INTRODUCTION

Lung cancer continues to be one of the most lethal malignant tumors. Lung cancer screening using low-dose CT has expanded in clinical medicine due to the presence of high risk populations and the relatively asymptomatic nature of the disease in the early stages. With the increased use of helical CT for lung cancer screening, the detection rate of small lung cancer lesions has also increased (1-4).

Small pulmonary nodules suspicious for a malignancy mandate a pathological diagnosis. CT-guided transthoracic needle aspiration biopsy is a well-established method for the cytological diagnosis of pulmonary nodules (5-8). However, histological evaluation by tissue-core cutting-needle biopsy is better than cytology for the determination of a specific diagnosis, especially for benign lesions and subsolid lesions (9, 10). CT fluoroscopy provides real-time imaging and allows radiologists to manipulate a patient in response to respiratory movement. Therefore, this imaging approach may permit rapid localization of lesions that are smaller and/or located in less accessible areas, as well as in patients that have difficulty cooperating with the procedure (11, 12). Kim et al. (13) reported that CT fluoroscopy-guided percutaneous biopsy of pulmonary lesions provided high diagnostic accuracy comparable to that of conventional CT-guided procedures, and with fewer complications. However, radiation exposure to both pa-
The present study evaluated the diagnostic accuracy and complications of CT fluoroscopy-guided core biopsy of small (≤ 20 mm) pulmonary nodules.

MATERIALS AND METHODS

Patients and Lesions

A retrospective analysis was performed on the imaging records of all patients that underwent CT fluoroscopy-guided core biopsy of pulmonary nodules at this institution between February 2007 and February 2010. The study included patients that underwent biopsy for small pulmonary nodules with a diameter of less than 20 mm and with a final diagnosis established by surgical resection of the nodule or imaging follow-up. Patients diagnosed with benign lesions by biopsy that remained stable in size and were followed for < 12 months, were excluded from the study. Finally, 62 patients (35 men and 27 women; age range, 36-85 years) were enrolled in the study. Among these patients, 35 underwent surgical resection and 27 patients underwent follow-up exams. The medical and imaging records of these 62 patients were reviewed by two radiologists. The diameter of all nodules and lesion depth (length of the aerated lung traversed by the needle from the surface of the pleura to the proximal margin of the target lesion) were measured on lung window settings. The patients were divided into two groups on the basis of nodule size (≤ 10 mm, n = 25 vs. > 10 mm, n = 37) and nodule density (solid, n = 49 vs. subsolid, n = 13) for comparison of the diagnostic accuracy. When the lesions contained a solid portion less than 50%, the lesion was defined as subsolid. Lesions containing more than 50% of a solid portion were defined as solid lesions. The complications associated with the procedure such as pneumothorax and thoracostomy insertion rates were recorded.

Procedures

The biopsies were performed by experienced chest radiologists that had four and 10 years of experience performing thoracic biopsy procedures, respectively. Written informed consent was obtained from patients before their biopsy. All biopsies were performed under CT fluoroscopy guidance using a 64-multi-detector CT scanner (Brilliance 64; Philips Medical Systems, Cleveland, OH, USA). At the time of the biopsy, selected images were obtained in the area of interest with 5-mm-thick contiguous transverse CT sections. Biopsies were planned such that they crossed the fewest pleural surfaces and avoided fissures or visible bullae. The procedure was performed with the patient in the prone, supine, or lateral decubitus position, depending on the location of the lesion. After local anesthesia, a core biopsy specimen was obtained with an 18-gauge automated cutting needle (Bio-gun; M.I.Tech, Seoul, Korea). The needle was inserted through the pleura and advanced to a position close to a target lesion under CT fluoroscopy guidance. To avoid irradiating the radiologists' fingers, the operator manipulated the needle with a needle holder during CT fluoroscopy-guided biopsy. To minimize the radiation to the patient and radiologist, the real-time scanning was limited to short glimpses to visualize the position of the needle tip. After the position of the needle tip was confirmed, the automated needle biopsy system was fired. Specimen acquisition was repeated until the radiologist determined that the specimens were adequate. Core specimens were immersed in 10% formalin for a subsequent pathology examination. A low dose CT was performed over the biopsy site immediately after the biopsy. Follow-up chest radiographs were obtained 1 hour and 24 hours after the biopsy to evaluate for a pneumothorax. A thoracostomy was considered when a patient had a symptomatic, large (> 30%) pneumothorax.

