Turk Gogus Kalp Dama 2016;24(1):83-88
doi: 10.5606/tgkdc.dergisi.2016.11016

Original Article / Özgün Makale

Should transbronchial needle aspiration and rapid on-site cytologic evaluation be performed before mediastinoscopy? "Analysis of 239 cases"

Mediastinoskopi öncesi transbronşiyal iğne aspirasyonu ve hızlı yerinde sitolojik değerlendirme yapılmalı mıdır? "239 olgunun analizi"

Ayten Kayı Cangır,[1] Cabir Yüksel,[1] Koray Ceyhan,[2] Serkan Enön,[1] Durdu Karasoy[3]

Institution where the research was done:
Medical Faculty of Ankara University, Ankara, Turkey

Author Affiliations:
Departments of [1]Thoracic Surgery, [2]Cytology, Medical Faculty of Ankara University, Ankara, Turkey
[3]Department of Biostatistics, Medical Faculty of Hacettepe University, Ankara, Turkey

ABSTRACT

Background: This study aims to assess the role and efficiency of transbronchial needle aspiration accompanied by rapid on-site cytologic evaluation performed in the operating room in patients who are planned to undergo mediastinoscopy.

Methods: A total of 239 patients (153 males, 86 females; mean age 53.3±13.7 years; range 14 to 85 years) who were diagnosed with or suspected to have lung cancer or mediastinal lymphadenopathy between January 2004 and December 2012 were performed transbronchial needle aspiration rapid on-site cytologic evaluation. Diagnosis success, localization and size of lymph nodes, and number of sampling were analyzed.

Results: Diagnostic specimens were obtained from a total of 227 patients (93.03%) and 297 lymph nodes were sampled. A statistically significant difference was detected between lymph node stations and dimensions (p=0.018). Subcarinal lymph nodes had the highest diagnosis rate (91.5%) and 49.5% of these were benign. Mean lymph node diameters were 23.9±10.4 mm in malignant group (n=123), 19.4±7.4 mm in benign group (n=135), and 19.1±8.8 mm in undiagnosed group (n=39) and the diameters were statistically significantly different from each other (p=0.001). A repeat transbronchial needle aspiration was performed in five patients and no metastasis was detected in three of them. All negative results (n=12) were confirmed with histopathological examination after resection.

Conclusion: On-site evaluation decreases the risk of inadequate specimens and increases diagnostic accuracy rate of transbronchial needle aspiration. Transbronchial needle aspiration may be the initial procedure of choice while staging lung cancer or diagnosing mediastinal lymph node. Procedure may be performed by thoracic surgeons in the operating room in patients planned for mediastinoscopy.

Keywords: Mediastinal lymphadenopathy; rapid on-site cytologic evaluation; thoracic surgery; transbronchial needle aspiration.

ÖZ

Amaç: Bu çalışmada mediastinoskopi yapılması planlanan hastalarda ameliyathanede yapılan transbronşiyal iğne aspirasyonu ile birlikte hızlı yerinde sitolojik değerlendirmenin rolü ve etkinliği değerlendirildi.

Çalışma planı: Ocak 2004 - Aralık 2012 tarihleri arasında akciğer kanseri veya mediastinal lenfadenopati tanısı konulmuş veya bu tanıdan şüphelenilen toplam 239 hastaya (153 erkek, 86 kadın; ort yaş 53.3±13.7 yıl; dağılım 14-85 yıl) transbronşiyal iğne aspirasyonu hızlı yerinde sitolojik değerlendirme uygulandı. Tanı başarısı, lenf nodlarının yerleşim yeri ve büyüklüğü ve örnekleme sayısı analiz edildi.

Bulgular: Toplam 227 (%93.03) hastadan tanı için örnek alındı ve 297 lenf nodu örneklendi. Lenf nodu istasyonları ve boyutları arasında istatistiksel açıdan anlamlı ilişki tespit edildi (p=0.018). Subkarinal lenf nodlarında tanı oranı en yüksek idi (%91.5) ve bunların %49.5'i benign idi. Ortalama lenf nodu çapları malign grupta (n=123) 23.9±10.4 mm, benign grupta (n=135) 19.4±7.4 mm, tanı konulamayan grupta (n=39) 19.1±8.8 mm idi ve lenf nodlarının çapları biribirinden istatistiksel olarak anlamlı düzeyde farklı idi (p=0.001). Beş hastaya tekrar transbronşiyal iğne aspirasyonu uygulandı ve bunların üçünde metastaz saptanmadı. Tüm negatif sonuçlar (n=12) rezeksiyon sonrası histopatolojik inceleme ile doğrulandı.

