Hindawi Publishing Corporation
ISRN Endoscopy
Volume 2013, Article ID 824693, 5 pages
http://dx.doi.org/10.5402/2013/824693

Clinical Study

The Diagnostic Yield of Navigational Bronchoscopy Performed with Propofol Deep Sedation

Uma Mohanasundaram,[1,2] Lawrence A. Ho,[1,2] Ware G. Kuschner,[1,2] Rajinder K. Chitkara,[1,2] James Canfield,[2] Lourdes M. Canfield,[2] and Ganesh Krishna[1,2,3]

[1] *Division of Pulmonary and Critical Care Medicine, Stanford University Medical Center, Stanford, CA 94305, USA*
[2] *Pulmonary Section, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA 94304, USA*
[3] *Palo Alto Medical Foundation, Palo Alto, 701 E. El Camino Real, Mountain View, CA 94040, USA*

Correspondence should be addressed to Ganesh Krishna; krishng1@pamf.org

Received 15 April 2013; Accepted 7 May 2013

Academic Editors: B. Braden and D. Stoyanov

Objective. To describe the diagnostic yield of electromagnetic navigation bronchoscopy (ENB) utilizing propofol for procedural deep sedation. *Methods*. We conducted a structured retrospective analysis of the medical records of patients who underwent ENB with propofol for the evaluation of pulmonary nodules and masses. We analyzed the relationships between lesion size and location, variance (CT-to-body divergence), and positron emission tomography findings on diagnostic yield. Diagnoses were established by histopathological evaluation and clinical-radiographic followup. *Results*. 41 patients underwent ENB during the study period. The overall diagnostic yield was 89% (42 of 47 target lesions). Among the 42 positive specimens, the diagnoses were squamous cell carcinoma ($n = 10$), adenocarcinoma ($n = 14$), small cell carcinoma ($n = 2$), adenocarcinoma in situ ($n = 2$), coccidioidomycosis ($n = 1$), and inflammatory processes ($n = 13$). Average lesion size was 3.01±0.21 cm and variance 3.6±0.15 mm. The diagnostic yield was greater when the lesion size was >4 cm (100%) and when variance was ≤4 mm (91% versus 87%, $P = 0.003$). *Conclusion*. The diagnostic yield of ENB utilizing propofol for procedural deep sedation at our center was excellent. ENB with deep sedation may result in superior diagnostic yield compared with ENB performed with moderate sedation.

1. Introduction

The diagnostic yield of flexible fiberoptic bronchoscopy is limited because of the inability to guide the biopsy needle directly to many pulmonary lesions. For lesions <2 cm in diameter, the diagnostic yield is 14% for lesions in the outer third of the chest and up to 31% in the proximal two-thirds [1].

Electromagnetic navigational bronchoscopy (ENB) is an emerging technology that improves the diagnostic yield of bronchoscopy for the assessment of peripheral pulmonary nodules. The diagnostic yield of ENB ranges from 59 to 74%, independent of lesion size and lobar distribution [2, 3]. It is designed to guide bronchoscopic biopsy tools to predetermined locations within the periphery of the bronchial tree. However, despite accurate navigation to within 10 mm of the target center in most cases, the ENB diagnostic failure rate remains clinically significant [4–6]. Respiratory variations causing larger than anticipated navigation errors [4] and dislodgement of biopsy instruments [6] may adversely affect diagnostic yield.

Most reports of ENB performance have assessed outcomes among patients receiving procedural moderate sedation or general anesthesia. Our center is one of few in the United States to perform ENB with propofol deep sedation. The goals of our investigation were to determine the diagnostic yield of ENB among patients undergoing deep sedation with propofol at our center. We also compared our experience with published reports of patients undergoing ENB with moderate sedation.

2. Methods

2.1. Overview. We conducted a structured retrospective review of consecutive patients who underwent ENB with

propofol sedation at the Veterans Affairs Palo Alto Health Care System (VAPAHCS) over a 2-year period beginning with our first case. The institutional review board at VAPAHCS approved this study. All ENB procedures conducted by one of us (G.K.) were included in the analysis. No other practitioners performed ENB. All patients had been referred to our interventional pulmonology service because they were candidates for nonemergent bronchoscopy of a suspected peripheral pulmonary lesion with or without enlarged mediastinal lymph nodes. Peripheral pulmonary lesions were defined as those surrounded by normal lung parenchyma without evidence of endobronchial abnormality on computed tomography (CT). All bronchoscopies were performed in an outpatient setting in our bronchoscopy suite.

