Complications After Transthoracic Needle Biopsy of Pulmonary Nodules: A Population-Level Retrospective Cohort Analysis

VISUAL ABSTRACT

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Abstract

Objective: To provide recent population-based estimates of transthoracic needle biopsy (TTNB) complications and risk factors associated with these complications.

Methods: This retrospective cohort analysis included adults from a nationally representative longitudinal insurance claims data set who underwent TTNB in 2017 or 2018. Complications that were evaluated included pneumothorax, hemorrhage, and air embolism. Separate logistic regression models estimated the association of pneumothorax or hemorrhage with the setting of care (ie, inpatient or outpatient) and selected baseline patient demographic and clinical characteristics including age, gender, history of chronic obstructive pulmonary disease, diagnosis of pleural effusion, tobacco use, use of oral anticoagulants and antiplatelet agents, prior lung cancer screening, previous bronchoscopy within 1 year, and Elixhauser comorbidity index.

Results: Among 16,971 patients who underwent TTNB, 25.8% experienced a complication within 3 days of the procedure (pneumothorax 23.3%, hemorrhage 3.6%, and air embolism 0.02%). Among patients who experienced pneumothorax, 31.9% required chest tube drainage. Among patients undergoing an outpatient TTNB (n = 12,443), 6.9% were hospitalized within 7 days. Biopsy in an inpatient setting, chronic obstructive pulmonary disease diagnosis, and prior bronchoscopy were associated with higher rates of both pneumothorax and hemorrhage. Prior lung cancer screening was associated with an increased risk of pneumothorax, and prior use of oral anticoagulants or antiplatelets was associated with higher rates of hemorrhage.

Conclusion: This contemporary population-based cohort study demonstrated that approximately one-quarter of patients undergoing TTNB experienced a complication. Pneumothorax was the most frequent complication, and hemorrhage and air embolism were rare. Among outpatients, complications from TTNB are an important cause of hospitalization.

Key Words: Complications, hemorrhage, pneumothorax, pulmonary nodules, transthoracic needle biopsy

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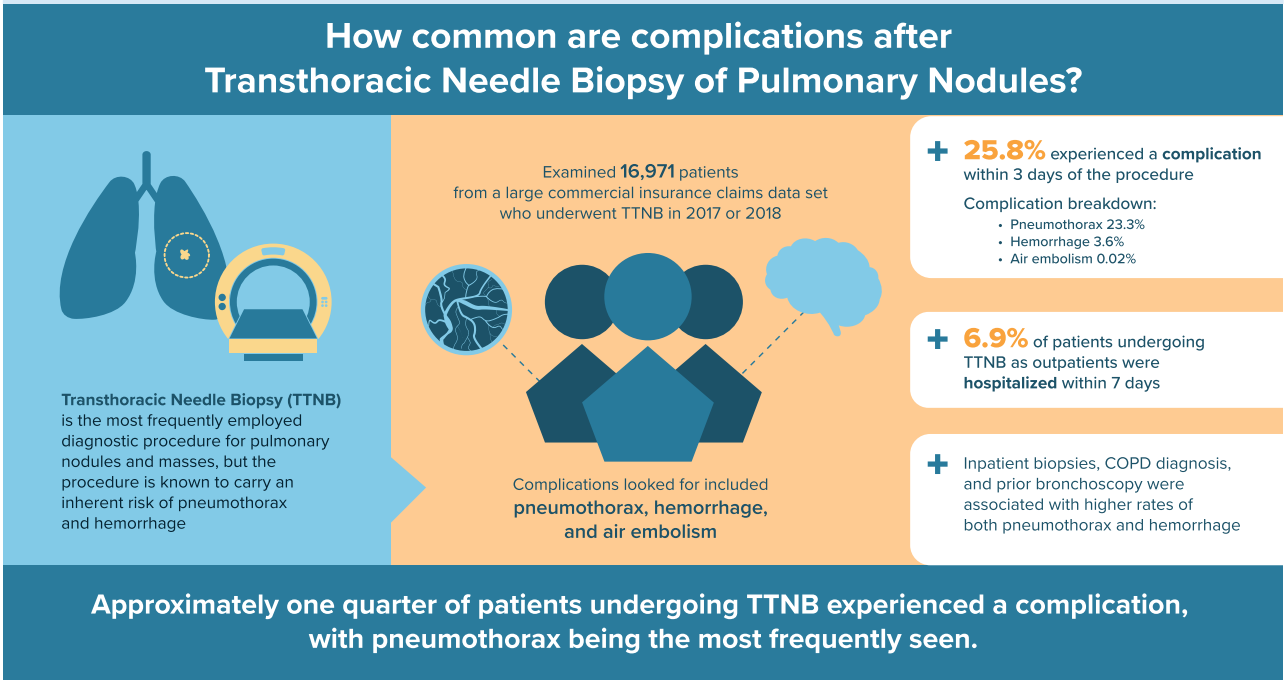
Visual Abstract



