs per year and who were at a high risk of lung cancer. Over the course of three years, participants were randomly assigned to either low-dose CT or chest X-ray screening groups and completed annual screening. Using low-dose CT instead of a chest X-ray for lung cancer screening resulted in a 20% reduction in lung cancer mortality overall after 6.5 years of follow-up, as per the findings of this trial.[10]

The NELSON trial, in contrast, compared no screening to low-dose CT screening at baseline, year 1, year 3, and year 5.5. Almost 15,792 participants between the ages of 50 and 74 who had a high risk of developing lung cancer were enrolled in this trial, including current and past smokers who had smoked for at least $\geq$30 pack-years. The NELSON trial's final findings were published in 2020, with a 10-year follow-up showing a cumulative rate ratio for lung cancer death in the screening arm of 0.76 compared to the control arm.[11] Results of a study by Bonney et al showed that compared to control groups that underwent chest x-rays or no screening at all, there was a 21% decrease in mortality with low-dose CT screening. Compared to men, women receiving low-dose CT screening appeared to benefit more from reduced lung cancer-related mortality. Additionally, there was a 5% decrease in deaths from all causes, including lung cancer. However, the low-dose CT group experienced an increase in invasive tests. However, there was no difference between groups in the analysis of 60-day postoperative mortality.[12]

Menezes et al demonstrated in their findings that in a population at risk, low-dose CT can detect small lung malignancies. Although the diagnostic algorithm generates a few invasive procedures that are falsely positive, the majority of cancers are detected or diagnosed when they are still treatable and have a good chance of being cured.[13] Similarly, results of a systematic review concluded that while using low-dose CT to screen high-risk individuals can lower lung cancer mortality, it also raises the risk of overdiagnosis, incidental findings, increased distress, and, only rarely, radiation-induced malignancies.[14] Contrarily, the results of a meta-analysis showed that the likelihood of false positive results, screening-related issues, overdiagnosis, and unintended findings were all considered to be low. However, the authors agreed that using the most recent randomised controlled trial data, it was shown that low-dose CT screening significantly lowers lung cancer mortality but does not lower overall mortality.[15]

Results of a single-centre population-based study revealed that the high-risk category of those under 50 with a confirmed family history of all types of cancer in first-degree relatives had a particularly high cancer detection rate of 6.2%. Almost 88% of malignancies were adenocarcinomas, and 99% of them were in the early stages. Cancer risk was much greater in nodules with interval growth. Ground glass opacity nodules and solid nodules both had a similar likelihood of developing cancer, and 61.76% of them were occult on chest radiographs. Therefore, for the early detection of lung cancer, low-dose CT is effective.[16]

Dezube and Jaklitch commented that there is growing evidence that low-dose CT reduces lung cancer-specific mortality with a stage shift in early-stage I lung cancer incidence. Additionally, there is mounting early evidence that screening may reduce mortality when inclusion criteria are expanded to include high-risk nonsmokers, as shown. Regarding the risk of harm from overdiagnosis caused by screening techniques that are unnecessary, there is still discussion about lung cancer screening. However, a long-term research analysis only discovered 3% of cases of overdiagnosis. There are also new, innovative approaches to lessening these risks. It has been demonstrated that standardised low-dose CT screening categorization can lessen risks and false-positive rates.[17] Among the new innovative procedures, Ardila et al. designed a model that they reported produced absolute reductions of 11% in false positives and 5% in false negatives when prior CT imaging was not available. The model's performance was comparable to that of the same radiologists in cases where previous CT imaging was available. This provides a chance to automate and computerize the screening process in order to improve it.[18] This model is illustrated in Figure 1.

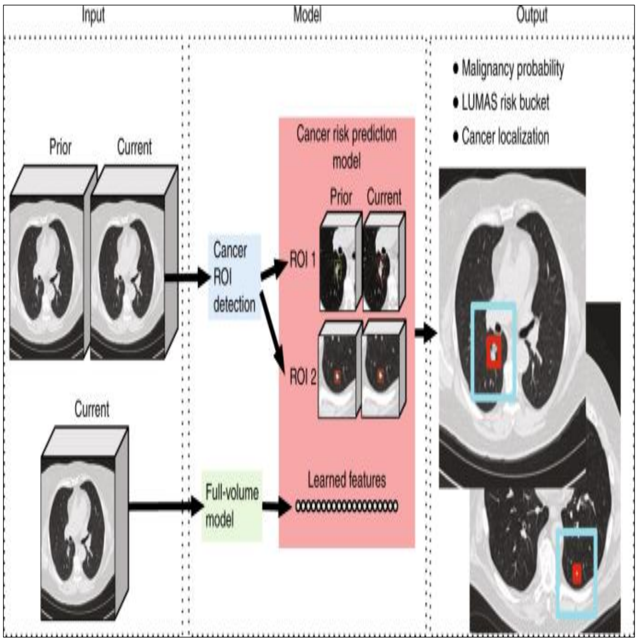

Figure 1: Model framework: The model takes as input a primary LDCT volume and, if possible, a preceding low-dose CT volume for each patient. After analyzing suspicious and volumetric ROIs as well as the entire low-dose CT volume, the model generates a risk bucket score (LUMAS), a location for anticipated malignant nodules, and a general prognosis of malignancy for the patient.[18]