2.2. Sedation and Airway Management. All patients received propofol at an initial dose of 1–1.5 mg/kg IV given as 30–40 mg q10 seconds until induction onset. Bronchoscopic intubation of the trachea was then performed and propofol infusion (25–75 mcg/kg/min IV) was used for management during the procedure. Hemodynamic and respiratory status was monitored throughout all procedures. Patients were extubated immediately after the procedure.

2.3. Cytopathologic Procedures. Suspicious cells were examined with rapid onsite cytology evaluation (ROSE) followed by diagnostic confirmation by a pathologist. The procedure was terminated once a preliminary diagnosis was obtained.

2.4. Electromagnetic Navigational Bronchoscopy. InReach, a three-phase system (SuperDimension Inc., Minneapolis, MN, USA), was used for ENB. Prior to ENB, all patients underwent imaging with a noncontrast CT of the chest with slice thickness of 1 to 1.5 mm and slice intervals of 1 to 1.5 mm with at least 20% overlap. The initial planning phase involved importing the CT scan data into Digital Communication in Medicine (DICOM) software (SuperDimension). This software is able to construct a three-dimensional virtual endoscopy. Endobronchial mapping is achieved when the virtual fiducial registration points are superimposed on actual patient position. After registration, a sensor probe with an eight-way steering mechanism to navigate the bronchial tree is advanced towards the target and directed to the lesion (phase two). The steerable probe is removed, allowing access to an extended working channel through which bronchoscopy instruments (forceps, brushes, and needles) can be advanced. For patients with enlarged mediastinal lymph nodes, a lymph node protocol was followed. Procedure start time was defined as occurring at the time of administration of the first intravenous bolus of propofol. Procedure end time was defined as occurring at the time of extubation.

2.5. Diagnostic Strategy. If the ENB-guided biopsy yielded a definitive histologic diagnosis, the procedure was judged successful. If the result was nondiagnostic, an additional procedure such as CT scan-guided transthoracic needle aspiration or surgery was undertaken; if this provided a diagnosis, then ENB was considered a failure. If the ENB-guided biopsy showed inflammatory cells, the lesion was followed radiologically every 3–6 months for up to 2 years to assess progression or regression.

The primary endpoint of our study was diagnostic yield. Secondary outcomes included analysis of yield by lesion size, lobar location, variance, and lesion pathology (malignant versus benign). Procedure safety was documented by tracking all complications.

2.6. Statistical Analysis. Continuous variables are described as mean ± SEM. Dichotomous variables are summarized in proportions. The following formula was used to compute yield of ENB biopsy: diagnostic yield (%) = 100 × ENB-diagnosed case/total number of patients with completed procedures. The yield of ENB was examined by lesion characteristics and CT-to-body divergence (the divergence between data obtained preoperatively by CT and data obtained during bronchoscopy).

3. Results

Forty-one patients (40 men, 1 woman; mean age 65 yr) were included in the analysis. Six patients had two lesions each, for a total sample size of 47. Patient characteristics are summarized in Table 1. The average lesion size was 3.01 ± 0.21 cm and CT-to-body divergence was 3.60 ± 0.15 mm. 36% of lesions were in the right upper lobe, with the left lower lobe as the second most frequent site (30%). All patients underwent imaging with fluorodeoxyglucose positron emission tomography (FDG-PET) prior to ENB. 37 lesions (79%) were FDG-PET positive, three were negative, and seven had intermediate FDG uptake based on the qualitative assessment of the nuclear medicine physician reviewing the images. Of the seven indeterminate lesions, six were inflammatory and one showed evidence of coccidioidomycosis. Over 3-month to 2-year followup, two of the six were stable and the other four decreased in size. The three PET-negative lesions were also inflammatory, but decreased in size when followed up over 2 years.

3.1. Diagnostic Yield. The target lesions reached 100% of the time regardless of a positive bronchus sign. The overall diagnostic yield was 89% (42 of 47). Different influencing factors are shown in Table 2. The yield was 100% when lesion size was >4 cm, and yield was significantly greater when CT-to-body divergence was ≤4 mm ($P = 0.003$). Upper lobe lesions had similar diagnostic yield compared with all other lobes (88% versus 90%).

In 28 samples, biopsy revealed cancer (10 squamous cell, 14 adenocarcinoma, 2 small cell carcinoma, and 2 adenocarcinoma in situ), and in 13 cases (28%) inflammatory cells.