Sonuç: Yerinde değerlendirme, yetersiz örnek riskini azaltmakta ve transbronşiyal iğne aspirasyonunun tanısal doğruluk oranını artırmaktadır. Akciğer kanserini evreler iken veya mediastinal lenfadenopati tanısı koyar iken transbronşiyal iğne aspirasyonu seçilecek ilk işlem olabilir. İşlem mediastinoskopi planlanan hastalarda göğüs cerrahları tarafından ameliyathanede uygulanabilir.

Anahtar sözcükler: Mediastinal lenfadenopati; hızlı yerinde sitolojik değerlendirme; göğüs cerrahisi; transbronşiyal iğne aspirasyonu.

Available online at
www.tgkdc.dergisi.org
doi: 10.5606/tgkdc.dergisi.2016.11016
QR (Quick Response) Code

Received: October 10, 2014 *Accepted*: January 20, 2015

Correspondence: Ayten Kayı Cangır, MD. Ankara Üniversitesi Tıp Fakültesi, Göğüs Cerrahisi Anabilim Dalı, 06100 Sıhhiye, Ankara, Turkey.
Tel: +90 312 - 508 31 65 e-mail: kayicangir@gmail.com

Transbronchial needle aspiration (TBNA) is a minimally invasive and safe technique for sampling mediastinal, hilar, and central pulmonary lesions and staging of patients with non-small cell lung carcinoma (NSCLC).[1,2] However, the diagnostic yield of TBNA varies widely in reported series, ranging from 20 to 90%.[1,3] Diagnostic yield of neoplasms can be improved with rapid on-site cytologic evaluation (ROSE) by a cytopathologist or endobronchial ultrasound (EBUS).[1,2,4] Transbronchial needle aspiration and rapid on-site cytologic evaluation can reduce risk, costs, morbidity, and anxiety for patients, as well as the time to definitive treatments.[1-5]

Surgical resection is considered as the best treatment method in NSCLC; however, clinical evidence indicates that patients with mediastinal lymph node (MLN) metastasis have poor prognosis.[2,3] Therefore, accurate MLN staging is critical for selecting patients suitable for surgery.[4] Mediastinoscopy remains the gold standard for mediastinal staging of NSCLC, but this procedure is associated with certain complications, such as bleeding, recurrent nerve damage, and thoracic duct injury. Particularly, remediastinoscopy after neoadjuvant chemotherapy or chemo-radiotherapy for N_2 disease have a higher complication rate than mediastinoscopy.[6,7] Transbronchial needle aspiration and rapid on-site cytologic evaluation (TBNA-ROSE) might be the first choice for staging N_2 disease to avoid complications of redo-mediastinoscopy in NSCLC.

Occasionally, establishing a diagnosis might be challenging in some patients with centrally located NSCLC without an endobronchial component and TBNA-ROSE may be used as a diagnostic procedure in such tumors.[6] Therefore, in this study, we aimed to assess the role and efficiency of TBNA accompanied by ROSE performed in the operating room in patients who are planned to undergo mediastinoscopy.

PATIENTS AND METHODS

Two hundred and thirty-nine patients (153 males, 86 females; mean age 53.3±13.7 years; range 14 to 85 years) who admitted to Medical Faculty of Ankara University, Department of Thoracic Surgery between January 2004 and December were subjected to TBNA-ROSE for a consecutive series of cytologic, aspirated material. The patients had a suspected or pathologically proven lung cancer or mediastinal/hilar adenopathy or mediastinal mass. Transbronchial needle aspiration and ROSE were performed as the first step for diagnosing or staging in our study. All TBNA-ROSE procedures were conducted under general anesthesia as all patients with MLN had been referred to our clinic for mediastinoscopy and at least one or two diagnostic procedures, namely bronchoscopy (79%, n=189) or TBNA (18%, n=43) was performed in the majority of patients before our hospitalization.

Preoperative investigations included medical history, physical examination, hemogram, routine blood chemistry, electrocardiogram, posteroanterior and lateral chest radiograms, computed tomographic scans of the chest, and positron emission tomography-computed tomography (PET-CT). When enlarged mediastinal/hilar lymph nodes (10 mm or more in the shortest axis) or a central lung or mediastinal mass were detected in CT scans, TBNA-ROSE was performed for staging and/or diagnosis.

