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Lung aeration, ventilation, and perfusion imaging

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Abstract

Purpose of review: Lung imaging is a cornerstone of the management of patients admitted to the intensive care unit (ICU), providing anatomical and functional information on the respiratory system function. The aim of this review is to provide an overview of mechanisms and applications of conventional and emerging lung imaging techniques in critically ill patients.

Recent findings: Chest radiographs (CXR) provide information on lung structure and have several limitations in the ICU setting; however, scoring systems can be used to stratify patient severity and predict clinical outcome. Computed tomography (CT) is the gold standard for assessment of lung aeration but requires moving the patients to the CT facility. Dual-energy CT has been recently applied to simultaneous study of lung aeration and perfusion in patients with respiratory failure. Lung ultrasound has an established role in the routine bedside assessment of ICU patients, but has poor spatial resolution and largely relies on the analysis of artefacts. Electrical impedance tomography is an emerging technique capable of depicting ventilation and perfusion at the bedside and at the regional level.

Summary: Clinicians should be confident with the technical aspects, indications, and limitations of each lung imaging technique to improve patient care.

Keywords

computed tomography; lung imaging; electrical impedance tomography; lung ultrasound; lung perfusion

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INTRODUCTION

Lung imaging is a cornerstone of the management of patients admitted to the intensive care unit (ICU). Critically ill patients often present with different degrees of respiratory failure, ranging from minimal multifactorial oxygenation impairment to established acute respiratory distress syndrome (ARDS)[1]. The definition of this syndrome underwent several revisions, but since its first description[2] up to the current Berlin definition[3], diffuse lung lesions documented with imaging techniques have been a key diagnostic criterion. As most ICU patients with lung injury receive some degree of respiratory and/or hemodynamic support, lung imaging techniques typically depict the interaction between such functional changes and the type and degree of artificial support delivered to the respiratory and cardiovascular systems. In this context, lung imaging in critically ill patients can be seen as functional imaging, not limited to the mere description of lung anatomy and pathology extension but rather of its physiological function[4]. Since the early phases of the ongoing COVID-19 pandemics, imaging techniques provided important insights on the disease with relevant implications for patient care[5–7]. This was reflected by a great increase in the research in this field, from simple techniques such as chest x-ray to complex analyses based on advanced imaging modes. The aim of this review is to provide an overview of mechanisms and applications of conventional and emerging lung imaging techniques applied in the ICU setting.

PHYSICAL AND TECHNICAL BASES OF LUNG IMAGING

From a technical standpoint, lung imaging techniques could be classified in radiation-free versus those requiring the use of ionizing radiation. From a clinical point of view, another important distinction is whether these can be used at the bedside or require transporting the patient to the radiology facility. Lung imaging techniques requiring the use of ionizing radiations include chest X-ray (CXR) and computed tomography (CT), both based on the concept of attenuation. Image intensity in X-ray projections represents the ability of tissues to attenuate a beam of high-energy photons—either through absorption or scattering—across all of the tissue along the beam's path from X-ray source to detector [8]. While CXR uses a single X-ray source and a single two-dimensional detector, CT spatially computes the X-ray attenuation for discrete volumetric elements (voxels) by combining many projections acquired while rotating the X-ray source and detector around the patient [8]. Generally, X-ray attenuation is proportional to tissue density and composition. Since alveolar gas has negligible density compared to water, the relative content of gas and water (including both soft tissue and blood) in each lung voxel is proportional to CT intensity [9]. Furthermore, iodinated contrast material can be administered to increase the attenuation coefficient of blood, revealing abnormalities in pulmonary perfusion and vascular structure [10]. Dissolved iodine increases attenuation coefficient of blood more for low- compared to high-energy photons. Based on this mechanism, dual-energy CT (DECT) has been developed, relying on the simultaneous acquisition of two CT scans using two X-ray sources of different energy. Post-acquisition analysis enables partitioning each voxel into gas, water (including soft tissue and blood), and iodine content [11]. Virtual non-contrast images of the lung are generated by removing the partitioned iodine signal—leaving only gas and water—while the iodine signal alone is proportional to regional pulmonary blood volume (PBV) [11]. This allows, in a single acquisition, to describe precisely in the whole lung the distribution of alveolar gases and blood.

