Comparison between endobronchial forceps-biopsy and cryo-biopsy by flexible bronchoscopy

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KEYWORDS
Cryobiopsy; Bronchoscopy; Lung cancer

Abstract  Background: Invasive procedures such as bronchoscopic biopsy, bronchial washing, and bronchial brushing are widely used in the diagnosis of lung cancers. The mean diagnostic rate with bronchoscopic forceps biopsy is 74% in central tumors; the new biopsy technique of cryobiopsy appears to provide better diagnostic samples.

Aim of the work: To compare the efficacy and diagnostic yield of endobronchial cryobiopsy with forceps biopsy in the diagnosis of lung cancer.

Methods: Twenty-five patients who underwent bronchoscopy were included in this study. Three forceps biopsies and one cryobiopsy with ERBE cryo probe were obtained from each subject. Biopsies interpretations were done by one expert pathologist.

Results: Hemorrhage was the only complication in both procedures, there was no significant difference between these two procedures in the incidence of hemorrhage (P > 0.05). There is significant difference as regarding crushing and loss of architecture under microscopy (P < 0.001), forceps biopsies shows crushing and loss of architecture more than cryo. Mean diameters of samples taken with forceps biopsy and cryo biopsy were 0.5 and 1.4 cm, respectively (P < 0.001), 20 patients (80%) were diagnosed with forceps biopsies, and 25 patients (100%) were diagnosed with cryo biopsy biopsies.

Conclusions: We concluded that cryo probe biopsies were more successful than forceps biopsies in the diagnosis of lung cancer. Nevertheless, further investigations are warranted to determine an efficacy of cryo probe biopsy procedures and a rationale to use as a part of routine flexible bronchoscopy.

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Introduction

Invasive procedures such as bronchoscopic biopsy, bronchial washing, and bronchial brushing are widely used in the diagnosis of lung cancers. The mean diagnostic rate with bronchoscopic forceps biopsy is 74% in central tumors [1].
A forceps-biopsy is performed to acquire tissue from patients with an endobronchial carcinoma using a flexible bronchoscope. Recently, a cryo-biopsy has also been used to acquire tissue samples. Cryo-biopsy is the diagnostic application of extreme cold for the local destruction of abnormal living tissue. This technique is safe, with no radiation danger, no risk of electrical accidents, and little risk of bleeding [2].

In studies assessing the histological material obtained using cryoprobes in cases of endobronchial tumors, the samples were found to be larger with preserved architecture and sufficient for diagnosis than those obtained with conventional forceps. This has led to considering the possibility of using cryoprobes for performing endobronchial biopsy [3,4].

Cryoprobe biopsies were more successful than forceps biopsies in diagnosis up to 92% [1].

**Aim of the work**

To compare the efficacy and diagnostic yield of endobronchial cryobiopsy with forceps biopsy in the diagnosis of lung cancer

**Subject & methods**

This study was carried out on 25 patients who attended the chest department, Minoufia university hospitals and a written consent was obtained from each patient participating in the study.

The patients underwent flexible Fiberoptic bronchoscopy; Using (Pentax FB, 19-TV, with an internal diameter of 2 mm).

Any patient having contraindication for fiber-optic bronchoscopy is excluded as;

1– Severe uncorrected hypoxemia despite the administration of supplemental oxygen.
2– Unstable cardiovascular or hemodynamic status.
3– Coagulation defects. The prothrombin concentration should be greater than 70%, and the platelet count greater than 60,000/mm³.
4– Acute exacerbation of chronic obstructive pulmonary diseases.

1- Pre-medication:

- Atropine 0.5–1 mg intramuscularly (I.M) half an hour before the procedure.
- Midazolam 2–5 mg (slow intravenous injection (I.V) over about 30 s).

2- Topical anesthesia:

A lignocaine gel was sprayed in nostrils and 10% Lidocaine solution directly into the larynx. Lidocaine 2% was used to anaesthetize the airways through the bronchoscope channel during the procedure as needed.

- The fiberoptic bronchoscopy was carried out trans-nasally except in two patients with nasal obstruction, where the trans-oral approach was used.
- Supplemental oxygen was given throughout the procedure when needed.

Full exploration of the endobronchial tree starting with the healthy side was done then 3 biopsies will be taken by forceps biopsy and one biopsy by cryoprobe from each patient with endobronchial lesion.

