

Conventional forceps or hot biopsy: comparative study of two methods in diagnosis of endobronchial lesions

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Abstract

Background: It is suggested that hot electrocoagulation-enabled forceps (hot biopsy) may reduce hemorrhage risk after the biopsy in endobronchial tumors. The main concern in this method is possible reduction of the specimen's quality.
Objectives: To compare the procedure related hemorrhage with hot biopsy and conventional forceps biopsy and the diagnostic quality of the obtained specimens with either technique.
Methods: In this prospective study, assessment of the biopsy samples and quantity of hemorrhage were done in a blind fashion. At first, for each patient a definite clinical diagnosis was made based on pathologic examination of all available samples, clinical data, and imaging findings. Then, second pathologist reviewed all samples to evaluate the quality of the samples.
Results: A total of 36 patients with endobronchial lesions were included in this study. Definite diagnosis was made in 83% of the patients. Diagnostic yield of the two methods were not statistically different, while the mean hemorrhage grades of all hot biopsy protocols were significantly lower as compared to that of conventional biopsy ($p=0.003$, $p<0.001$ and $p<0.001$ for 10, 20 and 40 voltages respectively). No significant difference was detected between the qualities of specimens obtained by hot biopsy methods in comparison with conventional biopsy ($p>0.05$ for all three voltages).
Conclusions: Hot biopsy can be a valuable alternative to forceps biopsy in evaluating endobronchial lesions.
Keywords: hot biopsy, endobronchial tumors, forceps biopsy, bleeding

Rezumat

Biopsia convențională cu forceps versus biopsia "caldă": studiu comparativ a două metode în diagnosticul leziunilor endobronșice

Introducere: A fost sugerat că biopsia cu pensă de electrocoagulare (biopsia prin căldură) poate reduce riscul de hemoragie după biopsie în tumorile endobronșice. Principala preocupare în această metodă este posibila reducere a calității specimenului obținut.
Obiectiv: Compararea hemoragiilor legate de procedură în biopsia prin căldură și în biopsia cu pensa convențională, precum și calitatea diagnostică a probelor obținute cu fiecare tehnică.
Metodă: În acest studiu prospectiv, evaluarea biopsiilor și a hemoragiei s-a realizat într-o manieră oarbă (blind). Inițial, pentru fiecare pacient s-a pus un diagnostic pe baza examenului histopatologic din toate probele disponibile, date clinice și imagistice. Apoi, un al doilea anatomopatolog a analizat toate probele pentru a evalua calitatea acestora.
Rezultate: Un număr de 36 de pacienți cu leziuni endobronșice au fost incluși în acest studiu. Diagnosticul definitiv a fost realizat la 83% dintre pacienți. Randamentul diagnostic dintre cele două metode nu a fost statistic diferit în timp ce hemoragiile protocoalelor de biopsie prin căldură au fost semnificativ mai mici în comparație cu biopsia convențională ($p=0,003$, $p<0,001$ și $p<0,001$ pentru voltaj de 10, 20 și 40). Nici o diferență semnificativă nu a fost detectată între calitățile specimenelor obținute prin metoda biopsiei prin căldură în comparație cu biopsia convențională ($p>0,05$ pentru toate cele trei voltaje).
Concluzii: Biopsia „prin căldură” poate fi o alternativă valoroasă la biopsia convențională cu pensa în evaluarea leziunilor endobronșice.
Cuvinte-cheie: biopsie prin căldură, tumori endobronșice, biopsie cu pensă, hemoragie

Introduction

Although advanced imaging modalities are widely available for diagnostic purposes in endobronchial diseases, fiberoptic bronchoscopy with forceps biopsy still remains the diagnostic method of choice in endobronchial lesions¹. Indeed, new modalities such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) can show the location and extension of the mass but pathologic evaluation of a suspected intrabronchial lesion is only available through evaluation of tissue biopsies.

Despite widely usage of conventional forceps for endobronchial biopsies, there are limitations regarding this technique. Small sample size and possible complications

including hemorrhage, bronchial spasm, arrhythmias, pneumonia, pneumothorax, and infections are the main obstacles with respect to this diagnostic technique^{2, 3}. To overcome sample size problem, larger forceps are suggested to improve diagnostic yield, but it may increase the chance of development of complications such as bleeding⁴⁻⁶. Cold saline instillation or/and adrenaline are widely used methods to control bleeding⁷. For preventing or controlling procedure-related bleeding, one of the newly introduced methods is the application of heat by electricity. In this method, electrocautery system has been connected to forceps. This "hot forceps" are available for using with flexible bronchoscopy. These forceps make heat energy after grasping the tissue to reduce bleeding and

Table I The clinical data of the study participants

Variable	Number	%
Cough	28	77.7
Hemoptysis	22	62.1
Tobacco smoking	23	63.8
Dyspnea	25	69.4
Pleural effusion	18	50
Weight loss	20	55.5

Table II Location of endobronchial lesions

Location	Number	%
Right main bronchus	9	25
Left main bronchus	9	25
Carina	3	8.3
Intermediate bronchus	5	13.8
Distal portion of the trachea	4	11.1
Other sites of the bronchial tree	6	16.6

improve coagulation. There are some expert views that hot biopsy forceps may reduce hemorrhage risk of biopsy. The main concern in this method is possible reduction of the specimen's quality⁸.