All patients were informed about the intervention and explained that if a diagnosis was established with TBNA-ROSE, the procedure was going to be ended; otherwise, mediastinoscopy would be conducted in the same session. This retrospective study was approved by the Ethics Committee of Ankara University.

Major complications were defined as hemorrhage causing surgical exploration, pulmonary embolus, and myocardial infarction. Minor complications were minimal hemorrhage and pneumothorax.

We performed the TBNA-ROSE procedure under general anesthesia, using laryngeal mask airway (LMA). We preferred LMA because it permitted the needle aspiration of the upper paratracheal nodes. Aspirations were performed using a video flexible bronchoscope. All specimens were obtained through a flexible video-bronchoscope using a standard, retractable 22 or 21-gauge cytology needle or a 19-gauge histology needle (ANSO-19, 21, 22-W Horizons International Corp., Barreal de Heredia, Costa Rica). The specific site from which the aspirate was obtained (subcarinal, paratracheal, hilar etc.) and number of sampling were recorded in every case.

No further intervention was carried out when the disease was diagnosed with TBNA-ROSE. But mediastinoscopy was performed if there was any suspicion for lymphoma or in undiagnosed cases.

One experienced cytopathologist evaluated all cytopathological samples on-site. The aspirated materials were immediately smeared onto glass slides, air-dried and immediately stained with Diff-Quik (Thermo Fisher Scientific, Waltham, MA, USA) for the interpretation to confirm adequate cell material. Furthermore, additional air dried and 95% of ethanol fixed wet smears were prepared and stained with May-Grünwald Giemsa and Papanicolaou stain for routine cytopathological evaluation. If possible, the rest

of the material (loose microtissue cores) on the glass slide was transferred into 10% buffered formalin solution with assistance of a needle tip and processed as cell block for histological examination. When the cytological material was considered adequate, the procedure was terminated. Multiple passes were performed for each targeted site until on-site assessment was diagnostic for a disease process or an adequate sample was obtained.

If numerous benign lymphoid cell or clusters of anthracotic pigment laden macrophages with scattered lymphoid cells were present, or if a specific cytopathological diagnosis could be rendered, aspirated material were considered as satisfactory for cytological evaluation. The ROSE results were compared with the corresponding results of the final pathologic diagnosis. Immunohistochemistry was also carried out in some patients. A reference standard was established for the final diagnosis. The patients with benign lymphadenopathy or mass were followed-up for at least 12 months for any clinical or radiological evidence of disease progression. In patients with malignant lymphadenopathy or mass, the determination of final status of the lesion was based on malignant cytological results at TBNA-ROSE, with a subsequent clinical course consistent with malignant disease. Transbronchial needle aspiration and ROSE diagnosis was confirmed by biopsy during thoracotomy in NSCLC patients with negative TBNA results.

Statistical analysis

Patients were evaluated for diagnosis success, LN localization and size, and number of sampling. Sensitivity, specificity, and accuracy of localization and size of MLNs were calculated. Distributions of these variables were compared between groups and between cell types using the chi-square test and Fisher's exact test for qualitative variables. Age analyses were performed using Student's t-test. All data comparisons and analyses were performed using SPSS for Windows version 10.0 software program (SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation and differences were considered as statistically significant when the p value was less than 0.05.

RESULTS

A total of 244 TBNA-ROSE procedures were performed in 239 patients and re-TBNA-ROSE was performed in five patients with NSCLC for re-staging after neoadjuvant chemotherapy. Of all 244 ROSE procedures, adequate or diagnostic specimens were determined in 227 (93.03%) procedures, but there was a failure in obtaining adequate or diagnostic specimens in 17 procedures (6.97%). Transbronchial needle aspiration and ROSE revealed benign disease in 117 and malignant disease in 110 procedures. Benign diseases diagnosed were granulomatous disease (n=70) and reactive LN hyperplasia (n=47). Malignant diseases were lung cancer (n=99) and other cancer types (n=11) including metastatic renal cell carcinoma, adenocarcinoma, and clear cell carcinoma.

