Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Review Article

Methods for Qualitative and Quantitative Assessment of Extravascular Lung Water–Clinical Application, Advantages, and Disadvantages

Gergana Petkova – Ivanova[1,4]*, Ivanka Karavelikova[2,5], Stanislav Karamitev[3,6]

[1]Department of Anesthesiology, Emergency and Intensive Care Medicine, Medical University of Plovdiv, Bulgaria.

[2]Department of Paediatrics and Medical Genetics "Prof. Dr.Ivan Andreev", Medical Faculty, Medical University of Plovdiv, Bulgaria.

[3]Department of Orthopaedics and Traumatology, Medical University of Plovdiv, Bulgaria.

[4]Clinic of Anesthesiology and Intensive care, University Hospital St. George, Plovdiv, Bulgaria.

[5]Department of Paediatrics, University Hospital St George, Plovdiv, Bulgaria.

[6]Clinic of Orthopaedics and Traumatology, University Hospital St George, Plovdiv, Bulgaria.

ARTICLE INFO

Article history:
Received 01 April 2025
Revised 21 April 2025
Accepted 05 May 2025

Keywords:
Acute respiritory distress syndrome;
Extravascular lung water;
Imaging methods;
Thermodilutional technique

ABSTRACT

Background: Lung edema is a life-threatening condition associated with prolonged intensive care unit stay and high mortality. The increased extravascular lung water (EVLW) causes impaired lung compliance and refractory hypoxemia. Although there are promising methods for the detection of EVLW, there is not yet a universally accepted one, and a systematic approach to the problem is missing. The discussion in this article is on the potential of the described assessment methods and techniques and reveals the strong and weak points according to their practical application.
Methods: The discussion in this article is on the potential of the described assessment methods and techniques. According to our comparative analysis, the strong and weak points regarding their practical application are presented in a table.
Results: This review article summerizes advantages and disadvantages of the most common methods in clinical practice.
Conclusion: Although there are promising methods for the detection of EVLW, there is not yet a universally accepted one, and a systematic approach to the problem is yet to be found.

Introduction

The amount of extravascular lung water (EVLW) is a determining factor for the clinical outcome in patients with ARDS [1].

Physiologically EVLW is considered to be around 500 ml [2] or 7 ml/kg predicted body weight [3]. Its amount depends on the balance between these forces:

$$EVLW = (L_p x S)((P_c - P_i) - k(\Pi_c - \Pi_i)) - \text{Lymph flow} \ [4]$$

where EVLW=extravascular lung water (ml), Lp=the hydraulic conductivity for water (cm/min/mmHg), S=surface area (cm^2), Pc and Pi=the hydrostatic pressure within the capillary and interstitial spaces, respectively (mmHg), s=the reflection coefficient for protein (no units), and Pc and Pi=the oncotic pressure within the capillary and interstitial spaces (mmHg).

Dysregulation in the balance of these forces causes abnormal elevation of EVLW, clinically presented as pulmonary edema [5].

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: gergana.ivanova@mu-plovdiv.bg

An approach for the estimation of the EVLW must be found for practice: it should be informative about the development of pulmonary edema before clinical manifestation. The ideal test should be accurate, sensitive, repeatable, comparative, noninvasive, practical and inexpensive [6].

Methods

Imaging methods

What is common in all imaging methods is that they are informative for the volume and spatial processes [4]. Every picture (pixel) or volume (voxel) element in a cross-sectional image of the lung represents a specific volume [4]. So, the variability of the image depends on the concentration (for example, ml EVLW/ml lung). Since the lung is an air-containing structure, the amount of parenchyma within each voxel can change depending on the underlying state of lung inflation (lung volume) [4]. To quantify EVLW, the signal from the entire organ should be investigated. Even though the specificity is different, no imaging method (except the positron emission tomography) cannot estimate quantitatively the amount of EVLW, but they all give information about the total water content (intravascular and extravascular) [4] (Table 1).