The biopsy results of 5 lesions were nondiagnostic. One patient had an FDG-PET-positive lesion that increased in size over 3-month followup, resulting in death shortly thereafter. One patient underwent CT-guided transthoracic needle aspiration of a left lower lobe lesion, and a diagnosis of hepatocellular carcinoma was made. In another FDG-PET-positive left lower lobe lesion, both ENB- and CT-guided

Table 1: Baseline characteristics in 41 patients undergoing electromagnetic navigational bronchoscopy*.

Characteristic	Number (%)	Mean (±SEM)
Gender		
Male	40 (98)	
Female	1 (2)	
Age (yr)		65 ± 1.55
Lesion size (cm)		3.01 ± 0.21
CT-to-body divergence (mm)		3.6 ± 0.15
Lobar location		
Right upper	17 (36)	
Right middle	2 (4)	
Right lower	5 (10)	
Left upper	8 (17)	
Lingula	1 (2)	
Left lower	14 (30)	
Positron emission tomography		
Positive	37 (79)	
Negative	3 (6)	
Intermediate	7 (15)	

*Six patients had two lesions, for a total sample size of 47.

Table 2: Diagnostic yield by size, location, and CT-to-body divergence in 47 samples.

	Number	Percentage yield
Size (cm)		
<2	11	91
2–4	27	85
>4	9	100
Lobar location		
Right upper*	14	82
Right middle	2	100
Right lower	5	100
Left upper*	8	100
Lingula	1	100
Left lower	12	86
CT-to-body divergence (mm)		
≤4	32	91
>4	15	87
Diagnosis		
Squamous cell carcinoma	10	21
Adenocarcinoma	14	30
Small cell carcinoma	2	4
Adenocarcinoma in situ	2	4
Inflammatory lesion	13	28
Coccidioidomycosis	1	2

*Mean percentage yield in upper lobe lesions was 88%.

transbronchial needle aspirations were nondiagnostic; however, the patient also had a rib lesion that surgical biopsy revealed to be carcinoid. The fourth patient had an FDG-PET-positive lesion for which he underwent right upper lobectomy, and a diagnosis of coccidioidomycosis was made. The fifth patient with an FDG-PET-positive lesion underwent endoscopic bronchial ultrasound of a right hilar lymph node that showed small-cell lung carcinoma.

Three patients also underwent biopsy of enlarged mediastinal lymph nodes through InReach lymph node sampling protocol, and results were similar to those obtained from the pulmonary nodules in each: two had inflammatory lesions and one small cell carcinoma.

3.2. Procedure Time. Mean procedure time was 72 ± 4.3 min (Table 3). Mean procedure time was shortest for right middle and left upper lobe lesions and longest for one in the lingula. Lesion size was not a factor. The mean distance to the center of a lesion after navigation from the tip of the locatable guide before diagnostic tools were inserted ranged from 0.2 to 0.7 cm.

3.3. Safety. Pneumothorax occurred in six patients (6 of 47 lesions, 13%). Four (66%) of these patients had peripheral lesions in the left lower lobe and the other two patients had lesions in the right upper lobe and left lower lobe, respectively. Treatment entailed placement of a Truclose thoracic vent valve in three patients and drainage by a small-bore catheter in two patients (one was managed by supplemental oxygen therapy and observation). No device-related adverse events were recorded and no significant bleeding was encountered.

4. Discussion

Patient anxiety, discomfort, coughing, and respiratory distress caused by bronchoscopy can adversely affect the diagnostic yield and safety of bronchoscopy. Accordingly, sedation is typically administered to achieve optimal patient comfort and clinical outcomes in routine and advanced diagnostic and therapeutic bronchoscopies [7].

An ideal sedative should have a predictable pharmacokinetic and pharmacodynamic profile, ease of use, a rapid onset, short duration, and quick recovery with a rapid return of cognition. The most commonly used agents, benzodiazepines, and opioids have some of these properties, but each has limitations [8]. Benzodiazepines are generally well tolerated and associated with improved patient satisfaction. In studies with diazepam, patient comfort [9] and tolerance of the procedure [10] were greater than in patients without sedation although recovery time was longer. Studies comparing opioids with benzodiazepines as single-agent regimens demonstrated similar efficacy [11, 12]. In general, benzodiazepines are often combined with opioids for bronchoscopy given the sedative and amnestic properties of the benzodiazepines and the analgesic and antitussive properties of opioids.

