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Early View

Task force report

ERS statement on chest imaging in acute respiratory failure

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ERS statement on chest imaging in acute respiratory failure

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ABSTRACT

Chest imaging in patients with acute respiratory failure plays an important role in diagnosing, monitoring and assessing the underlying disease. The available modalities range from plain chest x ray to computed tomography, lung ultrasound, electrical impedance tomography and positron emission tomography. Surprisingly, there are presently no clear-cut recommendations for critical care physicians regarding indications and limitations of these different techniques.

The purpose of the present European Respiratory Society (ERS) statement is to provide physicians with a comprehensive clinical review of chest imaging techniques for the assessment of patients with acute respiratory failure, based on the scientific evidence as identified by systematic searches. For each of these imaging techniques, the panel evaluated the following items: possible indications, technical aspects, qualitative and quantitative analysis of lung morphology and the potential interplay with mechanical ventilation. A systematic search of the literature was performed from inception to September 2018. A first search provided 1834 references. After evaluating the full text and discussion among the committee, 135 references were used to prepare the current statement.

These chest imaging techniques allow a better assessment and understanding of the pathogenesis and pathophysiology of patients with acute respiratory failure, but have different indications and can provide additional information to each other.

SHORT SENTENCE

Chest imaging in patients with acute respiratory failure plays an important role in diagnosing, monitoring and assessing the underlying disease. The available modalities range from plain chest x ray to computed tomography, lung ultrasound, electrical impedance tomography and positron emission tomography. Surprisingly, there are presently no clear-cut recommendations for critical care physicians regarding indications and limitations of these different techniques. A systematic search of the literature was performed from inception to September 2018. A first search provided 1834 references. After evaluating the full text, 135 references were used to prepare the current statement.

At first level exam, CXR, despite its intrinsic limitations and low accuracy may still play a relevant role. CT scan remains the gold standard, but it requires patient

transportation and use of radiations, which preclude an extensive use especially within the same patient. LUS, after a proper physician training, is able to provide an accuracy greater than CXR and similar to that of the CT scan. EIT is gaining a more clinical role after having represented a research tool for many years, while PET has a minimal role in the acute phase of respiratory failure. Future studies will assess if the information provided will improve clinical management and outcome.

List of abbreviation

ARF, acute respiratory failure;

ALI, acute lung injury;

AHF, acute heart failure;

ARDS, acute respiratory distress syndrome;

COPD, chronic obstructive pulmonary disease;

CT, chest computed tomography;

CXR, chest x-ray;

EIT, electrical impedance tomography;

ERS, European Respiratory Society;

FiO_2, fraction of inspired oxygen;

ICU, Intensive Care Unit;

LU, lung ultrasound;

MRI, magnetic resonance imaging;

PaO_2, partial pressure of oxygen in arterial blood;

PEEP, Positive end-expiratory pressure;

PET, Positron Emission Tomography;

PSV, pressure support ventilation;

PTCER, pulmonary trans-capillary escape rate for transferrin with PET.

INTRODUCTION

Patients with acute respiratory failure (ARF) require one or several imaging studies of the chest to diagnose underlying diseases, assess progression and evaluate treatment efficacy. Until a few decades ago, chest imaging of the critically ill consisted solely in chest x-ray (CXR). Additional imaging techniques have become widely available for the critically ill, including chest computed tomography (CT) and more recently, bedside techniques such as lung ultrasound (LU) and electrical impedance tomography (EIT), and Positron Emission Tomography (PET). Surprisingly, there are presently no clear recommendations for critical care physicians regarding indications and limitations of these five imaging techniques.

To date, the limited use of chest Magnetic Resonance Imaging (MRI) in pulmonary diseases is due to the physical properties of the pulmonary parenchyma and the long scan time. Although recent technical advances (i.e. parallel imaging, multi-array phase coils and ultra-short echo-time techniques enabling higher image quality and shorter scan time) have provided more detailed information on lung ventilation, inflammation, perfusion and structure, currently MRI is not used in the management of patients with acute respiratory failure. For all these reasons, MRI was not included in the current TF.

The purpose of this European Respiratory Society (ERS) statement is to provide physicians with a comprehensive clinical review of chest imaging techniques for the assessment of patients with ARF, based on the scientific evidence, as identified by systematic searches. Of the five imaging techniques selected by the Task Force Chairs, three are applicable at the bedside (CXR, LU, EIT) and two (CT and PET) require transfer to the radiological department.

For each of the included imaging techniques, the panel evaluated the following items: indications, technical aspects, qualitative and quantitative analysis of lung morphology and interaction with mechanical ventilation.

METHODS

The ERS Scientific Committee approved the development of a document on imaging techniques in acute respiratory failure by a task force (TF-2016-01) on May 2016 aimed to summarize the relevant literature. The task force was composed by several

experts (DC, GSP, AA, BB, AG, LH, KM, GP, LP, DR, MS, GS, PS, MZ, PN) and chaired by DC and PN. All members disclosed potential conflicts of interest according to ERS policies.

Search

The systematic search of the literature on the five imaging techniques (CXR, LU, CT, PET, EIT) was performed from inception to September 2018 on Medline (National Library of Medicine, USA) The search was limited to articles in English and to humans aged >18 years. The keywords included in table S1 to S5 were used as literature search terms and limited to original studies.

Manuscript preparation

Task force members were divided into five groups (LR and AA for CXR, DC and GSP for PET, LH, MS, MZ and KM for CT, GP and BB for LU, PS for EIT). Each group focused on a single technique and its use in a disease entity *a priori* selected by Task Force Chairs (pneumonia, chronic obstructive pulmonary diseases (COPD), acute heart failure (AHF), pneumothorax, pleural effusion, acute lung injury (ALI) and acute respiratory distress syndrome (ARDS). For each technique, a narrative summary was provided for contextualization, which summarized certainty of evidence and relevant features. Feedback was provided by electronic communication. This is a statement document, thus no formal assessment of the evidence quality was performed and it does not include recommendations for clinical practice. The final approved version was peer reviewed.

Results of literature search

Figure 1 provides an overview of the search. The initial search identified 1834 papers. After manual screening of titles and abstracts 1220 papers were excluded and 614 were considered as potentially relevant. After evaluation of the full texts and discussion among the committee 493 were excluded for the following reasons: 350 were case reports, 61 were reviews, 25 were deemed too small series (the expert and the methodologist agreed on two cut-offs: 10 subjects for PET and EIT, and 20 for CXR, LUS and CT), 16 were considered to be inappropriate for subject characteristics (e.g. pediatric studies); 41 references were discarded for other reasons.

An additional search of bibliographies and authors' personal files provided 9 papers. Thus, a total of 135 references were used to prepare the current statement.

CHEST X RAY

Bedside CXR remains one of the most frequently prescribed imaging techniques, providing helpful information for the monitoring of critically ill patients. Although lots of effort has been made to improve technical aspects, numerous limitations of bedside CXR persist, including: bedside attenuation factor, X-ray intensity and distance to the thorax and synchronization to mechanical ventilation. In addition, patients are often uncooperative and difficult to position, thus increasing procedure time and cost. All these factors may hinder the correct interpretation of CXR.

ARDS

ARDS is defined by the acute inset of bilateral opacities on chest radiograph not fully explained by effusions, lobar/lung collapse, nodules or edema [1].

Although the radiographic criterion of "bilateral pulmonary infiltrates or opacities" on CXR is essential for the diagnosis of ARDS, a significant interobserver variability has been reported [2]. Compared to chest CT, the accuracy of CXR in identifying pulmonary abnormalities in patients meeting criteria for ARDS is limited and unrelated to disease severity, as defined by the extent of oxygenation derangement [3]. A retrospective single-center study showed that only 31% of patients having ARDS according to the current definition, presented histo-pathological signs of diffuse alveolar damage (a finding pathognomonic for ARDS) [4]. A recent study evaluated whether diagnostic accuracy could be improved by an educational intervention based on a set of chest radiographs. Though some improvement in diagnostic accuracy after the educational intervention was observed, the overall accuracy remained poor [5]. A multicenter randomized trial using an online educational module of the Berlin definition on ARDS failed to demonstrate any improvement in the accuracy and in the identification of ARDS patients among critical care clinicians and research staff [6].