INTRODUCTION

Transthoracic needle biopsy (TTNB) of the lung is a commonly performed diagnostic procedure for obtaining tissue for the diagnosis of individuals with pulmonary nodules and masses [1-3]. Although TTNB can be performed with various guidance modalities, CT-guided biopsy is now the most common approach utilized [4]. Once a decision to proceed with biopsy has been made for a patient with a pulmonary lesion, the choice of modality is often complex and based on factors that include an assessment of clinical risks and benefits. Besides TTNB, the primary nonsurgical approach to lung biopsy is flexible bronchoscopy; however, TTNB is still the most frequently employed modality for peripheral located pulmonary lesions. The sensitivity and specificity of TTNB is excellent for malignant disease; however, the procedure is known to carry an inherent risk of pneumothorax and hemorrhage [1-3,5]. Prior studies are largely limited to single-center case series analyses with limited sample size [6-15] and one large cross-sectional analysis that used data before 2007 [16]. More recent population-based analyses of the characteristics of patients undergoing TTNB and the corresponding rates and nature of complications after TTNB are lacking.

The use of TTNB is increasing over time, which likely reflects higher incidence of pulmonary nodule identification and need for diagnosis as well as greater demands for tumor tissue for molecular testing to inform treatment selection at the time of recurrence or progression. It is unknown if complication rates have changed over time due to evolving clinical practice patterns, technological improvements, or changes in patient selection. We hypothesized that complications from TTNB remain a frequent cause of morbidity and would be higher among patients undergoing the procedure in the inpatient setting compared with other clinical settings. We further hypothesized that patient-specific factors, such as older age and greater comorbid illness, would be associated with higher complications rates. A better understanding of the contemporary rates and patterns of complications with TTNB and factors that predispose patients to these complications can be used by clinicians and patients to make decisions on the approach to lung biopsy. Thus, the objectives of this study were to calculate the frequency of complications with TTNB, explore risk factors associated with their occurrence, and measure resource utilization associated with these complications.

METHODS

Data Source and Study Population

We performed a retrospective cohort analysis using the Optum Clinformatics Data Mart, an administrative claims database of commercially insured and Medicare Advantage enrollees from a large US commercial health plan. The database included information on patient demographics, enrollment, pharmacy claims, medical claims, and

laboratory data for approximately 82 million enrollees between May 2000 and December 2019. The population is geographically diverse, spanning all 50 states.

We identified all patients who underwent a TTNB (defined as a Current Procedural Terminology [CPT] procedure codes of 32400 and 32405) between January 1, 2017, and December 31, 2018. The date of the first observed TTNB during this period was designated as the index date. Patients included in the analysis were ≥18 years of age; had continuous medical and pharmacy insurance coverage for ≥365 days before the index date (ie, baseline period); had a diagnosis of a pulmonary nodule, chest mass, or pulmonary neoplasm in the baseline period; and had continuous enrollment for at least 7 days after the procedure. Patients were excluded if they had a pulmonary resection, stereotactic body radiation therapy, TTNB, or pregnancy in the baseline period. Patients with a pulmonary resection, stereotactic body radiation therapy, mediastinoscopy, or bronchoscopy on the index date were also excluded. Diagnoses and procedures were measured using *International Classification of Diseases,* 10th rev, *Clinical Modification (ICD-10-CM)*; *International Classification of Diseases, Procedure Coding System*; and CPT procedure codes. The algorithm used to identify the diagnoses and procedures are presented in e-only Supplementary Table 1.

