A meta-analysis examining the risk factors associated with pneumothorax during CT-guided percutaneous lung biopsy

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ABSTRACT

Background: The study aimed to systematically evaluate the risk factors for pneumothorax after computed tomography (CT)-guided percutaneous lung biopsy. ***Materials and Methods:*** We conducted a search of several databases, including PubMed, Embase, the Cochrane Library, Web of Science, and CNKI, until May 2021, focusing on research related to risk factors for pneumothorax following CT-guided percutaneous lung biopsy. After screening and extracting the data, we conducted a meta-analysis using RevMan software (version 5.3) to calculate the odds ratio (OR) and 95% confidence interval (CI) for each relevant risk factor. Statistical significance was set at P<0.05. ***Results:*** Our study included 28 articles and 16,667 patients who underwent CT-guided lung biopsy, of whom 4,566 patients developed pneumothorax (27.40%). Our results showed that the incidence of pneumothorax was lower in the group with pulmonary nodules ≥ 2 cm, and the difference was statistically significant (OR=0.61, 95% CI=0.43–0.86, P=0.004). Additionally, patients with emphysema had a higher risk of developing a pneumothorax after the procedure, and the difference was statistically significant (OR=2.5, 95% CI=1.62–3.87, P<0.0001). Correlation analysis of sex, lung nodule size, needle track length, and CT-guided lung nodule biopsy showed no significant differences (P>0.05). ***Conclusion:*** Our findings indicate that pulmonary nodules smaller than 2 cm and emphysema significantly increase the risk of pneumothorax after puncture. Clinicians should be vigilant in monitoring patients with these risk factors after the procedure.

INTRODUCTION

CT-guided lung puncture biopsy is the most common method to obtain pathological specimens of lung nodules or masses. Pulmonary nodules are defined as soft tissue shadows with a diameter of ≤3 cm surrounded by aerated lung tissue, while solid nodules with a diameter >8 mm indicate non-surgical biopsy [1, 2]. The most commonly used method for distinguishing the nature of pulmonary nodules in clinical practice is computed tomography (CT)-guided lung puncture biopsy. This type of biopsy is a relatively safe and effective method that plays a crucial role in clinical practice due to its economically efficient diagnostic approach and its significance in guiding targeted therapies. In particular, the percutaneous CT-guided lung biopsy is a mature technique for lung lesions, with high diagnostic accuracy (83%-97%) and acceptable complication rate (22%-51%). Therefore, the expansion and development of lung cancer-screening programs may lead to an increase in the number of percutaneous lung biopsies. Complications associated with CT-guided lung biopsies include pneumothorax, pulmonary hemorrhage, and air embolism; among them, pneumothorax is the most severe. According to reports by the Society of Interventional Radiology (SIR) and the American College of Radiology (ACR), the estimated occurrence rate of pneumothorax ranges from 12% to 45%, with 2% to 15% of patients requiring chest tube placement. The incidence of pneumothorax and consequent tube placement is influenced by various intrinsic and extrinsic factors; the former includes the size and location of the tumor and the presence of emphysema, and presence of emphysema, and the latter encompass patient positioning during the procedure, needle size and angle with the pleura, puncture trajectory, number of punctures, and operator training and experience. Pneumothorax after lung biopsy usually occurs immediately or within an hour after surgery.

Using CT guidance, the biopsy needle can be inserted into the lesion under direct vision, which improves diagnostic accuracy and avoids damage to large blood vessels during puncture. CT-guided lung puncture biopsy is highly accurate for diagnosing pulmonary nodules and is commonly used in clinical practice. Despite being minimally invasive, safe, and

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fast, patients may experience postoperative complications, such as coughing blood and pneumothorax [3]. Pneumothorax is the most common CT-guided lung puncture biopsy complications, with an incidence of 25.9% [4]. Although pneumothorax is typically self-limiting following lung puncture biopsy, some patients may experience significant respiratory distress, which can necessitate the placement of a chest tube. This intervention can lead to increased hospital stay time and higher patient costs [4, 5]. Various studies have identified patient age, nodule size, puncture time, and puncture length as potential risk factors for pneumothorax following CT-guided lung puncture biopsy. However, evidence from the literature remains conflicting [6, 7].

