Editorial

Lung cancer screening and shared decision making in cancer survivors: the long and winding road

M. Patricia Rivera[1], Louise M. Henderson[2]

[1]Department of Medicine, [2]Department of Radiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Correspondence to: M. Patricia Rivera, MD. Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. Email: mprivera@med.unc.edu.

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The National Lung Screening Trial (NLST) showed a 20% relative reduction in lung cancer mortality among current and former (quit within the last 15 years) smokers aged 55–74 years with at least a 30 pack-year smoking history who underwent lung cancer screening (LCS) with low dose computed tomography (LDCT) versus chest radiography (1). The NLST enrolled participants who were younger and healthier than the general population of patients at high-risk for lung cancer and excluded participants unable to undergo thoracic surgery due to co-morbidities and those with prior history of cancer (2). Although several organizations recommended extending LCS to high-risk individuals outside of the NLST inclusion criterion, including long-term lung cancer survivors after 4 years of surveillance without recurrence (3,4), the US Preventive Services Task Force (USPSTF) recommends LCS in patients with the same eligibility criteria as the NLST cohort (with the exception of an upper age limit of 80 instead of 74) and after a careful discussion on the benefits and the harms of LCS through a shared decision making (SDM) process (5). Following the USPSTF recommendations, the Center for Medicare and Medicaid Services (CMS) approved LCS coverage only in patients who meet the NLST age and smoking criteria (extending upper age limit to 77) and added the requirements that eligible patients must be offered tobacco treatment and undergo a SDM discussion with their physician prior to the LDCT (6).

In real world settings, implementation of LCS in those eligible by USPSTF and CMS criteria has been challenging, resulting in very low LCS uptake rates (ranging from 3.6% to 7%) (7,8). Multiple barriers leading to low uptake of LCS include but are not limited to: lack of knowledge about screening among smokers and providers, lack of access to care, limited time to perform SDM and reimbursement (7,9). Expanding LCS to individuals at increased risk of lung cancer due to additional risk factors such as emphysema, prior history of cancer, and family history of cancer who do not meet NLST age and smoking history criteria is even more challenging because of a lack of evidence to support LCS in these patients. The much-awaited results of the NELSON trial, recently published in abstract form, support the benefit of lung cancer mortality reduction with LDCT (10), in a study population younger at entry (age 50 versus 55 years), with less tobacco exposure (10 cigarettes/day for 30 or more years or 15 cigarettes/day for 25 or more years) and quit within 10 years. However, the NELSON trial also excluded patients with a prior history of cancer and thus will not be informative for LCS in this patient population (10).

Survivors of common cancers (including lung, breast, colon, bladder, prostate) have an overall risk of 8.1% for developing a second primary malignancy (SPM) with lung cancer being the most commonly diagnosed SPM (11). Lung cancer occurring as a SPM currently accounts for about 8–14% of all lung cancer diagnoses (12-14), and those at increased risk for subsequent development of a second primary lung cancer (SPLC) are more likely to be smokers with a prior history of breast, lung, and head and neck cancer (HNC) (15,16). The risk of SPLC in patients with prior HNC is between 5–19%, is highest within 10 years of the initial HNC diagnosis (substantially higher than

in the general population), and results in excess mortality (17-21). An estimated 23% of deaths in HNC survivors are due to SPM, with the leading site being lung cancer which accounted for 53% of the SPM deaths (17). While there are no randomized controlled trials of HNC patients comparing survival with and without LDCT screening for lung cancer, a recent survey of Canadian head and neck surgeons showed that a majority believe LCS impacts mortality, and 31% were screening HNC survivors for lung cancer with LDCT (22).

