Incidental nodule management-should there be a formal process?

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Abstract: Indeterminate pulmonary nodules are commonly encountered and often result in costly and invasive procedures that eventually turn out to be unnecessary. Current prediction models can help to estimate the pretest probability of cancer and assist in determining a strategy of observation with serial imaging for a low pretest probability of cancer, and a more aggressive approach for those patients with a high pretest probability. However, the majority of patients will have an intermediate pretest probability which becomes complex. Decisions for further management are often based on preference by the clinician with the majority of physicians not following current guidelines in the management of pulmonary nodules. Poor adherence to pulmonary nodule guidelines is multifactorial with a variety of factors coming into play. These include inappropriate advice given by the radiologist, patient age, comorbidities, patient preference, and physician's technical skill all influencing the decision making.

Keywords: Solitary pulmonary nodule; lung nodule; lung cancer; lung neoplasms; decision making; guidelines

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Hundreds of thousands of pulmonary nodules are detected each year. Evaluation of these nodules has the potential to create a tremendous burden on the health care system as well as individual patients. Therefore, appropriate pulmonary nodule evaluation has important implications. Due to the complexity of pulmonary nodule management, in 2003 the American College of Chest Physicians (ACCP) published guidelines on the management of pulmonary nodules (1). This was followed by Fleischner Society guidelines in 2005 which sought to reduce the burden of lung nodule evaluation by recommending patients at lower risk of cancer receive fewer tests (2). Since that time, the ACCP has updated their own guidelines in 2007 (3), and again in 2013 (4) to reflect and be in concordance with Fleischner Society guidelines. Both guidelines stratify patients on the size and appearance of pulmonary nodules as well as the predicted or calculated risk of a

patient having lung cancer. They recommend a threestep approach which includes assessing the likelihood of malignancy, evaluating whether a patient is a candidate of invasive interventions, and engaging the patient in shared decision-making (1-4).

CT imaging of the chest done for various reasons frequently reveal incidental pulmonary nodules that were not previously known. For instance, CT angiography done for suspicion of pulmonary embolism has been demonstrated to be twice as likely to find a new incidental pulmonary nodule or thoracic adenopathy than a pulmonary embolism (5). Cardiac CT screening for coronary artery disease will discover incidental pulmonary nodules in 5–20% of patients (6). CT colonography increasingly being done to screen for colon cancer will also find pulmonary nodules that will need further evaluation (7). A review of 1,000 CT pulmonary angiographies ordered in the emergency department noted that in 9.9% of studies, pulmonary nodules were found. However, follow up for those nodules was extremely poor with less than a third of those patients having appropriate lung nodule follow-up imaging according to the Fleischner Society guidelines (8). A systematic review of 19 studies that had quantitative evidence of the number of tests not followed up for patients attending ambulatory settings demonstrated that up to 35.7% of radiology studies did not have appropriate follow-up by the ordering provider (9). Another study among veterans with incidental pulmonary nodules reported that almost a quarter of patients did not receive follow-up imaging concordant with Fleischner Society Guidelines (10).

Despite having guidelines, why is there a tremendous variation in achieving guideline-concordant care? Is the non-concordance with guidelines a reflection of a failure in communication between inpatient and outpatient medical teams? It has been shown that when guideline recommendations are not followed, many patients receive an over or under-evaluation with regards to their pulmonary nodule. An over-evaluation has been estimated to occur in 17.8% of patients with pulmonary nodules and resulted in either prolonged surveillance exposing patients to radiation, multiple biopsies with complications, and emotional stress and harm to the patient (11-13). In a more recent study, when looking at community pulmonologists in 18 different geographically diverse communities, a total of 20.4% of patients underwent surgery for lung nodules measuring 8-20 mm when the pretest probability of malignancy showed that 9.5% were at a low risk, 79.6% were at a moderate risk, and only 10.8% were at a high risk of malignancy. Having said this, the rate of surgical resection was similar among the three groups (14). This is despite advances in imaging and nonsurgical biopsy techniques. On the other hand, underevaluation occurs in 26.9% with no follow-up resulting in the possibility of a delayed cancer diagnosis (15). A multitude of factors have been associated with non-concordance. These include how the lung nodule was detected such as during a lung cancer screening evaluation, emergency room visit, inpatient admission, or during a pre-operative evaluation, radiologist recommendations on reports, patient preference or anxiety, patient's age and perceived life expectancy, physician preference, physician's technical experience, and malpractice concerns (15-19).

