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SCREENING AND EARLY DETECTION OF LUNG CANCER: A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: *Lung cancer is the second most commonly diagnosed cancer and the leading cause of cancer-related deaths globally, accounting for the greatest economic and public health burden of all cancers. In 2020, lung cancer accounted for approximately 2.2 million cases and nearly 1.8 million deaths worldwide.*

The aim: *The aim of this study to show about screening and early detection of lung cancer.*

Methods: *By the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. This search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed, SagePub, and Sciencedirect were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *Four publications were found to be directly related to our ongoing systematic examination after a rigorous three-level screening approach. Subsequently, a comprehensive analysis of the complete text was conducted, and additional scrutiny was given to these articles.*

Conclusion: *Early screening and diagnostic methods of lung cancer, x-ray screening is not recommended. LDCT has obvious advantages and is the most promising imaging method in early screening of lung cancer.*

Keyword: *Lung cancer, screening, detection, diagnosed.*

INTRODUCTION

Lung cancer is the second most common cancer and the leading cause of cancer-related mortality worldwide, with an estimated 2.2 million new cases and 1.8 million deaths in 2020, thus imposing severe social and economic burdens. According to histological type, lung cancer can be divided into non-small cell lung cancer (NSCLC) and small cell lung cancer. NSCLC accounts for approximately 85% of all lung cancers, and adenocarcinoma and squamous cell carcinoma are the main histopathologic subtypes. Despite advances in surgery, radiotherapy, chemotherapy, molecularly targeted therapy, and immunotherapy, the average 5-year survival rate for lung cancer is only 19%.[1–3]

Several strategies aim to detect lung lesions at an earlier stage: better public awareness of the 'alarm' symptoms of locoregional stage lung cancer (beyond the topic of this review), screening with imaging methods such as chest X-ray or chest CT, screening with biomarkers in blood, lung lavage fluid or exhaled air, and bronchoscopy in individuals at high risk to develop lung cancer. An overview of the most important developments in each of these fields is given.[4,5]

There is considerable relief in that statement given it has been over 30 years since the results of the Mayo Lung Project along with studies from Johns Hopkins University and Memorial Sloan Kettering Cancer Center showed lack of mortality reduction from screening with chest X-ray and sputum cytology. Advances in computed tomography (CT) technology with spiral low-dose CTs (LDCTs) allow for scanning of the entire chest in less than 15 seconds and in a single breath-hold, which is convenient and eliminates respiratory motion artefact. Early studies of screening for lung cancer with CT showed promise in detecting more cancers and more early stage cancers, and with improved survival, yet benefit in mortality reduction needed to be shown. The National Lung Screening Trial (NLST) was a trial of over 53,000 high-risk individuals (defined as current smokers aged 55–74 years with 30 pack-years or if quit had done so within 15 years) randomized between screening with LDCT versus chest X-ray. The three scans (baseline and annually for 2 years) in the LDCT arm resulted in a 20% lower mortality from lung cancer. Screening may result in detection at a time when treatment is more effective and so improves outcomes and functional abilities and enhances quality of life.[6–8]

After chest radiography had been unsuccessful for lung cancer screening in several randomised, controlled trials (RCTs) reported in the 1980s and 1990s, low-dose multidetector computed tomography (LDCT) of the chest has been investigated intensively in the last two decades. Chest CT is more sensitive than chest radiography for the detection of early lung cancers presenting as small, non-calcified, solitary pulmonary nodules (SPNs).[4,9,10]

METHODS

PROTOCOL

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

CRITERIA FOR ELIGIBILITY

For the purpose of this literature review, we compare and contrast screening and early detection of lung cancer. It is possible to accomplish this by researching of screening and early detection of lung cancer. As the primary purpose of this piece of writing, demonstrating the relevance of the difficulties that have been identified will take place throughout its entirety.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English, and it needs to determine about screening and early detection of lung cancer. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2014, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

SEARCH STRATEGY

We used " screening and early detection of lung cancer." as keywords. The search for studies to be included in the systematic review was carried out using the PubMed, SagePub, and Sciencedirect databases by inputting the words: *(("*Cancer*"[MeSH Subheading] OR "*Lung*"[All Fields] OR "*Lung cancer*" [All Fields]) AND ("*diagnostic*"[All Fields] OR "* Screening*"[All Fields]) AND ("*Risk factor*"[All Fields]) OR ("*Prevalence*" [All Fields]))* used in searching the literature.