In the study titled "*The complicated 'Yes': Decision-making processes and receptivity to lung cancer screening among head and neck cancer survivors*" (23), Seaman and colleagues conducted semi-qualitative interviews in 19 HNC survivors (15 males, all non-Hispanic white, 16 former smokers, all had received treatment with surgery, radiation and/or chemotherapy with a mean of 4.2 years since completion of treatment) to better understand the knowledge, attitudes and beliefs of patients with HNC about LCS and SDM. The interviews focused on five domains: (I) cancer history, (II) smoking and cessation history, (III) beliefs about and receptivity to screening, (IV) perceived risks, benefits, and challenges of LCS, and (V) preferences about LCS decision making (23). Many of the participants reported undergoing screening for other cancers (prostate, colon, breast) but the majority did not have knowledge and lacked an understanding of the purpose of LCS. Furthermore, the study participants did not appreciate the difference between monitoring for recurrence of HNC and screening for a new lung cancer. While a few participants expressed uncertainties about cancer screening due to their previous cancer experiences, the majority were receptive. For LCS in particular, there were few concerns regarding false positive results. Instead, participants focused on the positive benefits and reported beliefs that LCS would result in early detection and lead to successful treatment outcomes (23). Participants reported a preference for in-person discussions regarding LCS and most thought that decision aids (including written and online versions) were useful in conjunction with discussions with providers. Three groups were reported as the ideal person to engage in SDM discussions: (I) the otolaryngologist, given expertise in cancer care, (II) providers in healthcare (including specialists, primary care physicians and nurse practitioners), and (III) those with LCS knowledge regardless of their medical role. The authors conclude that prior cancer experiences result in a "heightened preference for screening" and may influence the LCS decision-making processes in HNC survivors. They suggest that when discussing LCS with cancer survivors, SDM should "frame the benefits and harms of LCS in a way that reflects the prior cancer history and how it might affect the individual's screening priorities" (23).

Herein when screening HNC survivors for lung cancer, healthcare providers face two challenges: (I) inclusion of high-risk individuals outside of the NLST criteria (prior cancer survivors) and (II) conducting effective SDM discussions and message framing that considers underlying co-morbidities such as a prior cancer history. The criteria of age and pack-years smoking history to identify patients at increased risk for lung cancer who benefit from LCS was effectual for enrollment of patients in the NLST; however, solely relying on these two variables may be too simplistic. Sex, race, prior history of cancer, family history of lung cancer and chronic obstructive lung disease (COPD) are predictors of developing lung cancer. These variables have been incorporated into risk-prediction models (24), and incorporation of these variables into patient selection for screening could lead to more benefits and less harms of LCS compared to the use of current recommendations (25). An argument against the use of risk-prediction models for selecting patients at highest risk for lung cancer is that they may result in the selection of patients who are too sick [because of comorbidities such as prior history of cancer, COPD, cardiovascular disease (CVD)] to benefit from LCS because they are unable to undergo treatment and are at increased risk of dying from a cause other than lung cancer (26). This argument however can be countered by the fact that dissemination of LCS in the real-world will not be limited to younger more healthy patients such as the "healthy participants" enrolled in the NLST. In a population-based survey comparing LCS outcomes in a general population of individuals eligible for LCS in the US based on USPSTF criteria versus NSLT participants, life expectancy was lower (18.7 *vs.* 21.2 years respectively), supporting the notion that individuals in the general population tend to be older, more likely to be current smokers and to have more underlying co-morbidities (27).

Offering LCS to high-risk cancer survivors is a difficult decision because they represent a heterogenous group of patients (breast cancer survivors may be younger and healthier than HNC and bladder cancer survivors) with variable comorbid conditions, prior cancer treatments and experiences. While at increased risk for SPLC, benefit of LCS in this group of patients is not known. A recent study of LCS with LDCT in 139 patients (mean age 66 years, median pack year smoking history of 50) with a personal

history of cancer (43% breast, 19% HNC, and 12% lung), 42 (30%) patients had a positive screening study and 7 (5%) were diagnosed with lung cancer (6 adenocarcinomas, 1 squamous cell carcinoma). All patients diagnosed with lung cancer underwent surgical resection, 5 were stage 1A and 2 were stage 1B. One patient died from lung cancer 11 months following diagnosis (15). Although a small study, the lung cancer detection rate is higher than reported in the NLST (15). While the lung cancer detection rate in cancer survivors may be higher, the clinical heterogeneity of this group of patients including variability in underlying comorbidities and prior cancer treatments (previous radiation therapy or chemotherapy that could affect ability to undergo surgery for lung cancer) may confound the benefits of LCS, improved survival.

