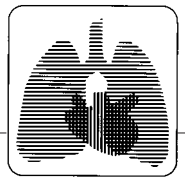

minimally invasive techniques

Predictors of Pleural Malignancy in Patients With Pleural Effusion Undergoing Thoracoscopy*

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Study objectives: **Thoracoscopic pleural biopsy is highly accurate in the diagnosis of pleural malignancy. However, no scientific evidence is currently available to guide the physician's decision as to when and in which patients with pleural effusion thoracoscopy is indicated. The application of predictive criteria of malignancy might improve the indication of thoracoscopy in patients with undiagnosed pleural effusion.**

Methods: **Prospective study of 93 patients referred for thoracoscopy at a tertiary hospital. Clinical variables were obtained prior to thoracoscopy by clinical history and review of previous data, patient interview, and physical examination. Radiologic variables were obtained by evaluation of chest radiograph and chest CT images by two independent readers. After thoracoscopy, all patients without a diagnosis were sent for long-term follow-up.**

Results: **Thoracoscopy demonstrated 94% sensitivity and 100% specificity in the diagnosis of pleural malignancy. Variables, which in a multivariate model are associated with pleural malignancy, include a symptomatic period > 1 month, absence of fever, blood-tinged pleural fluid, and chest CT scan findings suggestive of malignancy. Receiver operating characteristic analysis showed that the use of these four criteria offered adequate classification in 95% of patients. Twenty-eight patients had all four criteria, and all had malignancy; 21 patients had at most one criterion, and none had malignancy.**

Conclusion: **Clinical and radiologic criteria of patients with pleural effusion permit different risk levels for pleural malignancy to be distinguished. Consequently, application of the four proposed criteria permits better indication of thoracoscopy in patients with undiagnosed pleural effusion.**

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Key words: cancer; pleural effusion; thoracoscopy

Abbreviation: ROC = receiver operating characteristic

Pleural effusion is a manifestation of a variety of pulmonary and nonpulmonary conditions; however, consensus as to the tests that should be conducted in its diagnosis is not unanimous. Chest radiography and complete analysis of pleural fluid are performed in most patients, and a pleural biopsy is recommended in cases with no diagnosis.[1] Nevertheless, > 20% of patients with pleural effusion undergoing pleural fluid analysis and closed-needle pleural biopsy remain undiagnosed,[2–4] and in up to 22% of cases a diagnosis of neoplasia is posteriorly detected.[5]

Thoracoscopy, an established method in the diagnosis of pleural diseases, is highly sensitive for detecting pleural neoplasia with negative pleural fluid cytology and in the diagnosis of tuberculosis.[6] The possibility of visualizing the pleural cavity and obtaining directed biopsy specimens[7–9] accounts for

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the high performance of thoracoscopy in the diagnosis of pleural neoplasia, > 90%.[10] However, its precise indication in the workup of patients with pleural effusion remains controversial. In fact, in approximately half of the patients undergoing thoracoscopy, pleural biopsy does not demonstrate malignancy.[10,11] Since nonmalignant pleural disease may be diagnosed by noninvasive methods, the indication of thoracoscopy in patients with pleural effusion should be optimized.

The 2000 American Thoracic Society statement on management of malignant pleural effusions states that indications for performing thoracoscopy include "the evaluation of exudative effusions of unknown cause," among others, and that "in cases of undiagnosed exudative effusions with a high clinical suspicion for malignancy, some clinicians may proceed directly to thoracoscopy if the facilities for medical thoracoscopy are available."[12] Using clinical suspicion of malignancy to decide whether to perform thoracoscopy seems reasonable if the series of patients with undiagnosed pleural effusion are examined. In this series, malignancy was strongly suspected in the initial evaluation of patients in whom neoplasm was later detected[5,13,14]; and, alternatively, when malignancy was not initially suspected, it was detected in only 5% of the patients who were followed up.[15] However, what does "high clinical suspicion of malignancy" mean, and how can it be used in the workup of patients with undiagnosed pleural effusion? Patients with malignant pleural effusion present clinical differences compared with those with benign effusions[16,17]; however, the predictive value of malignancy of clinical variables has scarcely been studied. In a study of patients with chronic pleural effusion in whom a reduced number of variables was analyzed, blood-tinged pleural fluid was the single variable with the strongest positive predictability of malignancy.[16] Although it is therefore possible that clinical criteria may help physicians to improve the indication of thoracoscopy in patients with idiopathic pleural effusion, more data are required to confirm this possibility.

