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Transbronchial needle aspirates: how many passes per target site?

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Abbreviation list

ATS = American Thoracic Society

CT = computed tomography

EBUS = endobronchial ultrasound

NSCLC = non small cell lung cancer

ROSE = rapid on-site analysis

SCLC = small cell lung cancer

TBNA = transbronchial needle aspiration

Abstract

Background

Transbronchial needle aspiration is a bronchoscopic sampling method for a variety of bronchial and pulmonary lesions. This study investigated whether and how serial needle passes contribute to the yield of transbronchial needle aspiration at specific target sites.

Method

We prospectively recorded 1562 needle passes performed at 374 target sites rated for anatomical location, size, bronchoscopic appearance and underlying disease in 245 patients with neoplastic disease (82%), non-neoplastic disease (15%) or undiagnosed lesions (3%).

Results

Positive aspirates were obtained in 75% of patients and in 68% of target sites. A diagnosis was established with the first, second, third and fourth needle pass at 64%, 87%, 95% and 98% of targets, respectively. The absolute yield varied strongly with target sites features, but the stepwise increment to the maximum yield provided by serial passes was similar across target sites.

Conclusion

Three transbronchial needle passes per site are appropriate when only a tissue diagnosis is sought and when alternative sites or sampling modalities are available. At least four or five passes should be carried out at lymph node stations critical for staging of lung cancer.

Introduction

Transbronchial needle aspiration (TBNA) via flexible bronchoscopy (FB) is a well established sampling method for a variety of bronchial, peribronchial or pulmonary lesions [1]. Its ability to establish diagnosis and staging in a single non-invasive intervention has made TBNA the key technique for the evaluation of patients with suspected lung cancer [2, 3]. Endobronchial ultrasound (EBUS) [4], CT guidance [5] and rapid on-site evaluation (ROSE) improve TBNA yield [6, 7], but these methods require considerable resources and are not universally available. In the absence of EBUS and/or ROSE it is common practice to perform several TBNA passes at a target site to minimize false negative results. However, little is known about the value of serial aspirations. Chin et al reported a plateau in yield after seven aspirates per patient and per nodal site [8] while others report to perform two [9], two to three [10, 11], at least three [12], three to four [13]or three to five [14, 15] passes per site. It is well known that TBNA has a higher yield in neoplastic than in benign lesions as well as in small cell lung cancer (SCLC) compared to non-small cell lung cancer (NSCLC) [3, 16]. Other predictors of positive aspirates are greater size of lymph nodes, infracarinal or right tracheobronchial position, visible mucosal abnormalities such as a widened carina or erythema, and endobronchial mass lesions [1, 3, 9, 10, 17]. It is unknown whether these parameters also predict a higher yield when fewer aspirates are performed at these sites.

Demonstration of positive N2 or N3 lymph nodes with TBNA avoids unnecessary surgical exploration with the associated morbidity and cost [3, 18]. Such procedures often require TBNA sampling of multiple sites, proceeding in a stepwise fashion from the highest rated potentially involved nodal site to the primary tumor, followed by additional sampling modalities. Patient comfort and safety challenge the bronchoscopist to compromise between optimizing TBNA yield and possibly unnecessary prolongation of the intervention. This study investigated the yield of serial TBNA as a function of target site characteristics with the aim to establish a practical rule for sampling in routine practice.

Methods

Patients, interventions and diagnoses

All patients undergoing FB with TBNA at our institution (tertiary academic hospital) from June 2001 to June 2004 were prospectively recorded. Four chest physicians experienced with TBNA performed all procedures using standard fiberoptic or video bronchoscopes (models BF30 and BF1T160; Olympus; Tokyo, Japan; Exera; Hamburg, Germany) and standard TBNA for cytological specimens (Bard, Billerica, MA, USA) under topical anaesthesia (Lidocaine 1%) and conscious sedation (Midazolam iv as needed). TBNA was always the leading sampling method and was supplemented at the discretion of the physician with the appropriate additional modalities. For staging of suspected lung cancer the potentially highest rated nodal site was sampled first. If staging was not of concern, the most promising site for providing a diagnosis was sampled first. The final diagnosis was established with the results of the bronchoscopy or, in cases with negative FB, with appropriate repeat or additional examinations. All patients signed informed consent. The study was approved by the institutional ethical review board.

