Patient-Centered Outcomes among Lung Cancer Screening Recipients with Computed Tomography

A Systematic Review

Christopher G. Slatore, MD, MS,†‡§ Donald R. Sullivan, MD, MA,‡ Miranda Pappas, MA,§ and Linda L. Humphrey, MD, MPH§‖¶*

Introduction: Lung cancer screening using low-dose computed tomography (LDCT) is now widely recommended for adults who are current or former heavy smokers. It is important to evaluate the impact of screening on patient-centered outcomes. Among current and former smokers eligible for lung cancer screening, we sought to determine the consequences of screening with LDCT, and subsequent results, on patient-centered outcomes such as quality of life, distress, and anxiety.

Methods: We searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the fourth Quarter 2012), MEDLINE (2000 to May 31, 2013), reference lists of articles, and Scopus for relevant English-language studies and systematic reviews. To evaluate the effect of LDCT screening on patient-centered outcomes, we included only randomized controlled trials (RCTs) involving asymptomatic adults. To evaluate the association of particular results and/or recommendations from a screening LDCT with patient-centered outcomes, we included results from RCTs as well as from cohort studies.

Results: A total of 8215 abstracts were reviewed. Five publications from two European RCTs and one publication from a cohort study conducted in the United States met inclusion criteria. The process of LDCT lung cancer screening was associated with short-term psychologic discomfort in many people but did not affect distress, worry, or health-related quality of life. False-positive results were associated with short-term increases in distress that returned to levels that were similar to those among people with negative results. Negative results were associated with short-term decreases in distress.

Conclusions: As lung cancer screening is implemented in the general population, it will be important to evaluate its association with patient-centered outcomes. People considering lung cancer screening should be aware of the possibility of distress caused by false-positive results. Clinicians may want to consider tailoring communication strategies that can decrease the distress associated with these results.

Key Words: Lung cancer, Screening, Patient-centered outcomes.

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It is now widely recommended to consider lung cancer screening using low-dose computed tomography (LDCT) for middle-aged to elderly adults with a history of substantial cigarette smoking.[1–6] These recommendations are largely based on the National Lung Screening Trial which showed that three annual LDCT screens decreased lung cancer mortality by 20% and overall mortality by 7%.[7]

LDCT is associated with harms as well.[8,9] The most direct harm to individuals stems from the high rate of false-positive LDCT screens. In the National Lung Screening Trial, 39% of subjects received at least one positive test, 96% of which were falsely positive. Individuals with false-positive results may experience distress as a result of a "near-cancer" diagnosis. Other harms, such as the potential for overdiagnosis and increased risk of radiation-induced cancer, are important as well although are difficult to quantify for individual patients.[9,10]

We were particularly interested in understanding the influence of LDCT screening on patient-centered outcomes such as distress, anxiety, and quality of life (QOL). As part of a larger review of the benefits and harms of lung cancer screening conducted for the U.S. Preventive Service Task Force (USPSTF),[9] we conducted a systematic review of evidence that evaluated patient-centered outcomes for people who underwent screening and those who did not, and the association of specific LDCT screening findings with these outcomes.

*Health Services Research and Development, †Section of Pulmonary and Critical Care Medicine, ‖Division of Specialty and Hospital Medicine, Portland VA Medical Center, Portland, Oregon; and ‡Division of Pulmonary and Critical Care Medicine, Department of Medicine, §Pacific Northwest Evidence-Based Practice Center, Department of Medical Informatics and Clinical Epidemiology, ¶Department of Medicine, Oregon Health and Science University, Portland, Oregon.

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Address for correspondence: Christopher G. Slatore, MD, MS, Portland VA Medical Center, 3710 SW US Veterans Hospital Road, R&D 66, Portland, OR 97239. E-mail: slatore@ohsu.edu

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MATERIALS AND METHODS

A standard protocol was developed for this review. A technical report details the methods and includes search strategies and additional evidence tables.[11] Key questions addressing the benefits and harms of screening for lung cancer with LDCT were developed by the USPSTF with input from scientific staff at the Agency for Healthcare Research and Quality.[11] This report focuses on the association of LDCT lung cancer screening with patient-centered outcomes. Investigators created an analytic framework incorporating the key questions and outlining the patient populations, interventions, outcomes, and harms of LDCT screening for lung cancer. The Preferred Reporting Items for Systematic Reviews and Meta-analyses consensus was followed for the systematic review.[12]