Table 1- compare advantages and disadvantages of available methods in estimating EVLW from practical point of view

Method	Advantages	Disadvantages	References
Gravimetry	-referent for EVLW measurement -low price	-can be applied only in autopsy	[7-8]
Chest radiography	-easy applied in practice -can be done next to the patient's bed -noninvasive -gives information about possible etiology -repeatable -non expensive	-non quantitative method -relative subjectivity of the method -depends on the technical setting: equipment quality; preexposition; rotation/ posture of the patient, appliance of PEEP - depends on the clinical experience of the doctor who reads the chest xray -no sensitivity about small changes in the amount of EVLW	[9–11]
Computed tomography (CT)	-detailed information for structural changes -correlates with local pulmonary edema -noninvasive	- cannot be applied next to the patient's bed - cannot be applied for routine, repeatable investigations -relatively high doses of ionising radiation -expensive	[4,12]
Magnetic resonance imaging (MRI)	-high image credibility -no radiation during the investigation -comparable -noninvasive	-inability to be done next to the patient's bed -sensitive to the cardiac and respiratory movements -long duration of the investigation -cannot be applied for routine investigation of critically ill patients -high cost	[4,8,13]
Positron emission tomography (PET)	-precise in measurement of EVLW	-radioactive markers are used -not appliable for routine use -expensive -difficult access	[14]
Electrical impedance tomography (EIT)	-noninvasive -easy to be applied next to the patient's bed -repeatable -informative for ventilation features - non expensive	- it is not in the routine practice -missing protocols for proper position of the belt -non quantitative -cannot be applied whe there is chest bandage	[15-16]
Lung ultrasound (LUS)	-no radiation -repeatable -can be applied next to the patient's bed -quick access	-depends on the examinator experience -not appliable in chest trauma, obese patients, subcutaneous emphysema -Not quantitative test - contamination possibility	[17–21]

	- non expensive -informative for other pathologies		
Double indicator dilution method	-quantitative method -good correlation compared with the gravimetry - repeatable -applied next to the patient's bed	-invasive method -practically slow and difficult to be applied routinely -used dye could have impaired clearance in patients with compromised liver function -relatively expensive	[22]
Transpulmonary termodilution method (TPTD)	-quantitative method -good correlation with double indicator method and gravimetry -repeatable -mini-invasive -can be applied next to the patient's bed -no radiation or dye needed	- Mini invasive method - limitations: lung resection, massive obstruction of pulmonary vessel, high PEEP (above 15), continuous renal replacement therapy	[23–25]

Chest radiography (X-ray)

This is the most used imaging method in practice [26]. It provides information about the presence of pulmonary edema, the overall distribution, and the possible etiology. The EVLW should be increased by at least 30% [27] in order to detect some of the characteristic features: pulmonary congestion, peribronchial “cuffing,” perihilar “haze,” Kerley’s line, and the interstitial pattern of the radiographic patterns. As EVLW increases, the radiographic densities occupy a greater fraction of the total lung airspace; as edema worsens, densities become more and more “white” [6].

Research by Saugel et al. [28] on 71 patients confirms only 55% diagnostic accuracy in recognition of increased levels of EVLW. This fact proves that chest X-ray is not suitable for early recognition and estimation of pulmonary edema [8].

Computed tomography (CT)

Computed tomography is based on differential attenuation of X-ray absorption for cross-sectional imaging of the thorax and subsequent regional assessment of lung pathologies [26]. It provides detailed information about the type of pulmonary pathologies, including airway processes, interstitial ones, and thromboembolic incidents [26]. The main advantage of using CT over conventional radiography concerning EVLW measurement is that the density of the infiltrates can be determined quantitatively [4]. Also, during the transverse section, the spatial distribution of the edema can be detected [4]. Measurement of the density of the process can identify when EVLW is elevated by 50% (experimental animal study) [12].

In a research study, Leiser et al. [29] establish the ELW index (excess lung weight), which is achieved after manual segmentation and calculations of the lung CT scan. The index is compared with EVLW delivered from transpulmonary thermodilution, SOFA score, and oxygenation index, and there is a strong correlation [29]. This maneuver is time-consuming and specific and is not applicable in everyday practice.

Magnetic resonance imaging (MRI)

Technical development in the recent years allows a wide range of diagnostic options using MRI in pulmonary investigation: regional ventilation, perfusion, perfusion/ventilation mismatch, diffusion, and lung water estimation [30]. The estimation of EVLW is based on the ability to align hydrogen nuclei (protons) of water in the direction of an externally applied magnetic field. When the patient lies in a magnetic field being radiated with electromagnetic radiation, a resonance develops from the absorption and the consequent release of energy as the pulse is applied and then discontinued. This energy can be detected by properly placed amplifiers, producing signals with different strengths, varying according to the strength of the magnetic field and the frequency of the radio frequency pulse. The spin echo sequence is the only one to this moment to measure extravascular lung water [4]. A lot of studies report a good correlation between EVLW measured by MRI and the values measured by the gold standard—gravimetric method [31–35].