This study was reviewed by the New England Institutional Review Board and was determined to be exempt research as it did not involve human subjects.

Study Measures

Patient demographics were measured on the index date, which included age, gender, geographic region, and insurance type. Clinical characteristics evaluated in the baseline period include chronic obstructive pulmonary disease (COPD), pleural effusion, current or previous tobacco use, prior lung cancer screening, previous bronchoscopy, and Elixhauser comorbidity index [17-19]. Prior use of oral anticoagulants (including warfarin, dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban) or antiplatelet medications (including abciximab, anagrelide, aspirin, cilostazol, clopidogrel, dipyridamole, eptifibatide, prasugrel, ticagrelor, ticlopidine, and tirofiban) in the baseline period were also evaluated.

We evaluated the following outcomes: pneumothorax, hemorrhage, and air embolism. To measure the severity of pneumothorax, we assessed rates of pneumothorax requiring chest tube or mechanical ventilation and intubation. Similarly, among patients with hemorrhage, we evaluated the need for blood transfusion. Complications were measured using the presence of ICD-10-CM diagnosis codes or CPT procedure codes. In the primary analysis, we identified complications occurring within 3 days of TTNB as prior research has shown that most common complications of this procedure are identified within this period [20]. We performed four sensitivity analyses to assess the robustness of the measured complication rates. Two sensitivity analyses were performed by evaluating complications only on the index date and within 7 days of biopsy. To address the possibility that an identified complication may not be a consequence of TTNB, we performed a third sensitivity analysis in which we restricted the analysis to a subset of codes that are more specific for procedure-related pneumothorax or hemorrhage, respectively (e-only Supplementary Table 1). Furthermore, we performed an additional sensitivity analysis excluding patients who had a central venous catheterization, pulmonary venous catheterization, or pericardiocentesis or pacemaker insertion in the baseline period.

We classified the setting of care in which a TTNB was performed as either inpatient or outpatient (including outpatient hospital, office visit, emergency room, and skilled nursing facility). To measure inpatient health care utilization as a consequence of TTNB, hospitalization within 7 days was assessed for patients that underwent an outpatient biopsy.

Statistical Analyses

Study variables were analyzed descriptively (overall and stratified by setting of care) using counts and proportions for dichotomous variables and means and SDs for continuous variables. Complication rates of procedures performed in the inpatient versus the outpatient setting were compared using two-sample test of proportions. We conducted two main sets of analyses using multivariable logistic regression. First, we developed three separate models to evaluate patient factors associated with each of the three most common complications of TTNB (pneumothorax, pneumothorax requiring chest tube, and hemorrhage). Covariates included in these models were setting of care and patient baseline demographic and clinical characteristics including age, gender, COPD, pleural effusion, current or past tobacco use, prior use of oral anticoagulants or antiplatelet agents, prior lung cancer screening, previous bronchoscopy, and Elixhauser comorbidity index score. Odds ratios and 95% confidence intervals for each variable across the three models were calculated and graphed using Forest plots. Second, among patients who underwent TTNB as an outpatient, we modeled the risk of hospitalization within 7 days of biopsy for each type of complication. Patients who experienced no complications were used as the reference group in this analysis. Patients with missing values for variables included in the model were omitted from the analysis. A significance level of .05 was used for interpretation of results.

Adjustments for multiple hypotheses testing were not applied. An analytic data set was created using SQL workbench/J version 8.0.2. Statistical analyses were performed with Stata version 16.2 (StataCorp LLC, College Station, Texas).

RESULTS

Baseline Demographic and Clinical Characteristics

We assembled a retrospective cohort of 23,819 patients who underwent a TTNB during the study period, among whom 16,971 (71.3%) were eligible for the analysis (Fig. 1). Mean (SD) patient age was 72.5 (10.2) years, and 71.4% of patients were between the ages of 65 and 84 (Table 1). The proportion of females was 51.7%. Most patients resided in the South (40.3%), Midwest (24.4%), or West (23.1%) regions of the United States, and the majority of the cohort was insured with a Medicare Advantage plan (83.2%). The median Elixhauser comorbidity index was 13 and was higher among patients undergoing TTNB in the inpatient setting compared with outpatient setting (19 versus 11). One in 10 patients was prescribed oral anticoagulants and 1 in 10 patients was prescribed antiplatelet medications.