Statistical Analysis

The sensitivity, specificity, and diagnostic accuracy were calculated. The biopsy was considered as truly benign if the results of the biopsy evaluation were confirmed as benign by a surgically resected specimen, and if the lesion was stable in size for at least 12 months or decreased in size. A biopsy was considered to be truly malignant if the results of the biopsy were confirmed by a surgically resected specimen or if the lesion increased in size. A biopsy was considered non-diagnostic if the pathology yielded no specific benign or malignant diagnoses. Non-diagnostic cases were excluded from the calculation of sensitivity, specificity, and diagnostic accuracy. The results were compared between the two groups according to lesion size and lesion density. Fisher’s exact test and the
Student’s t-test were used to assess the statistical significance of the difference between the two groups. A p-value of less than 0.05 was considered to indicate statistical significance.

RESULTS

A total of 59 cases out of 62 were diagnosed by CT fluoroscopy-guided core biopsy. Malignant or premalignant lesions were finally diagnosed in 39 patients (adenocarcinoma in 20, metastases from an extrathoracic malignancy in 7, squamous cell carcinoma in 4, small cell carcinoma in 3, bronchioloalveolar carcinoma in 3, and atypical adenomatous hyperplasia in 2) with 36 true-positive (adenocarcinoma in 18, metastases from an extrathoracic malignancy in 7, squamous cell carcinoma in 4, small cell carcinoma in 2, bronchioloalveolar carcinoma in 3, and atypical adenomatous hyperplasia in 2) and 3 false-negative findings (chronic inflammation in 1, anthracofibrosis in 1, type II pneumocyte hyperplasia in 1) (Fig. 1). A benign lesion was finally diagnosed in 23 patients (chronic granulomatous inflammation in 6, organizing pneumonia in 4, tuberculosis in 4, chondroid hamartoma in 3, chronic interstitial inflammation in 1, fungus ball in 1, cryptococcosis in 1, actinomycosis in 1, rheumatoid nodule in 1, intrapulmonary lymph node in 1, and inflammatory pseudotumor in 1), with no false-positive results. Non-diagnostic results were obtained in three out of the 62 lesions (5%). All three non-diagnostic samples were lesions smaller than 10 mm and were benign lesions (intrapulmonary lymph node in 1, chondroid hamartoma in 1, and no change on follow up images at 24-month follow-up periods in 1); these lesions were excluded from the calculations of sensitivity, specificity and diagnostic accuracy.

The mean lesion diameter was 1.3 ± 0.4 cm (range, 0.5-2.0 cm). The overall sensitivity, specificity and diagnostic accuracy were 92%, 100%, and 95%, respectively. The sensitivity and diagnostic accuracy were 85% (11/13) and 91% (20/22) for nodules ≤ 10 mm, 96% (25/26) and 97% (36/37) for nodules > 10 mm. The sensitivity and diagnostic accuracy were 93% and 96% in the solid lesion group, and 90% and 92% in the subsolid group. The sensitivity and diagnostic accuracy were not significantly different between the two groups of nodule sizes and densities (Tables 1, 2).

Seventeen (27%) patients developed a pneumothorax, with two (3%) requiring placement of a thoracostomy tube. After the thoracostomy, all patients fully recovered without other complications. The frequency of pneumothorax for patients with a nodule size ≤ 10 mm and > 10 mm was similar (24%...
Table 1. Diagnostic Accuracy of Small (≤ 20 mm) Pulmonary Nodules Based on Lesion Size

<table>
<thead>
<tr>
<th>Lesion Diameter</th>
<th>Sensitivity</th>
<th>Accuracy</th>
<th>Lesion depth (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10 mm</td>
<td>85% (11/13)</td>
<td>91% (20/22)</td>
<td>2.0 ± 1.5</td>
</tr>
<tr>
<td>&gt; 10 mm</td>
<td>96% (25/26)</td>
<td>97% (36/37)</td>
<td>1.6 ± 1.4</td>
</tr>
</tbody>
</table>

Table 2. Diagnostic Accuracy of Small (≤ 20 mm) Pulmonary Nodules Based on Lesion Density

<table>
<thead>
<tr>
<th>Lesion Density</th>
<th>Sensitivity</th>
<th>Accuracy</th>
<th>Lesion size (cm)</th>
<th>Lesion depth (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subsolid (n = 12)</td>
<td>90% (9/10)</td>
<td>92% (11/12)</td>
<td>2.1 ± 1.3</td>
<td>1.1 ± 0.4</td>
</tr>
<tr>
<td>Solid (n = 47)</td>
<td>93% (27/29)</td>
<td>96% (45/47)</td>
<td>1.7 ± 1.5</td>
<td>1.4 ± 0.4</td>
</tr>
</tbody>
</table>

Table 3. Factors Influencing the Occurrence of Pneumothorax

<table>
<thead>
<tr>
<th></th>
<th>With Pneumothorax</th>
<th>Without Pneumothorax</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion size (cm)</td>
<td>1.34 ± 0.43</td>
<td>1.32 ± 0.42</td>
<td>0.874</td>
</tr>
<tr>
<td>Lesion depth (cm)</td>
<td>1.72 ± 1.38</td>
<td>1.80 ± 1.47</td>
<td>0.865</td>
</tr>
</tbody>
</table>

and 30%, respectively). The pneumothorax frequency for solid and subsolid nodules was found in 32% and 25% of procedures, respectively. Lesion size and depth were not significantly different between the two groups, with or without pneumothorax (Table 3). Post procedural pulmonary hemorrhage occurred near the pulmonary nodule in 35 patients (56%); however, no significant massive hemoptysis developed.

