INPLASY

Risk of re-expansion pulmonary edema after thoracentesis of pleural effusion in adult patients: a systematic review

INPLASY202610024
doi: 10.37766/inplasy2026.1.0024
Received: 7 January 2026
Published: 7 January 2026

Corresponding author:
Martin Müller

martin.mueller@insel.ch

Author Affiliation:
Department of Emergency Medicine, University Hospital Bern, University of Bern, Bern, Switzerland.

Schneider, C; Steffen, V; Kehrli, I; von Gernler, M; Speidel, V; Mosimann, V; Villiger, R; Henssler, J; Müller, M.

ADMINISTRATIVE INFORMATION

Support - The authors did not receive any specific grant or financial support from funding agencies in the public, commercial, or not-for-profit sectors for the preparation of this systematic review.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202610024

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 January 2026 and was last updated on 2 July 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review is to assess the risk of re-expansion pulmonary edema (REPE) following thoracentesis of pleural effusion in adult patients, with a particular focus on subgroups defined by the drained volume. To this end, the proposed systematic review will address the following questions: What is the risk and does the risk of REPE vary according to the amount of fluid drained in adult patients undergoing thoracentesis?

Rationale The occurrence of REPE after thoracentesis has been investigated in several studies. Some studies suggest that this complication is rare; however, its exact incidence remains unknown, and it can lead to serious consequences for patients. Prior research indicates a possible association with drainage of larger fluid volumes. Yet, there are patients who might benefit from drainage of greater volumes to achieve adequate symptom relief.
To support clinical decision making, a clear understanding of the risk of REPE and its relation to the drained volume is necessary. Therefore, we aim to systematically summarize and analyze existing literature.

Condition being studied Pleural effusion is an condition with a notably high prevalence, for example in an adult population of 4.6 in 1000 cases have been reported in Chinese People . The etiology of pleural effusion is diverse including parapneumonic, hemorrhagic or malignant effusions . Additionally, the clinical manifestation of a pleural effusion may vary among patients. The most common symptoms include cough , shortness of breath , and pain .
Along with clinical examination , imaging procedures help secure the diagnosis , most commonly with point of care ultrasound . Besides using ultrasound for detection of an effusion, it can

be used for thoracentesis . The drained fluid can be identified as a transudate or exudate through laboratory analyses which in turn can narrow down the etiology .
Besides direct treatment of the underlying cause , in many cases, especially in recurrent effusions, placement of a temporary drainage should be evaluated . The puncture and drainage of a pleural effusion can lead to REPE .
REPE is described as a potentially serious complication following thoracentesis . While it is often assumed to occur infrequently, its actual incidence has not been clearly established. The clinical main characteristics of REPE are cough, dyspnea, an increase in the respiratory rate , and hypoxia in hours following thoracentesis or drainage . In addition to the typical constellation of symptoms, imaging procedures are required to confirm the diagnosis of REPE and to exclude iatrogenic pneumothorax as a differential diagnosis . It can be visualized using tomographic imaging as well as ultrasound and chest X-ray . Common CT findings of REPE are ipsilateral ground-glass opacities . The presence of lung edema, associated with elevated extravascular fluid, is indicated by an increased number of B-lines on ultrasound .
REPE is believed to be caused by rapid removal of large volume or excessively negative pleural pressure during drainage . Chest discomfort or persistent cough during thoracentesis have been reported to correlate with a decline in pleural pressure and should prompt immediate interruption of the procedure . According to previous expert opinions, younger age has been considered an additional risk factor for an increased likelihood of REPE occurrence and the recommendation to drain a limited amount of less than 1.5 L was determined .
The treatment of REPE consists mainly of supportive measures . Several authors describe the administration of oxygen, in selected cases non-invasive and even invasive ventilation of patients was necessary . Evidence for the use of diuretics such as furosemide in REPE is limited to isolated case reports and anecdotal experience.