Complications

Approximately one-quarter (25.8%) of the cohort experienced at least one complication (ie, pneumothorax, hemorrhage, or air embolism) (Table 2). Most complications were identified on the day of the procedure (e-only Supplementary Table 2). Among the 16,971 patients who underwent TTNB, 12,443 (73.3%) were outpatients. Complications were more frequent when performed in the inpatient setting compared with the outpatient setting (34.7% versus 22.6%, $P < .001$).

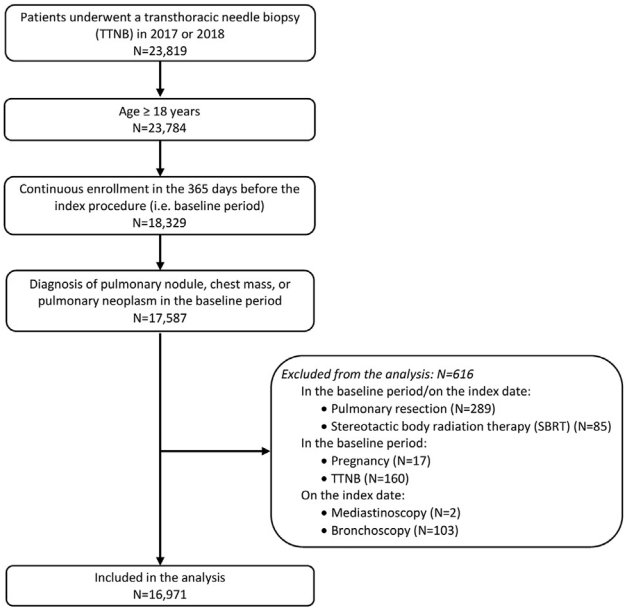


Figure 1. Cohort Assembly.

Pneumothorax occurred in 23.3% of patients overall and was more frequent among those undergoing TTNB in the inpatient compared with outpatient setting (30.5% versus 20.6%, $P < .001$). Chest tube drainage was performed in 31.9% of patients with pneumothorax, which represented 7.4% of all biopsy procedures. Chest tube drainage was performed more frequently in the inpatient compared with the outpatient setting (overall: 16.8% versus 4.0%, $P < .001$; among patients with pneumothorax: 55.1% versus 19.5%, $P < .001$). Pneumothorax requiring intubation and mechanical ventilation was rare (overall rate 0.1%). Hemorrhage was identified in 3.6% of biopsies; however, few required blood transfusion (0.1%). Air embolism was an extremely rare event (overall rate < 0.1%).

In the sensitivity analysis that used a restricted set of diagnosis codes (e-only Supplementary Table 2), the rates, compared with the primary analysis, were lower for pneumothorax (13.6% versus 23.3%), pneumothorax requiring a chest tube (6.5% versus 7.4%), and hemorrhage (0.8% versus 3.6%). In the sensitivity analysis excluding patients with a prior central venous catheterization, pulmonary venous catheterization, or pericardiocentesis or pacemaker insertion, the results are similar to the overall population (e-only Supplementary Table 3).

Factors Associated With Complications

There were a sufficient number of events for pneumothorax, pneumothorax requiring chest tube, and hemorrhage to allow for an exploratory analysis to identify factors associated with these complications (Fig. 2, e-only Supplementary Table 4). Younger age (age 18-44 versus 65-74), pleural effusion, and higher Elixhauser comorbidity index (≥20 versus 0) were associated with decreased likelihood of pneumothorax, and TTNB as an inpatient, history of COPD, prior lung cancer screening, and prior bronchoscopy were associated with increased risk of pneumothorax. The results were similar for the analysis that assessed factors associated with pneumothorax requiring chest tube. Finally, the factors associated with increased likelihood of hemorrhage included inpatient setting, history of COPD, prior bronchoscopy, and use of oral anticoagulants or antiplatelet agents.

