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Risks of Transthoracic Needle Biopsy: How High?

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Abstract

Transthoracic needle lung biopsy is a commonly performed diagnostic procedure for pulmonary nodules and masses. To make an informed decision about whether to pursue this procedure, doctors and patients must be aware of the possible risks of the procedure. We performed a MEDLINE search, 2003–2012 to identify relevant English-language studies that included at least 100 subjects and reported data on complications of transthoracic needle lung biopsy performed within the last 10 years. We found the most common complication to be any pneumothorax (risk 15–25%), with pneumothorax requiring chest tube occurring less often (risk 4–6%). Hemorrhage, defined as radiographically visualized blood along the needle tract was common, but clinically significant hemorrhage was infrequent (~1%). Rare complications, including air embolism and tumor seeding of the biopsy tract, occurred in fewer than 1% of cases but were potentially serious. We summarize data on factors associated with complications, including patient age, COPD, lesion size and location, and number of punctures. We also provide data on techniques to mitigate severity of pneumothorax post-biopsy, such as rapid patient rollover, manual aspiration, and instillation of substances into the biopsy tract.

Keywords

Needle Biopsy; Pulmonary nodule; Complications

INTRODUCTION

Indeterminate pulmonary nodules are an increasingly common clinical problem, and are expected to become even more common with more frequent use of low dose chest computed tomography (CT) scans for lung cancer screening. When an indeterminate nodule is found, clinicians and patients must decide whether to pursue biopsy to obtain a tissue sample of the nodule. Biopsy is most often pursued to confirm or exclude a malignant nodule; however, it may also be used to establish a specific benign diagnosis (e.g., infection) to help tailor treatment.¹ Professional society guidelines recommend that transthoracic needle lung biopsy be considered in the evaluation of indeterminate lung nodules measuring over 8 mm in size.^{1, 2}

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It is important for both clinicians and patients to be aware of the possible risks of transthoracic needle biopsy to make informed choices during the evaluation process. Much of the data regarding complications of transthoracic needle lung biopsy come from case series, though there are also data from surveys and large database analyses. The most commonly reported complications include pneumothorax and hemorrhage. Rare complications that have been described include tumor seeding along the needle biopsy tract and air embolism. In this paper we summarize recent data regarding the risks of complications resulting from transthoracic needle biopsy, factors associated with an elevated risk of complications, and methods to reduce the risk of adverse outcomes resulting from this procedure.

METHODS

We performed a MEDLINE search to identify English-language articles that were published in the last 10 years (2003–2012) that reported complications of transthoracic needle lung biopsy (search terms = “Biopsy, needle” AND “lung”; filters = English language, human). We supplemented this search through review of reference lists. To ensure reliable estimates of complications, we excluded studies that reported data on fewer than 100 transthoracic needle biopsy procedures. Because improvements in technology (e.g., better imaging quality, smaller gauge and more accurate needle systems) are likely to improve the safety of the procedure, we also excluded studies that reported data only on procedures performed more than 10 years ago (e.g., studies with most recent data from 2002 or earlier), with the exception of two studies examining rare complications that included data on several thousand patients who had undergone transthoracic needle biopsy prior to 2002. Finally, we excluded studies with incomplete information (full text unavailable [n=1] or insufficient details [n=1]). When investigators published multiple case series based on some or all of the same data, we included only the most comprehensive study.

We next abstracted data from the identified studies using a standardized form. We collected data on study design, study center, patient, and biopsy characteristics, as well as on reported complication rates, factors associated with risk of complications, and factors that were reported to mitigate complication rates. We used summary statistics (median, range) to describe complication rates reported in multiple case series.

RESULTS

Pneumothorax

Risk of Pneumothorax and Associated Factors—Pneumothorax is widely reported to be the most common complication of transthoracic needle biopsy. Pneumothorax severe enough to require chest tube placement is also generally agreed to be the most serious complication, necessitating a painful procedure (chest tube placement) and a hospital stay. In one study, the mean duration of chest tube drainage in 33 patients with pneumothorax complicating transthoracic needle biopsy was 3.8 days (range 1–9 days).³ The clinical significance of pneumothorax that does not require chest tube is more debatable.

