CURRENT OPINION

Lung ultrasound monitoring: impact on economics and outcomes

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Purpose of review
This review aims to summarize the impact of lung ultrasonography (LUS) on economics and possible impact on patients outcomes, proven its diagnostic accuracy in patients with acute respiratory failure.

Recent findings
Despite some previous ethical concerns on LUS examination, today this technique has showed several advantages. First, it is now clear that the daily use of LUS can provide a relevant cost reduction in healthcare of patients with acute respiratory failure, while reducing the risk of transport of patients to radiological departments for chest CT scan. In addition, LUS reduces the exposition to x-rays since can replace the bedside chest X-ray examination in many cases. Indeed, LUS is characterized by a diagnostic accuracy that is even superior to portable chest X-ray when performed by well trained personnel. Finally, LUS examination is a useful tool to predict the course of patients with pneumonia, including the need for hospitalization and ICU admission, noninvasive ventilation failure and orotracheal intubation, weaning success, and mortality.

Summary
LUS should be implemented not only in Intensive Care Units, but also in other setting like emergency departments. Since most data comes from the recent coronavirus disease 2019 pandemic, further investigations are required in Acute Respiratory Failure of different etiologies.

Keywords
chest X-ray radiography, critically ill patient, intensive care, lung ultrasound

INTRODUCTION

Lung ultrasonography (LUS) is a noninvasive tool that allows lung evaluation at the bedside in absence of ionizing radiations. Due to these reasons, LUS has gained popularity among clinicians since its first description more than 50 years ago [1].

In 1996, the American College of Radiology still recommended chest X-ray as the gold-standard to monitor lung and devices in critically ill patients, although the patient's positioning in the bed, the portable equipment and the antero-posterior approach may somehow limit its validity [2]. Therefore, at that time the application of LUS examination was very limited, lacking the pillars of ethics. Only in 2009, the American College of Chest Physicians and 'La Societe de Reanimation de Langue Francaise' published a joined consensus defining that general critical care ultrasonography (including LUS) could be performed and interpreted by trained intensivists to establish diagnoses and to guide procedures [3]. Intensivists required well established competences in technical and cognitive elements, such as the knowledge in basic semiology of LUS, identification, characterization and interpretation of lung consolidation and air-artifacts [3]. This document represented the 'Berlin wall fall', mainly for ethical concerns in LUS. However, the intensivist should assume the responsibility for all aspects of image acquisition [3].

After validation and growing evidence, LUS is now part of the medical assessment of patient with acute respiratory failure (ARF) and ethical concerns are now contracted. Although chest X-ray at the

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KEY POINTS

- Despite initial ethical and clinical concerns, lung ultrasonography (LUS) is today strongly introduced into clinical practice.
- LUS examination has advantages in terms of reduction of both cost and radiation exposure.
- When performed by trained personnel, LUS has an even higher diagnostic accuracy, as compared to traditional chest X-ray.
- LUS score can predict several clinical outcomes, such as need for hospitalization, noninvasive ventilation failure, need for ICU admission and mortality.

bedside remains the most frequently prescribed imaging techniques in patients with ARF, LUS has gained validity in the evaluation of these patients [4]. In addition, recent international guidelines recommend performing LUS assessment according to predefined imaging protocols, after the acquisition of an adequate (theoretical and practical) training before its implementation in the diagnostic process [5▪▪].

In recent years, LUS has progressively increased its application in and outside the intensive care unit (ICU) for the assessment of lung aeration in daily clinical practice [6–11]. Due to the widespread clinical use of LUS, we conducted the present review focused on describing the impact of LUS on economics and outcomes of patients. Technical and examination features are out of our aim, and we leave the reader to explore these issues elsewhere.

IMPACT ON ECONOMICS

Patients with ARF require chest imaging to monitor and/or assess their underlying disease and invasive devices. Bed-side chest X-ray has several limitations and sometime patients require to execute a control computed tomography (CT) scan. The mobilization of critically ill patients from the ICU to the radiological department is not without risk for complications or adverse events, occurring in up to 40–50% of patients [12,13]. The most important complications are modification of the heart rate and hemodynamics including arrhythmias and cardiac arrest, worsening of gas exchange, and increased intracranial pressure [13].

