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Mini review

Tobacco-Induced Disease: Advances in Policy, Early Detection and Management

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Abstract

In the United States, over 438,000 annual deaths are related to tobacco-exposure, and lung cancer is the most common cause of tobacco-related death, approaching 30% of this total mortality burden. In China, the smokers consume a majority of the world cigarettes, and consequently, the lung cancer rate has risen 6-fold during the last four decades. This mini review attempted to briefly summarize the recent advances in the policy, early detection and management of tobacco-induced disease, focusing on the application of CT as an effective tool for reducing lung cancer mortality.

Mini review

The majority of cigarettes consumed across the world are smoked in China. As a result the largest number of new lung cancers in the world, now occur in China. Lung cancer rates have risen six-fold across China over the last four decades so about one in three global cancer deaths occurs in China. Clearly more effective approaches to tobacco control are a national emergency in China but for those that heavy exposure to tobacco, even if they stop smoking their risk of lung cancer remains elevated for the rest of their lives.

Lung cancer screening has been demonstrated to effect a 20% reduction in lung cancer mortality as reported from the randomized National Lung Screening Trial (NLST). The United

小综述

烟草引起的疾病：政策，早期发现，和防治方面的进展

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摘　要

在美国，每年有 438,000 人死于烟草所引起的肺疾病。其中，肺癌是最常见的原因，约占总死亡率的百分之三十左右。在中国，吸烟者消耗世界香烟总量的大部分。故此，中国的肺癌发生率在近四十年内增加了六倍。 本综述旨在扼要总结近年来在烟草所诱发的疾病的政策，早期检测和防治方面的进展，侧重于介绍 CT 介导的筛查在降低肺癌死亡率中的作用。

小综述

世界上生产的大多数香烟消耗在中国。由此，世界上绝大多数新肺癌病例也见于中国。在过去四十年里，中国的肺癌发病率增加了六倍。目前，世界上每三例肺癌死亡，就有一例出现在中国。显然，以更有效的方法来控制抽烟是中国的当务之急，但对于这些重度吸烟者， 即使他们停止吸烟，在他们的余生中，肺癌的风险仍持续居高。

一近期发表的随机抽样的全国肺癌筛查实验（NLST）显示：肺癌筛查可导致肺癌死亡率下降约 20%。美国预防服务工作组提出了一

States Preventive Services Task Forces gave a "B" recommendation for low dose CT screening of for lung cancer in high risk populations (1). This favorable endorsement in turn led reimbursement the cost of providing this service by federal and commercial insurers for high risk smokers between the ages of 55-77 who have been smoking within the last 15 years. With these provisions, national lung cancer screening is now being implemented in the United States.

When the NLST was conducted in 2002, the study parameters were fixed to allow for the proper conduct of the trial. In 2002, a 4-detector CT scanner was the state-of-the-art for CT screening management and the diagnostic work up for suspected lung cancer cases was based on the existing community standard (2). In the time since the NLST was conducted there have been a number of developments that have improved the process of lung cancer screening services (3). These innovations range from the introduction of more capable CT scanners, lower medical radiation scanning protocols, more effective and efficient diagnostic work up approaches, as well as improved and more tailored surgical approaches. The aggregate effect of all of these advances is that the cost efficiency of this process has been greatly improved (4). Further improvements with clinical management may occur as the use of quantitative CT imaging allows for more consistent measurement of suspicious pulmonary nodules, as size criteria is emerging as a key determinant guiding invasive screening work-up (5). So for China, the current level of evidence to support screening implementation is greatly improved since 2002. However implementing national CT screening to ensure delivery of high quality, best-practice early lung cancer detection in the potential target population of tobacco-exposed individuals constitutes a profound challenge.

Still the public health impact of tobacco-exposure is singularly lethal. By comparison in the United States, over 438,000 annual deaths are related to tobacco-exposure with lung cancer being the most common cause of tobacco-related death approaching 30% of this total mortality burden.

