Diagnosis of intrathoracic lesions: are sequential fine-needle aspiration (FNA) and core needle biopsy (CNB) combined better than either investigation alone?

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AIM: To assess the diagnostic accuracy of sequential computed tomography (CT)-guided percutaneous fine-needle aspiration (FNA) and core-needle biopsy (CNB) in comparison with FNA and CNB performed separately for diagnosing intrathoracic lesions.

SUBJECTS AND METHODS: Five hundred and eighty-two consecutive patients with thoracic lesions who underwent same-session sequential CT-guided FNA and CNB procedures were studied. The final diagnosis, which was achieved by either agreement of percutaneous procedures with clinical follow-up, bronchoscopy or thoracotomy was available for all cases. The diagnostic yield of the combined FNA + CNB procedures was compared with that of each alone.

RESULTS: Adequate samples were obtained in 541 (93%) of FNAs and 513 (88%) of CNBs. Of 582 lesions, 419 (72%) were malignant and 163 (28%) were benign. For malignant lesions, the sensitivity, specificity and accuracy of the procedures were: 376/419 (89.7%), 136/163 (83.4%), and 88% for FNA; 317/419 (75.6%), 138/163 (84.7%), and 78% for CNB; 400/419 (95.5%), 154/163 (94.5%), and 95% for FNA + CNB. The sequential procedures showed significantly better sensitivity, specificity and accuracy compared with either FNA or CNB separately ($p < 0.003$). For the 163 benign lesions, 76 (47%) had a specific benign pathological diagnosis. The diagnosis was obtained in 16/76 (21%) by FNA, in 54/76 (71%) by CNB, and in 60/76 (79%) by FNA + CNB. There was no significant difference between the results of the sequential procedures and CNB alone ($p > 0.05$).

CONCLUSIONS: Sequential FNA and CNB improve the diagnostic accuracy of percutaneous CT-guided procedures in malignant lesions. There was only mild improvement, which was not statistically significant, for the diagnosis of benign specific lesions by the sequential procedures compared with the yield of CNB alone.

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Introduction

Radiologically guided transthoracic needle biopsy has emerged as one of the leading procedures for the diagnosis of pulmonary and mediastinal lesions. When successful, this method may obviate the need for more invasive diagnostic approaches, such as thoracoscopy, mediastinoscopy or thoracotomy. Fine-needle aspiration (FNA) provides a sample that is usually adequate for cytological and microbiological examinations, but not for a histological evaluation. The larger volume of tissue obtained by percutaneous core-needle biopsy (CNB) enables histopathological diagnosis and more sophisticated laboratory analysis. The optimal technique for the diagnosis of intrathoracic lesions has not yet been recommended. FNA with or without CNB are commonly used, while both techniques are used sequentially in some centres.
Sufficient attention has been given to the evaluation of both FNA and CNB techniques. However, the performance of sequential CT-guided FNA and CNB has been insufficiently evaluated and only on small groups of patients, showing various results. The aim of the present study was to evaluate the diagnostic accuracy of, and indications for, sequential CT-guided percutaneous FNA and CNB in comparison with FNA and CNB alone for the diagnosis of intrathoracic lesions on a large cohort of patients.

Materials and methods

The electronic medical records of our department were reviewed, and 1942 percutaneous transthoracic CT-guided procedures performed between 1 January 1996 and 31 December 2004 for the diagnosis of intrathoracic lesions were identified. Sequential FNA and CNB (obtained in the same session), were performed in 708 patients. Final diagnoses, which were arrived at by surgical resection, bronchoscopy, or concordance of percutaneous CT guided procedures with clinical-radiological follow-up of at least 6 months, were available in 582 patients, who constitute the study cohort. One hundred and twenty-six patients were excluded from the study because of incomplete or unavailable medical records or non-confirmed final diagnosis. The following characteristics were noted: patient’s age and gender; location, type (malignant or benign) and diameter of thoracic lesion, method of final diagnosis; and the rate of adequate samples for each sampling technique. The results of the combined percutaneous procedures (FNA and CNB) and of each of the procedures alone were reviewed and compared with the final diagnoses.