Mediastinoscopy (n=6) or mini thoracotomy (n=4) was performed in 10 cases in the undiagnosed group at the same session (malign, n=3; benign, n=7). No other procedures were carried out in the remaining seven patients as they refused any further interventions. In ROSE, 17 TBNA specimens were inadequate for diagnosis, but on final cytopathologic examination, one of them could be yielded with definitive diagnosis. In our series, overall discordance of preliminary and final diagnoses was 0.4% (1 out of 244 procedures).

In 239 patients, 297 LNs were sampled with TBNA and evaluated with ROSE. The characteristics of sampled lymph nodes are demonstrated in Table 1. Subcarinal station was the most punctured site (67.3%). A statistically significant difference was found between LN stations and dimensions (p=0.018); while the paratracheal MLN group had the largest mean LN size, the pretracheal MLN group had the smallest mean LN size (p=0.002). In all LN stations, results of TBNA were 45.5% (n=135) benign, 41.4% (n=123) malignant, and 13.1% (n=39) undiagnosed. Our success rate was 86.9% in TBNA results of LNs. Subcarinal station had the best diagnosis rate (91.5%) as well as the highest benign rate (49.5%). Paratracheal stations had the highest malignancy rate (60%) and the lowest benign disease rate (20%). Subcarinal position of LN was a predictor of positive aspirates and paratracheal LN station was a predictor of malignant disease. In ROSE, sampled materials in 39 cases (13.1%) were inadequate for diagnosis. There was a high failure rate (24.3%) in sampling of upper MLN stations.

The mean diameter of the lymph node in short axis was 21.2±9.2 mm (range, 8-60 mm) on CT image. The mean diameters were 23.9±10.4 mm in malignant group (n=123), 19.4±7.4 mm in benign group (n=135), and 19.1±8.8 mm in undiagnosed group, indicating a statistically significant difference among the groups. When each group was compared to each other, there was a statistically significant difference (malignant vs. benign p=0.001, malignant vs. undiagnosed p=0.006 and benign vs. undiagnosed p=0.5). The diameters of the malignant LNs were larger than the others. There was a correlation between the lymph node size and malignancy.

Table 1. Characteristics of sampled lymph nodes

	LN dimension (mm)				TBNA results								
					Malignant		Benign		Diagnostic		Non-diagnostic		
Lymph node station	n	%	Mean±SD	Range	n	%	n	%	n	%	n	%	*p**
Paratracheal	20	6.7	27.3±10.3	13-50	12	60	4	20	16	80	4	20	0.007
Pretracheal	20	6.7	17.1±6.4	10-32	5	25	9	45	14	70	6	30	0.07
Tracheobronchial	34	11.5	21.4±11.4	8-60	14	41.2	12	35.3	26	76.5	8	23.5	0.002
Subcarinal	200	67.3	20.9±8.9	5-70	84	42	99	49.5	183	91.5	17	8.5	0.000
Hilar/interlobar	23	7.8	21.6±5.4	11-30	8	34.8	11	47.8	19	82.6	4	17.4	0.002
Total	297		21.2±9.2	8-60	123	41.4	135	45.5	258	86.9	39	13.1	
P value			0.018**		0.001† 0.006‡		0.5¶						

LN: Lymph node; TBNA: Transbronchial needle aspiration; SD: Standard deviation; * Diagnostic compared with non-diagnostic in each lymph node groups; ** All lymph node station dimensions; † Malignant vs. benign lymph node dimensions; ‡ Malignant vs. non-diagnostic lymph node dimensions; ¶ Benign vs. non-diagnostic lymph node dimensions.

Multiple passes were performed until on-site evaluation was judged as diagnostic. The number of needle passes required for successful lymph node sampling was 2.8±2 in total, 2.5±1.6 in malignant group, and 2.6±2.2 in benign group, whereas it was 4.4±2 in undiagnosed group (Table 2). In our study, the threshold of needle passes for diagnosis was 2.5 and its sensitivity, specificity, and area under curve (AUC) were 60%, 87%, and 79%, respectively. When the relationship between character of the disease and the number of needle passes were evaluated, a statistically significant difference was found (p=0.001). When each group was compared to the others, the difference between the undiagnosed and the other two groups was statistically significant (malignant vs. undiagnosed, p=0.001 and benign vs. undiagnosed, p=0.001). The number of needle passes for the diagnosis of sampling of malignant disease was lower than in benign disease. Our study also showed that positive LN was easier to diagnose than benign LN but there was no statistically significant difference (malignant vs. benign p=0.5).