Image intensity in electrical impedance tomography (EIT) represents the ability of tissues to conduct (or rather, impede) electrical current between electrodes placed at the skin surface [12]. EIT signal in the lung is interpreted according to the relative contributions of high-impedance (low-conductance) gas and low-impedance ionic solutions (including soft tissue and blood) [13]. EIT can be acquired with extremely high temporal resolution (50 Hz), permitting post-processing of transient signals to estimate regional ventilation and perfusion according to fluctuations in impedance correlated with respiratory rate and heart rate, respectively [14].

Image intensity in ultrasonography (US) represents the ability of tissues to reflect high-frequency pressure waves (ultrasound) generated by a transducer at the skin's surface. Generally, reflections occur at boundaries between two materials with different acoustic impedances (e.g., gas and water), but detected echoes can also be affected by the structural arrangement of tissues and their relative motion [15]. Typically ultrasound cannot resolve anatomical structures within the lung, but several distinguishing features may indicate normal breathing motion, pneumothorax, or edema near the pleural surface [16].

CHEST X-RAY

The use of CXR in the ICU has been debated for several years. Its diagnostic accuracy in critically ill patients can be limited for several reasons. In ICU patients, the presence of internal and external medical devices presents a specific challenge, as patient positioning and other factors limit the ability to complement the antero-posterior projection with a lateral-lateral scan. Several societies recommend abandoning the practice of requiring daily CXR in ICU patients; however, the overall number of prescribed CXR has seen only a modest reduction over the last decades[17]. Despite being the most used radiographic exam in critically ill patients, it is associated with only around 2% the cumulative radiations dose received during the ICU stay, which are almost exclusively due to CT examinations associated with high per-exam doses, even though these represent only 12% of the performed exams[18]. During the COVID-19 pandemic CXR were widely used for their availability, and their visual assessment and scoring had similar performances compared to CT in defining disease severity and predicting mortality, with the potential role of reducing the overload of CT facilities during the peak phases[19]. Attempts of providing quantitative information from CXR dates back at least two decades. Nevertheless, this topic found renewed interest, and several score systems have been tested in COVID-19 patients. One approach consists of a manual quantification of opacified areas, expressed as total of the lung surface[20]. However, this approach is more time-consuming and less efficient compared to scoring systems such as the radiographic assessment of lung edema (RALE) [20] score and Brixia score[21]. Overall, while affected by several limitations, CXR still have a role in evaluating the respiratory function in critically ill patients.

COMPUTED TOMOGRAPHY

Computed tomography (CT) has been extensively used for quantitative analysis of the x-ray density of lung tissue. By evaluating the distribution of CT attenuation expressed in Hounsfield units (H)U, it is possible to quantify areas with no (atelectasis), poor, normal or relatively increased (hyperinflation) aeration[22]. The spatial resolution of clinical CT is around one millimeter. CT scan images acquired during a ventilatory hold depict the contingent regional distribution of air and therefore document lung aeration (*Static CT scan*). When a static CT scan is obtained in different conditions, e.g. at two levels of positive end-expiratory pressure (PEEP), functional information is derived, informing on the effects of ventilator settings on lung aeration changes [23,24]. When the acquisition is made during respiratory motion (*4-Dimensions Dynamic CT scan*) [25], dynamic regional changes of gas content can be tracked, thus evaluating ventilation. Moreover, it is possible to assess intra-tidal movement of air, e.g. *pendelluft*, when measuring gas changes during tidal breathing [26]. Since the lung's structures move when it is inflated with different volumes of gas, a process of image re-alignment, called *image registration*, is necessary [25] when comparing images taken in different inflation conditions. However, dynamic CT scans are associated with a moderate radiation exposure, and therefore mostly used for research purposes. By evaluating the effects of mechanical ventilation on gas/tissue distribution, CT scans have helped to improve the knowledge of ARDS pathophysiology, generating the concept of baby lung [27] and describing the anatomical changes after prone positioning [28]. However, its clinical use can be still limited by the exposure to radiation and the need for transport to the CT facility[4]. Modern computer-based algorithms recently allowed estimating lung perfusion with subtraction computed tomography (SCT) angiography [29]. This technique uses software-based motion correction between an unenhanced and an enhanced CT scan to obtain the iodine distribution in the pulmonary parenchyma. In addition to several innovative and experimental applications, CT represents the gold standard for assessment of lung aeration and is widely used in the clinical management in patients with ARDS.

