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REVIEW

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A versatile role for lung ultrasound in systemic autoimmune rheumatic diseases related pulmonary involvement: a narrative review

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Abstract

Systemic autoimmune rheumatic diseases (SARDs) related pulmonary disease is highly prevalent, with variable clinical presentation and behavior, and thus is associated with poor outcomes and negatively impacts quality of life. Chest high resolution computed tomography (HRCT) is still considered a fundamental imaging tool in the screening, diagnosis, and follow-up of pulmonary disease in patients with SARDs. However, radiation exposure, economic burden, as well as lack of point-of-care CT equipment limits its application in some clinical situation. Ultrasound has found a place in numerous aspects of the rheumatic diseases, including the vasculature, skin, muscle, joints, kidneys and in screening for malignancies. Likewise it has found increasing use in the lungs. In the past two decades, lung ultrasound has started to be used for pulmonary parenchymal diseases such as pneumonia, pulmonary edema, lung fibrosis, pneumothorax, and pleural lesions, although the lung parenchymal was once considered off-limits to ultrasound. Lung ultrasound B-lines and irregularities of the pleural line are now regarded two important sonographic artefacts related to diffuse parenchymal lung disease and they could reflect the lesion extent and severity. However, its role in the management of SARDs related pulmonary involvement has not been fully investigated. This review article will focus on the potential applications of lung ultrasound in different pulmonary scenarios related with SARDs, such as interstitial lung disease, diffuse alveolar hemorrhage, diaphragmatic involvement, and pulmonary infection, in order to explore its value in clinical daily practice.

Keywords Lung ultrasound, High resolution computed tomography, Systemic autoimmune rheumatic diseases, Interstitial lung disease, Diffuse alveolar hemorrhage, Diaphragmatic involvement, Pulmonary infection

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Introduction

Systemic autoimmune rheumatic diseases (SARDs) are a group of multi-system, inflammatory and autoimmune disorders arising from the loss of normal immune tolerance plus aberrant immune activation. Multiple pro-inflammatory cytokines that originate from innate and adaptive immune cells and auto-antibodies secreted by B cells are essential for the pathogenesis of SARDs [1–3]. The lung is one of the most vulnerable target organs attacked by abnormal immunity, and pulmonary involvement in SARDs is strongly associated with mortality and negatively impacts quality of life. However, due to the fact that most respiratory symptoms associated with SARDs are often insidious in onset and develop gradually, it is difficult to identify them early and intervene promptly [4]. Furthermore, joint and muscle inflammation, cardiovascular complication, and gastrointestinal symptom, can concomitantly affect the patients and mask the diagnosis of pulmonary disease.

Undoubtedly, high resolution computed tomography (HRCT) is presently the gold standard imaging modality for the identification of most pulmonary diseases associated with SARDs. It plays a critical role in the comprehensive assessment and management of SARDs-related lung disease. However, radiation exposure, economic burden, as well as lack of point-of-care CT equipment limits its application in some clinical situations.

Ultrasound has found a place in numerous aspects of the rheumatic diseases, including the vasculature, skin, muscle, joints, kidneys and in screening for malignancies. Likewise it has found increasing use in the lungs [5]. Generally, the aerated lung parenchyma is considered to be the forbidden zone for ultrasound, because the air is not an optimal medium for ultrasound wave propagation. However, in pathological conditions, when the ratio of air to non-air content in lung decreases because alveolar or interstitium space is occupied by fluid or fibrotic tissue, the resulting acoustic mismatch or the formation of an acoustic trap makes lung ultrasound feasible [6]. Although the biophysics and exact genesis of the sonographic signs have not been fully elucidated, lung ultrasound (LUS) B-lines and irregularity of the pleural line are recognized as important patterns associated with diffuse parenchymal lung disease (DPLD) [7]. B-lines, also called comet tail sign, were originally defined as discrete laser-like vertical hyperechoic reverberation artefacts which arise from the pleural line, extend to the bottom of the screen without fading and move synchronously with lung sliding [8]. Multiple B-lines patterns can be detected, such as single B-lines, numerous discrete B-lines, confluent B-lines, and sonographic white lung syndrome (Panels A-D in Fig. 1), which corresponds to different lung parenchymal alterations [9]. The identification of sonographic pleural lines is crucial during LUS

