Lung Cancer Detection in Patients With Airflow Obstruction Identified in a Primary Care Outpatient Practice*

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Introduction: **This prospective study describes a community-based lung cancer identification project focusing on high-risk patients who receive general care in a primary care outpatient practice. Within 1 calendar year, a simple questionnaire was completed in 1,296 patients > 50 years old to identify 430 patients at high risk of lung cancer (smoking, family history of aerodigestive tract cancer, or occupational exposures). Spirometric abnormalities were found in 126 of these patients.**

Methods: **Chest posteroanterior radiographs, thoracic CT scans, and sputum cytology were offered to subjects with airflow obstruction (n = 126). Eighty-eight patients underwent all tests. Thirty-eight patients refused or could not consent in a timely fashion.**

Results: **Six cancers were found in the screened group, and all were treated. Two more cancers were found in the nonscreened patients with airflow obstruction. Both were treated by surgical resection or radiation therapy. Costs per cancer found were $11,925 per patient.**

Conclusions: **Case finding in high-risk patients in a primary care population can be accomplished at a relatively low cost.** (CHEST 2005; 127:1140–1145)

***Key* words:** airflow obstruction; community detection; costs; lung cancer

Abbreviations: FNA = fine-needle aspiration; PCP = Primary Care Partners

Lung cancer continues to be the most common fatal malignancy in the United States in both men and women. The old dogma is that lung cancer detection by chest radiography and patient symptoms is ineffective, resulting in a 5-year survival rate of only 15%. Currently, there are no national or international guidelines for lung cancer screening. Studies from the Early Lung Cancer Action Project,[1,2] Mayo,[3] and Japan,[4] however, show that chest helical CT scans are more sensitive than standard chest radiographs in the detection of lung nodules and cancer.]-[4] This report describes a project designed to identify individuals at high risk for lung cancer in a family practice clinic setting, and to detect lung cancer in this high-risk group.

MATERIALS AND METHODS

Study Design

Patients who visited their primary care physicians for a variety of health-care issues but not primarily for respiratory complaints were asked to fill out a one-page questionnaire designed to identify individuals at high risk for lung cancer. Criteria for high risk of lung cancer were age ? 50 years old, and one of the following: (1) current or ex-cigarette smoker,

30 pack-years; or (2) an occupational exposure to asbestos or coal dust; or (3) a family history for esophageal, lung, or laryngeal cancer (so-called aerodigestive cancer). Patients at high risk for lung cancer underwent simple spirometrv. Those who were found to have airflow obstruction were offered lung cancer detection studies, which consisted of sputum cytology tests, chest radiographs_ and chest CT scans. This prospective study was approved by the St. Mary's Hospital Institutional Review Board, which approves research done within the St. Mary's Hospital Clinical System and the entire Western Slope of Colorado.

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Patient Population

Patients were enrolled from a busy 15-physician family practice group, Primary Care Partners (PCP) in Grand Junction, CO. Grand Junction is a rural town of 40,000 population with a drawing area of 250,000 persons. There were 52,336 patient visits to PCP from January 2001 through December 2001, the 1-year duration of the project. These included 14,459 visits by patients > 50 years old; 1,296 questionnaires were completed (Fig 1). Four hundred thirty of these questionnaires were indicative of high risk. From these 430 questionnaires, 126 patients showed spirometric abnormalities; of these, 88 high-risk patients were screened (80 by smoking history, 6 by occupational history, and 2 by family history) [one lung cancer and one esophageal cancer]. Many patients were seen more than once during the year.

