September 2015 Tucson Pulmonary Journal Club: Genomic Classifier for Lung Cancer

Silvestri GA, Vachani A, Whitney D, et al. A bronchial genomic classifier for the diagnostic evaluation of lung cancer. N Engl J Med. 2015;373(3):243-51. [CrossRef] [PubMed]

Pulmonary lesions are a common diagnostic dilemma for clinicians. Current literature describes the sensitivity of bronchoscopic techniques to be between 34 and 88%; which varies significantly depending on size and location of the biopsied lesion (1). Previously described gene expression patterns have been found to be associated with malignancy in healthy epithelial cells of the proximal airways\(2). The primary aim of this study was to prospectively validate a specific gene expression classifier in patients undergoing bronchoscopic biopsy for suspected lung cancer.

The study involved two independent, prospective, multicenter, observational studies (AEGIS-1 and AEGIS-2) conducted in the U.S., Canada and Ireland at 28 sites. Patients were excluded if they were never smokers, under age 21, or current cancer or former lung cancer patients. Patients were followed for 12 months after bronchoscopy or until a diagnosis was established. A wide array of bronchoscopic and surgical techniques were used to ultimately make a diagnosis. Prior to undergoing invasive diagnostic testing, the treating physician was asked to estimate the patient's pre-test probability of cancer.

The overall prevalence of lung cancer in the two cohorts was 76.5%. Bronchoscopy alone had 74% sensitivity (95% CI, 68 to 79) in AEGIS-1 and 76% (CI 95%, 71 to 81) in AEGIS-2 with a combined specificity of 100%. When combining the gene classifier with bronchoscopy, the sensitivity increased to 96% (95% CI, 93 to 98) in AEGIS-1 and 98% (95% CI, 96 to 99) in AEGIS-2 with a combined specificity of 47.9%.

The poor specificity of the gene classifier limits its clinical utility as an adjunct to bronchoscopy. Although the sensitivity was high, the low specificity makes this additional test of low diagnostic value for definitively ruling in cancer. When bronchoscopy was negative, the prevalence of lung cancer remained high, approximately 45%, and the resulting post-test probability of a positive gene-classifier test was 58% and the post-test probability of a negative test was 16%. Neither value is sufficiently predictive to avoid further invasive testing to definitely determine the presence or absence of cancer in this intermediate risk population. The racial composition of study participants was predominately white with a majority being males. The age range of study participants was between 55 and 71. Because of that, the generalizability is more limited. However, the gene classifier might have limited clinical utility for patients who are poor candidates for additional invasive testing. A positive result might tilt the balance in favor of additional testing whereas a negative result might warrant watchful waiting. Overall, this dual approach to diagnostic assessment for lung nodules suspicious of being lung cancer is not ready for widespread implementation.

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References

1. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013;143:Suppl 5: e142S-e165S. [CrossRef] [PubMed]
2. Spira A, Beane JE, Shah V, et al. Airway epithelial gene expression in the diagnostic evaluation of smokers with suspect lung cancer. Nat Med. 2007;13:361-6. [CrossRef] [PubMed]