Propofol is a highly lipophilic agent that has a rapid onset and short, predictable duration of action owing to its rapid penetration of the blood-brain barrier and distribution to the central nervous system followed by redistribution to inactive tissue depots such as muscle and fat. On the basis of pharmacokinetic and pharmacodynamic modeling, the mean blood-brain equilibration half-life is 2.9 minutes. After both a single

Table 3: Electromagnetic navigational bronchoscopy time and distance from lesion in 47 samples.

Lobar location	Number (%)	Lesion size (cm)	Procedure time (min)	Distance from lesion (cm)
Right upper	17 (36)	3.39 ± 0.49	84 ± 6.20	0.66 ± 0.05
Right middle	2 (4)	3.4 ± 1.4	51 ± 0	0.55 ± 0.05
Right lower	5 (11)	3.28 ± 0.42	82 ± 16.06	0.62 ± 0.08
Left upper	8 (17)	2.93 ± 0.26	51 ± 5.62	0.71 ± 0.08
Lingula	1 (2)	1.4 ± 0	95 ± 0	0.2 ± 0
Left lower	14 (30)	2.57 ± 0.23	67 ± 8.95	0.73 ± 0.04
Total	47	3.01 ± 0.21	72 ± 4.26	0.66 ± 0.03

intravenous injection and a continuous intravenous infusion, the blood concentrations of propofol rapidly decrease below those necessary to maintain sleep (around 1 mg/L), based on the rapid distribution, redistribution, and metabolism during the first and second exponential phases (more than 70% of the drug is eliminated during these two phases). The liver is the main eliminating organ, and renal clearance appears to play little part in the total clearance of propofol [13].

Propofol is currently used uncommonly for bronchoscopy in clinical practice. In a randomized trial comparing it with midazolam, patient tolerance of the procedure was similar as were local anesthetic requirements and the number of episodes of desaturation [14]. However, recovery from sedation was complete in the propofol group by 30 min, whereas the midazolam group had lower than baseline digital symbol substitution scores at 30 and 90 min.

The present study is the first to assess the diagnostic yield of ENB with the use of propofol to obtain deep sedation. The overall diagnostic yield was 89%—superior to reports with moderate sedation or general anesthesia. Gildea and colleagues showed an overall diagnostic yield of 74% with moderate sedation [6]. Makris and colleagues reported a yield of 62.5% with general anesthesia [2].

A principal reason for using propofol for procedural deep sedation in ENB is to minimize the variance between the patient's anatomy and planning CT. Conventional moderate sedation causes more respiratory movement and cough, and general anesthesia increases the variance by muscle relaxation. Intubation and deep sedation with propofol allow the bronchoscopist to minimize variance which, in turn, may improve biopsy yield. The diagnostic yield of lesions with CT-to-body divergence of ≤4 mm in our experience was higher (91%) than the previously documented yield of 77.2% [2]. The yield was also greater among lesions <2 cm (91% versus 43–75% in studies using moderate sedation or general anesthesia) [6]. There was limited comparative gain in lesions larger than 2 cm, possibly owing to some distortion of the lesion or occlusion of the airway leading up to it.

The design of our investigation did not allow direct comparisons with other techniques, and thus historical comparisons are made. There were also no comparative data for separate registration or navigational time. Differences in patient selection, lesion size, use of rigid bronchoscopy, moderate versus deep sedation or general anesthesia, biopsy techniques, the number of biopsies obtained, use of ROSE, and operator skill may affect the utility of any particular technology in a given setting.

It remains unclear why the rate of pneumothorax in our series (13%) was higher than in previous reports [15, 16]. Historically, the use of propofol for deep sedation has required the presence of an anesthesiologist for administration and hemodynamic monitoring. At our institution, pulmonologists, assisted by a registered nurse practitioner, may use propofol in an outpatient setting. In a recent study comparing nurse-administered propofol sedation (NAPS) for endoscopic ultrasound with midazolam and meperidine, NAPS offered faster sedation induction and full recovery time, higher postprocedure patient satisfaction, and a quicker anticipated return to baseline function [17].

5. Conclusions

In summary, the use of propofol infusion for procedural deep sedation with tracheal intubation during ENB is both safe and effective. The diagnostic yield of ENB in our series was superior to that reported in other series utilizing different sedation strategies. Our findings suggest that the use of propofol with deep sedation may improve the diagnostic performance of ENB. A prospective comparison of propofol with moderate sedation and general anesthesia should be considered.