DUAL-ENERGY COMPUTED TOMOGRAPHY

Contrast enhanced, DECT was initially proposed in the context of relatively healthy lung parenchyma to assess perfusion abnormalities, notably pulmonary embolism[30]. It has been proposed as an imaging tool covering the gray area between conventional CT-angiography of the pulmonary vessels and the more accurate, but much less available, ventilation-perfusion scintigraphy. Less frequently, DECT is used to assess ventilation distribution and ventilation defects via inhaled tracer gas (e.g., xenon) [31–33]. Advantages of DECT compared to single-energy CT include faster imaging and reduction of beam-hardening artifacts [34,35], although single-energy subtraction CT may provide better contrast than DECT [36] and similar added diagnostic value for pulmonary embolism detection compared to CT angiography [37]. DECT imaging performed in experimental models of acute lung injury demonstrated correlation between DECT-derived perfusion blood volume (PBV) and dynamic CT-derived perfusion blood flow [38], and dynamic single-slice DECT imaging revealed cyclic intra-tidal redistribution of PBV into poorly ventilated and dependent lung regions during inspiration [39,40].

Although routine use of DECT in critical care is uncommon, recently DECT has played an important role in characterizing the extent of pulmonary vascular dysregulation, perfusion defect (PD), and ventilation-perfusion mismatching occurring in COVID-19. DECT findings in case reports and clinical studies of COVID-19 included dilated peripheral vessels, PDs coinciding with parenchymal consolidation, increased perfusion in regions of ground-glass opacification, and increased perfusion in a "halo" surrounding consolidated regions [41–49]. PDs also occur throughout normally aerated parenchyma in COVID-19 [48,49], with greater frequency and extent in patients also showing pulmonary artery thrombosis [50], and with potential for improved peripheral PBV following thrombolysis treatment [51]. Presence of PDs and mismatched gas vs. blood distributions are associated with worse disease severity and gas exchange, as well as worse outcomes including ICU admission and length of stay [48,49,52–54]. A comparison of DECT findings in COVID-19 compared to non-COVID-19 pneumonia (with no macroscopic pulmonary embolism in either cohort) found increased PD frequency, patchiness, and coincidence with consolidation in patients with COVID-19 [55]. Follow-up DECT scans in COVID-19 survivors (3 months after hospitalization) exhibit long-term persistence of perfusion abnormalities [56]. Although available only on some CT scanners, DECT has interesting potential applications in critically ill patients, warranting future research in the field to better understand the interaction between respiratory function and perfusion in vivo.

ELECTRICAL IMPEDANCE TOMOGRAPHY

Lung EIT displays *relative changes* of air content, since the gas inflow modifies the impedance of the whole chest-wall/lung system [57]. The variation of the lung's air content is detected as a variation in the impedance and transformed into a 2D image representing the area inside the sensors belt. EIT, therefore, can show relative changes in air content, which mean variation in functional residual capacity (end-expiratory lung impedance, EELI) or intra-tidal regional variation of volume, but cannot provide absolute values of aeration[58]. The current technology allows the evaluation of both lung ventilation and perfusion at the bedside[59–61], but clinical consensus on EIT is still missing. Changes of EELI, ventilation and perfusion can be analyzed both globally and regionally, dividing the image in several regions of interest (ROIs) [62].