Thus far, there are few published studies comparing the outcomes of hot biopsy technique with the conventional sampling method. There are unanswered questions in this field and previous results are controversial^{1, 8, 9}. Moreover, to the best of our knowledge, there is no study that compared different voltages for the hot-biopsy. Moreover, an optimal electrocautery configuration is not yet proposed. The goal of the present study is to compare the procedure-related hemorrhage and diagnostic quality of samples that are obtained with hot-biopsy and conventional forceps. This study also compares the three different voltages for the hot-biopsy technique.

Materials and methods

Study Design

This study was a prospective study performed from June 2010 to April 2012 in National Research Institute

for Tuberculosis and Lung Diseases (Masih Daneshvari Hospital), Tehran, Iran. The entire study protocol has been reviewed and approved by the Health Research Ethics Board of the Shahid Beheshti University of Medical Sciences. All patients integrated in the study read and signed the written informed consent.

Patient selection

Patients older than 18 years with a visible endobronchial lesion larger than 1 cm in diameter investigated by computed tomography (CT) or routine diagnostic bronchoscopy, were eligible for the study. For all included patients, practicing pulmonologists of the patients had ordered a tissue biopsy and study investigators were not allowed to candidate a patient for invasive sampling. Patients with coagulation disorders and those with pacemaker or defibrillator implants were excluded. Poor cardiopulmonary function that may impose a high risk for interventional bronchoscopy was another exclusion criterion.

Procedure

Patients underwent flexible bronchoscopy under sedation with an intravenous opiate (fentanyl) and/or a

Table III Lesions types according to tissue examination findings

Endobronchial lesions	Number	%
Infiltrative lesions	17	47.2
Nodular lesions	6	16.6
Ulcerative lesions	13	36.1

Table IV Distribution of pathologic diagnoses

Diagnosis	Number	%
Non-Small Cell Lung Carcinoma	18	50
Small Cell Lung Carcinoma	6	16.6
Tuberculosis	1	2.7
Adenoid Cystic Carcinoma	1	2.7
Carcinoid Tumor	1	2.7
Amyloidosis	1	2.7
Clear Cell Carcinoma	1	2.7
No definite diagnosis could be made	7	19.5

short-acting benzodiazepine (midazolam). All patients had I.V lines in place, and supplemental oxygen was delivered by face mask. All patients were monitored for the heart function and their oxygen saturation status. Once an endobronchial lesion requiring endobronchial biopsy was recognized, 3 biopsy specimens were obtained using a conventional forceps (FD-7C-1, Olympus Co., Tokyo, Japan).

For hot biopsy 3 more biopsies were taken with an electrocoagulation-enabled forceps (K6118-A; manufactured by Endoflex, Germany) using 10, 20 and 40 voltages. The order of three consecutive conventional sampling or three consecutive hot-biopsies was random.

The procedure was abandoned prematurely if the patient developed severe hemorrhage or tachycardia. After procedure, patients were closely observed for a minimum period of two hours.

Estimation of procedure-related bleeding

Bleeding was graded as (1): no bleeding; (2): mild bleeding requiring no intervention; (3): moderate bleeding requiring intervention, such as ice-cold saline, topical adrenaline or electrocoagulation and (4): severe bleeding requiring termination of procedure, endotracheal intubation and hemodynamic stabilization.

Histopathological Examination

Endobronchial biopsy specimens were immediately placed in formalin solution for fixation, and examined the same day by a single specialized pulmonary pathologist who was unaware of the study purpose and sampling method. At first, for each patient a definite clinical diagnosis was made based on pathologic examination of all available samples; clinical data and imaging findings. When patients' diagnoses were established; a second pathologist who was blinded to the patients' data and diagnoses reviewed all samples to make diagnosis for each method separately. Hence, diagnostic yield of the both methods (using all these samples of a same method) were reported based on the comparison to the definite diagnosis. Second pathologist was also asked to evaluate the quality of the specimens. Sample's quality was graded as (1): mild damage or sufficient tissue (diagnosis could be easily made); (2): moderate damage or small amount of tissue (difficulty in making a diagnosis) and (3): severe damage or insufficient tissue (no histological diagnosis could be reached).