Intra-hospital transport of an ICU patient also requires organization, personnel, long times, which are adjunctive costs. Noteworthy, control CT scans within 12 h after ICU admission do not modify the clinical management in 70% of patients [14], which are certainly exposed to the potentially harmful effects of radiation or contrast dye. Furthermore, after the indication of the American College of Radiology to daily perform a chest X-ray in ventilated patients, Kroner *et al.* [15] reduced chest X-rays on an on-demand basis request and retrospectively analyzed their data. Noteworthy, the on-demand strategy reduced by the 50% the number of exams, with a minimal impact on chest CT scans or LUS examinations [15]. In keeping with the former study [15], another large multicenter randomized controlled trial confirmed that an on-demand strategy significantly reduced the need for bedside chest radiographs per patient-day by 10–56% across different centers, without any impact on days of mechanical ventilation, ICU length of stay or mortality [16].

LUS has been proposed as alternative to chest X-ray or CT scan, to reduce the risk of patients' transports, the costs, and the radiation exposure of patients. After introduction of LUS to assess the presence of pleural effusion, Peris *et al.* [17] significantly reduced the need of diagnostic chest X-rays and CT scans by 26% and 47%, respectively, with a 39% cost saving in radiological examination (around 27.000€) after only 6 months of LUS application. Interestingly, the cost for equipment and personnel training was approximately 25 000€ [17]. The reduction of costs, radiation exposure and risk associated with patients' transport have been also reported by an American study conducted in two medical ICU; the application of the point-of-care ultrasonography reduced by the 75% and 60% the need for chest X-ray and CT scan, respectively [18]. In keeping with the previous studies [17,18], Brogi *et al.* [19] retrospectively analyzed the costs associated to chest imaging before and after the introduction of LUS examinations as thoracic imaging technique of choice extending the indications to first diagnosis, follow-up and monitoring of pleuro-pulmonary conditions of critically ill patients. The authors reported to halve the number of chest X-ray and the costs related to radiological examinations without affecting the outcomes of patients [19]. Behind the cost saving reported by studies, every center may predict the possible economic impact of implementation of a LUS examination program. In fact, the cost to buy a small ultrasound machine is around 30 000€, whereas chest X-ray and CT scan costs are around 25€ and 130€ per exam, respectively [20]. Physicians in addition require a dedicated training that increases the required budget to start the program and a period (learning curve) to reach their best confidence and performance with the technique. Learning curve may last around 7 months [20], although even a 1-h theoretical course followed by 2-h hands-on training on

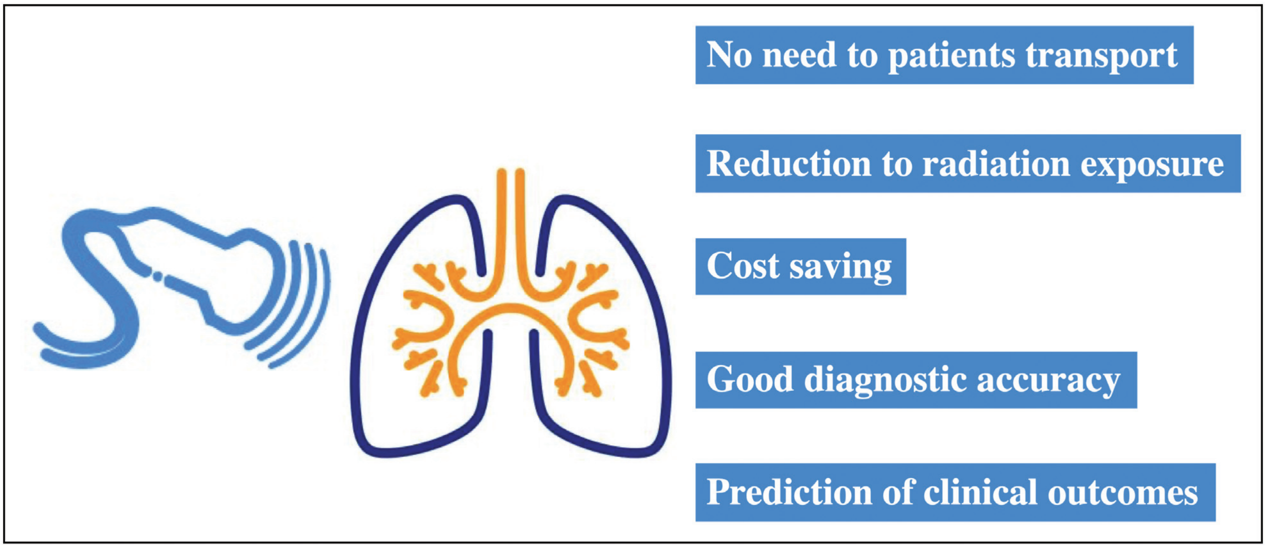

FIGURE 1. The application in clinical practice of LUS has several advantages which consist in reduction of costs, increased patients safety, diagnostic accuracy and prediction of outcomes. LUS, lung ultrasonography.

healthy subjects already improves the knowledge, image acquisition, and interpretation [21]. Certainly, the combination of theory and hand-on training has been reported to be successful in various ultrasonographic techniques [21,22]. All these findings are summarized in Fig. 1.

