Transforming Lung Cancer Care: Advancements in Screening, Treatment, and Survivorship

Author: Aleksandra Zurowska, EMJ, London, UK

Citation: Respir AMJ. 2024;2[1]:22-25. https://doi.org/10.33590/respiramj/JXDR3449.

INTRODUCTION

Matthew Triplette, Fred Hutchinson Cancer Center and University of Washington, Seattle, USA, delivered an insightful talk at the American Thoracic Society (ATS) International Conference 2024 on how landmark studies in lung cancer screening can affect recommendations and standards of care for pulmonary medicine specialists. Triplette highlighted that lung cancer remains the leading cause of cancer-related deaths, with 85% of all lung cancer cases related to tobacco smoke worldwide.

EPIDEMIOLOGY

Introducing the epidemiology of lung cancer, Triplette explained that, according to recent studies, lung cancer mortality rates are declining faster than incidence rates in the USA. A comprehensive analysis of registry data from the National Cancer Institute (NCI), Centers for Disease Control and Prevention (CDC), and the North American Association of Central Cancer (NAACCR; covering 90% of the USA population) between 2015–2019 demonstrated a significant decrease in lung cancer mortality rates compared to incidence rates for both men (5.0% versus 2.6% annually) and women (4.3% versus 1.1% annually), with a 1.4% annual improvement in 2-year relative survival.[1] Men showed greater annual incidence declines, but women experienced nearly twice the rate of annual mortality decline. These outcomes are attributed to advancements in treatments and better access to care, partly due to the Patient Protection and Affordable Care Act. However, disparities persist, with 5-year survival rates ranging from 26% among Asian American/Pacific Islanders to 19% among American Indian/Alaskan Natives. States with higher smoking rates, such as Mississippi and Kentucky, also have higher mortality rates. The study highlights the need for targeted tobacco control, smoking cessation programs, and increased lung cancer screening to improve outcomes and address these disparities.[1]

SCREENING GUIDELINES

Current low-dose CT (LDCT) screening guidelines vary among organizations like the United States Preventive Services Task Force (USPSTF), Centers for Medicare & Medicaid Services (CMS), National Comprehensive Cancer Network (NCCN), the American Cancer Society, and the UK National Screening Committee. While USPSTF and CMS require a smoking cessation period of 15 years, NCCN and the American Cancer Society have removed this criterion to broaden eligibility. The UK guidelines use a risk-based approach, including any current or former smokers. Triplette explained that dropping the restrictive smoking criteria might make it easier to identify patients for screening and thus increase screening rates.

A study by Choi et al.[2] examined the effectiveness of risk-based screening using data from the Multiethnic Cohort Study. The

study demonstrated that the 2021 United States Preventive Services Task Force (USPSTF) guidelines created significant disparities, especially for individuals who are African American, whose eligibility was 53% lower than that of individuals who are White. Conversely, the risk-based $PLCO_{m2012}$ model was more sensitive and equitable. These findings underscore the potential benefits of adopting risk-based criteria to improve lung cancer screening efficiency and reduce racial and ethnic disparities. This aligns with the goals of the new screening studies to enhance early detection and ensure more inclusive and effective screening practices.