The largest study to assess risk of complications of transthoracic needle lung biopsy was performed by Wiener et al using administrative databases from 4 large, geographically distinct states (California, Florida, Michigan, New York).⁴ They examined data from all transthoracic needle biopsies performed in non-federal hospitals in these states in 2006 (n=15,865). Based on these data, they estimated the risk of any pneumothorax to be 15.0% (95% CI 14.0–16.0%) and the risk of a pneumothorax severe enough to require chest tube placement to be 6.6% (95% CI 6.0–7.2%). Patients who experienced a pneumothorax that required chest tube placement had significantly longer lengths of stay ($p<0.001$) and were

significantly more likely to develop respiratory failure requiring mechanical ventilation ($p < 0.01$) than patients who did not experience a complication of transthoracic needle biopsy. Patient characteristics associated with increased risk of pneumothorax requiring chest tube included a history of tobacco use (OR = 1.50, 95% CI 1.26–1.77) or chronic obstructive pulmonary disease (COPD; OR = 2.52, 95% CI 2.16–2.92). They found risk of pneumothorax to be highest in patients aged 60–69 years, with a lower risk in young patients (likely reflecting a healthier, more robust population) and in elderly patients (likely reflecting a selection bias through which frail elderly patients at high risk of complications were not referred for biopsy). At the level of the medical center, there was no statistically significant association observed between number of biopsy procedures performed and risk of complications.

Several single-institution retrospective case series also reported data on complications of transthoracic needle lung biopsy. We summarized data on risk of pneumothorax complicating transthoracic needle biopsy from 19 recent single-institution, retrospective case series that met our inclusion criteria^{3, 5–22} (Table 1). These studies reported widely variable risks of complications, likely due to factors specific to the institution, such as patient population, biopsy procedure volume, experience of the biopsy operator(s), and technical factors. The median risk reported in these studies was 25% (range 4–60%) for any pneumothorax, and 4% (range 0.2–8%) for pneumothorax requiring chest tube.

It is notable that the median reported risk of pneumothorax based on data from single institution case series (25%) is higher than that observed in the multi-institution study by Wiener et al⁴ (15%). This discrepancy likely reflects the different ways in which pneumothorax was defined. Wiener et al⁴ relied on discharge records to estimate complication risks. Discharge records are unlikely to contain diagnostic codes that are based solely on radiographic findings without clinical significance. By contrast, single-institution case series often recorded a complication when a pneumothorax was observed on CT immediately post-biopsy, regardless of whether the patient had clinical symptoms. This radiographically defined pneumothorax risk tends to be much higher than if pneumothorax were based on clinical criteria, or even chest x-ray. For example, Noh et al¹⁸ contrasted the rate of pneumothorax observed by CT immediately post-biopsy (25%) with the much lower rate of pneumothorax identified by chest x-ray or clinical symptoms 4–16 hours after biopsy (12%). This “clinical” pneumothorax rate of 12% closely approximates the 15% risk of pneumothorax estimated by Wiener et al.⁴ Similarly, the median risk of pneumothorax requiring chest tube estimated based on the single-institution case series (4%) is similar to the 6% risk of pneumothorax requiring chest tube identified by Wiener et al in their multi-institution analysis.

A number of single-institution case series examined factors associated with increased risk of pneumothorax (Table 2). Factors that were associated with increased risk of pneumothorax in more than one study include patient characteristics (age > 60 years; COPD), lesion characteristics (small size, greater distance from pleura), and technical factors (increased number of punctures or aspirates, biopsy performed in supine or lateral rather than prone position). However, studies have not shown consistent results. Negative findings of the smaller case series should be interpreted with caution as they may be underpowered to identify statistically significant associations.

Strategies to Reduce Pneumothorax Rate—Some investigators have evaluated interventions to prevent or mitigate post-biopsy pneumothorax, including techniques for needle withdrawal and patient positioning,^{21, 23} injection of substances into the biopsy path to close the puncture site,^{24–26} and manual aspiration of any pneumothorax observed on

post-biopsy CT.^{3, 25} We review findings from studies that tested the effects of one or more of these interventions, as compared to either usual care or another intervention.

