A Randomized Controlled Trial of Electrocoagulation-Enabled Biopsy versus Conventional Biopsy in the Diagnosis of Endobronchial Lesions

Ajmal Khan^a Ashutosh N. Aggarwal^a Ritesh Agarwal^a Amanjit Bal^b
Dheeraj Gupta^a

Departments of ^aPulmonary Medicine and ^bHistopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Key Words

Bronchoscopy · Electrocautery · Endobronchial biopsy

Abstract

Background: Although electrocoagulation at time of endobronchial biopsy can potentially reduce procedure-related bleeding during fiberoptic bronchoscopy (FOB), it can also impair quality of tissue specimen; credible data for either are lacking. **Objective:** To evaluate the impact of hot biopsy on the quality of tissue samples and to quantify the amount of procedure-related bleeding during endobronchial biopsy. **Methods:** In this single-center, prospective, single-blind, randomized controlled study we included adult patients referred for FOB and having endobronchial lesions. Patients were randomized to bronchial biopsy using an electrocoagulation-enabled biopsy forceps, with (EC+ group) or without (EC– group) application of electrocoagulation current (40 W for 10 s in a monopolar mode). Procedure-related bleeding was semi-quantified by observer description, as well as through a visual analogue scale. Overall quality of biopsy specimen and tissue damage were assessed and graded by a pulmonary pathologist blinded to FOB details. **Result:** 160 patients were randomized to endobronchial biopsy with (n = 81) or without (n = 79) the application of electrocoagulation. There were no severe bleeding episodes in either group,

and severity of bleeding in the EC+ and EC– groups was similar (median visual analogue scale scores of 14 and 16, respectively). Histopathological diagnosis was similar in the EC+ and EC– groups (77.8% and 82.3%, respectively). There was no significant difference in tissue quality between the two groups. **Conclusion:** Use of electrocoagulation-enabled endobronchial biopsy does not alter specimen quality and does not result in any significant reduction in procedure-related bleeding.

Copyright © 2010 S. Karger AG, Basel

Introduction

Endobronchial biopsy through a flexible fiberoptic bronchoscopy (FOB) is a frequently performed procedure for visible endobronchial lesions that usually manifest as nodular, exophytic or ulcerative lesion, bronchial infiltration or submucosal lesions [1, 2]. Although diagnosis of cancer is perhaps the most common application of this technique, it can be applied to a wide range of pathologic processes. It is a relatively simple and safe procedure, with diagnostic yield between 76 and 97% [3–5]. Diagnostic

The trial was registered at www.clinicaltrials.gov (NCT00963716).

yield improves by increasing the number of biopsy specimens, but maximal yield can be achieved in three biopsies [6, 7].

Endobronchial biopsy can be routinely performed in an outpatient setting. However, bleeding from the biopsy site is a commonly encountered adverse event, which may impair further sampling and examination of tracheobronchial tree. Traditionally, local instillation of cold saline and/or adrenaline is commonly used to control procedure-related bleeding [5]. Application of heat during biopsy, by passage of electric current to the site of biopsy, is an attractive alternative to prevent/control bleeding. So far, the use of this electrocoagulation technique has been largely limited to gastrointestinal endoscopy [8, 9] and treatment of intraluminal tumors in the tracheobronchial tree [10, 11]. Although electrocoagulation at time of biopsy can potentially reduce procedure-related bleeding, it can also impair the quality of tissue specimen. Credible data for either are lacking.

Despite its low cost and the wide availability of electrocoagulation-enabled bronchoscopic biopsy forceps, endobronchial electrosurgery has failed to gain popularity due to cumbersome delivery systems and complications associated with the power units. Hooper and Jackson [12, 13] pioneered electrocautery in therapeutic bronchoscopy using a flexible bronchoscope in the mid-1980s. So far only one small study has objectively evaluated the use of electrocoagulation-enabled endobronchial biopsy [14]. This report demonstrated a small but significant reduction in procedure-related bleeding score, without an appreciable negative impact on the quality of tissue samples. However, this study employed both standard and electrocoagulation-enabled endobronchial biopsy alternatively during the same procedure in each patient. It is therefore difficult to ascertain how much each biopsy technique contributed to procedure-related bleeding [14, 15].