LUNG ULTRASONOGRAPHY DIAGNOSTIC ACCURACY AND PATIENTS' OUTCOMES

Proven the cost reduction, it is essential to evaluate the diagnostic accuracy of LUS compared to standard radiological imaging (chest X-ray or CT scan), and then analyzing the possible impact of this technique on patients' outcome.

LUS reveals combination of different images/artifacts and patterns according to the underlying disease. For example, in critically ill patients affected by acute respiratory distress syndrome, LUS shows a varying combination of B-lines, pleural line abnormalities (absent or reduced lung sliding, thickening or irregularities) and consolidated areas according to the severity of the lung impairment and presence of water lung [4,23]. Noteworthy, sometimes LUS may detect the interstitial involvement by viral pneumonia even earlier than chest X-ray [24].

The diagnostic accuracy of LUS has been extensively assessed in varying disorders and settings, in comparison with both chest X-ray and CT scan. Pneumothorax is the most common example of diagnostic accuracy for LUS. The absence of pleural sliding (i.e. the movement of the pleural line synchronous with the respiratory cycle) and the detection of a lung point (i.e., the alternation of normal and abolished sliding during tidal ventilation) highly suggest the presence of pneumothorax [25]. The absence of lung sliding had a sensitivity of 100%, a specificity of 78%, a negative predictive value of 100%, and a positive predictive value of 40%, in case of occult pneumothorax [26]. When the absence of lung sliding is associated to the 'A lines sign' (i.e., presence of A lines without B lines), diagnostic accuracy for pneumothorax further increases. LUS showed a sensitivity of 95%, a specificity of 94%, a negative predictive value of 99%, and a positive predictive value of 71% [26]. The presence of lung point has an overall sensitivity ranging between 66% and 79% in occult pneumothorax, a specificity of 100%, a negative predictive value of 97%, and a positive predictive value of 100% [25,26].

Systematic reviews demonstrate that LUS has a better diagnostic accuracy than chest X-ray, to detect lung consolidations, pleural effusion, pneumothorax, interstitial syndrome, and lung contusions [27,28▪]. A recent study has also reported that, by excluding the presence of pulmonary infarction, LUS provides useful information to rule out the suspicious of pulmonary embolism in patients with pleuritic chest pain (sensitivity 81.5% and specificity 95.4%), whereas in patients without pleuritic chest pain the sensitivity drops to 49.5% [29]. Therefore, LUS is a valid alternative to chest X-ray, not only for cost reduction, but also for diagnostic accuracy (Fig. 1). However, when the physician needs more precise and higher resolution of the abnormalities, CT scan still remains indicated.

After the outbreak of SARS-CoV-2 epidemic, a radiology panel of expert stressed on the importance of findings in CT scan in hospital admitted patients [30]; however, the limited resources to treat the high number of patients made CT scan for all patients unsustainable and LUS gained popularity in emergency departments, wards and ICU [31,32▪▪,33,34▪,35▪]. A recent Cochrane systematic review and meta-analysis reports that chest X-ray has a pooled sensitivity of 73.1% (95% confidence interval [CI] 64.1–80.5) and specificity of 73.3% (95% CI 61.9–82.2), whereas LUS is characterized by a sensitivity of 88.9% (95% CI 84.9–92.0) and specificity of 72.2% (95% CI 58.8–82.5) [36▪▪].

In addition, LUS score moderately correlates with findings of CT scan, although some abnormalities on CT scan cannot be detected with the LUS examination [37,38]. However, CT scan has a pooled sensitivity of 86.9% (95% CI 83.6–89.6), and a pooled specificity of 78.3% (95% CI 73.7–82.3), which is not so different from pooled data from LUS [36▪▪]. Therefore, despite similar specificity among the three imaging techniques, LUS and CT-scan still demonstrate a higher sensitivity in SARS-CoV-2 patients [36▪▪].

LUS has some correlations with the disease course, sometimes predicting clinical outcomes of patients. Although the most data belong from the COVID-19 epidemic, some studies assessed the ability of LUS to monitor and analyze the course of disease before the exploiting of SARS-CoV-2 pneumonia (Fig. 1).