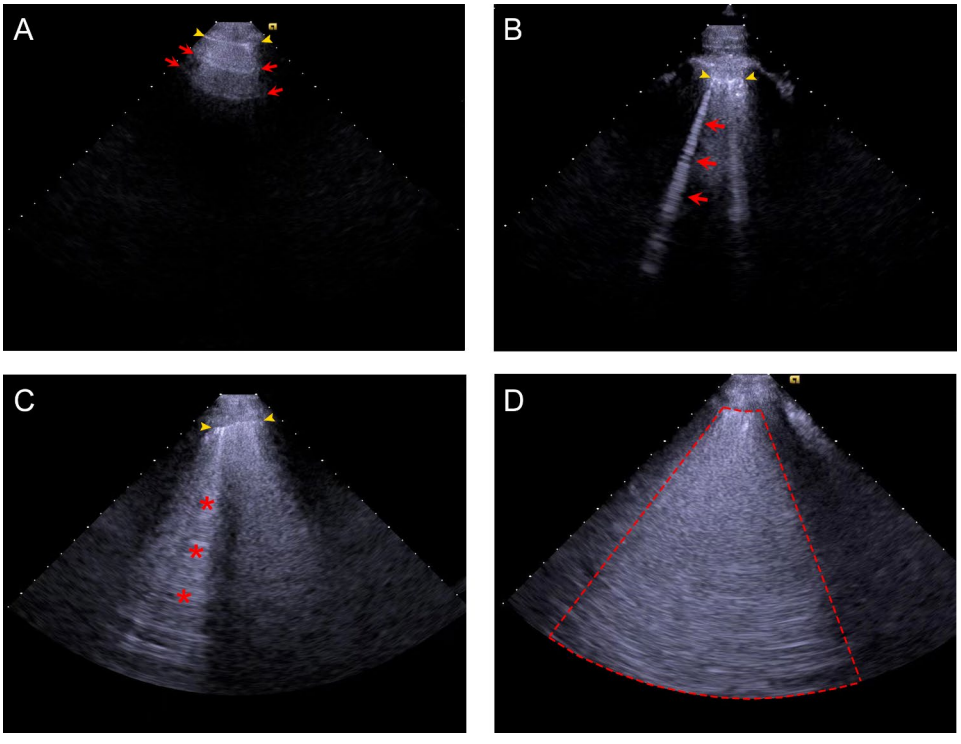

Fig. 1 Typical lung ultrasound patterns. Normal pleural line (yellow arrowheads) and A-lines (red arrows) (**Panel A**); two separate B-lines (red arrows) and fragmented pleural line (yellow arrowheads) (**Panel B**); confluent B-lines (red asterisks) and blurred and irregular pleural line (yellow arrowheads) (**Panel C**); sonographic white lung (delineated with red dotted line) (**Panel D**)

performance, as they are thin, smooth, hyperechogenic linear structures that move while breathing. Below the pleural line, another normal ultrasound finding of the lung is the sonographic A-line. A-lines are repetitive reverberation horizontal artefacts, with equal distances between them and the pleural line. Compared to the normal sonographic pleural line, the irregularity of the pleural line manifests with a coarse, blurred, fragmented or thickened appearance (Panels A-D in Fig. 1). When the subpleural region is involved, subpleural nodules and consolidations can be observed [10–12].

Over the past two decades, with the accumulation of clinical experience and technology innovation, LUS has been increasingly used as a complementary modality to traditional chest radiography to diagnose and monitor DPLD. Compared to chest X-rays or computed tomography (CT) scans, LUS not only has the advantages of portability, non-radiation, user-friendliness, and real-time imaging, but also exhibits a good sensitivity and negative predicted value, particularly when detecting lesions near the pleura. Although LUS has become a useful, sophisticated, and routine examination tool in intensive care unit (ICU), emergency department as well as neonatal unit [13–15], its role in the SARDs related pulmonary involvement has not been fully investigated [16]. This review article will focus on the potential applications of LUS in different pulmonary scenarios related to SARDs, in order to explore its value in clinical daily practice.

SARDs related interstitial lung disease

SARDs related interstitial lung disease (SARDs-ILD) is a common pulmonary feature, with protean clinical manifestations, behaviors, and outcomes [17]. Nonspecific interstitial pneumonia (NSIP), characterized by ground-glass opacity (GGO), reticular abnormality, and traction bronchiectasis with basilar and peripheral predominance is the most common pattern in SARDs-ILD, followed by usual interstitial pneumonia (UIP), organizing pneumonia (OP), and lymphocytic interstitial pneumonia (LIP) [18, 19]. A proportion of patients, particularly in anti-melanoma differentiated antigen 5 (MDA-5) antibody positive dermatomyositis, anti-synthetase syndrome, as well as diffuse scleroderma and rheumatoid arthritis with UIP-like, can develop a rapidly progressive phenotype most commonly with an acute interstitial pneumonia (AIP) pattern, which can result in significant mortality. However, how to identify early, follow up regularly, and monitor the development and progression of SARDs-ILD still remains a major challenge in the rheumatology community.

Since the first report regarding LUS in systemic sclerosis related interstitial lung disease (SSc-ILD) published by Gargani L. et al., numerous studies have investigated its application in various rheumatic diseases related ILDs [20]. According to a meta-analysis that included 349 patients with connective tissue diseases, the diagnostic sensitivity and specificity of LUS were 0.915 (95%CI 0.845 ~ 0.96) and 0.813 (95%CI 0.746 ~ 0.869), respectively. A significant correlation was found between lung US B-line scores and HRCT Warrick scores (correlation coefficient: 0.783; $P<0.001$) [21]. A recent prospective study involving 180 patients with SARDS showed the sensitivity and specificity of lung ultrasound as compared to HRCT in detecting pulmonary interstitial involvement were 99.3% and 96.4%, respectively; positive predictive value (PPV) 0.7, negative predictive value (NPV) 3.611. Excellent inter-observer agreement was found between the 2 investigators (weighted κ value between 0.846 and 0.969, and overall agreement between 92% and 97%) [22]. As per the data mentioned, LUS has the potential to be a valuable tool for managing SARDs-ILD.