Hospitalization After Outpatient TTNB

The rate of postprocedural hospitalization within 7 days among outpatients is presented in Table 3. Among patients

Table 1. Patient baseline demographic and clinical characteristics

Variable	Overall		Setting of Care			
			Inpatient		Outpatient	
	n	%	n	%	n	%
All	16,971	100.0	4,528	100.0	12,443	100.0
Age						
Mean (SD)	72.5 (10.2)	—	73.1 (10.5)	—	72.2 (10.1)	—
18-44	295	1.7	82	1.8	213	1.7
45-54	605	3.6	145	3.2	460	3.7
55-64	2,164	12.8	546	12.1	1,618	13.0
65-74	6,065	35.7	1,546	34.1	4,519	36.3
75-84	6,066	35.7	1,604	35.4	4,462	35.9
85+	1,776	10.5	605	13.4	1,171	9.4
Gender						
Female	8,769	51.7	2,246	49.6	6,523	52.4
Male	8,197	48.3	2,279	50.3	5,918	47.6
Unknown	5	0.0	3	0.1	2	0.0
Geographic region*						
South	6,832	40.3	1,948	43.0	4,884	39.3
Midwest	4,135	24.4	1,001	22.1	3,134	25.2
West	3,923	23.1	962	21.3	2,961	23.8
Northeast	2,055	12.1	611	13.5	1,444	11.6
Puerto Rico	1	0.0	0	0.0	1	0.0
Unknown	25	0.2	6	0.1	19	0.2
Insurance type						
Commercial	2,853	16.8	652	14.4	2,201	17.7
Medicare Advantage	14,118	83.2	3,876	85.6	10,242	82.3
CPT code for biopsy						
CPT 32405	16,632	98.0	4,436	98.0	12,196	98.0
CPT 32400	180	1.1	80	1.8	100	0.8
CPT 32405 and 32400	159	0.9	12	0.3	147	1.2
Image guidance for needle placement						
CT	16,417	96.7	4,299	94.9	12,118	97.4
Ultrasound or fluoroscopy	279	1.6	102	2.3	177	1.4
No image guidance	275	1.6	127	2.8	148	1.2
Pulmonary nodule	16,311	96.1	4,321	95.4	11,990	96.4
Chest mass	1,848	10.9	652	14.4	1,196	9.6
Pulmonary neoplasm	6,891	40.6	2,602	57.5	4,289	34.5
COPD	8,952	52.8	2,599	57.4	6,353	51.1
Pleural effusion	3,550	20.9	1,438	31.8	2,112	17.0
Tobacco use	10,380	61.2	3,156	69.7	7,224	58.1
Prior lung cancer screening	642	3.8	82	1.8	560	4.5
Prior bronchoscopy	1,791	10.6	540	11.9	1,251	10.1
Prior central venous catheterization	773	4.6	247	5.5	526	4.2
Prior pulmonary venous catheterization	50	0.3	19	0.4	31	0.3
Prior pericardiocentesis or pacemaker	26	0.2	14	0.3	12	0.1
Weighted Elixhauser comorbidity index†						
Median	13	—	19	—	11	—
<0	611	3.6	83	1.8	528	4.2
0	867	5.1	114	2.5	753	6.1
1-5	2,715	16.0	386	8.5	2,329	18.7
6-10	2,835	16.7	550	12.2	2,285	18.4
10-19	4,616	27.2	1,165	25.7	3,451	27.7
≥20	5,327	31.4	2,230	49.3	3,097	24.9

(continued)

Table 1. Continued

Variable	Overall		Setting of Care			
			Inpatient		Outpatient	
	n	%	n	%	n	%
Medication use[‡]						
Prior use of oral anticoagulants	1,692	10.0	498	11.0	1,194	9.6
Prior use of antiplatelets	1,719	10.1	444	9.8	1,275	10.3

COPD = chronic obstructive pulmonary disease; CPT = Current Procedure Terminology.
[†]Weighted using van Walraven method.
[‡]Oral anticoagulants include warfarin, dabigatran, rivaroxaban, apixaban, edoxaban, and betrixaban. Antiplatelets include abciximab, anagrelide, aspirin, cilostazol, clopidogrel, dipyridamole, eptifibatide, prasugrel, ticagrelor, ticlopidine, and tirofiban.
*South includes Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. Midwest includes Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. West includes Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. Northeast includes Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont.

who underwent TTNB in the outpatient setting, 6.9% were hospitalized within 7 days. Outpatients with complications were much more likely to be hospitalized (adjusted odds ratio range from 6.1 to 52.5), particularly for patients who experienced pneumothorax requiring chest tube (odds ratio = 52.5, 95% confidence interval 41.8-65.8).