References

[1] W. A. Baaklini, M. A. Reinoso, A. B. Gorin, A. Sharafkaneh, and P. Manian, "Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules," *Chest*, vol. 117, no. 4, pp. 1049–1054, 2000.

[2] D. Makris, A. Scherpereel, S. Leroy et al., "Electromagnetic navigation diagnostic bronchoscopy for small peripheral lung lesions," *European Respiratory Journal*, vol. 29, no. 6, pp. 1187–1192, 2007.

[3] R. Eberhardt, D. Anantham, F. Herth, D. Feller-Kopman, and A. Ernst, "Electromagnetic navigation diagnostic bronchoscopy in peripheral lung lesions," *Chest*, vol. 131, no. 6, pp. 1800–1805, 2007.

[4] H. D. Becher, F. Herth, A. Ernst, and Y. Schwarz, "Bronchoscopic biopsy of peripheral lung lesions under electromagnetic guidance: a pilot study," *Journal of Bronchology*, vol. 12, no. 1, pp. 9–13, 2005.

[5] Y. Schwarz, J. Greif, H. D. Becker, A. Ernst, and A. Mehta, "Real-time electromagnetic navigation bronchoscopy to peripheral lung lesion using overlaid CT images: the first human study," *Chest*, vol. 129, no. 4, pp. 988–994, 2006.

[6] T. R. Gildea, P. J. Mazzone, D. Karnak, M. Meziane, and A. C. Mehta, "Electromagnetic navigation diagnostic bronchoscopy: a prospective study," *American Journal of Respiratory and Critical Care Medicine*, vol. 174, no. 9, pp. 982–989, 2006.

[7] I. Matot and M. R. Kramer, "Sedation in outpatient bronchoscopy," *Respiratory Medicine*, vol. 94, no. 12, pp. 1145–1153, 2000.

[8] E. Horn and S. A. Nesbit, "Pharmacology and pharmacokinetics of sedatives and analgesics," *Gastrointestinal Endoscopy Clinics of North America*, vol. 14, no. 2, pp. 247–268, 2004.

[9] G. P. Maguire, A. R. Rubinfeld, P. W. Trembath, and M. C. F. Pain, "Patients prefer sedation for fibreoptic bronchoscopy," *Respirology*, vol. 3, no. 2, pp. 81–85, 1998.

[10] S. Putinati, L. Ballerin, L. Corbctta, L. Trcvisani, and A. Potcna, "Patient satisfaction with conscious sedation for bronchoscopy," *Chest*, vol. 115, no. 5, pp. 1437–1440, 1999.

[11] A. Papagiannis and A. P. Smith, "Fentanyl versus midazolam as premedication for fibre optic bronchoscopy," *Respiratory Medicine*, vol. 88, no. 10, pp. 797–798, 1994.

[12] C. M. Houghton, A. Raghuram, P. J. Sullivan, and R. O'Driscoll, "Pre-medication for bronchoscopy: a randomised double blind trial comparing alfentanil with midazolam," *Respiratory Medicine*, vol. 98, no. 11, pp. 1102–1107, 2004.

[13] J. Kanto and E. Gepts, "Pharmacokinetic implications for the clinical use of propofol," *Clinical Pharmacokinetics*, vol. 17, no. 5, pp. 308–326, 1989.

[14] K. Clarkson, C. K. Power, F. O'Connell, S. Pathmakanthan, and C. M. Burke, "A comparative evaluation of propofol and midazolam as sedative agents in fiberoptic bronchoscopy," *Chest*, vol. 104, no. 4, pp. 1029–1031, 1993.

[15] O. De Fenoyl, F. Capron, B. Lebeau, and J. Rochemaure, "Transbronchial biopsy without fluoroscopy: a five year experience in outpatients," *Thorax*, vol. 44, no. 11, pp. 956–959, 1989.

[16] J. T. Trkanjec, T. Peroš-Golubičić, D. Grozdek, A. Ivičević, and M. Alilović, "The role of transbronchial lung biopsy in the diagnosis of solitary pulmonary nodule," *Collegium Antropologicum*, vol. 27, no. 2, pp. 669–675, 2003.

[17] J. DeWitt, K. McGreevy, S. Sherman, and T. F. Imperiale, "Nurse-administered propofol sedation compared with midazolam and meperidine for EUS: a prospective, randomized trial," *Gastrointestinal Endoscopy*, vol. 68, no. 3, pp. 499–509, 2008.