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Prognostic value of extravascular lung water index in critically ill patients: A systematic review of the literature☆

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Abstract

Background: The prognostic value of extravascular lung water (EVLW) has been widely investigated; however, a wide range of its predictive accuracy has been reported.
Study Design: A meta-analysis of diagnostic test studies was conducted.
Setting and Population: Various patient populations in the intensive care unit were included, such as burned patients and patients with acute lung injury/acute respiratory distress syndrome and sepsis.
Selection Criteria: A computerized search of PubMed, Current Contents, CINAHL, and EMBASE from inception until March 1, 2011, was performed to identify potentially relevant articles. The inclusion criteria were studies investigating the prognostic value of EVLW in critically ill patients. There was no language restriction in the searching.
Index Tests: The EVLW index (EVLWI) was used.
Reference Tests: The outcome was mortality (including in-hospital mortality, intensive care unit mortality, and 28-day mortality).
Results: We analyzed data from 11 studies and 9 countries involving 670 patients. Overall, the EVLWI was significantly higher in nonsurvivors than in survivors, with a mean difference of 5.06 mL/kg (95% confidence interval, −7.53 to −2.58). The heterogeneity was significant with I^2 = 90%. The pooled statistics of diagnostic accuracy together with relevant 95% confidence interval were as follows: sensitivity, 0.81 (0.72-0.88); specificity, 0.66 (0.55-0.76); diagnostic odds ratio, 8.84 (3.83-20.4), positive likelihood ratio, 2.44 (1.69-3.52); negative likelihood ratio, 0.28 (0.16-0.46).
Limitations: The sample sizes of included studies were small.
Conclusion: The EVLWI appears to be a good predictor of mortality in critically ill patients.

1. Introduction

Extravascular lung water (EVLW) refers to the fluid within the lung but outside the vascular compartment. It includes extravasated plasma, intracellular water, lymphatic fluid, and surfactant. In circumstances of heart failure and lung injury, EVLW abnormally increases because of elevated hydrostatic pressure and pulmonary vascular permeability, respectively. A small amount of EVLW is

☆ This report is a meta-analysis. The author states that the report includes every item in the MOOSE checklist for meta-analysis clinical studies.

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often restricted to the interstitial space, but more extensive lung water reaches the distal air space, thereby impairing gas exchange. Extravascular lung water can be estimated by gravimetric method experimentally, which remains to be the golden standard of EVLW estimation. In clinical settings, EVLW can be estimated by physical examination and chest radiograph; both, however, are subject to many confounders, and their accuracy is suboptimal [1]. More recently, indicator dilution methods have been developed and used in clinical settings, and the estimated EVLW has been shown to be closely correlated with that estimated by the golden standard gravimetric method [2-4].

Clinical implications of EVLW have been widely investigated in recent years. Kuzkov et al [5] demonstrated that EVLW was moderately correlated with markers of acute lung injury, including lung compliance, oxygenation ratio, roentgenogram quadrants, and lung injury score. For clinicians, the prognostic value of EVLW is of particular interest, and many studies have focused on this issue. With accumulating evidence, the disparities among studies are evident, and the diagnostic accuracy of EVLWI in predicting mortality remained to be determined. Therefore, we performed a systemic review of the literature to accommodate the increasing body of evidence.

2. Methods

2.1. Data sources and searching strategy

Computerized search of PubMed, Current Contents, CINAHL, and EMBASE was performed to identify potentially relevant articles. Searching period was from inception to March 1, 2011. Our core search consisted of terms related to clinical outcome (*mortality* or *survival* or *outcome* or *prognosis*), combined with the term *extravascular lung water*. The reference lists of identified articles were reviewed manually to search potentially relevant articles. The Meta-analysis of Observational Studies in Epidemiology guidelines for the performance of meta-analyses of observational cohort studies were followed [6].

2.2. Study selection

Two reviewers independently searched literature and identified relevant studies for assessment of data on clinical outcomes and EVLW measurement. The study was considered to be eligible if it was a clinical observational study investigating the predictive value of EVLW in mortality. The methods used to estimate EVLW were not restricted. There was no language restriction on the search and study inclusion. The quality of each included study was assessed according to QUADAS document [7].

2.3. Data extraction

The following data were extracted from each study: year of publication, clinical setting or patient population, sample size, mean age of the patients, disease severity score (Acute Physiology and Chronic Health Evaluation [APACHE] II or Sequential Organ Failure Assessment [SOFA] score), devices for EVLW measurement, EVLW value in survivors and nonsurvivors (expressed as median and range, or mean and SD), time point of EVLW measurement, index of EVLW, cutoff value of EVLW to distinguish between survivors and nonsurvivors, and sensitivity and specificity of EVLW value in predicting mortality. Two reviewers independently extracted the data, and any disagreement was settled by a third opinion.

The numbers of true positive, true negative, false positive, and false negative of each included studies were calculated based on provided sensitivity and specificity. If the study provided median and interquartile range rather than mean and SD, we estimated the mean and SD using formulas described by Hozo et al [8].

2.4. Statistical analysis

Data syntheses comprised 2 parts. The first was to calculate the mean difference of EVLW between survivors and nonsurvivors. Data of the trials were combined using inverse variance method. Pooled effect of mean difference and 95% confidence interval (CI) were computed with a random-effects model when between-study variance was significant ($I^2 > 56\%$), or the fixed effect model when heterogeneity was insignificant. The heterogeneity was explored using statistic I^2, with I^2 less than 30% indicating unimportant heterogeneity, I^2 between 30% and 75% indicating moderate heterogeneity, and I^2 greater than 75% indicating significant heterogeneity. These calculations were performed by using the software Review Manager 5.0.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.) [9]. The second part involved the calculation of diagnostic accuracy of EVLW in predicting mortality. The meta-analysis was performed using summary receiver operating characteristics analysis as described by Rosman AS [10], and the computation was performed using the software Stata 10 (metandi syntax; College Station, TX 77845 USA). The primary statistical analysis was based on a bivariate meta-analytic approach. Based on this model, the pooled sensitivity and specificity, diagnostic odds ratio, and relevant 95% CI were obtained.

3. Results

3.1. Searching results and characteristics of included studies

The initial search identified 210 articles, and 195 were excluded based on of title and/or abstract because they were