A big advantage is the absence of ionizing radiation for the measurements [13]. An issue to consider is that normal to mildly edematous lungs produce weak signals, and MRI can underestimate true lung water content in 2-4% of the cases [34, 36]. Due to the method’s limitations, at this point MRI is more suitable for research-based applications of measuring EVLW than for clinical use. Also, most of the techniques used to date cannot differentiate intravascular lung water from extravascular lung water, complicating interpretation when pulmonary blood volumes are not constant. The practical application of MRI measurement of EVLW depends mainly on developing rapid and convenient techniques.

Lung ultrasound

An excellent diagnostic potential of lung ultrasound is presented by Lichtenstein et al. [37]. This method is reliable in diagnosing a variety of lung diseases: pleural effusion [38], parenchymal consolidation [39], and pneumothorax [40-41]. The presence of B lines is significant for diagnosing lung edema [42]. They are visualized as hyperechogenic artifacts, falling down from the pleural line, well outlined, synchronically moving with the respiratory movements [42]. If more than two B lines are visualized in an intercostal space, this is considered a diagnostic marker for interstitial syndrome [42]. Lung ultrasound technique has several advantages as a diagnostic tool: it is noninvasive, applicable next to the patient's bed, and repeatable [37]. With the admission of the new ARDS definition, it is expected for wider incorporation of this method in clinical practice.

Positron emission tomography (PET)

This is a nuclear medicine imaging technique that uses radioactively labeled positron-emitting isotope tracers, and by tracing them, lung water can be measured. The tracers are administered separately (intravenously and inhalationally) to distribute between the total and intravascular spaces of the lung. The emissions of these tracers are detected and reconstructed to form an image. PET scanner is considered a reliable standard of measuring EVLW because the tomographic image can be created and normalized for the attenuation of the structure being imaged using a transmission scan [43].

EVLW measurements by PET scan have good correlation with the gravimetric measured ones ($r = 0.86$–0.93) [44–45]. PET scan measurements have a high degree of reproducibility, as the coefficient of variations in the second measurement is <5% [44]. The method shows exquisite sensitivity—as little as 1 ml of additional extravascular water can be detected [4, 44].

Electrical impedance tomography (EIT)

The impedance technique is a noninvasive, non-radiational imaging method for personalized monitoring a range of lung function parameters, including functional residual capacity, regional ventilation, and perfusion [46]. This method can be applied next to the patient's bed [4, 15]. Measurement of lung water is based on the principle that air and fluid have different resistance to current flow. As intrathoracic water increases, electrical conductance across lungs improves and impedance decreases [47]. Although it is a measure of total pulmonary fluid rather than a direct measure of EVLW, Kunst et al. [48] demonstrate a strong correlation between measured EVLW by EIT and the thermal dye dilution technique. A new parameter, Lung Water Ratio (LWREIT) is established [49].

EVLW occupies the dependent parts of the lung, and the ventilation is in nondependent ones. These changes can be monitored by EIT. The body position also could cause gravity connected with redistribution of extravascular water and ventilatory changes, which can be reported. These ventilatory changes due to the body position determine EVLW and other fluid processes in the lung, for they could not change the ventilation after the change in the body position. This is how LWREIT is determined. In an animal model study, Trepte et al. [49] show good correlation between LWREIT proved pulmonary edema and the measured one by gravimetry method. LWREIT itself cannot assure quantitative information for pulmonary edema.

Indicator Dilution techniques

The double colorimetric thermodilutional method (TTD) consists of the injection of cold serum and an indicator (protein-bound coloring agent). It is considered that the thermoindicator will diffuse and fulfill the whole intrathoracic compartment, and the dye indicator will remain in the intravascular compartment. The difference in the volume of distribution is equal to EVLW [50]. This method is used in clinical practice, as Eisenberg et al. [51] prove that managed fluid therapy according to the values of EVLW affects the patient's outcome.

Nevertheless, the potential [52] of the method is slow for routine practice. Still, this method is important for investigating EVLW abilities and is fundamental for the development of the transpulmonary thermodilution technique [50].