TBNA and target sites

A target site for TBNA was defined as an area of interest on computed tomography (anatomical lymph node station or other lesion in reach of TBNA) or a visible abnormality identified during FB. Target site features were prospectively recorded. At least five successive aspirates in close proximity were performed. Every aspirate was immediately expressed onto a numbered glass slide and reported separately. TBNA sampling ended when all target sites had been aspirated or when sufficient diagnostic material was found with ROSE. ROSE was performed by a cytopathologist as previously described [7]. The anatomical location of lymph node target sites was classified according to the ATS system [18] into paratracheal sites above the tracheobronchial level (stations 2R and 2L), tracheobronchial sites (stations 4R, 4L and 7), and bronchial sites (all sites below tracheobronchial). All sites were rated for normal or altered appearance (i.e. widened carina, mucosal infiltration, extrinsic compression). Compression of a lumen was rated for its degree as partial or complete (passable with bronchoscope or not),

and for appearance (intrabronchial mass lesion opposed to submucosal or peribronchial disease). Post bronchoscopy the sites were further categorized for underlying disease (neoplastic or benign), type of lung cancer when applicable (SCLC or NSCLC), and short axis diameter in the case of treacheobronchial lymph nodes (assessed on contrasted spiral CT scan with 10mm sections).

Statistical analysis

We anticipated that sequential passes at a target site would result in stepwise yield increments to a plateau. From a published report [8] we deducted that five aspirates per site would provide enough data points to fit an exponential function with non linear regression (Newton Gauss). Every needle pass at a site was reported separately and entered into the database to provide yields after each sequential pass. Using these data, separate exponential functions were created to deduct the yields stratified for target site characteristics. Proportional data were analyzed with Chi square test of contingency tables or Fisher's exact test on 2x2 contingency tables in case of very small counts (≤ 5). P of <0.05 was considered significant. Two-sided tests were used. Values are mean ± standard deviation unless stated otherwise.

Results

Patients, diagnosis and interventions

We recorded 245 patients undergoing flexible bronchoscopy with TBNA (age range: 15-88 years, median 57 years, 66% male). The final diagnosis was neoplastic disease in 200 (82%), non-neoplastic disease in 36 (15%), and 9 (3%) remained undiagnosed (Table 1). Five of these patients died from clinically advanced malignancy before further investigations could be undertaken. One patient died undiagnosed from massive hemoptysis and three were lost to follow up. TBNA was diagnostic in 75% overall, in 84% in neoplastic disease and in 44% in benign lesions.

Target sites

In total, 374 target sites were sampled (mean per patient: 1.53 ±0.6) with 1562 needle

passes (mean passes per site: 4.2 ±1.6; range: 1-10). The site specific yields are demonstrated in Table 2. More than half of all target sites were at the tracheobronchial level (stations 4R, 4L, 7). Significantly higher yields were seen with increasing size of lymph nodes and at the tracheobronchial level in right sided (station 4R) and infracarinal (station 7) compared to left sided (station 4L) lymph nodes. Other statistically significant predictors of positive aspirates were the presence of a visible abnormality and neoplastic disease. Among abnormally appearing sites, endobronchial mass lesions were significantly more often positive than submucosal or peribronchial lesions. Of borderline significance was the better yield in SCLC compared to NSCLC. There was no significant difference between partial and complete endobronchial obstruction.

Sequential yield of TBNA

The cumulative yield obtained from the complete set of 1562 needle aspirates at 374 sites is displayed in Figure 1. The first needle pass contributed the largest proportion to the total yield at all sites, and all following passes increased the yield roughly by half of the increase of the previous pass until a plateau was reached. As expected, this pattern could be described with a simple non linear function. The functions and graphs established for sites with specific features came out very similar to Figure 1 and are not shown (all correlation coefficients: R^2>0.96). Table 3 shows the proportional yields of the plateau yield after the first five sequential passes for each site. The highest first pass contribution was achieved at sites with complete airway obstruction (82.6%) and in endobronchial mass lesions (76.7%). At all sites, at least 88% of the plateau yield is reached with three passes and at least 94% with four needle passes.