After puncture, the risk factors include fixed factors, such as clinical features and pathological characteristics, and modifiable factors, such as puncture technology. Therefore, this study aimed to determine the incidence, clinical significance, and risk factors of pneumothorax after a percutaneous lung biopsy. Stratifying patients according to their risk may help develop standardized evidence-based protocols to manage patients after a biopsy.

MATERIALS AND METHODS

Our methodology followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to perform systematic reviews and meta-analyses.

Data sources and searches

We conducted a comprehensive search of several prominent databases, including PubMed, Embase, Cochrane Library, Web of Science, and CNKI, to identify studies that examined the risk factors for pneumothorax after CT-guided percutaneous lung biopsy. The literature search was conducted up to May 2021 and utilized a variety of English and Chinese search terms, including “biopsy,” “fine-needle,” “FNA,” “fine needle aspiration,” “CT-guided,” “computerized tomography-guided,” “lung neoplasms,” “lung nodule,” “pulmonary,” “lung,” “transcutaneous,” “percutaneous,” “transthoracic,” “complication,” “pneumothorax,” “lung cancer,” “lung nodules,” “biopsy,” and “puncture.”

Selection of suitable studies

The suitable studies were selected through a process of independent screening performed by two authors, with 5 and 6 years of experience in radiology. Duplicate articles were identified and removed using Endnote, and an initial screening was conducted based on article titles and abstracts. Further screening of full-text articles was performed through careful reading. The screening results obtained by the two researchers were cross-checked, and discuss any discrepancies with the corresponding author to make a final decision on inclusion. The inclusion criteria were as follows: (I) studies on CT-guided lung puncture biopsy; (II) studies that assessed the risk factors for pneumothorax and non-pneumothorax patients after CT-guided lung puncture biopsy; (III) case-control or cohort studies; (IV) studies published in Chinese or English; (V) studies that could extract the odds ratio (OR), relative risk (RR), and 95% confidence interval (CI) or use tabulated data to calculate the OR and 95% CI of the correlation between risk factors and pneumothorax. The exclusion criteria were as follows: (I) studies with incomplete data on risk factors for pneumothorax; (II) case reports, conference papers, and reviews; and (III) studies not published in Chinese or English. In addition, the reference lists of the review articles were screened to find additional references. Studies conducted at the same institution during overlapping periods were considered duplicates, and data with larger sample sizes were included for further analysis.

Data extraction

The authors resolved any disagreements through consensus. The focus of data extraction was on the incidence of pneumothorax (confirmed by plain radiography or CT) after lung biopsy, and the risk factors most strongly associated with this complication. Two authors independently extracted data from the included literature, including the first author, date of publication, country, sample size, number of pneumothorax cases, age, sex, size of pulmonary nodules, length of needle path, and presence of pulmonary emphysema. If there were any disputes during the data extraction process, the corresponding author made the final decision.

Risk of bias and quality of the studies

The quality and risk of bias of the included studies were evaluated by two authors. The Newcastle-Ottawa Scale (NOS) was used to evaluate the quality of cohort studies and case-control studies. In contrast, the quality evaluation criteria of the Agency for Healthcare Research and Quality (AHRQ) were used to evaluate cross-sectional studies. Low quality was scored from 0 to 3, moderate quality from 4 to 7, and high quality from 8 to 11.

Statistical analysis

We used RevMan 5.3 software (Nordic Cochrane Centre, The Cochrane Collaboration, London, UK) for statistical analyses. A subgroup analysis was performed if the number of studies on a single risk factor was ≥ 5. We calculated the odds ratio (OR) and 95% confidence interval (CI) of the relevant risk factors. Statistical significance was set at $P < 0.05$. The study heterogeneity was evaluated using the chi-square test/chi-square goodness-of-fit statistic, and a fixed-effect model was used for analysis when I^2 was

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≤50%, while a random-effects model was used when I^2 was > 50%. The sensitivity of the studies was evaluated using the leave-one-out method, and publication bias was analyzed using funnel plots and Egger's test.