Transpulmonary thermodilution (TPTD)

Widely validated method for EVLW measurement is PICCO—thermodilution technique, based on the Steward Hamilton principle [23]. It is considered a minimally invasive method, as cannulation of the central vein and peripheral artery is only needed [53]. Cold serum is used as a thermal indicator [53].

The TPTD technique is validated by comparing results measured by the double colorimetric thermodilutional method [23], by the gravimetric method in animals [54-55], and by gravimetry in people [56]. Tagami et al. [56] in an autopsy study prove a strong correlation coefficient of 0.90 in EVLW measurement between TPTD and gravimetry. Via TPTD, it is possible to establish even a small elevation of EVLW, as after bronchoalveolar lavage [57]. Tagami et al. [58] label EVLW as "the bridge between pathology and clinical manifestation of ARDS."

High values of EVLW are associated with the severity of lung injury [59]. TPTD via PICCO monitoring provides detailed hemodynamic monitoring. EVLW and its dynamic changes have strong prognostic value for intensive care stay and mortality [60]. Moreover, EVLW is considered a helpful marker in the evaluation and guidance of the infusion strategy [61-64]. No serious complications are not being reported [65].

A change in the EVLW values during the first 48 hours is associated with 28-day survival [66]. EVLW changes represent the pathophysiological status of ARDS development. A systemic approach should be accepted for early recognition and evaluation of EVLW. In general, all the imaging methods present with limitations, affecting the accuracy or the range of application. TPTD measured EVLW over consecutive days is a quantitative and sensitive method and can provide rapid and sensitive information at the bedside. The benefit of detecting elevation of EVLW is applying early goal directed treatment.

Results

A detailed discussion of the advantages and disadvantages of the most common methods in clinical practice for estimation of EVLW was performed. Since imaging methods so far are the most used in clinical practice for estimation of the edema, the last decades TPTD takes advantage in the routine clinical practice. EVLW is undoubtedly a prognostic marker for severity, mortality and prognosis of ARDS and its values are of immense importance, regarding treatment behaviour.

Conclusion

There are several diagnostic approaches to measuring EVLW, validated against the gold standard—gravimetry. Each technique varies in its strong and weak features, also in practical accessibility. EVLW has the potential to be valuable for both clinicians and researchers for optimizing and taking advances in the diagnosis of ARDS. To fulfill this potential, optimization of the existing technologies should produce improvements in accuracy, sensitivity, and reproducibility in the measures.

References

[1] Laggner A, Kleinberger G, Haller J, Lenz K, Sommer G, Druml W. Bedside estimation of extravascular lung water in critically ill patients: comparison of the chest radiograph and the thermal dye technique. Intensive Care Med. 1984;10:309-13.

[2] Lewis FR, Elings VB, Sturm JA. Bedside measurement of lung water. J Surg Res. 1979;27(4):250-61.

[3] Kushimoto S, Taira Y, Kitazawa Y, Okuchi K, Sakamoto T, Ishikura H, et al. PiCCO Pulmonary Edema Study Group. The clinical usefulness of extravascular lung water and pulmonary vascular permeability index to diagnose and characterize pulmonary edema: a prospective multicenter study on the quantitative differential diagnostic definition for acute lung injury/acute respiratory distress syndrome. Crit Care. 2012;16(6):R232.

[4] Lange NR, Schuster DP. The measurement of lung water. Crit Care. 1999;3. Available from: http://ccforum.com

[5] Sakr Y, Vincent JL, Reinhart K, Groeneveld J, Michalopoulos A, Sprung CL, et al. High tidal volume and positive fluid balance are associated with worse outcome in acute lung injury. Chest. 2005;128(5):3098-108.

[6] Staub NC. Clinical use of lung water measurements. Report of a workshop. Chest. 1986;90(4):588-94.

[7] Michard F, Fernandez-Mondejar E, Kirov MY, Malbrain M, Tagami T. A new and simple definition for acute lung injury. Crit Care Med. 2012;40(4):1004-6.

[8] Fernández-Mondéjar E, Castaño-Pérez J, Rivera-Fernández R, Colmenero-Ruiz M, Manzano F, Pérez-Villares JM, et al. Quantification of lung water by transpulmonary thermodilution in normal and edematous lung. J Crit Care. 2003;18(4):253-8.