DATA RETRIEVAL

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to

the same trend, this conclusion was drawn. All submissions need to be written in English and cannot have been seen anywhere else.

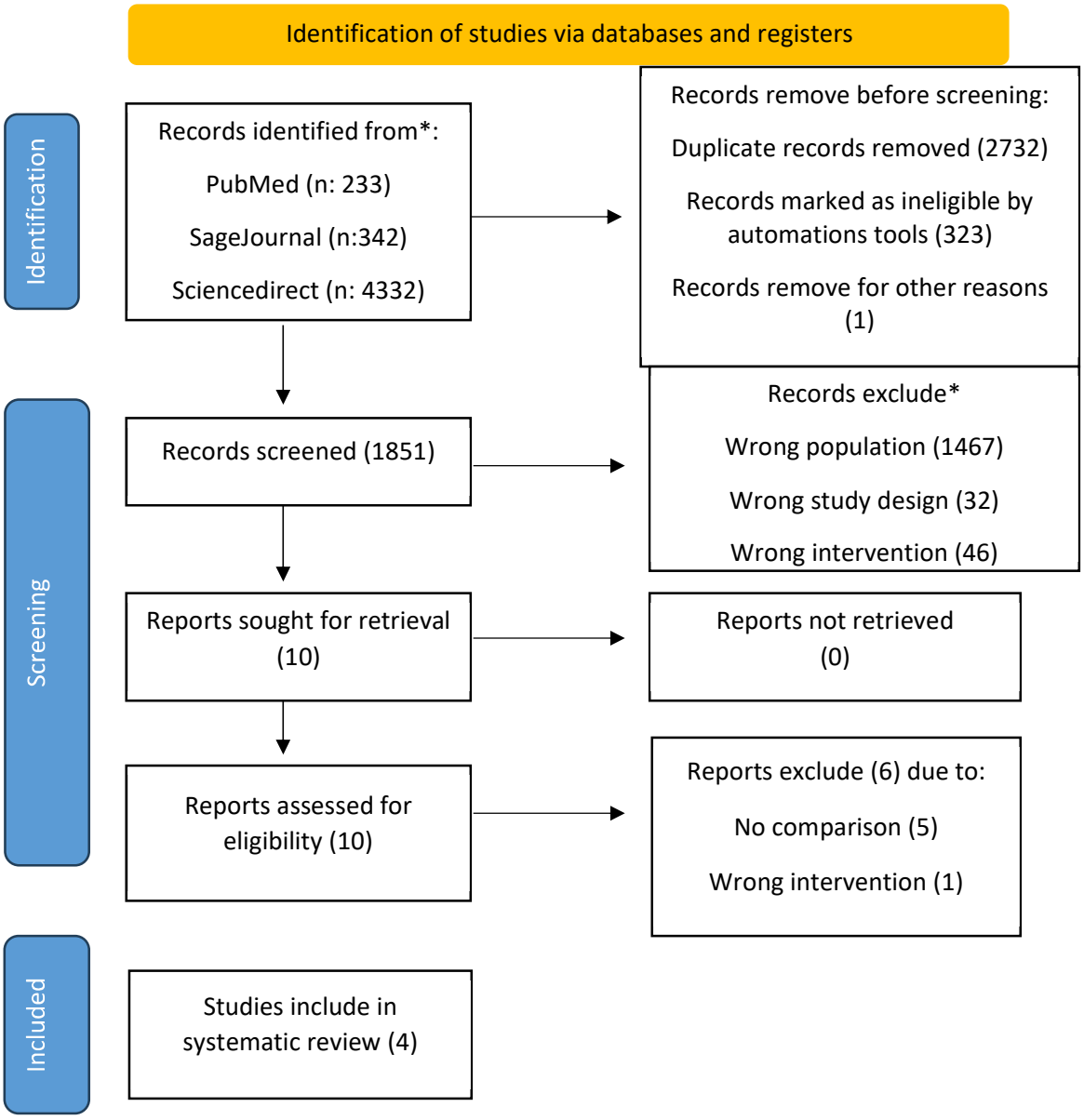

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

QUALITY ASSESSMENT AND DATA SYNTHESIS

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

Using reputable resources like Science Direct, PubMed, and SagePub, our research team first gathered 4907 publications. A thorough three-level screening strategy was used to identify only five papers as directly relevant to our ongoing systematic evaluation. Next, a thorough study of the entire text and further examination of these articles were selected. Table 1 compiles the literature that was analyzed for this analysis in order to make it easier to view.

Table 1. The litelature include in this study

Allehebi, A et al., 2024[11]	Saudi Arabia	A steering committee meeting was convened in October 2022, attended by a panel of ten key external experts in the field of oncology from the Kingdom of Saudi Arabia, United Arab Emirates, South Africa, Egypt, Lebanon, Jordan, and Turkey, who critically and extensively analyzed the current unmet needs and challenges in the screening and early diagnosis of lung cancer in the region.	100.000	As per the experts' opinion, lack of awareness about disease symptoms, misdiagnosis, limited screening initiatives, and late referral to specialists were the primary reasons for delayed diagnoses emphasizing the need for national-level lung cancer screening programs in the MEA region. Screening guidelines recommend low-dose computerized tomography (LDCT) for lung cancer screening in patients with a high risk of malignancy. However, high cost and lack of awareness among the public as well as healthcare providers prevented the judicious use of LDCT in the MEA region. Well-established screening and referral guidelines were available in only a few of the MEA countries and needed to be implemented in others to identify suspected cases early and provide timely intervention thus improving patient outcomes.
Zhao, Y et al., 2022[12]	China	The epidemic of COVID-19 outbreak in January 2020 in China, and routine CT examination was recommended to hospitalized patients in June 2020 and ended in July 2021.	