METHODS

Search strategy Search strategy: Ovid MEDLINE(R) ALL
1 pulmonary edema/ or drainage/ae
2 (((Reexpansion or re-expansion or lung or pulmonary) adj3 (edema? or oedema? or pseudoedema? or pseudooedema?)) or REPE or RPE or REPO or RPO).ti,ab,kf.
3 (complication? and ("pleura-centesis" or "pleuracenteses" or "pleuracentesis" or "pleuracentheses" or "pleuracenthesis" or "pleurocantensis" or "pleurocantenses" or "pleurocenteses" or "pleurocentesis" or "pleurocentheses" or "pleurocenthesis" or "thoracentesis" or "thoracenteses" or "thoracentesis" or "thoracentheses" or "thoracenthesis" or "thoracocenteses" or "thoracocentesis" or "thoracocentheses" or "thoracocenthesis" or "thorocentesis")).ti,ab.
4 or/1-3
5 paracentesis/ or thoracentesis/
6 ("pleural procedure?" or "paracentesis" or "pleura-centesis" or "pleuracenteses" or "pleuracentesis" or "pleuracentheses" or "pleuracenthesis" or "chest aspiration?" or "pleurocantensis" or "pleurocantenses" or "pleurocenteses" or "pleurocentesis" or "pleurocentheses" or "pleurocenthesis" or "thoracentesis" or "thoracenteses" or "thoracentesis" or "thoracentheses" or "thoracenthesis" or "thoracocenteses" or "thoracocentesis" or "thoracocentheses" or "thoracocenthesis" or "thorocentesis").ti,ab,kf.
7 ((pleur* or thora* or chest) adj3 (aspiration? or drain* or punction* or puncture* or paracentes* or centes* or centhes* or cantens#s or tap)).ti,ab,kf.
8 or/5-7
9 pleural effusion/ or chylothorax/ or hemothorax/ or hydrothorax/ or exp empyema, pleural/
10 ((pleura? adj3 (effusion? or fluid? or empyema? or ex?udat* or transudat*)) or pleurorrhea? or pleurorrhoea? or hydrothorax or hemothorax or haemothorax or pyothorax or chylothorax or parapneumonic effusion?).ti,ab,kf.
11 or/9-10
12 and/4,8,11
13 (exp animals/ or exp animal experimentation/ or e
• Time frame: from inception to present.

Participant or population Adult patients (aged ≥18 years) and mixed population (adult and children without documented focus on pediatric patients) with pleural effusion.

Intervention • Intervention: Thoracentesis/pleural puncture or thoracic drainage/chest tube.

Comparator Groups with different drained volumes, as defined in the included primary studies (e.g., lower vs. higher volume drainage thresholds). If no explicit comparator groups are reported, studies will still be included for estimation of REPE incidence, and subgroup analyses will be performed based on the extracted volume data.

Study designs to be included Randomized controlled trials, cohort studies (prospective and retrospective), case-control studies, cross-sectional studies, case series with >20 patients

Eligibility criteria Exclusion: studies with documented focus on pediatric patients or pneumothorax, reviews, non-original research, case reports, case series with <20 patients

Information sources • Databases: MEDLINE, Embase, Cochrane Library, Scopus, CINAHL, ClinicalTrials.gov, WHO ICTRP, Scopus, Google Scholar.

Main outcome(s) The primary outcome will be the incidence of re-expansion pulmonary edema (REPE) after drainage of a pleural effusion or other intrathoracic fluids.
Because the diagnostic criteria for REPE vary across studies, we will systematically document and compare the definitions used in each study during data extraction. If feasible, we will perform subgroup analyses using comparable subgroups with different diagnostic criteria (e.g. new unilateral pulmonary infiltrates following drainage combined with symptoms such as dyspnea or hypoxia within 24 hours vs. Radiological finding with/without symptoms).

Additional outcome(s) Secondary outcomes will include a detailed characterization of REPE, based on information reported in the included studies:
• Time to onset of REPE
• Clinical presentation (e.g., dyspnea, cough, tachypnea, hypoxia)
• Clinical severity, extracted as defined by the original studies; where possible, we will categorize severity using commonly accepted descriptors: mild symptoms without the need of oxygen; moderate symptoms with hypoxia requiring oxygen; severe symptoms in need for non-invasive or invasive ventilatory support)
• Radiological findings described on thoracic ultrasound, chest X-ray or CT associated with REPE (e.g., unilateral infiltrates, ground-glass opacities, ultrasound B-line increase)
• Management strategies (e.g., supplemental oxygen, non-invasive or invasive ventilation, diuretics)
• Mortality associated with REPE will be extracted and if possible a distinction between REPE associated and all-cause mortality will be conducted.

