Annals of Internal Medicine | ORIGINAL RESEARCH

Population-Based Risk for Complications After Transthoracic Needle Lung Biopsy of a Pulmonary Nodule: An Analysis of Discharge Records

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Background: Because pulmonary nodules are found in up to 25% of patients undergoing computed tomography of the chest, the question of whether to perform biopsy is becoming increasingly common. Data on complications after transthoracic needle lung biopsy are limited to case series from selected institutions.

Objective: To determine population-based estimates of risks for complications after transthoracic needle biopsy of a pulmonary nodule.

Design: Cross-sectional analysis.

Setting: The 2006 State Ambulatory Surgery Databases and State Inpatient Databases for California, Florida, Michigan, and New York from the Healthcare Cost and Utilization Project.

Patients: 15 865 adults who had transthoracic needle biopsy of a pulmonary nodule.

Measurements: Percentage of biopsies complicated by hemorrhage, any pneumothorax, or pneumothorax requiring a chest tube, and adjusted odds ratios for these complications associated with various biopsy characteristics, calculated by using multivariate, population-averaged generalized estimating equations.

Results: Although hemorrhage was rare, complicating 1.0% (95% CI, 0.9% to 1.2%) of biopsies, 17.8% (CI, 11.8% to 23.8%) of patients with hemorrhage required a blood transfusion. In contrast, the risk for any pneumothorax was 15.0% (CI, 14.0% to 16.0%), and 6.6% (CI, 6.0% to 7.2%) of all biopsies resulted in pneumothorax requiring a chest tube. Compared with patients without complications, those who experienced hemorrhage or pneumothorax requiring a chest tube had longer lengths of stay ($P < 0.001$) and were more likely to develop respiratory failure requiring mechanical ventilation ($P = 0.020$). Patients aged 60 to 69 years (as opposed to younger or older patients), smokers, and those with chronic obstructive pulmonary disease had higher risk for complications.

Limitations: Estimated risks may be inaccurate if coding of complications is incomplete. The analyzed databases contain little clinical detail (such as information on nodule characteristics or biopsy pathology) and cannot indicate whether performing the biopsy produced useful information.

Conclusion: Whereas hemorrhage is an infrequent complication of transthoracic needle lung biopsy, pneumothorax is common and often necessitates chest tube placement. These population-based data should help patients and physicians make more informed choices about whether to perform biopsy of a pulmonary nodule.

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With the increased use of computed tomography (CT) of the chest for indications that range from ruling out pulmonary embolism to lung cancer screening, pulmonary nodules are diagnosed in several hundred thousand persons in the United States each year (1). Such patients and their physicians then face the decision of whether to perform biopsy of the nodule. Although most nodules are benign incidental findings, some are lung cancer. Unfortunately, the invasive procedures needed for a conclusive determination can cause harm.

Transthoracic needle lung biopsy (CT-guided biopsy) is recommended for suspicious peripheral nodules (2). In 2004, more than 58 000 such biopsies were performed in Medicare fee-for-service patients (3). Biopsy guided by CT may cause hemorrhage or pneumothorax, which may then require hospitalization. Physicians and patients must therefore carefully weigh whether the risk for cancer justifies the risk for potential harms from biopsy.

Because the literature contains only case series from selected centers (4–13), the estimated risks of CT-guided biopsy are highly variable. For example, published studies from the past 10 years report risks for pneumothorax that range from 4% (11) to 42% (13). To provide patients and physicians with representative data to inform decision making, we determined population-based estimates of the risk for complications after CT-guided biopsy of a pulmonary nodule.

METHODS

Study Design

We performed a cross-sectional analysis of discharge records in 4 large, geographically diverse states in 2006. Our primary outcome was risk for complications of CT-guided biopsy of a pulmonary nodule, defined as the percentage of biopsies complicated by hemorrhage, pneumothorax, or pneumothorax requiring a chest tube (the **Appendix Table**, available at www.annals.org. shows all

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Appendix Table
Conversion of graphics into slides

Context

Although transthoracic needle biopsy is frequently considered for evaluation of a solitary pulmonary nodule, the risks of this procedure are not well-defined.

Contribution

In this assessment of national administrative databases, pneumothorax and hemorrhage were not rare complications after transthoracic needle biopsy. Patients often required treatment for these complications that included blood transfusion, chest tube placement, or mechanical ventilation. Patients aged 60 to 69 years and those who smoked or had chronic obstructive pulmonary disease were at increased risk.

Implication

These data may be helpful during consideration of how best to approach a solitary pulmonary nodule.