In the present study, a wide range of clinical and radiologic variables were used to predict malignancy in patients with pleural effusion referred for thoracoscopy. The hypothesis tested was that clinical predictors of malignancy permit a better indication of thoracoscopy in patients with undiagnosed pleural effusion.

Materials and Methods

All patients with pleural effusion consecutively referred for thoracoscopy to the Department of Thoracic Surgery between June 1993 and August 2001 were studied. The patients had been studied previously in respiratory and internal medicine departments on the decision of the attending physician, who indicated thoracoscopy. In all cases, this previous study included at least one thoracentesis with pleural fluid study (determination of glucose, proteins, lactodehydrogenase, adenosine deaminase, mycobacterial and cytologic examination, with total and differential counts and detection of neoplasic cells), chest radiograph, and chest CT scan.

Prior to thoracoscopy, patients were prospectively evaluated by one of the authors to obtain the clinical variables. Two readers unaware of the clinical history evaluated the radiologic images, and classification was obtained by consensus.

Thoracoscopy was performed with a standardized technique.[18]The macroscopic appearance of the pleura (pathologic/nonpathologic), days of hospitalization, and complications were recorded. Pleural samples were shipped for histologic study and cultured in Lowënstein-Jensen media for mycobacterial detection.

Diagnostic Criteria

Pleural effusion with neoplasic cells in pleural fluid and/or neoplasic infiltration in a pleural tissue biopsy sample was considered neoplasic. The diagnosis of malignant mesothelioma was made by histologic examination, histochemical techniques (positive periodic acid-Schiff diastase stain), and monoclonal antibodies (negative carcinoembryonic antigen and positive calretinin). Paramalignant effusion was defined as that occurring in a patient with neoplasia but with no evidence of malignancy in fluid or pleural tissue.[19] Pleural effusion with no evidence of malignancy in a patient with a history of asbestos exposure and in whom an alternative diagnosis was ruled out in a 3-year follow-up was considered a benign asbestos pleural effusion.[20] The diagnoses of tuberculosis and amyloidosis were based on the presence of caseating granulomas and amyloid in pleural tissue, respectively. Pleural effusion of unknown etiology after all diagnostic procedures was defined as idiopathic.

Clinical and Radiologic Variables

The following clinical variables were defined: sex, age, smoking, and asbestos exposure. Symptomatic variables were dyspnea, chest pain, and toxic syndrome, defined as the presence of anorexia, weakness, and weight loss. The symptomatic period was considered as acute-subacute if symptom duration was < 30 days, and chronic if longer. Fever was defined as body temperature > 37°C at the first evaluation. Red pleural fluid was considered as blood tinged.

Radiologic evaluation of pleural effusion included the extension measured in the chest radiograph as the ratio between height of the effusion and height of the affected hemithorax and expressed as a percentage. An effusion ≥ 75% was considered to be massive. The presence of pulmonary or pleural masses, pulmonary atelectasis, or adenopathies on plain chest radiograph and chest CT was considered suggestive of malignancy.

Follow-up

Patients with malignancy were referred to the Department of Oncology for treatment and control. Patients with idiopathic or suspected benign asbestos pleural effusions were referred to the outpatient department for follow-up control by one of the authors of the study. Those who did not attend for control were questioned by telephone.