**DISCUSSION**

CT fluoroscopy-guided core biopsy is a well-established accurate method used for the diagnosis of pulmonary nodules. According to Hiraki et al. (14), the diagnostic yield of CT fluoroscopy-guided core biopsies performed in 1,000 lesions was 99.4%, with only six non-diagnostic results (0.6%). The overall diagnostic accuracy was 95.2% regardless of lesion size. For lesions measuring less than 1 cm, the diagnostic accuracy was 92.7%. In our study, the diagnostic yield was 95% and the overall diagnostic accuracy was 95%. For lesions measuring less than 1 cm, the diagnostic accuracy was 91%. The results of our study showed a similar diagnostic accuracy compared to previously reported rates in the medical literature (10, 14). In our study, non-diagnostic samples were obtained in three out of 62 lesions (5%), which were all benign lesions measuring less than 1 cm.

The diagnostic accuracy for lesions < 1 cm in diameter (91%) was lower than that for lesions > 1 cm in diameter (97%). However, this difference was not statistically significant. Nodule size is an important factor influencing the diagnostic accuracy of CT fluoroscopy-guided core biopsy. Montaudon et al. (15) reported that a lesion size ≤ 1 cm was significantly associated with a higher rate of false negative diagnoses of malignancy. They suggested that by using a coaxial automated device, a high diagnostic yield could be obtained. Li et al. (16) reported that the diagnostic accuracy for lesions < 1.5 cm in diameter (74%) was statistically different from lesions > 1.5 cm in diameter (97%). These differences in the diagnostic accuracy of small and large pulmonary nodules might be associated with the aspiration needle used instead of the core biopsy needle. Two prior studies (15, 16) used conventional CT for biopsy guidance. However, the diagnostic accuracy could have been higher if CT fluoroscopy was used for guidance because it might have been easier to target small lesions < 1 cm in diameter.

Special attention to patients and radiologists is needed for CT fluoroscopy-guided biopsies due to the hazard of radiation exposure. During CT fluoroscopy-guided biopsy, a patient is exposed to radiation at or near the needle puncture site. The fixed position of the scanning plane in combination with high exposure factors may lead to a high accumulation of radiation exposure to the patient’s skin. Radiologists are also exposed to scattered radiation because of their close proximity to the scanning. Kim et al. (13) studied that radiation doses to the patients and doctors and diagnostic performance for CT-guided percutaneous needle aspiration biopsy of pulmonary lesions were performed with or without fluoroscopic guidance. The surface radiation doses to the patient and the doctor as well as the hand measured using a thermoluminescent dosimeter was significantly higher in the group with fluoroscopic guidance. However, the procedure time was significantly shorter, and the number of punctures and complication rate were lower. To minimize radiation exposure we wore lead covered clothing, gloves, and glasses. To avoid irradiating the hands, the needle was manipulated with a needle holder during CT fluoroscopy-guided biopsy and fluoroscopy time was
minimized.

Contrary to general assumptions that the diagnostic accuracy of CT-guided biopsy for ground-glass opacity (GGO) lesions is less than for solid lesions, Kim et al. (9) reported that CT-guided core biopsy of pulmonary GGO lesions could yield a high diagnostic accuracy approaching that of solid lesions. In fact, the diagnostic accuracy of GGOs was 91%, with a positive predictive value of 97%, and a negative predictive value of 75%. This result might be related to the use of a cutting needle rather than an aspiration needle. The results of our study showed a 92% diagnostic accuracy for GGO lesions. This result was lower than for solid lesions (96%); however, the difference was not statistically significant. Therefore, subsolid lesions could be biopsied when needed; if a cutting biopsy needle is used, the diagnostic accuracy for subsolid lesions is as high as for solid lesions. However, there is still debate over whether small pure GGO nodules need to be biopsied.