Discussion

This study showed that the stepwise increase in TBNA yield with serial needle passes is similar across target sites of variable position, aspect, size and underlying disease. Although the rate of positive TBNA was significantly different across target sites, the first needle pass consistently contributed at least 50% towards the maximum yield, three passes provided 89% to 99%, and five passes yielded at least 98% at all sites. TBNA was diagnostic in 75% in this large sample of patients representative for clinical practice.

The ideal number of TBNA passes per target site has not received much investigative attention in the past. A reason might be that a negative TBNA result can be due to a variety of other reasons such as inadequate puncture technique or suboptimal sample preparation and analysis [17]. Secondly, TBNA has a sensitivity of only 76% to 80% in the best hands under study conditions [10, 19, 20], which means that a negative result is of limited value even when established with a high number of aspirates. ROSE by a cytopathologist present in theatre will effectively optimize the number of aspirates in patients with positive TBNA but will contribute little when TBNA remains negative [7, 21]. In contrast, EBUS improves TBNA sensitivity by assisting the positioning of the needle inside the target lesion [4]. However, the majority of chest physicians performing TBNA do not have easy access to EBUS or ROSE and will rely on their clinical judgement and personal experience to decide on the number of aspirates in specific bronchoscopic situations.

Tracheobronchial lymph node sampling for staging of lung cancer is the best established and most widely used indication for TBNA. Our results in this subgroup of sites confirm previous reports that the yield of TBNA is strongly influenced by the size and location of the targeted lymph node as well as by the presence of erythema and a widened carina [3, 16]. Even though radiological size is a poor predictor for disease in the mediastinum [22] our yield in small nodes (<10mm small axis diameter: 29% yield) is surprisingly high. Harrow et al [10] reported 14% TBNA yield in tracheobronchial lymph nodes smaller than 10mm in a large sample of patients with lung cancer. The explanation for this discrepancy may be the inclusion of nodes with exactly 10mm into that group in the present study. Our yield in nodes measuring less than 10mm was only 16%. For sites other than tracheobronchial, our study confirms the prediction of positive aspirates by visible abnormalities such as a widened carina, submucosal infiltration, airway compression or endobronchial mass lesions [9, 16, 17].

The good overall yield of 75% in the present study encourages the use of TBNA regardless of the availability of EBUS support. While EBUS-guided TBNA is superior in

lymph node targets smaller than 10mm [23] or in peripheral lung lesions [24], most parabronchial lesions can be located using anatomical landmarks such as the carina or lobar bifurcations [25, 26]. Moreover, positive ROSE-TBNA makes EBUS redundant and shortens the sampling process [7]. The preferred method for mediastinal staging will not only depend on the available expertise but also on the prevalence of mediastinal metastases. Holty et al have recently shown that TBNA has a higher sensitivity in more advanced mediastinal disease than in situations with small lymph nodes [20]. This means that non-EBUS TBNA is probably sufficient for the majority of patients where confirmation of inoperability is sought. Conversely, EBUS-TBNA or even surgical staging is best used when a surgically operable stage is suspected and a high negative predictive value is important.

In conclusion, what can we recommended for general practice? TBNA is an elegant and effective technique that takes bronchoscopic sampling beyond visible abnormalities. Even though other sampling methods are often equally promising, we encourage frequent practice of TBNA to hone technical skills. In general, it seems reasonable to perform three serial TBNA passes per site when the main objective is establishing a tissue diagnosis and when alternative target sites or other sampling modalities are equally promising. Four or even five TBNA passes per site should be carried out if only a single site is available, if TBNA is the only potentially diagnostic sampling method, and if the objective is staging of lung cancer at critical lymph node stations.

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Table 1

Bronchoscopies, diagnoses and yield of TBNA

	Underlying disease		Diagnostic TBNA*
	n	%	%
All	245		75
Neoplastic disease	200	82	84
Non-small cell lung cancer	154	63	81
Adenocarcinoma	82	34	85
Squamous cell carcinoma	25	10	84
Undifferentiated carcinoma	47	19	72
Small cell lung cancer	39	16	95
Other neoplastic**	7	3	86
Non-neoplastic disease	36	15	44
Sarcoidosis	10	4	60
Tuberculosis	14	6	71
Other infective lesions	5	2	0
Other benign lesions	7	3	0
Undiagnosed	9	3	0

*At least one diagnostic aspirate.
** Metastasis (n=4), lymphoma (n=2), myeloma (n=1).
TBNA = transbronchial needle aspiration.