—The Editors

diagnosis and procedure codes used). At our institutions, studies that use deidentified, publicly available data are exempt from institutional board review.

Data Sources

We used the 2006 Healthcare Cost and Utilization Project State Inpatient Databases (14) and State Ambulatory Surgery Databases (15) from the largest participating state in each census region (California, Florida, Michigan, and New York). These states had a combined estimated adult population of 63 340 236, which represents 28.2% of the 2006 U.S. population (16).

The State Inpatient Databases include all discharge records from community hospitals (defined by the American Hospital Association as "all nonfederal, short-term, general, and other specialty hospitals, excluding hospital units of institutions") in each state (14). The State Ambulatory Surgery Databases contain all discharge records from ambulatory surgical procedures performed in nonfederal community hospitals and freestanding ambulatory surgery centers. These databases are fairly comprehensive; for example, the proportion of community hospitals represented in the 2006 State Inpatient Database (14) ranges from 92% (Michigan) to 99.5% (New York). Each record contains information on patient demographic characteristics; hospital characteristics; up to 31 diagnosis codes and up to 31 procedure codes in the International Classification of Diseases, Ninth Revision; and up to 21 Current Procedural Terminology codes.

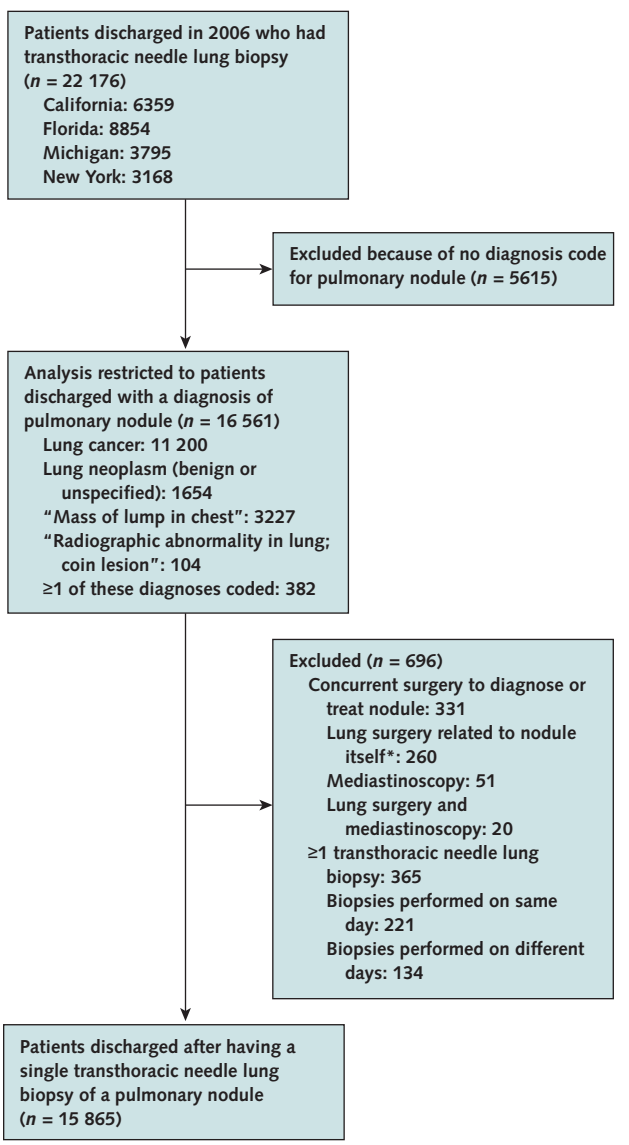
Study Population

We identified all adults who underwent CT-guided lung biopsy and then restricted our analysis to patients with a pulmonary nodule, as indicated by codes for coin lesion, chest mass, or lung neoplasm. Although some coding experts recommend using diagnosis code 518.89 ("Other diseases of lung not elsewhere classified") for pulmonary nodules (17), this code was not included in our definition because it is nonspecific. Because our data showed that patients who had concomitant chest surgery or multiple CT-guided lung biopsies were almost twice as likely to have complications, such patients were also excluded.

Statistical Analysis

The overall rate of CT-guided lung biopsies per 100 000 adults was calculated for each selected state and age-standardized by using the 2006 estimated U.S. adult population (16). We then measured our primary outcome: percentage of biopsies complicated by hemorrhage, pneu-

Figure 1. **Study flow diagram.**



* Includes open or video-assisted thoracoscopic surgical biopsy, excision, wedge resection, segmentectomy, lobectomy, or pneumonectomy.