Using a pre-post design, O'Neill et al²³ retrospectively reviewed their experience at a single institution with introduction of a policy for rapid patient roll-over into the biopsy side down position within 10 seconds after completing the biopsy. Using data from 201 consecutive cases (81 usual care, 120 rapid rollover intervention), they found significant reductions in the rapid rollover group in rates of any pneumothorax (23% vs 37%, $p=0.04$) as well as pneumothorax requiring chest tube (4% vs 10%, $p=0.03$).

A number of studies have examined injection of various agents into the biopsy tract to mitigate risk of pneumothorax. Billich et al²⁴ performed a prospective study in which they allocated 140 consecutive patients in an alternating fashion to receive instillation of saline (0.9% NaCl) into the biopsy path versus usual care; patients were similar with regard to characteristics that have been associated with risk of pneumothorax. Among patients receiving saline, as compared to usual care, they found a lower rate of any pneumothorax (8% [6 / 70] vs 34% [24 / 70], $p<0.001$) and pneumothorax requiring chest tube (1.4% [1 / 70] vs 11% [8 / 70], <0.001). Zaetta et al²⁶ performed a prospective, multi-center trial in which 339 patients undergoing transthoracic lung biopsy were randomly allocated to either injection of an expanding hydrogel plug into the biopsy tract or usual care. The primary outcome was absence of pneumothorax at 3 timepoints: 30–60 minute, 24-hour, and 30-day post-biopsy. More patients in the hydrogel plug group than in the control group achieved the primary outcome, but this difference only reached statistical significance ($p=0.002$) in the per-protocol analysis, not in the intention-to-treat analysis. The investigators also noted improvements in clinically important secondary outcomes of any pneumothorax (18% vs 31%), pneumothorax requiring chest tube (4% vs. 11%), and post-biopsy hospital admissions (9% vs. 14%), though statistical significance of these outcomes was not tested. There was no increase noted in adverse events in the treatment arm.

Other techniques have been proposed to mitigate the severity of a post-biopsy pneumothorax, such as pleural blood patching and manual aspiration of an observed pneumothorax.³ At the University of Wisconsin, the policy on treatment of immediate post-biopsy pneumothorax visualized on CT changed in February 2008 from simple aspiration to aspiration plus pleural blood patching (injection of autologous blood into the biopsy tract).²⁵ Using a pre-post design, Wagner et al²⁵ retrospectively compared outcomes of cases that received aspiration alone vs aspiration plus blood patching. Out of 463 consecutive transthoracic needle biopsies performed during the study period, 45 required intervention for a post-biopsy pneumothorax, including 15 patients who received aspiration only, 22 patients who also received pleural patching, and 8 patients (4.1% of all biopsies) who required chest tube placement. Success rate, defined as avoidance of chest tube placement, was higher in the pleural patching group (86% [19 of 22]) than the simple aspiration group (46.7% [7 of 15]). The authors did not report any adverse effects of pleural blood patching.

Hemorrhage

Estimates of risk of hemorrhage complicating transthoracic needle lung biopsy also vary widely. Based on data from 12 single-institution retrospective case series,^{5–10, 12, 15, 16, 19, 20, 22} the median risk of hemorrhage is 12% (range 2–66%). Based on the analysis of discharge records from 15,865 biopsies in 4 states, Wiener et al found a substantially lower risk of hemorrhage of 1.0% (95% CI 0.9–1.2%).⁴

