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Sensitivity and specificity of ultrasound for the diagnosis of acute pulmonary edema: a systematic review and meta-analysis

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Abstract

Aims: This study aimed to determine the sensitivity and specificity of ultrasound for the diagnosis of acute pulmonary edema by meta-analysis. **Materials and methods:** A systematic search was conducted through the following databases: Cochrane, PubMed, EMBASE and Ovid MEDLINE. Prospective cohort and prospective case-control studies that reported sensitivity and specificity of lung ultrasound in diagnosis of acute pulmonary edema were selected. An independent review of citations was carried out for inclusion and data extraction. Quality assessment was conducted using the QUADAS-2 tool. Sensitivity and specificity were taken from the studied articles and then calculated with the contingency tables. A total of 984 articles were identified but only eight studies (1301 patients) were included in this meta-analysis. One study was a case-control study and seven studies were prospective cohort study. **Results:** The overall sensitivity of ultrasound for the diagnosis of acute pulmonary edema is 97% (95% CI: 96%–98%) and the overall specificity was 98% (95% CI: 97%–99%). **Conclusion:** The diagnostic test accuracy suggests that lung ultrasound using B-lines is a useful and reliable diagnostic tool for critically ill patients with acute pulmonary edema.

Keywords: acute pulmonary edema; diagnosis; dyspnea; lung; ultrasound

Introduction

Understanding the microvascular fluid exchange in the lung is important for knowing the causes of acute pulmonary edema (PE). In a normal lung the outflow of fluid occurs though gaps between the capillary endothelial cells. A sudden increase of hydrostatic pressure in the pulmonary capillaries leads to edema [1]. The common causes of PE include arterial hypertension, severe coronary occlusion, cerebral diseases, pulmonary and heart diseases, infections, and shock [2].

Acute PE is produced by accumulation of the fluid in alveoli and pulmonary interstitial spaces, impairing in this way the diffusion of gases [3]. PE is one of the common causes of acute dyspnea. Selection of more sensitive and specific diagnostic approach of acute PE is a critical issue that continues to gain attention from medical staff. Accurate and rapid determination of the nature of acute dyspnea is an important and challenging issue in the intensive care unit (ICU) and the emergency department (ED) [4]. The common diagnostic methods that are used to determine the cause of acute dyspnea includes B-type natriuretic peptide (BNP) test, N-terminal (NT) proBNP test, X-ray, ultrasound, and thoracic computed tomography (CT) scan. Although chest radiography is the routine examination, CT scan remains the gold standard examination for pulmonary diseases. The chest radiography has some disadvantages, including inapplicability to pregnant women, the non-specific findings, the difficulties in acquiring the posteroanterior and laterolateral projections [4]. On the other hand, CT scan also has limitations such as high dosage of radiation that is required, lack of CT scan facility in certain hospitals, and patient the needs for moving the patient in the radiology room [5].

Diagnosis of acute PE with the non-invasive ultrasound method has been gaining popularity in the past

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decades. Lung ultrasound is a useful diagnosis imaging technique, particularly in a situation when a CT scan cannot be used, and allows a rapid bedside examination and immediate interpretation of scanning report by trained physicians [6]. Besides, the patient will not subject to any form of radiation. The main purpose of this study is to calculate the sensitivity and specificity of lung ultrasound from up-to-date studies regarding the diagnosis of acute pulmonary edema.

Materials and methods

Search strategy

This meta-analysis was carried out by following the PRISMA guidelines and the Cochrane Handbook for Diagnostic Test Accuracy Reviews [7,8]. Systematic search of published literature was carried out for dates prior to 17th July 2016 without limitation of start time in the following databases: Cochrane, PubMed, EMBASE and Ovid MEDLINE. Keywords that used to search in titles and abstracts were included "lung ultrasonography" or "lung ultrasound" and "acute pulmonary edema". Endnote software (version 7) was used to manage the literature.