LUS in rheumatoid arthritis related ILD

Rheumatoid arthritis related ILD (RA-ILD) is among the most frequent SARDs-ILDs, being the major extra-articular manifestation in this disease [23]. The prevalence of RA-ILD is reported as highly variable, owing to different methodologies, screening strategy, cohorts investigated and ILD definitions adopted [24]. The UIP pattern is more often encountered in RA-ILD than other SARDs and is associated with a poorer prognosis [25, 26]. A recent population-based cohort study revealed that even when asymptomatic and radiologically limited in extent, RA-ILD is associated with shorter survival [27]. Hence, there is no doubt that the detection of early interstitial lung lesions is of great clinical significance. Several predictive models have been constructed to identify patients at high risk of subclinical RA-ILD. These models include smoking, gender, age, disease duration, anti-cycling citrullinated peptide (CCP) antibody, rheumatoid factor, serum biomarkers, as well as the MUC5B genetic variant as predictive factors [28–31]. However, discrepancies in study results shows that these models need to be further studied and validated. Given that most RA-ILD progresses relatively slowly and is usually asymptomatic or oligosymptomatic in the early and intermediate stages. In addition, RA is more common than scleroderma and inflammatory myositis. Using HRCT to screen and monitor RA-ILD will not be available in remote and rural areas, and will place an increased burden on the radiology department, and is relatively expensive. Additionally, the low sensitivity of X-ray and pulmonary function tests (PFTs) limits their screening capacity. Therefore, LUS utilization can assist in bridging the gap in screening for early RA-ILD. Studies from different centers consistently demonstrated that LUS, and even the use of portable ultrasound devices, has good sensitivity and negative predictive value for detecting ILD in RA when compared

to HRCT [32–35]. Despite most of the studies were conducted in a single center, retrospective controlled, and with small sample size. Recently, we proposed an algorithm combining lung ultrasound B-lines and serum Krebs von den Lungen-6 (KL-6), two non-invasive and radiation-free biomarkers, to screen ILD in patients with early RA [36]. If ILD is suspected in the first step (B-line number > 10 and/or KL-6 ≥ 500 U/mL), the patient is recommended to undergo chest HRCT and PFTs examination, to confirm the radiological changes and quantify the physiologic impairment. If there is no radiological evidence of ILD, LUS and KL-6 test should be performed periodically, for close sonographic monitoring of ILD development. For individuals without the evidence of pulmonary involvement in the first step (B-line number ≤ 10 and/or KL-6 < 500 U/mL), LUS and KL-6 testing might be periodically repeated, within time-frames that depend on the presence of risk factors. However, the screening and follow-up strategy requires additional testing and validation among prospective, multicenter, and large-scale studies.

In a nutshell, the role of LUS in RA-ILD should be highlighted in early screening and dynamic monitoring.

LUS in anti-MDA-5 antibody positive dermatomyositis related ILD

Anti-MDA-5 antibody positive dermatomyositis (DM) is a special clinical phenotype that very frequently presents with mild muscular involvement and severe ILD manifestation [37]. Anti-MDA-5 positive ILD is one of the most difficult problems in the rheumatic community as a significant proportion of these patients progress rapidly to severe outcomes despite receiving aggressive and supportive treatment. High mortality of this entity is associated with an elusive pathophysiology, uncontrolled cytokine storm and superimposed viral and other pathogen infections [38]. NSIP, OP and AIP are the three predominant radiological and histopathologic patterns [39]. However, data regarding lung ultrasound in idiopathic inflammatory myositis related ILD (IIM-ILD) are scarce. One mono-center retrospective study including 39 patients with IIM-ILD showed that the lung ultrasound B-lines number positively correlated with the HRCT Warrick score and serum KL-6 concentration, and correlated inversely to PFTs [40]. In a case report, bedside ultrasound and KL-6 were used to evaluate the lung lesion, and their interpretation helped make the therapeutic decision in a DM patient with rapidly progressive ILD (RP-ILD) [41]. These data indicated that B-lines combined with KL-6 could be helpful in the assessment of IIM-ILD severity and in the close monitoring of ILD development.

Although the underlying mechanism is unknown, spontaneous pneumomediastinum or pneumothorax can occur in anti-MDA5 positive DM patients with RP-ILD, and this was demonstrated to be linked with poorer prognosis and higher mortality [42, 43]. In this clinical circumstance, bedside lung ultrasound is an alternative tool that can sensitively detect pneumothorax. The absence of lung sliding, as well as the identification of the lung point sign, are strongly indicative of the presence of pneumothorax, for which a chest tube would then be considered [44]. However, the concomitant presence of subcutaneous emphysema can affect the accuracy of the ultrasound reading. At this point, bedside X-ray or chest CT scan is indispensable [45, 46].