ACUTE HEART FAILURE

CXRs performed at the bedside with portable equipment are often used to identify and quantify the presence of pulmonary edema in the intensive care unit. However, supine position and the potential presence of other multiple radiographic abnormalities often hinder CXR interpretation. In addition, the distinction between hydrostatic and permeability pulmonary edema, as well as quantitating the amount of lung water is extremely problematic [7]. Although a relationship between a score based on CXR findings and the amount of extravascular lung water was found, nonetheless the evolution of extravascular lung water was not associated with score changes [7]. To improve diagnostic accuracy in patients with acute heart failure, some radiologic signs, such as the cardiothoracic ratio, vascular pedicle width, and dimensions of the mediastinal silhouette of the great vessels have been proposed [8, 9]. A vascular pedicle width exceeding 70 mm was found to have acceptable sensitivity and specificity in discriminating cardiogenic from non-cardiogenic pulmonary edema [10]**.**

COPD

Although CXR is usually performed in patients with COPD exacerbation, it has low sensitivity for the detection of airflow obstruction. During acute exacerbation the predominant pathological changes are found within the airways, with abnormal images only in very few cases. In this setting, CXR is useful to rule out pneumonia or to exclude alternative diagnoses and complications such as decompensated heart failure, massive pleural effusion, atelectasis or pneumothorax.

PNEUMONIA

Conventional CXR is the preferred imaging modality in critical care settings for both the detection of new infiltrates and for monitoring response to therapy with the possibility to detect early complications including cavitations, abscesses, pneumothoraces and pleural effusions. However, due to the well-known difficulties involved in radiographic interpretation of portable CXR in the critical care, the diagnosis of pneumonia may be difficult. Using protected brush catheter specimens as gold standard for the diagnosis of nosocomial pneumonia, Lefcoe et al. demonstrated that CXR sensitivity in detecting pneumonia associated with positive cultures was 0.60 and 0.64, as interpreted by two radiologists, with low reproducibility

between the two examiners [11]. In a small group of patients with clinical suspicion of ventilator-associated pneumonia, the sensitivity of CXR in determining the presence of ventilator-associated pneumonia was 25%, with a specificity of 75% and an accuracy of 0.45 using protected brush catheter and microbiology as reference [12]. A multicentre French study found that the occurrence of alveolar consolidations with lobar distribution was more frequently associated with severe pneumococcal pneumonia, although the value of this prediction was indeed rather limited [13].

PNEUMOTHORAX

Controversy exists regarding the optimal time interval to identify a pneumothorax on CXR both after chest tube positioning and removal. Schulman et al. evaluated both an immediate and a delayed approach (following morning) with CXR after chest tube positioning [14]. Thirty one patients had a pneumothorax on follow up, of these 22 were “early” and 9 “late”, but none of the patients of the late group presented a clinically significant pneumothorax. Concerning the timing of CXRs after tube removal, Pizano et al showed that serial CXRs performed at approximately 1, 10 and 36 hours did not identify different rates of pneumothoraces in mechanically ventilated patients [15].

PLEURAL EFFUSION

Due to technical limitations, pleural effusions, particularly when small, may be difficult to diagnose on CXR performed in supine position. A previous report on the detection of pleural effusions on supine CXR has shown an overall accuracy of 82%, with better results for larger pleural effusions (>300 ml) [16]. The accuracy on parapneumonic effusions was similar for the anteroposterior and the lateral CXR [17].

ULTRASOUND

Because the ultrasound beam does not penetrate the lung, LU is able to explore only the pleural line and the related artifacts that are generated at the pleural line. The pleural line appears as a hyperechoic sliding line, moving forward and backward in the course of inspiration and expiration. The key artifacts are A- and B-lines. B-lines correspond to various degrees of lung aeration and the quantity is related to the amount of the extra-vascular lung water. Multiple and well separated vertical B lines

correspond to a moderate decrease in lung aeration resulting from interstitial syndrome. Coalescent B-lines correspond to a more severe decrease in lung aeration resulting from partial filling of alveolar spaces by pulmonary edema or confluent bronchopneumonia. Lung consolidation is a tissue-like echotexture pattern due to a loss of aeration of lung parenchyma [18].

ARDS

Lung infiltrates of the pulmonary alveolar-interstitial space caused by ARDS may show consolidations and B-line patterns. Yet, these findings are non-specific of ARDS as the syndrome encompasses consolidated regions, ground glass areas and normally aerated regions. As a consequence, LU patterns of ARDS may encompass B-lines, pleural line abnormalities (absent or reduced lung sliding, thickening or irregularities), consolidations and spared areas [19, 20]. These LU findings, together with an impaired oxygenation, are simple tools to diagnose ARDS [21] [21] especially when combined with echocardiography [22]. LU has helped assess the incidence and outcomes of patients with ARDS in settings with limited resources [23].

The increase of lung water in ARDS can be detected by LU, and the LU score of B-lines is closely related to several prognostic indices [24].

Given that LU patterns are determined by the level of aeration, lung re-aeration may be assessed by tracking LU changes. This was first demonstrated by trans-esophageal echography [25–27]. It has been proven that during positive end expiratory positive pressure (PEEP) recruitment maneuvers the gas increase can be monitored by measuring the area of consolidated, dependent right lower lobes [28]. Yet, it may be more accurate to use scores based on a whole lung examination protocol [29]. Despite LU scores have proven to represent a valid tool to assess regional and global lung aeration, global LUS score variations should not be used for bedside assessment of PEEP-induced recruitment. In addition, LU cannot be used to estimate lung hyperinflation [30].

ACUTE HEART FAILURE

Although non-specific, B-lines may detect extra vascular lung water. Simple scores based on numbers of B-lines correlated to surrogate markers of pulmonary edema [31–33], as B-lines have been proven to decrease during hemodialysis [34, 35]. B lines could also be correlated to pulmonary wedge pressure [24, 36].

Cardiogenic pulmonary edema results from increased intravascular hydrostatic pressure. As a consequence, the distribution of alveolar flooding is homogeneous. LU pattern of cardiogenic pulmonary edema is characterized by the presence of multiple B-lines in all thoracic regions [19]. Pleural effusion, moderately or severely decreased left ventricular function, and a small inferior vena cava diameter point towards cardiogenic pulmonary edema instead of ARDS in acutely hypoxemic patients [20]. LU was used in the pre-hospital setting [37] and in the emergency department to manage patients with cardiogenic pulmonary edema, thus proving to be a reliable bedside tool to guide therapy [38, 39].

COPD

In COPD patients, acute exacerbation usually shows a normal LU pattern despite the presence of acute respiratory failure. On the contrary, the presence of B-lines suggests the presence of an associated alveolar interstitial syndrome with an acceptable accuracy [40]. Chest ultrasonography (heart and lung) in patients admitted with acute respiratory failure allows a more accurate diagnosis of decompensated COPD compared to a standard diagnostic approach, based on physical examination, CXR and biological data [41].

PNEUMONIA

LU is a valid alternative for the bedside diagnosis for lung consolidations in community acquired pneumonia in adults [42], and can provide early detection of interstitial lung involvement in viral pneumonia [43]. In addition, LU can also provide guidance for transthoracic needle aspiration for etiologic diagnosis of patients with complicated pneumonia. This was confirmed in the intensive care unit and the emergency department [44–52].

Performing an accurate diagnosis of ventilator-associated pneumonia in mechanically ventilated patients frequently represents a challenge. By identifying ventilator-associated pneumonia-specific signs (focal areas of interstitial syndrome, small subpleural consolidations, large consolidations, and fluid bronchogram) LU can discriminate pneumonia from resorptive atelectasis [53]. Furthermore, LU can accurately estimate the changes in lung aeration in patients with ventilator associated pneumonia treated with antibiotics [54].

In a multicenter study the diagnostic performance of a score based on the presence of subpleural consolidations, lobar consolidations, and dynamic arborescent / linear air bronchograms was investigated in patients with suspected ventilator-associated pneumonia [55]. The LU-based score presented a higher sensitivity and specificity in predicting ventilator-associated pneumonia than the clinical-based one (i.e. Clinical Pulmonary Infection Score) [55].

PNEUMOTHORAX

Pneumothorax is the interposition of gas between visceral and parietal pleura. LU findings in pneumothorax are A-lines and the absence of lung sliding, B-lines and visualization of a lung point [56]. The lung point corresponds to the area on the chest wall adjacent to the pneumothorax where the respiratory movement of the lung reappears. This transition between sliding and non-sliding pattern represents the limit of the pneumothorax and is a measure of its extension and volume [57].