Each procedure was performed by a senior physician experienced in CT-guided biopsies and in the presence of a cytopathologist, after informed consent was obtained from the patient. All patients had a diagnostic chest CT examination with a 5-mm collimation and 3–5 mm section interval before the biopsy. The CT biopsy protocol included 3–5 mm contiguous axial sections obtained through the lesion, with a tube voltage of 120 kVp, and tube current of 50 mA. After the preliminary examination the patients’ position, the site of needle insertion and the direction of the biopsy were planned using the safest and most direct route to the lesion. Precise needle placement was documented by CT in all cases. During the early years of the study a dual-section Elscint Twin CT machine (Haifa, Israel) and an Elscint Helicat CT machine (Haifa, Israel) were used, and since the beginning of the year 2003, a Philips MX-8000, 16-section CT machine was used. The procedure was performed under local anaesthesia using 1% lidocaine, during breath-hold or shallow respiration.

For all patients FNA was performed first. FNAs were executed with a 20-gauge aspirating needle as described elsewhere. Some of the cytological material was stained with a rapid air-dried Diff-Quick Giemsa method and the rest was fixed in alcohol. The cytopathologist assessed the adequacy of the air-dried Diff-Quick specimens without delay. Whenever the immediate cytopathologist’s impression of the air-dried Diff-Quick specimens was that there is inadequate material or when no clear malignant features were observed, a CNB was performed sequentially, by a second puncture, without using a coaxial technique. The CNBs were performed using an 18-gauge Temno Tru-Cut automatic cutting needle. This needle is designed to obtain core specimens for histopathological analysis through a spring-activated mechanism that fires a cutting cannula that snare a biopsy specimen adequate for histological examination in a 1.7 cm stylet. A touch preparation of the core biopsy was stained with the Diff-Quick stain for immediate evaluation by the cytopathologist, while the specimen was submitted to the histopathology laboratory in formalin solution. In all cases where an infectious process was included in the differential diagnosis, material was also submitted from both FNA and CNB for microbiological assessment.

After the biopsy, axial CT sections were obtained through the lesion and sometimes through the entire chest to rule out pneumothorax. The size of the pneumothorax was not quantified, but the cases were divided into those requiring chest tube insertion and cases that resolved spontaneously. The presence of haemoptysis and development of a late pneumothorax were noted in the patient’s medical chart. Haemoptysis was defined as mild when the sputum was only stained, moderate when the sputum was bloody and increased in quantity, and severe when the patient required treatment. All complications during and after the procedure were recorded.

The results of both procedures were classified as malignant or benign based on the presence or absence of malignant cells in the sample. Specific cell types were also identified when possible. Specimens were defined as inadequate if there was insufficient pathological material for diagnostic evaluation such as “necrotic material”, “blood only”, or “lung cells”. The institutional review board approved the study. An informed consent was not required for this retrospective study.
Statistical analysis

Statistical analyses were performed by using a computer software package (SAS for Windows version 8.02; SAS Institute, Cary, NC, USA). For each procedure (either FNA, CNB, or their combination), there were four possible results: (1) true-positive, defined as a diagnosis of malignancy obtained by the invasive procedure and a final diagnosis of malignancy; (2) false-positive, defined as a diagnosis of malignancy obtained by the invasive percutaneous procedure and a final diagnosis of a benign process; (3) false-negative, defined as no malignancy found by the invasive procedure and a final diagnosis of malignancy; and (4) true-negative, defined as no malignancy found by the invasive procedure and a final diagnosis of a benign process. The results of each procedure were compared with the combination of the two procedures (i.e., FNA + CNB), with the presence of malignant cells on either of them being enough to consider the case as "positive" for malignancy.

The McNemar test of symmetry compared the diagnostic performance of the two methods. Comparisons of sensitivity or specificity of the two methods were done using the Chi square test or Fisher’s exact test as applicable.

Results

Five hundred and eighty-two patients comprised the final study group (347 males and 235 females with a mean age of 66 ± 16 years, range 16–94 years). The mean diameter of the thoracic lesions was 3.8 ± 1.8 cm (range 0.5–11 cm). The lesions were located in the right lower lobe (n = 126, 22%), right upper lobe (n = 128, 22%), left upper lobe (n = 123, 21%), left lower lobe (n = 116, 20%), right middle lobe (n = 33, 6%), and mediastinum (n = 56, 10%). The final diagnosis was determined by concordance of the percutaneous CT-guided FNA or CNB with clinical-radiological follow-up in 483 (83%) cases, by thoracotomy in 80 cases (14%), bronchoscopy in nine cases (2%), and mediastinoscopy in 10 cases (2%).