In addition, diaphragmatic myositis in IIM, a very rare complication, was reported to contribute to respiratory failure [47]. Recently, Grignaschi et al. reported the case of a patient with MDA5 + DM who presented with progressive dyspnea due to concomitant ILD and diaphragmatic myositis. Lung and diaphragm ultrasound revealed remarkable B-lines and diaphragm dysmotility. After therapy with intravenous immunoglobulins and mycophenolate mofetil, the patient's condition gradually improved and subsequent ultrasound examination showed marked improvement of the diaphragmatic dysfunction and a reduction of the B-lines score [48].

LUS in systemic sclerosis related ILD

SSc-ILD is a major pulmonary manifestation in this disease which deserves attention as it represents a leading cause of death [49]. HRCT is the fundamental imaging tool for identifying radiological pattern, the type of involvement, pulmonary artery enlargement as well as esophageal dilatation in SSc patients. Notwithstanding, emerging evidence indicates that lung ultrasound can play a supporting role in the whole journey of SSc-ILD [50]. The published promising data demonstrated that LUS B-lines and irregularity of the pleural line significantly correlate with HRCT score, PFTs, serological biomarkers and clinical parameters in SSc-ILD [20, 22, 51–53]. As per a recent meta-analysis that included nine studies with a total of 888 participants, LUS had high diagnostic accuracy, with good sensitivity (94%) and moderate specificity (64%) [54]. Additionally, one retrospective and mono-center study enrolled 77 patients with SSc found that LUS B-lines correlate with radiomic quantitative indexes, including mean lung attenuation ($r = 0.568$, $P < 0.001$), skewness ($r = -0.368$, $P = 0.004$), and kurtosis ($r = -0.283$, $P = 0.028$). Sub-analysis further confirmed the similar results in anterior and posterior chest separately [55]. The prognostic value of B-lines for SSc was investigated in 396 consecutive patients. The posterior B-lines ≥ 5 was found to associate with new development or worsening ILD [hazard ratio (HR) 3.38, 95% CI 1.137–9.994; $P = 0.028$]. The prognostic value of B-lines was further confirmed in the subgroup of patients with

known ILD at baseline (HR 1.010; 95% CI 1.003–1.018; $P=0.008$) [56].

In light of the fact that SSc-ILD screening is mandatory, chest HRCT scans combined with PFTs are the main modalities for this purpose. Nevertheless, LUS can serve as a complementary tool in initial clinical phase, providing baseline sonographic data as a guide for later flexible follow-up. For example, LUS can be performed more intensively depending on clinical requirements for patients at high risk of developing progressive pulmonary fibrosis (PPF). Recently, a screening strategy including LUS, HRCT, and PFTs was recommended for every patient with SSc at baseline. Routine screening for ILD through LUS andd PFTs should be done every 3 to 6 months during the first two years in cases of non-radiographic ILD. If the screening test results show signs of deterioration, chest HRCT scan is required [50].

LUS in SARDs related diffuse alveolar hemorrhage

Diffuse alveolar hemorrhage (DAH) is a rare but potentially life-threatening complication of some SARDs, particularly systemic lupus erythematosus (SLE) and antineutrophil cytoplasmic antibody associated vasculitis [57]. The alveolar capillaries are attacked by various inflammatory cytokines and abnormal immune cells, leading to increased permeability and capillaritis, and ultimately cause red blood cells accumulation within the alveolar space [58]. The triad of DAH encompasses acute dyspnea, hemoptysis and progressive hypoxemia. Chest CT reveals emerging non-specific patchy or diffuse, bilateral GGO, and alveolar consolidation with air bronchogram [59, 60]. DAH is an emergency condition that requires rapid identification and timely intervention to avoid catastrophic consequences and death [61]. Point-of-care lung ultrasound is a useful imaging modality that can be used to rapidly and sensitively detect patients with suspected DAH when related clinical features are presented. The sonographic pattern identified in DAH includes multiple confluent or discrete B-lines, with or without pleural irregularity depending on prior pleural involvement [62]. After aggressive treatment, the B-lines gradually dissolve and finally disappear. Therefore, in this context, lung ultrasound could become an applicable, rapid alternative to detect and closely follow-up DAH, as well as to identify the response to treatment. The interpretation of lung ultrasound pattern can facilitate the clinical decision making process. Panels A–H in Fig. 2 demonstrate the clinical application of lung ultrasound to identify, monitor a SLE patient with DAH.

LUS in SARDs related shrinking lung syndrome

Shrinking lung syndrome (SLS) is an uncommon complication of SARDs (mainly associated with SLE) in which the diaphragmatic muscle is involved, resulting in reduced lung volume and restrictive ventilation impairment on PFTs [63]. The patient will be highly suspected of SLS when progressive exertional dyspnea, pleuritic chest pain, and elevation of the diaphragm on chest X-rays as well as restrictive pattern on PFTs are present, but there is no obvious evidence of ILD, pulmonary vasculopathy or pleural disease is detected [64]. Although the precise mechanism of SLS is unknown, diaphragm dysfunction is suggested to play a crucial role in its pathogenesis. In this clinical scenario, diaphragm ultrasound could directly evaluate the diaphragm both structurally and functionally by measuring diaphragmatic thickness and mobility [46, 65]. Using this technique, a recent study found that SLE patients had reduced diaphragmatic muscle thickness compared to those with primary Sjögren's syndrome (pSS). Diaphragmatic function testing by evaluating maximum expiratory pressure (MEP) and maximum inspiratory pressure (MIP), also demonstrated that SLE patients had significant lower MEP and MIP compared to pSS (80% vs. 92% and 76% vs. 120%, respectively; $p<0.05$). These findings indicated that diaphragmatic muscle abnormality is common in SLE patients. To explain whether this could be the underlying reason for the increased risk of lower respiratory tract infections and SLS in SLE patients, prospective studies and larger sample size are needed [66]. One mono-center study including 11 pediatric SLE patients complicated with SLS used M-mode ultrasound and showed diaphragmatic hypomotility in 100% by obtaining the range, duration and velocity of the diaphragmatic contraction [67].