REAL-WORLD SCREENING

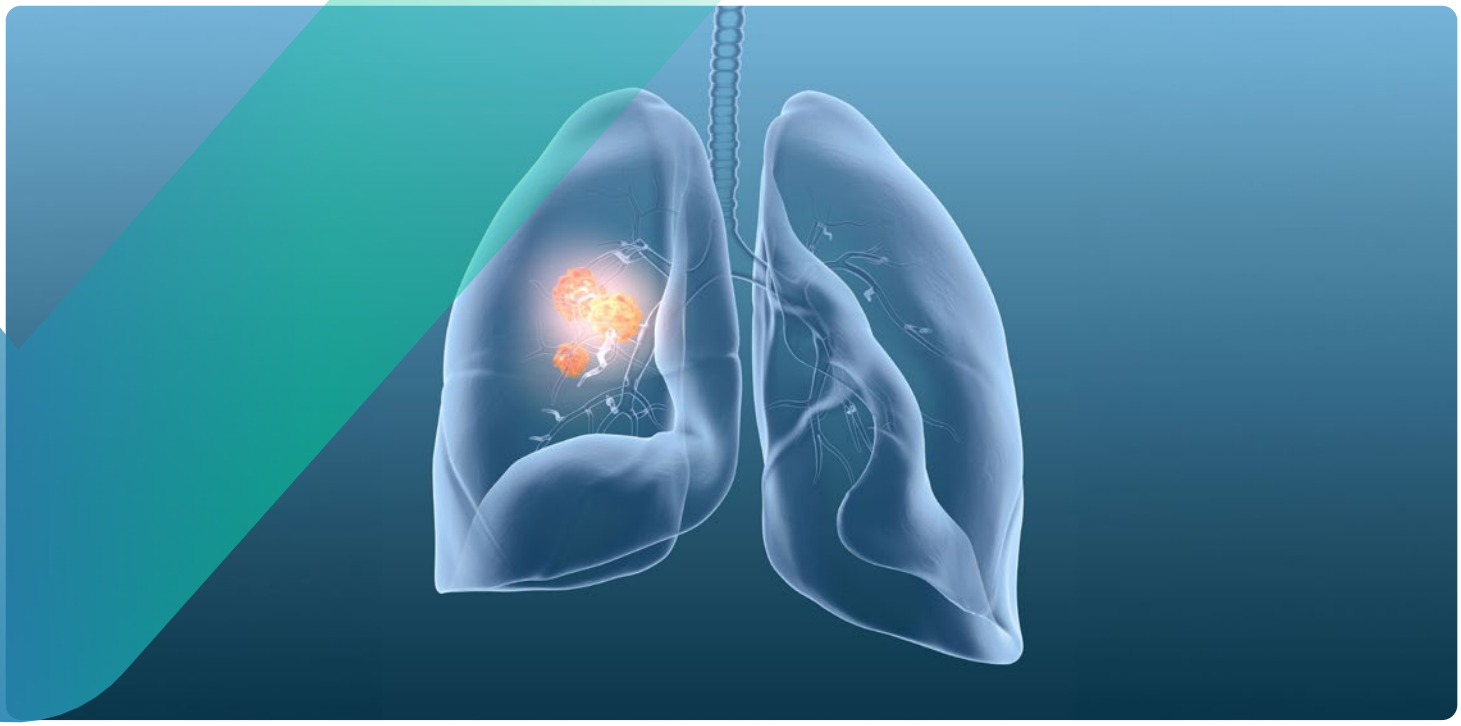
Triplette went on to question the applicability of clinical trial results in real-world settings. A study by Slivestri et al.[3] addressed this by analyzing individuals undergoing baseline LDCT for lung cancer screening (LCS) from 2015–2019. The study compared outcomes from the American College of Radiology's LCS Registry with those from the National LCS Trial (NLCST). The study demonstrated that 14.3% of over one million screened individuals had positive results, similar to NLCST data. However, the cancer detection rate (0.56%) was half that of NLCST (1.1%). Additionally, only 22.3% of participants with negative baseline scans followed up within 11–15 months, highlighting a gap in adherence that impacts real-world effectiveness.

Another study by Rendle et al.[4] investigated downstream procedures and complications in real-world LCS across five American healthcare systems between 2014–2018. Among nearly 10,000 patients, 15.9% had abnormal LDCT results, with a 9.5% lung cancer diagnosis rate within 12 months. The positive predictive value was 9.5%, and the negative predictive value was 99.8%, with high sensitivity (92.7%) and specificity (84.4%). Despite the effectiveness of LDCT in detecting lung cancer, there were significant rates of follow-up imaging (31.9%) and invasive procedures (2.8%), with higher complication rates than NLCST, suggesting a need for improved diagnostic management to balance the benefits and harms of screening.