Moreover, Benzaquen et al described that, in the context of lung cancer screening, low-dose CT interpretation may be challenging. The straightforward algorithm design ought to be predicated on two inquiries about the primary lesion identified by low-dose CT. First, if the person has a nodule and the response is no, the patient will be offered a date and time for the subsequent screening round. If the response is yes, the next inquiry is: Is this nodule cancerous? The nodule will be categorized as malignant, benign, or undetermined depending on its characteristics. The variety of challenges faced by clinicians at lung cancer clinics in the context of lung cancer screening is exemplified in Figure 2. When using low-dose CT alone, lung cancer screening takes time. In fact, most decision-making algorithms for lung nodules recommend a repeat CT to examine the volume-doubling time, a statistic that, along with the nodule's morphology, has the most bearing on whether or not to undergo invasive procedures such as surgery.[19] However, it is still unclear what factors contribute to the underutilization of low-dose CT screening. As a relatively new recommendation, physicians might not be aware of appropriate screening standards or be unsure of the validity of the body of research supporting low-dose CT screening. Patients may be less likely to choose to get yearly examinations that were previously not advised. Additional study is required to characterise the potential benefits of low-dose CT screening more fully in order to support physicians' and patients' informed decision-making, particularly in light of the formation and recent extension of national screening recommendations.[20]

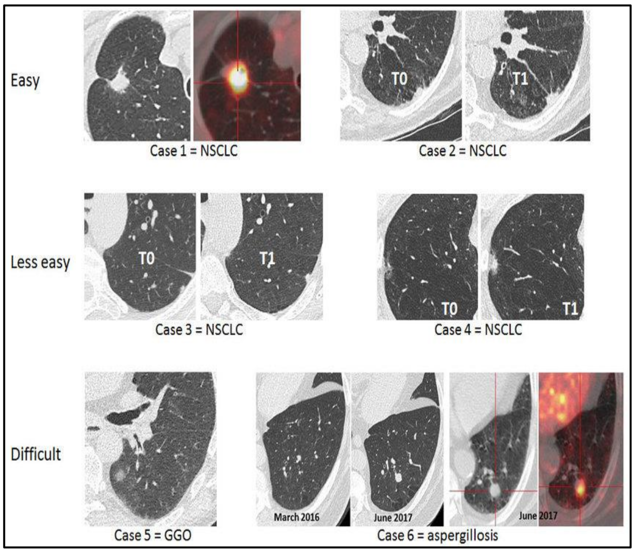

Figure 2: Six lung cancer screening examples demonstrate the potential difficulty in interpreting low-dose CT.

NSCLC: non-small cell lung cancer, GGO: ground glass opacities.[19]

One of the challenges associated with low-dose CT is referral from a family physician, as reported by Ersek et al who stated that although the majority of family physicians report discussing low-dose CT with patients who are at high risk for lung cancer, referrals are still insufficient. Physicians' understanding of screening recommendations and reimbursement is lacking, which points to the need for more educational outreach.[21] Similarly, Lewis et al commented that chest X-rays are more frequently requested by primary care physicians than low-dose CT. Primary care physicians' knowledge of low-dose CT effectiveness and lung cancer screening recommendations was poor when analyzed. Hence, interventions to educate healthcare providers are required to encourage patient-centred decision-making.[22] Awareness and training sessions for family physicians are therefore recommended since timely referral would initiate a timely and early diagnosis. Our study signifies the importance of the use of low-dose CT in lung cancer screening, which has the potential to reduce lung cancer-related mortality, as backed by the evidence from research studies. However, we could not more elaborately compare the advantages and disadvantages associated with low-dose CT, which is the limitation of this review since it is beyond the scope of this paper. However, we aim to conduct a more comprehensive review illustrating and comparing the advantages and limitations of low-dose CT in lung cancer screening in the future.