Inclusion and exclusion criteria for article selection

Our outcome of interest in this study was the diagnosis of acute PE using the lung ultrasound with B-lines. Prospective case-control and prospective cohort studies that involved lung ultrasound B-lines in diagnosis of acute PE were included in this study. Commentaries, letters, reviews, and case reports were excluded from this analysis. Studies that enrolled patients with clinical suspicion of acute PE and acute dyspnea were included. Studies without acute PE and asymptomatic pulmonary diseases were excluded. No restriction was applied to the ultrasound scanning protocol that was used for diagnosis. Lung ultrasound procedure has to be performed by trained personnel at the patient's bed-side.

Titles and abstracts of the literature that were identified were independently reviewed by 2 reviewers. Then, the full-texts in the filtered list of references were reviewed by the same reviewers. If both reviewers had disagreements, a discussion was carried out. The inclusion and exclusion criteria were followed to find out suitable studies for the meta-analysis. All data were extracted by the same reviewers. For quality assessment, the same reviewers independently reviewed the included studies using the QUADAS-2 tool [9]. The QUADAS-2 quality assessment was structured to evaluate the four key points, including patient selection, index test, reference standard, and flow and timing.

Data analysis

Data analyses were performed by using the Stata (version 14) statistical software. Results for sensitivity and specificity of all the included studies were plotted on a forest plot for heterogeneity assessment.

Results

A total of 984 studies were retrieved from PubMed, Ovid MEDLINE, EMBASE and Cochrane databases (fig 1). After removing the duplicate studies and the studies that did not fulfill the inclusion criteria, 8 studies were included in the meta-analysis (1301 patients; Table I) [10-17]. Two studies were performed in the ICU, three studies in the ED, two studies in the ward and one study in a pre-hospital setting and ED. The ultrasonographers of all studies were blinded to the results of the reference standard. Only one study was a case-control study, while the others were prospective cohort studies. Four studies followed the procedure reported by Volpicelli et al [10,14-16,18]. Two studies diagnosed the PE by detecting B-line in anterior and lateral chest and three or more B-lines in at least two zones on each hemithorax [12,13]. Another two studies followed comet-score scanning protocol for diagnosis of PE [11,17]. The QUADAS-2 quality assessment revealed that quality of the included studies was from moderate to high (Table II). Low risk of bias showed that the quality evaluation of the studies is high.

The ultrasound examinations were carried out by trained physicians from the ED and ICU, nurses and medical students (Table III). In three studies the inter-rater reliability was reported. Sensitivity and specificity of included studies are presented in a forest plot (fig 2). The overall sensitivity of lung ultrasound using B-lines for the diagnosis of acute pulmonary edema is 97% (95% CI: 96%–98%), and 98% overall specificity (95% CI: 97%–99%).

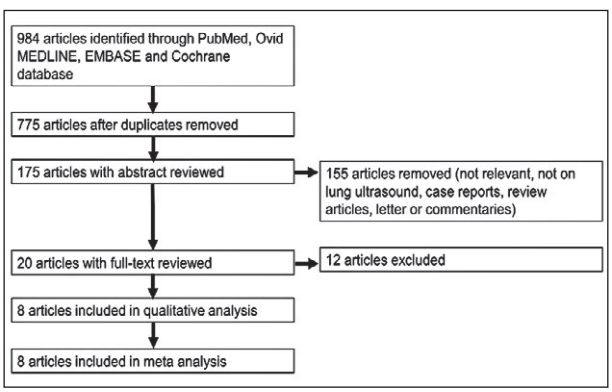

Fig 1. Study selection flow diagram.