In the United States patient advocacy groups have worked with academic medical centers as well as community hospitals to address this implementation challenge by creating a consortium of institutions that are conducting screening programs to systematically adopt best standard of screening practice for all components of clinical management (6). They have called this consortium the Lung Cancer Screening Framework Process. This

个"B" 方案, 建议以低剂量 CT 对在高危人群中的肺癌进行筛查 (1)。这一有益的提议使得为 55 到 75 岁，近 15 年来一直吸烟者提供筛查的医学中心或医疗服务单位， 能从联帮政府或商业保险公司中得到财经补助。由于这些政策的推行，对肺癌的全国性筛查正在铺开。

在 2002 年的随机筛查中，为方便实验的展开，临床参数是固定的。所用的 CT 扫描仪是当时分辨率最高的；对可疑病例的检查和诊断是参照当时已有的标准〈2）。随着时间推移而带来的技术进步和条件改善，逐步提高了筛查的效果 （3）。这些技术进步和条件改善主要包括：分辨率更高的扫描议的问世，低放射量扫描技术的诞生，更有效和准确诊断方法的形成，以及更有效、更定位外科手术的应用。所有这些进步的综合效应，不仅降低了筛查成本，而且显著地提高了筛查的效果 （4）。由于定量 CT 扫描图像技术的发展和应用，一些可疑病灶可得到更规范可靠的定量分析，从而确定病壮的大小，并进而指导应对策略。这些方法可望更进一步提高筛查效果 （5）。目前，中国对肺癌筛查的力度和水平自 2002 年来已有显著提高。然而，实行全国性 CT 扫描普查，以确保高质量高效益的筛查服务能落实到每个吸烟者，面临重大挑战。

由吸烟而引起的公共健康危害，至今依然十分严重和致命。在美国，每年有越过 438,000 人死于烟草所引起的肺疾病。其中，肺癌是最常见的原因，约占总死亡率的百分之三十左右。

在美国，一些维护病人权益的组织已经和学术性医学中心或者社区医院，在应对肺癌筛查所遇挑战的问题上达成协议。具体作法是：成立一个医患共同体，以确保筛查项目能全面、系统性采用其他临床服务项目的金标准（6）。 他们将此共同体称为肺癌筛查框架程

process includes the expectation that participating institutions will prospectively acquire clinical follow-up information so that the outcomes of lung cancer screening efforts can be accessed and reported (6). This effort builds on previous models of cooperative research such as with using institutional feedback to accelerate learning curve in allowing new screening institutions to rapidly implement effective screening process. The best example to date of this approach with screening is the use of the recent International-Early Lung Cancer Action Project (I-ELCAP) screening outcomes to evaluate the most favorable pulmonary nodule size to use as a threshold for a more invasive diagnostic work-up (7). Increasing the nodule size as the threshold for further diagnostic work-up markedly improves the efficiency of the screening management while reducing the rate of false positive work-ups, cost and morbidity (7).

An indispensible element in the national implementation of screening is the simultaneous provision of best practice smoking cessation services for those individuals that continue to smoke. Pyenson and co-workers have reported that routine integration of smoking cessation with the annual CT screening process can improve the cost utility ratio of quality adjusted life years by close to 40% (4). Indisputably implementing national annual CT screening in high risk populations is a significant societal cost. However there are attractive opportunities to leverage this new pattern of care to further benefit health outcomes in this at-risk cohort. For example, the annual CT visit provides a scaffolding to support more intensive research to define better smoking cessation measures. In Poland and Spain cost economic studies are underway to determine the cost of providing national screening support in those countries.

In asymptomatic tobacco-exposed individuals, a growing body of research suggests that the CT scan done to evaluate for early lung cancer also commonly finds individuals with evidence of asymptomatic COPD/emphysema or coronary artery disease (8, 9). These diseases along with lung cancer account for close to 70% of the excess mortality in heavily tobacco-exposed populations. Lung cancer screening will permit additional research opportunities in this tobacco-exposed cohort including catalyzing the development for more effective drugs to manage the early stage of lung cancer. With screening, the frequency of finding early stage lung cancer is greatly increased and focusing on these early stage patients could allow for much more rapid evaluation of new targeted therapeutic agents compared to the current setting. For the same reason, lung cancer

