Cost-Effectiveness of Initial Diagnostic Strategies for Pulmonary Nodules Presenting to Thoracic Surgeons

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Background. Patients presenting to thoracic surgeons with pulmonary nodules suggestive of lung cancer have varied diagnostic options including navigation bronchoscopy (NB), computed tomography-guided fine-needle aspiration (CT-FNA), 18F-fluoro-deoxyglucose positron emission tomography (FDG-PET) and video-assisted thoracoscopic surgery (VATS). We studied the relative cost-effective initial diagnostic strategy for a 1.5- to 2-cm nodule suggestive of cancer.

Methods. A decision analysis model was developed to assess the costs and outcomes of four initial diagnostic strategies for diagnosis of a 1.5- to 2-cm nodule with either a 50% or 65% pretest probability of cancer. Medicare reimbursement rates were used for costs. Quality-adjusted life years were estimated using patient survival based on pathologic staging and utilities derived from the literature.

Results. When cancer prevalence was 65%, tissue acquisition strategies of NB and CT-FNA had higher quality-adjusted life years compared with either FDG-PET or VATS, and VATS was the most costly strategy. In sensitivity analyses, NB and CT-FNA were more cost-effective than FDG-PET when FDG-PET specificity was less than 72%. When cancer prevalence was 50%, NB, CT-FNA, and FDG-PET had similar cost-effectiveness.

Conclusions. Both NB and CT-FNA diagnostic strategies are more cost-effective than either VATS biopsy or FDG-PET scan to diagnose lung cancer in moderate- to high-risk nodules and resulted in fewer nontherapeutic operations when FDG-PET specificity was less than 72%. An FDG-PET scan for diagnosis of lung cancer may not be cost-effective in regions of the country where specificity is low.


The management of pulmonary nodules suggestive of lung cancer is a combination of art and science as the clinician balances the advantages and disadvantages of a range of tests at each stage in the diagnostic process. The US Preventive Services Task Force recently recommended low-dose computed tomographic (CT) screening of healthy individuals at high risk for lung cancer [1]. Based on current smoking estimates in the US population and given the rates of nodule discovery found in the National Lung Screening Trial, as many as 1 to 2 million more suspicious nodules will be discovered annually given current clinical screening recommendations [2]. Patients with suspicious nodules will require additional tests for diagnosis, and some will require evaluation by a surgeon.

Currently, 18F-fluoro-deoxyglucose positron emission tomography (FDG-PET) is suggested for noninvasive diagnosis of a nodule larger than 0.8 cm with a clinical probability for lung cancer between 5% and 65%. Computed tomography-guided fine-needle aspiration (CT-FNA) is an alternative diagnostic technique with a diagnostic accuracy of 77% (range, 59% to 96%) in peripheral nodules accessible to needle biopsy; however, as many as 41% of CT-FNA biopsies are nondiagnostic [3].

Several image-guided bronchoscopy techniques have been developed to improve the yield of transthoracic and transbronchial biopsy for lung nodule diagnosis. Computer-assisted navigation bronchoscopy (NB), virtual bronchoscopy, and radial endobronchial ultrasound allow the clinician to navigate beyond the hilum to biopsy suspicious lesions in the peripheral lung fields with increased diagnostic yield [4, 5]. Using a decision analysis model, we examined the cost-effectiveness of NB compared with FDG-PET, CT-FNA, and video-assisted thoracoscopic surgery (VATS) biopsy.

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Material and Methods

A decision analysis model was developed to estimate the costs and outcomes of four different diagnostic strategies for the workup of a patient with a 1.5- to 2-cm nodule detected by CT. Compared strategies included FDG-PET scan, NB, CT-FNA, and surgical biopsy (Fig 1). The model includes key outcomes after each treatment or diagnostic alternative with estimated probabilities of these events, quality-adjusted life years (QALYs), and total costs associated with each strategy. Model construction and cost-effectiveness analysis were performed using TreeAge Pro 2013 (Williamstown, MA). This study was not deemed human research by Vanderbilt Institutional Review Board.