200	During the period of routine CT examination, more early stages of lung cancer were detected and the tumor size was reduced to 2.14 cm from 3.21 cm at pre-period (p = 0.03). The proportion of lung adenocarcinoma and early stage adenocarcinoma was increased by 12% and 30% in the period of routine CT examination, with referral to the pre-period of CT examination ($p < 0.05$). A total of 61% of diagnosed patients had the wild type of TP53 gene during the period of routine CT examination, compared to 45% of patients at the pre-period of CT examination (p = 0.001). The median Ki-67 index was 15% among patients diagnosed at the period of routine CT examination and increased to 35% at the pre-period of CT examination ($p < 0.001$). The

				period of routine CT examination was associated with a 78% higher probability of detecting an early stage of adenocarcinoma (OR = 1.78, 95%CI 1.03, 3.08) but no significant association was observed for squamous cell carcinoma. From the pre-period to the period of routine CT examination, the proportion of female patients and non-smoking patients increased by 57% and 44%, respectively ($p < 0.001$).
Mazzone, PJ et al., 2021[13]	USA	Approved panelists reviewed previously developed key questions using the Population, Intervention, Comparator, Outcome format to address the benefit and harms of low-dose CT screening, and key areas of program implementation .	75	The systematic literature review identified 75 additional studies that informed the response to the 12 key questions that were developed. Additional clinical questions were addressed resulting in seven graded recommendations and nine ungraded consensus statements.
Sikosek, T et al., 2023[14]	Germany	We prospectively recruited 1384 individuals meeting the National Lung Screening Trial demographic eligibility criteria for lung cancer and collected stabilized whole blood to enable the pipetting-free collection of material, thus minimizing preanalytical noise.	1384	We generated diagnostic models and report a median receiver-operating characteristic area under the curve of 0.86 (95% confidence interval [CI]: 0.84–0.86) in the discovery cohort and generalized performance of 0.83 in the validation cohort. Diagnostic performance increased in a stage-dependent manner ranging from 0.73 (95% CI: 0.71–0.76) for stage I to 0.90 (95% CI: 0.89–0.90) for stage IV in the discovery cohort and from 0.76 to 0.86 in the validation cohort. We identified a tumor-shed, plasma-bound ribosomal RNA fragment of the L1 stalk as a dominant predictor of lung cancer. The fragment is decreased after surgery with curative intent. In additional experiments, results of dried blood spot collection and sequencing revealed that small RNA analysis could