DISCUSSION

Our results from this contemporary population-based cohort confirm that complications from TTNB remain a common cause of morbidity and are considerably more frequent in the inpatient setting. Complications after TTNB occurred in approximately 25% of all patients undergoing this procedure. Pneumothorax was the most frequent (23.3%) complication, followed by hemorrhage (3.6%), and air embolism was extremely rare. Complications were more frequent in patients evaluated in the inpatient setting (34.7%) compared with the outpatient setting (22.6%). An outpatient TTNB resulted in the need for hospitalization in approximately 7% of patients.

Our findings also suggest that complication rates have potentially increased over time based on a comparison to a prior population-based study by Wiener et al [16] that used 2006 state-level ambulatory surgery and inpatient data for California, Florida, Michigan, and New York and reported a lower rate of pneumothorax (15.0%) or pneumothorax requiring chest tube placement (6.6%) compared with our estimates (23.3% and 7.4%, respectively). However, our estimates from the sensitivity analysis restricted to procedure-related diagnosis codes (that are potentially more specific for these complications) resulted in very similar findings for pneumothorax (13.6% in both analyses), and chest tube insertion rates (6%-7% in both analyses). The higher rates of pneumothorax based on the use of broader diagnosis codes may reflect true differences or represent an artifact due to differences in patient population and change in coding system (*International Classification of Diseases,* ninth rev, *Clinical*

Table 2. Complications after transthoracic needle biopsy

Complication	Overall		Setting of Care				*P* Value
			Inpatient		Outpatient		
	n	%	n	%	n	%	
All	16,971	100.0	4,528	100.0	12,443	100.0	
Any complications	4,383	25.8	1,570	34.7	2,813	22.6	<.001
Pneumothorax	3,950	23.3	1,382	30.5	2,568	20.6	<.001
Pneumothorax requiring chest tube	1,262	7.4	761	16.8	501	4.0	<.001
Pneumothorax requiring mechanical ventilation and intubation	16	0.1	11	0.2	5	<0.1	<.001
Hemorrhage	603	3.6	268	5.9	335	2.7	<.001
Hemorrhage requiring transfusion	9	0.1	6	0.1	3	<0.1	.007
Air embolism	4	<0.1	2	<0.1	2	<0.1	.292