Table 1. **Baseline Characteristics of Computed Tomography–Guided Biopsies of a Pulmonary Nodule**

Characteristic	Overall (*n* = 15 865)	California (*n* = 4382)	Florida (*n* = 6408)	Michigan (*n* = 2820)	New York (*n* = 2255)	*P* Value
Patient, %						
Women	48.4	49.4	47.5	48.1	49.8	0.132
Age						<0.001
18–49 y	6.9	8.2	5.8	7.6	6.7	
50–59 y	13.4	14.9	12.1	15.5	11.9	
60–69 y	25.4	23.4	25.8	26.2	27.1	
70–79 y	34.1	32.6	35.4	33.0	34.8	
≥80 y	20.2	20.9	21.0	17.7	19.4	
Comorbid pulmonary condition						
Current or former tobacco use	36.4	40.4	36.3	35.5	30.0	<0.001
Chronic obstructive pulmonary disease	27.4	26.1	28.4	25.3	29.9	<0.001
Pleural effusion	4.8	5.6	4.0	4.1	6.3	<0.001
Visit, %						
Scheduled procedure	67.1	59.2	75.4	72.9	51.3	<0.001
Concurrent bronchoscopy	1.9	1.4	2.0	0.6	4.3	<0.001
Hospital						
Perform computed tomography–guided biopsy, *n*	713	286	174	90	163	
Listed in both inpatient and ambulatory surgery databases, *n*	440	153	146	67	74	
Listed only in inpatient databases, *n*	247	125	22	14	86	
Listed only in ambulatory surgery databases, *n*	26	8	6	9	3	
Biopsy volume per year						
Median (range), *n*	55 (1–245)	35 (1–151)	77 (1–245)	77 (1–169)	33 (1–114)	<0.001
Procedures per year, %						<0.001
1–50	46.9	67.8	30.4	27.4	77.5	
51–100	26.7	23.5	27.8	37.8	16.3	
101–245	26.4	8.7	41.8	34.8	6.2	

mothorax, or pneumothorax requiring a chest tube. Associations were investigated between each complication and clinically important adverse outcomes, including need for blood transfusion (for hemorrhage), increased mean length of stay, respiratory failure (defined by the presence of codes for mechanical ventilation and intubation within 1 day after the biopsy), or hospital death. The SVY mean and proportion functions in STATA, version 10.1 (StataCorp, College Station, Texas), were used with postestimation Wald tests to compare these outcomes, clustered by hospital and stratified by state, among patients with versus those without complications. *P* values less than 0.05 were considered statistically significant.

We used logistic regression to explore the association between each biopsy characteristic and complication. Characteristics of patients (age, sex, and comorbid pulmonary disease), visits (scheduled procedure and concurrent bronchoscopy), and hospitals (hospital state and volume of CT-guided biopsies performed per year) were examined. Comorbid pulmonary disease was defined by codes for current or former tobacco use, chronic obstructive pulmonary disease (COPD), or pleural effusion. Scheduled procedures were those in which the CT-guided biopsy was performed as an ambulatory procedure or within 1 day of hospital admission (as opposed to biopsy performed during a hospital stay). Concurrent bronchoscopy was defined as bronchoscopy performed on the same day as CT-guided biopsy.

Adjusted odds ratios and 95% CIs for complications were calculated on the basis of robust SE estimates that included all biopsy characteristics (patient, visit, and hospital characteristics) as covariables. Interactions between state and patient characteristics were investigated, but none were identified. Generalized estimating equations were used to account for clustering by hospital, assuming the binomial family, a logit link function, and an exchangeable correlation structure. Analyses were performed with STATA by using the xtgee function. To determine whether residual variation across hospitals was important, we ran a random-effects model with a random intercept for hospital.

We performed 2 sensitivity analyses to address the potential limitations of using administrative databases. To address the possibility that a discharge diagnosis of pneumothorax may not represent a complication of CT-guided biopsy, a sensitivity analysis for the outcome of any pneumothorax was performed by using the more specific code for iatrogenic pneumothorax and eliminating discharges that included other procedures that could have caused pneumothorax (such as central venous catheterization or bronchoscopy with transbronchial biopsy). To address the possibility that pneumothorax requiring a chest tube may not be a complication of CT-guided biopsy, the first sensitivity analysis was repeated for the outcome of pneumothorax requiring a chest tube, with patients who had pleural effusion also excluded to ensure that chest tube placement was for pneumothorax.