Table I. Characteristics of the included studies in the meta-analysis

First author, year of publication	Lichtenstein, 1998 [12]	Lichtenstein, 2008 [13]	Gargani, 2008 [11]	Liteplo, 2009 [14]	Prosen, 2011 [16]	Vitturi, 2011 [17]	Cibinel, 2012 [10]	Mumoli, 2016 [15]
Journal	Intens Care Med	Chest	Eur J Heart Fail	Acad Emerg Med	Crit Care	J Ultras	Intern Emerg Med	Medicine
Study country	France	France	Italy	USA	Slovenia	Italy	Italy	Italy
Place of study	ICU	ICU	CPD	ED	Prehospital and ED	Internal medicine ward	ED	ED
Number of patients	146	260	149	94	218	152	56	226
Ultrasound machine	Hitachi-405, ADR 400	Hitachi-405	Philips Sonos 7500	Sonosite	Sonosite	Toshiba Aplio XV	GE Electric LOGIQ 3	GE Vivid S5
Probe type	3.5 MHz cardiac	5.0 MHz micro-convex	2.5–3.5 MHz cardiac	2.5 MHz curved-array	Not specified	3.5 MHz convex	3.5 MHz convex	2.0–5.5 MHz curved-array
Protocol	Lichtenstein	Lichtenstein	Comet score	Volpicelli	Volpicelli	Comet score	Volpicelli	Volpicelli
Reference standard	Blinded	Blinded	Blinded	Blinded	Final hospital diagnostic	Blinded	Final hospital diagnostic	Final hospital diagnostic
Examination time	<1 min	<3 min	<5 min	<5 min	<1 min	<3 min	<5 min	<6 min
Study type	Case-control	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort	Cohort
Sensitivity, % (95% CI)	100	97	76.2	58 (36–77)	100 (98–100)	97	93.6	95.3 (92.6–98.1)
Specificity, % (95% CI)	97	95	88	85 (69–95)	95 (91–100)	79	84	88.2 (84.0–92.4)
Conflict of interest	Unclear	Unclear	Unclear	Unclear	None	None	None	None

ICU – intensive care unit; ED – emergency department; CPD – cardiology and pneumology division; CI – confidence interval

Table II. QUADAS-2 assessment of methodologic quality of the included studies

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Criterion standard	Flow and timing	Patient selection	Index test	Criterion standard
Lichtenstein, 1998 [12]	High	Unknown	Unknown	High	Low	Low	Low
Lichtenstein, 2008 [13]	Unknown	Low	Low	Unknown	Low	Low	Low
Gargani, 2008 [11]	Low	Unknown	Low	Low	Low	Low	Low
Liteplo, 2009 [14]	Unknown	Low	Low	Low	Low	Low	Low
Prosen, 2011 [16]	Unknown	Low	Low	Low	Low	Low	Low
Vitturi, 2011 [17]	Low	Low	Low	Unknown	High	High	Low
Cibinel, 2012 [10]	Low	Low	Low	Low	Low	Low	Low
Mumoli, 2016 [15]	Low	Low	Low	Low	Low	Low	Low

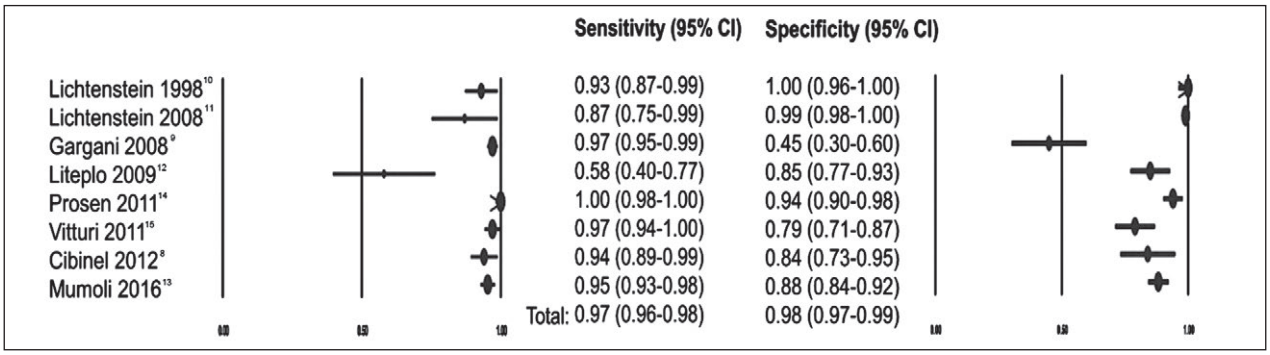

Fig 2. Forest plot of sensitivity and specificity of the included studies. CI: confidence interval.