To clarify some of these issues, we planned a randomized controlled trial to (1) evaluate the impact of electrocoagulation-enabled biopsy forceps on the quality of bronchial biopsy tissue samples and (2) quantify reduction in procedure-related bleeding (if any) during endobronchial biopsy using such forceps.

Patients and Methods

This was a single-center, prospective, single-blind, randomized controlled study conducted between July 2007 and September 2008. Informed consent was obtained from all patients and the study was approved by our institutional ethics committee.

Selection and Preparation of the Patients

All adult patients (aged >18 years) undergoing routine diagnostic FOB for the first time and having visible endobronchial lesions were eligible for inclusion in the study. Patients receiving anticoagulants or having known bleeding diathesis, those with pacemaker or defibrillator implants and those with poor cardiopulmonary reserve or marked hypoxemia at rest were excluded. Uncooperative patients and patients enrolled previously in the study were also excluded. Baseline demographic characteristics, clinical features, results of relevant radiological and laboratory investigations, and the provisional diagnosis (based on clinicoradiological features) were recorded prior to FOB. As part of the prebronchoscopic work-up, blood pressure of all patients is measured and bronchoscopic biopsies were performed only in patients with well controlled blood pressure (less than 140/90 mm Hg) prior to the procedure. Intraprocedure monitoring of blood pressure was performed using noninvasive blood pressure monitoring.

Randomization

Eligible participants, willing for inclusion into the study, were randomized to undergo endobronchial biopsy with (EC+ group) or without (EC- group) electrocoagulation. The randomization sequence was computer-generated using the statistical package StatsDirect (StatsDirect version 2.6.2 for MS Windows). The assignments were placed in sealed opaque envelopes and each patient's assignment was made prior to endobronchial biopsy by the attending physician. Blinding of allocation was not possible.

Bronchoscopic Procedure

FOB was performed by an experienced faculty, or by fellows under direct supervision, using a wide channel bronchoscope (BF-1T20 or BF-TE2; Olympus Optical Co., Tokyo, Japan; Pentax FB-19TV; Asahi Optical Co., Tokyo, Japan) and with patient lying supine. All patients received nebulization with 4% lignocaine solution immediately before the procedure. In addition, topical lignocaine jelly was applied in the nasal cavity, and 3 ml of 2% lignocaine solution sprayed over the carina through the working channel of the fiberoptic bronchoscope, and repeated at other sites as necessary, during the procedure. Oxygenation status was continuously monitored using pulse oximetry and supplemental oxygen was administered as per requirement. Procedure-related bleeding, if any, was controlled by instillation of cold saline or epinephrine (2 ml of 1:10,000 solution). As a policy, we do not administer any prebronchoscopic sedation.

Once an endobronchial lesion requiring endobronchial biopsy was identified, its exact location was recorded. These eligible participants, if willing for inclusion into the study, were then randomized to either the EC+ or EC- group. At least 2 or 3 biopsy specimens were obtained under direct vision for all subjects using an electrocoagulation-enabled forceps (DK2518W; Pentax.), with (EC+ group) or without (EC- group) the application of electrocoagulation current. For the hot biopsy, an electrosurgical unit (GN300; Aesculap AG and Co. KG, Melsungen, Germany) powered the electrocoagulation current. A power setting of 40 W through a soft coagulation monopolar mode was used for 10 s for this purpose. The power setting of 40 W was chosen empirically to minimize the deleterious effects of heat on biopsy specimens without adversely compromising hemostasis. FOB was terminated prematurely if the patient developed tachycardia, desaturation

Table 1. Baseline characteristics of the study population

	EC+ group (n = 81)	EC- group (n = 79)
Male gender	64 (79.0)	63 (79.7)
Age, years	58 ± 12.01	55 ± 13.12
Symptoms		
Cough	52 (64.2)	54 (68.4)
Hemoptysis	37 (45.7)	22 (27.8)
Tobacco smoking	42 (51.9)	38 (48.1)
Clinical diagnosis of lung cancer	75 (92.6)	69 (87.3)

Figures in parentheses are percentages. All p values are non-significant.

Table 2. Bronchoscopic findings of various endobronchial lesions

	EC+ group (n = 81)	EC- group (n = 79)
Infiltrative lesions	34	26
Nodular lesions	7	10
Ulcerative lesions	40	43

All p values are nonsignificant.

or wheezing. All patients were monitored for at least 2 h after the FOB.