				potentially be conducted through home sampling.

Allehebi, A et al., 2024 showed the incidence of lung cancer has increased significantly in the MEA in region recent years. Lack of awareness about disease symptoms, misdiagnosis, limited screening initiatives, and late referral to specialists are the major reasons for delayed diagnosis. The high incidence and poor survival rates of patients with lung cancer in the region are primarily due to delayed presentation and diagnosis, emphasizing the need for national-level lung cancer screening programs. High cost, lack of public awareness, and lack of expertise among the healthcare providers prevent the judicious use of LDCT in the MEA region. A well-established screening and referral guideline can aid the healthcare providers in early identification enabling timely intervention and reducing delays. Research on risk factors, awareness programs for physicians and patients and integration of lung cancer screening initiatives with tobacco control programs have the potential to improve clinical outcomes by facilitating higher adherence to screening and may also prove to be cost-effective over the long term. This holistic and evidence-based approach also supports rational decision-making for fund allocation, emphasizing high-impact interventions to reduce the overall burden of lung cancer. Local governments in the MEA region need to be made aware of the importance of lung cancer screening and should be convinced to initiate large-scale programs targeting high-risk individuals to improve survival outcomes.[11]

Zhao, Y et al., 2022 showed a routine CT examination was effective to detect the early stages of lung adenocarcinoma among hospitalized patients. The detected cases had less aggressive and better prognosis features. The definition of high-risk people for lung cancer screening programs might need to be reconsidered, especially for females and non-smokers. This study was significant for lung cancer screening programs, especially for the definition of high-risk people. Further studies are warranted to explore the target clinical patients for screening by routine CT scan.[12]

Mazzone, PJ et al., 2021 showed an update of the evidence related to the benefit and harms of lung cancer screening, and evidence that assists programs with selecting individuals to screen and implement high-quality LDCT screening. Based on this review, we have developed recommendations where evidence allowed and consensus-based statements in areas that we thought warranted comment despite a lack of high-quality evidence. Future updates to this guideline are planned, with literature reviews every 3 months, and editing of the guideline when new evidence suggests recommendations and suggestions should change.[13]

Sikosek, T et al., 2023 showed if successfully validated, we envision broad applicability of this technology in the management of individuals at risk for lung cancer. This is due to the 1520 Sikosek et al Journal of Thoracic Oncology Vol. 18 No. 11 relatively simple use of a peripheral blood test that could be routinely performed during the annual physician examination, does not require ordering and scheduling of additional examination (c.f., LDCT), and could potentially even be conducted at home.[14]

DISCUSSION

Lung cancer is the second most diagnosed cancer, but the most prevalent cause of cancer-related deaths worldwide. This rather high death rate is due mainly to the fact that most patients are diagnosed with advanced-stage cancer, for which the conventional treatment does not work. In order to overcome this problem, the US changed in 2013 the guidelines for lung cancer screening and recommended low-dose CT (LDCT) scan for adults between 55 and 80 years that smoke 30 packs yearly or have quit smoking less than 15 years. Different trials tried to identify different screening methods for lung cancer diagnosis, and it was observed that chest radiography or sputum sample are less efficient than LDCT. The choosing of screening methods has aroused different debates regarding the pros and cons of CT scan and how it can be implemented with a larger population range. In this way, Hofmann et al. presented in their analysis on LDCT that its implementation is costly but it presents a better alternative that standard CT scans, obtaining a risk reduction of lung cancer between 0.76-4.7 percent. Previous data suggested that in order to improve the early diagnosis of lung cancer, better selection of target population, based on age and smoking habit are not enough.[15–17]