Role of the Funding Source

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RESULTS

Of the 22 176 CT-guided lung biopsies in the 4 U.S. states, 15 865 met our criteria of a single biopsy of a pulmonary nodule (**Figure 1**). **Table 1** shows characteristics of the study population, stratified by state. States differed significantly in patient, visit, and hospital characteristics.

Risk for Complications

Among all CT-guided biopsies of a pulmonary nodule, 1.0% (95% CI, 0.9% to 1.2%) were complicated by hemorrhage, 15.0% (CI, 14.0% to 16.0%) by any pneumothorax, and 6.6% (CI, 6.0% to 7.2%) by pneumothorax severe enough to require a chest tube. The sensitivity analyses showed little change in the estimated risks (any pneumothorax, 13.6% [CI, 12.6% to 14.6%]; pneumothorax requiring a chest tube, 6.1% [CI, 5.4% to 6.7%]).

Risk for complications varied across hospitals (1.0% [CI, 0% to 5.9%] for hemorrhage, 15.0% [CI, 0% to 50%] for any pneumothorax, and 6.6% [0% to 25%] for pneumothorax requiring a chest tube). After we accounted for the fixed effects in our models, significant residual variation across hospitals remained for each complication ($P = 0.020$ for hemorrhage, $P < 0.001$ for any pneumothorax, and $P < 0.001$ for pneumothorax requiring a chest tube). Although the estimated residual correlation within hospitals seemed small ($\rho = 0.003$, 0.03, and 0.03, respectively, for the 3 outcomes), these results are consistent with meaningful variation in outcomes across hospitals.

Several findings suggest that these complications were clinically important. Among patients with hemorrhage from biopsy, 18% (CI, 11.8% to 23.8%) required a blood transfusion, compared with 4.3% of patients with no documented complications ($P < 0.001$). Complications were also significantly associated with other adverse outcomes (**Table 2**). Patients with complications required hospitalization more often (if performed in the outpatient setting) or had longer lengths of stay (if performed in the inpatient setting) than did patients without complications. Among all patients who had CT-guided biopsy, respiratory failure requiring mechanical ventilation occurred more often in patients with hemorrhage (4.3%; $P = 0.017$) or pneumothorax requiring a chest tube (1.4%; $P = 0.019$) than in those without recorded complications (0.6%).

Characteristics Associated With Complications

Table 3 shows the characteristics associated with complications. Age (60 to 69 years vs. <60 or ≥70 years), female sex, and comorbid pulmonary disease (COPD or pleural effusion) were significantly associated with hemorrhage. Age 60 to 69 years, tobacco use, and COPD were significantly associated with higher rates of any pneumothorax and pneumothorax requiring a chest tube, whereas patients who had concurrent bronchoscopy had a lower risk for any pneumothorax ($P < 0.001$) and pneumothorax requiring a chest tube ($P < 0.002$). Patients who had a scheduled procedure (ambulatory or within 1 day of hospital admission) had significantly higher rates of all com-

Table 2. **Clinical Outcomes in Patients Who Had Computed Tomography–Guided Lung Biopsy, by Presence of Complication and Timing of Biopsy**

Variable	No Complication*	Complication		
		Hemorrhage	Any Pneumothorax	Pneumothorax Requiring a Chest Tube
All patients who had biopsy (n = 15 865)				
Percentage in group (95% CI), %	84.2 (83.2–85.2)	1.0 (0.9–1.2)	15.0 (14.0–16.0)	6.6 (6.0–7.2)
Mean length of stay (95% CI), *d*	4.8 (4.5–5.2)	7.6 (5.5–9.6)†	5.3 (4.9–5.8)‡	6.3 (5.6–7.0)§
Respiratory failure (95% CI), %	0.6 (0.4–0.7)	4.3 (1.3–7.3)‡	0.8 (0.5–1.2)	1.4 (0.7–2.1)‡
Died in the hospital (95% CI), %	1.8 (1.5–2.0)	4.3 (1.2–7.4)	1.6 (1.1–2.2)	2.0 (1.2–2.9)
Patients with a scheduled biopsy (n = 10 638)				
Percentage in group (95% CI), %	83.8 (82.5–85.1)	1.0 (0.8–1.2)	15.4 (14.2–16.7)	6.8 (6.0–7.6)
Mean length of stay (95% CI), *d*	1.0 (0.8–1.1)	1.7 (1.0–2.4)‡	1.9 (1.6–2.1)§	2.7 (2.3–3.0)§
Respiratory failure (95% CI), %	0.1 (0.1–0.2)	4.6 (0.1–8.7)‡	0.3 (0.0–0.6)	0.7 (0.1–1.3)
Died in the hospital (95% CI), %	0.4 (0.3–0.6)	0.9 (0.0–2.7)	0.5 (0.2–0.8)	1.0 (0.2–1.7)
Patients who had biopsy during a hospital stay (n = 5227)				
Percentage in group (95% CI), %	85.0 (84.0–86.1)	1.1 (0.8–1.3)	14.1 (13.1–15.2)	6.1 (5.4–6.8)
Mean length of stay (95% CI), *d*	10.8 (10.4–11.3)	17.1 (13.4–20.7)§	11.6 (10.9–12.4)	13.1 (12.0–14.2)§
Respiratory failure (95% CI), %	1.5 (1.1–1.8)	3.6 (0.0–8.7)	2.0 (1.0–3.0)	3.1 (1.2–5.0)
Died in the hospital (95% CI), %	4.3 (3.7–5.0)	10.9 (2.6–19.3)	4.2 (2.7–5.7)	4.4 (2.2–6.6)