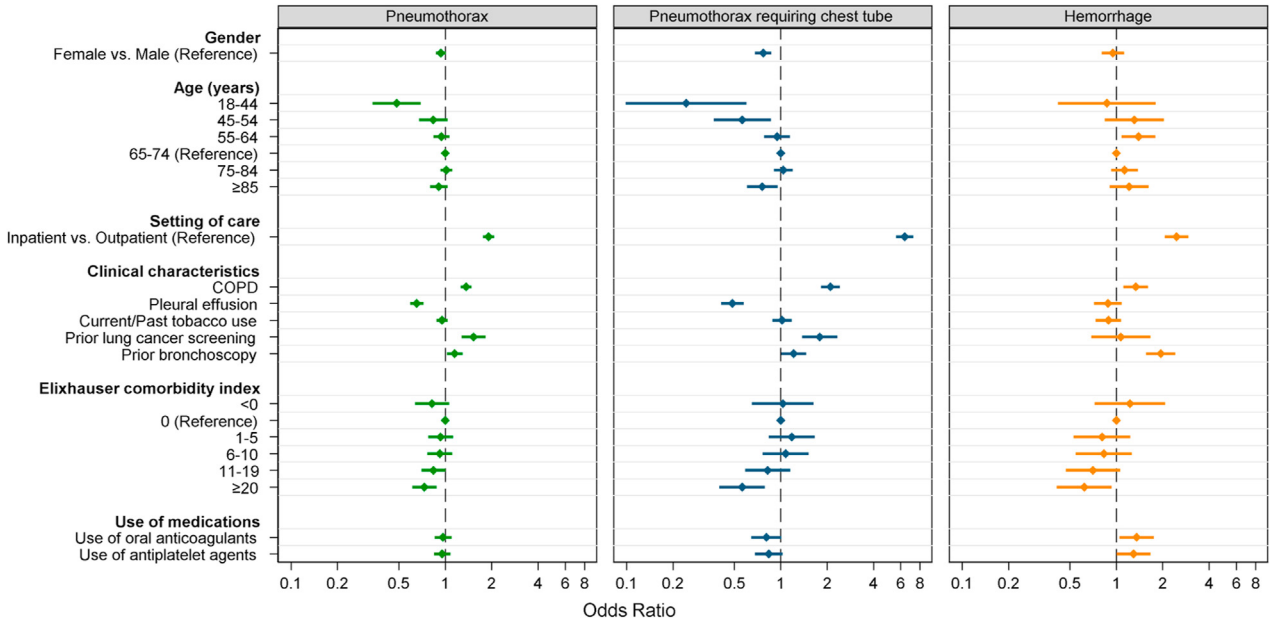


Figure 2. Factors associated with complications.

Modification versus ICD-10-CM) over time. Nevertheless, our study demonstrates that pneumothorax after TTNB remains common and often results in chest tube placement and subsequent hospitalization.

In comparison to the analysis by Weiner et al, we also found a slightly higher rate of hemorrhage after TTNB (3.6% versus 1.0%) but a much lower rate of hemorrhage requiring blood transfusion (1.5% versus 17.8%). Estimates of hemorrhage from TTNB reported in the literature vary widely (1%-66%), which may be due to variations in the definition of hemorrhage (eg, diagnosis code-based algorithms using claims data, clinical definitions using patient-reported symptoms, and radiographical evidence) [1,21]. Although Wiener et al reported a high rate of transfusion after TTNB, the rate reported in most other studies has been quite low, usually under 1%. For example, in one single-center case series study, 94 (29.3%) of 321 TTNB procedures were complicated by pulmonary hemorrhage and only 2 (0.6%) required intervention [22]. In a separate study, pulmonary hemorrhage was reported in 483 (41.1%) of 1,175 biopsies, and only 5 (0.4%) patients necessitated admission; 1 (0.1%) patient required transfusion and a second patient required surgical evacuation for persistent bleeding [21].

Table 3. Postprocedural hospitalization within 7 days

Variable	Patients With Outpatient TTNB, n	Patients Hospitalized Within 7 Days, n (%)	Odds Ratio	
			Unadjusted	Adjusted*
Overall	12,443	863 (6.9)	—	—
No complication	9,630	345 (3.6)	Reference	Reference
Any complications	2,813	518 (18.4)	6.1 (5.3-7.0)*	6.1 (5.3-7.1)†
Pneumothorax	2,568	491 (19.1)	6.4 (5.5-7.4)*	6.4 (5.5-7.5)†
Pneumothorax requiring chest tube	501	316 (63.1)	46.0 (37.2-56.8)*	52.5 (41.8-65.8)†
Hemorrhage	335	64 (19.1)	6.4 (4.7-8.5)*	6.8 (5.0-9.2)†

TTNB = transthoracic needle biopsy.

*Adjusted for age, gender, chronic obstructive pulmonary disease, pleural effusion, current or past tobacco use, prior use of oral anticoagulant, prior use of antiplatelets and prior low-dose CT scan for lung cancer screening or consultation, prior bronchoscopy, and weighted Elixhauser comorbidity index as a categorical variable. The odds ratios for all variables included in the model are presented in e-only Supplementary Table 5.

†$P < .05$.

In our analysis of factors that predispose patients to complications after TTNB, we identified several potentially interesting findings, while confirming some previously established associations. A higher risk of pneumothorax was observed in patients with a diagnosis of COPD, recent lung cancer screening, and prior bronchoscopy. Patients with COPD have been previously shown to have an increased risk of pneumothorax, which is likely related to the presence of emphysema. Recent lung cancer screening may also reflect increased risk from COPD given that screening is generally restricted to individuals with >30 pack-year tobacco history, a population that is more likely to have radiographic emphysema. Given the concerns regarding the harms of biopsy in patients with screening detected nodules [23,24], future analyses should further characterize optimal biopsy approaches among patients with lung cancer screening–detected pulmonary abnormalities. Finally, the findings of an increased risk of pneumothorax in patients who have undergone a prior bronchoscopy may reflect patients with less peripherally located lesions in whom bronchoscopy was chosen first but was nondiagnostic. The use of TTNB in these patients may therefore require deeper needle placement or reflect the use of biopsy approaches (eg, multiple pleural punctures, crossing of a fissure) that are associated with a higher risk of complications.