In trauma patients in the emergency department, LU performs better than CXR in diagnosing pneumothoraces and can also detect the presence of occult pneumothoraces [58, 59]. A CXR is routinely requested after central venous catheter placement to exclude the presence of a iatrogenic pneumothorax. LU ultrasonography combined with contrast enhanced ultrasonography presented a high accuracy in excluding both a pneumothorax and catheter malposition [60, 61], with a significant reduction in the mean time required for the examination [62]. In addition LU can be used to exclude a pneumothorax, in alternative to CXR, after chest tube removal [63].

PLEURAL EFFUSION

LU can reliably identify free pleural effusion that appears as a dependent echo-free space between the parietal and visceral pleura [64]. LU may also allow semi quantitative, clinically useful estimations of effusion volume. The expiratory interpleural distance measured at the thoracic base with ultrasonography has been proven to correlate with the fluid volume [65]; LU is able to detect pleural effusion in different clinical conditions, irrespective of the underlying disorder [66–69].

Ultrasound-guided thoracentesis in patients receiving mechanical ventilation reduces the risk of pneumothorax to less than 1% [70].

Miniaturized ultrasound systems such as hand carried ultrasound imagers are now available. These systems allow a more prompt bedside diagnosis and immediate therapeutic measures, and could provide a helpful technique for primary assessment of pleural effusions [71].

COMPUTED TOMOGRAPHY

CT scanning is frequently performed in critically ill patients either at admission, or later in case of worsening of respiratory failure. A retrospective analysis conducted in medical critically ill patients reported that a CT scan was performed in 11.5% of all patients admitted to the intensive care unit [72]. Consolidations, pleural effusions and parenchymal abnormalities were each present in more than one-fifth of the patients. The most common CT findings included consolidations (46%), other parenchymal abnormalities (29%) and pleural effusions (35%). Clinical changes clearly linked to chest CT were made in 24% of the patients [72].

ARDS

DESCRIPTION OF THE FINDINGS

Since the first description of chest CT in ARDS, the described disease patterns included ground glass opacifications, parenchymal distortion, areas of consolidation, reticular and linear opacities [73]. These alterations detected by CT scan were significantly related to the impairment of gas exchange and to the lung injury score [74]. ARDS patients are characterized by a lower end expiratory lung gas volume, increase in lung edema with a typical diffuse or patchy distribution of attenuation in the lung [75–77]. However it should be noted that a single-slice CT compared to an overall lung study, due to the inhomogeneous distribution of the disease, cannot accurately describe the amount of reopening of collapsed lung regions due to PEEP changes [78]. An important technical issue with CT is the spatial resolution. Vieira et al. demonstrated that low spatial resolution CT may underestimate the degree of hyperinflation due to PEEP compared to high spatial resolution CT, particularly when the lung morphology has a focal loss of aeration [79].

ARDS is characterized by different levels of hypoxemia due to different amounts of non-aerated lung regions (i.e. alveolar shunt) which can be precisely quantified by CT. The logarithmically transformed PaO_2/FiO_2 due to pure oxygen ventilation allows

estimation of CT shunt [80]. According to the recent Berlin definition of ARDS which proposed three exclusive categories according to the degree of hypoxemia, a PEEP of 5 cmH2O should be applied to stratify the patients at intensive care admission. This relatively low PEEP level was accurate in predicting the severity and recruitability compared to higher PEEP levels [81]. At 5 cmH_2O of PEEP the potential for lung recruitment was significantly different according to each ARDS category of the Berlin definition, being two and three times higher in patients with moderate and severe ARDS compared to mild ARDS [81] suggesting that low PEEP levels should be applied upon intensive care admission to stratify patients according to the severity.

Patients with diffuse attenuations presented a higher mortality rate compared to lobar attenuations [82]. Up to fifty percent of patients with sepsis suffering from ARDS had a CT scan score higher than survivors and less ground glass opacities [83]. Pulmonary findings on CT did not allow to discriminate between a pulmonary and extrapulmonary focus of infection [83].

In patients with ARDS caused by H1N1 influenza the amount of total lung consolidation and ground glass were not different. However, the total lung consolidation significantly increases, whereas total lung ground glass decreases from the anterior toward the posterior. The total lung disease was significantly higher in patients who required ExtraCorporeal Membrane Oxygenation (ECMO) compared to those who did not require ECMO [84]. Chest CT has substantially changed the understanding and management of patients with ARDS. Simon et al. reported that chest CT affected treatment in 27% of the cases, in particular alteration in antibiotic therapy (8%), drainage of pleural fluid (8%) and modification in antimycotic therapy (4%) [85]. A major disadvantage of CT is the requirement of transportation of the patient to the radiological department and radiation exposure. Chiumello et al. demonstrated that low dose CT showed a high agreement with conventional CT for quantitative analysis in ARDS patients [86]. The current standard technique for quantitative CT scan analysis is based on a manual lung segmentation, which is time consuming and depends on the skills of the operator. Klapsing et al. reported a very good precision of an automatic lung segmentation software compared to manual segmentation [87]. This automatic lung CT segmentation was able to reduce the processing time by more than 99%.

Trauma patients are at risk for developing ARDS, and CT scan could be used to detect possible lung and heart disease [85]. In chest trauma patients with pulmonary contusion the volume of the contusion was related to higher risk of ARDS [88]. The quantitative CT scan analysis offers the possibility to compute the total lung weight and could be used to discriminate lung atelectasis from consolidation. In a group of trauma patients with ARDS, 60% of the patients had a lung weight volume similar to trauma patients without ARDS, suggesting a higher amount of atelectasis compared to consolidation [89].

In the early phase of ARDS, the amount of pleural effusion is quite of modest entity (an average amount of 340 ml) and does not affect the respiratory system elastance, amount of lung collapse and oxygenation [90].

TREATMENT EFFECT

Chest CT has been used to determine complications of mechanical ventilation or in the follow-up of ARDS patients. Late ARDS had a significantly higher incidence of pneumothoraces and number of bullae compared to early ARDS [91]. Treggiari et al. performed chest CT in ARDS patients on prolonged ventilation (interval between ARDS and CT scan 22 ± 19 days). They found that development of air cysts and bronchiectasis in ventilated patients with ARDS mainly developed in non-dependent lung regions and severity was correlated with peak pressures [92].

Despite the mortality rate of ARDS patients has significantly decreased through the years it still ranges between 40-50%, with surviving patients having significant reduction in their quality of life. Decrements in quality of life attributable to pulmonary dysfunction were strongly associated with higher radiologic scores [93]. In a small study, 87% (13 / 15) of patients with ARDS exhibited fibrotic changes in the lung, in particular in the ventral parts, as assessed by high resolution CT scan [94]. A significant correlation was found between the severity of ARDS and severity of CT findings. In a subsequent study, [95] it was reported that in 75% of the patients, lung abnormalities were found six months after recovery on high resolution CT scans. A reticular pattern was the most frequent finding. A predominance for the ventral parts was noted in 37% of the patients. Kim et al. [96] found that patients with pulmonary ARDS had more severe lung sequelae on chest CT after 20±12 months compared to patients with extrapulmonary ARDS.

CT has been used to evaluate or predict the response to PEEP changes and to recruitment maneuvers in patients with ARDS. Analyzing lung recruitability as the decrease in the non-aerated tissue from 5 to 45 cmH_2O of PEEP, an average of 15% of the total lung tissue was found to be unrelated to the amount of compressive forces (lung edema and characteristics of the chest wall). This suggests that the amount of PEEP required to keep open the lung was independent from the amount of tissue which should be kept open and other factors such as the distribution of edema within the lung mainly intra or extraalveolar and the nature of the disease play an important role [97]. In patients with diffuse attenuation PEEP induced a significant alveolar recruitment without overdistension, whereas in patients with lobar CT attenuation PEEP induced mild alveolar recruitment with overdistension of the already inflated lung regions [98] Patients with focal ARDS at zero end-expiratory pressure are at increased risk for hyperinflation during recruitment maneuver and are less likely to recruit compared to patients with a non focal lung morphology [99]. The effect of body mass index in ARDS was not associated to significant differences in lung recruitability and respiratory mechanics [100]. In addition according to the protective ventilation between 10-30% of the potentially recruitable lung remains always closed and furthermore increasing the PEEP up to 15 cmH_2O did not prevent the cyclic lung tissue opening and closing [101].

In an ARDS lung the distribution of the lesions (consolidations and atelectases) are inhomogeneous, promoting a regional increase in transpulmonary pressure, acting as stress raiser. Thus a safe transpulmonary pressure could become harmful, (i.e reaching high levels) in presence of stress raisers. It was found that the extent of lung inhomogeneities increased with the severity of ARDS; the increase in PEEP significantly decreased the amount of lung inhomogenetis [102].