The base case is a 60-year-old man with a 15-pack-year smoking history, no prior history of lung cancer, and a 1.5- to 2-cm nodule in an upper lobe incidentally observed on a CT scan. The nodule is either spiculated or has grown at least 15% in diameter on serial radiographs, but does not have both radiographic risk factors. The individual is a good operative candidate and would tolerate a lobectomy. With a clinical risk for lung cancer of approximately 65% based on the Mayo Clinic model, this case reflects a patient presenting to thoracic surgeons for surgical evaluation for suspected lung cancer without a preoperative diagnosis [6]. Several diagnostic choices are available to the surgeon for diagnostic workup of this patient who is at the margin between high and intermediate risk for lung cancer [7].

![Diagram](https://via.placeholder.com/150)

**Figure 1.** Decision analysis model for patient presenting with a 1.5- to 2-cm nodule and likelihood of lung cancer is 65%. (A = outcomes resulting from a video-assisted thoracoscopic surgery [VATS] biopsy; B = outcomes resulting from a lobectomy given pathologically determined malignancy; CT-FNA = computed tomography-guided fine-needle aspiration; PET = positron emission tomography; SPN = suspicious pulmonary nodule.)

### Abbreviations and Acronyms

- **CT-FNA** = computed tomography-guided fine-needle aspiration
- **FDG-PET** = $^{18}$F-fluoro-deoxyglucose positron emission tomography
- **ICER** = incremental cost-effectiveness ratio
- **NB** = navigation bronchoscopy
- **QALYs** = quality-adjusted life years
- **VATS** = video-assisted thoracoscopic surgery
with a clinical risk for lung cancer of 50% while holding all other model parameters constant was also considered.

Data Sources
We examined published literature for estimates and ranges of diagnostic test characteristics (sensitivity and specificity), complication and outcome probabilities, 5-year survival rates, and costs included in the decision analysis model (Table 1). Recent meta-analyses examining values of a model component (such as 5-year survival) were the preferred source [8, 9]. Next, systematic reviews were considered with preference for evidence-based reviews to support practice guidelines [7, 10, 18, 24]. When neither systematic reviews nor meta-analyses were available, a limited review of the relevant literature was conducted, and applicable but broad ranges of values were used in sensitivity analysis of the characteristic or event’s impact on cost and outcomes. We used Medicare-reimbursable amounts for societal costs representing the mean Medicare hospital reimbursement for the indicated inpatient procedure using a base year of 2011 based on combined diagnostic resource group reimbursement and Common Procedural Terminology (CPT). Outpatient procedures were calculated using their respective combined professional and facility CPT code reimbursement for 2011. Costs were abstracted from existing literature or Center for Medicare Services publications (Table 2) [26]. Cost ranges were assumed to be base-reimbursable amount plus or minus 50.

Outcomes
Both CT-FNA and NB biopsies could be either diagnostic (malignant or definitely benign) or nondiagnostic. We refer to diagnostic yield as the percent of biopsies that result in a malignant or definitely benign diagnosis. Patients with malignant biopsies underwent a lobectomy (Fig 1). All lesions that underwent a CT-FNA or NB that had a diagnosis of cancer were assumed to undergo VATS for a lobectomy. We assumed 85% of all nondiagnostic biopsies underwent VATS biopsy. The remaining 15% of nondiagnostic biopsies and all non-avid FDG-PET nodules entered the watchful waiting strategy. In the watchful waiting strategy, a nodule was monitored with three CT scans over 2 years with the first scan occurring 3 months after the decision to initiate the watch and wait strategy. Patients with malignancy after a VATS biopsy were assumed to undergo lobectomy, whereas patients with a pathologically determined benign nodule at VATS biopsy were assumed to undergo a wedge resection. Surgical biopsy was considered the gold standard for diagnosis.