Table 2

Target sites and yield of TBNA

	Target sites aspirated		Diagnostic	Chi Square	
	n	%	%*	p**	
All sites	374	100	68		
Anatomical location* **					
Paratracheal sites (stations 2R, 2L)	32	8	75	0.043	ns
Tracheobronchial sites (stations 4R, 4L, 7)	212	57	56	<0.001	
Bronchial sites	130	35	85		
Underlying disease					
Neoplastic	309	85	76	<0.001	
Non-neoplastic	55	15	35		
Bronchial carcinoma					
Small cell lung cancer	64	18	86	0.052	
Non-small cell lung cancer	230	63	74		
Paratracheal and tracheobronchial lymph node sites					
Visible abnormality					
Present	124	34	75	<0.001	
Absent	120	33	42		
Lymph node short axis diameter					
≤10mm	39	11	28	0.004	<0.001
11-20mm	97	27	56	0.016	
>20mm	108	30	72		
Tracheobronchial position					
Right (station 4R)	49	13	61	0.004	ns
Left (station 4L)	34	9	29	<0.001	
Subcarinal (station 7)	129	35	61		
Bronchial sites					
Degree of bronchial obstruction					
None or partial	70	19	80	ns	
Complete	60	16	92		
Bronchoscopic appearance					
Peribronchial or submucosal disease	76	21	76	<0.001	
Endobronchial mass lesion	54	14	98		

* At least one diagnostic TBNA per target site.

** All p in the right column are between values directly above and below. All p <0.10 are shown, others = ns.

*** Lymph node station according to ATS [18].

TBNA = transbronchial needle aspiration.

Table 3

Target sites and yield of sequential needle passes

	Yield after needle pass (%)					Fit*
	1	2	3	4	5	R^2
All sites	64.5	87.4	95.5	98.4	99.4	0.998
Anatomical location**						
Paratracheal sites (stations 2R, 2L)	59.6	83.8	93.5	97.4	99.0	0.996
Tracheobronchial sites (stations 4R, 4L, 7)	57.4	82.0	92.4	96.8	98.8	0.997
Bronchial sites	73.5	93.0	98.1	99.5	99.9	0.996
Underlying disease						
Neoplastic	64.2	87.2	95.4	98.3	99.4	0.998
Non-neoplastic	68	89.7	96.7	98.9	99.7	0.978
Bronchial carcinoma						
Small cell lung cancer	59.5	83.6	93.4	97.3	98.9	0.998
Non-small cell lung cancer	65.8	88.3	96.0	98.6	99.5	0.998
Paratracheal and tracheobronchial lymph node sites						
Visible abnormality						
Present	53.4	78.2	89.8	95.2	97.8	0.991
Absent	60.1	84.2	93.7	97.5	99.0	0.998
Lymph node short axis diameter						
≤10mm	64.8	87.8	95.8	98.5	99.5	0.968
11-20mm	59.2	83.2	93.1	97.2	98.8	0.995
>20mm	51.5	76.7	88.8	94.6	98.8	0.991
Tracheobronchial position						
Right (station 4R)	54.5	79.4	90.7	95.8	98.1	0.995
Left (station 4L)	60.3	84.3	93.8	97.5	99.0	0.992
Subcarinal (station 7)	57.1	81.7	92.2	96.7	98.6	0.998
Bronchial sites						
Degree of bronchial obstruction						
None or partial	67.4	89.3	96.5	98.9	99.6	0.997
Complete	82.6	97.0	99.5	99.9	100.0	0.992
Bronchoscopic appearance						
Peribronchial or submucosal disease	71.2	91.7	97.6	99.3	99.8	0.996
Endobronchial mass lesion	76.7	94.6	98.7	99.7	99.9	0.996

* Non linear function curve fit. For explanation see Figure 1.

** Lymph node station according to ATS [18].

TBNA = transbronchial needle aspiration.

Figure legends

Figure 1

Incremental yield to plateau with sequential needle passes. This graph describes the yield to plateau in 1562 TBNA passes at 374 target sites. The measured yield after each sequential needle pass is plotted as a single dot. The curved line is the extrapolated yield from an exponential function obtained by nonlinear regression. The function is: "yield = 100 - b0 * exp (b1 * needle passes)". The correlation is excellent ($R^2 = 0.999$).