LUS in SARDs related pulmonary infection

Pulmonary infection is the most common complication of SARDs patients who receive therapy with glucocorticoids, immunosuppressants, biologic agents or Janus Kinase inhibitors, and remains a leading cause of respiratory failure and intensive care unit admission [68]. In addition to bacterial pneumonia, immunocompromised patients are prone to infection by opportunistic infections, including viral, pneumocystis, fungal, non-tuberculosis mycobacteria and other agents. Although there are no specific sonographic findings as a diagnostic hallmark of pneumonia, lung ultrasound could provide information comparable to standard radiographs. Systemic literature reviews and meta-analyses have demonstrated that lung ultrasound had higher sensitivity, specificity, and diagnostic accuracy than chest X-ray, using CT as the referent [69]. The presence of sonographic consolidation (subpleural echo-poor region or one with tissue-like echotexture), fluid or air bronchograms, focal multiple B lines, and pleural effusion would suggest pneumonia. To accurately interpret ultrasonographic patterns associated with pneumonia, a comprehensive judgment should be made by integrating clinical, serological and, when

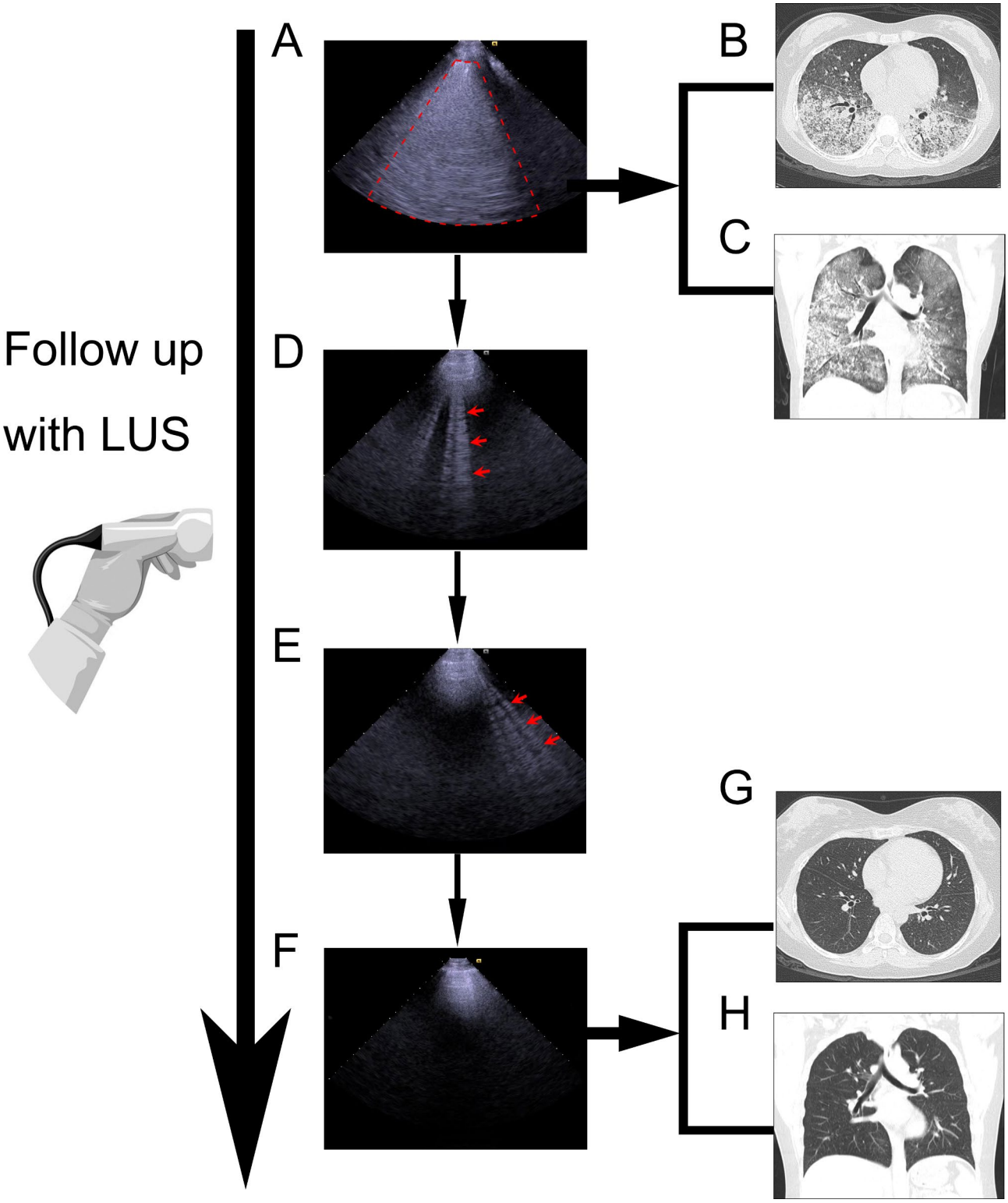

Fig. 2 A hospitalized patient with active SLE suddenly presented with hemoptysis, hypoxemia and progressive hemoglobin decline. Timely bedside lung ultrasound revealed diffuse sonographic "white lung" (confluent B-lines) (**Panel A**), subsequently confirmed by chest HRCT scan (**Panel B and C**). The patient was treated with intravenous methylprednisolone (250 mg per day for 3 days, and tapered 80 mg per day for 3 days, then 40 mg per day) combined with intravenous belimumab (10 mg/kg) injection. Intensive lung ultrasound monitoring over a period of 14 days indicated B-lines score diminished sequentially (**Panel D-F**), corresponding improvement in chest HRCT imaging (**Panel G and H**) and the patient's condition

available, radiological information. After administration of antibiotic, the therapeutic efficacy can be ascertained by assessing lung reaeration and pleural fluid absorption through tracking changes in sonographic findings. However, there are no relevant recommendations or guidelines on the use of lung ultrasound to follow-up pneumonia in patients with SARDs. Panels A–H in Fig. 3 demonstrate a patient with pneumocystis jiovecii pneumonia to show HRCT findings plus use of LUS to follow a patient to resolution of her pneumonia.

LUS in SARDs patients with COVID-19 pneumonia

The vast majority of SARDs individuals are vulnerable to the SARS-CoV-2 infection, whether the illness is quiescent or active [70]. Pulmonary parenchymal involvement characterized by diffuse interstitial alterations is a feature of COVID-19 pneumonia, and contributes to a worse prognosis and significant mortality [71]. Separated and coalescent B-lines with patchy distribution, peripheral consolidation, as well as irregularities of the pleural line and rare pleural effusion are the main ultrasonographic manifestations of COVID-19 pneumonia [72, 73]. The value of lung ultrasound in the management of COVID-19 pneumonia was comprehensively reviewed previously, focused on its applications for triaging, monitoring and prognostic management of these patients [74]. Compared with classical radiological modalities, lung ultrasound could play a more flexible role in different clinical settings, from home monitoring to emergency department and ICU bedside assessment. The implementation of lung ultrasound might help minimize exposure to ionizing radiation, reduce unnecessary transport of infected patients in the hospital setting, decrease the strain on imaging modalities such as the radiology department while enabling rapid clinical decision-making [74–77].

Lung fibrosis is one of the severe complications after SARS-CoV-2 infection, also called post-COVID-19 pulmonary fibrosis (PCPF) [78]. The diagnosis of PCPF requires a combination of clinical, serological, radiological and pathological (if available) information [79]. The long-term outcome and clinical behaviour of PCPF remains unknown, and how to manage it is still uncertain. Nonetheless, close follow-up of high-risk patients, such as older age individuals, those who are immunosuppressed, those with higher acute-phase reactants and pro-inflammatory cytokine levels and with known autoantibody positivities (e.g. anti-CCP, anti-MDA-5, Ro52, Scl-70) is essential [80]. Research into this LUS use is needed because, in this context, lung ultrasound could be an excellent tool for the screening and monitoring of PCPF.

The diverse role of LUS in SARDs patients with various clinical pulmonary complications is outlined in Fig. 4.

Limitations

Although LUS is becoming increasingly popular as a new imaging modality in the field of pulmonary disease, it must be noted that there are some limitations that prevent its further clinical application. First, the standardization and validation of LUS examination in patients with SARDs have not yet been fully established. Because of acquisition of ultrasound image is mostly dependent on detecting and evaluating artefacts, which are highly dependent on imaging frequency and settings. Therefore, in order to improve the diagnostic reproducibility and accuracy, standardization of imaging protocols is urgent. Second, the calculation of the number of B-lines and the description of pleural line morphology are mainly dependent on the operator, making the results subjective and prone to variation. Third, discriminating various underlying lung pathologies by analyzing and comparing different B-lines patterns is still a challenge. In this respect, artificial intelligence and machine learning algorithms can help to interpret LUS data more accurately, thereby avoiding subjective errors and making the more correct diagnosis [81]. In addition, combining clinical, serological, and radiographic information can enhance understanding of LUS findings.

Regarding the clinical application of LUS in patients with SARDs, there is little data on other pulmonary complications except for in ILD. Moreover, most studies that were published focused on LUS as a screening, diagnostic, and monitoring tool for ILD. Therefore, it is necessary to conduct more clinical studies to establish its validity in various pulmonary diseases. Additionally, due to its high sensitivity and moderate specificity, LUS should be utilized as a promising tool for assessing therapeutic response to anti-fibrotic agents in ILD. In order to confirm this effect, a large-scale, prospective, multicenter clinical trial is needed.