The main application of EIT is still at the moment bedside monitoring of lung ventilation and of the relative changes occurring when mechanical ventilation is titrated[63]. EIT enables bedside exploration of the regional heterogeneity of lung disease in ARDS and COVID-19[64]. In ARDS, it has been used to evaluate regional distribution of ventilation, areas of hypoventilation[58], inhomogeneity[65] and regional inflection point in lung mechanics[66]. In this context, EIT could have a clinical role in in PEEP titration. Its use can indeed identify each patient's level of PEEP that is able to balance overinflation and derecruitment, thus reducing – at least theoretically – the occurrence of VILI[67]. The evaluation of perfusion with EIT is based on the method of the first-pass contrast agent, which usually is a hypertonic saline solution. The saline is injected in a central line and transiently changes the impedance of blood, by modifying the saline content and osmolarity. This change can be recorded by the EIT and transformed into a 2-d cumulative perfusion map[68]. Independently of several limitations related to its low spatial resolution and inability of providing absolute values of ventilation and perfusion, EIT is currently the only bedside imaging tool able to unveil the relative regional heterogeneity of $\dot{V}_A/\dot{Q}$ matching in ventilated patients.

LUNG ULTRASOUND

Lung ultrasound has gained an increasing popularity and clinical use in critically ill patients. Lung ultrasound interpretation is based on both artifactual images of normal/pathologic lung (respectively A-lines and B-lines) and on real images of pathologic conditions (e.g. lung consolidations, pleural effusion) [69]. The ultrasound (US) lung evaluation is mainly qualitative, since it is based on the characteristics of the US image, but an attempt to quantify the ultrasound-derived data has been done with the introduction of the Lung Ultrasound Score (LUS). The LUS has a good correlation with lung aeration measured by CT scan, but its performance is lower when used to quantify lung recruitment [70]. The low sensitivity of the technique and the limited access to the deep lung parenchyma are the greatest limitations when applied as a ventilation monitoring technique. An effort to improve this aspect has been recently made by software based US texture analysis, which was recently found to be able to discriminate ARDS from acute cardiogenic pulmonary edema [71]. Another possible implementation of US imaging may derive from the addition of a soluble contrast agent. Contrast-enhanced ultrasound (CEUS) consists in the intravenous injection of microbubbles, having the approximate size of a red blood cell, made of a phospholipid shell surrounding a perflourocarbon gas, providing information on regional lung perfusion. This technique has been recently applied to evaluate the perfusion patterns of peripheral pulmonary lesions in COVID-19 patients [72,73]. Peripheral subpleural consolidations with no or inhomogenous enhancement on CEUS can be, indeed, highly suggestive of embolic consolidations[74]. While lung ultrasound has an established role in detecting loss of aeration and pneumothorax, its use as a tool to titrate mechanical ventilation is still limited.

CONCLUSIONS

Lung imaging in critically ill patients aims at providing both pathophysiological and functional information on the respiratory system. There is increasing interest in the role of lung perfusion in determining the severity of gas exchange impairment in respiratory failure. Clinicians should be confident with the technical aspects, indications, and limitations of each lung imaging technique to improve the process of care in critically ill patients admitted to the ICU.

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KEY POINTS

- Lung imaging is often used in ICU patients to obtain anatomical and functional information on the impairment of the respiratory function
- Computed tomography provides a detailed three-dimensional map of lung aeration, dual-energy computed tomography also provides information on lung perfusion
- Lung ultrasound and electric impedance tomography are radiation-free bedside techniques. The former has an established role in describing lung loss of aeration, the latter allows monitoring ventilation and perfusion.