Data management • Data will be extracted independently by two reviewers; disagreements will be solved by a third, senior reviewer
• Extracted items will include the following items. If the data is missing it will be marked as not reported:
1. Study identification and characteristics: First author, year, journal, country, study setting, study design, sample size, study period
2. Population Characteristics: mean age, sex, etiology of pleural effusion, healthcare setting (e.g. emergency department, hospitalized or critically ill patients)
3. Procedural Characteristics: thoracentesis technique, evacuation method, operator qualification, needle/catheter size, drainage technique, volume of drainage,
4. Outcomes: definition of REPE used by authors, incidence of REPE, time to onset (meaning the time after the procedure until the appearance of the first symptom confirmed with radiologic findings), clinical presentation, severity, radiological findings, management, mortality, routine imaging
5. Confounders and risk factors: pressure measurements, duration/chronicity of effusion, reported adjusted effect sizes
6. Quality and reporting: bias assessment results, reporting of missing data handling, follow-up.
• Software systems being used for recording decisions, for conducting data extraction and statistical analysis are Covidence. The extracted data will be recorded with Excel.
• References will be managed using Zotero throughout the review process.

Quality assessment / Risk of bias analysis The methodological quality of the reviewed studies will be assessed with the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data. Since the primary objective of this review is to estimate the incidence of re-expansion pulmonary edema after thoracentesis, we apply the above-mentioned checklist irrespective of the original study design. This approach is justified because all included studies contributed data to a prevalence/incidence estimate of REPE rather than to a comparative intervention effect. Regarding the secondary objective concerning drainage volume, we additionally assess whether studies reported drainage volume at the patient/procedure level, whether REPE events were stratified by drainage volume, and whether analyses accounted for clinically relevant confounding factors. This supplementary assessment is used to judge the interpretability of evidence regarding a possible volume–risk relationship and was not incorporated into the primary prevalence risk-of-bias rating.
Evidence regarding the association between drainage volume and REPE is interpreted cautiously, because many studies were designed to estimate complication rates rather than to

evaluate drainage volume as an independent risk factor.

Strategy of data synthesis The primary analysis will be a meta-analysis of the pooled incidence of REPE following thoracentesis or pleural drainage. The extraction of incidence will be accomplished by dividing the number of REPE events by the number of thoracentesis/pleural puncture or thoracic drainage/chest tube.
The pooled proportions will be obtained with Stata's Meta-Analysis command for prevalences. Statistical heterogeneity will be assessed by using I^2 statistic and Cochran's Q test.
If there is relevant heterogeneity, we will perform a subgroup analysis based on drainage volume and other predefined variables (e.g. type of pleural effusion, drainage method etc.) to find a possible clinical explanation. The aim of the subgroup analysis is to investigate clinically comprehensible causes for the variability between studies.
If there is relevant heterogeneity (>50%) according to the I^2 test and we can include 5 or more studies, we will perform meta-regression.
For studies reporting comparative data, effect estimates such as odds ratios (OR) or relative risks (RR) with 95% confidence intervals will be calculated. The calculation of pooled effect estimates will only be performed if we have at least two studies with comparable data (such as volume 1L).
If it is not possible to conduct the meta-analysis, we will provide a descriptive and narrative summary of the trends, differences and possible risk factors. Reasons for not performing a meta-analysis include excessive clinical heterogeneity (e.g. patient population, significant differences in the definition of REPE, different pleural puncture techniques) or methodological heterogeneity, incomplete numerical data (e.g. missing event rates), or if there are too few studies available for a meta-analysis (at least 2 studies) or meta-regression (at least 5 studies).

