Diagnostic accuracy of lung ultrasound in identifying connective tissue disease related interstitial lung disease: a systematic review and meta-analysis

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Abstract

Objective

The diagnosis of connective tissue disease-associated interstitial lung disease (CTD-ILD) primarily relies on high-resolution computed tomography or lung biopsy, while several challenges persist in the clinical application of these modalities. This study aims to investigate the performance of lung ultrasound (LUS) in diagnosis of ILD in patients with CTD.

Methods

Records from five electronic databases were screened and selected for eligible studies. Quality assessment of eligible studies was performed via Quality Assessment of Diagnostic Accuracy Studies-2. The pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and area under the curve (AUC) of LUS was calculated. Sensitivity analyses, subgroup analyses and meta-regression were applied to identify sources of heterogeneity.

Results

Twenty-eight eligible studies were selected from 417 records, with a total of 2,196 participants (1,117 with CTD-ILD and 1,079 CTD patients without ILD). All studies reached moderate to high quality. LUS has shown good diagnostic performance in detecting CTD-ILD, with a sensitivity of 0.92, a specificity of 0.88 and an AUC of 0.96. Further stratified analyses suggested that good performance of LUS was also observed in diagnosing rheumatoid arthritis-associated ILD (sensitivity: 0.91, specificity: 0.90, AUC: 0.96) and systemic sclerosis-associated ILD (sensitivity: 0.96, specificity: 0.78, AUC: 0.94). Significant heterogeneity and publication bias was observed.

Conclusion

Although LUS has shown good performance in diagnosing CTD-ILD, this approach does not yet justify routine application due to heterogeneity and publication bias. Further studies may focus on performance of LUS in other subtypes of CTD-ILD.

Key words

connective tissue disease related interstitial lung disease, lung ultrasound, diagnosis, meta-analysis

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Introduction

Connective tissue diseases (CTD) refer to a group of autoimmune disorders characterised as immune dysregulation and systematic involvement (1, 2). Interstitial lung disease (ILD) is an essential pulmonary manifestation of CTD, which may lead to significant risk of mortality (3). Diverse prevalence of ILD was observed in different types of CTD, ranging from 6% in systemic lupus erythematosus (SLE) to 56% in mixed connective tissue disease (MCTD) (4). To identify patients with ILD, high resolution computed tomography (HRCT) has been regarded as the primary diagnostic approach in clinical practice (5). However, application of HRCT may be restricted by multiple factors, including insufficient availability, high costs and potential risk of radiation exposure (6). Therefore, finding more available and affordable diagnostic approaches to address these factors is necessary for management of CTD-ILD.

Lung ultrasound (LUS) is an emerging approach to detect potential pulmonary pathologies via identifying characteristic signs (7). Application of LUS has also been reported in multiple pulmonary diseases, including pneumonia, pleural diseases and acute respiratory distress syndrome (7-9). Compared with HRCT, LUS offers the advantages of real-time capability, cost-effectiveness, and radiation-free operation (10). These merits may potentially enable it to overcome limitations of HRCT to become another diagnostic approach of CTD-ILD. However, although two previous systematic reviews supported the good performance of LUS in detecting CTD-ILD, their results were far from drawing the conclusion due to small sample size and non-rigorous study selection (6, 11). Moreover, performance of LUS in identifying different subtypes of CTD-ILD still warrants further investigations (12, 13). Therefore, as evidence accumulated in recent years, we conducted an updated systematic review and meta-analysis to address these issues.

Methods

Registered on the PROSPERO website (registration no.: CRD420251018143), this systematic review and meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (14).

Literature search and study selection

Two investigators have independently searched Web of Science, Scopus, PubMed, China National Knowledge Infrastructure (CNKI) and Wanfang for eligible studies from inception of database to March 31st 2025. The detailed search strategies can be found in Supplementary Table S1. References of related systematic reviews were also manually evaluated to avoid potential omissions.

The inclusion criteria of this systematic review were listed as follows:

1. Studies focusing on diagnostic performance of LUS in detecting ILD in patients with CTD, with data of true positive (TP), true negative (TN), false positive (FP) and false negative (FN).
2. Studies with a sample size of over 20.
3. The gold diagnostic criteria of ILD were clearly demonstrated, such as HRCT or lung biopsy.

There were also some exclusion criteria:

1. Studies using duplicated data. Duplicated data were defined as the same types of CTD-ILD in the same institutions during the same study period. In this case, only the study with the largest sample size was enrolled. 2. Studies not published in English or Chinese. 3. Review, comments or systematic reviews.

All eligible studies were grouped by the specific types of CTD.

Data extraction and quality assessments

Two investigators independently extracted the following data for further analysis: 1. Baseline information of each article, including the first author, publication year, geographical location, number of centres and study design (prospective or not). 2. Characteristics of participants (number of participants, sex, age, types of CTD, duration of diseases, history of smoking) and diagnostic criteria of CTD and ILD. 3. Baseline information of LUS, including criteria for ultrasound-defined ILD, type and frequency of probe and number of intercostal spaces for examination. 4. Value of TP, FP, TN

and FN of LUS for CTD-ILD. If critical data were missing from any studies, we would contact the original authors for clarification. Quality assessments were performed by two independent reviewers applying the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 and virtualised via Revman 5.3. To evaluate the certainty of evidence, we applied the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach (GRADEpro).

