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COMMENTARY

Lung water assessment: from gravimetry to wearables

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Abstract
Several techniques are now available to detect and quantify pulmonary edema, from the laboratory postmortem method (gravimetry) to non-invasive wearable sensors. In critically ill patients with adult respiratory distress syndrome (ARDS), computed tomography scans are often performed to visualize lung lesions and quantify lung aeration, but their value seems somewhat limited to quantify pulmonary edema on a routine basis and of course to track changes with therapy. In this context, transpulmonary thermodilution is a convenient technique. It is invasive but most patients with ARDS have a central line and an arterial catheter in place. In addition to extravascular lung water measurements, transpulmonary thermodilution enables the measurement of hemodynamic variables that are useful to guide fluid and diuretic therapy. Echo probes are about to replace the stethoscope in our pocket and, if B lines (aka comet tails) do not allow a real quantification of pulmonary edema, they are useful to detect an increase in lung water. Finally, wireless and wearable sensors are now available to monitor patients on hospital wards and beyond (home monitoring). They should enable the detection of pulmonary congestion at a very early stage, and if combined with a proactive therapeutic strategy, have potential to improve outcome.

Keywords Pulmonary edema · Lung water · Transpulmonary thermodilution · Point of care ultrasound · Wearable

1 Introduction

Pulmonary edema is a common cause of respiratory failure characterized by an accumulation of fluid in the interstitial and alveolar space. It may result from an increase in pulmonary capillary pressure (aka hydrostatic pulmonary edema) or an increase in pulmonary capillary permeability (aka acute lung injury and adult respiratory distress syndrome—ARDS) or both. Several methods have been proposed to quantify lung water. They are useful to detect pulmonary edema at an early stage or when chest X-rays are difficult to interpret, which is often the case in supine ICU patients [1]. They also have value to assess the effects of diuretic therapy or ultrafiltration, and to predict outcome in patients with ARDS [1].

The gravimetric method is known as the reference to measure lung water. This is a laboratory post-mortem technique that consists in weighting the lungs before and after desiccation (Fig. 1). The weight difference gives a precise measure of the total lung water content. Assuming red blood cells do not cross the alveolar-capillary barrier (which is actually not always true), a comparison of the hematocrit in systemic blood and lung specimen is used to estimate the intravascular lung water, which is subtracted from total lung water to calculate extravascular lung water (EVLW).

Computed tomography (CT) scans are regularly performed in patients with ARDS. They enable the visualization of lung lesions, from the apex to the bottom, from the anterior to the posterior regions (Fig. 1). They are useful to quantify lung aeration during mechanical ventilation and recruitment maneuvers. They can also be used to quantify tissue density (quantitative CT) and hence estimate lung water [2]. However, CT is not (yet?) a bedside method. The transfer of hypoxemic, and sometimes hemodynamically unstable, mechanically ventilated patients to the radiology department is often risky. It is always time-consuming and expensive.

Bedside or ambulatory methods to estimate lung water are therefore highly desirable. They include the thermo-green dye dilution, thermodilution, echography, bioimpedance, bioreactance and remote dielectric sensing.