Mediastinal staging of NSCLC was performed in 64 patients with TBNA-ROSE, which resulted in a change of therapy recommendation from curative surgery to neo-adjuvant chemotherapy or curative chemo-radiotherapy. Nine patients underwent curative surgery after negative results of final TBNA evaluation for MLN metastases. All these negative results were confirmed with final histopathological examination after curative surgery. Re-TBNA-ROSE was performed in five patients after neoadjuvant chemotherapy and three of them were detected as negative with TBNA. All the negative results were also confirmed with final histopathological examination during resection materials. Two cases had persistent N_2 disease in MLN staging with TBNA. Negative results of TBNA evaluation of 12 cases were confirmed with histopathological examinations after curative surgery. One patient with renal failure had a minor complication (hemorrhage); however, there was no major complication in our interventions.

DISCUSSION

Transbronchial needle aspiration is a valuable and safe technique for mediastinal staging of NSCLC; however, the reported diagnostic yield is highly variable, with meta-analysis reporting the pooled sensitivity and specificity to be only 39% (95% confidence interval,

Table 2. Relationship between number of sampling and lymph node location

	Total number of sampling		Number of sampling in malignant disease		Number of sampling in benign disease		Number of sampling in nondiagnostic disease		
LN location	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median	*p**
Paratracheal	3.3±2.2	3	2.7±0.8	3	2±1.4	1.5	6.5±3.1	6.5	0.007
Pretracheal	2.9±1.9	2.5	2.6±1.5	2	2.1±2	1	4.5±1.4	4	0.020
Tracheobronchial	3.2±2.3	2	2.9±1.8	2.5	3.2±2.6	2	4±2.8	3	0.236
Subcarinal	2.7±2	2	2.4±1.7	2	2.7±2.2	2	4.1±1.5	4	<0.001
Hilar	2.3±1.4	2	2±1.1	2	1.7±1	1	4.5±0.6	4.5	0.001
Total	2.8±2	2	2.5±1.6	2	2.6±2.2	2	4.4±2	4	<0.001
P value	0.29		0.51		0.38		0.38		

LN: Lymph node; SD: Standard deviation; * Statistical comparisons were done between diagnostic and nondiagnostic disease.

range 17 to 61) and 99% (95% confidence interval, range 96 to 100), respectively.[7,8] This perception was changed with TBNA-ROSE and EBUS-guided TBNA and their use is encouraged.[9-11]

In recent years, many authors clearly demonstrated the improved diagnostic accuracy of real-EBUS-guided TBNA, but equipment for EBUS-TBNA is costly and therefore is not available in every hospital.[8-11] However, TBNA-ROSE can be performed in every hospital with a thoracic surgeon and cytopathologist. Baram et al.[1] and Diette et al.[2] reported that on-site cytopathology assessment was associated with greater diagnostic success. The results of a randomized trial that evaluated the utility of ROSE for the diagnosis of adenopathy using TBNA showed that ROSE significantly reduces the number of TBNAs and the complication rate of the bronchoscopy with TBNA.[5,12] Our TBNA-ROSE procedures were performed under general anesthesia with the use of a laryngeal mask airway and intravenous anesthesia as in EBUS-TBNA.[13] We have successfully performed TBNA-ROSE on 244 procedures without any major complications thanks to the procedure itself or general anesthesia.

Mediastinal staging is of importance for planning the treatment of NSCLC patients but mediastinoscopy allows access to only a limited number of MLN stations (1,2,3,4,7). Transbronchial needle aspiration is less invasive than mediastinoscopy and allows access to a wider range of MLN stations (2,3,4,7,10,11).[14] In our series, mediastinal staging of NSCLC was performed in 64 patients with TBNA-ROSE, which resulted in the change of therapy recommendation from curative surgery to neo-adjuvant chemotherapy or curative chemo-radiotherapy.

A number of imaging techniques, including multislice CT, 18-fluoro-deoxyglucose positron emission tomography-PET, and integrated PET-CT have recently been developed to investigate the mediastinum.[15,16] However, reliance on imaging alone is unacceptable and tissue diagnosis is still required to guide management.[17,18] Therefore, re-mediastinal staging after induction therapy is necessary for selecting the appropriate treatment strategy, but redo mediastinoscopy after induction therapy may be inaccurate.[19] The first mediastinoscopy might cause local fibrosis and adhesions, which make it technically difficult to perform re-mediastinoscopy. These problems may be overcome by EBUS or TBNA-ROSE especially for mediastinal staging after neoadjuvant chemotherapy. Transbronchial needle aspiration and ROSE may be a safer alternative modality for MLN sampling before or after induction therapy. In our series, re-TBNA-ROSE was performed in five patients after neoadjuvant chemotherapy and three of them had negative results. We operated on three patients and their N_2 stations were histopathologically negative. Our limited experience has shown that the re-TBNA-ROSE may be safely performed for re-mediastinal staging in NSCLC.