Statistical analysis

We performed a pooled analysis focusing on diagnostic performance of LUS in identifying CTD-ILD, providing the summarised results of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR). The summary receiver operating characteristic (sROC) curve was also conducted to further evaluate the diagnostic efficacy of LUS. We also explored the performance of LUS for different subtypes of CTD-ILD if data were available. We applied I square (I^2) statistic and Q test for assessment of heterogeneity. A random-effect model was applied if I^2>50% or p<0.05, otherwise a fixed-effect model was applied. Sensitivity analyses, which include goodness-of-fit, bivariate normality, influence analysis and outlier detection, was conducted to detect the stability of the results (15). Subgroup analyses and meta-regression were performed to evaluate the source of heterogeneity. To detect the potential risk of publication bias, the Deek's funnel plot was also applied. All statistical analyses were performed via Stata 16, and p<0.05 was considered as statistically significant.

Results

Study selection and quality assessments

A total of 417 records were identified during the literature search. After primary and full-text screening, a total of 28 eligible studies were enrolled in this systematic review and meta-analysis (Fig. 1) (16-43). The baseline characteristics of eligible studies are shown in Table I. The protocols and number of TP, FP, FN and TN in each study are shown in Supplementary Table S2. The results of quality assessments are shown in Figure 2, with all studies reaching moderate to high quality. Low certainty of evidence was observed according to the GRADE approach (Suppl. Fig. S1).

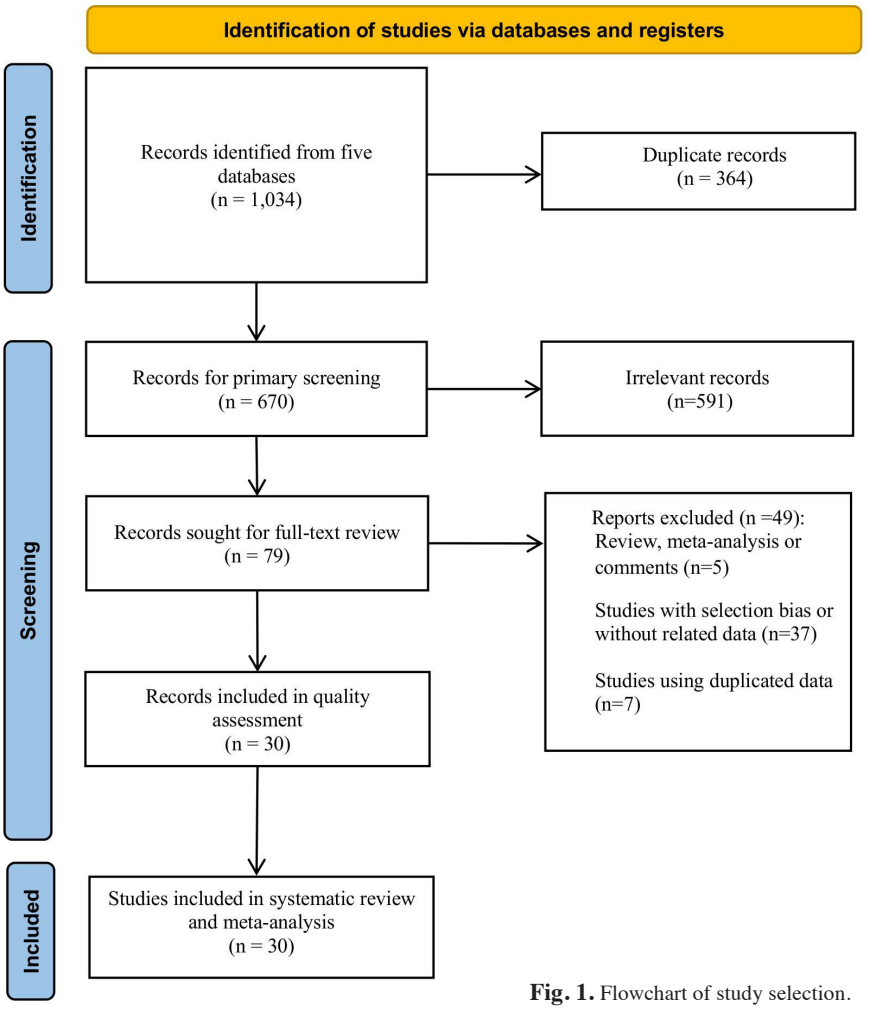

Fig. 1. Flowchart of study selection.

Performance of LUS for patients with CTD-ILD

All eligible studies including 2,196 participants (1,117 with CTD-ILD and 1,079 CTD patients without ILD) reported performance of LUS in detecting CTD-ILD, with the sensitivity ranging from 0.72 to 1.00 and specificity ranging from 0.34 to 1.00. The pooled sensitivity and specificity of LUS reached 0.92 (95%CI 0.88, 0.95, I^2=74.68%) and 0.88 (95%CI 0.81, 0.92, I^2=90.71%), respectively (Fig. 3A). The pooled PLR, NLR and DOR was 7.5 (95%CI 4.8, 11.6), 0.09 (95%CI 0.06, 0.13) and 86 (95%CI 45, 164), respectively (Suppl. Table S3). The results of sROC curve showed that the area under the curve (AUC) was 0.96 (95%CI 0.94, 0.97) (Fig. 3B).

