CHEST

Use of [^{18}F]Fluoro-2-deoxy-D-glucose Positron Emission Tomographic Imaging in the National Lung Screening Trial

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BACKGROUND: Positron emission tomography (PET) is a diagnostic tool for lung cancer evaluation. No studies have ascertained practice patterns and determined the appropriateness of PET imaging in a large group of US patients with screen-detected lung nodules.

METHODS: We analyzed participants in the National Lung Screening Trial (NLST) with positive screening test results and identified individuals with a PET scan performed prior to lung cancer diagnosis (diagnostic PET). Appropriate scan was defined as one performed in a patient with a nodule ≥ 0.8 cm. Logistic regression was used to assess factors associated with diagnostic PET scan use and appropriateness of PET scan use.

RESULTS: Diagnostic PET imaging was performed in 1,556 of 14,195 patients (11%) with positive screen results; 331 of these (21%) were inappropriate. PET scan use by endemic fungal disease area was comparable although patients from the Northeast/Southeast were twice as likely as the West to have a diagnostic PET. Trial arm, older age, sex, nodule size ≥ 0.8 cm, upper lobe location, and spiculated margin were variables positively associated with use. Trial arm, older age, and spiculated margin were positively associated with appropriate use. Only 561 diagnostic PETs (36%) were recommended by a radiologist and 284 PETs performed for nodules < 0.8 cm (86%) were ordered despite no recommendation from a radiologist.

CONCLUSIONS: PET imaging was differentially used in the NLST and inappropriately used in many cases against radiologist recommendations. These data suggest PET imaging may be overused in the lung cancer screening population and may contribute to excess health-care costs.

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KEY WORDS: [^{18}F]Fluoro-2-deoxy-D-glucose positron emission tomography; lung cancer; National Lung Screening Trial; positron emission tomography; screening

ABBREVIATIONS: CDAS = Cancer Database Access System; CXR = chest radiograph; FDG = [^{18}F]fluoro-2-deoxy-D-glucose; NCI = National Cancer Institute; NLST = National Lung Screening Trial; PET = positron emission tomography; SPN = solitary pulmonary nodule

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[^{18}F]Fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) imaging was introduced into clinical practice 15 years ago for the diagnosis of solitary pulmonary nodules (SPNs), based on decision models that suggested it was an accurate and cost-effective imaging test.[1] Meta-analyses shortly thereafter confirmed that FDG-PET imaging was a potentially specific and sensitive tool for both SPN diagnosis and lung cancer staging.[2-4]

The National Lung Screening Trial (NLST) was a prospective, multicenter, randomized trial of lung cancer screening by chest radiography (CXR) vs chest CT scan in patients 55 to 74 years of age with a recent or current smoking history of at least 30 pack-years. The NLST demonstrated that older, high-risk patients with an at least 30 pack-year smoking history who underwent yearly CT scans compared with CXR over 3 years had a decreased lung cancer-specific mortality (relative risk reduction, 20%).[5] Comparatively, this is more efficacious than mammography or colon cancer screening.[6,7] While impressive, the NLST results came with recognition that 96% of identified lesions, where a "positive" screen result was defined as a nodule ≥ 4 mm in diameter, were not cancer.[5] Many of these patients with false positive findings were subjected to additional downstream testing, including imaging in the majority of cases, and invasive biopsies or surgeries in a minority of cases. Despite these additional tests, current cost-effectiveness analyses suggest that lung cancer screening may be effective by modern cost metrics,[8] but there is strong interest within the medical community to minimize the morbidity and cost of screening by identifying the highest risk patients using mathematical modeling,[9] or blood biomarker integration.

At present, the American College of Chest Physicians, the National Cancer Center Network, and the American College of Radiology recommend that clinicians consider using FDG-PET imaging to risk-stratify indeterminate SPNs of adequate size for downstream management.[10,11] For the American College of Chest Physicians, these recommendations have decreased in emphasis from 2007 (grade 2a) to the present (grade 2c), which reflects a more stringent appraisal of the quality of evidence and risk of bias.[10,12] Practice patterns, however, remain poorly characterized at a population level despite the rapidly increasing use of PET scans, with an estimated 2,000 imaging stations in the United States alone.[13] Since FDG-PET imaging is costly, how it is used in screen-detected nodules for patients who have a positive—or a false positive—result will undoubtedly affect health-care costs and use.

Several European studies have previously examined PET scan use in a lung cancer screening population, but on a much smaller scale when compared with the US-based NLST.[14-16] We now add to this literature a secondary analysis of a large number of patients who had a positive screen result (≥ 4-mm nodule) and subsequently underwent a diagnostic PET scan to ascertain the etiology of an indeterminate finding prior to a diagnosis in the NLST. Our goal was to characterize diagnostic FDG-PET scan use for screen-detected nodules.

Methods

Data Sources

The NLST enrolled more than 54,000 patients from 2002 to 2004 at 33 medical centers.[5,17] Follow-up for diagnostic evaluation and treatment was left to the enrollment centers and was therefore not standardized. Thus, the NLST was a reflection of medical center practice patterns—the majority of which were academic—for nodule evaluation in addition to a lung cancer screening trial. The NLST was a collaboration between the National Cancer Institute (NCI) and the American College of Radiology Imaging Network (ACRIN). The NCI maintains the Cancer Database Access System (CDAS), which has developed a repository of data dictionaries and patient-level data files for participants in the NLST. These data were posted to the website in locked form in 2012 and consist of 16 de-identified SAS files that are available for statistical analysis. We reviewed variables from these NLST data sets and extracted pertinent variables for our analysis. The CDAS also provided to us at request additional unblinded center locations for regional analyses and to examine the effect of endemic fungal disease on PET scan use (e-Appendix 1). Data specific to individual centers were blinded for publication at the request of the NCI.

All patient data were de-identified and received from the CDAS after (1) proposal approval and (2) material transfer agreements had been signed as part of this institutional review board-exempt study at the Stanford University School of Medicine.

Study Cohort and Variable Definitions

We selected all patients who had a positive finding on any of the three annual screening scans in either group (Fig 1). A positive finding was defined as a nodule coded as "Positive, Change Unspecified, nodule(s) ≥ 4 mm or enlarging nodule(s), mass(es), other nonspecific abnormalities suspicious for lung cancer"; "Positive, No Significant Change, stable abnormalities potentially related to lung cancer, no significant change since prior screening exam"; or "Positive, other" in the participant data set from the NLST files. This corresponds to a code of 4, 5, or 6 in the participant identification data dictionary, which specifies the finding of a new ≥ 4-mm lesion requiring further evaluation.

We assessed whether patients had undergone PET or PET-CT imaging (defined in the data sets as "Radionuclide scan—FDG-PET scan" or "Radionuclide scan—Fusion PET/CT scan"). We defined a diagnostic PET scan as a scan that was performed after a positive finding on a