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Clinical Medicine COMMENTARY

Is LDCT sufficient for screening central-type lung cancer?

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INTRODUCTION

Lung cancer ranks as the leading cause of cancer-related incidence and mortality worldwide. Effective screening is crucial for improving patient outcomes. The widespread application of low-dose computed tomography (LDCT) has been confirmed by large randomized controlled trials to significantly increase the early detection rate of lung cancer (particularly peripheral-type adenocarcinoma) and reduce lung cancer-specific mortality. However, LDCT screening strategies have significant anatomical limitations: its efficacy for screening central-type lung cancers arising in segmental or more proximal bronchi is markedly insufficient, while its advantage is primarily manifested in the detection of nodules located in the lung periphery.

BLIND SPOT FOR CENTRAL-TYPE LUNG CANCER SCREENING

Central-type lung cancer has a strong epidemiological association with smoking. Its main pathological types are squamous cell carcinoma (accounting for approximately 25%-30% of all lung cancers) and small cell lung cancer (accounting for approximately 15%-20%). LDCT has very poor sensitivity for detecting early-stage central-type lung cancer, especially lesions still in the precancerous stage or carcinoma in situ. This is primarily due to the complex anatomy of the hilar region, where overlapping images of major blood vessels, bronchi, and surrounding soft tissues make it difficult to distinguish early mucosal lesions or micro-invasive foci from normal structures. Data from landmark studies, such as the National Lung Screening Trial (NLST), the Dutch–Belgian lung cancer screening trial (NELSON) and other studies, consistently demonstrate this phenomenon. These trials specifically enrolled populations at high risk for lung cancer, namely heavy smokers. Despite this, the distribution of cancer types found by LDCT screening was skewed. The proportions of squamous cell carcinoma and small cell lung cancer detected were only in the ranges of approximately 14% to 24% and 6% to 15%, respectively. These detected proportions are far lower than the known epidemiological incidence of these cancers. Furthermore, most of these detected cases were already in the local advanced or advanced stages.[1] This indicates that reliance on LDCT-based screening may lead to a significant proportion of central-type lung cancers being missed until clinical symptoms appear, by which time the optimal window for treatment has often passed. This is a critical factor that requires careful consideration in the formulation of public health policies and clinical decision-making.

Currently, no guideline-recommended screening method exists for early central-type lung cancer in the general population. In clinical practice, most early central-type lung cancers are discovered incidentally during bronchoscopy performed for other reasons, while the corresponding CT images may still show no definite abnormalities. This highlights the decisive advantage of bronchoscopy in directly visualizing the airway mucosa and detecting early superficial lesions. Multiple studies show that autofluorescence bronchoscopy is more sensitive than white light bronchoscopy to identify these lesions.[2] However, using bronchoscopy as a screening tool faces numerous practical obstacles: it is an invasive procedure carrying certain risks; the equipment is expensive, its operation requires specialized training, and disinfection is complex and time-consuming; most importantly, patient acceptance and compliance are low, making it unsuitable for large-scale screening of asymptomatic high-risk populations.

EMERGING NON-INVASIVE SCREENING ALTERNATIVES

To address this screening gap, various non-invasive techniques are under investigation:

1. Exhaled Breath Biomarker Detection: This technology identifies cancer-associated abnormal patterns by detecting the spectrum of volatile organic compounds (VOCs) in exhaled breath, which reflects the body's metabolic fingerprint. It is a completely non-invasive, rapid, and potentially cost-effective method. In recent years, advancements in artificial intelligence, particularly machine learning technologies such as deep learning, have significantly improved the diagnostic accuracy and stability of these devices. Using electronic nose technology to assist in the diagnosis of lung cancer among specific populations (such as patients with chronic obstructive pulmonary disease) with suspected lung cancer shows an accuracy of up to 95% and can effectively avoid approximately 75% of unnecessary invasive procedures.[3] However, challenges for this technology include standardizing detection protocols, improving sensor stability and sensitivity, and accumulating data from large-scale, multicenter, prospective studies to confirm its general applicability.

2. Blood Biomarkers: Although traditional tumor markers have poor sensitivity, novel liquid biopsy technologies such as circulating tumor DNA and microRNA profiles are rapidly developing. Their potential for screening central-type lung cancer, particularly small cell lung cancer,[4] is a current focus of cutting-edge research. While their sensitivity is still insufficient for standalone screening at present, they may potentially serve as part of a multimodal screening strategy in the future.

3. Sputum Cytology Examination: This is the most classic non-invasive method. However, the sensitivity of conventional smears for diagnosing lung cancer does not exceed 10%, with a specificity of around 40%. Although improved liquid-based cytology techniques can increase sensitivity to around 20%, it still falls far short of screening requirements. Current research directions include using automated flow cytometry, and developing artificial intelligence models based on deep learning to automatically analyze sputum cytopathological images, aiming to improve identification accuracy.[5] Although promising, these new technologies are still in the research and validation phase, and their standardization and large-scale application require further time.