Subgroup analysis The subgroup analysis aims to explain relevant heterogeneity with clinically effect modifiers. If enough studies are available, we will perform random-effects meta-regression analyses to explore whether between-study heterogeneity in the incidence of REPE can be explained by study- and patient-level characteristics. The primary effect modifier will be the volume of fluid drained per procedure, analyzed as a continuous variable (mean) where possible and additionally as a categorical variable according to prespecified or study-reported thresholds (for example, ≤1 L versus >1 L or ≤1.5 L versus >1.5 L).
Prespecified additional potential effect modifiers will include:
• Volume of drained fluid (continuous or categorical, as defined above).
• The use of pleural manometry and pleural pressure measurements
• Chronicity of the pleural effusion (acute versus long-standing, according to study definitions)
• Etiology of pleural effusion (e.g. malignant, parapneumonic, heart failure-related)
• Drainage method (such as single thoracentesis versus indwelling or chest tube drainage; use of suction versus no suction)
• Thoracentesis technique and operator characteristics (for example, physician specialty, level of training, ultrasound guidance)
• Patient characteristics (e.g. age, sex distribution, and relevant comorbidities)
• Study design and methodological quality, including overall risk-of-bias rating: The incidence could be distorted by studies with high risk of bias and thus the incidence could be over- or underestimated.
Where data permits, each effect modifier will first be examined in univariable meta-regression models. If the number of studies is adequate (at least 5 studies for each subgroup), we will consider multivariable models including more than one effect modifier. We will calculate the heterogeneity effects of the various subgroups using a Q interaction test. We consider a p-value <0.10 to be statistically significant. The robustness of meta-regression findings will be interpreted cautiously, given the observational and study-level nature of these analyses. We will exclude studies without data on the various subgroups from this analysis.

Sensitivity analysis We will carry out a sensitivity analysis if heterogeneity is high, which we define as an I2 value >75% or p10% in the incidence or a shift of >20% or change of the heterogenity category (low, moderate, high) of the I2 value, the shift is considered relevant. We will provide a visualization of the results using an influence plot.

Language restriction • Language restrictions: We only consider studies published in English, German and French.

Country(ies) involved Switzerland and Germany.

Other relevant information Meta-analysis and -regression:
For the statistical analysis, we will use the meta command collection of Stata/MP 18.0 (StataCorp, USA).
Assessment of certainty of evidence about prognosis (GRADE)

Two reviewers will assess the certainty of evidence for the primary and each secondary outcome using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. Given that our systematic review assesses the question about the incidence of REPE the classical GRADE framework is not suitable. Therefore we will apply the adaptation of GRADE as mentioned by Iorio et al.(31).
In contrast to the classical approach GRADE about prognosis rates the certainty of evidence across observational cohort studies as high and not low. Evidence may be downgraded based on five domains, which consist of risk of bias, inconsistency, indirectness, imprecision or publication bias. Afterwards the final certainty rating will be conducted independently and rated as high, moderate, low or very low. If consensus can not be reached a third, more experienced reviewer will make a final decision. As the outcome of interest represents rare events, we will specifically focus on imprecision including small numbers of events, zero-event studies and wide confidence intervals.
GRADE assessments for each outcome will be summarized in Summary of Findings tables.

Keywords Re-expansion pulmonary edema; pleural effusion; fluid drainage; thoracentesis; drainage; volume drained; systematic review.

Contributions of each author

• First author: Dr. med. Claudio Schneider1
• Second shared authors: Vera Steffen2, Isabelle Kehrli2
• Co-authors: Dr. rer. nat. Marc von Gernler3, Dr. med. Victor Speidel4, Dr. med. Vincent Mosimann5, Dr. med. Rahel Villiger1, Prof. Dr. med. Priv.-Doz. Dr. med. Jonathan Henssler6
• Corresponding author: Prof. Dr. med. Dipl.-Math. Martin Müller, PhD MSc2 (email: martin.mueller@insel.ch)

• 1 Department of Internal Medicine, University Hospital Bern, University of Bern, Bern, Switzerland
• 2 Department of Emergency Medicine, University Hospital Bern, University of Bern, Bern, Switzerland
• 3 University Library Bern, Medical Library, University of Bern, Switzerland
• 4 Department of Emergency Medicine and Internal Medicine, Hospital SRO Langenthal, Langenthal, Switzerland
• 5 Oberwallis Hospital Centre, Pflanzettastrasse 8, 3930 Visp, Switzerland
• 6 Charité University Hospital Berlin, Department of Psychiatry and Psychotherapy at St. Hedwig Hospital, Große Hamburger Str. 5-11, 10115 Berlin, Germany.