RESULTS

Results of literature search

Following the database searches, a total of 4,893 articles were initially retrieved. After the removal of duplicate studies, 4,452 articles remained for further screening. From these, based on title and abstract, 4,243 articles were excluded. Upon reviewing the full texts of the remaining 209 articles, 176 were found ineligible for the current meta-analysis, ultimately leaving 28 articles for inclusion (6-32). The flow chart of the literature screening process is shown in figure 1.

Assessment of study quality

The quality of the 28 studies included in the meta-analysis was considered good in all cases. The scoring results are shown in table 1, and all the studies considered were of medium or high quality.

Risk factors for pneumothorax following CT-guided lung biopsy

A meta-analysis was conducted to examine the risk factors for pneumothorax after CT-guided lung puncture biopsy. The results are shown in table 2. In the current meta-analysis, a total of 16,667 patients underwent CT-guided lung puncture biopsies, of which 4,566 patients developed pneumothorax (27.40%). The incidence of pneumothorax was significantly lower in patients with pulmonary nodules ≥2 cm in size (OR = 0.61, 95% CI = 0.43–0.86, P <0.01) (figure 2). In addition, the risk of pneumothorax after CT-guided lung biopsy is significantly increased in patients with emphysema (OR = 2.5, 95% CI = 1.62–3.87, P <0.01). However, sex, pulmonary nodule size, needle tract length were not significantly correlated with the incidence of pneumothorax after CT-guided lung biopsy (P >0.05).

Risk of bias and quality of the studies

A publication bias risk analysis was conducted using subgroups stratified according to the presence of pulmonary nodules ≥2 cm in diameter as an indicator. The funnel plot is shown in figure 3. The scatter was mainly distributed within the funnel, with high symmetry, indicating that the publication bias was negligible (figure 3). After excluding each study, the meta-analysis results remained consistent.

Table 1. The basic clinical features of included studies.

First Author	Country	Gender male/ female	Year	Diameter of nodules/cm	Track length/ cm	Pulmonary emphysema	Sample size	Pneumothorax	Non-pneumothorax	Bias risk
Chen 2021[30]	China	157/171	-	-	-	-	328	82	246	7
He 2017[6]	China	83/35	-	-	-	36/82	118	59	59	6
Wang 2020[7]	China	118/84	-	-	-	-	202	37	165	6
Xiao 2018[31]	China	62/50	-	-	-	21	112	25	87	6
Yan 2017[32]	China	47/33	-	-	-	25/55	80	12	68	6
Ashraf 2017[8]	Denmark	155/146	68 (29–91)	-	-	-	301	123	178	-
Besir 2011[9]	Turkey	-	-	-	-	70/32	102	16	86	7
Branden 2021[10]	Sweden	239/224	-	-	-	-	463	119	344	9
Chakrabarti 2009[11]	UK	73/61	68±10	-	-	-	134	32	102	5
Covey 2004[12]	USA	230/223	68 (21-90)	2.5(0.5-1.5)	-	-	453	116	337	7
Drumm 2019[13]	Ireland	177/196	67.7 (23-90)	-	-	178/195	373	70	303	8
Geraghty 2003[14]	USA	471/375	-	-	-	-	846	226	620	6
Hiraki 2010[15]	Japan	377/656	67.2 ± 11.2	2.27 ± 1.50	-	302/731	1115	452	663	8
Khan 2008[16]	Germany	-	-	-	-	-	135	23	112	8
Kim 2015[17]	Korean	713/514	-	-	-	-	1227	263	964	6
Kolderman 2020[18]	USA	-	69.9 (11.6)	-	-	-	559	154	405	6
Kuban 2015[19]	USA	1987/ 1930	63.5 ±12.63	2.478 ±1.903	2.917 ±2.172	421/3841	4262	1286	2976	6
Lee 2016[20]	Korea	397/194	64.25 (18-89)	3.71 (0.5-12.5)	-	136/455	591	100	491	7
Lee 2014[21]	Korea	624/470	-	-	-	95/998	1153	196	957	6
Loubeyre 2005[22]	Switzerland	-	-	-	-	-	63	12	51	8
Noh 2009[23]	Korea	172/65	-	-	-	54/183	237	92	145	6
Ozturk 2018[24]	Turkey	655/167	-	-	-	127/695	822	127	695	8
Patel 2014[25]	USA	82/92	67±11.4	2.7±2.1	-	-	174	63	111	9
Rong 2021[26]	USA	277/279	66 ± 14	-	-	-	553	146	407	7
Ruud 2021[27]	Norway	382/404	67.8 (22-92)	2.2 (4-11.0)	-	318/557	875	343	532	8
Sabatino 2021[28]	Italy	-	69.6 ± 10.8	3.57 ± 2.33	-	-	904	306	598	7
Weon 2021[29]	Australia	149/106	-	-	-	78/207	255	77	178	8
Zhuang 2013[33]	China	80/22	-	-	-	-	102	9	93	7