Conclusion

The harmful outcomes of lung involvement in patients with SARDs has attracted increasing attention and is great challenge for most rheumatologists. Accumulated evidence and promising data in the past two decades indicate that lung ultrasound may be a useful tool to detect pulmonary abnormalities. Incorporating sonographic information into clinical and radiological data may help rheumatologists to achieve more comprehensive management of these diseases, particularly in the screening and follow-up of SARDs-related pulmonary disease. However, high-quality studies and rigorous data are still scarce in this area. Hence, its role in screening and monitoring of pulmonary alteration need to be further investigated and validated. Much work remains to be done to reach a consensus on standard practice of lung ultrasound in different clinical scenarios. In addition,

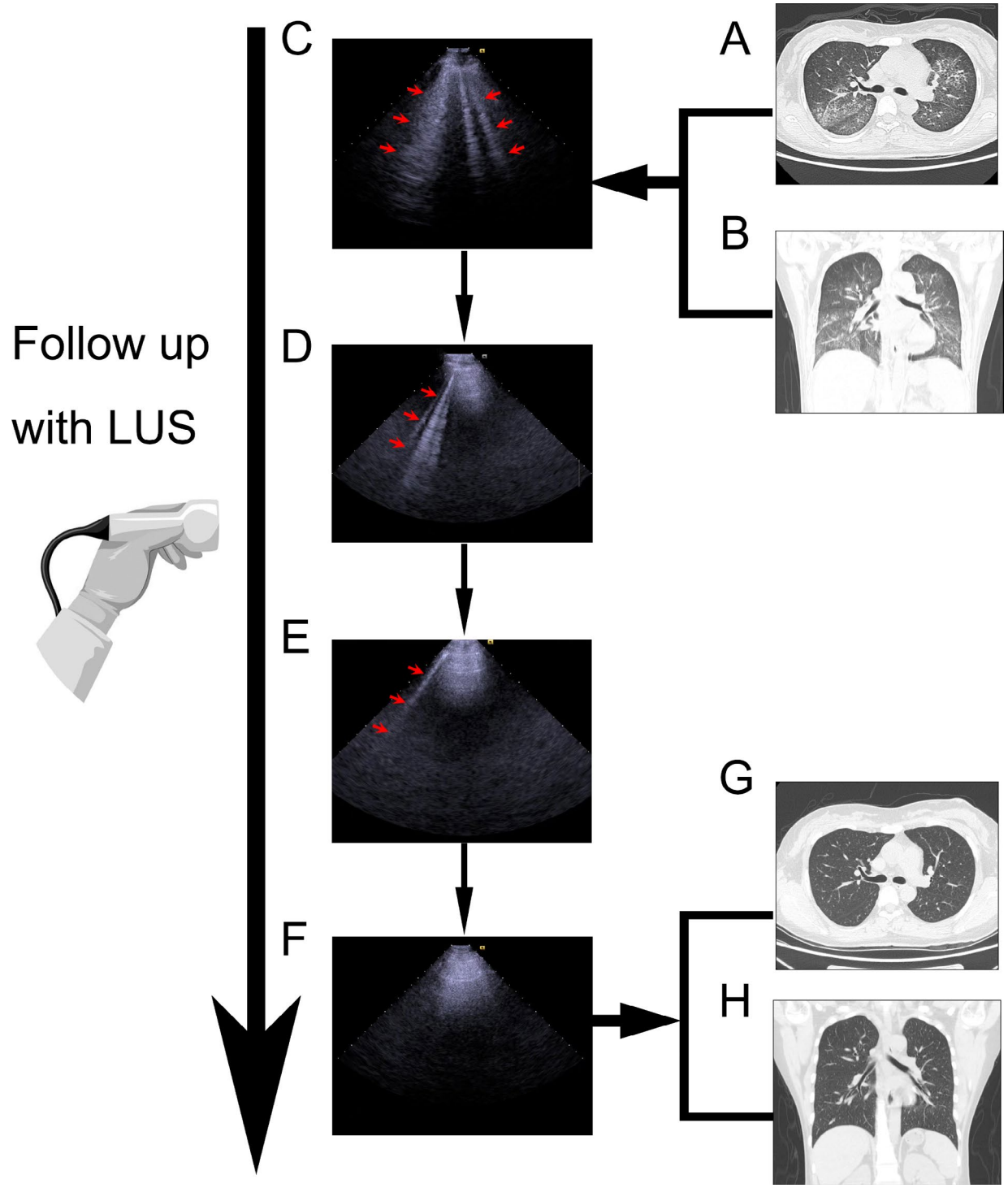

Fig. 3 A refractory and recurrent young lupus patient complicated with severe enteritis, thrombocytopenia, and nephropathy admitted to our department. After received high dose glucocorticoid (2 mg/kg) and cyclophosphamide (total dose 1 gram) therapy, she presented fever, dry cough, and mild exertional dyspnea. Subsequent chest HRCT examination revealed new diffuse ground-glass opacity and reticular abnormality (**Panel A and B**). Simultaneous bedside lung ultrasound showed multiple B-lines, blurred pleural line, and no pleural effusion (**Panel C**). Pneumocystis jirovecii pneumonia (PJP) was confirmed by bronchoalveolar lavage fluid smear. Trimethoprim-sulfamethoxazole (2 tablets, three time per day) was added while glucocorticoid was reduced (1 mg/kg) and cyclophosphamide was discontinued. In order to avoid radiological exposure, lung ultrasound was used to closely follow up the PJP infection. Ultrasound was performed every two weeks for the first two months, and subsequently performed monthly for follow-up. B-lines elimination and normal pleural line indicated that PJP infection was controlled (**Panel D-F**), further confirmed by chest HRCT findings (Panel G and H) and improved clinical symptom

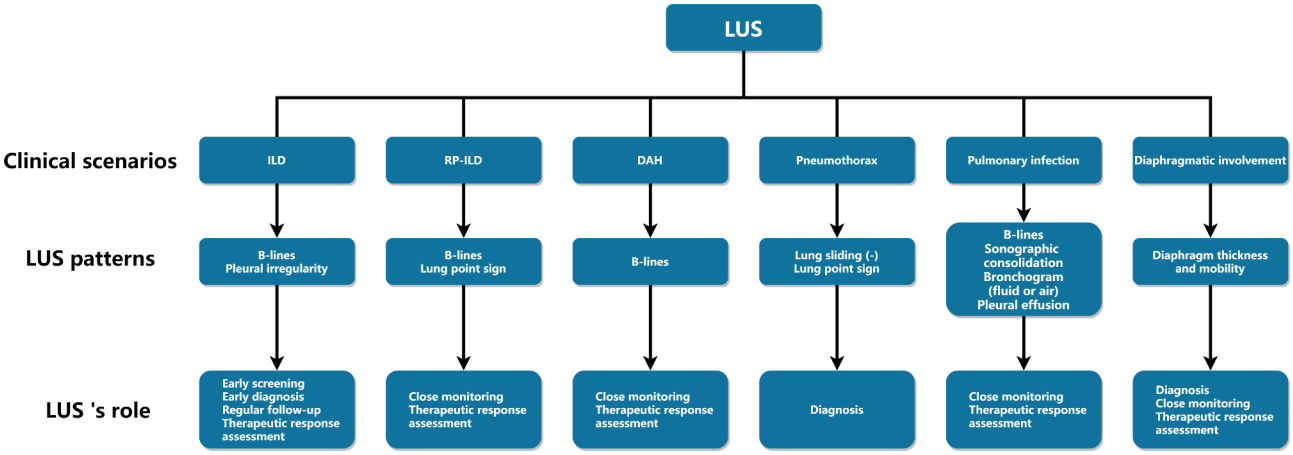