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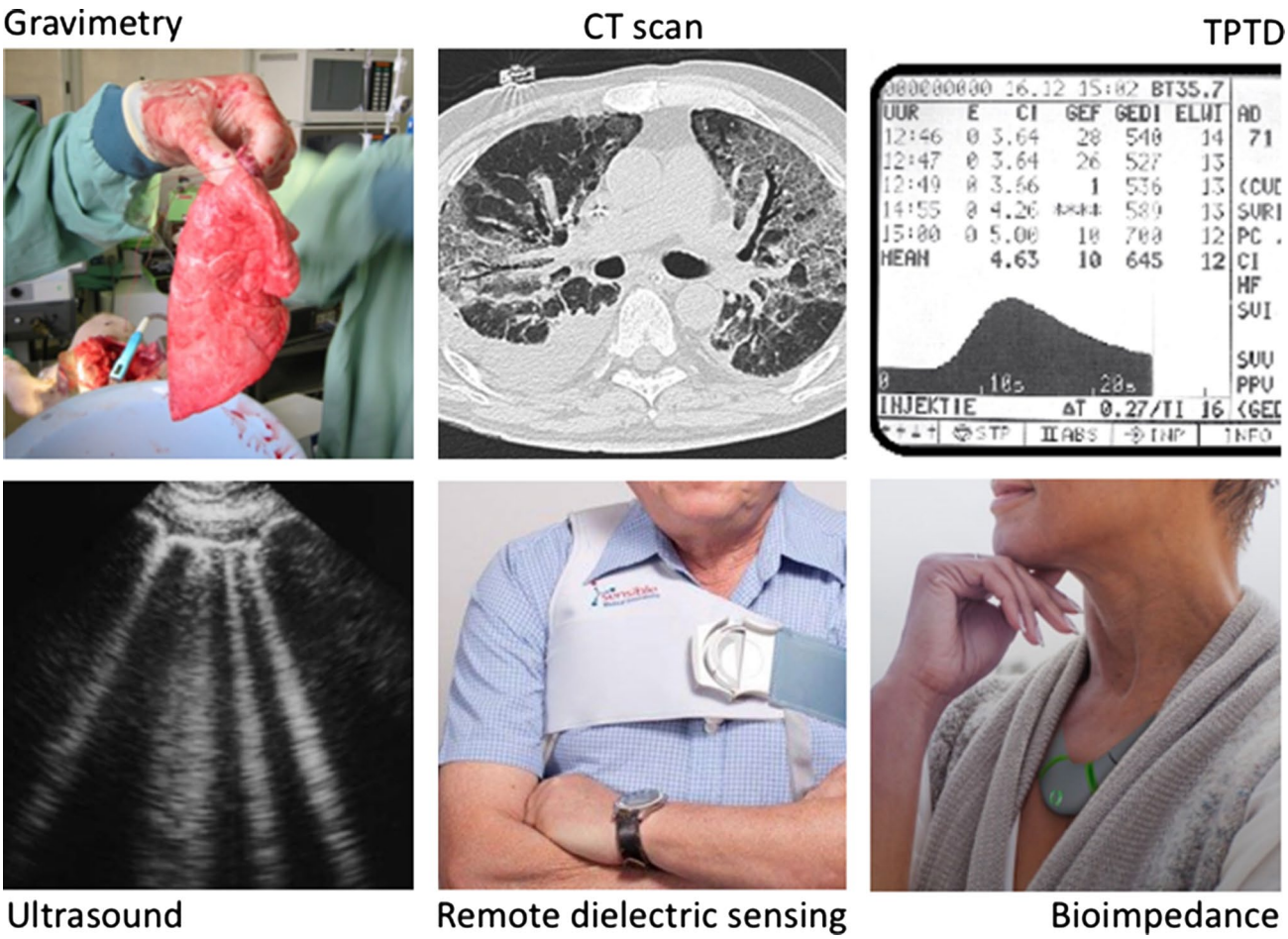

Fig. 1 An illustration of methods currently available to detect and quantify pulmonary edema, from the laboratory postmortem technique (gravimetry) to wearable solutions (remote dielectric sensing from Sensible-medical.com with permission, and bioimpedance necklace from Tosense.com with permission). *CT* computed tomography, *TPTD* transpulmonary thermodilution

2 Dilution methods

In an attempt to propose a bedside method for assessing EVLW, the thermo-green dye dilution technique was first proposed in the eighties [3]. A cold green dye is injected into the central circulation and a thermistor-tipped fiber-optic femoral catheter is used to simultaneously record the thermodilution and dye dilution curves. The difference between the volume of distribution of the indicator diffusing into the extravascular space (cold) and of the green dye remaining in the circulation gives the EVLW volume. This method has been validated against gravimetry [4] and used in many experimental and clinical studies to assess EVLW. It is no longer available on the market and has now been replaced by the single indicator thermodilution technique, aka transpulmonary thermodilution (TPTD).

The TPTD method is a simplification of the thermo-green dye dilution method. It is based on the assumption that the pulmonary blood volume represents 20% of the intra-thoracic blood volume (or 25% of the so-called global end-diastolic volume). This assumption comes from observations made in 57 critically ill patients and published in 2000 by Sakka et al. [5]. The relationship between pulmonary blood volume and intrathoracic blood volume may obviously be slightly different from one patient to the other, so that TPTD represents at best an estimation—and not a precise measure—of EVLW [1].

In the present issue of the Journal, Saugel et al. [6] compared the estimation of EVLW by quantitative CT and TPTD in 21 critically ill patients. They reported a poor agreement between the two methods. At first sight, these findings are somewhat surprising. Indeed, both quantitative CT and TPTD have been shown to provide reasonable estimates of EVLW when compared to gravimetry (the reference experimental method) and to thermo-green dye dilution (the reference clinical method) [1, 2, 7]. In addition, a recent study [8] comparing quantitative CT and TPTD in patients with

ARDS concluded that both methods give more or less the same information. However, as speculated by Saugel et al. [6], the fact that quantitative CT was not standardized as in previous studies, but rather used in "real life conditions" (no end-expiratory pause), may explain, at least in part, the observed discrepancies. Moreover, according to TPTD measurements, only 6 patients had permeability pulmonary edema (EVLW index > 10 ml/kg and pulmonary vascular permeability index > 3), making hazardous any conclusion regarding the value of quantitative CT to assess EVLW in patients with ARDS. In any case, CT is not a bedside method and TPTD remains the only way to obtain non-operator dependent, nurse-performed estimations of EVLW as often as needed (e.g. before, during and after therapeutic interventions).

