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ORIGINAL ARTICLE

The diagnostic yield of cryobiopsy versus forceps biopsy of malignant endobronchial lesions

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KEYWORDS

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Abstract *Background:* In patients with endoscopically visible lesions, flexible bronchoscopy with FB is the most frequently used technique to obtain specimens for pathologic analysis with sensitivity of approximately 74%. The flexible cryoprobe, so far used for cryotherapy and endoluminal tumor debulking, also seemed to be suitable for biopsies from visible lesions.

Objective: The aim of this study was to prospectively evaluate the diagnostic yield and safety of cryobiopsy and forceps biopsy.

Patients and methods: For each patient group with a confirmed endobronchial lesion, diagnostic yield and safety of forceps biopsy and cryobiopsy were recorded.

Results: The diagnostic yield was significantly higher with cryobiopsy (95%), compared with forceps biopsy (80%) ($p < 0.001$).

Conclusion: Cryobiopsy is a safe high diagnostic yield technique in sampling endobronchial tumor lesions.

Introduction

The determination of histopathological cell type and stage of primary lung tumor is crucial to develop an appropriate treatment approach that affects morbidity and mortality. Invasive methods widely used in histopathological diagnosis of lung cancer are bronchoscopic mucosal biopsy, bronchial washing, bronchial brushing, and transthoracic needle aspiration [1,2].

The traditional approach to the diagnosis of visible endobronchial disease has been through forceps biopsy (FB) via a flexible bronchoscope. Previous studies have concluded that the diagnostic yield of bronchoscopy is augmented when multiple procedures are performed, including brushings, needle aspirates, and washings. Flexible bronchoscopy now is the diagnostic tool of choice to diagnose endobronchial malignancies [3–5].

The major drawback of the forceps biopsy technique is the relatively small amount of tissue obtained; with a moderate yield of sections per biopsy specimen, the mechanical damage of the biopsy specimen, and because vital tumor tissues do not always present further, immunohistochemical staining is hampered [6,7].

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Searching for a biopsy tool of choice that should be safe, capable of obtaining large biopsy samples without causing any morphologic alteration to the tissue samples, thereby reducing number of additional sampling techniques required and need for repeated bronchoscopies. Flexible cryoprobe appears to have most of these characteristics [8,9].

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 [10,11]. 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 [12].

Aim of the study

This study aimed to evaluate the diagnostic yield and safety of endobronchial biopsies using the flexible cryoprobe, compared to conventional forceps biopsy.

Patients and methods

This study was carried out on 40 patients with suspected endobronchial malignant lesions, based on clinical diagnosis, and enhanced C.T. chest.

Inclusion criteria

Exophytic endobronchial tumor (endoscopically visible lesion), signed informed consent form, and sufficient respiratory function (oxygen saturation $>90\%$ with 2 liters of supplementary oxygen).

Exclusion criteria

Patient with bleeding tendency or on anticoagulant therapy, previous cancer-specific treatment or endobronchial diagnostic technique, O_2 saturation $<90\%$ on $\geqslant 2$ L/min, or recent severe unstable cardiac diseases.

Patients with endoscopically visible lesion were randomized into 2 groups (using 2 closed envelops with one selected for randomization):

Group I: Included 20 patients in whom biopsy was carried out using forceps biopsy (2 samples).

Group II: Included 20 patients in whom biopsy was carried out using cryobiopsy (one sample).

Bronchoscopy and biopsy

Both procedures were carried out during flexible bronchoscopy. The patients were deeply sedated with intravenous midazolam and local anesthesia was achieved with 10% xylocaine solution. Before biopsy sampling, a bronchoscopic assessment of patients' bronchial systems was performed.

The forceps biopsy, two biopsies, was performed conventionally (using a reusable fenestrated forceps FB-21C or FB-52C-1, Olympus Corp, Hamburg, Germany). For cryobiopsy, a cryoprobe was used with carbon dioxide as the cryogen. The temperature of the probe tip was approximately -89 °C (Erbokryo, ERBE Medizintechnik GmbH, Tuebingen, Germany). The flexible cryoprobe was placed onto the endobronchial lesion, and the freezing process was started for 3–5 s or until the ice front reached the bronchial wall. The probe was pulled out enbloc together with the bronchoscope and the frozen tissue sample on the probe's tip. The tissue was then released from the probe's tip by thawing in a sterile 0.9% sodium chloride water bath and placed in formalin.

Histopathology

All samples were fixed in 10% formalin for at least 24 h before pathological analysis. Using centimeters (cm), biopsies were measured in the largest diameter prior to sectioning for microscopic evaluation.

Statistical analysis

All data were expressed as median (IQR) or as numeric values (%). The diagnostic accuracy of the cryotechnology and that of the forceps biopsy procedures was compared with an x^2 test, and the size of the specimens obtained by cryotechnology and forceps biopsy was compared with a t test. The level of statistical significance was set at $p\_0.05$. All analyses were performed with SPSS software (version 13.0, SPSS, Chicago, IL).

Results

A total of 40 patients with suspected endobronchial malignant lesion were randomized into two groups, patients included in group I underwent conventional forceps biopsy, while patients in group II had been cryobiopsied. The characteristics of the study population are illustrated in Table 1.

Based on enhanced CT, tumor size was classified into tumor size more than 3 cm in the largest diameter, and tumor size less than 3 cm Table 2. On bronchoscopy, endobronchial lesion was confirmed and localized Table 2.

Median size of biopsies with cryoprobe and forceps were 1.7 cm (0.8–2.2 cm), and 0.6 cm (0.2–1.1 cm) respectively ($p < 0.001$). Furthermore, histopathological examination of tissue samples obtained via cryobiopsy was demonstrated to be of good quality in terms of necrosis and artifact-free sample area, with the artifact-free tissue areas of each slide significantly larger with cryobiopsies than with forceps biopsies (1.56 vs 0.4 cm, $p < 0.001$) Table 3, Figs. 1 and 2.

Table 1 Basic characteristics of the study population.

Parameter	Group I		Group II	
	$N = 20$		$N = 20$	
Age (years)				
Mean ± SD	53.93 ± 8.37		57.83 ± 10.88	
Sex				
Male	14	70%	15	75%
Female	6	30%	5	25%
Smoking history				
Non smoker	5	25%	4	20%
Ex-smoker	4	20%	6	30%
Current smoker	11	55%	10	50%