EVIDENCE-BASED REVIEW

Lymphatic Interventions for Chylothorax: A Systematic Review and Meta-Analysis

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ABSTRACT

Purpose: To perform a systematic review and meta-analysis of published studies to evaluate the efficacy of lymphatic interventions for chylothorax.

Materials and Methods: The MEDLINE, EMBASE, and Cochrane databases were searched for English-language studies until March 2017 that included patients with chylothorax treated with lymphangiography (LAG), thoracic duct embolization (TDE), or thoracic duct disruption (TDD). Exclusion criteria were as follows: a sample size of less than 10 patients, no extractable data, or data included in subsequent articles or duplicate reports.

Results: The cases of 407 patients from 9 studies were evaluated. The pooled technical success rates of LAG and TDE were 94.2% (95% confidence interval [CI], 88.4%–97.2%; $I^2 = 46.7\%$) and 63.1% (95% CI, 55.4%–70.2%; $I^2 = 37.3\%$), respectively. The pooled clinical success rates of LAG, TDE, and TDD, on a per-protocol basis, were 56.6% (95% CI, 45.4%–67.2%; $I^2 = 5.4\%$), 79.4% (95% CI, 64.8%–89.0%; $I^2 = 68.1\%$), and 60.8% (95% CI, 49.4%–71.2%; $I^2 = 0\%$), respectively. The pooled major complication rate of LAG and TDE was 1.9% (95% CI, 0.8%–4.3%; $I^2 = 0\%$) and 2.4% (95% CI, 0.9%–6.6%; $I^2 = 26.4\%$), respectively. The pooled overall clinical success rate of lymphatic interventions, on an intention-to-treat basis, was 60.1% (95% CI, 52.1%–67.7%; $I^2 = 54.3\%$). Etiology of chylothorax was identified as a significant source of heterogeneity for the pooled clinical success rate of TDE and overall clinical success rate.

Conclusions: Lymphatic interventions have a respectable efficacy for the treatment of chylothorax.

ABBREVIATIONS

CI = confidence interval, ITT = intention-to-treat, LAG = lymphangiography, PP = per-protocol, TDD = thoracic duct disruption, TDE = thoracic duct embolization

Chylothorax is a condition characterized by the accumulation of chyle in the pleural space (1). It is caused by disruption or obstruction of the lymphatic system, due often to trauma or malignancy, respectively, and can lead to chyle depletion (2,3). The optimal management of chylothorax is as yet unknown because no prospective or randomized trials exist to guide the treatment, although conservative measures are generally initially used (1). If these measures fail to provide sufficient symptom relief, surgery has traditionally been the mainstay of treatment (3). However, although surgery has shown high success rates of 82%–100% (4–8) and 64%–87% (7,9) in traumatic and non-traumatic cases, respectively, it has a high morbidity rate reaching 16% (10).

Lymphatic interventions (i.e., lymphangiography [LAG], thoracic duct embolization [TDE], and thoracic duct disruption [TDD]) have been increasingly used for treating chylothorax due to their minimally invasive nature and excellent safety profile (11–14). However, the efficacy of these interventions is not well-documented, because of a paucity of large studies owning to the rarity of chylothorax (11,13,15–17). Meta-analysis is a useful tool for synthesizing the results of multiple studies to obtain a more precise estimate of the effect of interest. The purpose of our study was to perform a systematic review and meta-analysis of published studies to evaluate the efficacy of lymphatic interventions for chylothorax.

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P.H.K. and J.T. contributed equally to this work and are co-first authors.

Tables E1–E3 and Figures E1–E7 are available online at *www.jvir.org*.

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MATERIALS AND METHODS

Institutional review board approval is not required for review articles at our institution. This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (18).

Search Strategy and Selection Criteria

A literature search of the MEDLINE/PubMed, EMBASE, and Cochrane databases was conducted using pertinent MeSH or EMTREE terms with common keywords (**Table E1** [available online at *www.jvir.org*]) for relevant studies until March 2017. Reference lists of relevant articles were also searched, as well as Google and Google Scholar. After eliminating duplicate reports, articles identified through the search were initially screened for their relevance based on titles and abstracts. Case reports, review articles, letters, and conference abstracts were excluded at this stage. Full-text articles were then assessed for their eligibility according to the selection criteria. Articles were included if they reported regarding patients with chylothorax treated with LAG, TDE, or TDD and were published in the English language. Articles with a sample size of less than 10 patients, with no extractable data, or with data included in subsequent articles or duplicate reports were excluded. Two authors (P.H.K., J.T.) independently performed the literature search and application of the selection criteria; any discrepancy was resolved through discussion and consensus, with a third author (J.H.S.) making the final decision as required.

