Feasibility and therapeutic implication of computed tomography-guided TruCut biopsy in cases of recurrent adenocarcinoma lung

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INTRODUCTION

Lung cancer is one of the leading causes of cancer deaths worldwide. The common histologic types are Adenocarcinoma (ADC), Squamous Cell Carcinoma (SCC) and Small Cell Lung Cancer (SCLC). Clinical staging is performed with noninvasive diagnostic modalities, such as total body CT scan with contrast, and/or Positron Emission Tomography (PET). Diagnostic tissue biopsies may be obtained through percutaneous route with image-guided needle biopsy or bronchoscopic biopsy for endobronchial lesions or open biopsy if the former modalities could not obtain tissue. TruCut biopsy is a simple procedure, is relatively safe, rapid and a reliable technique for the diagnosis of lung lesions. But all patients may not be ideal candidates for needle biopsy at recurrence because of various tumour related and patient-related factors. This study of ours tried to find out the feasibility of image-guided transthoracic needle biopsy and compared its therapeutic implications with those who could not undergo the procedure.

Result: Overall adequacy rate of obtaining tissue samples was 89.7% (35/39). All patients who undergo needle biopsy tolerated it well. Most common complications were pneumothorax (12.8%) (5/39) and pulmonary haemorrhage (10.2%) (4/39). Two (5.1%) patients developed hydropneumothorax. The cumulative percentage of side effects was 17.9% (7/39) and no procedure-related fatal. 42.8% of patients who underwent needle biopsy were started with the second line targeted/Immunotherapy. Only 21.0% of the patients who underwent liquid biopsy instead, received targeted therapy in the second line.

Conclusion: TruCut biopsies of NSCLC’s at recurrence are feasible and are adequate in appropriately selected patients and associated with acceptable rates of complications. Rebiopsy may explore new tumour characteristics and give the opportunity to act on changes in tumour behaviour. For those patients who are not candidates for a needle biopsy, in them, liquid biopsy is a comparable alternative.

Key words: recurrent lung cancer, repeat needle biopsy, liquid biopsy

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safety of CT guided lung biopsy of NSCLC (Adenocarcinoma) at recurrence. Finer molecular characterization through next-generation sequencing and immunohistochemistry and to find out the pros and cons of image-guided lung biopsy in comparison to liquid biopsy.

METHODOLOGY

Sixty-six non-small cell lung cancer (Adenocarcinoma) patients irrespective of the stage of presentation, who were being treated in our hospital, were enrolled in the study and followed up prospectively. Over time 12 patients were lost to follow up. All of the 54 patients on follow up eventually had recurrence/progression of the disease, which was documented with contrast, enhanced CT scan. All of them were evaluated for trans-thoracic CT guided needle biopsy at progression. The feasibility of needle biopsy was studied according to the various tumour and patient-related factors and reasons for not being able to conduct needle biopsies were documented. Patients in whom, a needle biopsy was not possible for whatever reasons, were subjected to liquid biopsy. Between the liquid biopsies and needle biopsies, therapeutic implications were compared.

Pre-procedure evaluation and the procedure

Prothrombin Time (PT), International Normalized Ratio (INR), Activated Partial Thromboplastin Time (APTT), and platelet count was checked before a needle biopsy. Those patients, who were on aspirin or clopidogrel, were asked to discontinue it 5 days before the biopsy. Patients on oral anticoagulants were switched to low molecular weight heparin before 3 days, which in turn was withheld on the day of the procedure. CT studies were performed on 128 SLICE CT SCANNER [GE OPTIMA CT660] in all patients. Location of the lesions, location of fissures adjacent to the lung lesions or within the pathway of the biopsy needle trajectory, location of adjacent arteries and veins were evaluated, in order to plan the needle trajectory. The angle of entry of the needle, route of entry and distance between skin and the lesion and the length of throw was documented on the CT scan monitor. Patients were positioned either in prone, supine or lateral position depending on the skin site entry point chosen. The breath-holding technique was followed during the procedure and it was explained to the patient and was practised beforehand. Patients were asked to avoid coughing and taking deep breaths during the procedure (Figures 1-3).

Statistical evaluation

Quantitative data is represented in form of a percentage. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 25.0.

RESULTS

Baseline patient and tumour characteristics are mentioned in Table 1. All of the 54 patients on follow up eventually had recurrence/progression of the disease. Forty-six (n=46) of these 54 patients had a recurrence in the lung with or without other sites of metastasis. And the rest 8 patients had recurrences at distant sites only and did not involve lung at recurrence. Out of the 46 patients who had lung lesions at recurrence, 39 patients underwent trans-thoracic needle biopsy. Among them, viable tumour tissue could be obtained for 35 patients. Among the 7 patients who did not undergo needle biopsy, 3 had a poor general condition with low oxygen saturation. For 4 patients, lung lesions were close to the great vessels, which made them unfit for needle biopsies. Patients in whom viable tissue could not be acquired through needle biopsy, or whose who could not undergo needle biopsy because of technical issues, or those who did not have a lung lesion at recurrence and other lesions were not amenable for biopsy, were subjected to liquid biopsy.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
</tr>
<tr>
<td>Female</td>
<td>22</td>
</tr>
<tr>
<td>Age (in years)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>63(29-87)</td>
</tr>
<tr>
<td>Primary treatment</td>
<td></td>
</tr>
<tr>
<td>CT+RT</td>
<td>12</td>
</tr>
<tr>
<td>Palliative chemotherapy</td>
<td>20</td>
</tr>
<tr>
<td>TKIs</td>
<td>34</td>
</tr>
<tr>
<td>Sites of disease on recurrence/progression</td>
<td></td>
</tr>
<tr>
<td>Lung ± others</td>
<td>46</td>
</tr>
<tr>
<td>Other sites without lung lesion</td>
<td>8</td>
</tr>
<tr>
<td>Location of the largest lung lesion</td>
<td></td>
</tr>
<tr>
<td>RUL</td>
<td>12(26%)</td>
</tr>
<tr>
<td>RML</td>
<td>6(12%)</td>
</tr>
<tr>
<td>RLL</td>
<td>10(22%)</td>
</tr>
<tr>
<td>LUL</td>
<td>11(24%)</td>
</tr>
<tr>
<td>LLL</td>
<td>7(16%)</td>
</tr>
</tbody>
</table>
### Tab. 2. Results of molecular analysis