Forceps biopsies were performed by passing the forceps into the bronchoscope working channel, opening the forceps, advancing the bronchoscope or forceps onto the lesion, closing the forceps thus grasping, gently tugging so as not to tear the tissue while retrieving the forceps through the working channel or barrel, and then placing it in 10% formalin. In the patients that were studied, a minimum of 3 endobronchial forceps biopsies were performed initially then endobronchial CB is performed with the following protocol; the cryotherapy probe (ERBE flexible probe used nitrous oxide which induces a temperature of -89.5 °C at the tip of the probe, seen below in Fig. 1) is placed in direct contact with the lesion that is being sampled, and when approaching exophytic lesions, the probe is frozen for 3–5 s (or until the initiation of the frosting at the tip of the probe is visible). After this short period of freezing, the bronchoscope is removed en bloc with the cryotherapy probe.

Frozen biopsy material was separated from the cryoprobe by way of plunging into saline.

After having a specific code, each specimen is grossly examined to measure the largest diameter of the biopsy. After that biopsies were fixed separately in 10% buffered formalin. Then, 4 mm sections were obtained from paraffin embedded blocks and stained by hematoxylin and eosin (H&E). The slides were histologically evaluated by one pathology specialist using a light microscope.

**Results**

This study was done on 25 patients who attended the Chest department Minoufia University hospitals. 18 of them were males and 7 females with a mean age of 57.04 ± 6.4 years.

The above table showing the diagnosis was achieved in 100% of cases in cryo biopsy, while the diagnostic yield by forceps biopsy was 80.0% and 20.0% were not diagnosed and all of them were squamous cell carcinoma as reported by cryo (see Figs. 2–5).

**Discussion**

Diagnostic bronchoscopy with endobronchial forceps biopsy (FB) is primarily practiced in patients with suspected thoracic malignancy and visible endobronchial pathology.
A comprehensive review of the literature indicates a diagnostic yield of FB of approximately 74% [5] and biopsy specimens have a diameter of approximately 2 mm [6].

The diagnostic utility is limited by their small size, which may result in several problems. First, there is a moderate yield of sections per biopsy specimen. Second, the mechanical damage of the biopsy specimen causes difficulties in interpretation of anatomic structure and histopathologic changes. Finally, because vital tumor tissues do not always present further, immunohistochemical staining is hampered. The diagnostic yield can be increased by combining bronchial biopsy with complementary diagnostic methods, such as needle aspiration, bronchial lavage cytology, and brush cytology; however, this leads to a relevant increase in time and costs [7–12].

The introduction of a new sampling technique is another opportunity to increase the diagnostic yield. The flexible cryoprobe is primarily used for cryoextraction of malignant airway stenosis and was introduced as an alternative method for mechanical tumor debulking, which is immediately effective. Because of extraordinarily well-preserved tissue samples (larger in size with less mechanical damage and mostly vital tumor) from cryorecanalization procedures, the technique has been transferred to the biopsy of endobronchial lesions [13,14].

So, the aim of this study was to assess the diagnostic yield and to show the feasibility and safety of endobronchial biopsies using the flexible cryoprobe. In addition, for the new diagnostic method, the sensitivity of cryobiopsy (CB) compared with FB was evaluated.
This study was done on 25 patients who attended the chest department Minoufia University hospitals. 18 of them were males and 7 females with a mean age of 57.04 ± 6.4 years. This result is logical as males are more liable to lung cancer than females which come in agreement with [15] (see Tables 1–3).

CB can be performed using both the flexible and rigid bronchoscope. The use of the cryo flexible probe guided by a flexible bronchoscope allowed endobronchial cryobiopsies of central airways, as well as more distal airways, provided that the lesion is visible on bronchoscopic evaluation. Though all lesions were deemed approachable at the outset, one operator noted that it was difficult to flex the bronchoscope in order to biopsy a lesion in the right upper lobe even with the use of the smaller diameter cryo probe (although this was eventually accomplished). Thus, one potential limitation is that lesions located in airways requiring significant flexure of the bronchoscope may not be reached with the current cryo probes [16].

Operators found that sampling lesions lying parallel to the axis of the bronchoscope (rigid and flexible) was much easier with the cryo probe than with the endobronchial forceps [16].

A disadvantage of CB via a flexible bronchoscope is that the frozen probe with the attached biopsy material cannot be removed through the working channel. In order to remove the specimen from the airway, it is necessary to remove both the bronchoscope with the cryoprobe and the attached specimen en block. The procedure is repeated by reinserting the bronchoscope and the cryoprobe [16,17].

Endotracheal intubation could be utilized to minimize the possibility of the vocal cord and airway trauma. In this regard, Hetzel et al. in their recent study of CB actually indicated that a disadvantage of CB was that it is recommended to intubate all patients, either with a flexible endotracheal tube or through rigid bronchoscopy [16], while we agree with them in that though the complication risk from intubation is small; we do not consider it negligible. Additionally, such a practice is certainly not commonly accepted in many institutions. In our experience, the use of a supraglottic airway mask to perform routine bronchoscopies can many times be advantageous, as is the case when performing bronchoscopies with CB. It provides similar advantages to endotracheal intubation yet carries a lower risk of direct damage to the vocal cords or trachea [16].