A total of 10 studies reported diagnostic accuracy of LUS in rheumatoid arthritis associated ILD (RA-ILD), with the sensitivity ranging from 0.72 to 1.00 and specificity ranging from 0.52 to 1.00, respectively (16, 17, 19, 20, 25, 27, 29, 30, 42, 43). The pooled sensitivity and specificity reached 0.91 (95%CI 0.83, 0.96, I^2=71.35%) and 0.90 (95%CI 0.76, 0.96, I^2=94.98%), respectively (Fig. 3C-D). The PLR, NLR, DOR and AUC reached 9.3 (95%CI 3.5, 24.7), 0.10 (95%CI 0.05, 0.20), 96 (95%CI 24, 379) and 0.96 (95%CI 0.94, 0.97), respectively (Suppl. Table S3).

A total of 8 studies reported performance of LUS in systemic sclerosis associated ILD (SSc-ILD), with the sensitivity ranging from 0.74 to 1.00 and specificity ranging from 0.34 to 0.92,

Table I. Baseline characteristics of eligible studies.

Author	Continent	Centre	Design	Diagnostic criteria of ILD	Type of ILD	Diagnostic criteria of CTD	CTD-ILD (n)	CTD without ILD (n)	Total (n)
Vermant 2025 (16)	Europe	Single-centre	R	HRCT	RA-ILD	ACR/EULAR	12	97	109
Ottaviani 2025 (17)	Europe	Single-centre	R	HRCT	RA-ILD	ACR/EULAR	44	57	101
Ferro 2025 (18)	Europe	Single-centre	R	HRCT	SjS-ILD	ACR/EULAR	23	38	61
Sofíudóttir 2024 (19)	Europe	Multi-centre	P	HRCT	RA-ILD	ACR/EULAR	23	54	77
Otaola 2024 (20)	South America	Single-centre	P	HRCT	RA-ILD	ACR/EULAR	32	74	106
Han 2024 (21)	Asia	Single-centre	P	HRCT	CTD-ILD	Medical records	75	29	104
Zhang 2023 (22)	Asia	Single-centre	P	HRCT	CTD-ILD	ACR/EULAR	45	15	60
Koshy 2023 (23)	Asia	Single-centre	R	HRCT	CTD-ILD	Medical records	31	11	42
Huang 2023 (24)	Asia	Single-centre	R	HRCT	CTD-ILD	ACR/EULAR	65	23	88
Gutierrez 2022 (25)	South America	Multi-centre	R	HRCT	RA-ILD	ACR/EULAR	27	47	74
Gargani 2022 (26)	Europe	Single-centre	R	HRCT	SSc-ILD	ACR/EULAR	33	36	69
Carlo 2022 (27)	Europe	Single-centre	R	HRCT	RA-ILD	ACR/EULAR	25	47	72
Xie 2021 (28)	Asia	Single-centre	R	HRCT	CTD-ILD	ACR/EULAR	66	34	100
Mena-Vázquez 2021 (29)	Europe	Single-centre	R	HRCT or lung biopsy	RA-ILD	ACR/EULAR	35	36	71
Fotoh 2021 (30)	Africa	Single-centre	R	HRCT	RA-ILD	ACR/EULAR	75	75	150
Fairchild 2021 (31)	North America	Single-centre	P	HRCT	SSc-ILD	ACR/EULAR	11	9	20
Buda 2021 (32)	Europe	Single-centre	P	HRCT	CTD-ILD	ACR/EULAR	28	148	176
Wang 2020 (33)	Asia	Single-centre	R	HRCT	CTD-ILD	ACR/EULAR	48	12	60
Tu 2020 (34)	Asia	Single-centre	P	HRCT	CTD-ILD	ACR/EULAR	39	24	63
Ji 2019 (35)	Asia	Single-centre	R	HRCT	CTD-ILD	Medical records	50	20	70
Hassan 2019 (36)	South America	Single-centre	P	HRCT	SSc-ILD	ACR/EULAR	29	38	67
Tardella 2018 (37)	Europe	Single-centre	R	HRCT	SSc-ILD	ACR/EULAR	27	13	40
Edis 2016 (38)	Asia	Single-centre	R	HRCT	SSc-ILD	ACR/EULAR	29	19	48
Sperandeo 2015 (39)	Europe	Single-centre	R	HRCT	SSc-ILD	ACR/EULAR	149	26	175
Moazedi-Fuerst 2015 (40)	Europe	Single-centre	R	HRCT	SSc-ILD and SLE-ILD	ACR/EULAR	13	7	20
Mohammadi 2014 (41)	North America	Single-centre	R	HRCT	SSc-ILD	ACR/EULAR	53	17	70
Moazedi-Fuerst 2014 (42)	Europe	Single-centre	P	HRCT	RA-ILD	ACR/EULAR	17	47	64
Cogliati 2014 (43)	Europe	Single-centre	R	HRCT	RA-ILD	ACR/EULAR	13	26	39