Estimation of Procedure-Related Bleeding

Procedure-related bleeding was subjectively graded by the bronchoscopist through a visual analogue scale (a 100-mm straight line bound at two ends by 'no bleeding' and 'severe bleeding'). Bleeding was also categorized as (1) mild, if it was easily controlled by instillation of cold saline and/or adrenaline, (2) moderate, if significant effort was required to control the bleeding, and (3) severe, if further bronchoscopic examination was not possible and the procedure had to be abandoned.

Histopathological Examination

Endobronchial biopsy specimens were immediately placed in 40% w/v formalin solution for fixation, and examined the same day by a pulmonary pathologist blinded to the patient's clinical and randomization details. Information regarding quality of the biopsy specimen, tissue damage subjectively visible on microscopic examination and the histopathological diagnosis was recorded. Tissue damage, represented by coagulative necrosis on microscopic examination, was graded as (1) mild, if the histological diagnosis could be easily made, (2) moderate, if there was difficulty in making a diagnosis, and (3) severe, if the tissue damage was extensive and no histological diagnosis could be reached.

Statistical Analysis

Data are presented in a descriptive fashion using numbers (with percentages in parentheses), medians (with interquartile ranges in parentheses) or means ± SD. The differences between continuous variables were analyzed using the Mann-Whitney test and the differences between categorical variables were analyzed using the χ^2 test. p values less than 0.05 were considered statistically significant.

Results

A total of 160 patients were randomized to undergo electrocoagulation-enabled endobronchial biopsy (EC+ group, n = 81) or standard endobronchial biopsy (EC- group, n = 79). The baseline demographic and clinical profiles were similar in the two groups (table 1). Most patients studied were men (127, 79.3%) with a mean age of 57.1 ± 12.4 years. Eighty (50.0%) patients were current or past tobacco smokers, and were almost equally distributed in the two groups. A provisional diagnosis of lung cancer was suspected in 146 (91.3%) patients at the time of initial presentation, based on clinical features and other relevant investigations (table 1). The majority of patients had ulcerative lesions (table 2).

No significant difference was found in the number of biopsy specimen in the two groups (2.9 ± 1.5 vs. 2.9 ± 1.4 in the EC+ and EC- groups, respectively; median 3 in both groups; table 3). There was no significant difference in specimen quality on histopathology. Diagnosis could be achieved in 144 (80.0%) patients, and overall diagnostic yield was similar in the two groups (table 3). Most patients in either group had no evidence of fibrin or hemorrhage that may have obscured the histopathological diagnosis (table 3). Presence of fibrin and hemorrhage obscured the histopathological diagnosis partly in 14 patients and completely in 3 patients; however, there was no statistically significant difference in the amount of fibrin and hemorrhage between the two groups.

All included subjects tolerated the procedure well and no premature termination of procedure related to bleeding or other complication was seen. There was no episode of severe bleeding in either group and the amount of procedure-related bleeding was similar in both groups (table 3).

Discussion

This is the first randomized controlled study designed to study the effects of endobronchial biopsy with electrocoagulation on procedure-related bleeding and specimen

Table 3. Histopathological findings and severity of bleeding

	EC+ group (n = 81)	EC- group (n = 79)
Number of biopsy samples	3 (2–4)	3 (2–4)
Fibrin and hemorrhage		
Absent	50 (61.7)	40 (50.6)
Present but not obscuring diagnosis	21 (25.9)	32 (40.5)
Present and partly obscuring diagnosis	9 (11.1)	5 (6.3)
Present and completely obscuring diagnosis	1 (1.2)	2 (2.5)
Histopathological diagnosis		
Malignancy	55 (67.9)	54 (68.4)
Inflammation	4 (4.9)	6 (7.6)
Infection	4 (4.9)	5 (6.3)
Necrosis	0	5 (6.3)
Nondiagnostic	18 (22.2)	9 (11.4)
Severity of bleeding		
Mild	70 (86.4)	65 (82.3)
Moderate	11 (13.6)	14 (17.7)
Severe	0	0
Visual analogue scale score for bleeding, mm	14 (6–21)	16 (9–23)

Figures are presented as medians (with interquartile ranges in parentheses) or numbers (with percentages in parentheses) as appropriate. All p values are nonsignificant.