The utility of TBNA-ROSE has been previously reported and it has been shown that at least five to seven TBNA needle passes would be needed to achieve a plateau diagnostic yield.[20,21] In our study, the number of needle passes required for successful lymph node sampling was 2.8±2 in total, 2.5±1.6 in malignant disease, and 2.6±2.2 in benign disease; however, this number was 4.4±2 in undiagnosed group (Table 2). Our threshold of needle passes for diagnosis was 2.5 and its sensitivity, specificity and AUC were 60%, 87%, and 79%, respectively. The number of needle passes did not correlate with the diagnosis after the fourth pass. The TBNA-ROSE significantly improves the diagnostic yields and also reduces the number of passes necessary for achieving high diagnostic yields.[1,12] Conversely, EBUS-TBNA samples are often difficult to interpret because of the low quality of samples. The amount of lymphoid tissue depends not only on the technical aspect but also on cellularity of the lymph node.[22] Endobronchial ultrasound and TBNA can evaluate the morphologic features of LN but not the cellularity of the lymph node; therefore, ROSE may be preferred for determining the adequacy of TBNA with or without EBUS samples by the presence of normal lymphocytes, especially for non-malignant lymph nodes. In this study, adequate or diagnostic specimens were determined in 93.03% (n=227) of the procedures with TBNA-ROSE. Transbronchial needle aspiration and ROSE is a valuable method for identifying good quality samples.

Endobronchial ultrasound is a new and promising TBNA technique for improving diagnostic yield; however, ROSE not only improves the yield of procedure but also enables triage of material to secondary investigations (i.e. culture, flow cytometry).[23] From this point of view, ROSE is an important part of TBNA or EBUS-TBNA for diagnosing tissues and staging lung cancer.

However, the importance of improving the performance of TBNA through education and experience cannot be completely overemphasized, we believe that these factors really lead an significant role for improving.[1,24] Rapid on-site cytopathological evaluation decreases the frequency of inadequate specimens and increases diagnostic accuracy of TBNA.[1,6,24]