ILD: interstitial lung disease; LUS: lung ultrasound; CTD: connective tissue diseases; R: retrospective; P: prospective; HRCT: high resolution computed tomography; ACR/EULAR: American College of Rheumatology/European Alliance of Associations for Rheumatology; RA: rheumatoid arthritis; SjS: Sjögren's disease; SSc: systemic sclerosis; SLE: systemic lupus erythematosus.

respectively (26, 31, 36-41). The pooled sensitivity and specificity were 0.96 (95%CI 0.82, 0.99, I^2=75.81%) and 0.78 (95%CI 0.62, 0.89, I^2=84.93%) (Fig. 3E-F). The PLR. NLR, DOR and AUC reached 4.4 (95%CI 2.4, 8.1), 0.05 (95%CI 0.01, 0.23), 95 (95%CI 20, 439) and 0.94 (0.91, 0.96), respectively (Suppl. Table S3).

Only one study reported performance of LUS for Sjögren's disease-related ILD (SjS-ILD), with a sensitivity of 86.6% and a specificity of 84.2% (18).

Sensitivity analyses, subgroup analyses and meta-regression

Sensitivity analyses suggested that three studies were detected in influence analysis (30, 32, 36), and two studies was observed as outliers in outlier detection (32, 36) (Suppl. Fig. S2). After excluding studies identified by sensitivity analyses, LUS reached a pooled sensitivity of 0.90 (95%CI 0.86, 0.93), a specificity of 0.85 (95%CI 0.80, 0.90) and an AUC of 0.94 (95%CI 0.92, 0.96) (Suppl. Fig. S3). The results of subgroup analyses and meta-regression for categorial variables are shown in Table II. Geographical location (Europe *vs.* Non-Europe) (p<0.001), sample size (≥100 *vs.* <100) (p=0.01) and number of intercostal spaces for examination (≥50, <50 or unknown) (p=0.02) may contribute to the heterogeneity of sensitivity, while study design (prospective *vs.* retrospective) (p=0.01) may contribute to the heterogeneity of specificity. The results of meta-regression for continuous variables are shown in Table III, suggesting that age (year), duration of CTD (year), smoking (%), male (%), body mass index (BMI), positive rate of rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), percentage of forced vital capacity (FVC%) and percentage of diffusion lung capacity for Carbon Monoxide (DLCO%) were not responsible for the heterogenous results.

Publication bias assessments

Result of Deek's funnel plot asymmetry test is shown in Supplementary Figure S4, with significant publication bias observed in this study (p=0.04).

Discussion

LUS has been shown to demonstrate substantial diagnostic utility in multiple pulmonary diseases, including CTD-ILD (6, 7). A meta-analysis published in 2019 reported a sensitivity of 0.859 and a specificity of 0.839 for LUS in detecting CTD-ILD (6). However, this meta-analysis was restricted to a limited number of participants and included a study not focused on CTD-ILD (44). With a total of 28 studies and 2,196 participants, this updated meta-

