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Economic analysis of combined endoscopic and endobronchial ultrasound in the evaluation of patients with suspected non-small cell lung cancer

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ABSTRACT

Lung cancer remains the most common cause of cancer-related death in the United States. This study evaluated the costs of alternative diagnostic evaluations for patients with suspected non-small cell lung cancer (NSCLC). Researchers used a cost-minimization model to compare various diagnostic approaches in the evaluation of patients with NSCLC. It was less expensive to use an initial endoscopic ultrasound (EUS) with fine needle aspiration (FNA) to detect a mediastinal lymph node metastasis ($18,603 per patient), compared with combined EUS FNA and endobronchial ultrasound (EBUS) with FNA ($18,753). The results were sensitive to the prevalence of malignant mediastinal lymph nodes; EUS FNA remained least costly, if the probability of nodal metastases was <32.9%, as would occur in a patient without abnormal lymph nodes on computed tomography (CT). While EUS FNA combined with EBUS FNA was the most economical approach, if the rate of nodal metastases was higher, as would be the case in patients with abnormal lymph nodes on CT. Both of these strategies were less costly than bronchoscopy or mediastinoscopy. The pre-test probability of nodal metastases can determine the most cost-effective testing strategy for evaluation of a patient with NSCLC. Pre-procedure CT may be helpful in assessing probability of mediastinal nodal metastases.

1. Introduction

Lung cancer remains the most common cause of cancer death in the United States. The optimal treatment for patients with non-small cell lung cancer (NSCLC) is surgical resection. Unfortunately, metastatic involvement of mediastinal lymph nodes (stage III disease) precludes surgery in most cases; N2 disease is defined as involvement of the ipsilateral mediastinal lymph nodes, while N3 disease involves contralateral nodes. The 5-year survival rate for patients with N2 disease detectable on preoperative computed tomography (CT) is universally poor after surgical resection, ranging from 3% to 8% [1–7]. Consequently, it is crucially important to detect stage III disease, so that these patients may avoid unnecessary surgery.

Although thoracic CT is the most commonly used non-invasive staging modality of the mediastinum, it cannot always reliably differentiate between benign and malignant mediastinal nodes, as enlarged nodes may also be inflammatory, whereas normal-sized lymph nodes may contain malignancy [8–20]. Procedures that facilitate sampling of mediastinal nodes, such as endoscopic ultrasonography (EUS)-guided fine-needle aspiration (FNA), endobronchial ultrasound (EBUS) FNA, mediastinoscopy and transbronchial needle aspiration (TBNA), have become established means for tissue confirmation. EUS FNA of posterior mediastinal lymph nodes is a highly accurate modality for cytodiagnosis [11,21–36]. Mediastinoscopy, on the other hand, offers visualization as well as tissue diagnosis of accessible lymph node stations, but is an invasive procedure, carries a substantial cost, and has a small but definite morbidity [12,14,19,35,37–43]. TBNA has been used to evaluate suspicious subcarinal, paratracheal and hilar lymph nodes [42–53], but its blind approach is a limitation. More recently, EBUS FNA has emerged as an approach to overcome this limitation [54–56].

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This study aimed to compare the costs of alternative diagnostic approaches in modeled patients with non-small cell lung cancer (NSCLC), using a cost-minimization approach.

2. Methods

We used standard decision analysis software (DATA 3.5, TreeAge Software Inc., Williamstown, MA) to construct our decision model (Fig. 1). Decision analysis uses data available in the medical literature to produce a model of possible outcomes associated with a particular disease, in order to facilitate the determination of the most economical health care strategy, among different alternatives. The model attaches costs and health outcomes to each health state, and estimates the total costs and outcomes associated with a particular health care strategy.

A cost-minimization analysis, which assumes that competing diagnostic strategies have equivalent outcomes, is the most appropriate form of economic analysis to use in this setting. The benefit of each diagnostic test lies in their respective abilities to detect malignant mediastinal lymphadenopathy, i.e., to detect stage III disease. Detecting stage III disease is useful because it prevents subjecting the patient to a more expensive procedure (thoracotomy) to achieve the same endpoint. Recognizing that:

- There is a well-defined outcome in each arm of our decision model (detection of stage III disease).
- The long-term outcomes (i.e., measure of effectiveness) are equivalent in each model arm, i.e., the survival of all patients with stage III disease is similar regardless of how the disease extent was diagnosed.
- The downstream costs of medical care in patients with stage III disease are similar in all arms, once the extent of disease has been established.