Adequate samples were obtained in 541 (93%) lesions by FNA and in 513 lesions (88%) by CNB. When combining the FNA and CNB together, adequate samples were obtained in at least one of the techniques in 577 (99.1%) patients. Of the 582 patients, 419 (72%) had malignancy and 163 (28%) had benign disease. The most common malignancy was bronchogenic carcinoma, which was diagnosed in 279 patients (Table 1). Eighty-seven of the 163 cases of benign disease had non-specific features such as fibrosis or inflammation. The most common benign specific diagnosis was cryptogenic organizing pneumonia (Table 2).

Malignant diseases

The sequential procedures, FNA and CNB, showed significantly better sensitivity, specificity and
accuracy (Table 3) when compared with each method separately (p < 0.0003). The sensitivity of FNA was higher than the sensitivity of CNB, but when the two procedures were combined the sensitivity increased markedly to 96% (Table 3). The specificity of both procedures was similar, but increased significantly to 95% when the two procedures were combined. FNA was more accurate than CNB (88 versus 77%, respectively) confirming malignancy in 376 cases compared to only 317 cases, respectively. However, the accuracy of the combined procedures increased to 95%. The combined procedures yielded 24 more diagnoses of malignancy compared with FNA alone, whereas they added 83 more cases of diagnosed malignancies compared with CNB alone. This difference was statistically significant (p < 0.0001).

Benign processes

FNA was able to exclude malignancy in 136 of 163 (83%) patients and CNB in 138 of 163 patients (85%), whereas the combined procedures excluded malignancy in 154 patients (95%). There were four cases of false positive diagnoses of bronchogenic carcinoma by FNA, and one of them also had a false-positive diagnosis by CNB, yielding a total of four patients that had a false-positive diagnosis by the combined procedures (p > 0.05). Their final diagnoses obtained by thoracotomy were: aspergillosa, hamartoma, granuloma, and infarction.

A specific benign diagnosis was obtained in 76/163 cases (47%). The rate of identification of specific benign lesions was significantly higher with CNB (54/76, 71%) than with FNA (16/76, 21%). The combination of both techniques yielded the highest number of specific benign diagnoses (60/76, 79%). There was no significant difference between the performance of CNB alone and the combined procedures in the diagnosis of specific benign lesions (p > 0.05).

Pneumothorax was the most common complication in the present study, occurring in 140 (24%) of the procedures. However, it was usually small and required placement of chest tubes and hospitalization in only 21 patients (3.6%). Twenty-five patients (4%) had mild or moderate and well-tolerated haemoptysis that resolved spontaneously. There were no cases of severe haemoptysis. There were no serious adverse events following the procedures.

Discussion

FNA and CNB are well-established techniques for the diagnosis of focal lesions. Overall sensitivity for the diagnosis of intrathoracic malignancy ranges between 70–100%. Several studies recommend using FNA when there is a strong suspicion of malignancy, and when a pathologist is available on-site. However, due to the non-specific cytopathological appearance of benign disease, a specific benign diagnosis (e.g., granuloma, hamartoma) can be achieved by FNA in only 16–68% of the cases. CNBs have been shown to be more accurate in the specific diagnosis of benign lesions, lymphoma and when a CT-guided procedure is performed in the absence of a cytopathologist. We performed FNA and CNB sequentially, at the same session, in 582 patients. To the best of our knowledge, this is the largest series to examine the yield of a sequential percutaneous CT-guided FNA and CNB approach in the diagnosis of intrathoracic lesions using a non-coaxial technique.

The findings of the present study suggest that the use of sequential FNA and CNB results in a higher rate of adequate specimens and an improvement in the diagnostic yield of percutaneous CT-guided procedures in malignant lesions, similar to the findings of some previous reports. The sensitivity for diagnosing malignant lesions in the present study using combined FNA and CNB was 96%, and 6% more lesions were diagnosed in comparison with FNA alone. The present results agree with those of Yamagami et al. who showed that using sequential FNA and CNB improves the rate of adequate specimens obtained and the rate of precise diagnosis. In their study, specific cell types could be proven in 89 of 90 malignant lesions and in 30 of 44 benign lesions. It is important to note that, in contrast to the present study, CT fluoroscopy was used for the biopsy procedures in the Yamagami et al. study. This technique is reported to have