CONCLUSION

In conclusion, LDCT has blind spots for screening central-type lung cancer and is far from sufficient. The field of lung cancer screening is evolving from a single LDCT model towards precise and personalized strategies tailored to different risk factors and lung cancer subtypes. The ideal future model likely involves a "stepwise" or "complementary" strategy: initial LDCT screening for lung cancer in high-risk populations, with positive results evaluated by a multidisciplinary team to determine whether further clinical diagnosis and treatment pathways are required. Meanwhile, non-invasive techniques such as VOCs detection, blood biomarkers or sputum analysis are employed for the initial screening of central-type lung cancer in individuals with negative LDCT results who are heavy smokers. Individuals testing positive on these non-invasive tests would then undergo more precise examinations for confirmation, such as autofluorescence bronchoscopy (Figure 1). Achieving this vision requires vigorous advancement in the clinical validation and standardization of the aforementioned emerging technologies, along with well-designed, large-scale prospective screening studies, to ultimately establish a comprehensive screening system capable of effectively detecting both early-stage peripheral-type and central-type lung cancers.

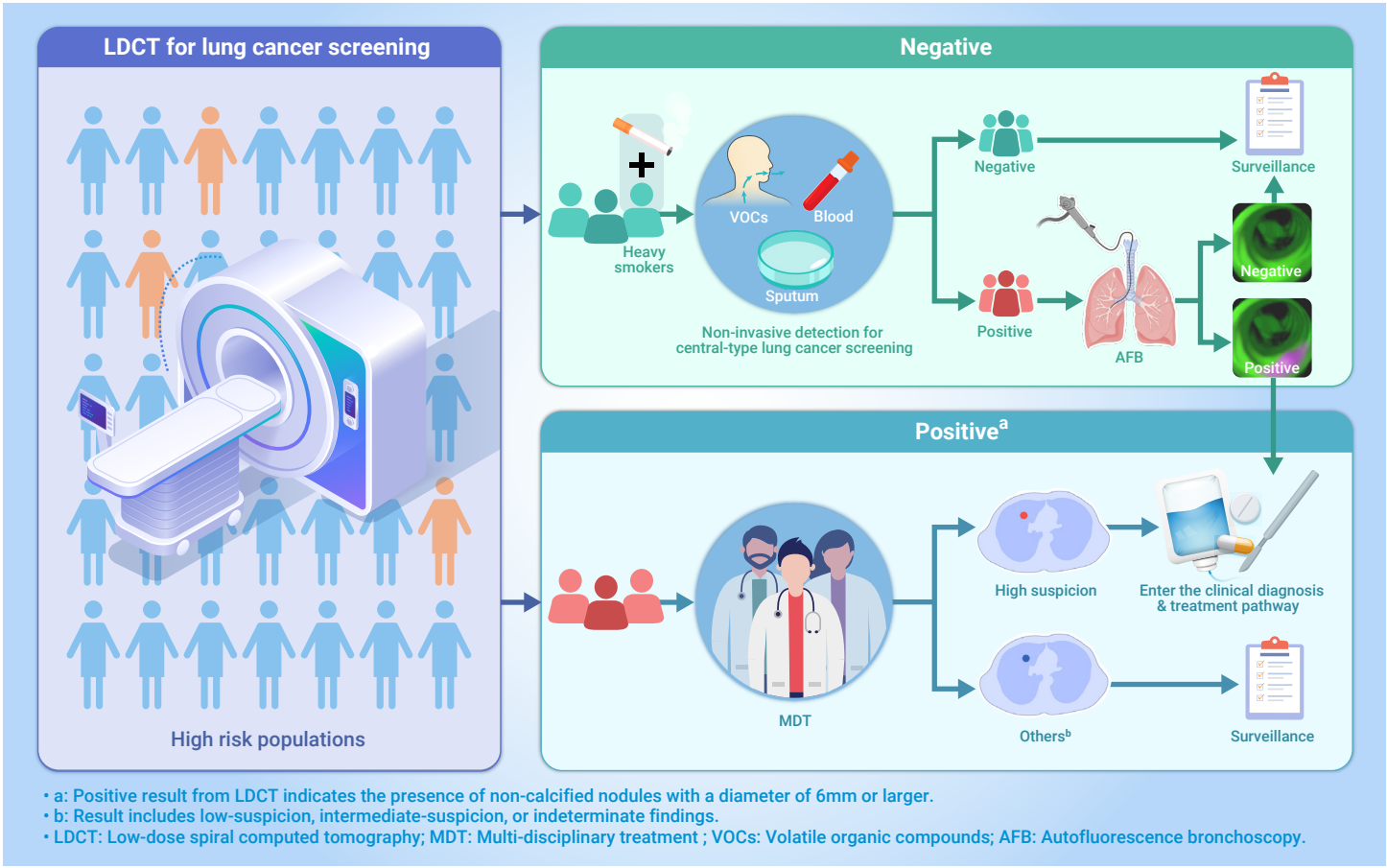

Figure 1. Ideal future screening strategy.

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AUTHOR CONTRIBUTIONS

FFQ drafted the manuscript and conducted the data analysis. BZ contributed to conceptualization and writing. Huakang Tu contributed to conceptualization, review, and editing. YWZ contributed to conceptualization, data analysis, visualization, review, and editing. HZ and BHH reviewed the manuscript. All authors contributed to and approved the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.