CN, Core biopsy; FNA, fine needle aspiration

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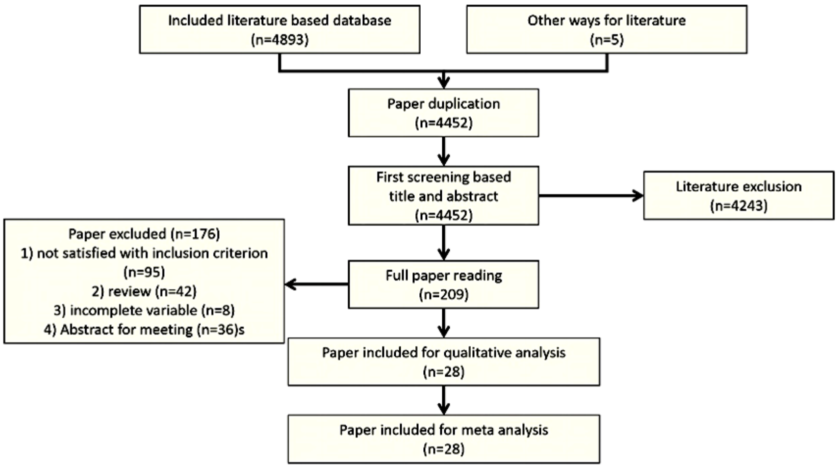

Figure 1. Flowchart outlining the literature search and article evaluation process. Identification, inclusion and exclusion of studies on the meta analysis of risk factor for pneumothorax after CT-guided lung biopsy.

Table 2. Analysis of risk factors for pneumothorax during computed tomography (CT)-guided percutaneous lung biopsy.

Risk factors	Included studies	Meta analysis		Heterogeneity test P-value	Egger analysis P value
		OR (95% CI)	P value		
Gender/male	19	1.08 (0.96, 1.23)	0.19	<0.01*	0.050
Year	7	1.10 (0.99, 1.03)	0.16	<0.01*	0.204
Year≥60 years	5	1.4 (0.89, 2.21)	0.06	<0.01*	0.664
Diameter of nodules	12	0.99 (0.97, 1.00)	0.08	<0.01*	0.423
Lung nodules ≥2 cm	9	0.61 (0.43, 0.86)	<0.01*	<0.01*	0.983
Pneumonectomy	12	2.50 (1.62, 3.87)	<0.01*	<0.01*	0.815
Track length	7	1.02 (0.99, 1.06)	0.23	<0.01*	0.694

* denotes statistically significant differences. CI, confidence interval.