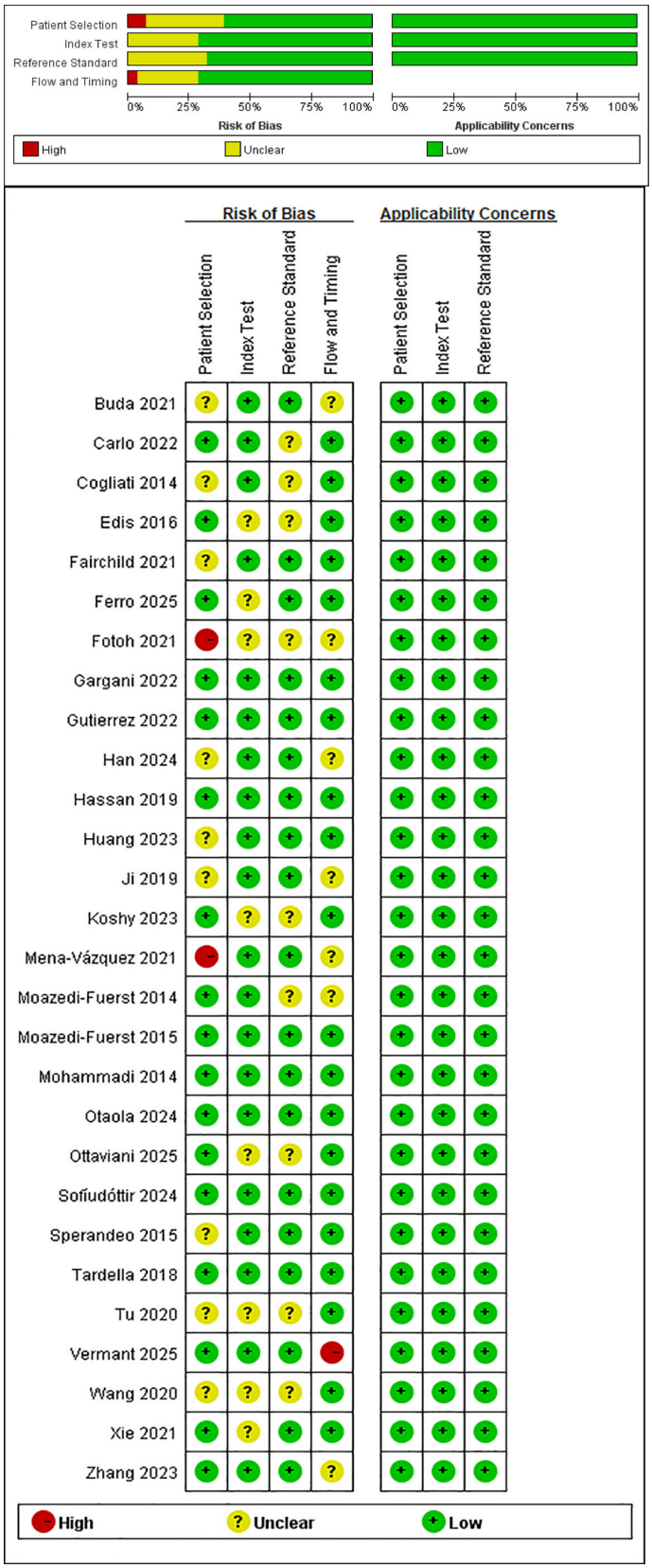

Fig. 2. Quality assessments of eligible studies.

analysis suggested that LUS exhibited good diagnostic performance in detecting CTD-ILD, RA-ILD and SSc-ILD, which reinforced the conclusion from the previous study. However, due to the high heterogeneity, risk of publication bias and low-certainty evidence in the available studies, it was still premature to recommend LUS to be applied in diagnosis of CTD-ILD.

To date, multiple specific signs of LUS have been identified to diagnose CTD-ILD, such as B-lines and pleural line alternations (45, 46). B-line, which is defined as vertical, discrete laser-like hyperechoic reverberation artifacts, emerges from the pleural line to bottom of screen without disappearing (47, 48). A study reported that B-lines showed good sensitivity in detecting patients with very early SSc (49). Another study reported high sensitivity but low specificity of posterior B-lines in detecting worsening and development of CTD-ILD (50). Pleural line alternation, including thickening, fragmentation and irregularity, was another indicator of ILD (45, 51). A pleural irregularity score ≥15 has been reported to reach a sensitivity of 86.6% and specificity of 84.2% for patients with SjS-ILD (18). As there are multiple specific signs in ILD diagnosis, future studies may consider incorporating these signs to develop a standardised criteria of LUS (52). By taking all specific signs into account, this criterion may achieve better diagnostic performance and facilitate broader implementation of LUS in future large-scale applications.

Other features of using LUS for ILD diagnosis should also be noted. For example, LUS has shown a sensitivity of 84.2% and a specificity of 84.5% in identifying >50% HRCT involvement in ILD patients with UIP pattern. However, no correlation was observed between LUS findings and > 50% HRCT involvement in ILD patients with NSIP pattern (53). Moreover, as LUS is more sensitive to pleural abnormalities and superficial lung assessment, it may fail to detect ILD cases with little pleural involvement or central pulmonary fibrosis. As both B-lines and pleural line alternations are not specific markers of ILD, it may also misdiagnose other diseases or subpleural interstitial lung abnormalities as ILD. Future studies may combine LUS with other ILD-related laboratory tests such as Krebs Von den Lungen-6 (KL-6) to improve its sensitivity and specificity (54).