In the watch and wait strategy, 10% of benign lesions were assumed to demonstrate malignant growth on the

<table>
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<tr>
<th>Table 1. Variables Used in Model</th>
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<td>Variable</td>
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<tr>
<td>PET sensitivity</td>
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<tr>
<td>PET specificity</td>
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<td>NB % diagnostic</td>
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<td>NB sensitivity</td>
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<tr>
<td>NB specificity</td>
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<tr>
<td>CT-FNA % diagnostic</td>
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<td>CT-FNA sensitivity</td>
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<td>CT-FNA specificity</td>
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<tr>
<td>Surgical biopsy sensitivity</td>
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<td>Surgical biopsy specificity</td>
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<th>Table 2. Cost of Diagnostic Strategies</th>
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<tr>
<td>Procedure or Complication</td>
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<td>-------------------------------</td>
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<tr>
<td>Procedures</td>
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<tr>
<td>FDG-PET</td>
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<tr>
<td>CT-FNA</td>
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<tr>
<td>NB</td>
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<tr>
<td>Lobectomy</td>
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<tr>
<td>Wedge</td>
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<tr>
<td>Surgery with complications</td>
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<tr>
<td>Computed tomography</td>
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Complications:
| Pneumothorax needing observation | 8.4% | 1.5% | [9] |
| Pneumothorax needing chest tube | 6.6% | 0.6% | [9] |
| Hemorrhage | 1% | 0% | [9] |

Lobectomy Wedge
| Mortality | 2.2% | 1.2% | [22] |
| Major morbidity | 6.4% | 4.6% | [23] |

CT-FNA = computed tomography-guided fine-needle aspiration; NB = navigation bronchoscopy; PET = positron emission tomography; QALY = quality-adjusted life year.

a Costs are given in 2011 dollars.

CT-FNA = computed tomography-guided fine-needle aspiration; FDG-PET = 18F-fluoro-deoxyglucose positron emission tomography; NB = navigation bronchoscopy.
3-month follow-up CT scan as used in previous cost-effectiveness studies [27]. Lesions demonstrating malignant growth underwent VATS biopsy. Malignant nodules were assumed to be identified at 3 months as used in previous effectiveness analyses [27]. To incorporate the hazard of delayed diagnosis from the watchful waiting strategy, disease progression caused by delayed diagnosis resulted in stage progression and reduced life expectancies as modeled in previous effectiveness analyses [28]. Patients with benign lesions who underwent surgical biopsy were assumed to have a nontherapeutic wedge resection that would not affect life expectancy if the initial surgery did not result in mortality. The Society of Thoracic Surgeons National General Thoracic Surgery Database was the source for perioperative mortality and complications with lobectomy, and National Lung Cancer Screening trial data were used for perioperative mortality from wedge resection [21, 22].

The changes in survival as a result of a diagnosis of benign disease or cancer were converted to quality-adjusted life years (QALYs) by multiplying the expected years of survival by the utility or quality of life of the patient for those remaining years. One QALY represents the quality and quantity of life equivalent to a healthy individual with no disease burden for a year. United States life expectancy tables were used to calculate life expectancy for patients with benign nodules [17]. The utility or quality of life of this patient population was assumed to be 1.0. The only decrease in QALYs in this group was from morbidity and mortality from diagnostic procedures. Survival curves for lung cancer were used to determine stage-specific survival after resection [18].

Expected 5-year survival was converted to overall life expectancy using the declining exponential approximation for life expectancy method to estimate excess mortality attributable to disease. This method uses a competing risks for mortality model in which risks of mortality are a function of age [29]. Because older patients have multiple competing risks for death, the absolute effect of a new diagnosis on life expectancy is often relatively small. The prevalence of each pathologic stage for suspected clinical stage 1 disease (T1N0M0) was based on the American College of Surgeons, Oncology Group Z4031 trial [19]. A prior publication by Gould and colleagues [28] was the source for utilities associated with patient health states arising from procedures and the complications associated with those procedures.