> **Despite the effectiveness of LDCT in detecting lung cancer, there were significant rates of follow-up imaging**

SCREENING: ON THE HORIZON

According to Triplette: "New screening methods, technologies, and adjuvant approaches are on the horizon." Two new studies highlight significant advancements in LCS and multi-cancer early detection, which promise to revolutionize how we approach early cancer detection, potentially leading to better outcomes and more personalized screening strategies.



A recent study introduced a deep learning model named 'Sybil', which accurately predicted lung cancer from a single LDCT.[5] Validated on three independent datasets (National Lung Screening Trial, Massachusetts General Hospital, and Chang Gung Memorial Hospital), Sybil demonstrated high accuracy with area under the receiver-operator curves of 0.92, 0.86, and 0.94, respectively.

This model's capability to run in real-time on radiology stations showcases its potential to enhance personalized screening efforts.[5] Triplette also discussed a significant National Health Service (NHS)-Galleri trial led by Neal et al.,[6] which evaluates a multi-cancer early detection blood test. This randomized controlled study, involving over 140,000 participants aged 50–77 in the UK, aims to assess the test's effectiveness in reducing late-stage cancer incidence, helping the NHS decide on its potential implementation in routine screening programs. The results are anticipated in 2026. Additionally, the NCI Cancer Screening Network, with Triplette as the Health Equity and Access Chair, is investigating non-steroidal anti-inflammatory drugs and other screening technologies through a flexible research framework, including a Vanguard pilot RCT study involving 24,000 individuals randomized to different multi-cancer early detection tests.

TREATMENT

Triplette explained that there is ongoing evidence to refine treatment for early-stage non-small cell lung cancer (NSCLC), especially with the emergence of more precision approaches to multimodal therapy in NSCLC. Additionally, the role pulmonologists play is the key to expanding the role of neoadjuvant therapy and multi-disciplinary management. Triplette mentioned two new studies in particular, that he expects to have significant implications for lung cancer treatment and screening. The first study compared sublobar resection to lobectomy in patients with small (≤2 cm), node-negative peripheral NSCLC.[7] The study showed that sublobar resection was non-inferior to lobectomy in terms of disease-free and overall survival, suggesting that less invasive surgery might be a viable option for early-stage NSCLC, potentially preserving more lung function. The second study, the ADAURA trial, demonstrated that adjuvant osimertinib significantly improved

5-year overall survival rates in patients with resected, EGFR-mutated stage IB to IIIA NSCLC compared to placebo (88% versus 78%).[8] These findings highlight the potential of personalized treatments based on genetic markers and less invasive surgical options to improve patient outcomes and reduce the burden of late-stage lung cancer, reinforcing the importance of early detection and tailored treatment strategies in lung cancer management.

SURVIVORSHIP

Triplette noted that there aren't many studies on survivorship, and with that physicians and researchers need to consider interventions to support lung cancer survivors through treatment and beyond. Triplette mentioned one study as an example, in which physicians investigated the sleep quality of patients with lung cancer, who often experience sleep disturbances. A randomized trial in Hong Kong compared aerobic exercise and tai chi in 226 patients with advanced lung cancer.[9] Over 16 weeks, both aerobic exercise and tai chi groups showed significant improvements in sleep quality, psychological distress, physical function, and circadian rhythm compared to a control group. Tai chi provided greater benefits in sleep and survival rates.[9] These results suggest that incorporating physical activities, especially tai chi, can enhance lung cancer care and survivorship. This study is just one of the examples of continued efforts of physicians to improve the survivorship of patients with lung cancer.

CONCLUSION

In his concluding remarks, Triplette highlighted the ongoing advances and challenges in LCS and treatment. He noted that the decline in mortality rates can be attributed to improved treatments and access to care. However, there is still a need to address the significant disparities among different racial and ethnic groups. Triplette advocated for broader LDCT screening guidelines and emphasized the potential of risk-based models.

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