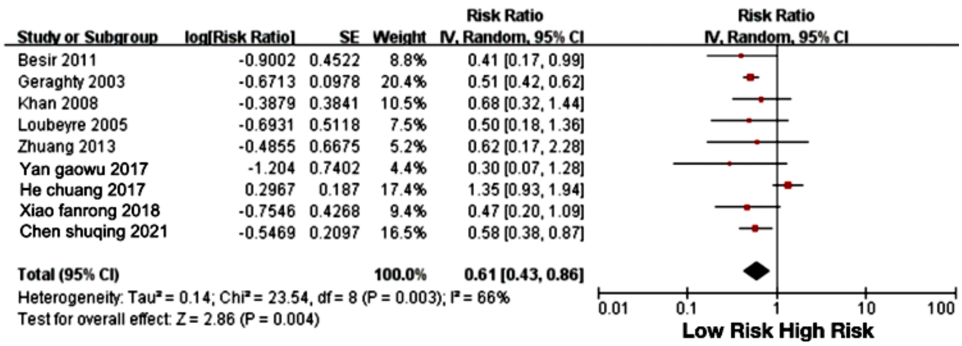

Figure 2. Funel pot of publication bias. Meta-analysis forest plot showing the effect of pulmonary nodules ≥2 cm in diameter as a risk factor for pneumothorax after computed tomography (CT)-guided lung biopsy.

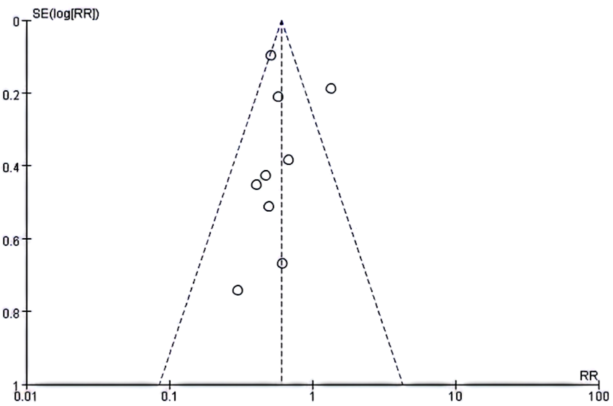

Figure 3. Forest plots for pneumothorax after CT-guided lung biopsy.

DISCUSSION

Under CT guidance, percutaneous biopsy provides precise localization of pulmonary nodules, elucidating the relationship between the lesion and surrounding blood vessels and organs. The accuracy of biopsy is enhanced by adhering to predetermined puncture paths and depths, with repeated confirmations of the biopsy needle's position. However, the challenges of small volumes and the inherent difficulty of puncturing pulmonary nodules increase the risk of complications, notably pneumothorax. This article seeks to conduct a meta-analysis based on prior clinical studies to identify risk factors for pneumothorax induced by CT-guided percutaneous biopsy. The objective is to refine these risk factors through a literature analysis, offering insights to guide clinical practices aimed at reducing the incidence of pneumothorax.

Pneumothorax is the most common complication of lung puncture biopsy under CT guidance [33]. However, the risk factors for pneumothorax following CT-guided lung biopsy remain controversial. In the era of personalized medicine, reliable and safe pathological sampling is crucial for establishing a diagnosis, assessing prognosis, and tailoring

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treatment plans. CT-guided lung puncture biopsy allows for the visualization of dynamic phenomena in the thoracic cavity and surrounding structures during the puncture process. It is less invasive than surgical biopsy and can access nearly all mediastinal regions, including those that are inaccessible for bronchoscopic and endoscopic ultrasound-guided biopsies. This technique enables the diagnosis of lung parenchymal, mediastinal, chest wall, and pleural lesions. Previous studies have reported an incidence rate of pneumothorax complications following CT-guided percutaneous lung biopsy ranging from 17% to 26.6%, with an incidence of major complications ranging from 4% to 27% in the postoperative period. A patient's medical history, nodule characteristics, and puncture factors may influence the risk of developing postoperative pneumothorax. The current meta-analysis of 28 studies explored the significance of age, sex, nodule size, needle tract length, and history of emphysema as risk factors for pneumothorax following CT-guided lung puncture biopsy.