序。这一程序包括：所有参与单位均前瞻性地收集随访和追踪资料，以致肺癌筛查和相关努力的结果能被如实记载， 并随时供相关人员查用和报告（6）。这一系统是建立在以前已有的合作模式（如利用体制的反馈，选择方便学习的曲线），允许新筛查机构迅速选择、实施有效的筛选程序。这一筛查方法至今最成功的实例是：利用国际早期肺癌干预计划（IEFCAP）筛查结果，找出一最佳体积的肺结节，作为更进一步检测的阈值。结节的体积增加而导致的更进一步检查，能显著地改善筛查效果。相反，结节体积减少则增加筛查费用和发病率 （7）。

在实施全国性肺癌筛查中，一个必不可少的条件是为吸烟者提供戒烟服务。Pyenson 等报道：戒烟加每年常规 CT 筛查，可提高成本效用比率和生活质量高达近 40%（4）。在全国实施对高危人群的肺癌普查，毋庸置疑是一个沉重的社会经济负担。然而，这一措施可吸引新的机遇。这些机遇可能会有助于进一步改善这一高危人群的健康状况。例如，每年的常规 CT 检查结果可提供一个技术平台，此平台有助于找到更好的个性戒烟措施。波兰和西班牙正在进行经济效益方面的调研，以确定实行全国筛查所需的费用。

越来越多的研究提示：在给无肺病症状的吸烟者作 CT 扫描检测早期肺癌时，也可很常见的发现慢性阻塞性肺病 / 肺气肿或者冠状动脉疾病(8，9）。在严重吸烟的人群中，这些慢性疾病和肺癌是铸成此组病人的死亡率较其他人群高 70%的主因。肺癌筛查同时可为吸烟者提供其他人一些额外的科研机遇，如催化研发更为有效的防治早期肺癌的药物。与既往作法相比，CT 扫描检测可显著提高发现早期肺癌的比例，从而可让这些早期肺癌患者更迅速地体验新开发的药物的疗效。同时，肺癌筛查可发

screening will also find many more early asymptomatic COPD patients and quantitative CT provides an economical biomarker to allow much more efficient COPD drug development research than is currently possible. Particular classes of drug targets such as immunomodulators could conceivably show benefit in arresting the progression of both early lung cancer and COPD.

This time of initial US national screening dissemination is allowing a full national discussion not only about how to provide high quality lung cancer screening services, but also about how to thoughtfully leverage this newly reimbursed screening service to extend the utility of the thoracic imaging encounter and greatly accelerate progress with improving health outcomes in heavily tobacco-exposed populations. At the very least, evidence for one or more of these additional diseases on annual screening may heighten a smoker's motivation to stop that habit. Other lifestyle interventions such as diet modification and exercise are being successfully employed to manage the consequence of asymptomatic coronary calcification. Lifestyle counseling could also emerge as integral part of the annual CT evaluation as these interventions can have markedly positive impact for a range of tobacco-dependent conditions.

The emergence of lung cancer screening as a public health tool has evoked a lively global debate regarding its potential merits. While this healthy debate should continue, there are potentially unprecedented opportunities arising with this new approach to the lethality of chronic tobacco exposure that merit serious consideration.

现更多的早期、无症状的 COPD 病人。再者，定量性 CT 可提供更为经济实惠的生物标记，有助于研发更为有效的 COPD 拮抗剂。可以预测：一些新型药物，如免疫调节剂，无疑会阻断早期肺癌和 COPD 的进展。

启动全国性肺癌筛查项目将会给全体国民一个充分发言的机会；不仅可讨论如何提供高质量的肺癌筛查服务，而且可讨论如何将这一有益的筛查服务扩展到胸部影像的充分应用，以加速在严重吸烟人群中科研的进程。至少，在每年的常规筛查中查出一或多个和吸烟相关的疾病可能会说服病人戒断吸烟的习惯。此外，生活习惯的改良，如适当饮食和运动，已经破证明可显葬改观无症状型冠状动脉硬化的后果。生活习惯的疏导也是每年常规 CT 评估的一个重要环节。既往实验已充分证实：正常的生活习惯对一系列烟草依耐性的肺疾患有积极影响，

肺癌筛查作为一种公共卫生工具的出现及其潜在价值已在全球引起了活跃的争论。这种健康的争论应该继续。然而，我们应该充分认识：肺癌早期筛查项目为拮抗烟草所致疾病的致命作用提供了前所未有的机遇。

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