CONCLUSION

Screening for lung cancer can lower the mortality associated with it by employing low-dose CT. This has now been conclusively demonstrated in numerous clinical studies. As a result, low-dose CT in lung cancer screening shall be effectively practiced in high-risk groups. To ensure effectiveness, it will be necessary to continuously monitor participant eligibility, lung cancer detection rate, false-positive and false-negative rates, lung cancer screening interval, adherence, and referral rate, along with CT radiation exposure.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. National Lung Screening Trial Research Team; Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, et al. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. N Eng J Med. 2011;365(5):395-409.
2. Thandra KC, Barsouk A, Saginala K, Aluru JS, Barsouk A. Epidemiology of lung cancer. Contemporary Oncol (Poznan, Poland). 2021;25(1):45-52.
3. Martínez PE, De Aguiar QK, Arrarás MM, Mojarrieta JC, De Moya EFE, Benito MB, et al. Lung Cancer Screening: Use of Low-Dose Computed Tomography. Archivos de Bronconeumología (English Edition). 2019;55(10):526-31.
4. Collins LG, Haines C, Perkel R, Enck RE. Lung cancer: diagnosis and management. Am Family Physician. 2007;75(1):56-63.
5. Gopal M, Abdullah SE, Grady JJ, Goodwin JS. Screening for Lung Cancer with Low-Dose Computed Tomography: A Systematic Review and

Meta-Analysis of the Baseline Findings of Randomized Controlled Trials. J Thoracic Oncol. 2010;5(8):1233-9.
6. Silva M, Picozzi G, Sverzellati N, Anglesio S, Bartolucci M, Cavigli E, et al. Low-dose CT for lung cancer screening: position paper from the Italian college of thoracic radiology. La radiologia Medica. 2022;127(5):543-59.
7. Maki KG, Shete S, Volk RJ. Examining lung cancer screening utilization with public-use data: Opportunities and challenges. Preventive Med. 2021;147:106503.
8. Diederich S, Wormanns D, Heindel W. Lung cancer screening with low-dose CT. Eur J Radiol. 2003;45(1):2-7.
9. Lancaster HL, Heuvelmans MA, Oudkerk M. Low-dose computed tomography lung cancer screening: Clinical evidence and implementation research. J Internal Med. 2022;292(1):68-80.
10. Aberle DR, Adams AM, Berg CD. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395-409.
11. De Koning HJ, Van der Aalst CM, De Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020;382(6):503-13.
12. Bonney A, Malouf R, Marchal C, Manners D, Fong KM, Marshall HM, et al. Impact of low-dose computed tomography (LDCT) screening on lung cancer-related mortality. Cochrane Database Systematic Rev. 2022;8(8):Cd013829.
13. Menezes RJ, Roberts HC, Paul NS, McGregor M, Chung TB, Patsios D, et al. Lung cancer screening using low-dose computed tomography in at-risk individuals: the Toronto experience. Lung Cancer. 2010;67(2):177-83.
14. Jonas DE, Reuland DS, Reddy SM, Nagle M, Clark SD, Weber RP, et al. Screening for Lung Cancer With Low-Dose Computed Tomography: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2021;325(10):971-87.
15. Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung Cancer Screening with Low-Dose CT: a Meta-Analysis. J General Internal Med. 2020;35(10):3015-25.
16. Chen CY, Chen CH, Shen TC, Wen-Chien C, Cheng-Nan H, Chun-Han L, et al. Lung cancer screening with low-dose computed tomography: Experiences from a tertiary hospital in Taiwan. J Formosan Med Asso. 2016;115(3):163-70.
17. Dezube AR, Jaklitsch MT. New evidence supporting lung cancer screening with low dose CT and surgical implications. Europ J Surgical Oncol. 2020;46(6):982-90.
18. Ardila D, Kiraly AP, Bharadwaj S, Choi B, Reicher JJ, Peng L, et al. End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography. Nature Med. 2019;25(6):954-61.
19. Benzaquen J, Boutros J, Marquette C, Delingette H, Hofman P. Lung Cancer Screening, Towards a Multidimensional Approach: Why and How? Cancers. 2019;11:212.
20. Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325(10):962-70.
21. Ersek JL, Eberth JM, McDonnell KK, Strayer SM, Sercy E, Cartmell KB, et al. Knowledge of, attitudes toward, and use of low-dose computed tomography for lung cancer screening among family physicians. Cancer. 2016;122(15):2324-31.
22. Lewis JA, Petty WJ, Tooze JA, Miller DP, Chiles C, Miller AA, et al. Low-Dose CT Lung Cancer Screening Practices and Attitudes among Primary Care Providers at an Academic Medical Center. Cancer Epidemiol Biomarkers Prevention. 2015;24(4):664-70.

Cite this article as: Jamal AD, Ali AA, Ali AS, Mufadhi AM, Qirati BA, Hassani AA et al. The use of low-dose computed tomography for lung cancer screening. Int J Community Med Public Health 2023;10:3875-9.