**Baseline and Sensitivity Analysis**

Baseline estimates were used to calculate outcomes for the model. One-way sensitivity analyses were performed by varying single variables across clinically plausible ranges to assess changes in cost-effectiveness of modeled strategies and to identify potential thresholds at which the preferred treatment option would change. Two-way sensitivity analyses were performed by varying two factors simultaneously to assess whether the optimal treatment strategy changed within clinically plausible values. Incremental cost-effectiveness ratio is used to compare the cost-effectiveness of different treatments and indicates the additional cost required to gain one additional QALY. Differences in the incremental cost-effectiveness were expressed as an incremental cost-effectiveness ratio and were calculated using the additional cost associated with a diagnostic decision and its associated net increase or decrease in quality-adjusted life.

**Results**

The FDG-PET had the lowest expected cost for diagnosing patients ($10,410) with an expected QALY of 14.12 (Table 3). Compared with FDG-PET, patients diagnosed using NB incurred an expected incremental cost of $191 to obtain an additional 0.05 QALYs and resulted in an incremental cost-effectiveness ratio of $4,602 per additional QALY. Diagnosis by CT-FNA had a similar cost ($193) and efficacy with a QALY of 14.17 as compared with FDG-PET and marginally higher QALY (<0.01) when compared with NB. Diagnosis by VATS had both higher

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Total Cost ($)</th>
<th>Incremental Cost ($)</th>
<th>QALYs</th>
<th>Incremental Effectiveness</th>
<th>ICER* ($ per QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base case scenario—65% prevalence of cancer</strong></td>
<td></td>
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<tr>
<td>FDG-PET</td>
<td>10,411</td>
<td></td>
<td>14.12</td>
<td>0.05</td>
<td>3,998</td>
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<td>CT-FNA</td>
<td>10,603</td>
<td>193</td>
<td>14.17</td>
<td>0.04</td>
<td>4,602</td>
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<tr>
<td>NB</td>
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<td>191</td>
<td>14.17</td>
<td>0.03</td>
<td>43,578</td>
</tr>
<tr>
<td>VATS</td>
<td>11,720</td>
<td>1,294</td>
<td>14.15</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td><strong>Base case scenario—50% prevalence of cancer</strong></td>
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<tr>
<td>FDG-PET</td>
<td>9,256</td>
<td></td>
<td>15.55</td>
<td>0.03</td>
<td>9,533</td>
</tr>
<tr>
<td>CT-FNA</td>
<td>9,542</td>
<td>286</td>
<td>15.58</td>
<td>0.03</td>
<td>7,333</td>
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<tr>
<td>NB</td>
<td>9,476</td>
<td>220</td>
<td>15.58</td>
<td>0.03</td>
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<tr>
<td>VATS</td>
<td>11,623</td>
<td>2,367</td>
<td>15.54</td>
<td>−0.02</td>
<td>−118,350</td>
</tr>
</tbody>
</table>

* Incremental cost-effectiveness ratio is the ratio of the differences in the cost of decisions divided by the increase in QALY, where FDG-PET is the reference decision (Cost_{decision} − Cost_{FDG-PET})/QALY_{decision} − QALY_{FDG-PET}.

**CT-FNA** = computed tomography-guided fine-needle aspiration; **FDG-PET** = 18F-fluoro-deoxyglucose positron emission tomography; **ICER** = incremental cost-effectiveness ratio; **NB** = navigation bronchoscopy; **QALY** = quality-adjusted life year.
expected cost of $11,720 and a lower effectiveness (14.15 QALYs), and the other two biopsy strategies provided higher QALYs at a lower cost than VATS biopsy.