* Reference group for P values.
† $P < 0.010$.
‡ $P < 0.050$.
§ $P < 0.001$.

Table 3. **Odds Ratios for Complications Associated With Various Characteristics Included in Multivariate Generalized Estimating Equation Models**

Characteristic	Odds Ratio for Complication (95% CI)*		
	Hemorrhage (n = 163)	Any Pneumothorax (n = 2381)	Pneumothorax Requiring Chest Tube (n = 1047)
Patient			
Women	1.42 (1.03–1.96)†	0.99 (0.91–1.08)	0.93 (0.81–1.05)
Age			
18–49 y	0.42 (0.17–1.04)	0.72 (0.58–0.89)‡	0.63 (0.45–0.88)‡
50–59 y	0.43 (0.22–0.83)†	0.83 (0.72–0.97)†	0.83 (0.68–1.00)
60–69 y	Reference	Reference	Reference
70–79 y	0.92 (0.63–1.37)	0.89 (0.80–0.99)†	0.78 (0.67–0.91)‡
≥80 y	0.51 (0.30–0.84)‡	0.93 (0.82–1.05)	0.78 (0.66–0.92)‡
Comorbid pulmonary condition			
Current or former tobacco use	1.13 (0.78–1.63)	1.37 (1.23–1.54)§	1.50 (1.26–1.77)§
Chronic obstructive pulmonary disease	1.61 (1.08–2.39)†	1.88 (1.69–2.09)§	2.52 (2.16–2.95)§
Pleural effusion	6.32 (4.18–9.55)§	1.04 (0.83–1.29)	1.09 (0.81–1.47)
Visit			
Scheduled procedure	1.64 (1.10–2.45)†	1.60 (1.40–1.82)§	1.86 (1.53–2.25)§
Concurrent bronchoscopy	1.20 (0.43–3.36)	0.27 (0.15–0.49)§	0.28 (0.13–0.64)‡
Hospital			
Biopsy volume per year			
1–50	Reference	Reference	Reference
51–100	0.75 (0.49–1.14)	0.92 (0.78–1.09)	1.10 (0.86–1.41)
101–245	0.82 (0.47–1.43)	1.02 (0.81–1.27)	1.14 (0.84–1.55)

* Multivariate generalized estimating equation models also included hospital state; **Table 4** lists odds ratios for complications associated with each state relative to the reference state of Florida.
† $P < 0.050$.
‡ $P < 0.010$.
§ $P < 0.001$.

plications than patients whose biopsy was performed during a hospital stay. **Figure 2** shows adjusted rates of complications stratified by age, which illustrate that patients aged 60 to 69 years experienced significantly more complications than younger or older patients.

Variation Among States

Overall, 25.0 CT-guided biopsies of a pulmonary nodule (CI, 24.7 to 25.4 biopsies) were performed per 100 000 adults. **Table 4** highlights the substantial variation among states in rates of biopsy use and complications. Age-standardized biopsy rates in New York (14.7 per 100 000 adults) and California (17.5 per 100 000 adults) were less than one half of those in Michigan (35.9 per 100 000 adults) and Florida (36.2 per 100 000 adults). **Table 4** also shows that states with low biopsy use had lower relative rates of complications at the population level but higher relative rates of complications at the biopsy level (for example, higher odds for pneumothorax requiring a chest tube among patients who had a biopsy in New York than among those in Florida).