Randomized clinical trials comparing high and low PEEP values in ARDS did not find any difference in the outcome, probably due to several factors such as the potential of lung recruitability, the amount of edema or severity that were not taken into account. When different PEEP selection methods (based on lung mechanics, esophageal pressure and oxygenation) were compared according to lung recruitability, the oxygenation method provided higher PEEP levels (i.e. higher PEEP in patients with higher recruitability) [103].

Constantin et al. compared two recruitment maneuvers, CPAP with 40 cmH2O for 40 seconds vs PEEP maintained at 10 cmH2O above the lower inflection point of the

pressure volume curve for 15 minutes. Although the increase in oxygenation was different, lung recruitment estimated by CT scan was significantly lower with the CPAP maneuver [104]. Galiatsou et al. demonstrated that pronation in patients with ARDS recruited lung tissue in dependent lung areas and reversed overinflation of the ventral areas [105]. Surfactant deficiency in ARDS also contributes to alveolar derecruitment. The administration of surfactant in mechanically ventilated patients was associated to a significant increase in volume of gas in poorly/non aerated lung areas and a significant increase in tissue volume in normally aerated lung areas [106]. Concerning the estimation of the lung recruitment with the CT or pressure volume curve, they were well related despite having very large limits of agreements [107].

Two studies have used CT to compare different ventilator modes on lung aeration in patients with ARDS [108, 109]. The first one found that airway pressure release ventilation significantly decreased the amount of atelectasis and increased the normally aerated lung volume compared to pressure support ventilation [108]. On the contrary, a latter study failed to identify any differences between airway pressure release ventilation and pressure support ventilation from admission to day seven [109].

ACUTE HEART FAILURE

Practical issues limit the application of CT in the acute phase for the diagnosis of acute cardiogenic pulmonary edema. In a retrospective study, CT markers for acute pulmonary edema (i.e. engorged peripheral pulmonary vessels, thickening of inter and intralobular septa, ground glass opacities and consolidations) were compared with transpulmonary thermodilution technique variables [110]. The authors concluded that hemodynamic parameters obtained with transpulmonary thermodilution cannot be accurately estimated by CT scan. In a small study in ARDS patients, a good correlation was found between transpulmonary thermodilution and CT markers for pulmonary edema [111]. Patients with acute pulmonary edema presented a similar amount of ground glass attenuation and a lower amount of airspace consolidations [112].

PNEUMONIA

CT scan is more sensitive than CXR in detecting pulmonary infiltrates in patients with clinical suspicion of pneumonia [113, 114]. Similarly, in patients admitted to the emergency department with clinically suspected community acquired pneumonia, CT scan modified the likelihood of diagnosing community acquired pneumonia in 58% of the cases [115].

In addition, CT can also provide a detailed morphological description of patients with ventilator-associated pneumonia. CT scans of a group of patients with ventilator-associated pneumonia at diagnosis and at day 7 of antimicrobial therapy, were characterized by the presence of intraparenchymal and subpleural rounded CT attenuations disseminated within the upper and lower lobes, with consolidations of the lower and upper lobes [54]. Patients who responded successfully to antimicrobial therapy showed predominant disappearance of the rounded opacities, whereas antibiotic failures correlated with new onset of rounded opacities within the lungs. A significant correlation was found between chest CT diagnosis of pneumonia and electronic nose sensor of the expired gases, a new promising adjunct tool for the diagnosis of pneumonia [116].

COPD

Patients with severe acute exacerbation COPD, due to infection or cardiac failure, frequently require mechanical ventilation with PEEP to improve oxygenation and to reduce the work of breathing. However, the increase in PEEP is associated with an increase in lung volume with possible risks of overinflation [117].

In addition, COPD patients are at increased risk of developing pulmonary thromboemboli. During a five year follow-up from an acute exacerbation of COPD, 17% of the patients developed pulmonary embolism; the intensive care unit length of stay and mortality were significantly higher in patients with pulmonary embolism [118].

PNEUMOTHORAX

CT is commonly used for the diagnosis of pneumothorax. It is known that supine CXR is not sensitive for the diagnosis of pneumothorax in non-ICU patients [119, 120].

Very few studies compared conventional chest X-ray with CT in ICU patients. However, in a prospective study of 42 ICU patients, none of the 8 pneumothoraces diagnosed by CT were seen with CXR [121].

PLEURAL EFFUSION

The quantitative computation of pleural effusion with whole chest CT has been demonstrated to significantly relate to the amount of pleural effusion computed with LU using a multiplanar ultrasound approach considering the cephalocaudal extension and the area measured at mid length [122].

POSITRON EMISSION TOMOGRAPHY

PET can provide a functional examination, detecting the presence of a radioactive tracer which is usually administered to patients linked to a biological molecule. One of the most common tracers is [18F] fluorodexoxyglucose (18FDG). In presence of an inflammatory status there is an increase in cellular metabolism and glucose consumption, mainly linked to neutrophilic activity.

ARDS

ARDS lung is characterized, in addition to abnormalities in gas exchanges, by an increase in pulmonary vascular permeability [1]. The pulmonary vascular permeability may be assessed by the pulmonary trans-capillary escape rate for transferrin with PET (PTCER), which evaluates the protein flux between the pulmonary intravascular and extravascular compartment. ARDS and pneumonia patients presented a significant higher PTCER compared to heart failure patients and healthy subjects [123]. In pneumonia patients PTCER was also higher in the regions contralateral to focal pneumonia [123]. ARDS in the early phases had a higher PTCER compared to the late phases [124], which was still higher than that of healthy subjects [124].

The current lung ARDS model, extensively explained by CT, indicates that regions of normal aeration coexist with poorly and not aerated lung regions, and that lung densities are mainly located in the dependent lung regions [125]. Similarly, PET showed a significant increase in lung density in dorsal compared to ventral lung regions with a higher amount of the same lung regions compared to healthy subjects [126]. Surprisingly, no difference was found in the PTCER distribution between the

dorsal and ventral lung regions. Despite a lack of difference between the ventral and dorsal regions, PTCER was not uniformly distributed in ARDS patients, thereby suggesting a possible blood bore delivery of injurious agents to the lung.

Combining PET and CT with 18FDG it is possible to assess the distribution and magnitude of inflammation within the lung. Different approaches have been proposed, such as the simple static model that measures the standardized uptake volume, dynamic models that analyze the spectral analysis filter, and the Patlak analysis. In a comparison of the static and the dynamic model in ARDS patients, the dynamic model provided a better description of lung inflammation [127]. In ARDS patients the metabolic activity of the lungs was significantly higher in comparison with healthy subjects, and did not correlate with the mean lung density or with the relative weight of either non aerated or normally aerated tissue [128]. The inflammation activity negatively correlated with oxygenation levels. In the normally aerated tissue the metabolic activity was significantly higher, up to seven times, compared to that of healthy subjects. Additionally, lung inflammation was very differently distributed considering the distribution of inflation (from non inflated to well inflated regions).

The same authors analyzed the relationship between gas volume changes induced by tidal ventilation, from end expiration to end inspiration, and pulmonary inflammation [129]. The lung regions undergoing intra-tidal recruitment and de-recruitment during tidal breathing presented similar lung inflammation as the collapsed ones. Airway pressure positively correlated with lung inflammation [129].

Due to the greater distribution of lung edema in the dorsal regions, greater lung inhomogeneities of lung parenchyma may be present along the sternum vertebral axis. Concerning the distribution of lung inhomogeneity and inflammation within the lung, the amount of lung inflammation and inhomogeneity increased from mild to severe ARDS [130]. The homogeneous lung compartment with normal PET signal was mainly composed by well inflated tissue and was located in the ventral regions. On the contrary, the inhomogeneous compartment with high PET signal was composed of non or poorly inflated tissue and located in the dorsal regions. The homogeneous lung compartment with high PET signal was composed of mixed lung aeration from non inflated to well inflated and was similarly distributed with the lung.

ACUTE HEART FAILURE

Pulmonary hypertension, which is frequent in ARDS patients, has been associated to pulmonary vasoconstriction in response to hypoxia, which could redistribute pulmonary blood flow within the sick lung. The ventral to dorsal regional distribution of pulmonary blood flow has been analyzed in a group of patients with pulmonary lung edema and in healthy subjects [131]. Although the amount of lung water concentration was significantly higher in ARDS and cardiogenic pulmonary edema, the regional distribution of pulmonary blood flow was similar among ARDS and healthy subjects [131].