3 Ultrasound methods

Ultrasounds are useful to detect pleural effusion, pneumothorax, lung consolidation, and to assess diaphragmatic function [9]. They can also be used to detect comet tails or B lines (Fig. 1). The number of B lines has been shown to correlate with the importance of pulmonary edema so that a semi-quantitative estimation of EVLW is now possible [10, 11]. From a technical standpoint, echo devices are becoming smaller and cheaper [12]. If appropriate skills remain the limiting factor for clinical adoption, the current boom in simulation and training programs explains that point of care ultrasound (aka POCUS) evaluations are becoming a new reality in a growing number of medical centers.

4 Bioimpedance, bioreactance and remote dielectric sensing

The thorax electrical impedance depends on its fluid content. Changes in thoracic impedance can be detected non-invasively from chest electrodes. Cyclic changes in thoracic fluid content (TFC) are typically observed with cardiac cycles. Therefore, bioimpedance methods have first been proposed to assess stroke volume and cardiac output. Bioreactance emerged over the last decade and is an evolution of bioimpedance techniques, relying on phase shifts of the electrical currents traversing the thorax, instead of amplitude of voltage changes. It enables a higher signal to noise ratio, and ultimately a more accurate and precise estimation of hemodynamic variables [13]. Both techniques (bioimpedance and bioreactance) also have potential to assess changes in TFC related to pulmonary edema. Validation and clinical usefulness studies are scarce but are promising regarding the ability to discriminate between cardiac and non-cardiac causes of acute dyspnea [14], as well as to assess the efficacy of ultrafiltration during hemodialysis [15].

Chronic heart failure is a public health issue, hospital readmissions are frequent and costly. Most patients are readmitted for pulmonary edema that progressively developed over a few days or weeks. These patients may benefit from proactive interventions based on the early detection of cardiac decompensation. Implantable sensors have been used with success to monitor pulmonary artery pressures on a daily basis and detect deterioration before patients develop symptoms [16]. Recently, non-invasive and wearable sensors have been proposed to detect lung water changes in ambulatory patients. A chest vest or belt uses remote dielectric sensing (ReDS) to detect changes in lung water [17]. It is a radar system that employs low-power electromagnetic signals. Two sensors are embedded in the front and back side of the chest belt (Fig. 1). They do not require contact to the skin so that the belt can be worn on top of clothing. The analyzed signal reflects the dielectric properties of the section of the lung between the sensors. The dielectric coefficient of a material depends on its water content. A good agreement was reported between CT scan and ReDS measurements in patients with and without chronic heart failure [17]. A study done in patients with chronic heart failure suggests that ReDS-guided therapy may help to decrease hospital readmissions [18]. A bioimpedance necklace able to assess the TFC was recently cleared by the FDA (Fig. 1). Clinical studies are now needed to confirm it enables the detection of pulmonary congestion and is useful to trigger early therapeutic interventions in ambulatory patients with chronic heart or kidney failure.

5 Conclusion

There are now various methods available to detect and quantify pulmonary edema. CT scans are regularly performed in critically ill patients with ARDS but, as suggested by Saugel's study [6], their value seems somewhat limited to quantify pulmonary edema on a routine basis and of course to track changes with therapy. In this context, TPTD is a convenient technique. It is invasive but most patients with ARDS have a central line and an arterial catheter in place anyway. In addition to EVLW, TPTD enables the measurement of hemodynamic variables (Fig. 1) that are useful to guide fluid and diuretic therapy [19]. Echo probes are about to replace the stethoscope in our pocket and, if B lines do not allow a real quantification of pulmonary edema, they are useful to detect an increase in lung water. Finally, wireless and wearable sensors are now available to monitor patients on hospital wards and beyond (home monitoring). They should enable the detection of pulmonary congestion at a

very early stage, and if combined with a proactive therapeutic strategy, have potential to improve outcome.

Compliance with ethical standards

Conflict of interest FM is the founder and managing director of MiCo, a Swiss consulting firm. MiCo does not sale any medical product. FM does not own shares and does not receive royalties from any medtech company.

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