

DOES PERCUTANEOUS FINE-NEEDLE ASPIRATION BIOPSY AID IN THE DIAGNOSIS AND SURGICAL MANAGEMENT OF LUNG MASSES?

Michael J. Odell, BSc;* Kenneth R. Reid, MD

OBJECTIVES: To evaluate the ability of percutaneous, transthoracic fine-needle aspiration biopsy (FNAB) to correctly diagnose intrathoracic masses, to determine what complications were experienced and at what rate they occurred and to define more clearly the role of this technique in the surgical management of lung masses.

DESIGN: A chart review.

SETTING: Kingston General Hospital, Kingston, Ont., a tertiary care centre and university-affiliated teaching hospital.

PATIENTS: One hundred and thirteen patients who underwent 117 percutaneous transthoracic FNABs between Jan. 1, 1991, and July 1, 1996.

OUTCOME MEASURES: Patient demographics, size and location of the lesion, diagnostic result of FNAB, complications of the procedure, smoking history, number of needle passes made by the radiologist and results of any other available biopsy (i.e., through bronchoscopy, mediastinoscopy, pleuroscopy) and of surgical resection, as well clinical information pertaining to the disease state in patients with nondiagnostic or negative FNAB.

RESULTS: Eighty-six masses (73.5%) were diagnosed as malignant, 31 biopsy specimens (26.5%) were either nondiagnostic or negative for malignancy. Of these specimens, 15 (48.4%) were subsequently shown to be cancer. In 64 biopsies (54.7%), the patient suffered pneumothorax, requiring hospitalization and chest tube insertion in 35 (29.9%) and 24 (20.5%) cases respectively. The size of the lesion was related to both the diagnostic accuracy and the incidence of pneumothorax.

CONCLUSIONS: Percutaneous transthoracic FNAB should not be used routinely in the assessment of patients with lung masses who are medically fit to withstand surgery and are free of widespread disease. The results of FNAB do little to modify the course of surgical management in these patients.

OBJECTIFS : Évaluer la capacité de la biopsie percutanée transthoracique par aspiration à l'aiguille fine de permettre de diagnostiquer correctement la présence de masses intrathoraciques, déterminer les complications et leur fréquence et définir plus clairement le rôle de cette technique de biopsie dans le traitement chirurgical de masses pulmonaires.

CONCEPTION : Étude de dossiers.

CONTEXTE : Hôpital général de Kingston, Kingston (Ontario), centre de soins tertiaires et hôpital d'enseignement affilié à une université.

PATIENTS : Cent-treize patients qui ont subi 117 biopsies percutanées transthoraciques par aspiration à l'aiguille fine entre le 1^{er} janvier 1991 et le 1^{er} juillet 1996.

MESURES DE RÉSULTATS : Caractéristiques démographiques des patients, dimensions et emplacement de la lésion, diagnostic découlant de la biopsie, complications de l'intervention, antécédents de tabagisme, nombre de ponctions effectuées avec l'aiguille par le radiologiste et résultats de toute autre biopsie disponible (c.-à-d. par bronchoscopie, médiastinoscopie, pleuroscopie) et de toute résection chirurgicale, ainsi que renseignements cliniques portant sur l'état de la maladie chez les patients dont la biopsie ne permet pas de poser un diagnostic ou donne un résultat négatif.

From the Division of Cardiothoracic Surgery, Department of Surgery, Queen's University, Kingston, Ont.

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Correspondence to: Dr. Kenneth R. Reid, Department of Surgery, Division of Cardiothoracic Surgery, 102 Stuart St., Kingston ON K7L 2V6; fax 613 549-2902

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RÉSULTATS : On a diagnostiqué la présence de 86 masses (73,5 %) malignes, 31 spécimens de biopsie (26,5 %) n'ont pas permis de poser de diagnostic ou ont donné un résultat négatif quant à la malignité. On a montré par la suite que 15 (48,4 %) de ces spécimens étaient cancéreux. Dans le cas de 64 biopsies (54,7 %), le patient a été victime d'un pneumothorax qui a entraîné une hospitalisation et l'insertion d'un drain thoracique dans 35 (29,9 %) et 24 (20,5 %) cas respectivement. Les dimensions de la lésion étaient liées à la fois à l'exactitude du diagnostic et à l'incidence du pneumothorax.

CONCLUSIONS : Il ne faudrait pas utiliser la biopsie percutanée transthoracique par aspiration à l'aiguille fine de façon routinière pour évaluer les patients qui ont une masse au poumon, qui sont médicalement aptes à subir une intervention chirurgicale et qui n'ont pas de maladie généralisée. Les résultats de la biopsie n'ont guère d'incidence sur l'évolution du traitement chirurgical chez ces patients.