In sensitivity analysis of individual model components, decreasing the diagnostic yield of NB to less than 54% causes FDG-PET to be preferred. When the diagnostic yield of NB is greater than 65%, then tissue acquisition by NB is the preferred decision for diagnosis. Similarly, for CT-FNA, increasing the diagnostic yield to 85% caused it to be preferred over FDG-PET or NB; however, FDG-PET was preferred when CT-FNA diagnostic yield dropped to less than 70%. When FDG-PET sensitivity was fixed at 87% and the specificity of an FDG-PET scan fell to less than 72%, then CT-FNA or NB were the preferred diagnostic strategies. When the sensitivity of FDG-PET was greater than 94% and specificity was fixed at 77%, then FDG-PET was less costly than tissue biopsy or surgery and similarly effective.

In two-way sensitivity analysis, FDG-PET remained the least costly diagnostic strategy across all combinations of sensitivity between 80% and 100% and specificity between 60% and 90% (Fig 2). Efficacy for FDG-PET ranged from 14.08 to 14.22 QALYs across these combinations of sensitivity and specificity. Diagnosis by FDG-PET was the most effective and least costly strategy at the upper ranges of sensitivity and specificity when expected QALYs exceeded 14.17.

When the risk of malignancy was decreased to 50% in the base case, then all estimated QALYs increased, making the non-VATS strategies similar in efficacy (Table 3). The cost of care for each diagnostic modality was lower compared with the model with higher prevalence of lung cancer (Table 3). Both FDG-PET and CT-FNA were the preferred strategies compared with NB and VATS biopsy, although the difference between CT-FNA and NB in overall cost-effectiveness was negligible. Sensitivity analysis on single diagnostic components when cancer prevalence was 50% was similar to that observed when the prevalence of malignancy was 65%.

Comment

In clinical practice, surgeons are frequently asked to see patients with suspicious lesions. Based on American College of Chest Physicians 2013 guidelines, an estimation of the likelihood of cancer should be made first and the subsequent workup follow this estimation [3]. Predictive models such as the Mayo Clinic model exist to help clinicians but these cancer risk prediction models are poorly calibrated for the higher prevalence of cancer a surgeon encounters, so we are left with our best clinical judgment [30]. In the diagnostic algorithm presented in the updated guidelines, patients with a probability of cancer in the 5% to 65% range needed a diagnostic workup such as FDG-PET or a noninvasive biopsy (CT-FNA or NB). Patients who have greater than a 65% likelihood of cancer were recommended to go to VATS biopsy. In this study, we focused on the patient with a 65% likelihood of cancer for whom a difficult decision exists between VATS or further diagnostic workup. We also performed sensitivity analyses for cancer likelihoods between a 50% and 85% range to represent the cancer prevalence range frequently encountered in surgical practices. Within these cancer likelihood and practice prevalence patterns, we varied the model variables to determine the important drivers of the outcomes.

In populations in which the prevalence of lung cancer is at least 65%, we found that pursuit of tissue diagnosis with biopsy (CT-FNA or NB) was more cost-effective than FDG-PET or VATS. The method of biopsy made little difference in effectiveness as measured by quality of life. Navigation bronchoscopy is slightly less expensive than CT-FNA in this analysis owing to fewer complications, but given the range in costs of each method, they are equivalent in this scenario. The use of CT-FNA or NB is highly dependent on both clinical expertise and physical accessibility of the nodule to the proposed modality. For 1.5- to 2.0-cm nodules, centralized location, lesions distant from an airway, or smaller lesions increase the likelihood of a nondiagnostic biopsy and decrease the efficacy of their respective diagnostic modalities [4, 31]. In our model we assumed that 85% of nondiagnostic biopsies would be followed by VATS biopsy. The aggressive pursuit of tissue diagnosis is logical in populations in which the prevalence of malignancy is
high, as we assumed here. The increased quality of life after tissue biopsy (0.05 QALYs) compared with imaging was modest; however, the less than $200 cost for this increase of life was modest as well. Instituting a strategy of aggressive tissue diagnosis in a population with a moderate to high likelihood of cancer would result in a gain of about 1 QALY per 20 patients, assuming an increase of adjusted life years of 0.05, treated at a modest cost of an additional $4,000 to Medicare for those 20 patients.