In this study we use fiberoptic bronchoscopy pentax type while [17] use rigid bronchoscopy and compare it with fiberoptic bronchoscopy also [16,18] use fiberoptic bronchoscopy as it doesn’t need anesthesia and can reach deeper than the rigid one, also some use endotracheal intubation during procedures as done by Hetzal et al. [16] but we don’t use it.

The diagnosis was achieved in 100% of cases in cryo biopsy, while the diagnostic yield by forceps biopsy was 79.2% which comes with a diagnostic yield of FB generally accepted to be below 80%, though it can improve with the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic data.</th>
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<tr>
<td></td>
<td>Frequency</td>
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<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>Male</td>
<td>18</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
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<td>Age</td>
<td>Mean ± S.D.</td>
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<th>Table 2</th>
<th>Diagnostic yield of two biopsies.</th>
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<tr>
<td>Biopsy</td>
<td></td>
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<tr>
<td>Cryo</td>
<td>3</td>
</tr>
<tr>
<td>Forceps</td>
<td>3</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>SCC</td>
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<td>Squamous</td>
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<td>Adeno</td>
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<td>Undiagnosed</td>
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<tr>
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<th>Table 3</th>
<th>showing significant difference as regarding size of biopsies (cryo size &gt; forceps size), also there was significant difference as regarding crushing and architecture under microscopy (forceps showed crushing and loss of architecture more than cryo). But as regards hemorrhage in biopsies there were no significant differences between both.</th>
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<tbody>
<tr>
<td>Biopsy</td>
<td></td>
</tr>
<tr>
<td>Cryo</td>
<td></td>
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<tr>
<td>No</td>
<td></td>
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<tr>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
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</tr>
<tr>
<td>No</td>
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<td>Crushing</td>
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<td>No</td>
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<tr>
<td>Architecture</td>
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</tr>
<tr>
<td>No</td>
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<tr>
<td>Size (X ± SD)</td>
<td>1.4 ± 0.29</td>
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<td>Cm</td>
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performance of additional sampling techniques [5,6], while [17] report 89.1% and 65.5% for cryo and forceps biopsies respectively, also [16] report 95% and 85% for cryo and forceps biopsies respectively.

CB has a previously reported sensitivity of 89%, when biopsying exophytic malignant lesions, and more recently an overall 95% diagnostic yield for all malignant lesions [9]. Our diagnostic yield is comparable or higher than those previously reported for both CB and FB. For FB one reason may be related to the sampling technique and the use of deeper sedation, allowing more accurate targeting of the suspicious lesion. Repeated biopsy sampling of each lesion may have resulted in a greater volume of material, which has been demonstrated to improve the diagnostic yield [19]. Interestingly, Hetzel et al. [16] also demonstrated a higher yield of FB when this was performed under rigid bronchoscopy (reported at 89.5%) and noticed that CB did not provide a statistically significant advantage in these cases. The authors comment also on the fact that “due to general anesthesia and a reduced breathing amplitude, positioning of the forceps becomes easier, thus diminishing the benefit of cryobiopsy” [9].

One must also wonder if this simply led to more FB samples. In their study the number of biopsies was left to the bronchoscopist discretion, and the number of biopsies obtained or an analysis of this during the rigid bronchoscopy cases is not provided [9].

It was reported that adequacy and size of the specimens may improve the histological accuracy of NSCLC. There is evidence that the size of the biopsies correlates with the diagnostic yield: larger samples obtained through a rigid bronchoscope have a yield of 78% [20].

In this study there was significant difference as regarding size of biopsies (the mean cryobiopsy size was 1.4 ± 0.29 in comparison to the forceps biopsy which was 0.5 ± 0.27, also there was significant difference as regarding crushing and architecture under microscopy (forceps showed crushing and loss of architecture more than cryo), so the cryobiopsy sample is large in diameter with preserved architecture and one biopsy in each setting which increases the diagnostic yield and saves time, but as regards hemorrhage in biopsies there was no significant difference between both. Also the above results come with [1,15–17].

Biopsies performed with the cryoprobe proved extremely safe. One minor complication was reported, related to a small bleed that resolved spontaneously, following instillation of cold saline as regarded by Hetzel et al. and Shuman et al. [16,17].

In conclusion this study showed that cryobiopsy is a safe technique with a diagnostic yield, which is comparable to that of conventional forceps biopsy. A larger specimen size and better tissue quality along with a low incidence of bleeding in cryobiopsy makes this method an acceptable alternative to forceps biopsy.

Conflict of interest

There is no conflict of interest.

References