Statistical Analyses

All qualitative values were reported as frequency and percentage. For paired comparisons, nonparametric McNemar's test was used. Cochran's Q test was used to

Table V Diagnostic quality of the samples regarding the method of biopsy and the diagnostic quality of samples

Technique	Samples	Tissue damage			Total
		Mild	Moderate	Severe	
Hot biopsy	10 Volts	22	10	4	36
	20 Volts	19	13	4	36
	40 Volts	20	9	7	36
	Total	61	32	15	108
Conventional Forceps	Sample 1	20	10	6	36
	Sample 2	21	12	3	36
	Sample 3	25	9	2	36
	Total	66	31	11	108

Table VI Comparison of procedure related hemorrhage in different methods and voltages

Biopsy Method		None	Mild	Moderate	Severe
Hot Biopsy	40 V	19	12	5	0
	20 V	11	20	4	1
	10 V	10	20	6	0
Conventional technique		5	10	18	3

compare diagnostic yield of the methods. Chi-square was used to compare categorical variables. A p-value less than 0.05 was considered to be statistically significant. All analyses were performed using SPSS version 20.0 for Mac OS.

Results

A total of 36 patients with endobronchial lesions were included in this study. Most of the patients were men (n=30, 83%). Median age of our patients was 59.4 years (range 27-86). The presenting symptoms and other clinical information of the patients are shown in table I.

The location and type of endobronchial lesions as revealed during diagnostic bronchoscopy are summarized in tables II and III.

Definite diagnosis could be obtained in 29 patients (80.5%). Distribution of pathologic diagnoses is shown in table IV. Using all three samples of the conventional forceps biopsy, correct diagnosis could be obtained in 25 patients (69.4%). Moreover, evaluation of the accuracy results revealed justifiable efficacy of the new

hot-biopsy technique in all three voltages. Our findings showed that hot-biopsy in 10 Volts, 20 Volts and 40 Volts led to the final diagnosis in 20 patients (55.6%), 22 patients (61.1%) and 26 subjects (72.2%). Cochran's Q test showed that the achieved diagnostic yields for all four sampling methods were not statistically different ($p > 0.05$). The most common diagnosis was non-small cell lung carcinoma (n=18, 50%).

Table V summarizes tissue quality of each method. Neither the two by two comparisons of the methods, nor overall comparisons of the tissue quality between the sampling methods showed a statistically significant difference ($p > 0.05$ for all one-by-one comparisons). As it is evident in table V, for the three samplings of the hot-biopsy, mild; moderated; and severe tissue damage were encountered in 61 (56% of all 108 observations for hot-biopsy), 32 (29.6%), and 15 (13.8%) patients. This is while for the three samplings with the conventional method these numbers showed to be 66 (61.1%), 31 (28.7%), and 11 (10.2%). These proportions were not statistically different ($p=0.66$).

This study also evaluates hemorrhage as one of the most prevalent complications during endobronchial sampling. Our results showed that in 4 patients (11%), biopsy was terminated due to severe bleeding (grade 4). Magnitude of bleeding in regards to methods of biopsy is shown in table VI.

Hemorrhage grades of all hot biopsy methods were significantly different when compared to that of conventional biopsy ($p=0.003$, $p<0.001$ and $p<0.001$ for 10, 20 and 40 voltages respectively). As it is shown in table VI, the number of bleeding-free procedures for hot-biopsy technique far exceeds its number for the conventional method. Indeed, most of the observed bleedings for the hot-biopsy sampling were mild, whereas the bleeding for the conventional method tends to be more severe.

Within-group analysis of the three utilized voltages for the hot-biopsy showed no statistically significant difference with regard to the hemorrhage grading ($p>0.05$).

Discussion

Endobronchial biopsy is a relatively safe and effective technique of diagnosis in a wide variety of pulmonary diseases including infections, interstitial lung diseases, malignant neoplasms and lung transplant rejection¹⁰. Larger forceps size is considered to have a greater diagnostic yield, although the use of larger forceps instinctively may lead to increase in major bleeding and pneumothorax rates that can potentially threaten the life of the patient⁵. Bleeding is an uncommon event during a bronchoscopy. A leading study with a relatively large sample size has illustrated two deaths due to hemorrhage in a questionnaire survey of 48,000 bronchoscopy procedures¹¹. This is while procedure related hemorrhage is one of the most important factors that increase patient's hospital stay and healthcare costs. Conventionally, electrocautery has been applied in different fields for controlling and management of bleeding. It has also been used in treatment of various pulmonary diseases such as hemoptysis and neoplastic obstruction of the respiratory tract with acceptable outcomes.