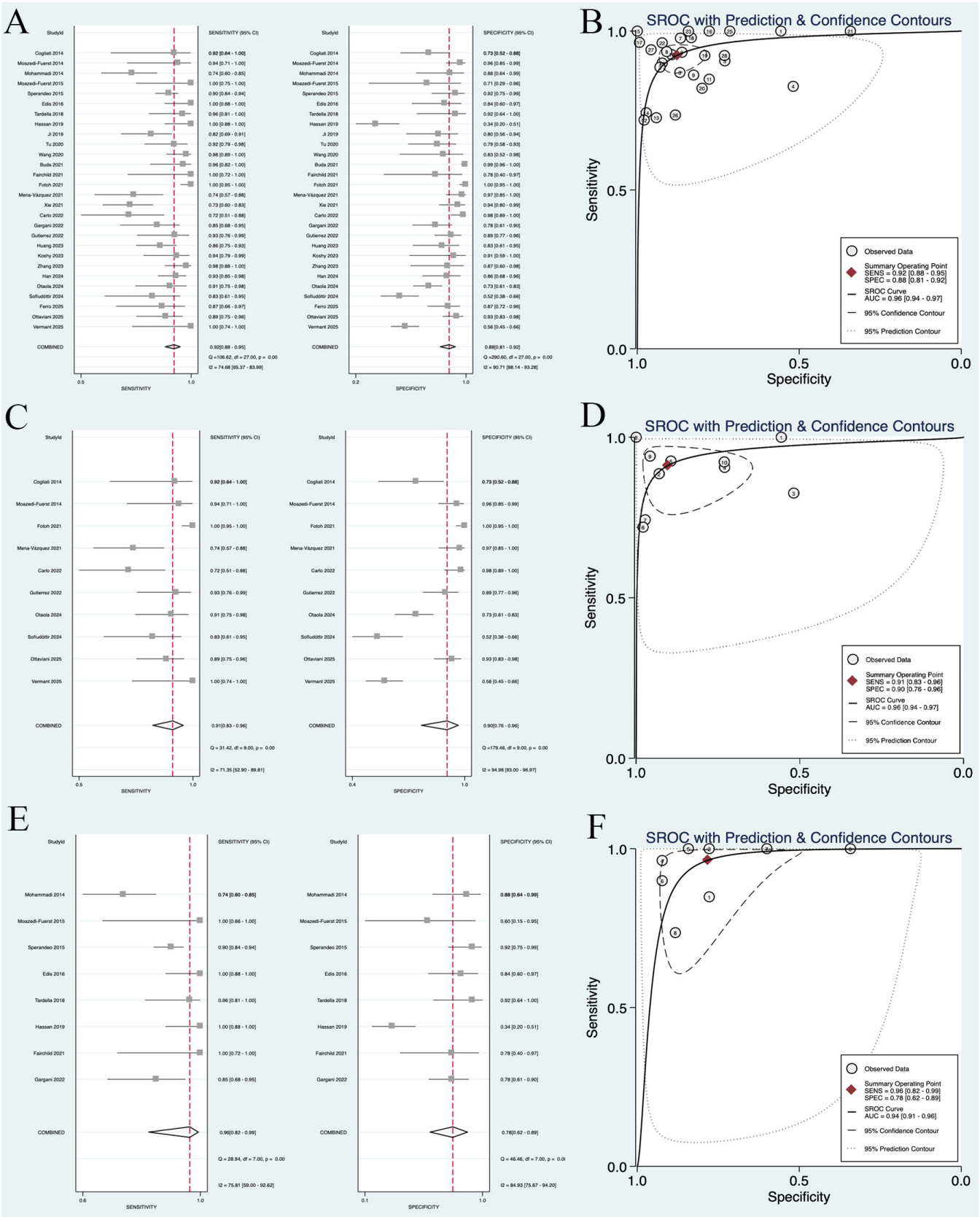

Fig. 3. Diagnostic performance of LUS for detection of CTD-ILD, RA-ILD and SSc-ILD.
A. Forest plot of LUS for CTD-ILD. **B.** sROC curve of LUS for CTD-ILD. **C.** Forest plot of LUS for RA-ILD. **D.** sROC curve of LUS for RA-ILD. **E.** Forest plot of LUS for SSc-ILD. **F.** sROC curve of LUS for SSc-ILD.
CTD-ILD: connective tissue disease-related interstitial lung disease; sROC curve: summary receiver operating characteristic curve; RA-ILD: rheumatoid arthritis-related interstitial lung disease; SSc-ILD: systemic sclerosis-related interstitial lung disease.

Table II. Subgroup analyses and meta-regression for categorial variables.

Parameter	Subgroup	n. of studies	Sensitivity (95% CI)	I^2 (meta-regression)	$p1$	Specificity (95% CI)	I^2	$p2$ (meta-regression)
Geographical location								
	Europe	13	0.89 (0.84, 0.93)	50.61%	<0.001	0.90 (0.79, 0.95)	93.78%	0.14
	Non-Europe	15	0.94 (0.89, 0.97)	83.56%		0.86 (0.77, 0.92)	86.34%	
Sample size								
	≥100	8	0.93 (0.85, 0.97)	86.36%	0.01	0.94 (0.79, 0.98)	96.71%	0.47
	<100	20	0.92 (0.87, 0.95)	69.47%		0.84 (0.76, 0.90)	85.15%	
Study centre								
	Single-centre	26	0.93 (0.89, 0.96)	76.35%	0.99	0.88 (0.82, 0.93)	90.25%	0.42
	Multi-centre	2	NA	NA		NA	NA	
Study design								
	Prospective	9	0.94(0.91, 0.96)	57.89%	0.06	0.84 (0.65, 0.94)	94.10%	0.01
	Retrospective	19	0.91 (0.85, 0.95)	73.63%		0.89 (0.83, 0.93)	87.38%	
Number of intercostal spaces for examination	≥50	6	0.98 (0.88, 1.00)	81.6%	0.02	0.75 (0.51, 0.90)	90.43%	0.82
	<50	18	0.92 (0.87, 0.95)	75.11%		0.90 (0.82, 0.94)	87.86%	
	Unknown	4	0.87 (0.77, 0.93)	76.44%		0.91 (0.83, 0.95)	0	
Diagnostic criteria of CTD	ACR/EULAR	25	0.93 (0.88, 0.96)	76.64%	0.32	0.88 (0.81, 0.93)	91.80%	0.74
	Medical records	3	NA	NA		NA	NA	

CTD: connective tissue disease.

The results of sensitivity analyses suggested that Buda *et al*. (32) and Hassan *et al*. (36) may be the outliers affecting the stability of the results. Buda *et al*. reported a good performance of LUS for CTD-ILD, with both sensitivity and specificity exceeding 96%. However, Hassan *et al*. reported a specificity of 34%, which was different from the general findings. The results of subgroup analyses and meta-regression suggested that geographical location, sample size, number of intercostal spaces for examination and study design were responsible for the heterogeneous results. Both findings highlighted the importance of standardising criteria and procedure of LUS in future clinical practice, calling for further high-quality studies to address this issue further.