Data Sources and Searches

In conjunction with a research librarian, investigators searched the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the fourth Quarter 2012), MEDLINE (2000 to May 31, 2013), reference lists of articles, and Scopus for relevant English-language studies and systematic reviews. These dates overlap with those of the previous review of the effectiveness of lung cancer screening.[13]

Study Selection

Each abstract was initially reviewed by one investigator, and if possibly relevant to the key question, then independently reviewed by two investigators to determine eligibility for inclusion. To evaluate the effect of LDCT screening on patient-centered outcomes, we included only randomized controlled trials (RCTs) involving asymptomatic adults at high risk of lung cancer because of smoking behaviors that compared screening with no screening. To evaluate the association of specific results and/or recommendations from a screening LDCT with patient-centered outcomes, we included results from RCTs and cohort studies that involved asymptomatic adults at high risk of lung cancer because of smoking behaviors.

Data Extraction and Quality Assessment

For each included study, one investigator abstracted details about the patient population, study design, screening procedure, LDCT findings, and patient-centered outcomes which were confirmed by a second investigator. By using predefined criteria for RCTs and cohort studies developed by the USPSTF,[14] two investigators rated the quality of studies (good, fair, or poor) and resolved discrepancies by consensus. We assessed the overall quality of the body of evidence (good, fair, or poor) using methods developed by the USPSTF on the basis of the number, quality, and size of studies; consistency of results; and directness of evidence.[14,15] When studies reported findings in more than one article, data from the most recent publication were used unless unique data were presented in a previous publication.

Data Synthesis and Analysis

Values and ranges for summary statistics are reported based on information provided by the study authors. Trial results could not be meaningfully combined because of heterogeneity of the outcome measures.

External Review

The draft report, from which the current analysis is based, was reviewed by content experts, USPSTF members, Agency for Healthcare Research and Quality Project Officers, and collaborative partners.[11]

RESULTS

A total of 8215 abstracts were reviewed. Five publications from two RCTs[16–20] and one publication from a cohort study[21] were included (Fig. 1). In general, the quality of these studies was fair. Table 1 includes details about the screening studies. Quality ratings are reported in Supplementary Tables 1 and 2 (Supplementary Digital Content, http://links.lww.com/JTO/A624).

Influence of LDCT Screening

Two reports each from the Danish Lung Cancer Screening Trial (DLCST) and the *Ne*derlands-Leuvens *L*ongkanker *S*creenings *On*derzoek (NELSON) study evaluated patient-centered outcomes.[16–18,20] The DLCST compared LDCT with no screening[22] and enrolled healthy men and women with ages 50 to 70 years, who were current or former (quit after age 50 and <10 years prior) smokers with 20 pack-years or greater smoking history.[22] All subjects were administered the Consequences of Screening (COS) scale (includes items on anxiety, negative impact on behavior, dejection, and sleep) and Consequences of Screening in Lung Cancer (COS-LC) scale (includes items on self-blame, focus on airway symptoms, stigmatization, introvert, harm of smoking, and anxiety)[23] at two time points: before randomization and at the time of the second LDCT.[16] Subjects with positive LDCT results for lung cancer (including false positives) were excluded. Before randomization, there were no differences in the COS scores between screen and control subjects. More subjects in the control arm did not complete the second survey compared with LDCT subjects (92% versus 97%). Control subjects at baseline had worse scores in the anxiety, behavior, dejection, self-blame, focus on symptoms, and introvert domains of the COS and COS-LC surveys. Subjects in both arms reported statistically significant increases in several scales, including the negative impact on behavior, dejection, and sleep scales, but the degree of change was similar in both groups. This study did not report on the minimally important difference (the smallest change that a patient would consider as significant) of the COS or COS-LC scales or domains (Table 2).

DLCST investigators also examined the new prescription of antidepressant and anxiolytic medications as recorded in the Danish National Prescription Registry among all control and LDCT subjects.[17] Subjects were followed for up to 3 years after randomization and censored from analysis if they died, emigrated, or were diagnosed with lung cancer. No differences were found between the screen or control group in terms of prescriptions for antidepressant or anxiolytic medications (hazard ratio, 1.00; 95% confidence interval [CI],