Testing Methods

Spirometry was performed by trained nurses in the PCP offices on the same day of the office visit. American Thoracic Society standards were followed, and airflow obstruction was diagnosed in patients with FEV_1 < 70% of predicted and < 70%. Posteroanterior and lateral chest radiographs were performed in standard fashion, and overread by two physicians. Sputum cytology examinations consisted of induced and spontaneous coughed specimens prepared and analyzed using the Saccomanno technique. All sputa were interpreted by qualified sputum cytopathologists (G.K. and D.S.). Chest CT scans were performed on individuals using a helical CT scanner (GE Lightspeed QXI; GE Healthcare Technologies: Waukesha, WI), taking noncontrast, 7.5-mm, sequential images. These were indepen-

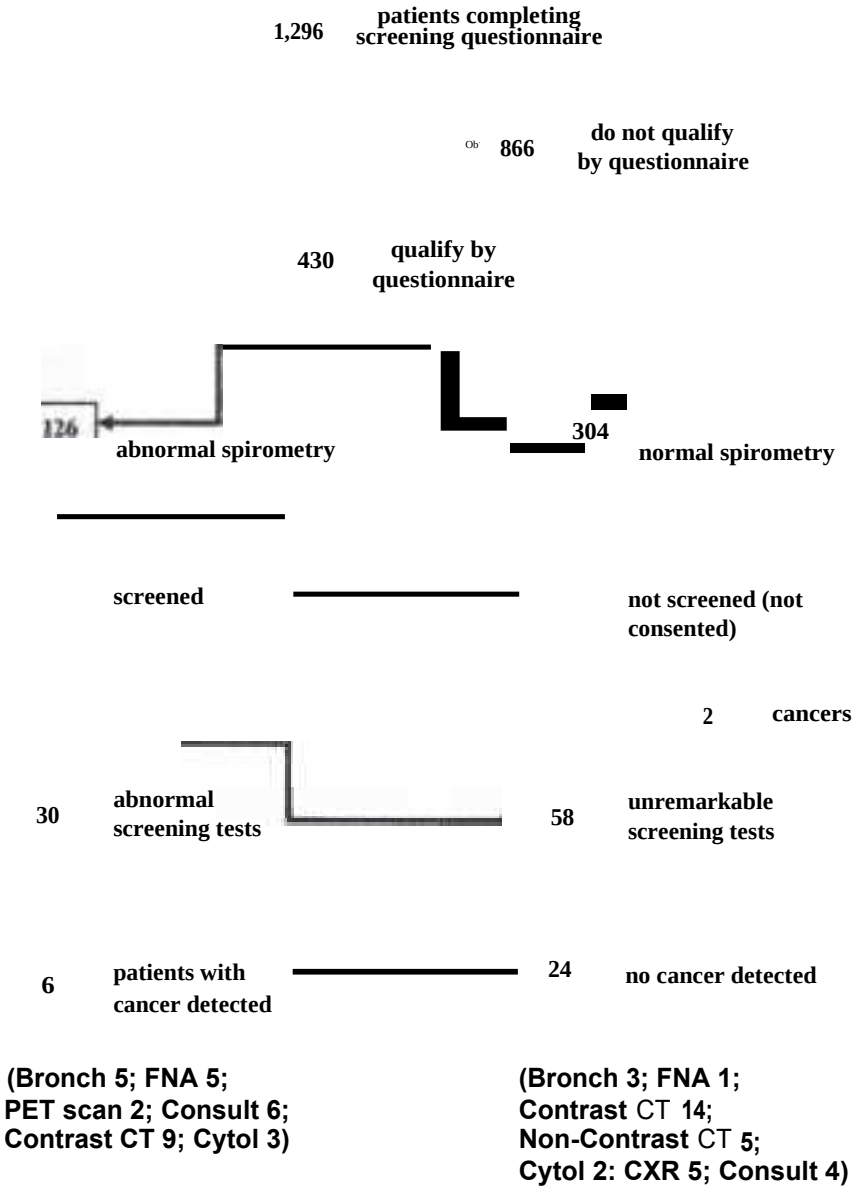

FIGURE I. Patient population for the Early Lung Cancer Detection Study. Bronch = bronchoscopy; CXR = chest radiography. Cytol = cytology; PET = positron emission tomography.

dently overread by a second radiologist and a pulmonologist who did not know the results of the initial readings. Patients with suspicious sputum cytology, abnormal chest radiographic findings, or worrisome nodules on CT scan were either monitored by their family physician with follow-up studies or referred to a pulmonologist for evaluation.