We have also shown a conceptual framework for future application of CTD-ILD (Fig. 4). CTD patients may first undergo LUS examination and ILD-related laboratory such as KL-6 (55, 56). Patients with negative results are identified as low-risk and underwent periodic check-up, while patients with positive results are categorised as high-risk and underwent HRCT examination. Patients with HRCT-confirmed ILD may receive anti-fibrotic drugs and oxygen therapies to improve their long-term outcome, and periodic re-evaluation is still required to optimise therapeutic management. Future studies may

Table III. Results of meta-regression for continuous variables.

Parameter	Coefficient	Standard error	T	95% CI	P>|t|
Age (year)					
Sensitivity	-0.01	0.02	-0.29	-0.05, 0.04	0.78
Specificity	-0.02	0.04	-0.66	-0.10, 0.05	0.52
Duration of CTD (year)					
Sensitivity	-0.01	0.07	-0.17	-0.17, 0.15	0.87
Specificity	0.03	0.10	0.28	-0.19, 0.25	0.78
Smoking (%)					
Sensitivity	-0.63	1.09	-0.57	-3.66, 2.41	0.60
Specificity	0.65	2.57	0.25	-5.65, 6.95	0.81
Male (%)					
Sensitivity	-0.90	1.51	-0.60	-4.12, 2.31	0.56
Specificity	1.51	2.57	0.59	-3.88, 6.91	0.56
BMI (kg/m^2)					
Sensitivity	-0.12	0.12	-0.92	-0.65, 0.42	0.45
Specificity	-0.21	0.17	-1.19	-0.96, 0.54	0.36
RF+ (%)					
Sensitivity	-0.77	1.81	-0.42	-5.43, 3.89	0.69
Specificity	0.06	3.52	0.02	-8.56, 8.68	0.99
ACPA+ (%)					
Sensitivity	-1.37	3.05	-0.45	-9.84, 7.11	0.68
Specificity	1.70	5.53	0.31	-12.53, 15.93	0.77
UIP (%)					
Sensitivity	-3.70	2.77	-1.34	-12.51, 5.12	0.27
Specificity	9.96	4.13	2.41	-3.19, 23.11	0.10
NSIP (%)					
Sensitivity	1.59	6.06	0.26	-17.71, 20.89	0.81
Specificity	-6.98	9.80	-0.71	-38.18, 24.22	0.53
FVC%					
Sensitivity	-0.04	0.02	-1.88	-0.09, 0.01	0.12
Specificity	-0.01	0.04	-0.32	-0.10, 0.07	0.76
DLCO%					
Sensitivity	0.00	0.02	0.18	-0.05, 0.05	0.87
Specificity	-0.02	0.03	-0.87	-0.10, 0.05	0.42
Number of intercostal spaces					
Sensitivity	0.00	0.01	0.47	-0.02, 0.02	0.64
Specificity	-0.01	0.01	-1.54	-0.04, 0.01	0.14

CTD: connective tissue disease; BMI: body mass index; RF: rheumatoid factor; ACPA: anti-citrullinated peptide antibodies; UIP: usual interstitial pneumonia; NSIP: non-specific interstitial pneumonia, FVC%: percentage of forced vital capacity; DLCO%: percentage of diffusion lung capacity for carbon monoxide.