Table 3 Diagnostic performances of fine-needle aspiration (FNA), core needle biopsy (CNB), and the combined procedures (FNA + CNB) in a total of 582 patients (malignant n = 419, benign n = 163)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Inadequate sample</th>
<th>False positive</th>
<th>False negative</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>FNA</td>
<td>38</td>
<td>4</td>
<td>28</td>
<td>376/419 (89.7%)</td>
<td>136/163 (83.4%)</td>
<td>88%</td>
</tr>
<tr>
<td>CNB</td>
<td>69</td>
<td>1</td>
<td>57</td>
<td>317/419 (75.6%)</td>
<td>138/163 (84.7%)</td>
<td>78%</td>
</tr>
<tr>
<td>FNA + CNB</td>
<td>5</td>
<td>4</td>
<td>14</td>
<td>400/419 (95.5%)</td>
<td>154/163 (94.5%)</td>
<td>95%</td>
</tr>
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</table>
advantages over conventional CT-guided technique, but is not available in most centres. The results of the present study are also in agreement with the studies of Boiselle et al.\textsuperscript{4} and Klein et al.\textsuperscript{15} However, a major difference in the biopsy technique between the studies exists, as they used a coaxial technique, therefore sampling the exact same location by both FNA and CNB, rather than the two separate punctures that were performed the present study, providing sampling of two different locations of the same thoracic lesion. Another difference relates to the types of benign lesions in the prior studies. In the present study there was a higher rate of benign tumours in contrast with the other studies,\textsuperscript{3,4} that had mostly infectious lesions. Given that FNA is usually sufficient for microbiological analysis, this explains the greater added value of CNB in the present study in comparison with the other studies.\textsuperscript{3,4}

Based on the evidence from the present study and in the literature,\textsuperscript{4,5,7,15,16} FNA should be performed first. FNA alone may be sufficient to provide an accurate diagnosis when the cytopathologist is present at the time of the procedure, immediately confirming the adequacy of the specimen with unambiguous malignant characteristics. This is especially the case in patients likely to have bronchogenic carcinoma on the basis of pre-biopsy evaluation. CT-guided FNA with rapid expert cytopathological examination of the aspiration specimen can provide a definitive diagnosis in the vast majority of cases, as it can accurately distinguish between small cell and non-small cell carcinoma, and no substantial advantage is provided by obtaining histological specimens.\textsuperscript{15,20} A subsequent CNB should be undertaken when the FNA specimen are interpreted as benign and when the specimen diagnosis is considered indefinite and there is an uncertainty about the presence of malignancy. In contrast, the sequential procedures apparently have no advantage over CNB alone for the diagnosis of benign specific lesions due to CNB’s significantly higher specificity over FNA. The present study confirms and further emphasizes the conclusion of the prior studies, that CNB is most useful for the diagnosis of benign lesions,\textsuperscript{3,4,7,16} and suggest that CNB alone may suffice, with consequent reduction in cost and risk, where there is a high pre-test probability of benign disease.

The improvement in diagnostic performance when using the sequential FNA and CNB approach should be weighed against the risk of higher complication rate related to more punctures and longer procedural duration, and to the higher costs.\textsuperscript{17,18} The reported frequency of pneumothorax in prior studies that included large patient cohorts was 15–54\%.\textsuperscript{7,8,15,19} The pneumothorax rate of the present study of 24\% is within this reported rate and is also similar to the accepted rates of a single-needle biopsy technique (either FNA or CNB).\textsuperscript{6,7} Given the large size of the patient cohort, it may be reasonable to conclude that, if performed carefully using state of the art biopsy technique and all the necessary precautions, the use of the combined technique may not be associated with an additional significant risk to the patients.

The present study is limited due to the relatively short follow-up period of 6 months, while 2 years are generally considered as confirmation of benign disease. However, 6 months was the minimal follow-up period for inclusion in the present study, and most patients have been under close clinical-radiological follow-up for several years.

In conclusion, the present study demonstrates, in a large patient cohort with diverse lesion types, that sequential FNA and CNB may improve the
diagnostic yield of percutaneous CT-guided procedures in malignant lesions, especially in cases of uncertain diagnosis, without an increase in complication rate. In cases highly suggestive of a benign process, CNB alone may be considered as its yield is similar to that of the sequential procedures.

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References