Fig. 4 The diverse role of LUS in SARDs patients with various clinical pulmonary complications. DAH, Diffuse alveolar hemorrhage; ILD, Interstitial lung disease; LUS, Lung ultrasound; RP-ILD, Rapidly progressive interstitial lung disease

lung ultrasound operation training, as well as sonographic patterns identification and interpretation, must be carried out urgently in the rheumatology community. We hope that in the near future, lung ultrasound will become a powerful stethoscope for rheumatologists in daily clinical practice.

Abbreviations

AIP	Acute interstitial pneumonia
CCP	Cycling citrullinated peptide
CT	Computed tomography
DAH	Diffuse alveolar hemorrhage
DM	Dermatomyositis
DPLD	Diffuse parenchymal lung disease
GGO	Ground-glass opacity
HRCT	High resolution computed tomography
ICU	Intensive care units
IIM	Idiopathic inflammatory myositis
ILD	Interstitial lung disease
KL-6	Krebs von den Lungen-6
LIP	Lymphocytic interstitial pneumonia
LUS	Lung ultrasound
MDA-5	Melanoma differentiated pneumonia
MEP	Maximum expiratory pressure
MIP	Maximum inspiratory pressure
NPV	Negative predictive value
NSIP	Nonspecific interstitial pneumonia
OP	Organizing pneumonia
PCPF	Post-COVID-19 pulmonary fibrosis
PFTs	Pulmonary function tests
PPF	Progressive pulmonary fibrosis
PPV	Positive predictive value
pSS	primary Sjögren's syndrome
RA-ILD	Rheumatoid arthritis related ILD
RP-ILD	Rapidly progressive ILD
SARDs	Systemic autoimmune rheumatic diseases
SLE	Systemic lupus erythematosus
SLS	Shrinking lung syndrome
SSc-ILD	Systemic sclerosis related interstitial lung disease
UIP	Usual interstitial pneumonia

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Author contributions
YKW, SQC, BR, CB, AMHV, LG, MMC and DEF participated in the literature review, writing and reviewing of the manuscript. SYZ, ZXZ, WJZ, GZD and AM participated in the clinical data collection and preparation of Figs. 1, 2 and 3. All authors reviewed the manuscript.

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Data availability
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Declarations

Ethics approval and consent to participate
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Consent for publication
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Competing interests
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