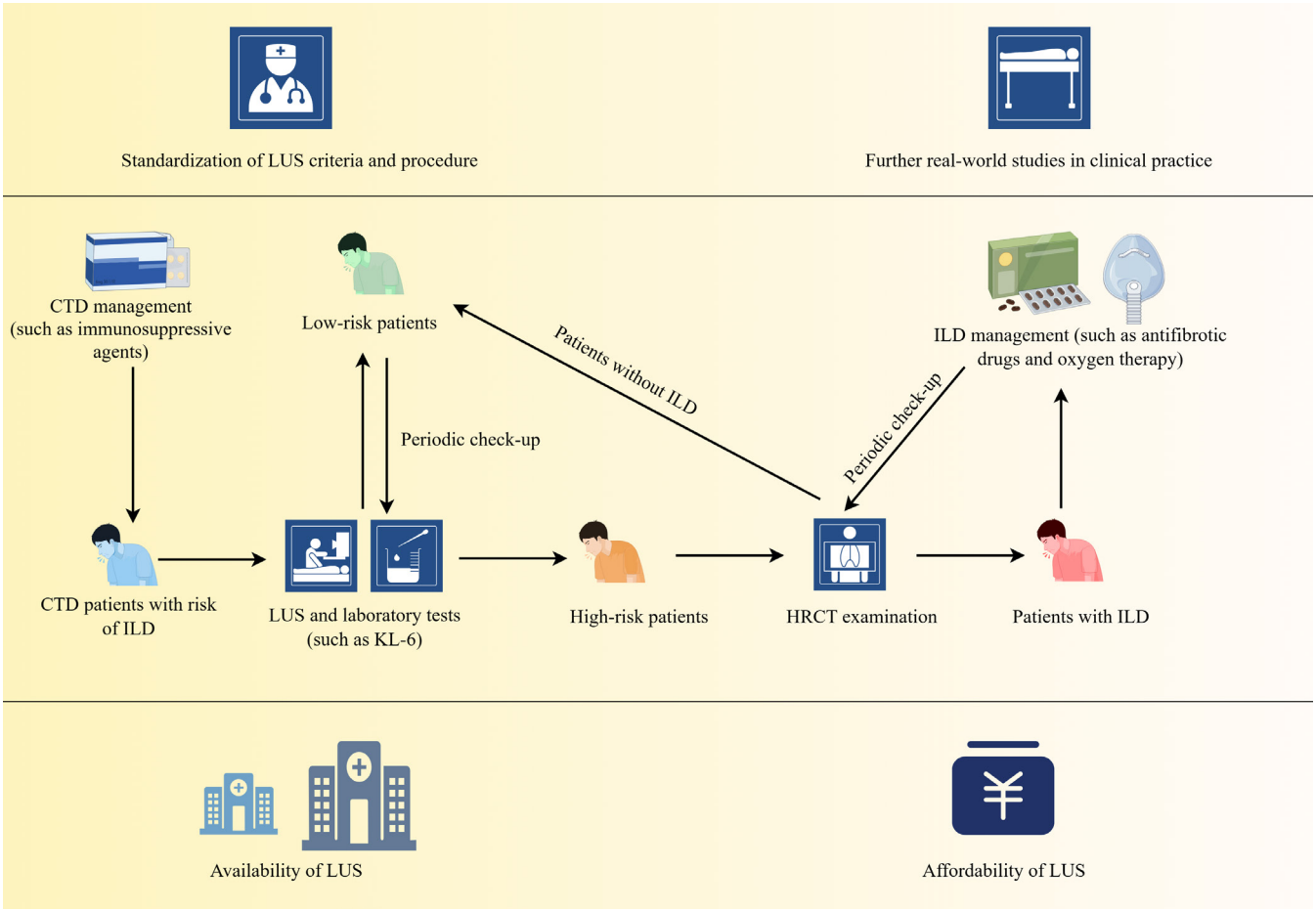

Fig. 4. A conceptual framework of LUS application.
LUS: lung ultrasound, CTD: connective tissue disease, ILD: interstitial lung disease, KL-6: Krebs Von den Lungen-6. HRCT: high resolution computed tomography.

also focus on the optimal time intervals for follow-up assessments for both low-risk and high-risk CTD patients as well as those with confirmed CTD-ILD.

The results of this study exhibited high heterogeneity, which may be attributed to multiple factors including the probe type and frequency, number of intercostal sites for examination, the criteria for LUS positivity, and operator expertise. The significant heterogeneity observed in our study constituted a major barrier to the direct application of meta-analysis findings to individual patients. It underscored the necessity for judicious interpretation and contextual adaptation of this evidence in routine practice: taking specific clinical scenarios, patient characteristics, standard clinical training and local healthcare resources into account rather than simply adopting the 'average' effect.

There are also other approaches that may be applied for diagnosis of CTD-ILD. Cheng *et al*. reported that combining spirometry with impulse oscillometry was more beneficial than spirometry alone in detecting RA-ILD (57). Niu *et al*. developed a nomogram combining age, anti-dsDNA, C-reactive protein, disease activity index of SLE and pericarditis to predict ILD or pulmonary arterial hypertension of SLE, with an AUC of 0.871 (58). Future studies may consider adding spirometry results into predictive nomograms of CTD-ILD to reach better diagnostic performance.

This study still has some limitations that need to be mentioned. 1. CTD-ILD was composed of multiple subtypes with different pathogenesis. However, we could only summarise the performance of LUS in RA-ILD and SSc-ILD. The performance of LUS in other types of CTD-ILD, such as SLE-ILD and SjS-ILD, was still under investigation. 2. Most eligible studies were conducted in a single centre, and 20 out of 28 studies enrolled less than 100 participants, which may reduce the reliability of study results. As eligible studies were conducted mostly in specialised care settings, our findings can only indicate the considerable potential of LUS within such contexts. Whether LUS can be widely adopted in community settings requires further validation. 3. Furthermore, although LUS has shown good diagnostic accuracy in identifying CTD-ILD, few studies have investigated whether imaging characteristics of LUS were associated with prognosis of patients, which may need to be addressed by future studies. 4. Potential comorbidities of CTD patients, such as pulmonary hypertension and heart failure, may share similar artifacts like B lines, thereby necessitating the need of LUS to differentiate ILD from other comorbidities. Future studies may also need to investigate how to differentiate ILD from other comorbidities of CTD.

5. Significant publication bias was observed in this study, which suggested that studies with lower diagnostic efficacy of LUS may have remained unpublished, leading to an overestimation of its diagnostic performance. The result should therefore be interpreted as an optimistic diagnostic accuracy in an ideal research setting, rather than its expected performance in routine practice.

Conclusion

Despite good diagnostic accuracy, the high heterogeneity, risk of publication bias and low-certainty evidence in the available studies suggested that the evidence was insufficient to recommend LUS for routine application. The generalisability of pooled estimates to clinical practice also remains uncertain. Standardisation of diagnostic criteria and procedure was still necessary before its broader application in clinical practice, and future prospective studies with large sample size were still needed to investigate performance of LUS in detecting other subtypes of CTD-ILD.

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