The surgeon's role in bronchogenic carcinoma, the leading cause of death in North America, is to assess the patient and determine the most appropriate course of management. A significant number of the solitary pulmonary nodules seen by thoracic surgeons are nonmalignant and do not require surgical management. Given the risks of general anesthesia, thoracotomy and pulmonary resection, it is critical that the nature of the mass is determined. Although clinical and radiographic assessment can raise or lower the probability that a lesion is malignant, a histologic examination is the ultimate tool in this decision-making process. Cytologic examination of sputum or bronchoscopy can sometimes provide a diagnosis; however, negative findings do not rule out the presence of cancer. Transcutaneous fine-needle aspiration biopsy (FNAB) is frequently used when cytologic examination and bronchoscopy have failed to provide a diagnosis. The value of transcutaneous FNAB in this process is quite controversial, however, and some investigators advocate its use only when a patient with a suspicious but nondiagnosed lesion either refuses surgery or is medically unfit to undergo thoracotomy.^{1,2} Our goal was to evaluate, through a chart review, the ability of percutaneous transthoracic FNAB to correctly diagnose intrathoracic masses and to determine the complication rate at our centre. We also wanted find out which patients would be best served by this procedure and more clearly define

the role of FNAB in the surgical management of lung masses.

PATIENTS AND METHODS

The records of 129 patients who underwent FNAB of an intrathoracic mass between Jan. 1, 1991, and July 1, 1996, were examined retrospectively. Biopsy specimens obtained in the operating room under direct visualization were excluded. Data from the remaining 117 biopsies, taken from 113 patients, form the basis of the study. The following information gathered from chart notes, radiology and cytology reports was analysed for each biopsy: patient demographics, size and location of the lesion from which a biopsy was taken, diagnostic result of FNAB, complications of the procedure, smoking history in pack-years, number of needle passes made by the radiologist and results of any other biopsy (i.e., specimens obtained at bronchoscopy, mediastinoscopy or pleuroscopy) or of surgical resection. Lesions were placed in 1 of 4 anatomic categories, according to radiologic data:

- peripheral — a lesion involving or within 1 cm of the visceral pleura
- central/hilar — a pulmonary lesion in close proximity to hilar structures
- parenchymal — pulmonary lesions not satisfying the criteria for either peripheral or central/hilar
- mediastinal.

The course of all patients with negative biopsy specimens was carefully examined for evidence of undiagnosed

malignancy (i.e., the pathologic characteristics of resected lesions, progression of lesions either radiographically or clinically, response of lesions to empirical courses of chemotherapy or radiotherapy and the appearance of metastatic lesions without evidence of another possible primary lesion). Biopsy results that fitted this category were considered to be false negative. Negative biopsy results were considered to be true negative if resection or other biopsy established a benign diagnosis, or if radiologic or clinical evidence suggested that the mass was indeed benign (i.e., no radiographic changes for more than 2 years, spontaneous regression of the lesion). Biopsy specimens that contained malignant cells were considered to represent true positives and repeat biopsy was not done. For the purpose of this study, cytologic results described as suspicious for malignancy but nondiagnostic were considered to represent malignant disease, and repeat biopsy was not done.

Data were organized and analysed with use of a Microsoft Access database and Microsoft Excel spreadsheets. Statistical analysis was carried out using Instat software from GraphPad Software, San Diego, Calif. Differences between means were tested for statistical significance by the 2-tailed *t*-test. Risk factors and outcomes were examined for correlation using 2 × 2 contingency tables tested with Fisher's exact test; the odds ratio and 95% confidence intervals were also calculated.

RESULTS

Demographics

Demographic data concerning the study population are contained in Table I.

Biopsy results

In 2 cases the biopsy could not be completed. The biopsy yielded a diagnosis of malignancy in 86 (73.5%) cases (Table II). Thirty-one (26.5%) biopsy specimens were nondiagnostic for the following reasons: insufficient material for diagnosis (16), sufficient material but a nondiagnostic biopsy (15). Although 9 (29.0%) of the 31 lesions were eventually proven benign, 15 (48.4%) were subsequently shown to be malignant. Seven (22.6%) lesions remain undiagnosed. Thus, the sensitivity of FNAB in diagnosing intrathoracic malignant disease was 85% in our series. Since all positive biopsies were assumed to represent true positives, the specificity was 100%. Twenty-seven patients in our study had negative or nondiagnostic percutaneous transthoracic FNAB: in 7 cases the patient refused further investigation, in 5 cases the patient opted for resection or open lung biopsy, in 3 cases the patient chose to undergo other investigations (e.g., mediastinoscopy) and in 9 cases a repeat biopsy was done. Five of these were positive for malignancy.