RESULTS

Eighty-eight of the 126 patients who qualified for cancer "screening" (imaging and cytology) based on high-risk history and airflow obstruction were studied. Two of the remaining 38 patients could not be scheduled for the consenting process in a timely fashion, but lung cancer was subsequently diagnosed; others refused to undergo screening tests for personal reasons. The majority of screened patients completed all tests (Table 1).

Thirty of the 88 screened patients showed radiologic or cytologic abnormalities requiring diagnostic procedures or follow-up studies. Primary lung cancer in six of these high-risk patients was diagnosed using surgical biopsy[5] or fine-needle aspiration (FNA) biopsy (Tables 2, 3).[1] CT size for the nodular lesions is listed in Table 2 (0.9 to 2.5 cm). One endobronchial lesion was 1-mm thick with extensive local endobronchial spread. Diagnoses were made in four patients at the initial testing, while diagnoses in the other two patients (patients 5 and 6, Table 2) were made when follow-up CT scans showed growth of a suspicious nodule. Biopsies were not performed initially in these two patients because of clinical concerns; one patient showed pulmonary silicosis with multiple nodules on CT scan (patient 5), and the other patient was an elderly woman with advanced emphysema (patient 6). All six patients with cancer underwent surgical resection or radiation therapy for cure. The remaining 24 of the 30 patients with screening abnormalities showed no evidence of cancer on biopsy or follow-up studies (Fig 1).

Table 1—*Patient Visits to PCP for 1 Year and Studies Performed**

Variables	Data
Total patient visits to PCP	52,336
Patient visits > 50 years old	14,459
Questionnaires completed	1,296
High-risk patients qualifying for spirometry	430
Patients with airflow obstruction eligible for screening	126
Patients screened	88
Completing chest radiography	88 (100)
Completing at least one cytology	78 (89)
Completing CT scan	87 (99)

*Data are presented as No. or No. (%).

Of the 38 patients with spirometric abnormalities who were not screened, two additional cancers were found on radiograph follow-up. Both patients received surgical resection.

Cost Analysis

The cost for the initial screening of the 430 high-risk patients identified by the questionnaire was $50,055. The cost of diagnosis in six patients with lung cancer was $12,632, and the cost of follow-up studies for the 24 high-risk patients with abnormal initial screening tests was $8,861. The total cost to screen, follow-up abnormal test results, and diagnose lung cancer was $11,925 per patient detected with cancer (Table 4). The costs recorded in this article are actual costs based on Medicare reimbursement rates for our region, and include hospital. radiology, and pathology technical fees and physician professional fees. Screening CT scans and cytology costs were negotiated at Medicare reimbursement rates.

Preliminanj Follow-up

Patients 1, 2, and 3 are alive without evidence of recurrences 2 to 3 years after diagnosis. Patient 4 died of heart failure after coronary artery bypass 2 years after diagnosis. Patient 5 died of silicosis, COPD, and lung cancer. Patient 6 died of emphysema. One of the two patients who did not consent is alive after 2 years; one patient is dead.

A follow-up of all 430 high-risk patients both with airflow obstruction (n = 126) and with normal airflow (n = 304) is now underway. It will be the subject of a later report.

Comments

This was not a screening study for lung cancer. Instead, it attempted to find patients with previously unsuspected lung cancer in a general private practice setting.

The 6.8% lung cancer incidence (six cancers in 88 screened patients) found in this study is higher than reported elsewhere in a screening study.[5] This is attributed to the following three factors: (1) only high-risk patients > 50 years old with extensive smoking history or an occupation or family history risk were studied. Lung cancer certainly occurs in patients with fewer risk factors; however, this study focused on very high-risk individuals, *ie,* a "case management" approach. (2) High-risk patients were screened only if airflow obstruction measured by spirometry was present. Tockman et al[b] showed years ago that cancer was up to six times more common in smokers with airflow obstruction compared to smokers with normal lung function.