PNEUMONIA

By analyzing the uptake of tracer by activated inflammatory cells PET may provide a quantitative assessment of lung infection and assess the response to therapy. The pulmonary trans-capillary escape rate proved to be significantly higher in areas of radiographic infiltrates in patients with pneumonia compared to normal subjects [123]. Cystic fibrosis patients are characterized by persistent lung inflammation with high levels of neutrophil activation, translating clinically into frequent episodes of lung infections. In patients with cystic fibrosis PET showed a higher uptake of [18F] FDG compared to healthy subjects, and this feature positively correlated with the number of neutrophils in the BAL fluid [132].

PET has also been proposed in the diagnosis of interstitial lung diseases. In a small group of patients with diffuse interstitial lung disease, the tracer uptake was not different in patients with and without idiopathic lung fibrosis (IPF) [133]. On the contrary in cryptogenic organizing pneumonia the tracer uptake was significantly higher compared to IPF and non-specific interstitial pneumonia (NSIP), while similar levels were detected between IPF and NSIP [134].

COPD

COPD patients are characterized by significant alterations in the distribution of ventilation and perfusion. Vidal et al, by applying a quite innovative PET analysis, analyzed ventilation and perfusion within the lung imaging resolution unit (voxel) [135]. COPD, compared to healthy subjects. showed a larger perfusion heterogeneity with no dorso-ventral ventilation gradient.

PLEURAL EFFUSION

Due to the intrinsic differences in glucose metabolism between normal and tumour cells, PET may distinguish benign from malignant pleural effusions. Malignant pleural effusions have shown a significantly higher glucose uptake compared to benign effusions, with a good sensitivity and a relatively low specificity of the technique in detecting malignant pleural effusions (93% and 68% respectively) [136, 137].

ELECTRICAL IMPEDANCE TOMOGRAPHY

EIT uses multiple electrodes applied on the external chest surface and the application of a low voltage current to measure both absolute and relative variations of body impedance. A two-dimensional image, of approximately 10 cm, is created with good correlation to intrapulmonary lung gas volume and intrathoracic blood volume. EIT applications range from monitoring mechanical ventilation (PEEP selection, lung recruitability, distribution of ventilation), to estimating the lung perfusion and pulmonary function [138–140].

Based on our criteria selection no articles have been found on this topic.

CONCLUSIONS AND NEEDS FOR FUTURE RESEARCH

Patients with acute respiratory failure due to different lung causes and high mortality risk require numerous lung studies. As a first level exam, CXR, despite its intrinsic limitations and low accuracy may still play a relevant role. CT scan remains the gold standard, but it requires patient transportation and use of radiations, which preclude an extensive use especially within the same patient. LUS, after a proper physician training, is able to provide an accuracy greater than CXR and similar to that of the CT scan. EIT is gaining a more clinical role after having represented a research tool for many years, while PET has a minimal role in the acute phase of respiratory failure.

As bedside lung imaging techniques, LUS and EIT will become more frequently used in patients with acute respiratory failure. Future studies will assess if the information provided will improve clinical management and outcome. Regarding the CT the possibility to have dose reduction protocols and safer patients transport to the radiology department will be extend its application. There is a clinical need for studies combining different methods for the diagnosis and in the monitoring of patients.

FIGURES AND TABLES

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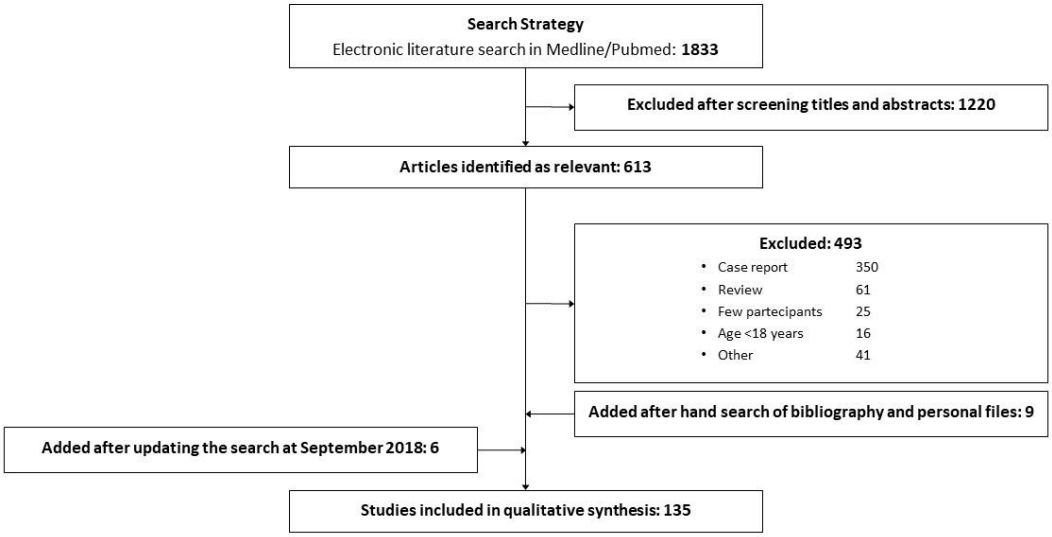
Search Strategy
Electronic literature search in Medline/Pubmed: 1833
Excluded after screening titles and abstracts: 1220
Articles identified as relevant: 613
Excluded: 493
Case report 350
Review 61
Few partecipants 25
Age <18 years 16
Other 41
Added after hand search of bibliography and personal files: 9
Added after updating the search at September 2018: 6
Studies included in qualitative synthesis: 135

Table 1. Studies included on chest-x-ray

Disease	*Reference*	*First Author*	*Aim*	*Subjects*	*Study design*	*Main results*
ARDS	2	Rubenfeld GD	To study the interobserver variability in applying the American European radiographic criteria for ARDS	28	Prospective	The radiographic criterion showed high interobserver variability
ARDS	3	Figueroa-Casas JB	To evaluate the diagnostic accuracy of CXRs to detect pulmonary abnormalities in ARDS	90	Retrospective	Accuracy of CXRs to detect pulmonary abnormalities was limited
ARDS	4	Frolich S	To evaluate accuracy of clinical diagnoses of ARDS	51	Retrospective	Only one third of ARDS were recognized on clinical records
ARDS	5	Peng J-M	To examine the effect of training material on the accuracy of CXR interpretations for ARDS diagnosis	286 intensivists	Prospective	The radiographic diagnostic accuracy and inter-rater agreement were poor and not improved by training
ARDS	6	Goddard SL	To test an educational intervention to improve the radiographic identification of ARDS	464 intensivists	Prospective	Recognition of radiographic criteria for ARDS was low, with poor agreement.
AHF	7	Halperin BD	To identify presence of excess lung water	12	Prospective	CXRs were not accurate in monitoring modest changes in lung water in critically ill patients.
AHF	8	Martin GS	To identify temporal changes in fluid balance	37	Prospective	Objective radiographic measures of intravascular volume were more accurate than subjective measures
AHF	9	Thomason JW	To identify hydrostatic and permeability pulmonary edema	33	Prospective	Objective measurements of CT ratio and VPW correlated with pulmonary artery occlusion pressure
AHF	10	Farshidpanah S	To identify hydrostatic and permeability pulmonary edema	80	Retrospective	Objective measurements of CT ratio and VPW correlated with cardiogenic pulmonary edema

PNEUMONIA	11	Lefcoe MS	To examine diagnostic accuracy of CXRs for pneumonia	62	Prospective	CXRs was not accurate in predicting the presence of pneumonia
PNEUMONIA	12	Butler KL	To examine diagnostic accuracy of CXRs for pneumonia	20	Prospective	CXRs did not improve the clinician's ability to diagnose pneumonia
PNEUMONIA	13	Moine P	To describe radiological features of severe community-acquired pneumococcal pneumonia	132	Prospective	CXRs were not accurate in detecting pneumonia etiology
PNEUMOTHORAX	14	Schulman CI	To determine optimal time for CXRs after chest tube positioning	75	Prospective	Early CXRs excluded the development of a clinically significant pneumothorax
PNEUMOTHORAX	15	Pizano LR	To determine optimal time for CXRs after chest tube removal	75	Prospective	After one hour from tube removal the CXRs identified all the pneumothoraces
PLEURAL EFFUSION	16	Emamian SA	To determine the diagnostic accuracy of pleural effusion by CXR	24 measures	Prospective	Diagnostic accuracy of pleural effusion on supine CXRs was acceptable
PLEURAL EFFUSION	17	Brixey AG	To determine the diagnostic accuracy of pleural effusion by CXR	61	Retrospective	Diagnostic accuracy of pleural effusion was the same between lateral and anterior-posterior CXRs

AHR, acute heart failure; ARDS, acute respiratory distress syndrome; CT, chest computed tomography; CXR, chest x-ray.