The observed discrepancy in estimated risk of hemorrhage likely relates to how the complication was defined. Wiener et al⁴ based their estimated risk on frequency of procedure-related hemorrhage coded on the discharge record. Coding of hemorrhage likely

only occurred in clinically significant cases. Supporting this contention, Wiener et al⁴ found that 18% (95% CI 11.8–23.8%) of patients who experienced hemorrhage required a blood transfusion (as compared to 4.3% of patients without a biopsy-related complication, $p<0.001$), and that patients who experienced biopsy-related hemorrhage had significantly longer lengths of stay ($p<0.05$) and a higher incidence of respiratory failure requiring mechanical ventilation ($p<0.05$) than patients without biopsy-related complications. By contrast, in many case series, hemorrhage was defined radiographically, by the visualization of bleeding around the biopsy site under CT guidance. Defining hemorrhage based on radiographic findings led to much higher estimates of risk of hemorrhage, though it is likely that many of these cases had little clinical significance. In a single institution case series of 321 biopsies, Priola et al¹⁹ demonstrate how the definition of hemorrhage can affect the estimated risk. They report that 94 of 321 biopsies (29%) were complicated by hemorrhage defined as bleeding visualized along needle path on immediate post-biopsy CT; however, only 11 of these patients (3.4%) experienced hemoptysis; and only 2 patients (0.6% of all biopsies) had hemoptysis significant enough to require medical treatment.

Several studies assessed factors associated with hemorrhage, with mixed results. Both Wiener et al⁴ and Heyer et al¹² found COPD to be associated with an elevated risk of hemorrhage. Wiener et al⁴ also found female sex to be associated with higher rates of hemorrhage (OR 1.42, 95% CI 1.03–1.96). Yildirim et al²² found female sex to be significantly associated with hemorrhage in univariate, but not multivariate analysis. Chang et al,⁷ Rizzo et al,²⁰ and Yildirim et al²² each found smaller nodule size to be significantly associated with an increased risk of hemorrhage. Rizzo et al identified technical factors significantly associated with risk of hemorrhage including longer biopsy path (>40 mm), and a biopsy path that crossed a fissure. By contrast, Chakrabarti et al⁶ did not find a significant association between nodule size or biopsy path and hemorrhage.

Rare Complications: Tumor seeding and Air embolism

Tumor seeding along needle biopsy tract—Case reports have anecdotally reported that seeding of tumor along the needle tract can complicate transthoracic needle lung biopsy. Two recent larger studies provide an estimate of the frequency of this complication. First, Tomiyama et al²⁷ conducted a survey of 124 centers in Japan to identify frequency of rare but serious complications. Out of 9783 transthoracic needle biopsies reported in the survey, 6 were complicated by tumor seeding along the needle tract (0.06%). In a large, single-institution case series, Ibukuro et al²⁸ retrospectively reviewed 1400 consecutive transthoracic needle lung biopsies performed between 1993–2008; among these cases, 713 patients had a pathologically confirmed thoracic malignancy and at least 2 months follow-up post-biopsy. Four of these 713 patients (0.6%) developed a pathologically confirmed tumor implantation along the needle tract. Of note, this risk is an order of magnitude higher than the risk reported in the multi-center survey by Tomiyama et al.²⁷ However, as Ibukuro et al point out, the proper denominator is not *all* transthoracic needle biopsies, as reported by Tomiyama et al, but rather the subset of procedures performed on a patient with a malignant lesion (data which is not provided by Tomiyama et al). As a limitation to their study, Ibukuro et al acknowledge that they were only able to identify patients with tumors large enough to be detected with CT, and could not comment on the frequency of microscopic tumor seeding.

Sano et al²⁹ have attempted to address this concern with a prospective study. They performed intraoperative pleural lavage on 412 patients undergoing resection of a lung cancer, 171 of whom had undergone transthoracic needle biopsy prior to surgery. They found no difference in the percentage of patients with malignant cells found on pleural lavage cytology between those who had versus had not undergone transthoracic needle

biopsy prior to surgery (2.9% vs. 5.4%, $p=0.22$). They also found no difference in frequency of pleural dissemination or malignant pleural effusion (3.3% vs. 2.3%, $p=0.77$). No patients in either group had a clinical presentation of seeding in the chest wall after a median of 20 months follow-up.

Finally, Wisnivesky et al³⁰ performed an analysis using the Surveillance, Epidemiology and End Results (SEER) registry to determine whether the possibility of tumor seeding along the needle tract led to worsened survival among lung cancer patients who had undergone transthoracic needle lung biopsy prior to resection ($n=3082$) versus those who had not ($n=5525$). They found no difference in either overall survival or lung-cancer specific survival in crude or adjusted analyses.