We observed that a high Elixhauser comorbidity index score was associated with decreased odds of pneumothorax, which seems counterintuitive to the relationship that would be anticipated. One potential explanation is that providers are more selective in patients with higher comorbidity burden, only offering it to patients with relatively less pulmonary disease and more peripherally located lesions, and the proceduralist may avoid the use of core needle biopsy and perform fewer passes, resulting in lower pneumothorax risk. Further studies are needed to explore whether these patient selection mechanisms and provider-level decisions on procedural approach are the true underlying mechanisms or whether there are alternative explanations for this association.

Most of the factors associated with complications identified in our analysis are not modifiable by patients or providers; however, the presence of these risk factors may allow for the identification of patient subgroups that warrant greater monitoring for complications. Alternatively, some patients at highest risk of TTNB-associated complications may be potentially better served with alternative approaches to tissue sampling.

This study is unique in that it was a contemporary analysis with a sufficiently large and representative study population that employed the use of multiple analytic approaches and sensitivity analyses to facilitate an exploration of TTNB-associated complications. We assessed all patients who underwent TTNB including those with a diagnosis pulmonary nodule, mass or pre-existing malignancy, whereas most previous studies provided findings from single-institution experience focused on patients with confirmed lung cancer. The longitudinal nature of our study also allowed the identification of patient-level clinical characteristics in the year before TTNB and the associated risk of hospitalization after a complication for biopsies performed in the outpatient setting. Although biopsy-related pneumothorax frequently occurs during or immediately after procedure, pneumothorax can be identified on follow-up chest radiographs or even after discharge due to the development of symptoms (delayed pneumothorax) [20], and coding for complications may be delayed in such setting. We therefore identified complications over a 3-day period after the index TTNB but performed sensitivity analyses to assess alternative time horizons.

However, our study has limitations. First, as with all administrative data, we used diagnostic or procedure codes to measure medical events, which can potentially result in misclassification of exposure, outcomes, and covariates of interest. To minimize the risk of misclassification, we selected algorithms based on literature review that were supported by validation studies, when possible. Moreover, we also used procedure-based algorithms that are more reliable as they are directly linked to reimbursement as opposed to diagnosis codes that may lead to over- or underestimation. Second, minor complications may not be fully documented in claims data, which may lead to an underestimation of complication rates. On the other hand, diagnoses that may or may not be procedure-related tend to be documented for reimbursement purposes, which may lead to an overestimation of complications. Finally, there may be residual unmeasured confounding given that we lacked information on factors that may influence the rate of complications such as clinical details of the pulmonary lesion and provider and hospital characteristics.

Biopsy is an important approach for the diagnosis of pulmonary lesions and management of lung cancer or other malignancies involving the chest. The choice of biopsy approach needs to carefully weigh the diagnostic accuracy and the safety profile of the procedure itself. To minimize the complication risk and optimize the diagnostic yield, future studies are needed to determine the best practice to customize the biopsy approach based on patient factorsand risk for lung cancer. Moreover, studies examining other aspects of biopsy performance such as diagnostic accuracy, access to the target nodule, efficiency of the procedure, costs of the biopsy, and economic burden of complications associated with the biopsy are needed to improve clinical decision making.

TAKE-HOME POINTS

- Approximately one-quarter of patients undergoing TTNB experienced a complication (ie, pneumothorax, hemorrhage, or air embolism).
- Pneumothorax was the most frequent complication, occurring in 23.3% of patients, and hemorrhage and air embolism were rare.
- Chest tube drainage was performed in 31.9% of patients who developed a pneumothorax.
- Complications were more frequent when performed in the inpatient setting compared with the outpatient setting (34.7% versus 22.6%).
- Among patients that underwent TTNB in the outpatient setting, 6.9% were hospitalized within 7 days.

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ADDITIONAL RESOURCES

Additional resources can be found online at: https://doi.org/10.1016/j.jacr.2022.04.010.

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