Table I

Demographic Data in 113 Patients Who Underwent 117 Percutaneous Transthoracic Fine-Needle Aspiration Biopsies

Parameter	Biopsy (N = 117)
Age, yr (mean [and SD])	68.3 (8.7)
Men, no. (and %)	67 (57)
Women, no. (and %)	50 (43)
Smokers, no. (and %)	106 (91)
Lesion size, cm (mean [and SD])	4.3 (3.1)
Smoking history, pack-yr (mean [and SD])	43.7 (4.0)

In the 4 cases associated with 2 negative biopsies the patient opted for clinical and radiologic observation. Two patients were lost to follow-up.

Complications

In 64 (54.7%) of the biopsies the patient was shown to have iatrogenic pneumothoraces. Of these, 35 biopsies (54.7% associated with pneumothorax and 29.9% of the total number), the patient required hospitalization for either observation or treatment of the pneumothorax. Mean (and standard deviation) length of hospital stay for the patients was 2.1 (0.9) days (range 1 to 4 days). In 24 cases (37.5% associated with pneumothorax and 20.5% of the total number), the patient required chest tube placement. In 6 (5.1%) cases, the patient suffered hemoptysis, with 1 requiring admission to hospital. Other complications included hematoma surrounding the biopsy site (5 cases), subcutaneous emphysema (4), pleural effusion or hemothorax (2) and syncope and recurrent laryngeal nerve palsy (1 each). One patient suffered a cerebrovascular accident while on the operating table. This caused generalized tonic-clonic seizures that rapidly progressed to status epilepticus. It is not clear whether the biopsy was responsible for this, as the patient in question had locally advanced disease and was later shown to have brain

metastases. No deaths were recorded during the study period.

Correlations

The risk of pneumothorax was related to the location of the lesion and inversely related to the size of the lesion. Patients with peripheral lesions had a pneumothorax rate of 39.0% (16 of 41), whereas those with either central or parenchymal lesions had a significantly higher rate (47 of 72 [65.3%], $p = 0.01$, odds ratio = 2.938, 95% confidence intervals 1.329 to 6.494). The development of pneumothorax was not related to age, sex or smoking history. Patients who had pneumothorax during FNAB had a mean (and standard deviation) lesion size of 3.28 (1.4) cm, significantly smaller than those who did not experience pneumothorax during the procedure (5.74 [4.1] cm, $p < 0.0001$).

Lesion size was also related to the diagnostic outcome of the biopsy. In biopsies giving nondiagnostic results (31) the patient had a mean (and SD) lesion size of 2.62 (1.3) cm, compared with 4.96 (3.4) cm for biopsies giving diagnostic results ($p < 0.0002$). This appears, at least in part, to be related

Table II

Cytologic Diagnosis of Positive Fine-Needle Aspiration Biopsies

Diagnosis	No. of biopsies
Large cell carcinoma	26
Squamous cell carcinoma	17
Adenocarcinoma	14
Small cell carcinoma	9
Metastatic carcinoma	5
Sarcoma	2
Mesothelioma	1
Thymoma	1
Lymphoma	1
Unable to classify	3
Suspicious for malignancy	7

to the inability to obtain sufficient material for diagnosis. In FNABs labelled "insufficient material" by the pathology laboratory, the mean (and SD) lesion size was 2.39 (1.1) cm compared with 4.70 (3.2) cm for lesions in which the biopsy produced sufficient material for diagnosis ($p < 0.005$).

If the patient population was subdivided into those with lesions larger than 3 cm and those with lesions 3 cm or smaller, some patterns develop. Those with smaller lesions are at a clear disadvantage, owing to a higher risk of pneumothorax (OR = 2.7; 95% CI 1.2 to 6.3) as well as to a lower probability of obtaining a diagnostic biopsy (OR = 0.17; 95% CI 0.06 to 0.4812).

DISCUSSION

In many areas, the results of our series are comparable to those of similar studies.¹⁻⁷ Needle aspiration had an 85% sensitivity for intrathoracic malignancy in our study; comparable to the 64% to 97% reported by Weisbrod.⁷ Our incidence of pneumothorax was somewhat higher than that reported elsewhere,⁶ which relates directly to the technique employed by the radiologist performing the majority of the procedures. The individual in question uses 2 needles in every biopsy, 1 to stabilize the lung and 1 to perform the biopsy. Thus, the higher complication rate is due to the increased number of perforations of the lung. Also, the yield is significantly lower when the lesions are smaller. These results should be used to guide the decision to perform FNAB in a patient who may not be able to tolerate a moderate or severe pneumothorax due to coexistent pulmonary disease. Twenty-seven patients in our study had negative or nondiagnostic FNAB.