This ensures that a cost-minimization approach is most appropriate. We assumed that each of the FNA techniques has perfect specificity; i.e., no false-positive FNA results. Therefore, no patient would mistakenly forgo potentially life-saving treatment, and each strategy would be equally effective in clinical patient outcomes.

2.1. Patient model

The model assumed a patient diagnosed as having either (1) verified NSCLC or (2) suspected NSCLC, based on a primary pulmonary mass with or without enlarged mediastinal lymph nodes detected by CT. The seven main branches of the tree represent the management options: (1) mediastinoscopy with biopsy of any visualized lymph nodes; (2) EUS FNA of any visualized lymph nodes; (3) EBUS FNA of visualized lymph nodes; (4) TBNA biopsy of any lymph nodes seen on CT; (5) combined EUS FNA and EBUS FNA; (6) combined EUS FNA and TBNA; (7) combined EBUS FNA and TBNA. Pathologic evidence of benign nodal tissue on FNA prompted thoracotomy, which provided a view to surgical resection. The false-negative rates of each FNA procedure determined the likelihood of malignant disease being found at surgery. A positive biopsy at sampling confirmed stage III disease and precluded thoracotomy.

2.2. Assumptions

The model is based on a series of assumptions:

1. Patients referred for mediastinoscopy, EUS FNA, EBUS FNA and TBNA are clinically similar.
2. All patients underwent initial luminal bronchoscopy; only patients in the TBNA study arms underwent bronchoscopic FNA.
3. All patients have undergone CT and PET scanning prior to invasive staging in order to guide further management.
4. The aim of each procedure is to detect nodal metastases. However, there is no reason to preferentially favor performance of one procedure over another.
5. Detection of mediastinal nodal metastases signifies stage III disease and precludes thoracotomy.
6. For calculation of pathology interpretation costs, one cytology sample was acquired in patients undergoing TBNA; two cytology samples were acquired in patients undergoing EUS FNA, EBUS FNA or mediastinoscopy while three separate cytology samples were acquired in patients undergoing combination procedures.
7. The following procedure-related complication rates requiring hospitalization were assumed: EUS FNA and EBUS FNA and TBNA, all 0.5% [23–36,43–59], mediastinoscopy, 2% [35,37–42] and thoracic surgery, 8% [60].
8. EUS FNA/EBUS FNA/TBNA combination procedure sensitivities vary linearly with changes in sensitivity of the individual component procedures.
9. Because 50–60% of patients undergoing mediastinoscopy with an indication of NSCLC in our institution do so as hospital inpatients, 50% inpatient plus 50% outpatient reimbursement rates were used to represent the direct costs of mediastinoscopy.
10. The total cost of a procedure-related complication was calculated using the diagnosis related group (DRG) for hospitalization of a patient with NSCLC.
11. The positive predictive value of a cytologic finding of malignancy is 100%.
12. From a Bayesian perspective, the initial FNA test result and the subsequent histologic examination of tissue from mediastinoscopy with biopsy are independent tests when used sequentially for diagnostic purposes in the sense that the two tests are independent given disease state.

2.3. Baseline costs

The base-case analysis took the payer's perspective expressed in US dollars, based on 2007 Medicare reimbursement rates. Direct medical costs were estimated from Medicare ambulatory patient classification (APC) payments (combined professional plus facility fee) for hospital-based outpatient procedures. Inpatient hospital facility fees were calculated as the amount Medicare pays, based on assignment to a DRG, for a patient with a diagnosis of NSCLC. In the case of hospitalization required for a procedure-related complication, the facility fee component was calculated using the DRG for hospitalization for a post-procedure complication. This amount remains constant regardless of the nature of the complication, e.g., hemorrhage, infection, and perforation. The professional fee component was calculated using the CPT codes for the initial consultation, daily physician visit, and discharge consultation. The total cost for each procedure is obtained from the following formula: [(cost of procedure without complications) (1 − complication rate)] + [(cost of procedure with complications) (complication rate)]. Taking into account the procedure complications in this way provides a precise estimation of costs involved. Costs for outpatient visits and hospitalizations are illustrated in Table 1.

Direct costs were used in preference to charges or total costs because direct costs reflect true resource utilization better and tend to be more generalizable. Indirect health and institutional costs, such as the cost to society for lost work, quality of life, and institutional administration or maintenance of buildings or costs involved in the original diagnosis were not included. Discounting was not performed as the diagnostic evaluation only lasts several days.