[9] Meade MO, Cook RJ, Guyatt GH, Groll R, Kachura JR, Bedard M, et al. Interobserver variation in interpreting chest radiographs for the diagnosis of acute respiratory distress syndrome. Am J Respir Crit Care Med. 2000;161(1):85-90.

[10] Rubenfeld GD, Caldwell E, Granton J, Hudson LD, Matthay MA. Interobserver variability in applying a radiographic definition for ARDS. Chest. 1999;116(5):1347-53.

[11] Halperin BD, Feeley TW, Mihm FG, Chiles C, Guthaner DF, Blank NE. Evaluation of the portable chest roentgenogram for quantitating extravascular lung water in critically ill adults. Chest. 1985;88(5):649-52.

[12] Forster BB, Muller NL, Mayo JR, Okazawa M, Wiggs BJR, Pare PD. High-resolution computed tomography of experimental hydrostatic pulmonary edema. Chest. 1992;101(5):1434-7.

[13] Effros RM, Pornsuriyasak P, Porszasz J, Casaburi R. Indicator dilution measurements of extravascular lung water: basic assumptions and observations. Am J Physiol Lung Cell Mol Physiol. 2008;294:L1023-31.

[14] Wollmer P, Rhodes CG. Positron emission tomography in pulmonary edema. J Thorac Imaging. 1988;3(3):44-50.

[15] Minev I, Jukic V, Gogova T, Tarykova N. Personalized approach in defining the level of interest during lung electrical impedance tomography. Bulg Chem Commun. 2023;55(Special Issue C):75-9.

[16] Minev I. Unconventional application of electrical impedance tomography in patients with significant thoracic deformities due to trauma. Intensive Care Med Exp. 2024;12(S1):642-3.

[17] Soldati G, Demi M, Demi L. Ultrasound patterns of pulmonary edema. Ann Transl Med. 2019;7(S1):S16.

[18] Wooten WM, Shaffer LET, Hamilton LA. Bedside

ultrasound versus chest radiography for detection of pulmonary edema: a prospective cohort study. J Ultrasound Med. 2019;38(4):967-73.

[19] Phillips CR, Chesnutt MS, Smith SM. Extravascular lung water in sepsis-associated acute respiratory distress syndrome: indexing with predicted body weight improves correlation with severity of illness and survival. Crit Care Med. 2008;36(1):69-73.

[20] Lichtenstein DA. Lung ultrasound in the critically ill. Ann Intensive Care. 2014;4:1. Available from: http://www.annalsofintensivecare.com/content/4/1/1

[21] Muradali D. Can ultrasound probes and coupling gel be a source of nosocomial infection in patients undergoing sonography? An in vivo and in vitro study. AJR Am J Roentgenol. 1995;164(6):1521-4.

[22] Boussat S, Jacques T, Levy B, Laurent E, Gache A, Capellier G, et al. Intravascular volume monitoring and extravascular lung water in septic patients with pulmonary edema. Intensive Care Med. 2002;28(6):712-8.

[23] Sakka SG, Rühl CC, Pfeiffer UJ, Beale R, McLuckie A, Reinhart K, et al. Assessment of cardiac preload and extravascular lung water by single transpulmonary thermodilution. Intensive Care Med. 2000;26(2):180-7.

[24] Sakka SG, Klein M, Reinhart K, Meier-Hellmann A. Prognostic value of extravascular lung water in critically ill patients. Chest. 2002;122(6):2080-6.

[25] Schreiber T, Hüter L, Schwarzkopf K, Schubert H, Preussler N, Bloos F, et al. Lung perfusion affects preload assessment and lung water calculation with the transpulmonary double indicator method. Intensive Care Med. 2001;27(11):1814-8.

[26] Gupta RK, Nathani N, Mishra P. Methods of measuring lung water. Intensive Care Soc. 2012;13(3).

[27] Snashall PD, Keyes SJ, Morgan BM, McAnulty RJ, Mitchell-Heggs MA, McLvor JM, et al. The radiographic detection of acute pulmonary oedema: a comparison of radiographic appearances, densitometry and lung water in dogs. Br J Radiol. 1981;54(640):277-88.