DISCUSSION

We examined population-based risk for complications after CT-guided biopsy of a pulmonary nodule. Whereas hemorrhage was infrequent (1%), pneumothorax was common (15%). Complications were associated with adverse outcomes, including longer length of stay and higher rates of respiratory failure. Our analysis confirms previous reports (4, 8, 9, 13) that older age and COPD increase complications. Of note, we also show that more than 6% of CT-guided biopsies result in pneumothorax requiring a chest tube, a clinically important complication that entails pain, serial imaging and radiation exposure, and hospitalization for an average of 2 to 5 days (18).

A recent study (12) showed that physicians do not accurately predict risk for pneumothorax after CT-guided biopsy; this may due in part to a lack of representative data. Case series over the past decade (4–13) report hemorrhage in 2% to 10% and pneumothorax in 4% to 42% of patients. Some estimates are clearly lower than the risk faced by a typical patient, which reflects the expertise of specialized centers. Other estimates seem high, perhaps because they include all complications visualized under CT guidance, regardless of clinical relevance.

Comprehensive databases offer important advantages over case series. Our analysis of more than 15 000 CT-guided lung biopsies in 4 states offers a more representative picture of complication risk than do smaller case series of a few hundred patients. Our estimated risks for complications are more likely to be clinically important than complications defined by imaging findings at the time of biopsy (as is often done in case series), which may be irrelevant to

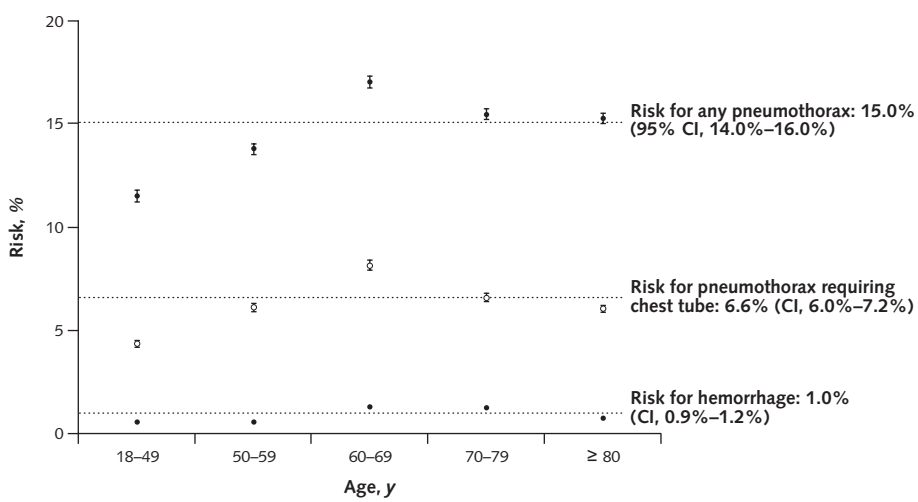
the patient if no symptoms result. For example, we found that hemorrhage recorded on discharge records was associated with several clinically important adverse events, including longer length of stay, need for blood transfusion, and respiratory failure requiring mechanical ventilation. Similarly, our estimated risk for pneumothorax requiring a chest tube should be reliable and precise because it is based on billing for a clinically important invasive procedure with a coding specificity of 99% and a positive predictive value of 86% (19). Our estimated risk for pneumothorax requiring a chest tube (6.6% [CI, 6.0% to 7.2%]) is consistent with (but far more precise than) estimates from case series, which range from 0.2% to 9.0% (4–13).

Analyzing administrative databases has disadvantages. Although such databases can be used to estimate the short-term risks of such procedures as CT-guided biopsy, these data are deidentified and cannot be linked to other sources to provide information on the diagnostic yield of biopsy or the long-term risks and benefits of the procedure. Some complications, particularly minor ones, are probably systematically undercoded. However, an increasing emphasis has been placed on accurately coding complications (20), and procedure-related adverse outcomes of hemorrhage and pneumothorax have been shown to have positive predictive values greater than 70% (20–22). Without access to clinical progress notes, we cannot be certain of the sequence of events: for example, whether a discharge diagnosis of pneumothorax is truly a complication of CT-guided biopsy. However, because our more specific sensitivity analyses produced little change in estimated risks, our reported risks for any pneumothorax or pneumothorax requiring a chest tube are indeed likely to reflect complications of CT-guided biopsy.