Taken together, these 3 studies suggest that tumor seeding of the biopsy tract is a rare complication that does not appear to substantially affect survival.

Air embolism—Air embolism is an even more infrequent complication than tumor seeding along the biopsy tract, but it is nonetheless important because of the risk of immediate death. Two large studies provide estimates of the frequency and outcomes of air embolism complicating transthoracic needle lung biopsy. In their survey of 124 Japanese hospitals, Tomiyama et al found that 6 of 9783 biopsies (0.06%) were complicated by air embolism. In two large single institution case series, Hiraki et al (2007)³¹ and Ibukuro et al²⁸ report risk of air embolism complicating transthoracic needle biopsy to be 0.4% (4 of 1010 biopsies) and 0.2% (3 of 1400 biopsies), respectively. Ibukuro et al also summarize the outcomes of the 19 cases of air embolism complicating transthoracic needle biopsy that had been reported in the literature through 2008. Of these 19 cases, 10 patients experienced paresis (53%), 7 had cardiac complications (37%), and 5 died (26%). Tactics to minimize risk of air embolism include patient breath holding during biopsy (with particular avoidance of coughing) and closing off the introducer needle to atmospheric air as quickly as possible. The treatment of choice for air embolism is Trendelenburg position and hyperbaric oxygen therapy.

Air embolism is likely under recognized. For example, in the survey conducted by Tomiyama et al,²⁷ there were 5 cases of unexplained cardio-pulmonary arrest or shock reported that may have been due to unrecognized air embolism. Meanwhile, Freund et al⁹ report on systematic use of CT of the entire thorax immediately after the biopsy needle was removed in 610 consecutive transthoracic needle biopsy procedures. In this way they were able to radiographically identify 23 cases of systemic air emboli (3.8%); however, only 3 of these patients (0.5%) presented with clinical symptoms. Using multivariable logistic regression, they identified the following modifiable risk factors for air embolism: needle tip not fully penetrated into nodule; use of general anesthesia; increasing height above level of left atrium; and prone position during biopsy.

DISCUSSION

As use of CT continues to rise for a variety of indications including lung cancer screening, more and more patients will have a pulmonary nodule detected, leaving patients and their providers to decide whether or not to pursue transthoracic needle biopsy. In this review we have summarized the recent data on risk of complications of transthoracic needle biopsy. We have shown that risk of any pneumothorax is not uncommon (approximately 15–25%), but that the more clinically important outcome of risk of pneumothorax requiring chest tube is lower (4–6%). Risk of hemorrhage varies widely, depending in part on how hemorrhage is defined, but clinically significant hemorrhage appears to complicate approximately 1% of transthoracic needle biopsies. Air embolism and seeding of the biopsy tract with malignant

cells are rare complications, with a risk well under 1%. While seeding of the biopsy tract does not appear to affect overall survival, air embolism is a potentially fatal complication.

In deciding whether to pursue transthoracic needle biopsy of a pulmonary lesion, providers and patients should consider not only these “average” risks but also factors that may elevate the individual patient’s risk of complications. Important considerations include the patient’s age, presence of comorbidities such as COPD, the size and location of the nodule (proximity to pleura). In general, older patients, those with COPD, those with smaller nodules or nodules deep in the lung parenchyma are at increased risk of complications. Other technical factors that may differ from one institution to the next (e.g., CT vs. fluoroscopic guidance, needle size, cutting vs. fine needle, presence or absence of cytopathologist) may also influence risk of complications. However, the included studies did not directly examine the association of these factors with complications; most single-institution case series used a standard protocol for all cases (Table 1), and the multi-center study by Wiener et al⁴ did not have data on technical factors of biopsies. Of note, with rising use of biomarker testing of tumor specimens for personalized treatment of cancer, which requires larger core biopsies that may put the patient at higher risk of complications, it will be particularly important to be cognizant of the risks of transthoracic needle lung biopsy.