In addition to the reduction in exposure to tobacco smoke, screening for the early detection of lung cancer has been considered to be a major strategy for decreasing the rate of lung cancer mortality. At present, low-dose CT (LDCT) screening in the high-risk population is the predominant tool used for detecting lung cancer in the early stages. The results of the US National Lung Screening Trial found that compared with chest X-ray examination, LDCT screening was associated with a 20% reduction in lung cancer-specific mortality in a high-risk group of participants defined by their smoking status. In addition, other previous studies have also confirmed the validity of LDCT screening for the early detection of lung cancer to reduce mortality rate. However, potentially healthy individuals are also at risk of being subjected to expensive and potentially harmful diagnostic procedures, such as positron emission tomography, transthoracic/bronchoscopic biopsy or even surgery, due to the considerably high false-positive rate of LDCT (nearly 96.4%). Therefore, the combination of LDCT with additional biomarker-based tests has been proposed to be a more favorable strategy for improving the effectiveness of lung cancer screening programs whilst reducing the cost and harmfulness to otherwise healthy individuals.[18,19]

There were several studies done in the 1960s and 70s using chest X-rays as screening tools. These studies, though limited by the lack of a control group, showed no mortality benefit for chest x-ray screening. The 2010 prostate lung colorectal

and ovarian cancer screening trial (PLCO) definitively proved the lack of screening benefit with x-rays for lung cancer. In 2011 the national lung screening trial was published and was the most significant trial conducted globally to determine the benefit of screening for lung cancer. The trial found that with low dose CT scans; detection of more stage-1 cancers took place. The results from this study showed a mortality benefit in a subset of the general population. It showed a decrease in lung cancer deaths in heavy smokers or people with a history of heavy smoking. The low dose CT scan (LDCT), when used for screening, led to approximately 3 fewer deaths per 1000. Overall, the use of LDCT when compared to chest x-ray reduced lung cancer-related deaths by 20%.[20–22]

PET/CT is an integrated fusion of PET and CT equipment and imaging, which can display accurate anatomical images and tissue metabolic function images. It has been widely used to identify the property and stage of tumors. Wang et al. integrated 1330 patients with lung-occupying lesions in four clinical studies and found that PET/CT has higher sensitivity (98.7%) and higher specificity (58.2%) in distinguishing benign or malignant lung lesions. Yet, PET/CT also has a high FPR in lung cancer screening, and reducing FPR is still a dilemma in the early diagnosis of lung cancer through PET/CT. In contrast with CT, PET/CT can enhance the accuracy of diagnosis of solitary pulmonary nodule (SPN). The standard uptake value (SUV) of PET/CT reflects the metabolism and malignancy of diseased tissues under certain circumstances. However, PET/CT also has its shortcomings. For instance, there are respiratory motion artifacts. FDG metabolism is not unique to tumors and the higher cost limits the application.[23,24]

Nowadays, pathological diagnosis has been regarded as gold standard for diagnosing cancer. There are several methods for obtaining histological specimens, including bronchoscopy, ultrasound or CT-guided percutaneous lung biopsy. Among them, bronchoscopy has been developed rapidly and widely recognized in recent years. It not only expands the field of vision for diagnosis, but also improves the efficiency of diagnosis.[23,25]

CONCLUSION

In conclusion, early screening and diagnostic methods of lung cancer, x-ray screening is not recommended. LDCT has obvious advantages and is the most promising imaging method in early screening of lung cancer. Bronchoscopy has a greater advantage in direct vision of intraluminal lesions and can be used as a diagnostic tool. Liquid biopsy, VOCs and special tumor autoantibodies detection are simple and non-invasive.

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