This study included 16,667 patients who underwent lung puncture biopsy under CT guidance, with a pneumothorax incidence rate of 27.40%. The presence of pulmonary nodules <2 cm in size was a risk factor for pneumothorax after CT-guided lung puncture biopsy. The study conducted by Yeow *et al.* (35) reveals that the size of the lesion is not associated with the positive pathological diagnosis during percutaneous lung puncture biopsy procedures. However, it is correlated with the occurrence of pneumothorax complications post-biopsy. The research findings demonstrate that patients have the highest probability of developing pneumothorax when the lesion size is approximately 2.1cm and they undergo CT-guided lung puncture biopsy.

The placement of a puncture is more challenging with smaller pulmonary nodules, which renders it more vulnerable to respiratory influence after positioning. This susceptibility may necessitate repeated positioning and puncture, raising the risk of developing pneumothorax. At the same time, the study found that puncturing normal lung tissue was associated with a higher incidence of pneumothorax. When nodules are smaller, it is easier to damage normal lung tissue (5). However, a subgroup analysis of nodules based on size measurements showed no correlation between nodule size and pneumothorax risk after lung puncture biopsy under CT guidance. Since this study included a relatively small number of patients, high-quality, large-sample case-control or cohort studies are needed to further validate the relationship between nodule size and pneumothorax after puncture. Nodule characteristics may also be one of the factors that affect the risk of pneumothorax after puncture; however, since there are no relevant detailed data reported in the literature, this study did not analyze the correlation between nodule characteristics and pneumothorax after puncture, and further clinical research is needed to explore the impact of nodule characteristics.

In addition, this study also found that the risk of post-puncture pneumothorax was significantly increased in patients with coexisting emphysema. This study indicates that emphysema, especially at the needle insertion site, leads to a lack of elasticity in the lung tissue, obstructs gas expansion, and increases the risk of pneumothorax (34). This suggests that emphysema and bullae sites should be avoided when selecting a puncture needle pathway in clinical practice. Simultaneously, postoperative monitoring should be strengthened for patients with coexisting emphysema, and pneumothorax should be detected early and promptly addressed to avoid severe complications. The puncture technique is also an important factor affecting post-puncture pneumothorax; however, limited research literature has yet to examine certain risk factors. Kolderman *et al*., conducted a retrospective study comparing the complications of 18G and 20G puncture needles for CT-guided lung biopsy and found no statistically significant differences in puncture accuracy and post-puncture pneumothorax rate between the two (18). Branden *et al*., found that an increased number of pleural punctures did not increase the incidence of post-puncture pneumothorax but may increase the risk of post-puncture hemoptysis (10). High-quality clinical studies investigating the technical risk factors affecting post-puncture pneumothorax remain lacking.

This study had certain limitations that should be considered. First, the studies included in this literature were retrospective, which may have confounded the effects of certain risk factors for developing pneumothorax following CT-guided lung biopsy. Therefore, the conclusions of this study require further validation in prospective, large-sample, multicenter cohort studies. Second, certain risk factors, such as the number of pleural punctures, smoking history, size of the puncture needle, puncture angle, operator experience, and nature of lung nodules, were excluded from the subgroup analysis due to the limited studies available. Further exploration is needed through meta-analysis of large samples and high-quality individual case data. Third, the included studies demonstrated significant heterogeneity, which may have contributed to research bias. However, the sensitivity analysis demonstrated that the results of this meta-analysis were relatively stable. The research results should be verified by a meta-analysis of individual case data to reduce heterogeneity.

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CONCLUSIONS

The most relevant risk factors for pneumothorax after a biopsy are lung nodules < 2 cm and coexisting emphysema. Our findings can help select safer puncture techniques, strengthen post-puncture monitoring, and reduce the incidence of postoperative pneumothorax.

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