Although attempts were made to classify specimens histologically, positive biopsies were generally not investigated further and a relatively small proportion of patients went on to resection, making

confirmation of cell type difficult. As a result, no conclusions could be reached regarding the reliability of FNAB in accurately determining cell type. Because of the retrospective nature of the study, it was frequently impossible to determine whether attempts were made at histologic as well as cytologic diagnosis, as this was frequently not specified in the patient record.

The malignancy rate in our study is somewhat higher than that found in other studies, suggesting that our patient population may have been preselected. Given the average age (68.3 years) and the very high rate of smokers (91%) in our study population, a higher malignancy rate than expected is not surprising. A malignancy rate of 66% was reported by Calhoun and associates¹ in their study in which the average patient age was 61 years.

The value of fine-needle aspiration biopsies

The value of any test lies in its ability to modify the course of management for a particular patient. If the outcome of the procedure has little or no effect on the decision-making process, its use cannot be justified. FNAB is a relatively safe procedure that can often be performed on an outpatient basis. As histologic or cytologic diagnosis is a prerequisite to nonsurgical therapy in most centres, a positive FNAB can alter management decisions, especially in the setting of small cell carcinoma. There is little doubt that FNAB is a useful and necessary tool in the nonsurgical management of lung masses, especially since smaller lesions are harder to diagnose than larger lesions and the patients are more likely to suffer complications requiring costly interventions. In a surgical setting, however, the value of FNAB is questionable. As demonstrated by the 48% false-negative rate at our institution, a negative FNAB result does not rule out malignancy. The false-

negative rate in our series is comparable to that of other investigators^{1,3} and dictates that further investigation, including open lung biopsy if necessary, be done before malignancy is ruled out. In this instance, proceeding directly to thoracotomy in an operable patient saves the patient and the surgeon from the frustration of a negative FNAB, the risks of complications and the costs associated with those complications. In an operable patient with a suspicious mass and no evidence of distant metastases, proceeding directly to thoracotomy represents the safest, most cost-efficient course of action.

It can be argued that a benign diagnosis made by FNAB can save the patient from a painful and invasive procedure; however, in our study, not one specific benign diagnosis was made using FNAB, even though 9 patients were eventually shown to have benign conditions.

Alternatives to FNAB and traditional thoracotomy

Newer methods of making diagnoses in patients with lung masses are now available to thoracic surgeons. Recent advances in video-assisted thoracic surgery (VATS) have led to increasingly frequent use of this technique to diagnose intrathoracic malignant disease.⁸ VATS avoids a traditional thoracotomy and therefore results in less morbidity. There are, however, numerous reports of seeding of malignant cells along the video and instrumentation tracts. Clearly, methods of reducing this risk to negligible levels are required before VATS can be widely employed as a diagnostic tool for intrathoracic tumours.

Use of positron emission tomography (PET) to differentiate benign from malignant tumours of the chest has been investigated and shown to possess equal or superior diagnostic ability to FNAB, with fewer complications.⁴ However, it is only capable of

differentiating benign from malignant, whereas a positive FNAB can also indicate histologic type, and therefore differentiate between small cell and non-small cell lung cancers. In addition, PET is generally only available in larger tertiary care centres.

Recommendations

We believe that FNAB has no role in the management of the suspicious solitary lung mass in patients who are willing surgical candidates. In such cases, the outcome of the biopsy is irrelevant, as thoracotomy will be undertaken regardless, given the high false-negative rate. One concern is that the surgeon may be operating on patients with small cell lung cancer. In such cases, however, surgery plays an important role as part of a multidisciplinary approach to the disease.⁵

FNAB should be used for the following:

- patients who are medically unfit and could not tolerate surgery
- patients who refuse surgery
- patients with advanced disease (local or metastatic).

In these instances, FNAB may provide a diagnosis and thus allow institution of appropriate therapy. Biopsy of centrally located lesions less than 1 cm in diameter is unlikely to be successful and is associated with a higher complication rate.

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Clinical signs and symptoms of mandibular fractures include facial asymmetry and swelling, trismus and limitation of mandibular movement, malocclusion, lengthening of the face, paresthesias of the lower lip and chin due to injury to the inferior alveolar nerve, and ecchymosis of the floor of the mouth.

Consistent clinical signs and symptoms of malar or zygomatic complex fractures (tripod fractures) include ecchymosis and edema and numbness of the anterior cheek due to injury to the infraorbital nerve. Depending on the degree of displacement, other possible signs and symptoms include flattening of the cheek, infraorbital rim step defect, and decreased extraocular muscle function. Unilateral malar fractures do not produce malocclusion or facial lengthening. Trismus or limitation of mandibular movement may be caused by pressure on the coronoid process of the mandible by the zygoma as well as by swelling in the temporal region.

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