[28] Saugel B, Ringmaier S, Holzapfel K, Schuster T, Phillip V, Schmid RM, et al. Physical examination, central venous pressure, and chest radiography for the prediction of transpulmonary thermodilution-derived hemodynamic parameters in critically ill patients: a prospective trial. J Crit Care. 2011;26(4):402-10.

[29] Leiser P, Kirschning T, Weiß C, Hagmann M, Schoettler J, Centner FS, et al. A quantitative CT parameter for the assessment of pulmonary oedema in patients with acute respiratory distress syndrome. PLoS One. 2020;15(11):e0241048.

[30] Hopkins SR, Levin DL, Emami K, Kadlecek S, Yu J, Ishii M, et al. Advances in magnetic resonance imaging of lung physiology. J Appl Physiol. 2007;102(3):1244-54.

[31] Caruthers SD, Paschal CB, Pou NA, Roselli RJ, Harris TR. Regional measurements of pulmonary edema by using magnetic resonance imaging. J Appl Physiol. 1998;84(6):2143-53.

[32] Phillips DM, Man SF, Froese AB. Assessment of temporal changes in pulmonary edema with NMR imaging. J Appl Physiol. 1989;66(3):1197-208.

[33] Wexler HR, Nicholson RL. Quantitation of lung water by nuclear magnetic resonance imaging. Invest Radiol. 1985;20(7):583-90.

[34] Cutillo AG, Morris AH. Determination of lung water content and distribution by nuclear magnetic resonance imaging. J Thorac Imaging. 1986;1(3):39-51.

[35] Morris AH, Blatter DD, Case TA, Cutillo AG, Ailion DC, Durney CH, et al. A new nuclear magnetic resonance property of lung. J Appl Physiol. 1985;58(3):759-62.

[36] Cutillo AG, Goodrich KC, Ganesan K, Watanabe S, Ailion DC, Albertine KH, et al. Lung water measurement by nuclear magnetic resonance: correlation with morphometry. J Appl Physiol. 1995;79(6):2163-8.

[37] Lichtenstein D, Goldstein I, Mourgeon E, Cluzel P, Grenier P, Rouby JJ. Comparative diagnostic performances of auscultation, chest radiography, and lung ultrasonography in acute respiratory distress syndrome. Anesthesiology. 2004;100(1):9-15.

[38] Lichtenstein D. Feasibility and safety of ultrasound-aided thoracentesis in mechanically ventilated patients. Intensive Care Med. 1999;25(9):955-8.

[39] Yang PC, Luh KT, Chang DB, Yu CJ, Kuo SH, Wu HD. Ultrasonographic evaluation of pulmonary consolidation. Am Rev Respir Dis. 1992;146(3):757-62.

[40] Lichtenstein DA, Menu Y. A bedside ultrasound sign ruling out pneumothorax in the critically ill: lung sliding. Chest. 1995;108(5):1345-8.

[41] Lichtenstein D, Mezière G, Biderman P, Gepner A. The "lung point": an ultrasound sign specific to pneumothorax. Intensive Care Med. 2000;26(10):1434-40.

[42] Volpicelli G, Elbarbary M, Blaivas M, Lichtenstein DA, Mathis G, Kirkpatrick AW, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med. 2012;38(4):577-91.

[43] Schuster DP. Positron emission tomography: theory and its application to the study of lung disease. Am Rev Respir Dis. 1989;139(3):818-40.

[44] Velazquez M, Haller J, Amundsen T, Schuster DP. Regional lung water measurements with PET: accuracy, reproducibility, and linearity. J Nucl Med. 1991;32(4):719-25.

[45] Schuster DP, Marklin GF, Mintun MA. Regional changes in extravascular lung water detected by positron emission tomography. J Appl Physiol. 1986;60(4):1170-8.

[46] Bodenstein M, David M, Markstaller K. Principles of electrical impedance tomography and its clinical application. Crit Care Med. 2009;37(2):713-24.

[47] Pomerantz M, Baumgartner R, Lauridson J, Eiseman B. Clinical evaluation of transthoracic electrical impedance as a guide to intrathoracic fluid volumes. Ann Surg. 1970;171(5):686-94.

[48] Kunst PW, Vonk Noordegraaf A, Raaijmakers E, Bakker J, Groeneveld AB, Postmus PE, et al. Electrical impedance tomography in the assessment of extravascular lung water in noncardiogenic acute respiratory failure. Chest. 1999;116(6):1695-702.