In several studies, investigators have compared the frequency of pneumothorax after CT fluoroscopy-guided lung biopsy. Kirchner et al. (17) showed that the frequency of pneumothorax was 38% (8/21) after CT fluoroscopy-guided biopsies of lung lesions. In our study, complications such as pneumothorax and thoracosomy occurred in 27% of 62 patients, which is in the mid range of reported complication rates (12.5-69%) (13). The prevalence of pulmonary hemorrhage in our study was relatively higher than rates reported (20.2-30%) in the literature (9, 15, 18). Further, pulmonary hemorrhage along the needle path or around the target lesion developed in 35 patients (56%), but none required specific treatment. Our study included a higher proportion of small nodules and GGO nodules, which are risk factors for bleeding, compared to previous studies (18). Laurent et al. (19) found that when using a coaxial 20-gauge automated cutting needle, there was a 43% alveolar hemorrhage rate and a 6% hemoptysis rate in 67 biopsies of lung nodules < 20 mm in size, compared to a 14% alveolar hemorrhage rate and a 5% hemoptysis rate in 135 biopsies of larger lesions. When taking a biopsy from a small lesion or GGO lesion, the cutting needle often includes a portion of aerated lung, which results in a lower tamponading effect than solid tissue. Therefore, embedding the cutting needle into lung lesions without violating the aerated lung and avoiding the trauma incurred by the rapidly firing needle used in an automated gun are important precautions in avoiding unnecessary bleeding complications (18).

The limitations of our study include the following. First, our study had a relatively small number of enrolled patients, especially in the subsolid nodule group and the group of nodules equal to or less than 10 mm. To achieve statistical significance, more studies with large data sets will be needed. Second, our study had a follow-up period of 12 months. Pulmonary nodules are generally considered benign if they are stable in size for two years. GGO lesions such as atypical adenomatous hyperplasia or bronchioloalveolar carcinoma may persist without size change over two years. Therefore, a 12-month follow-up period might have missed a lung malignancy in patients without histological confirmation. However, our study patients were followed with CT that had a specific benign pathology such as tuberculosis and chondroid hamartoma. Patients that had a nonspecific pathological diagnosis such as chronic inflammation underwent surgical resection. None of the patients that were followed with CT had subsolid nodules. Only solid nodules were followed by CT; therefore, a short follow-up period does not appear to significantly affect the overall diagnosis. Third, biopsies were performed in patients that had a chest CT that was suspicious for a malignant pulmonary lesion. The diagnostic accuracy for malignant disease was 90%, compared to 80% for benign disease. Our study included more malignant lesions than benign lesions, which might have contributed to the high diagnostic accuracy.

In conclusion, CT fluoroscopy-guided core biopsy was demonstrated to be a safe and accurate modality for the diagnosis of small (≤ 20 mm) pulmonary nodules. This technology could be used with high diagnostic accuracy even in lesions equal to or less than 10 mm and for subsolid nodules.

REFERENCES

목적: 폐 소결절(≤ 20 mm)의 진단에 있어 CT 투시촬영 유도하 중심부바늘생검의 유용성에 대해 알아보고자 하였다.

대상과 방법: 폐 소결절(≤ 20 mm)에 대하여 CT 투시촬영 유도하 중심부바늘생검을 시행 받은 62명의 환자를 대상으로 진단적 정확도와 합병증에 대해 알아보았다. 조직검사 결과와 수술(n = 35) 또는 추적검사(n = 27)로 확인된 최종 결과를 비교하여 진단적 정확도를 계산하였으며, 진단적 정확도는 소결절의 크기(≤ 10 mm 대 > 10 mm)와 결절의 밀도(고형결절 대 아 고형결절)에 따라 차이가 있는지 알아보았다.

결과: 최종적으로 39명의 환자에서 악성 또는 전암 병소가 확인되었다. CT 투시촬영 유도하 중심부바늘생검을 통해 이 중 36명은 진양성, 3명은 가음성으로 나왔다(민감도, 92%). 23명의 환자들은 양성 병소로 밝혀졌으며 가양성 결과는 없었다(특이도, 100%). CT 투시촬영 유도하 폐 결절 중심부바늘생검의 진단적 정확도는 95%였다. 10 mm 이하의 폐 결절의 민감도와 진단적 정확도는 각각 85%와 91%였으며, 10 mm보다 큰 폐 결절의 민감도와 진단적 정확도는 각각 96%와 97%였다(p > 0.05). 고형 폐 결절의 민감도와 진단적 정확도는 각각 93%와 96%였으며, 아 고형 폐 결절의 민감도와 진단적 정확도는 각각 90%와 92%였다(p > 0.05). 17명의 환자(27%)에서 기흉이 발생하였으며 이 중 2명(3%)은 흉강 배액관 삽입을 시행하였다.

결론: CT 투시촬영 유도하 중심부바늘생검은 폐 소결절(≤ 20 mm) 진단에 있어 비교적 정확하고 안전한 검사이다.

1고려대학교 의과대학 구로병원 영상의학과학교실, 2가천의과학대학교 길병원 영상의학과학교실, 고려대학교 의과대학 구로병원 3흉부외과학학교실, 4병리학교실