Table 2. Studies included on lung ultrasound

Disease	*Reference*	*First Author*	*Aim*	*Subjects*	*Study design*	*Main results*
ARDS	19	Copetti R	To assess the ability of LU to identify ARDS compared to cardiogenic pulmonary edema	58	Prospective	LU was able to discriminate between ARDS and cardiogenic pulmonary edema
ARDS	20	Sekiguchi H	To assess the ability of LU to identify ARDS compared to cardiogenic pulmonary edema	134	Prospective	LU was able to discriminate between ARDS and cardiogenic pulmonary edema
ARDS	21	Bass CM	To assess the ability of LU and arterial saturation to identify ARDS	123	Prospective	LU was a useful tool to screen oxygenation impairment consistent with ARDS
ARDS	22	Huang D	To assess the ability of LU to identify ARDS in elderly patients	51	Prospective	LU presented similar accuracy compared to CT scan
ARDS	23	Riviello ED	To estimate incidence of ARDS according to the Berlin definition and LU	42	Prospective	Using these criteria the incidence of ARDS was significantly improved
ARDS	24	Zhao Z	To assess prognostic values of LU in ARDS	21	Prospective	Early use of LU was a useful prognostic indicator in ARDS patients
ARDS	25	Tsubo T	To evaluate daily lung density changes in ARDS	15	Prospective	LU was able to detect density changes in in dependent lung regions in ARDS
ARDS	26	Tsubo T	To evaluate lung density in ARDS	40	Prospective	LU was able to detect density changes in in dependent lung regions in ARDS
ARDS	27	Tsubo T	To evaluate lung density in ARDS during prone positioning	10	Prospective	LU was able to detect changes in density during prone positioning
ARDS	28	Stefanidis K	To evaluate LU in the	10	Prospective	LU could detect non aerated lung

			measurement of pulmonary recruitment			areas during PEEP trials
ARDS	29	Bouhemad B	To evaluate LU in the measurement of pulmonary recruitment	30	Prospective	LU could detect lung recruitment during PEEP changes
ARDS	30	Chiumello D	To assess LU score in the measurement of pulmonary recruitment	20	Prospective	LU score should be not used to assess pulmonary recruitment
AHF	31	Enghard P	To evaluate LU in predicting extravascular lung water	50	Prospective	LU correlated with extravascular lung water
AHF	32	Jambrick Z	To evaluate LU in predicting extravascular lung water	121	Prospective	LU correlated with extravascular lung water
AHF	33	Volpicelli G	To evaluate LU in predicting extravascular lung water	73	Prospective	LU correlated with extravascular lung water
AHF	34	Mallamaci F	To evaluate LU in predicting extravascular lung water	47	Prospective	LU correlated with extravascular lung water in hemodialysis patients
AHF	35	Noble VE	To evaluate LU in predicting extravascular lung water	45	Prospective	LU score changes correlated with real time extravascular lung water changes during hemodialysis
AHF	36	Lichtenstein DA	To evaluate LU in predicting pulmonary arterial occlusion pressure	102	Prospective	LU score could predict a low pulmonary arterial occlusion pressure
AHF	37	Laursen CB	To evaluate LU in predicting the diagnosis of cardiogenic pulmonary edema	40	Prospective	LU was able to rule out cardiogenic pulmonary edema
AHF	38	Cortellaro F	To evaluate LU in monitoring the response to therapy in cardiogenic pulmonary edema	41	Prospective	LU allowed to guide therapy titration in cardiogenic pulmonary edema

AHF	39	Martindale JL	To evaluate LU in monitoring changes in pulmonary edema	20	Prospective	LU improved the clinical management
COPD	40	Lichtenstein DA	To assess the relationship between comet tail artifacts and alveolar interstitial syndrome	121	Prospective	Good correlation between the ground glass and comet tail artifacts
COPD	41	Silva S	To compare LU with clinical, radiological and biological data	78	Prospective	Cardiothoracic ultrasound was a useful diagnostic approach
PNEUMONIA	42	Yang PC	To identify LU features associated with pneumonia	161	Prospective	LU was a useful tool in the evaluation of pulmonary consolidation
PNEUMONIA	43	Testa A	To evaluate LU features in interstitial pneumonia	98	Prospective	LU could provide an early detection of interstitial pneumonia
PNEUMONIA	44	Reissig A	To identify LU features associated with pneumonia	30	Prospective	LU was a useful tool in the evaluation and follow up of patients with pneumonia
PNEUMONIA	45	Parlamento S	To evaluate LU in confirming the clinical suspicion of pneumonia	49	Prospective	LU should be considered in the diagnostic workup of pneumonia
PNEUMONIA	46	Sperandeo M	To evaluate LU in confirming the clinical suspicion of pneumonia	15	Prospective	LU was a useful tool in the evaluation and follow up of patients with pneumonia
PNEUMONIA	47	Cortellaro F	To evaluate LU to confirm the clinical suspicion of pneumonia	120	Prospective	LU should be considered in the diagnostic workup of pneumonia
PNEUMONIA	48	Reissig A	To evaluate LU in the diagnosis of community acquired pneumonia	30	Prospective	LU had a high accuracy in diagnosing community acquired pneumonia
PNEUMONIA	49	Bourcier J-E	To evaluate LU in confirming the clinical suspicion of pneumonia	144	Prospective	LU should be considered as a first line diagnosis tool for pneumonia

PNEUMONIA	50	Corradi F	To compare LU with CXR in suspected community acquired pneumonia	32	Prospective	LU should be considered in the first line diagnosis of pneumonia
PNEUMONIA	51	Liu X	To compare LU with CXR in suspected community acquired pneumonia	179	Prospective	LU had a better diagnostic sensitivity and accuracy for diagnosing community acquired pneumonia
PNEUMONIA	52	Pagano A	To compare LU with CXR in suspected community acquired pneumonia	107	Prospective	LU should be considered in the first line diagnosis of pneumonia
PNEUMONIA	53	Lichtenstein DA	To evaluate LU features and diagnosis of pneumonia	66	Prospective	LU could distinguish pneumonia from reabsorption atelectasis
PNEUMONIA	54	Bouhemad B	To evaluate LU for lung reaeration in ventilator associated pneumonia	30	Prospective	LU accurately estimated lung reaeration
PNEUMONIA	55	Mongodi S	To evaluate LU for early diagnosis of ventilator associated pneumonia	99	Prospective	LU was a reliable tool for early ventilator associated pneumonia diagnosis
PNEUMOTHORAX	56	Lichtenstein DA	To evaluate the presence of lung point as specific sign of pneumothorax	66	Prospective	The lung point allowed the diagnosis of pneumothorax
PNEUMOTHORAX	57	Volpicelli G	To compare the pneumothorax volume between LU and CT	124	Prospective	Good correlation between LU and CT
PNEUMOTHORAX	58	Dulchavsky SA	To evaluate LU for diagnosis of pneumothorax	382	Prospective	LU was a reliable tool for diagnosis of pneumothorax
PNEUMOTHORAX	59	Kirkpatrick AW	To evaluate LU for diagnosis of pneumothorax	225	Prospective	LU was a reliable tool for diagnosis of pneumothorax
PNEUMOTHORAX	60	Weekes AJ	To compare LU with CXR for	151	Prospective	No difference between LU and

			confirmation of central venous catheter placement			CXR
PNEUMOTHORAX	61	Vezzani A	To compare LU with CXR for confirmation of central venous catheter placement	111	Prospective	No difference between LU and CXR
PNEUMOTHORAX	62	Maury E	To compare LU with CXR for confirmation of central venous catheter placement	58	Prospective	LU was a more rapid method compared to CXR
PNEUMOTHORAX	63	Saucier S	To evaluate LU for the detection of pneumothorax after chest tube removal	50	Prospective	LU was accurate to detect pneumothorax
PLEURAL EFFUSION	64	Lichtenstein DA	To evaluate the safety of thoracentesis guided by LU	40	Prospective	LU guaranteed safety during thoracentesis
PLEURAL EFFUSION	65	Vignon P	To assess the ability of LU to predict the amount of pleural effusion	97	Prospective	Expiratory interpleural distance was related with the amount of pleural effusion
PLEURAL EFFUSION	66	Rozycki GS	To evaluate LU for diagnosis of pleural effusion	47	Prospective	LU was a reliable tool for the diagnosis of pleural effusion in surgically ill patients
PLEURAL EFFUSION	67	Rocco M	To compare LU with CXR in trauma patients	15	Prospective	LU was a reliable tool for diagnosis of pleural effusion in trauma patients
PLEURAL EFFUSION	68	Gallard E	To evaluate LU in patients with acute dyspnea in the emergency department	130	Prospective	LU permitted rapid detection of pleural effusion in presence of acute dyspnea
PLEURAL EFFUSION	69	Yu CJ	To assess the ability of LU to predict the amount of pleural effusion	320	Prospective	LU accurately detected pleural effusion in critically ill patients
PLEURAL	70	Mayo PM	To assess the safety of ultrasound	211	Prospective	Ultrasound thoracentesis in