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Study characteristics and complication rates reported in retrospective series of patients undergoing transthoracic needle lung biopsy

Table 1

Author, year	Study location	Subjects, N	Study period	Study characteristics			Study characteristics				
				Inclusion criteria*	Biopsy method	Mean Age (SD), years	Male, %	Mean lesion diameter (SD), mm	Pneumothorax, %	Pneumothorax requiring chest tube, %	Hemorrhage, %
Multi-center study											
Wiener, 2011 ⁴	California, Florida, Michigan, New York	15,865	2006	Adults with pulmonary nodule, mass, or cancer in non-federal facilities in 4 states	Unknown; defined by ICD-9 or CPT codes for CT-guided or fluoroscopic transthoracic needle lung biopsy	--	52%	unknown	15%	6.6%	1.0%
Single center studies											
Ayyappan, 2008 ⁵	Canada	107	1/06–8/06	Consecutive adults with upper lobe lesion; excluded if larger gauge needle or nodule abutting chest wall	Ultrathin FNA with 25G needle under fluoroscopic guidance, transfixsural approach	62 (range 36–88)	55%	range (11–80)	28%	8%	6%
Chakrabarti, 2008 ⁶	UK	134	1/00–12/04	Consecutive patients exclusion: uremic patients, pleural-based masses	co-axial cutting needle system (19G outer, 20 G cutting) under CT guidance	68 (10)	55%	Median 30–40	24%	4%	3.7%
Chang, 2008 ⁷	Taiwan	582	10/97–6/04	Consecutive patients with non-vascular pulmonary lesion >4 mm	19-gauge coaxial guiding needles and 20-gauge biopsy needles under CT guidance	62.8 (13.5)	58%	36 (20)	38%	1%	46.9%
D'Alessandro, 2007 ⁸	Italy	583	5/95–9/05	Consecutive patients with thoracic lesion and no evident intrabronchial neoplasm	CT-guided fine needle aspiration biopsy	Range 14–86	77%	median 47 (range 10–160)	18%	5.2%	4%
Freund, 2012 ⁹	Austria	610	3/07–9/09	Consecutive patients	CT guided core biopsy using coaxial needle 17G with 18G cutting needle	61.7 (13.4)	41%	--	15%	1.6%	66%; clinically significant 0.7%
Guimaraes, 2010 ¹⁰	Brazil	362	7/96–6/04	Consecutive patients	CT-guided fine needle aspiration biopsies using 22 gauge needles	61 (16)	59%	51.5 (24.3)	11%	3.0%	3%
Halloush, 2007 ¹¹	Michigan	150	1/98–4/04	Consecutive patients	Fine needle aspirations under fluoroscopic or CT guidance using 23 or 25G needle	63.6 (range 27–85)	54%	--	12%	2.2%	
Heyer, 2008 ¹²	Germany	159	8/95–3/07	Consecutive patients	16 gauge core biopsy needle 10 cm length, automated biopsy device; chose shortest vertical intercostal approach that avoided bulla, vascular structures, and pleural fissures	66 (11)	72%	46 (30 mm)	26%	6%	10%
Hiraki, 2009 ¹³	Japan	901	4/00–8/08	Consecutive patients	CT fluoroscopy guidance, 19G introducer, 20G cutting biopsy needle coaxial system	66.9	63%	23 (15)	42%	5%	