Application of electrocautery system that is connected to forceps is possibly a good method to increase the ability of obtaining large lung tissue samples with minimal side effects. The diagnostic yield following hot biopsy is showed to be excellent (sensitivities ranging 76–97%)^{7,13}. It is hypothesized that hot biopsy may facilitate the procedure, particularly in patients with complications, such as those with a coagulation disorders (who were excluded from the present study) or when the biopsy is to be obtained from a very brittle or hypervascularized lesion⁷. The amount of bleeding after sampling with hot biopsy could be influenced by several factors such as utilized voltage, the surface involved, time of the electric current and the existence of blood or mucus at the biopsy¹². In this study, we demonstrated that hot biopsy technique reduces risk and amount of procedure related hemorrhage in comparison with conventional forceps biopsy method. There was no significant difference between utilization

of different voltages in the amount of procedure related hemorrhage.

Another important issue regarding tissue biopsies is the specimen quality. Diagnostic quality of bronchial biopsy is related to variety of factors. Clinical condition of the patient and presence of necrosis in the obtained specimen are among the most important considerations¹⁴. One of the intriguing findings of the present study showed that by increasing the voltage, tissue damage was increased but the diagnostic quality of samples was not affected. In other words, we revealed that there is no statistically significant difference between diagnostic qualities of biopsies obtained using different voltages.

To the best of our knowledge, this technique has not been studied as the extent as it is entitled. In a recent study conducted by Tremblay et al., 40 patients with endobronchial tumor underwent endobronchial biopsy via two methods of hot and cold techniques. In that study, the voltages used for coagulation were 80, 60, 40, and 100. From each tumoral site, six biopsy samples were taken via either hot or cold techniques. A total of 238 pathologic samples were obtained. In their study, significant decrease in amount of mild bleeding has been shown in the hot biopsy group. For the clinical pathologist, concordance between the diagnoses made by cold and hot biopsies was 92.5%. This ratio for the blinded pathologist was 87%¹. Our results in the present study is consistent with the Tremblay's study, except that in our study incidence of both mild and severe bleeding during the hot biopsy method was significantly less than the conventional forceps biopsy method.

Similar results have been achieved in another study by Firoozbakhsh and colleagues¹⁵. They investigated 40 patients with variety of endobronchial pathologies and obtained three hot and three cold biopsies in a random sequence. A total of 240 biopsies were obtained. For the quantification of bleeding, a four-point scale was used. All samples were reviewed by a single blinded pathologist. Electrocoagulation damage was recorded with a three point scaling system. The average procedure related hemorrhage in hot biopsy technique was significantly lower than the cold biopsy method. Positive concordance between the two methods was 85%. There was no major difference between the diagnostic yields of two biopsy methods. In another published study by Khan et al.⁹, 160 patients were randomized to endobronchial biopsy with ($n = 81$) or without ($n = 79$) the application of electrocoagulation. No severe bleeding was recorded in both groups, and severity of bleeding in both groups was comparable. In addition, pathological diagnoses were comparable in the electrocoagulation + and electrocoagulation – groups (77.8% and 82.3%, respectively). In that study, tissue quality between the two groups was not statistically different. Hence they concluded that the use of hot biopsy does not affect the quality of the samples. Meanwhile, they showed that hot biopsy could not reduce the amount of the procedure-related hemorrhage¹⁶.

In comparison with other similar studies, our study demonstrates several strengths. One of these strengths is the blindness of individual who measured the bleeding quantity. In the other studies, bronchoscopist, who was not blinded to the biopsy method, measured the amount of hemorrhage during the biopsy procedure. This may result in a major bias.

In our study, both biopsy approaches were used in all patients. Hence, each patient could be served as his/her own control. This strategy would not have any negative effect on the histologic diagnostic performance. It is very difficult to discriminate and categorize the severity of the consecutive bleedings after six repeated biopsies in a single lesion during a bronchoscopy procedure. Application of hot biopsy was done after collection of conventional biopsies to avoid this limitation, so with this strategy we just may have an overestimation in bleeding quantity in hot biopsy method for the reason that the hot biopsies was obtained at last. One of the methodological concerns with regard to our study was utilizing a single study group. It should

be noted that dividing patients into two similar study arms could raise possible ethics considerations because this methodological approach may prevent half of the patients from having the reference diagnostic method (conventional forceps biopsy).

In conclusion, our results show that the hot biopsy can be a good alternative to forceps biopsy in evaluating endobronchial lesions. Hot biopsy method prevents or reduces bleeding during flexible bronchoscopic examination of endobronchial lesions. It also provides a greater diagnostic yield for pathologist without any reduction in diagnostic quality of the samples. However, the cost of the conventional forceps biopsy is relatively lower than that of hot biopsy method (cost of the electrosurgical generator). Application of hot biopsy seems to be justifiable in selected patients who are prone to bleeding since a major reduction in post-operation costs may compensate for the procedure expenses. Bronchoscopist's expertise with this method and patient's selection issues should be addressed in future studies. ■

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