Table 2—Six *High-Risk Patients With Lung Cancer Detected by Screening Tests

Patient Therapy	Age, yr	Sex	Smoking, Pack-yr	Chest Radiograph Finding	Sputum Cytology Finding	CT Scan Finding (cm)	Diagnosis by Stage	Cell Type	Stage	Treatment
1	79	Female	45	Negative	Negative	Positive (2.1)	FNA	Adeno	II IA	R
2	70	Female	46	Positive	NA	Positive (2.5)	FNA	Adeno	IA	S
3	62	Male	76	Negative	Positive	Negative	Bronch	Squa	IA	S
4	62	Male	50	Positive	Negative	Positive (2.3)	FNA	Sq/Ad	3Cas	S/R
5	84	Male	12f	Negative	Positive	Positive (1.8)	Bronch	Adeno	IIIA	R
6	79	Female	40	Negative	Negative	Positive (0.9)	Bronch	Adeno	IA	R

*Adeno = adenocarcinoma; Bronch = bronchoscopy; FNA = fine-needle aspiration biopsy; NA = not able to produce sample; R = radiation therapy; Sq/Ad = squamous/adenocarcinoma; Squa = squamous cell carcinoma; and S = surgical therapy. An additional two patients who completed questionnaires and wanted to participate in the study, but were not allowed, were found to have primary lung cancer and have undergone treatment, but are not included here.

}Also occupational exposure to radon.

(3) Detection studies included chest CT scan, chest radiography, and sputum cytology analysis. Chest CT scanning is a powerful tool to identify lung lesions as shown in the Early Lung Cancer Action Project,[1,2] Mayo,[3] and several Japanese studies[4,5]; CT scanning detected the cancer in five of the six patients in this study. Our group has previously shown[6] that tiny endobronchial cancers not seen on radiography could be detected only by sputum cytology testing. The long-term survival of sputum-diagnosed lung cancer is > *50%* after *5* years.[3] One of the six cancers found here was identified only by cytology testing, with the screening CT scan and follow-up contrast CT scan findings both negative. *(4)* The *24* of 30 patients with screening abnormalities who did not show evidence of lung cancer on biopsy or follow-up represents an *80%* false-positive rate. This is lower but of similar magnitude to the false-positive rate reported in other studies[5] of as high as *98%.*

Based on the above observations, we conclude that identifying high-risk patients by questionnaire, and testing those who show airflow obstruction with CT scan and sputum cytology improves the results in a high rate of lung cancer detection. The cost of $11,925 per patient with lung cancer detected includes all costs for screening, diagnostic testing, and follow-up of abnormal findings in those with and without cancer.

Arguments have been made that lung cancer screening is not cost-effective.° These projections were made on the basis of many assumptions and concluded that the spending of *$42,000* for quality-adjusted life-year gained is the most favorable projection. It has generally been accepted for prevention and therapeutic intervention that *$50,000* per year of life saved could be accepted as cost-effective.[10] Our study does not include a computation of cost-effectiveness, because the number of patients and the follow-up is now between *2* years and 3 years at this writing, *ie,* incomplete. Also, the number of patients is small. The costs of care of lung cancer when diagnosed by symptoms or chest radiograph observation, *ie,* in late stages, was nearly *$50,000* per patient in 1998 dollars." Early diagnosis may improve on cost of later diagnosis of lung cancer.

The patients participating in the study were visiting their primary care physicians for routine health-care concerns, annual physical examinations, or a variety of acute and chronic illnesses. Only a few (estimated 10%) had respiratory complaints. The physicians, office staff, and patients were mostly enthusiastic about the study and concluded that the process involving questionnaires and spirometry performed at the time of the clinic visit was not too disruptive to patient care. No additional costs for the routine office visit and questionnaire were charged. This is a model that could be employed in many small or large family physician offices, with some adjustments.

