Using Clinical Risk Models for Lung Nodule Classification

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Evaluation and diagnosis of indeterminate pulmonary nodules is a significant and increasing burden on our health care system. The advent of lung cancer screening with low-dose computed tomography only exacerbates this problem, and more surgeons will be evaluating smaller and screening discovered nodules. Multiple calculators exist that can help the clinician diagnose lung cancer at the bedside. The Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) model helps to determine who needs lung cancer screening, and the McWilliams and Mayo models help to guide the primary care clinician or pulmonologist with diagnosis by estimating the probability of cancer in patients with indeterminate pulmonary nodules. The Thoracic Research Evaluation And Treatment (TREAT) model assists surgeons to determine who needs a surgical biopsy among patients referred for suspicious lesions. Additional work is needed to develop decision support tools that will facilitate the use of these models in clinical practice, to complement the clinician's judgment and enhance shared decision making with the patient at the bedside.

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INTRODUCTION

Lung cancer is the most common cancer in the world with an estimated 1.8 million new cases a year.[1] It is the leading cause of cancer-related mortality among men and women with an estimated 224,000 new cases and 159,000 annual deaths due to lung cancer in the United States.[2] The United States spends an estimated $10.3 billion on lung cancer care, which comprises 10% of all cancer-related health care expenditures.[3] Lung cancer prognosis remains poor despite the steady decline in lung cancer incidence, declining smoking rates, increased awareness in the general population, and the advent of new technologies to detect lung cancer early. A lung nodule suspicious for lung cancer can present to the clinician in 3 ways: symptomatically, incidental discovery of the nodule after imaging for another clinical indication, and from periodic screening. Irrespective of source, the diagnosis of lung cancer begins with radiographic imaging of the chest and review of a detailed history and physical of the individual. Previously, most lung cancer was diagnosed symptomatically (estimated 75%), but incidental discovery has increased recently with the proliferation of imaging modalities like computed tomography (CT) scans.[4] Once a national screening program is fully initiated in the United States, a dramatic increase in asymptomatic lung nodules requiring diagnosis will occur. Irrespective of the source of a lung nodule, clinical risk models have been developed and employed to determine who should be screened, who should receive continued radiographic surveillance, and who should be referred to a surgeon. We discuss these models and their use across the spectrum of lung cancer risk and look in depth at those models designed for evaluation of lung nodules.

PREDICTIVE MODELS IN LUNG CANCER

When considering the spectrum of lung cancer risk, we begin with the "at-risk" patient before developing a suspicious lung lesion and move through time until a definitive diagnosis of cancer

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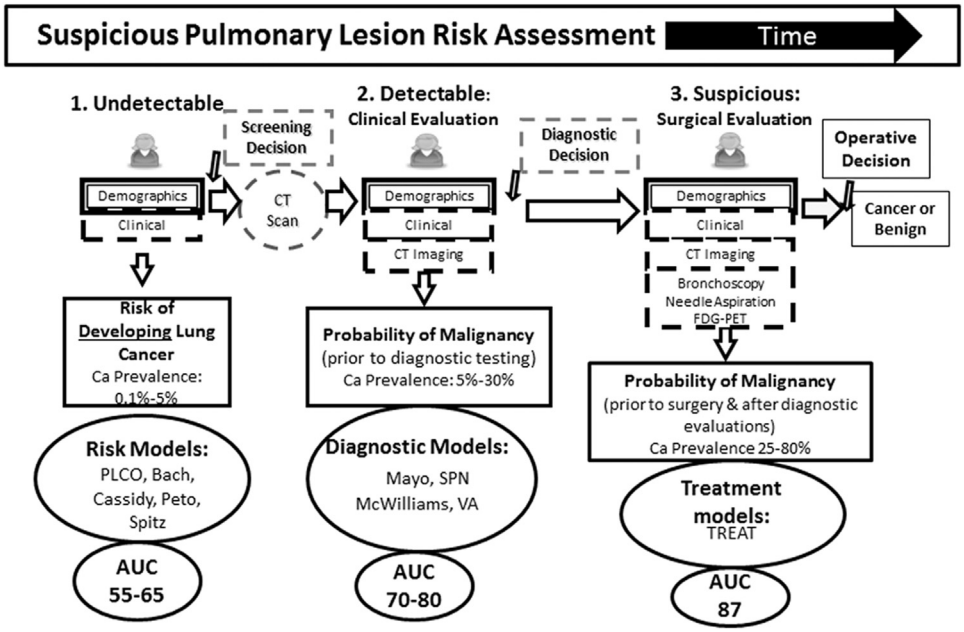

Figure 1. Existing predictive models. At each step in the pathway, the patient accumulates more diagnostic information. Predictive models with disease prevalence are located at the 3 steps.

or benign disease occurs at the time of an operation. At each step along their evaluation, patients accumulate more diagnostic information until presenting to the surgeon for an operative decision (Fig. 1). Risk models exploit the increasing amount of diagnostic information to create more accurate estimates of malignancy risk. In the first step, an individual is asymptomatic. Each person has genetic, demographic, environmental, clinical, and behavioral risk factors for the development of lung cancer. So, for example, lung cancer risk in nonsmokers is 23 per 100,000 person years in individuals between the ages of 60 and 80 years. This risk is 20-fold higher in current smokers.[5] The person then undergoes imaging, and a lesion is either present or absent. If a lung lesion is present, the individual is then further evaluated. In the second step, a lung lesion has been detected radiographically, and clinical symptoms may or may not be present. Lesion imaging characteristics that change the likelihood for malignancy are added to the epidemiologic data generated by a history and physical examination. Nodules are then evaluated by a clinician who makes an assessment of the probability of cancer and decides to either follow the lesion with continued CT imaging or obtain additional diagnostic testing such as ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) scans in accordance to current clinical guidelines. In the third step, the nodule is suspicious enough to warrant a referral to a surgeon for additional assessment. At this point in the evaluation, surgeons have access to all available data including patient risk factors, clinical and imaging characteristics, and the results of additional procedural and clinical evaluations. A final estimate of cancer or benign disease occurs, and the operative decision is made.

Screening Models

Population-level predictive risk models at step 1, such as the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) model published by Tammemägi et al that was developed from the PLCO cohort, the Liverpool model created by Cassidy et al, or the Bach model, exist to assess a patient's multiyear risk for developing cancer before conducting imaging. These models are epidemiologic in nature and assess large, asymptomatic populations. Their primary purpose is to determine who would most benefit from lung cancer screening.[6-8] They have been extensively used to estimate cancer risk by age and tobacco burden and to help assess the efficacy of lung cancer screening across strata of risk.[7,9,10] In North America, the 2 most popular models for this population are the Bach and PLCO models.[6,8] The Bach model is known for its simplicity in estimating the likelihood of cancer over 6 years. Only age, sex, smoking history (pack years and years quit), and any work-related asbestos exposure are needed to estimate risk. The PLCO model is more complex than Bach and has been extended to include nonsmokers. It requires age, race, years of education, body mass index, diagnosis of chronic pulmonary disease,