quality. Our observations suggest that there was no significant difference in the rate of bleeding and quality of endobronchial tissue in both groups. These results are largely similar to those obtained in an earlier study [14]. Previous data in this area are rather limited and suggest that application of electrocoagulation to airway mucosa during endobronchial biopsy may lead to some pathological changes in the tissue specimen obtained [16, 17]. It is, however, not clear if these changes are substantial enough to reduce interpretability in a clinical scenario. Our study shows a diagnostic yield of over 80% in the group evaluated with electrocoagulation-enabled biopsy. These figures are comparable to results from earlier studies using standard biopsy techniques [5, 18, 19], and suggest that the new approach does not have any significant negative impact on the histopathological diagnosis. The mean number of biopsy samples obtained in this study was 2.92 ± 1.46 , and it is possible that additional samples could have improved the diagnostic yield further [6].

In addition to problems in making a histopathological diagnosis, electrocoagulation via the bronchoscope has several other potential hazards. There remains a theoretical possibility of hemorrhage or perforation, as well as ignition of the fiberoptic bronchoscope itself. Specific precautions must also be taken whenever electrocautery

is used as an adjunct to FOB in order to avoid electrical hazards such as low-frequency electrical shock or high-frequency burns [8, 9]. We did not encounter any such problems in any of our study subjects.

In contrast to a previous report by Tremblay et al. [14], wherein the investigators reported significant reduction in bleeding score with electrocoagulation-enabled biopsy, our results suggest that such biopsy does not result in any significant reduction in procedure-related bleeding. We observed similar bleeding in both the EC+ and EC- groups. A possible explanation for this variation could be the different biopsy technique applied in individual patients in the two studies. While Tremblay et al. [14] used both electrocoagulation-enabled and standard biopsy in each patient, we used only one of the two approaches in any given patient to obtain the endobronchial biopsy. As with earlier studies [20, 21], our study also showed only mild, self-limiting bleeding in the vast majority of patients, in both the EC+ and EC- groups. Absence of visible fibrin and hemorrhage on histopathological examination of biopsy specimens in most patients in both groups provides further evidence of minimal procedure-related bleeding during endobronchial biopsy in this study. Absence of severe bleeding in our study requiring endotracheal intubation or use of rigid bronchoscopy to control

the bleeding confirms the earlier finding of safety of endobronchial biopsy as an outpatient procedure [22, 23].

An important limitation of this study was that we excluded patients at higher risk for procedure-related bleeding. These results therefore may not get extrapolated to the general patient population for which FOB is carried out. For example, electrocoagulation-enabled forceps can be selectively used for biopsy in patients where there is an indication for electrocoagulation such as central obstruction with endobronchial tumor, where even minimal bleeding is unwarranted. Further studies are needed in these high-risk patients.

Thus it appears that routine use of an electrocoagulation-enabled forceps for endobronchial biopsy is not appropriate in routine bronchoscopic practice. Although hot biopsy does not impair diagnostic yield, it neither decreases the frequency or the severity of bleeding episodes. On the other hand, such an approach increases overall equipment cost, and may be associated with other potential hazards associated with the use of electric currents. Instead, simpler methods of hemostasis followed routinely, such as topical application of cold saline or adrenaline, or wedging the bronchoscope into bleeding segments, may be better in day to day practice.