EFFUSION			guided thoracentesis			mechanical ventilation was a well tolerated procedure
PLEURAL EFFUSION	71	Schleder S	To evaluate hand carried LU for the diagnosis of pleural effusion	24	Prospective	Hand carried LU had high diagnostic accuracy

AHR, acute heart failure; ARDS, acute respiratory distress syndrome; COPD, Chronic obstructive pulmonary disease; CT, chest computed tomography; CXR, chest x-ray; LU, lung ultrasound.

Table 3. Studies included on computed tomography

Disease	*Reference*	*First Author*	*Aim*	*Subjects*	*Study design*	*Main results*
ARDS	72	Awerbuch E	To evaluate diagnostic and clinical impact of CT	134	Retrospective	Up to one quarter of the patients received clinical changes
ARDS	73	Owens CM	To compare morphological CT abnormalities with severity of lung injury score	8	Prospective	Extent of CT abnormalities correlated with lung injury score
ARDS	74	Bombino M	To compare CT and CXR with clinical data	17	Prospective	CT and CXR scores were related to the degree of gas exchange impairment
ARDS	75	Puybasset L	To compare CT distribution of gas and tissue analysis in ARDS and healthy subjects	82	Prospective	Different lung morphology corresponded to different distribution of gas within the lung
ARDS	76	Patroniti N	To compare Helium dilution technique with CT to assess lung gas volume in patients with ARDS	21	Prospective	Helium dilution technique showed good agreement with CT
ARDS	77	Patroniti N	To compare CT and indocyanin green dye double dilution technique for measurement of pulmonary edema in ARDS	14	Prospective	Estimation of edema with indo-cyanine green showed good correlation and reproducibility with CT
ARDS	78	Lu Q	To assess PEEP changes in single- or three section, or whole lung CT	39	Retrospective	Single and three section differed from whole CT lung
ARDS	79	Vieira SRR	To compare pulmonary hyperinflation measured by low and high spatial resolution CT	30	Prospective	In ARDS accurate estimation of lung hyperinflation on CT required high spatial resolution
ARDS	80	Reske AW	To evaluate the ratio between PaO_2/FiO_2 and shunt	71	Prospective	Logarithmic PaO_2/FiO_2 allowed estimation of CT shunt and its changes

ARDS	81	Caironi P	To assess a standardized low PEEP strategy	148	Retrospective	The PaO_2/FiO_2 computed at 5 cmH2O of PEEP accurately reflected the lung injury severity and recruitability
ARDS	82	Rouby JJ	To assess differences in lung morphology with different lung mechanics and outcome	71	Prospective	A severity score based on CT lung morphology accurately identified patients with the most severe forms of ARDS
ARDS	83	Stelter L	To evaluate CT findings in patients with sepsis and ARDS	36	Prospective	A CT scoring system based on pulmonary findings was related to the outcome
ARDS	84	Lazoura O	To correlate CT morphology with clinical severity and outcome	33	Retrospective	A greater extent of airspace disease was associated with higher clinical severity
ARDS	85	Simon M	To assess clinical utility of CT	204	Retrospective	CT yielded useful information for diagnosis, prognosis and alternative diagnosis in ARDS patients
ARDS	86	Chiumello D	To investigate if low dose CT can provide accurate quantitative and visual anatomical results	45	Prospective	Low dose CT showed good agreement with conventional CT both for quantitative and visual anatomical results
ARDS	87	Klapsing P	To investigate an automatic software for quantitative lung analysis	10	Prospective	Automatic software computation allowed an accurate computation
ARDS	88	Miller PR	To identify high risk patients according to pulmonary contusion volume	49	Prospective	Contusion volume on chest CT was predictor for ARDS development
ARDS	89	Reske AW	To evaluate quantitative CT in posttraumatic lung dysfunction	78	Prospective	Quantitative CT might help to discriminate atelectasis from consolidation

ARDS	90	Chiumello D	To assess the effect of pleural effusion on respiratory mechanics, gas exchange and lung recruitability	179	Prospective	Pleural effusion was of modest entity and did not affect respiratory system elastance
ARDS	91	Gattinoni L	To assess CT changes in early and late ARDS	81	Prospective	Lung structure markedly changed with ARDS duration
ARDS	92	Treggiari MM	To investigate prevalence / distribution of air cysts and bronchiectasis	21	Retrospective	A predominant localization of lesions in better ventilated areas (non-dependent)
ARDS	93	Burnham EL	To determine relationship between pulmonary dysfunction and high resolution CT	89	Prospective	Among survivors, high resolution CT findings correlated with quality of life
ARDS	94	Nobauer IM	To evaluate changes in high resolution CT at 6-10 months after ARDS	15	Prospective	ARDS frequently resulted in fibrotic changes in the lung, particularly in the ventral regions.
ARDS	95	Masclans JR	To evaluate the quality of life in survivors of ARDS and related CT changes	38	Prospective	Six months after ARDS, there were mild radiological abnormalities in 76% of the patients
ARDS	96	Kim SJ	To determine if outcome differs between pulmonary and extra pulmonary ARDS	29	Retrospective	Pulmonary lesions were more extensive in pulmonary compared to non-pulmonary ARDS
ARDS	97	Cressoni M	To assess the relationship between lung recruitability and pressure to overcome the compression forces	51	Prospective	Lung recruitability was not related to the pressure to overcome compression forces
ARDS	98	Puybasset L	To evaluate PEEP changes and lung morphology	71	Retrospective	PEEP effects were more related to lung morphology compared to the cause of lung injury
ARDS	99	Constantin J-M	To determine if differences in lung morphology may predict the	19	Prospective	Lung morphology predicted response to recruitment. Focal

			response to recruitment maneuvers			lung morphology was at high risk for hyperinflation with recruitment maneuver
ARDS	100	Chiumello D	To evaluate the effects of body mass index in ARDS	101	Retrospective	Obese ARDS had similar chest wall elastance and lung recruitability compared to non obese ARDS patients
ARDS	101	Cressoni M	To assess the amount of lung recruitability and opening and closing	33	Prospective	With PEEP up to 25 cmH_2O and Plateau pressure up to 30 cmH_2O were not adequate to maintain open the lung
ARDS	102	Cressoni M	To quantify lung inhomogeneities	148	Retrospective	Lung inhomogeneities were related to disease severity and mortality
ARDS	103	Chiumello D	To determine bedside PEEP selection is related to lung recruitability	51	Prospective	Oxygenation based method provided PEEP related to lung recruitability
ARDS	104	Constantin J-M	To compare two recruitment maneuvers s in ARDS	19	Prospective	Extended sigh promoted higher alveolar recruitment and oxygenation compared to CPAP RM
ARDS	105	Galiatsou	To quantify the lung volume changes during prone position	21	Prospective	Prone position recruited significantly more lung compared to recruitment maneuver
ARDS	106	Lu Q	To evaluate the effects of exogenous surfactant on pulmonary aeration in patients with ARDS	20	Prospective	Surfactant administration induced an improvement in lung aeration of poorly and non aerated lung regions
ARDS	107	Lu Q	To compare PV curves and CT during PEEP-induced lung recruitment	19	Prospective	Alveolar recruitment assessed by CT and PV curve were strongly correlated but with very high