The diagnosis and follow-up of pneumonia is one of the first clinical application of LUS in ICU [39]. A recent randomized controlled trial enrolled all patients after 48 h of mechanical ventilation with clinical signs for ventilator associated pneumonia (VAP) [40]. Patients were then randomized to confirm the diagnosis of VAP or with chest X-ray (controls) or LUS. In the latter groups of patients, the ventilator free days improved by >4 days, as explained by an earlier VAP diagnosis through LUS, as compared to traditional X-ray imaging [40]. Similarly, Zagli *et al.* [41] demonstrated that a new diagnostic score called Chest Echography and Procalcitonin Pulmonary Infection Score (CEPPIS), replacing chest X-ray with LUS, was superior to the Clinical Pulmonary Infection Score (CPIS) in predicting the development of VAP. In 2012, another study enrolling 361 patients with pneumonia in 14 European centers demonstrated that the area of pneumonic lesions decreased from 15.3 cm^2 at the diagnosis to 0.2 cm^2 after 2 weeks of treatment, in line with the reduction of C-reactive protein levels [42].

LUS has been also applied to predict weaning success or failure. Based on the hypothesis that lung aeration defect before weaning and/or the evidence of a significant lung derecruitment during a spontaneous breathing trial may predict weaning failure, Soummer *et al.* [43] reported that patients developing postextubation respiratory failure had a greater lung derecruitment during the weaning process. In addition, a LUS score ≤12 at the end of the spontaneous breathing trial was a good predictor of weaning and extubation success, whereas a score ≥17 highly predicted extubation failure [43]. These findings were also supported by other studies included in a pooled data analysis of a systematic review [44]. In addition, the application of LUS combined with diaphragm [45] or diaphragm and cardiac sonography [46▪] showed a contrasting result requiring further investigations.

In COVID-19 patients, LUS has been investigated as a tool to predict several clinical outcomes, such as need for hospitalization and ICU admission, noninvasive ventilation (NIV) failure requiring orotracheal intubation and survival.

In a study conducted in the emergency department by Brahier *et al.* [47▪▪], COVID-19 patients requiring or not hospital admission showed different LUS score, normalized for the examined number of regions (median value of 1.1 vs. 0.5, respectively) and even predicting those patients requiring intubation (median value of 1.5). LUS integrated with the clinical status of the patient was also shown to improve the outcome prognostication over clinical judgment alone by an Italian group [48]. The absence of (or minimal) alterations at LUS may suggest a low-risk condition and the patient can be safely discharged at home [48].

Another challenge during the pandemic was to discriminate which patients would fail or not NIV. Biasucci *et al.* [49▪▪] computed the LUS score in 85 patients undergoing NIV. In NIV failure patients, the median LUS score (12 vs. 6) was significantly higher than in those patients succeeding with NIV [49▪▪]. Of note, not all the lung regions could be examined by the authors, resulting in relatively 'low' LUS scores [49▪▪]. Indeed, another study by de Alencar *et al.* [50] reported that a global LUS score ≥ 25 at hospital arrival well predicts the need for invasive mechanical ventilation and ICU admission.

LUS score has also been tested to predict ICU mortality in COVID-19 patients. In the literature, the reported cut-offs vary from 18 to 26. During the first wave of SARS-CoV-2 infection, Lichter *et al.* defined a LUS score cut-off of 18 within the first 24 h of admission to predict the 30-days mortality (area under the curve [AUC] 0.76; sensitivity = 62%, specificity = 74%) and an unadjusted hazard ratio of death equal to 2.65 [1.14–6.3] ($P = 0.02$) [51]. In keeping with Lichter *et al.* [51], Rubio-Gracia *et al.* [52] reported that a LUS score ≥22 at hospital admission was a good predictor for a composite outcome of ICU admission or mortality, whereas de Alencar *et al.* [50] found a LUS score ≥26 at emergency department arrival a risk factor for mortality. These findings were further confirmed by several other studies [53–55], although not all the literature is univocal [56].

CONCLUSION

Today, LUS examination plays a major role in the clinical management of critically ill patients. This is particularly true in situation such as the COVID-19 pandemic, wherein the assistance requirements overcame the available resources. Therefore, based on the safety, diagnostic accuracy, the low cost, and, not least, the ability to predict clinical outcomes, LUS should be widely implemented and it can be considered ethical.

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Conflicts of interest

Prof. Gianmaria Cammarota declares speaking honoraria from MSD and Getinge outside the present work. Prof. Federico Longhini contributed to the development of a new helmet and he is designated as inventor (European Patent number 3320941) not related to the present manuscript. He also received speaking fees from Draeger, Intersurgical and Fisher & Paykel. Prof. Luigi Vetrugno has no conflict of interest to declare.

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