References

- 1 Karahalli E, Yilmaz A, Turker H, Ozvaran K: Usefulness of various diagnostic techniques during fiberoptic bronchoscopy for endoscopically visible lung cancer: Should cytologic examinations be performed routinely? *Respiration* 2001;68:611–614.
- 2 Dasgupta A, Jain P, Minai OA, Sandur S, Meli Y, Arroliga AC, Mehta AC: Utility of transbronchial needle aspiration in the diagnosis of endobronchial lesions. *Chest* 1999; 115:1237–1241.
- 3 Herth FJ, Eberhardt R, Ernst A: The future of bronchoscopy in diagnosing, staging and treatment of lung cancer. *Respiration* 2006; 73:399–409.
- 4 Chaudhary BA, Yoneda K, Burki NK: Fiberoptic bronchoscopy. Comparison of procedures used in the diagnosis of lung cancer. *J Thorac Cardiovasc Surg* 1978;76:33–37.
- 5 Zavala DC: Diagnostic fiberoptic bronchoscopy: techniques and results of biopsy in 600 patients. *Chest* 1975;68:12–19.
- 6 Popovich J Jr, Kvale PA, Eichenhorn MS, Radke JR, Ohorodnik JM, Fine G: Diagnostic accuracy of multiple biopsies from flexible fiberoptic bronchoscopy. A comparison of central versus peripheral carcinoma. *Am Rev Respir Dis* 1982;125:521–523.
- 7 Shure D, Astarita RW: Bronchogenic carcinoma presenting as an endobronchial mass. *Chest* 1983;83:865–867.
- 8 Barlow DE: Endoscopic applications of electrosurgery: a review of basic principles. *Gastrointest Endosc* 1982;28:73–76.
- 9 Curtiss LE: High frequency currents in endoscopy: a review of principles and precautions. *Gastrointest Endosc* 1973;20:9–12.
- 10 Sutedja G, Postmus PE: Bronchoscopic treatment of lung tumors. *Lung Cancer* 1994;11: 1–17.
- 11 Sutedja TG, van Boxem AJ, Postmus PE: The curative potential of intraluminal bronchoscopic treatment for early-stage non-small-cell lung cancer. *Clin Lung Cancer* 2001;2: 264–270; discussion 271–262.
- 12 Hooper RG, Jackson FN: Endobronchial electrocautery. *Chest* 1985;87:712–714.
- 13 Hooper RG, Jackson FN: Endobronchial electrocautery. *Chest* 1988;94:595–598.
- 14 Tremblay A, Michaud G, Urbanski SJ: Hot biopsy forceps in the diagnosis of endobronchial lesions. *Eur Respir J* 2007;29:108–111.
- 15 Nath A, Srinivas R, Agarwal R: Hot and cold biopsy: implications of study design on outcomes. *Eur Respir J* 2007;29:1067–1068.
- 16 van Boxem TJ, Westerga J, Venmans BJ, Postmus PE, Sutedja TG: Tissue effects of bronchoscopic electrocautery: bronchoscopic appearance and histologic changes of bronchial wall after electrocautery. *Chest* 2000;117:887–891.
- 17 Verkindre C, Brichet A, Maurage CA, Ramon P, Homasson JP, Marquette CH: Morphological changes induced by extensive endobronchial electrocautery. *Eur Respir J* 1999;14:796–799.
- 18 Dreisin RB, Albert RK, Talley PA, Kryger MH, Scoggin CH, Zwillich CW: Flexible fiberoptic bronchoscopy in the teaching hospital. Yield and complications. *Chest* 1978; 74:144–149.
- 19 Kvale PA, Bode FR, Kini S: Diagnostic accuracy in lung cancer; comparison of techniques used in association with flexible fiberoptic bronchoscopy. *Chest* 1976;69:752–757.
- 20 Bilaceroglu S, Gunel O, Cagirci U, Perim K: Comparison of endobronchial needle aspiration with forceps and brush biopsies in the diagnosis of endobronchial lung cancer. *Monaldi Arch Chest Dis* 1997;52:13–17.
- 21 Cordasco EM Jr, Mehta AC, Ahmad M: Bronchoscopically induced bleeding. A summary of nine years' cleveland clinic experience and review of the literature. *Chest* 1991;100:1141–1147.
- 22 Ackart RS, Foreman DR, Klayton RJ, Donlan CJ, Munzel TL, Schuler MA: Fiberoptic bronchoscopy in outpatient facilities, 1982. *Arch Intern Med* 1983;143:30–31.
- 23 Donlan CJ Jr, Foreman DR, Klayton RJ: Fiberoptic bronchoscopy in nonhospitalized patients. *Arch Intern Med* 1978;138:698–699.

Conclusions

Electrocoagulation-enabled endobronchial biopsy does not alter the specimen quality. No significant reduction in procedure-related bleeding can be achieved with the use of electrocoagulation-enabled biopsy forceps when compared to the standard biopsy forceps.

Acknowledgement

The authors wish to acknowledge Mr. Babu Ram, Senior Technician, and all other supporting staff at the bronchoscopy suite for their assistance with this study.

Financial Disclosure and Conflicts of Interest

There are no conflicts of interest or financial disclosures.