<table>
<thead>
<tr>
<th></th>
<th>Needle biopsy at recurrence (n=35)</th>
<th>Liquid biopsy at recurrence (n=19)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR exon 19 mutation</td>
<td>13</td>
<td>9</td>
<td>P value not significant</td>
</tr>
<tr>
<td>EGFR exon 21 (L858R)</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>EGFR Exon 20(T790M)</td>
<td>5</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>PD L1</td>
<td>7</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>ALK rearrangement</td>
<td>2</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>ROS1</td>
<td>1</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>BRAF (V600E)</td>
<td>2</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

*Chi-square test

### Tab. 3. Complications in rebiopsies performed in relapsed cases of Non-small cell lung cancer

<table>
<thead>
<tr>
<th>Complications</th>
<th>(n=39)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax</td>
<td>5</td>
<td>12.82%</td>
</tr>
<tr>
<td>Pulmonary Hemorrhage</td>
<td>4</td>
<td>10.25%</td>
</tr>
<tr>
<td>Hydropneumothorax</td>
<td>2</td>
<td>5.12%</td>
</tr>
<tr>
<td>No complication</td>
<td>32</td>
<td>82.05%</td>
</tr>
</tbody>
</table>

**Fig. 1.** Representative case of percutaneous transthoracic core needle biopsy in a Relapsed NSCLC patient. Axial CT image (lung window) [5 mm section thickness] shows a mass in the right middle lobe; (a): Surface Markers; (b): Coaxial needle approach; (c): Advancement to lesion. Repeat CT scan obtained after needle insertion ensures that the needle tip (arrow) is located within the target mass.

**Fig. 2.** Representative case of percutaneous transthoracic core-needle biopsy in a Relapsed NSCLC patient. Axial CT image (lung window) [5 mm section thickness] shows mass in the right lower lobe; (a): Repeat CT scan obtained after needle insertion ensures that the needle tip (arrow) is located within the target mass; (b): Post Procedure—Pulmonary Hemorrhage.
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location of the tumour. Out of 39 patients who underwent

limiting factors such as poor performance status and difficult

patients, 7(15.3%) patients did not undergo biopsy due to the

lung lesions at recurrence, rebiopsy was performed in 39(84.7%)

NSCLC (adenocarcinoma) patients. Out of 46 patients who had

feasibility and safety of CT guided TruCut biopsy in recurrent

The study was conducted with the objective to determine the

DISCUSSION

The study was conducted with the objective to determine the

feasibility and safety of CT guided TruCut biopsy in recurrent

NSCLC (adenocarcinoma) patients. Out of 46 patients who had

lung lesions at recurrence, rebiopsy was performed in 39(84.7%)

patients, 7(15.3%) patients did not undergo biopsy due to the

limiting factors such as poor performance status and difficult

location of the tumour. Out of 39 patients who underwent

needle biopsy, adequate tumour tissue could not be obtained

in 4(10.3%) patients. So the adequacy rate of obtaining tissue

samples was 89.7% (35/39). All patients who underwent needle

biopsy tolerated well, cumulative percentage of side effects was

17.9% (7/39) and no procedure-related fatality (Tables 2 and 3)

(Figures 2 and 3). According to studies, pneumothorax has been

reported to be the most common complication of needle biopsy

of the lung lesions and is reported to occur in 17%-27% of

patients; pulmonary haemorrhage is the second most common

complication, with reported frequencies ranging from 4%-27%

[6-10]. Our complication rates for pneumothorax (12.82%)

and pulmonary haemorrhage (10.25%) were comparable to

the above-mentioned studies. Patients treated with EGFR-

TKIs, frequently leads to the appearance of drug-resistant

mutations within the target kinase [11-13]. A few of these new

mutations are targetable, so the molecular characterisation of

the additionally acquired mutations is the need of the hour. In

our study, there was no statistically significant difference in the

probability of finding a driver mutation or a resistance causing

mutation like T790M, between needle biopsy and liquid biopsy.

But in comparison to the liquid biopsy, a needle biopsy can

procure tissue for histopathologic examination and IHC, so

can detect histologic transformations or second primary if any,

as well (Table 2). 42.8% (15/35) of patients who underwent

needle biopsy were started with the second line targeted/

Immunotherapy. Only 21.0% (4/19) of the patients who

underwent liquid biopsy instead, received targeted therapy in

the second line.

CONCLUSION

Rebiopsy and mutational analysis of NSCLC’S are feasible and

are adequate in appropriately selected patients and associated

with acceptable rates of complications. Rebiopsy may explore

new tumour characteristics and give the opportunity to act on

changes in tumour behaviour. Rebiopsy can be used to predict

therapeutic resistance and consequently redirect targeted

therapies. Thus changes in treatment facilitate better tumour

control. For those patients who are not candidates for a needle

biopsy, in them, liquid biopsy is a comparable alternative.


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