In sensitivity analysis, the preferred strategy of tissue biopsy did not change when the prevalence of morbidity and mortality from VATS ranged from 0.5 to 2.5 times the reported rates found in the literature [21-23]. Use of VATS biopsy for diagnosis was not preferred over other diagnostic methods unless the prevalence of malignancy was greater than 85% (data not shown). In our base-case scenario, VATS biopsy for diagnosis became competitive as a diagnostic strategy but remained inferior to CT-FNA or NB when the likelihood of mortality dropped to half that observed for wedge resection (0.6%) and lobectomy (1.1%). Variables materially influencing diagnostic method choice were the rates of nondiagnostic biopsy for NB and CT-FNA and the sensitivity and specificity of FDG-PET. Increases in diagnostic yield by 6% for NB and 7% for CT-FNA caused each modality to be preferred over FDG-PET. Comparable decreases in diagnostic biopsy yield made FDG-PET preferred. As the prevalence of lung cancer decreases, the noninvasive FDG-PET scan becomes more effective as a lower cost alternative to tissue diagnosis. However, surgeons should also consider tissue acquisition strategies even in instances when the likelihood of cancer is lower (50%) if there is reason to believe that the accuracy of FDG-PET is reduced as a result of smaller lesion diameter or high rates of false-positive scans.

Following the recommendations of Gold and colleagues [26], we used Medicare-reimbursable charges when possible to estimate the relative cost of performing a procedure or diagnostic test. The lack of uniformity of costs or charges across providers required reliance on published reimbursement from Medicare and a perspective that can be considered from the payers’ perspective. Societal costs arising from lost workdays, transportation costs, and waiting-induced anxiety were not included in this analysis. One weakness of our study was the use of QALY data from previous studies in lung cancer and cancer treatment rather than direct estimation of utilities from surgery patients. We assumed that the stress from watchful waiting would be equivalent to that incurred from a benign pathologic diagnosis after VATS wedge biopsy. Our analysis of the preferred diagnostic strategy may not be applicable to nodules less than 1.5 cm in which the sensitivity of FDG-PET is lower, the diagnostic yield of FNA and NB decreases, and the risk of lung cancer is lower. Conversely, FDG-PET accuracy and diagnostic yields of biopsy likely increase for nodules greater than 2 cm in diameter.

When evaluating a suspicious lung lesion, surgeons should first provide their best estimate of the likelihood of cancer. Guidelines suggest using either a validated clinical risk model, like the Mayo Clinic model, or physician expertise to estimate a lesion’s risk for cancer. Based on our effectiveness model, if the likelihood of cancer approaches 85%, VATS would be the most cost-effective choice. If the likelihood of cancer is 50% to 85%, then a tissue acquisition is best. Navigational bronchoscopy should be used when expected diagnostic yield is greater than 65%, and CT-FNA is chosen if its expected yield is greater than 85%. If the lesion has an estimated likelihood of cancer less than 50%, then FDG-PET is a cost-effective option provided that the sensitivity and specificity are greater than 87% and 76%, respectively.

Navigational bronchoscopy and CT-FNA diagnostic strategies were more cost-effective than VATS biopsy or FDG-PET strategies in the workup of a 1.5- to 2-cm nodule in populations with lung cancer prevalence greater than 50%. In circumstances in which FDG-PET accuracy is reduced, the cost-effectiveness of FDG-PET scans for diagnosis of lung cancer may be reduced. Selection of a predefined diagnostic strategy using the surgeon’s estimate of the likelihood of lung cancer and the accuracy of the diagnostic tests available will be cost-effective and may result in fewer nontherapeutic operations.

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References

DISCUSSION

DR BRYAN F. MEYERS (St. Louis, MO): Nice job on your presentation. I have followed your work. I think Dr Grogan does a great job with this type of analysis of what we do in clinical practice. I think this type of work is very important because it allows us to look simultaneously at all aspects of the whole process of taking care of a patient and then focus on the multiple decisions we make and try to figure out where our weakest area of decision-making lies.