Table III. Characteristics of ultrasonographers in the included studies

Study	Number of ultrasonographer	Training level of ultrasonographer	Inter-rater reliability
Lichtenstein, 1998 [12]	2	ICU physicians	Not reported
Lichtenstein, 2008 [13]	2	ICU physicians	Not reported
Gargani, 2008 [11]	Not reported	Not reported	Not reported
Liteplo, 2009 [14]	7	2 Emergency physicians, 5 trained medical students	0.82
Prosen, 2011 [16]	10	Emergency physicians	Not reported
Vitturi, 2011 [17]	2	Not reported	0.98
Cibinel, 2012 [10]	Not reported	Emergency physicians	0.92
Mumoli, 2016 [15]	5	Trained nurses	Not reported

Discussions

A rapid diagnosis using non-invasive methods ensures an appropriate and timely treatment. In the present study, the lung ultrasound using B-lines were evaluated for sensitivity and specificity in the diagnosis of acute PE. Three studies that employed scanning protocol of Volpicelli et al [18] showed different values of sensitivity and specificity as different methodologies were applied in the mentioned studies. The ultrasound scanning in the Liteplo et al study was performed by trained medical students, Mumoli et al study was conducted by trained nurses, and Cibinel et al study was implemented by attending physicians [10,14,15]. Operation of scanning by different methodologies and people with different training levels leads to inconsistent results.

The comet tail artifacts B-line was used for the detection of extravascular lung water and it enables differentiation of acute PE from chronic obstructive pulmonary disease [12]. The ultrasound scanning protocol described by Volpicelli et al involved a single scan on eight zones at anterior and lateral of each lung [18] and they were interpreted as abnormal when two or more zones presented B-lines in both hemithoraces. The protocol of Lichtenstein et al involved scanning of comet-tail artifact produced from pleural line [12]. Comet score scanning protocol as described by Picano et al [19] was applied by Vitturi et al [17] and Gargani et al [11] in determination of extravascular lung water; the test was considered as abnormal when the number of B-lines was greater than five [11] or eight [17]. Subgroup analysis was not carried out in these studies and this contributed to the heterogeneity of our data.

The sensitivity of chest radiography, BNP, and NT proBNP tests in the diagnosis of acute dyspnea ranged from 56%–93%, 86%–99% and 92%–97%, respectively, while the specificity ranged from 51%–98%, 74%–99% and 44%–93%, respectively [11,15-17,20-25]. Although high sensitivity and specificity of the mentioned diagnostic methods were reported, real-time valuation of the outcome is almost impossible and the assessments are not available in the pre-hospital setting. Besides, the BNP test is not accessible to all clinicians in hospitals.

Limitations in this study included incomplete retrieval of identified research, publishing bias, reporting bias, and inconsistencies of the ultrasonic inspection method. Besides, patients included in analysis were from different populations. A larger number of patients presenting with acute PE should be included in future studies. In addition, standardization of ultrasound scanning protocol and qualification of ultrasonographers should be applied to minimize heterogeneity of the analysis.

Conclusions

The diagnostic test accuracy suggests that lung ultrasound using B-lines is one of the best tools for the diagnosis of acute PE especially for the critically ill patients. Lung ultrasound provides high sensitivity and specificity diagnosis for moderate to severe acute PE. In addition, negative lung ultrasound helps to exclude the PE.

Conflict of interest: none

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