Another disadvantage of deidentified administrative databases is the lack of clinically detailed variables to predict complications, such as previously identified patient risk factors of nodule size and location; physician characteristics, such as specialty or years of experience (7, 9); or concentration of physicians or CT scanners in a hospital or region. Coding for the comorbid conditions we tested, such as COPD and tobacco use, may have varied on discharge records, and such coding may have been more thorough on records that also showed a complication. Without clinical detail, some observed associations seem counterintuitive at first glance. For example, pleural effusion was associated with a 5-fold higher likelihood of hemorrhage; however, we could not distinguish whether the effusion increased the risk for complication or was itself the complication (hemothorax from biopsy). Although some variables associated with lower complication rates (such as concurrent bronchoscopy or biopsies performed during a hospital stay as opposed to a scheduled procedure) initially seem counterintuitive, we believe that the explanation lies in patient selection. Physicians choose to perform bronchoscopy and CT-guided biopsy on the same day only for patients who can best tolerate both procedures (those with lower risk for complications); similarly, physicians tend to defer elective procedures, such as CT-guided biopsy, for patients at high risk for complications (such as those with severe COPD) during acute hospital admissions. We suspect the lower risk for complications in younger patients (age <60 y) reflects a relatively healthier population, whereas the lower risk in older patients (age >70 y) suggests that physicians may reserve biopsy for older adults who are healthy enough to tolerate treatment if the nodule is malignant.

Table 4 shows that states with low biopsy use had a higher complication rate per biopsy than those with high biopsy use; for example, the odds ratio for pneumothorax requiring a chest tube was 1.85 (CI, 1.35 to 2.54) for

Figure 2. **Adjusted risk for complications after transthoracic needle biopsy of a pulmonary nodule.**



Adjusted for all variables in **Table 3** by using generalized estimating equation models.

Table 4. **Rates of Complications at the Population and Biopsy Levels, by State**

Variable	High Biopsy Use		Low Biopsy Use	
	Florida (n = 6408)	Michigan (n = 2820)	California (n = 4382)	New York (n = 2255)
Age-adjusted population biopsy rate per 100 000 adults (95% CI), %	36.2 (35.3–37.1)	35.9 (34.6–37.2)	17.5 (16.9–18.0)	14.7 (14.1–15.3)
Population-level analyses				
Age-adjusted complication rate per 100 000 adults (95% CI), %				
Hemorrhage	0.33 (0.2–0.4)	0.32 (0.2–0.5)	0.23 (0.2–0.3)	0.15 (0.1–0.2)
Any pneumothorax	5.2 (4.4–5.9)	5.4 (4.6–6.3)	2.7 (2.4–3.0)	2.4 (1.9–2.9)
Pneumothorax requiring a chest tube	2.2 (1.8–2.6)	2.0 (1.5–2.4)	1.2 (1.0–1.4)	1.3 (0.9–1.7)
Age-adjusted relative rate of complications in the population (95% CI), %				
Hemorrhage	Reference	0.98 (0.57–1.63)	0.71 (0.48–1.07)	0.45 (0.26–0.77)*
Any pneumothorax	Reference	1.06 (0.94–1.20)	0.53 (0.47–0.59)†	0.47 (0.41–0.53)†
Pneumothorax requiring a chest tube	Reference	0.90 (0.74–1.10)	0.54 (0.46–0.64)†	0.61 (0.50–0.73)†
Biopsy-level analyses				
Age-adjusted complications per 1000 biopsies (95% CI), %				
Hemorrhage	7 (5–9)	9 (5–13)	14 (10–18)	10 (5–14)
Any pneumothorax	112 (96–129)	148 (126–172)	166 (145–187)	157 (124–192)
Pneumothorax requiring a chest tube	48 (40–57)	54 (42–66)	73 (60–87)	86 (61–113)
Adjusted odds ratio of complications in patients who had biopsy (95% CI), %‡				
Hemorrhage	Reference	1.08 (0.64–1.80)	1.45 (0.91–2.29)	1.05 (0.63–1.77)
Any pneumothorax	Reference	1.06 (0.89–1.27)	1.17 (0.99–1.38)	1.30 (1.04–1.63)§
Pneumothorax requiring a chest tube	Reference	0.85 (0.67–1.08)	1.32 (1.04–1.68)§	1.85 (1.35–2.54)†

* $P < 0.010$ compared with reference state (Florida).
† $P < 0.001$ compared with reference state.
‡ Ratios are the result of multivariate generalized estimating equations, adjusted for variables shown in **Table 3** as well as state.
§ $P < 0.050$ compared with reference state.

patients who had biopsy in New York versus Florida. States with a high rate of biopsy use probably achieved a lower rate of complications per biopsy by expanding the pool of patients who had biopsy to include healthier patients with a lower risk for both cancer and complications. A greater proportion of CT-guided biopsies in New York were performed in patients who had COPD or were aged 60 to 79 years (factors associated with both lung cancer and biopsy complications) than were performed in states with a high rate of biopsy use, which supports this hypothesis. However, states with low biopsy use had a lower rate of complications at the population level because they performed fewer biopsies per 100 000 adults in the state; for example, the age-adjusted relative rate of pneumothorax requiring a chest tube in New York versus Florida, at the population level, was 0.61 (CI, 0.50 to 0.73).