With these cost-effectiveness studies, which I think are quite valuable, there are times where the differences in effectiveness are so small that it actually becomes a different type of a study. I did the quick math on your survival estimates and they describe days, less than a month, of survival difference for all the different pathways, so it really then becomes a cost-reduction study rather than a cost-effectiveness study because the effectiveness is essentially equivalent. How big of an effectiveness difference do you think there ought to be in order to consider the effectiveness as part of the answer?

DR GROGAN: That’s a great question. Let me see if I can actually go back. This is sort of the way that my statisticians buried me beneath the $50,000 to $100,000 limit. So the...

DR MEYERS: To elaborate a little on that slide, a QALY is a quality-adjusted life year, and so if you just assume that the
quality of life scores are the same for all paths, you are really looking at years of survival from the point of the decision-making. If you need to go 2 digits beyond the decimal point to show a difference, one tenth of a QALY is 30 days and one one-hundredth is 3 days.

DR GROGAN: Right.

DR MEYERS: So you are looking at really 15 days of survival difference between arms. So it’s a cost study more than anything else.

DR GROGAN: It is, and that is a great point. So when you look at these two strategies, which it’s decimal-point differences, it doesn’t matter, but when you start comparing this and you start comparing the cost and the effectiveness, then the incremental cost-effectiveness ratio starts to matter. I think your point is excellent. That’s one of the reasons why we did the sensitivity analysis with FNA (fine-needle aspiration) and navigational bronchoscopy, because then it becomes what is the best strategy as clinicians. When I look at the lesion, am I going to have a bronchoscopy, because then it becomes what is the best strategy cost-effectiveness ratio starts to matter. I think your point is comparing the cost and the effectiveness, then the incremental cost-effectiveness ratio starts to matter.

DR MEYERS: And that is my other question. When the survival is identical and the costs are pretty close, I mean the difference of $191, I think the sequential compression boots to prevent DVTs (deep venous thrombosis) cost more than that, so you are finding that the differences are small. Then it falls to local expertise. If you have a radiologist who is really good or really lousy at your local hospital, that’s going to affect your decision-making here: local strengths and weaknesses rather than some global answer.

DR GROGAN: That is correct. The other thing that we can’t forget is actually PET (positron emission tomography) and the accuracy of PET. PET where we are is not as good. When you start varying the sensitivity and specificity of PET at your local institution, then it becomes less and less attractive as an option.

Your points are well taken and I have followed your work as well and I appreciate your comments.

DR MEYERS: Thank you.

DR KAMAL G. KHALIL (Houston, TX): Congratulations on considering cost as part of the decision tree. The problem I have is a patient with a central solitary lesion who had negative tissue sampling by limited means. You take him to VATS (video-assisted thoracoscopic surgery). You can’t do VATS on a central lesion. Would you then do a lobectomy for diagnosis or would you back off and observe?

My second question is the medicolegal implications of depending on limited sampling that is negative and then a year later you come back with metastases and so forth.

DR GROGAN: That’s a great question. It’s hard to take a case-by-case basis because our decision making is all driven by the likelihood and the probability that we as clinicians feel that this lesion is cancer, and that can only drive how willing we are to wait and watch this, and if there is a high probability of cancer, there are other options, such as navigational bronchoscopy, that are a possibility. A lobectomy is still well within the realms of our diagnostic capabilities to perform for a highly suspicious lesion. However, I think all of us are starting to see, even from a medicolegal perspective, cases of physicians being sued for benign diagnoses and doing lobectomies. So all of these things must be balanced and I’m not sure I have the perfect solution for that.

DR LAURIE B. REEDER (Warwick, RI): Did size play any role in the differences? I mean it’s a wide range from 0.8 to 3.