						limits of agreements
ARDS	108	Yoshida T	To compare airway pressure release ventilation compared to PSV on lung atelectasis	18	Retrospective	Airway pressure released ventilation resulted in better lung aeration compared to PSV
ARDS	109	Varpula T	To compare airway pressure release ventilation compared to PSV on lung atelectasis and gas distribution	23	Retrospective	No differences in airway pressure release ventilation or PSV on CT characteristics
AHF	110	Saguel B	To compare CT estimation of cardiac preload and pulmonary hydration in predicting volume status	30	Prospective	CT estimation of end diastolic volume index and extravascular lung water were not accurate in predicting volume status
AHF	111	Zhang F	To evaluate quantitative CT analysis to measure pulmonary edema	10	Prospective	Acceptable agreement between CT analysis and thermodilution
AHF	112	Vergani G	To compare quantitative CT analysis in cardiogenic pulmonary edema and ARDS	80	Prospective	Similar presence of ground glass and different airspace consolidation regions
PNEUMONIA	113	Syriala H	To compare CT with CXR in the diagnosis of pneumonia	47	Prospective	CT was more sensitive compare to CXR
PNEUMONIA	114	Gruden JF	To compare CT with CXR in AIDS patients	33	Prospective	CT was more sensitive compare to CXR
PNEUMONIA	115	Claessens Y-E	To compare CT with CXR in the diagnosis of community acquired pneumonia	319	Prospective	CT was more sensitive compared to CXR
PNEUMONIA	116	Hockstein NG	To compare CT with electronic nose sensor	33	Prospective	Acceptable agreement between CT and nose sensor for pneumonia
COPD	117	Nieskowska A	To assess the regional distribution of inflation in COPD	32	Prospective	PEEP significantly increased lung overinflation

COPD	118	Bahloul M	To assess the incidence and outcome of pulmonary embolism in COPD	131	Retrospective	Higher mortality and length of stay in COPD patients with an acute exacerbation and pulmonary embolism
PNEUMOTHORAX	119	Lichtenstein DA	To compare CT with LU in the diagnosis of occult pneumothorax	200	Retrospective	LU might decrease the need for CT
PNEUMOTHORAX	120	Soldati G	To compare CT with LU in the diagnosis of occult pneumothorax	109	Prospective	LU might decrease the need for CT
PNEUMOTHORAX	121	Xirouchaki N	To compare CT with LU and CXR	42	Prospective	LU could be an alternative to CT
PLEURAL EFFUSION	122	Remerand F	To assess the accuracy of LU to measure pleural effusion	58	Prospective	The multiplane LU approach could estimate pleural effusion volume better than the conventional technique

AHR, acute heart failure; ARDS, acute respiratory distress syndrome; COPD, Chronic obstructive pulmonary disease; CT, chest computed tomography; CXR, chest x-ray; FiO_2, fraction of inspired oxygen; LU, lung ultrasound; PaO_2, partial pressure of oxygen in arterial blood; PEEP, Positive end-expiratory pressure; PSV, pressure support ventilation.

Table 4. Studies included on positron emission tomography

Disease	*Reference*	*First Author*	*Aim*	*Subjects*	*Study design*	*Main results*
ARDS	123	Kaplan JD	To measure pulmonary vascular permeability	43	Prospective	ARDS and pneumonia had higher PTCER
ARDS	124	Calandrino FS	To measure pulmonary vascular permeability	27	Prospective	Early vs Late ARDS had higher PTCER
ARDS	125	Sandiford P	To measure regional distribution of vascular permeability	8	Observational	No difference in the distribution of PTCER
ARDS	126	Grecchi E	To investigate PET static and dynamic model analysis	11	Observational	Dynamic model better described lung inflammation
ARDS	127	Bellani G	To investigate inflammation distribution	10	Observational	Lung inflammation was diffusely distributed within the lung
ARDS	128	Bellani G	To assess gas volume changes and metabolic activity	13	Observational	No difference in lung inflammation between recruited-derecruited and collapsed regions
ARDS	129	Cressoni M	To determine size and location of lung inhomogeneities and inflammation	20	Observational	Different regional distribution of inhomogeneities and inflammation
AHF	130	Schuster DP	To assess perfusion distribution	21	Observational	Similar pulmonary blood flow among the groups
PNEUMONIA	131	Chen DL	To investigate the relationship between lung inflammation and lung function	27	Observational	Patients with cystic fibrosis had higher inflammation compared to healthy
PNEUMONIA	132	Nusair S	To assess possible use of PET in interstitial lung disease	21	Observational	No difference in tracer uptake between patients with different interstitial lung diseases
PNEUMONIA	133	Umeda Y	To assess the degree of inflammation and disease progression	50	Observational	Possible use in analysis of disease progression and response to therapy

COPD	134	Vidal Melo MF	To assess ventilation distribution in COPD	12	Observational	High heterogeneity of ventilation distribution in COPD
PLEURAL EFFUSION	135	Nakajima R	To discriminate benign from malignant pleural effusion	79	Retrospective	Good accuracy in discriminating benign from malignant pleural effusion
PLEURAL EFFUSION	136	Duysink BC	To discriminate benign from malignant pleural effusion	36	Retrospective	Good accuracy in discriminating benign from malignant pleural effusion

AHR, acute heart failure; ARDS, acute respiratory distress syndrome; COPD, Chronic obstructive pulmonary disease; PET, positron emission tomography; PTCER, pulmonary transcapillary escape rate.

Table S1. The following keywords were used for search on Medline for chest-x-ray

COPD

((("Pulmonary Disease, Chronic Obstructive"[Mesh] OR "COPD")) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ARDS

((("Respiratory Distress Syndrome, Adult"[Mesh] OR "ARDS" OR "acute respiratory distress syndrome")) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ALI

((("Acute Lung Injury"[Mesh] OR "ALI" OR "acute lung injury")) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMOTHORAX

(("Pneumothorax"[Mesh]) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PLEURAL EFFUSION

(("Pleural Effusion"[Mesh]) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMONIA

(("Pneumonia"[Mesh]) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PULMONARY EDEMA

(("Pulmonary Edema"[Mesh]) AND ("Radiography, Thoracic"[Mesh] OR "chest x-ray" OR "chest radiography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

Table S2. The following keywords were used for search on Medline for lung ultrasound

COPD

((("Pulmonary Disease, Chronic Obstructive"[Mesh] OR "COPD")) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ARDS

((("Respiratory Distress Syndrome, Adult"[Mesh] OR "ARDS" OR "acute respiratory distress syndrome")) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ALI

(("Acute Lung Injury"[Mesh]) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMOTHORAX

(("Pneumothorax"[Mesh]) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PLEURAL EFFUSION

(("Pleural Effusion"[Mesh]) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMONIA

(("Pneumonia"[Mesh]) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PULMONARY EDEMA

(("Pulmonary Edema"[Mesh]) AND ("Ultrasonography"[Mesh] OR "lung ultrasonography" OR "lung ultrasound")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

Table S2. The following keywords were used for search on Medline for computed tomography (CT)

COPD

((("Pulmonary Disease, Chronic Obstructive"[Mesh] OR "COPD")) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ARDS

((("Respiratory Distress Syndrome, Adult"[Mesh] OR "ARDS" OR "acute respiratory distress syndrome")) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ALI

((("Acute Lung Injury"[Mesh] OR "ALI" OR "acute lung injury")) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMOTHORAX

((("Pneumothorax"[Mesh]) AND "Pleural Effusion"[Mesh]) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PLEURAL EFFUSION

(("Pleural Effusion"[Mesh]) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMONIA

(("Pneumonia"[Mesh]) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PULMONARY EDEMA

(("Pulmonary Edema"[Mesh]) AND ("Tomography, X-Ray Computed"[Mesh] OR "CT scan" OR "computed tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

Table S4. The following keywords were used for search on Medline for positron emission tomography

COPD

((("Pulmonary Disease, Chronic Obstructive"[Mesh] OR "COPD")) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ARDS

((("Respiratory Distress Syndrome, Adult"[Mesh] OR "ARDS" OR "acute respiratory distress syndrome")) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

ALI

((("Acute Lung Injury"[Mesh] OR "ALI" OR "acute lung injury")) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMOTHORAX

(("Pneumothorax"[Mesh]) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PLEURAL EFFUSION

(("Pleural Effusion"[Mesh]) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PNEUMONIA

(("Pneumonia"[Mesh]) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")

PULMONARY EDEMA

(("Pulmonary Edema"[Mesh]) AND ("Positron-Emission Tomography"[Mesh] OR "PET" OR "positron emission tomography")) AND (("Critical Care"[Mesh]) OR "Intensive Care Units"[Mesh] OR "intensive care" OR "critical care")