A personal history of HNC has been reported to predict worse survival after lung cancer diagnosis (28). A study using the NCI Surveillance, Epidemiology, and End Results (SEER) database evaluated survival from lung cancer for patients between ages 55–74 who were diagnosed with an early stage SPLC at least 1 year after HNC diagnosis compared with survival from patients with early stage lung cancer and no prior malignancy. Median survival for patients with lung cancer was 38 months with 5-year survival of 40% while median survival of SPLC 1-year after HNC diagnosis was 22 months with a 5-year survival of 26% (P<0.0001) (28). The authors suggest that LCS in patients with a history of HNC may not result in the same survival benefit as LCS in those without it (28). On the contrary, several studies have determined that a prior cancer history does not adversely impact survival in lung cancer. In a study using the SEER database that included 51,542 patients aged 65 or older diagnosed with locally advanced lung cancer, 15.8% had a prior history of cancer (most common were prostate, gastrointestinal, breast cancer, and other genitourinary) and in 54%, the prior cancer had been diagnosed within 5 years of the lung cancer diagnosis. Patients with prior cancer had slightly better all-cause [hazard ratio (HR) =0.96; 95% CI: 0.94–0.99, P=0.005] and lung cancer-specific (HR =0.84; 95% CI: 0.81–0.86, P<0.001) mortality when compared to patients without a prior cancer (29). A study of 42,910 patients aged 65 or older diagnosed with stage I and II NSCLC found that 21% had a history of prior cancer, 68% either *in situ* or early stage and the median time between the most recent prior cancer and the diagnosis of lung cancer was 3.6 years (mean 5.3 years) (30). Patients with a prior cancer had similar all-cause mortality (HR =1.01; 95% CI: 0.98–1.04) but decreased lung-cancer specific mortality (HR =0.79; 95% CI: 0.76–0.82) compared to patients without a prior cancer history (30).

SDM involves a thorough discussion of benefits and harms of LCS and should occur between clinicians and patients prior to ordering a LDCT. Though it sounds straightforward, in reality the process of SDM in the setting of LCS has been problematic due to multiple factors including but not limited to: insufficient time during the visit to assess competing priorities and access decision aids to conduct SDM (31), lack of knowledge regarding when to conduct the SDM consultation and who should spearhead the discussion (PCP *vs*. specialist) (32), how to best incorporate medical co-morbidities and patient's preferences in the SDM discussion (33), and understanding how patient's preferences and perceptions of benefits and risk may differ based on cultural beliefs, underlying co-morbidities, prior history of cancer and the clinical setting where the SDM visit is conducted (32). In one study, the quality of SDM communication by primary care physicians or pulmonologists was studied by analyzing audio from 14 doctor-patient conversations about LCS. Seven patients had Medicare and eight were current smokers. Using the OPTION (Observing Patient Involvement in Decision Making) scale, significant deficiencies were found in the SDM discussion. Most were very brief, one-sided and lacked discussions regarding the rate and consequences of false positive results and risk of overdiagnosis of lung cancer (34). Another qualitative study using semi-structured interviews and focus groups recruited clinicians who referred patients for LCS and patients who had undergone LCS. In this study, clinicians varied in the information communicated and shared with patients and reported inconsistent use of decision aids. Interestingly, patients reported receiving little information regarding benefits and risks of LCS from the clinicians (31).

Extending LCS to smokers with a prior history of cancer is a complicated decision. In this group of patients, the risk for developing lung cancer must be balanced against increased complications from procedures to evaluate screen-detected nodules, lung cancer treatment, and recurrence or dying from prior cancer (35). Cancer survivors are a heterogeneous group (sex, tumor characteristics, underlying comorbidities and prior cancer treatments) for whom there is little data on the effectiveness of LCS. As these patients are enrolled in screening, evaluating if LCS benefits outweigh potential harms will be crucial. Furthermore, little is known about the ideal content for SDM for LCS

in patients with underlying co-morbidities that may limit life expectancy including cancer survivors. Seaman and colleagues recommend that providers frame LCS-SDM discussions to better understand and clarify HNC survivors' understanding of the benefits and risks of LCS and that they consider the likelihood that a patient's prior history of cancer may influence decisions regarding LCS, potentially resulting in a heightened receptivity to LCS (23). This will require development of SDM tools that are tailored to the needs of cancer survivors and studies that will enhance our knowledge on LCS benefits across different populations.

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Footnote

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