DR GROGAN: Correct. Size is actually very problematic from a decision analysis modeling standpoint, which is why we focused on that size, less than 2 cm, basically between 1.5 and 2 cm. As you start to vary the size, the probabilities change. So I can’t comment for the smaller lesions or the larger lesions. I can really only comment for the ones that we modeled here. But that is a very good question.


We had some experience with this back in the dark ages of 1998 when we looked at PET and ways to diagnose mediastinal lymph nodes. Decision analysis is a very sensitive tool and the assumptions are very important. In the watch-and-wait arm of the analysis, the number of tests can add up and lead to increasing expenses for multiple CT (computed tomography) scans and other tests. Did you assume that there would be just one CT scan, three CT scans?

DR GROGAN: We assumed following for up to 2 years, and when we put our model together, we made some assumptions about serial CT scans at 3-month and 6-month intervals and tried to put that in from a cost perspective. When you model that, though, as you can see, the watch-and-wait strategy is really in all of the trees, so when you change that number, if you change it in all of them, it kind of washes out in the model, if that makes sense.

DR SCOTT: I see. Again, nice work. Thank you.

DR LARRY L. STEPT (Pittsburgh, PA): On the CT-fine-needle aspiration and on the navigational bronchoscopy, you said that 85% of the people eventually went to VATS or some sort of invasive diagnostic procedure. Is that because 85% of the people had a positive tissue diagnosis or is that because in 85% you eventually had to do something in order to get to the bottom of this lesion?

DR GROGAN: That’s a great question. Let me see if I can go back here real quick. With regard to the model itself, we modeled the nondiagnostic and diagnostic probabilities of CT-FNA. So you could say 60% of the time you had a nondiagnostic biopsy rate. If you are at our institution, our radiologists for CT-FNA, it seems like it’s even higher than that. In this probability for the nondiagnostic, then you can model the VATS probability, and we chose a very conservative estimate that 85% of the time, because this is a suspicious lesion, I’m not going to trust that negative or the nondiagnostic FNA. I’m going to go to VATS because I’m worried about this lesion. So this is a conservative approach, and when we did sensitivity analyses, it didn’t seem to change our results when you varied that number.

DR STEPT: And of those patients who went to VATS because they were in the watch-and-wait, what percentage of those patients actually turned up with a malignant diagnosis?

DR GROGAN: In the model, then, and this is based on the probability of a 65% chance of being cancer, you can go back to that A category, which is the VATS model, and model the probabilities that it’s going to be 35% cancer and 35% benign
disease. So it’s a model and there are limitations, but we did our best.

DR THOMAS K. WADDELL (Toronto, Ontario, Canada): I enjoyed it as well. It was very well done.

My question is about the sensitivity analysis about the basal prevalence estimate. You set up the question very nicely from the CT screening, but I think it’s worth remembering that the prevalence of cancer in the screened group is about 1%, the prevalence in the group that has a nodule is only 4%, and you presented that algorithm where right at the beginning there was a certain strategy, but then you did the modeling on 65%.

DR GROGAN: That’s a great question. I didn’t have time to present this, but if you change the base scenario to 50% prevalence of cancer—.

DR WADDELL: I would like to know if you modeled it down to 5%.

DR GROGAN: But those aren’t the people that I’m seeing as a surgeon. That’s a good point, but I had to pick something, so I chose the suspicious lesions, and as you get down to 50%, PET becomes more and more a better option for diagnosis. It’s more and more cost-effective. Once you get up to above 80% to 85%, VATS actually becomes the best strategy. So we have got a little bit more work to do to figure out sort of what these breakpoints are and where the best options are for us as surgeons. But I can tell you that clinically, this will drive my practice a little bit. I will be doing a lot more tissue-acquisition strategies because it does appear to be more cost-effective for those intermediate lesions.

DR WADDELL: I am really surprised if you say that you are seeing patients at the 50% from the screening program, because that means somebody else, radiologists or pulmonary people, are removing 90% of the false positives, in which case I would like to know what strategies they are using. It sounds like they are doing a very good job.