The strongest predictor of guideline inconsistent care is inappropriate radiologist recommendations (8,15,20). In one study, radiologist recommendations were found to be inconsistent with guidelines in 17.8% of cases (16.2% more intensive, 2% less intensive) (15). In national surveys, 39-73% of radiologists had non-concordance with guidelines with regards to follow-up recommendations (17,21). In addition, in another study PCP's almost universally report always selecting the follow-up interval of a CT chest for a pulmonary nodule based on the radiologist's recommendations (22). The majority of these recommendations result in an over-evaluation resulting in further invasive testing. For this reason attempts have been made to implement standardized interpretation and recommendations for chest CT scans. This has been demonstrated and proven to increase appropriate guidelinedriven care (23). With the implementation of the National Lung Screening Trial (NLST), the American College of Radiology has created a structured reporting system for LDCT lung cancer screening and reports improved positive predictive value without increasing the number of examinations with false negative results (24). However, these recommendations are for the screening cohort and not incidental nodules found on imaging.

The pretest probability of cancer by far determines the most cost-effective strategy for the diagnosis and management of a pulmonary nodule. These include nodule size and appearance, patient age, and smoking history. Therefore, the approach to a patient with a pulmonary nodule should be based on an estimate of the probability of cancer using prediction models. Using these prediction models, the NLST only examined individuals thought to be at the highest risk for lung cancer. Even in that study of the 24.2% of positive screening tests found during the NLST, 96.4% were false positives. This resulted in 42% of invasive procedures being performed in patients with benign nodules and resulted in reduced quality of life and increased anxiety. Complications following these invasive procedures were 10% (15). The NLST's number of invasive procedures and 10% complication rate is likely unrealistically low and has a comprehensive cancer center study bias when compared to all centers nationally. Therefore, the actual number of procedures and complications are realistically much higher when evidence-based guidelines are not appropriately followed.

Another area in which recommendations for testing are not aligned with current guidelines is subcentimeter lung nodules which are <6 mm in size. In one study, invasive testing was recommended for 23% of patients with a <6 mm lung nodule when the risk of malignancy ranged from less than 1% (25,26). Given the level of complication risks associated with invasive procedures, guidelines recommend serial imaging when pulmonary nodules are

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<6 mm however, in this study there was a wide variation in the management. In addition, it has been found that guideline recommendations are not adhered to when it comes to the elderly population. Patients are approximately half as likely to undergo invasive testing despite it being indicated (26).

Pulmonary nodule management is only going to become more problematic over time as the annual frequency of chest CT imaging is increasing which results in increasing number of nodules being found. By extrapolation, over 1.5 million Americans will be expected to have an incidental pulmonary nodule identified each year (27). The combination of increased volume of chest imaging, and improved image technology, is going to create a large burden of patients with nodules that need to be managed. Improvements in individual components of nodule care are most likely not going to be enough to ensure a high rate of appropriate guidelinedriven follow-up. Patients whose nodules are initially deemed likely to be benign are generally followed up by CT scans performed over a 2-year interval. If the clinician's initial assessment of the patient's lung nodule is later found to be incorrect, then the cancers are usually discovered early in the follow-up period and remain at an early enough stage for therapeutic intervention.

In contrast, when physicians initially assess their patient's nodule to have a higher probability of lung cancer, they often undergo biopsies or surgeries to identify cancer. However, these procedures often end up identifying the nodules as benign or turn out to be non-diagnostic, meaning that many patients may undergo costly, invasive procedures that turn out to be unnecessary.

Current prediction models do not present the clinician with a sufficient specificity, negative predictive value and large enough area under the receiver operating characteristic curve to prevent a false positive diagnosis. In addition, it has been reported that only 28% of physicians follow current guidelines in the management of pulmonary nodules. Therefore, systems need to be implemented that include a dedicated coordinator or clinician to be notified for followup and evaluation of all new pulmonary nodules that are detected at each institution. In addition, we need a national formal tracking program with structured reporting systems and applications of registries (28).

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Footnote

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