[49] Trepte CJ, Phillips CR, Solà J, Adler A, Haas SA, Rapin M, et al. Electrical impedance tomography (EIT) for quantification of pulmonary edema in acute lung injury. Crit Care. 2016;20(1):6.

[50] Brown LM, Liu KD, Matthay MA. Measurement of extravascular lung water using the single indicator method in patients: research and potential clinical value. Am J Physiol Lung Cell Mol Physiol. 2009;297(4):L547-58.

[51] Eisenberg PR, Hansbrough JR, Anderson D, Schuster DP. A prospective study of lung water measurements during patient management in an intensive care unit. Am Rev Respir Dis. 1987;136(3):662-8.

[52] Mitchell JP, Schuller D, Calandrino FS, Schuster DP. Improved outcome based on fluid management in critically ill patients requiring pulmonary artery catheterization. Am Rev Respir Dis. 1992;145(5):990-8.

[53] Litton E, Morgan M. The PiCCO monitor: a review. Anaesth Intensive Care. 2012;40(3):393-409.

[54] Katzenelson R, Perel A, Berkenstadt H, Preisman S, Kogan S, Sternik L, et al. Accuracy of transpulmonary thermodilution versus gravimetric measurement of extravascular lung water. Crit Care Med. 2004;32(7):1550-4.

[55] Kirov MY, Kuzkov VV, Kuklin VN, Waerhaug K, Bjertnaes LJ. Extravascular lung water assessed by transpulmonary single thermodilution and postmortem gravimetry in sheep. Crit Care. 2004;8(6):R451-8.

[56] Tagami T, Kushimoto S, Yamamoto Y, Atsumi T, Tosa R, Matsuda K, et al. Validation of extravascular lung water measurement by single transpulmonary thermodilution: human autopsy study. Crit Care. 2010;14(5):R162.

[57] Dres M, Teboul JL, Guerin L, Anguel N, Amilien V, Clair MP, et al. Transpulmonary thermodilution enables to detect small short-term changes in extravascular lung water induced by a bronchoalveolar lavage. Crit Care Med. 2014;42(8):1869-73.

[58] Tagami T, Sawabe M, Kushimoto S, Marik PE, Mieno MN, Kawaguchi T, et al. Quantitative diagnosis of diffuse alveolar damage using extravascular lung water. Crit Care Med. 2013;41(9):2144-50.

[59] Martin GS, Eaton S, Mealer M, Moss M. Extravascular lung water in patients with severe sepsis: a prospective cohort study. Crit Care. 2005;9(2):R74-82.

[60] Letourneau JL, Pinney J, Phillips CR. Extravascular lung water predicts progression to acute lung injury in patients with increased risk. Crit Care Med. 2012;40(3):847-54.

[61] Craig TR, Duffy MJ, Shyamsundar M, McDowell C, O'Kane CM, Elborn JS, et al. A randomized clinical trial of hydroxymethylglutaryl-coenzyme a reductase inhibition for acute lung injury (the HARP study). Am J Respir Crit Care Med. 2011;183(5):620-6.

[62] Kirov MY, Kuzkov VV, Bjertnaes LJ. Extravascular lung water as a target for intensive care. ICU Manag Pract. 2019;19(1):46-50.

[63] Wang H, Cui N, Su L, Long Y, Wang X, Zhou X, et al. Prognostic value of extravascular lung water and its potential role in guiding fluid therapy in septic shock after initial resuscitation. J Crit Care. 2016;33:106-13.

[64] Cordemans C, De Laet I, Van Regenmortel N, Schoonheydt K, Dits H, Huber W, et al. Fluid management in critically ill patients: the role of extravascular lung water, abdominal hypertension, capillary leak, and fluid balance. Ann Intensive Care. 2012;2(Suppl 1):S1.

[65] Belda FJ, Aguilar G, Teboul JL, Pestaña D, Redondo FJ, Malbrain M, et al. Complications related to less-invasive haemodynamic monitoring. Br J Anaesth. 2011;106(4):482-6.

[66] Tagami T, Nakamura T, Kushimoto S, Tosa R, Watanabe A, Kaneko T, et al. Early-phase changes of extravascular lung water index as a prognostic indicator in acute respiratory distress syndrome patients. Ann Intensive Care. 2014;4(1):27.