The late outcome of all of the six patients (mean age, *72.6* years) [three patients with stage Ia lung cancer, two patients with stage IIIa lung cancer, and

Table *3—Demographics of 6 Patients With Lung Cancer Compared to 82 Patients Without Cancer*

Patients	Age, yr		Male/Female Gender, No.	Smokin , Pack-yr	FEV_1, % Predicted
	Range	Mean			
Without cancer (n = 82)	52—85	67.5	44/38	56	54.7
With cancer (n = 6)	62—84	72.6	3/3	45	51.5

Table 4—Costs to Diagnose Lung Cancer and Follow Up Patients With Screening Abnormalities but No Cancer*

Variables	Costs, US Dollars
Screening costs (430 patients)	
Office visits	NC
Spirometry (430 × $40)	17,200
Chest radiograph (88 × $51)	4,488
Sputum cytology (149 × $52)	7,748
Noncontrast CT scan (87 × $237)	20,619
Total	50,055
Cost to diagnose cancer (6 patients)	
Bronchoscopy (5 × $724)	3,620
FNA (5 × $557)	2,785
Positron emission tomography scan (2 × $1,375)	2,750
Consults (6 × $108)	648
Contrast CT scan (9 × $297)	2,673
Sputum cytology (3 × $52)	156
Total	12,632
Follow-up diagnostic tests; no cancer found (24 patients)	
Bronchoscopy (3 × $724)	2,172
FNA (1 × $557)	557
Contrast CT scan (14 × $297)	4,158
Noncontrast CT scan (5 × $237)	1,185
Sputum cytology (2 × $52)	104
Chest radiograph (5 × $51)	255
Consults (4 × $108)	432
Total	8,863
Costs summary	
Total costs	71,550
Costs to screen, diagnose, and follow up all 88 patients ($71,550 ± 6)	11,925 per cancer patient

*NC = no charge.

one patient with three cancers] will be determined by follow-up. A continuation of the long-term follow-up of the entire 430 patients at high risk is currently underway. The patients who were originally screened will undergo repeat CT and sputum cytology at year 3 and year 5 of the follow-up. The nonscreened subjects with airflow obstruction and those with risk factors but normal airflow will be followed up during their scheduled clinic visits for symptoms of lung cancer. Some will undergo chest radiographs for various indications. This follow-up is in keeping with the present standard of care in which no general screening is recommended.

The strengths and weaknesses of the study deserve comment. The main strength is that the study was done in offices of primary care practitioners during routine appointments for other medical problems (usually not respiratory symptoms). This was not a lung cancer screening study. It was a case-finding study limited to high-risk patients. A simple one-page standard questionnaire was used. By agreement, the study was limited to 1 calendar year, but the study enrolled all patients fulfilling the high-risk definition.

Weaknesses include of the study are as follows: (1) 38 of the 126 high-risk patients with airflow disorders refused or otherwise did undergo the screening tests. Two additional cancers were found in this group who did not consent in a timely fashion. All of these patients are available for follow-up, however. (2) The primary clinical diagnosis for each patient seen, which was sometimes multiple, was not systematically recorded. (3) It is possible that the Grand Junction community could be considered unique and not representative of the United States. This area is where modern sputum cytology became established, originally because of the large number of uranium workers with lung cancer in the region. Uranium has not been mined on the Colorado Plateau for nearly 30 years, but the community culture still remains alert to the possibility of diagnosing lung cancer early through sputum cytology. (4) Some costs were minimized due to agreements with St. Marv's Hospital and Rocky Mountain Health Maintenance Organizations, but actual cost dollars were recorded. It could be argued that our costs are inaccurate, as many of the diagnostic and screening tests were negotiated to a lower fee than usually charged. It must be noted, however, that these fees are equal to Medicare-allowed fees for our area, and most physicians accept these rates. (5) Because of the practice setting study design, there is no internal comparison (control group).

In conclusion, patients at high risk for lung cancer can be identified by questionnaire and spirometry in a busy family practice clinic. Lung cancer can be detected in high-risk patients using CT scans, radiographs, and sputum cytology. Chest CT scan was the most sensitive test to identify lung cancer in our patients; standard chest radiographs added little additional information.

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