Study characteristics							Study characteristics				
Author, year	Study location	Subjects, N	Study period	Inclusion criteria *	Biopsy method	Mean Age (SD), years	Male, %	Mean lesion diameter (SD), mm	Pneumothorax, %	Pneumothorax requiring chest tube, %	Hemorrhage, %
Kothary, 2010 ¹⁴	California	262	1/03-9/08	Consecutive adults with a pulmonary mass or nodule with indeterminate radiologic characteristics	Coaxial technique with 19G introducer needle and 21G aspiration needle; all patients underwent FNA, some cutting biopsy as well with 20G needle	59	51%	28 (18)	23.70%	4.2%	
Laspas, 2008 ¹⁵	Greece	409	unknown ("over a 5-year period")	Consecutive adults	CT-guided fine needle aspiration using 21–23 gauge needle	65	73%	range 6–100	4.2%	0.2%	2.0%
Mazza, 2005 ¹⁶	Italy	312	6/00-3/04	Consecutive adults	CT-guided fine needle aspiration with 20–25G needle or fine needle biopsy with small cutting needle (19–22G)	66	70%	range 5–80	13%	6.7%	15%
Nakamura, 2011 ¹⁷	Japan	156	7/03-10/06	Consecutive patients	CT-guided needle lung biopsy using noncoaxial technique with 9–15 cm and 20–22G needle	74.2	63%	--	60%	7.7%	
Noh, 2009 ¹⁸	Korea	934	5/03-6/07	Consecutive patients	CT-guided transthoracic needle aspiration-biopsy	--	--	--	25% by immediate CT; 12% by CXR 4–16h later	2.2%	
Priola, 2010 ¹⁹	Italy	321	4/05-2/07	Consecutive patients with a lung nodule or mass	CT-guided fine needle aspiration biopsy using a 21 or 20 G aspirating needle or 17G/18G coaxial cutting needle	65.8 (8.9)	72%	37.2 (21)	27%	4.0%	29% bleeding in needle path; 3% any hemoptysis; 0.6% hemoptysis requiring treatment
Rizzo, 2011 ²⁰	Italy	157	1/07-7/08	Consecutive patients; excluded if prior lung resection, presence of pleural effusion, pleural-based lesion	Fine needle aspiration with 20–25G needle; core biopsy with 14–20G needle	--	--	40.1 (25.6)	overall: 45.6%; for nodule<20 mm: 61%	8%	overall: 35%; for nodule<20 mm: 55%
Wang, 2009 ²¹	Taiwan	146	1/00-12/05	Consecutive adults	CT-guided lung biopsy with 17G/18G coaxial cutting needle; single puncture, 3-step needle withdrawal technique	66.1 (1.2)	58%	--	16%	1.4%	
Yamagami, 2009 ³	Japan	642 biopsies (594 patients)	10/00-8/08	Consecutive adults	CT fluoroscopic guided biopsy using 18, 20, or 21G needle and 1-I device	66.1 (range 5–92)	60%	20.8 (range 3–100)	38%	5.1%	
Yildirim, 2009 ²²	Turkey	225 biopsies (213 patients)	6/00-3/07	Consecutive patients	CT-guided coaxial cutting needle lung biopsy using 17G guiding needle, 22G biopsy needle, followed by 19G guiding, 20G core needle	62.5 (13.1)	76%	41.3 (20.1)	26%	7.5%	13%

* All patients included in these studies underwent CT-guided biopsy

Table 2

Findings of studies evaluating factors associated with increased risk of pneumothorax

Author, year	Possible Factors Associated with Pneumothorax*									
	Age (years)	Gender	Tobacco	COPD	Small Lesion	Distance from pleura / length of biopsy path	Number of punctures	Fissure traversed	Operator experience	Patient position
Multi-center study										
Wiener, 2011 ⁴	+ (60–70)	–	+	+						
Single center studies										
Ayyappan, 2008 ⁵				–		–	+			
Chakrabarti, 2008 ⁶	–	–	–	–	+	+		–	–	
Guimaraes, 2010 ¹⁰				+	–	+				
Halloush, 2007 ¹¹	–						–			
Heyer, 2008 ¹²	–	–		–	+	+				–
Mazza, 2005 ¹⁶	+	(>60)				+	–			
Nakamura, 2011 ¹⁷	–			–	–		–			+ (supine)
Noh, 2009 ¹⁸				–						
Priola, 2010 ¹⁹	–				–	–	**			
Rizzo, 2011 ²⁰				–	+	+		+	–	
Wang, 2009 ²¹	–	–			+	+				–
Yamagami, 2009 ³	–	–		+	–	+	–			+ (lateral)
Yildirim, 2009 ²²	–	–		–	–	–				

* Plus sign indicates significant association between factor and increased risk of pneumothorax; minus sign indicates no association found in that study

** Number of pleural punctures did not affect the risk, but number of needle aspirates and cutting specimens was associated with increased risk (p=0.02)