In conclusion, transbronchial needle aspiration rapid on-site cytologic evaluation was shown to be an easy and rapid technique with good outcomes and reduced the number of mediastinoscopy procedures. In our series, mediastinoscopy was prevented in 222 (92.9%) of 239 patients. Transbronchial needle aspiration and rapid on-site cytologic evaluation with or without endobronchial ultrasound may be the initial procedure of choice by thoracic surgeons in the staging or diagnosing of the mediastinal lymph node or mass before mediastinoscopy.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Baram D, Garcia RB, Richman PS. Impact of rapid on-site cytologic evaluation during transbronchial needle aspiration. Chest 2005;128:869-75.
2. Diette GB, White P Jr, Terry P, Jenckes M, Rosenthal D, Rubin HR. Utility of on-site cytopathology assessment for bronchoscopic evaluation of lung masses and adenopathy. Chest 2000;117:1186-90.
3. Baram D. Comparison of the diagnostic accuracy of transbronchial needle aspiration for bronchogenic carcinoma and other malignancies. J Bronchol 2004;11:87-91.
4. Nakajima T, Yasufuku K, Saegusa F, Fujiwara T, Sakairi Y, Hiroshima K, et al. Rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for nodal staging in patients with lung cancer. Ann Thorac Surg 2013;95:1695-9.
5. Iyoda A, Baba M, Shibuya K, Moriya Y, Yasufuku K, Sekine Y, et al. Transbronchial fine needle aspiration cytological examination: a useful tool for diagnosing primary lung cancer. Thorac Cardiovasc Surg 2006;54:117-9.
6. Yasufuku K, Fujisawa T. Staging and diagnosis of non-small cell lung cancer: invasive modalities. Respirology 2007;12:173-83.
7. Kunst PW, Lee P, Paul MA, Senan S, Smit EF. Restaging of mediastinal nodes with transbronchial needle aspiration after induction chemoradiation for locally advanced non-small cell lung cancer. J Thorac Oncol 2007;2:912-5.
8. Holty JE, Kuschner WG, Gould MK. Accuracy of transbronchial needle aspiration for mediastinal staging of non-small cell lung cancer: a meta-analysis. Thorax 2005;60:949-55.
9. Krasnik M, Vilmann P, Larsen SS, Jacobsen GK. Preliminary experience with a new method of endoscopic transbronchial real time ultrasound guided biopsy for diagnosis of mediastinal and hilar lesions. Thorax 2003;58:1083-6.
10. Herth FJ. Mediastinal staging--the role of endobronchial and endo-oesophageaL sonographic guided needle aspiration. Lung Cancer 2004;45:63-7.
11. Yasufuku K, Nakajima T, Motoori K, Sekine Y, Shibuya K, Hiroshima K, et al. Comparison of endobronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer. Chest 2006;130:710-8.
12. Trisolini R, Cancellieri A, Tinelli C, Paioli D, Scudeller L, Casadei GP, et al. Rapid on-site evaluation of transbronchial aspirates in the diagnosis of hilar and mediastinal adenopathy: a randomized trial. Chest 2011;139:395-401.
13. Sarkiss M, Kennedy M, Riedel B, Norman P, Morice R, Jimenez C, et al. Anesthesia technique for endobronchial ultrasound-guided fine needle aspiration of mediastinal lymph node. J Cardiothorac Vasc Anesth 2007;21:892-6.
14. Groth SS, Andrade RS. Endobronchial and endoscopic ultrasound-guided fine-needle aspiration: a must for thoracic surgeons. Ann Thorac Surg 2010;89:2079-83.
15. Vansteenkiste J, Dooms C. Positron emission tomography in nonsmall cell lung cancer. Curr Opin Oncol 2007;19:78-83.
16. Gonzalez-Stawinski GV, Lemaire A, Merchant F, O'Halloran E, Coleman RE, Harpole DH, et al. A comparative analysis of positron emission tomography and mediastinoscopy in staging non-small cell lung cancer. J Thorac Cardiovasc Surg 2003;126:1900-5.
17. De Leyn P, Stroobants S, De Wever W, Lerut T, Coosemans W, Decker G, et al. Prospective comparative study of integrated positron emission tomography-computed tomography scan compared with remediastinoscopy in the assessment of residual mediastinal lymph node disease after induction chemotherapy for mediastinoscopy-proven stage IIIA-N2 Non-small-cell lung cancer: a Leuven Lung Cancer Group Study. J Clin Oncol 2006;24:3333-9.
18. Mateu-Navarro M, Rami-Porta R, Bastus-Piulats R, Cirera-Nogueras L, González-Pont G. Remediastinoscopy after induction chemotherapy in non-small cell lung cancer. Ann Thorac Surg 2000;70:391-5.
19. Cerfolio RJ, Bryant AS. When is it best to repeat a 2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography scan on patients with non-small cell lung cancer who have received neoadjuvant chemoradiotherapy? Ann Thorac Surg 2007;84:1092-7.
20. Chin R Jr, McCain TW, Lucia MA, Cappellari JO, Adair NE, Lovato JF, et al. Transbronchial needle aspiration in diagnosing and staging lung cancer: how many aspirates are needed? Am J Respir Crit Care Med 2002;166:377-81.
21. Diacon AH, Schuurmans MM, Theron J, Brundyn K, Louw M, Wright CA, et al. Transbronchial needle aspirates: how many passes per target site? Eur Respir J 2007;29:112-6.
22. Stoll LM, Yung RC, Clark DP, Li QK. Cytology of endobronchial ultrasound-guided transbronchial needle aspiration versus conventional transbronchial needle aspiration. Cancer Cytopathol 2010;118:278-86.
23. Nakajima T, Yasufuku K, Iyoda A, Yoshida S, Suzuki M, Sekine Y, et al. The evaluation of lymph node metastasis by endobronchial ultrasound-guided transbronchial needle aspiration: crucial for selection of surgical candidates with metastatic lung tumors. J Thorac Cardiovasc Surg 2007;134:1485-90.
24. Hsu LH, Liu CC, Ko JS. Education and experience improve the performance of transbronchial needle aspiration: a learning curve at a cancer center. Chest 2004;125:532-40.