The striking variation in rates of biopsy use between states suggests a lack of consensus on optimal management of pulmonary nodules, which reflects the lack of evidence in this area. To our knowledge, no randomized trials have compared strategies of pulmonary nodule management (such as serial imaging, biopsy, or early surgery) or addressed whether, when, and how to perform biopsy, and guidelines on pulmonary nodule management are based primarily on expert opinion (2). Although full results have yet to be released, the National Cancer Institute recently put an early stop to its National Lung Screening Trial, which compared chest CT with radiography screening, because of a reported 20% reduction in lung cancer mortality in the CT group (23). This announcement received substantial media coverage and has led to renewed public and physician enthusiasm for lung cancer screening and aggressive pulmonary nodule management in general. Data from a feasibility study for this trial (24) suggest that one third of smokers who undergo chest CT have a false-positive result (a pulmonary nodule that does not turn out to be malignant over the next year). These patients would then have to choose whether to proceed with biopsy, an area not addressed by the design of the trial. Although our study does not address the long-term risk–benefit trade-off of whether to pursue biopsy, our population-based data on short-term risk for complications of CT-guided biopsy may help both patients with pulmonary nodules and their physicians make more informed decisions.

Our data suggest that several thousand persons in the United States experience complications of CT-guided biopsy each year. These harms will no doubt continue to increase as more patients are diagnosed with nodules and undergo biopsy. For many patients, including those with a low risk for cancer, those who are too frail to undergo

cancer treatment, or those with a high risk for cancer who should proceed directly to surgery, this procedure may be unnecessary. Before exposing patients to potential harm from CT-guided biopsy, physicians must ensure that patients understand the risks.

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Appendix Table. ICD-9 and CPT Codes Used for This Study

Diagnosis, Complication, or Procedure	ICD-9 Diagnosis Codes	ICD-9 Procedure Codes	CPT Codes
Diagnosis of pulmonary nodule			
Pulmonary coin lesion	793.1		
Chest mass	786.6		
Lung neoplasm	162.2–162.9, 197.0, 212.3, 235.7, 239.1		
Complication			
Procedure-related hemorrhage	998.1		
Hemorrhage requiring blood transfusion	998.1	99.03, 99.04	36430
Pneumothorax	512		
Iatrogenic pneumothorax*	512.1		
Pneumothorax requiring a chest tube	512	34.04	32002, 32020
Respiratory failure requiring mechanical ventilation		96.04 plus 96.7	31500
Comorbid pulmonary disease			
Current or former tobacco use	305.1, 649.0, V15.82		
Chronic obstructive pulmonary disease	491, 492, 496		
Pleural effusion	510, 511		
Procedure			
Transthoracic needle lung biopsy		33.26	32405
Lung surgery for pulmonary nodule, including open or thoracoscopic surgical biopsy, excision of lung or bronchus, wedge resection, segmentectomy, lobectomy, or pneumonectomy		32.09, 32.1, 32.20, 32.29, 32.3–32.5, 32.9, 33.20, 33.25, 33.28	31786, 32095, 32100, 32440, 32442, 32445, 32480, 32482, 32484, 32486, 32488, 32500–32501, 32503–32504, 32520, 32602, 32657, 32663
Mediastinoscopy		34.22, 34.26	32605–32606, 32662, 38746, 39000, 39010, 39220, 39400
Bronchoscopy		33.21–33.24, 33.27	31620, 31622–31625, 31628–31633, 31635–31638, 31640–31641, 31643, 31645–31646
Other procedures that could cause pneumothorax*			
Central venous catheterization		38.93, 38.94, 89.62	36425, 36556, 36558, 36561, 36563, 36569, 36571
Pulmonary artery catheterization		89.63–89.64, 89.66–89.68	36013–36015, 93503
Bronchoscopy with transbronchial biopsy		33.27	31628–31629, 31632–31633
Pericardiocentesis or pacemaker insertion		37.0, 37.7–37.8	33010–33011, 33015, 33206–33207, 33212

CPT = Current Procedural Terminology; ICD-9 = International Classification of Diseases, Ninth Revision.
* Used for sensitivity analysis.