Data Extraction and Definition

The following data were extracted from the included studies: first author; publication year; study type; study location and time period; number of patients; patient age and sex; etiology and location of chylothorax; high-output (>500 mL/d) chylothorax; previous unsuccessful surgical treatment; approach for performing LAG; technical success; embolic agent used; clinical success; and complications. Data extraction was independently performed by the 2 authors using a standardized form, with any discrepancy resolved through discussion and consensus with the involvement of a third author when required. When necessary, the authors of a study were contacted to obtain further individual patient data. Technical success of LAG was defined as successful injection of contrast agent into the lymphatic system; technical success of TDE was defined as total occlusion of the target lymphatic duct. Clinical success was defined as complete resolution of chylothorax without further surgical treatment. Complications were categorized as major or minor according to the Society of Interventional Radiology clinical practice guidelines (19).

Quality Assessment

The quality of the included studies was independently assessed by the 2 authors (P.H.K., J.T.) using the U.S. National Institutes of Health Quality Assessment of Case Series Studies tool (20).

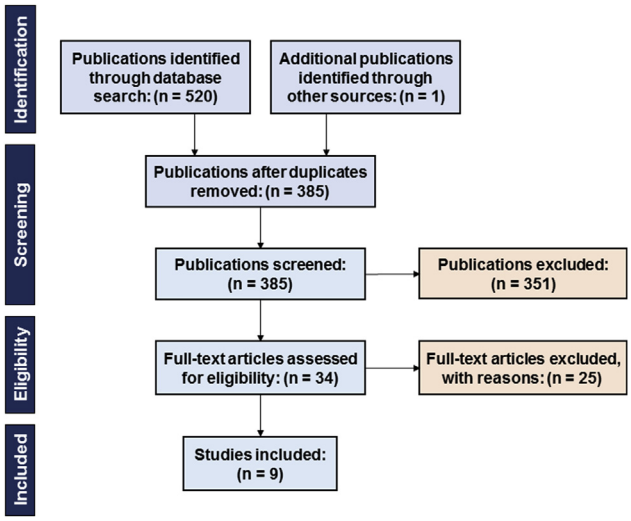

Figure 1. Flowchart of the study selection process.

Data Synthesis and Statistical Analysis

Meta-analytic pooling was based on the inverse variance method for calculating weights, and the pooled technical and clinical success rates with their 95% confidence intervals (CIs) were determined using DerSimonian-Laird random-effects modeling. Heterogeneity across studies was assessed using the Q test ($P < .05$ indicating significant heterogeneity) and the I^2 statistic (21). Publication bias was evaluated using the funnel plot and Egger's test (22). The value of the I^2 statistic was interpreted as follows: 0%–40% indicates that heterogeneity might not be important; 30%–60% may represent moderate heterogeneity; 50%–90% may represent substantial heterogeneity; and 75%–100% may represent considerable heterogeneity (23). A value of $P < .1$ was considered to indicate significant publication bias. Publication bias-adjusted rates of pooled estimates were also obtained using the trim and fill method. If the unadjusted and adjusted rates were similar, the results were considered to be robust against publication bias. Meta-regression analysis was conducted to identify the source of heterogeneity. A value of $P < .05$ was considered to indicate a significant source of heterogeneity. All statistical analyses were performed using R software (version 3.1.2; R Foundation for Statistical Computing, Vienna, Austria) with the "meta" packages.

RESULTS

Literature Selection and Characteristics

A total of 385 non-duplicated publications were identified through the database search (n = 384) and Google (n = 1) (**Fig 1**). An initial screening of titles and abstracts led to the assessment of 34 full-text articles for eligibility. Of these, 9 met the selection criteria and were included (**Table 1**) (11,13–17,24–26). The other 25 articles were excluded because they had a sample size of less than 10 (n = 21), they had no extractable data (n = 2), or the data were included in subsequent articles (n = 2) (**Table E2** [available online at