Risk Factors for Pneumothorax Complicating Radiofrequency Ablation for Lung Malignancy: A Systematic Review and Meta-Analysis

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ABSTRACT

Purpose: To assess the potential risk factors for pneumothorax secondary to pulmonary radiofrequency (RF) ablation.

Materials and Methods: Six electronic databases were searched from inception to February 2014 for studies assessing potential patient-related, tumor-related, or treatment-related risk factors for pneumothorax during pulmonary RF ablation. Study selection, data collection, and quality assessment were done by three independent reviewers.

Results: Among 771 studies identified in the search, 10 retrospective cohort studies met inclusion criteria. There were 981 patients (61.5% male) with a mean age of 64.2 years included (259 primary lung tumors, 722 metastatic tumors). The prevalence of pneumothorax was 37% (95% confidence interval [CI], 29%–46%) in 1,916 RF ablation sessions. The potential patient-related and tumor-related risk factors for pneumothorax were increased age (mean difference [MD], 2.09; 95% CI [0.11–4.06]; $I^2 = 0\%$), male gender (unadjusted odds ratio [OR], 2.20; 95% CI [1.49-3.27]; $I^2 = 0\%$), no history of lung surgery (unadjusted OR, 0.29; 95% CI [0.19–0.44]; $I^2 = 0\%$), and a greater number of tumors ablated (MD, 0.50; 95% CI [0.27–0.73]; $I^2 = 0\%$).

Conclusion: Based on available observational studies, the results suggest risk factors for pneumothorax secondary to pulmonary RF ablation may include increased age, male gender, no history of lung surgery, number of tumors ablated, and increased length of the aerated lung traversed by the electrode. The findings from this systematic review should be interpreted with caution because of the inherent limitations of the retrospective observational design.

ABBREVIATIONS

CI = confidence interval, MD = mean difference, NOS = Newcastle-Ottawa scale, OR = odds ratio, PPAP = post–pulmonary ablation pneumothorax

First described by Dupuy et al in 2000 (1), image-guided percutaneous radiofrequency (RF) ablation has become an effective modality to treat both primary and metastatic lung tumors in patients who are not surgical candidates because of advanced stage of the disease or associated comorbidities (2,3). Compared with traditional surgical options for the treatment of lung tumors, benefits of RF ablation include decreased mortality and morbidity, reduced hospitalization time, preserved pulmonary functional reserve, and reduced cost (1–3).

Pulmonary RF ablation has a reported complication rate of 15.2%–55.6% and a mortality rate ranging from 0%–5.6% (2). Potential complications of lung RF ablation include pneumothorax, pleural effusion, pneumonia, pulmonary abscess, hemothorax, pulmonary hemorrhage, and hemoptysis (2–4). Pneumothorax after pulmonary ablation (post–pulmonary ablation pneumothorax [PPAP]) is the most common complication; it is estimated to occur in 4.5%–61.1% of cases (2). Large, symptomatic pneumothoraces requiring chest tube insertion have been reported in 3.3%–38.9% of patients (2).

PPAP is the most common cause of morbidity after lung RF ablation (3). Various conflicting risk factors for pneumothorax have been described in the literature,

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Figure E1 is available online at *www.jvir.org*.

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including emphysema, number of tumors ablated, and length of lung traversed to ablate the target tumor (2,3). The present systematic review and meta-analysis aims to assess risk factors for PPAP. It is hoped that this review will help interventionalists develop appropriate prevention and monitoring strategies in patients at high risk for developing pneumothorax.

MATERIALS AND METHODS

This systematic review and meta-analysis was conducted in accordance with a protocol developed a priori and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (5).

Eligibility Criteria

The eligibility criteria were developed based on input of all authors. The study inclusion criteria were as follows: (*a*) studies of any type examining potential patient-related, tumor-related, and treatment-related risk factors for PPAP following RF ablation; (*b*) studies including patients $\geq$ 18 years old with any type of primary or metastatic lung malignancies; and(*c*) studies published in the English language at any date. The exclusion criteria were as follows: (*a*) case reports and case series ($<$ 10 patients), (*b*) commentaries or editorials discussing pulmonary RF ablation without reporting methodologies and extractable results, (*c*) conference and meeting abstracts, (*d*) animal or basic science studies, and (*e*) review articles. Studies that combined other therapies with RF ablation (ie, microwave ablation, chemoembolization) were also excluded.

Definition of Pneumothorax

In the included studies, pneumothorax was defined as the accumulation of air in the pleural space that was documented by either computed tomography (CT) scan or chest radiograph at any time during or after RF ablation.

Search Strategy

An electronic search strategy was developed a priori in conjunction with an experienced medical librarian. Electronic searches were conducted in the following databases from database inception date to February 2014: MEDLINE (Ovid and PubMed), Embase, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials. The searches included the following key words or medical subject heading or both: "pneumothorax," "pneumothoraces," "pneumatothorax," "aerothorax," "collapsed lung," "catheter ablation," "radiofrequency ablation," "RF ablation," "thermal ablation," "ablative therapy," "ablation," "lung neoplasm," "lung tumor," "lung," and "pulmonary." Electronic searches were limited to the English language and human study populations (**Figure E1** [available online at *www.jvir.org*]).

Study Selection

Three reviewers (S.K., L.M., D.D.) independently assessed all study abstracts based on criteria defined beforehand. Subsequently, eligibility of full-text articles of the studies that passed the abstract review was assessed by all reviewers. Disagreements on study inclusion were resolved through discussion and unanimous agreement among the reviewers. During discussion, the entire article was read by all reviewers to ensure all eligibility criteria were met. The corresponding author (M.M.) reviewed all articles meeting eligibility criteria as well as articles excluded from the study before data extraction. The authors of the articles included were contacted if pneumothorax risk factors were mentioned in the text but statistical data or information regarding methodologies or both were insufficient in their published series.

Data Extraction

Using a data extraction form developed a priori, two reviewers (S.K., L.M., or D.D.) independently extracted the following information from included studies: study design and time frame, study location, number of patients with primary and metastatic lung cancer, patient demographics, number of RF ablation sessions performed, modalities for and timing of pneumothorax diagnosis, definitions, severity and prevalence of pneumothorax, and data on pneumothorax risk factors assessed. For risk factors assessed, we recorded odds ratio (OR), relative risks, corresponding 95% confidence interval (CI), mean, standard deviation (SD), and statistical methods used, where appropriate.

Quality Assessment

Three reviewers (S.K., L.M., and D.D.) assessed the methodologic quality of the included studies using the Newcastle-Ottawa scale (NOS) (6). The NOS is a validated tool that uses a star system to assess observational studies based on selection of the study cohorts, comparability of the cohorts, and assessment of outcome. A maximum of nine stars can be given to a study. Consensus on the number of stars (quality score) given per study was reached through discussion between the three reviewers (S.K., L.M., D.D.) to ensure unanimous agreement. During discussion, the entire study publication was read by all reviewers to assign stars accurately.

Statistical Analysis

With respect to the study selection and quality assessment, interreviewer agreement was measured with Fleiss κ statistic and intraclass correlation coefficient using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp, Armonk, New York) (7). Weighted means (SD) were also calculated. A random-effects model was used for all meta-analyses based on a priori decision.