

Diagnostic Tests

What Physicians Need to Know

PAULA's Test for Lung Cancer Screening

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PAULA's test (Protein Assays Utilizing Lung Cancer Analytes) is a blood test for early detection of lung cancer in high-risk adults.¹ Eligible patients are 50 years or older, current or former smokers with more than a 20-pack-year history and less than 15 years of smoking cessation, asymptomatic, and not being treated for lung cancer.^{2,3} The test is composed of a panel of three tumor markers (carcinoembryonic antigen, cancer antigen 125, and CYFRA 21-1 [a fragment of cytokeratin 19]) and one autoantibody marker (New York esophageal squamous cell carcinoma 1 [NY-ESO-1]).

Accuracy

A 2015 retrospective study used a training set of 115 patients with confirmed non-small cell lung carcinoma and 115 patients (matched in age and smoking history) in a control group to evaluate the predictive model used in PAULA's test.³ It was then validated in an independent set of 150 matched patients. This study found that the panel of four biomarkers was 77% sensitive and 80% specific for the detection of lung cancer in the validation group (positive likelihood ratio = 3.8; negative likelihood ratio = 0.29).³ Given a 1% likelihood of lung cancer in the target screening population, the positive predictive value is estimated to be 3.7%, and the negative predictive value is estimated to be 99.7%.

A 2018 study that included a training set of 268 patients with lung cancer and 336 patients

Test	Indication	Population, age range, and frequency	Cost*
PAULA's test	Lung cancer screening	Adult patients at high risk of lung cancer; testing frequency not yet established	\$150 (plus shipping and any venipuncture fees charged by the medical office)

PAULA = Protein Assays Utilizing Lung Cancer Analytes.

*—Payment rate according to Genesys Biolabs.

†—Eligible patients are 50 years or older, current or former smokers with more than a 20-pack-year history and less than 15 years of smoking cessation, asymptomatic, and not being treated for lung cancer.^{2,3}

in a control group, plus a validation set of 155 patients with lung cancer and 245 patients in a control group, explored adding a fifth biomarker (hepatocyte growth factor) to the established panel.⁴ Both the four- and five-biomarker panels had a sensitivity of 49% and a specificity of 96%.

The U.S. Preventive Services Task Force recommends annual screening for lung cancer with low-dose chest computed tomography (CT) in adults 55 to 80 years of age who have a 30-pack-year smoking history and currently smoke or have quit within the past 15 years.⁵ The National Lung Screening Trial (NLST) randomized 53,439 asymptomatic participants, 55 to 74 years of age with at least a 30-pack-year smoking history, to annual screening with low-dose CT or chest radiography for three years. Low-dose CT had a sensitivity of 93.8% and specificity of 73.4% for lung cancer.⁶

Benefit

There have been no prospective studies demonstrating that PAULA's test improves patient-oriented outcomes.

Harms

PAULA's test combines tumor markers with an autoantibody marker to increase the overall

This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

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Author disclosure: No relevant financial affiliations.

sensitivity of the test, although it is still less sensitive than screening with low-dose CT. Preliminary testing of PAULA's test demonstrated increased expression of biomarkers in patients with benign pulmonary disease (e.g., chronic obstructive pulmonary disease, asthma, bronchitis), which could lead to false-positive findings.³ As a result, patients may undergo unnecessary and potentially invasive diagnostic testing, including full-dose CT and biopsy. The 2018 validation study also demonstrated lower sensitivity than previously documented, but the reasons for this are unclear.⁴

Cost

PAULA's test costs \$150 in addition to shipping and any venipuncture fees charged by the medical office.² In comparison, the current fair price for chest CT without contrast media is \$300.⁷

Bottom Line

Because of insufficient evidence of benefit, no recommendations can be made regarding PAULA's test. Prospective cohort studies of a screening population and randomized controlled trials comparing cancer mortality outcomes using PAULA's test vs. low-dose CT and no

screening are needed before the test can be recommended as a screening option.

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