Patz E, et al. Overdiagnosis in Low-dose Computed Tomography Screening for Lung Cancer JAMA Int Med (1)

Reviewed by CPT Sarah Petteys

Publication of the National Lung Screening Trial (NLST) in 2011 has resulted in increased implementation of lung cancer screening guidelines and programs. One criticism of lung cancer screening is the risk for overdiagnosis: detection of malignancies that would never become clinically relevant, and could result in unnecessary testing and treatment with potential for physical and psychological harm to the patient. The article by Patz et al. published in JAMA Internal Medicine attempts to estimate the amount of overdiagnosis that occurred in the NLST cohort. The researchers performed an empirical analysis of the NLST data, determining that 120 excess cancers were detected with low dose CT scan (LDCT) compared to CXR alone. Utilizing this value, two different overdiagnosis rates were calculated to detect the percent of clinically irrelevant cancers diagnosed during screening (Pₚₛ) and in total in the screening group (Pₚₐ). The upper bound rates of overdiagnosis were 11% and 18% for PA and PS respectively. These estimates were also calculated for subtypes of lung cancer, with the estimated overdiagnosis rates for bronchoalveolar carcinoma (BAC) were quite high at 67.6% and 78.9% for PA and PS respectively.

The researchers also performed mathematical modeling in 500,000 simulated cases to estimate overdiagnosis rates with varying surveillance periods of 5 years, 7 years and lifetime follow-up. As expected with the effects of screening over time, the amount of overdiagnosis declined as the years of follow-up increased. The rate of overdiagnosis for BAC remained elevated however and was estimated at 51% versus 3.2% for non-BAC NSCLC if the screening was extended to lifetime (Table 5). One presumes this is generally due to the indolent behavior of these lesions. The study has limitations as it is based on mathematical models, and the estimates based on current data are subject to lead time bias. Additionally, the lead authors are affiliated with companies that research molecular markers for screening which represents a potential conflict of interest. In summary, this article presents upper bound estimates of overdiagnosis with lung cancer screening and suggests that overdiagnosis is highest for cancers formerly characterized as BAC. Overdiagnosis rates for non-BAC lung cancer decreased significantly with lifetime screening. The phenomenon of overdiagnosis is well
established in areas, including breast cancer screening, where estimates of up to 3 cases of overdiagnosis for one life saved have been found.\textsuperscript{2-3} Despite the eye-catching reported 18\% overdiagnosis rate, the authors’ calculation of 1.38 cases of overdiagnosis for each life saved by lung cancer screening can therefore be interpreted favorably and can serve as starting point for patient counselling.

References

Black W, et al. Cost-Effectiveness of CT Screening in the National Lung Screening Trial. NEJM. (1)

Reviewed by LCDR Joseph Zeman

The National Lung Screening Trial (NLST) demonstrated a 20% reduction in lung-cancer mortality (2), leading the United States Preventive Services Task Force to release a grade B recommendation for CT screening in 2014 (3). Black and colleagues performed a cost-effectiveness analysis including an estimation of mean-life years, quality adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICER) based upon several assumptions. They used baseline costs from Medicare 2009 reimbursement data, including CT scans ($285) and incidental CT scan finding work-ups ($500), and baseline quality of life adjustments for a diagnosis of Stage 1A lung cancer (-.03 on Short Form Health Survey SF-36 questionnaire). They also assumed that there would be only one additional CT scan to the NLST protocol (which has 3 annual scans) and that any positive CT scan finding would not cause a change in quality of life.

With the above assumptions, they found that screening with low-dose CT provides an additional 0.0316 life-years per person and 0.0201 QALYs per person, at a cost of an additional $1,631 per person as compared to no screening. The ICER with the baseline assumptions was calculated at $81,000, below the accepted $100,000 threshold of cost per QALY gained. Subgroup ICER analysis revealed that CT scanning was more cost effective for women, current smokers, higher risk cancer patients and those between the ages 60-69. A sensitivity analysis determined that CT scans (through either increased cost or increased frequency outside of protocol) and an assumed lower quality of life following positive CT scan result (- 0.03 on SF-36) were the only variables found to be at risk of being cost prohibitive.

An important limitation of this analysis is the assumption that a positive CT scan result would have negligible impact upon the patient’s quality of life. Even small adjustments to the patient’s quality of life became cost prohibitive, highlighting the importance for education both prior and after a screening CT scan to minimize patient anxiety. Given the dramatic cost superiority in screening women, further research is warranted to evaluate if there is benefit in screening them at a younger age. Additionally, institutions which minimize additional CT scans, perhaps using a refined surveillance protocol such as the LUNG-RADS program (4), will be most cost effective in implementing a Lung Cancer Screening program.

References:


Louie AV, et al. When is a Biopsy-Proven Diagnosis Necessary Before Stereotactic Ablative Radiotherapy for Lung Cancer? A Decision Analysis. CHEST (1)

Reviewed by Capt Charles Stahlmann

Lung cancer is the leading cause of cancer-related deaths in the United States.\(^1\) Screening high-risk patients offers hope for early detection and higher cure rates.\(^2\) However, many patients with suspected lung cancer have comorbidities that significantly impact treatment options.\(^3\) Stereotactic ablative radiotherapy (SABR) offers hope for local control rates with low toxicity in such patients. In a subset of patients, even diagnostic procedures may entail unacceptable risks, which has led to increasing use of SABR without a confirmed tissue diagnosis.

Louie and colleagues compared the relative merits of three strategies: (1) PET scan-biopsy-SABR (2) surveillance and (3) PET scan-directed SABR without biopsy, when faced with a >1cm noncalcified solitary pulmonary nodule (SPN) at different probabilities of lung cancer. Published literature was used to create a cohort of 75-year-old patients meeting this description. A decision tree was constructed to compare strategies. Quality adjusted life years (QALYs) were derived from a prospective trial using SABR to treat early stage NSCLC. Overall survival (OS) was compared at 1, 3, and 5 years for treatment with and without pathologic confirmation of malignancy. SABR-without-biopsy OS rates were within 2% of OS rates for the biopsy-proven treatment group. Varying the lung cancer probability from 0 to 100% in a one-way sensitivity analysis revealed that the threshold for decision between PET scan-biopsy-SABR and PET scan-directed SABR strategies was 85.0%; between PET scan-biopsy-SABR and surveillance, the prior probability threshold was 17.0%. Biopsy sensitivity and CT scan false negative rate had the greatest influence on decision thresholds.

The authors suggest a blueprint for medically inoperable patients with SPN suspicious for stage I NSCLC; Limitations of this mathematical model include the assumption that all patients with recurrence are not fit for salvage therapy, which is an oversimplification.\(^4\) Additionally, PET-CT false negative rates were assumed, due to a lack of randomized controlled data. Furthermore, electromagnetic navigation bronchoscopy (ENB) was not considered in the decision tree despite several published studies demonstrating it to be a safe and effective biopsy option in certain high-risk patients.\(^5,6\) Finally, a lack of consensus regarding cancer pre-test probability determination may also influence real-life decision making; further research incorporating use of techniques such as volume doubling time for enlarging nodules is needed. This model suggests that if there are concerns about morbidity related to biopsy, a PET scan-directed SABR strategy is warranted when the prior probability of lung cancer exceeds 85%. Although clinically useful, the limitations of this model highlight the importance of a multidisciplinary approach, taking into account individual patient factors and local expertise with evolving therapies for the optimal management of high risk patients with suspected lung cancer.

References


