

Early View

Invited review

ERS International Congress 2021: highlights from the Clinical Techniques, Imaging and Endoscopy assembly

C Bal, C Falster, A Carvalho, N Hersch, J Brock, CB Laursen, S Walsh, J Annema, D Gompelmann

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ERS International Congress 2021: highlights from the Clinical Techniques, Imaging and Endoscopy assembly

Bal C¹, Falster C², Carvalho A^{3,4}, Hersch N⁵, Brock J⁶, Laursen CB⁷, Walsh S⁸, Annema J⁹, Gompelmann D¹

¹Division of Pulmonology, Department of Internal Medicine II, Medical University of Vienna, Vienna, Austria

²Department of Respiratory Medicine, Odense University Hospital, Odense, Denmark

³Department of Radiology, Centro Hospitalar Universitário de São João, Porto, Portugal

⁴Department of Medicine, Faculdade de Medicina da Universidade do Porto, Portugal⁵

Department of Respiratory Medicine, St George Hospital, Sydney, Australia

⁶Department of Pneumology and Critical Care Medicine, Thoraxklinik University of Heidelberg, Heidelberg, Germany

⁷Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

⁸National Heart and Lung Institute, Imperial College, London, UK

⁹Department of Respiratory Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Address correspondence to:

Prof. Dr. med. Daniela Gompelmann
Department of Internal Medicine II, Division of Pulmonology
Medical University of Vienna
Währinger Gürtel 18-20
1090 Vienna
Vienna, Austria

Abstract

This manuscript summarises the highlights from the virtual European Respiratory Society's "Clinical techniques, imaging and endoscopy" Assembly 14 presented at the 2021 European Respiratory Society International Congress. Cutting-edge innovative developments in both diagnostic approaches and therapeutic strategies in patients with lung cancer, interstitial lung disease, obstructive airway disorders and infectious diseases were presented on this year's interactive congress platform. In this manuscript, the Assembly 14 subgroups summarise the key take home messages given new research outcomes and place them in the context of the current knowledge.

In this article, early career members of the Assembly 14 subgroups “Interventional pulmonology”, “Imaging” and “Ultrasound” review the highlights of novel diagnostic approaches and innovative therapeutic strategies in patients with various lung diseases. Results of numerous trials in the field of lung cancer, interstitial lung disease, obstructive airway disorders and infectious diseases presented at the 2021 international European Respiratory Society International Congress are summarised.

Group 14.01: interventional pulmonology

Peripheral pulmonary lesions and lung cancer

Effective and minimally invasive diagnosis of peripheral pulmonary nodules (PPNs) has emerged as a key issue at this year’s ERS congress. As guidelines recommend lung cancer screening, solutions to safely and effectively obtain tissue from PPNs are required. More than in previous years, several new techniques have been established and synergistically combined to address this emerging challenge. Additionally, localised malignant PPN ablation treatment is being studied, enhancing the importance of bronchoscopy in both diagnostic and therapeutic approaches.

Bronchoscopy-guided ablation is a novel therapeutic approach for malignant PPNs. Few pilot and model studies of radiofrequency ablation and microwave ablation (MWA) in porcine and canine models are published [1; 2] and a few first trials have described encouraging results of bronchoscopic ablation techniques in human beings [3]. At the ERS congress 2021, Lau et al. presented MWA of peripheral lung tumours in the NAVABLATE study as a late-breaking abstract [4]. This prospective study used MWA in combination with navigation bronchoscopy to target PPNs <30 mm. Thirty patients with lung cancer or oligometastatic disease, 68 ± 10 years, with a mean nodule size of 14 ± 5 mm, were enrolled, and 39 ablations were performed using 75-100 Watt. All ablations were technically satisfactory without serious adverse events. One patient experienced mild haemoptysis as an adverse event, possibly related to the ablation device as it occurred in the first 30 days. At one-month, technique efficacy was 100%, and the planned two-year follow-up regarding efficacy is in progress [4].

Robotic navigational bronchoscopy (RNB) provides increased reach, stability, dexterity and needle proximity for small PPNs. In a recent study with 131 patients, RNB provided a diagnostic yield of 82% in PPNs with a mean size of 18mm. Nodule size remains the major determining factor in diagnostic feasibility [5]. RNB combined with cytologic rapid on-site evaluation (ROSE) was found to be a successful and safe method with a pneumothorax rate of 3.7% as the sole adverse event in another

recent study with 55 patients [6]. A new idea that was presented at the ERS congress 2021 was the combination of RNB with the needle-based confocal endomicroscopy (nCLE), that is able to differentiate between malignant and benign processes with a concordance with cytopathology of 95% [7]. Thereby, the combination of RNB with nCLE seems to reduce the amount of near-miss events. In a late-breaking study, Manley et al. combined nCLE with RNB in 17 patients with a mean nodule size of 15mm [8]. After identifying the nodule by RNB, nCLE was performed for correcting needle position. After confirming the correct position of the catheter within the malignant nodule using CLE, transbronchial needle aspiration was performed. The sensitivity of nCLE was 93% for detecting malignant patterns, and diagnostic yield was 82%, without relevant adverse events. Importantly, nCLE identified near-miss events leading to reposition of sampling location in 35%. Thus, the combination of nCLE and RNB improved the diagnostic yield in very small lesions and reduced near-miss events, displaying a synergistic benefit when used in diagnostic procedures.

For patients with suspected lung cancer, fast and accurate tissue diagnosis is important for therapeutic decisions and prognostication. A laser-based real-time visualisation of tissue with higher harmonic generation (HHG) microscopy seems to be an innovative tool that provides the ability to identify pathological features in small bronchoscopic biopsies without the need for tissue processing. One study presented at ERS 2021 reported about 29 biopsies from 11 patients that were imaged by using the HHG microscope within a few minutes after bronchoscopic sampling and compared results to routine pathological practice [9]. The HHG microscope was able to identify pathological hallmarks so that in future the use of HHG microscopes within the endoscopy units may reduce the number of biopsy samples required and may reduce endoscopy time.

The use of cryoprobes for diagnosis of malignancy is well established. Thus, the diagnostic yield of endobronchial biopsies of endoluminal lesions and of transbronchial cryobiopsies of periphery pulmonary nodules were found to be 90% and 93% respectively [10; 11]. When added to conventional sampling methods, cryobiopsy improved the diagnostic success rate in 8.6% of patients, and with low adverse events (1.2% severe bleeding and 0.8% pneumothorax events) [12]. At ERS 2021, Gonuguntla and co-authors described endobronchial ultrasound-guided transbronchial Cryo Nodal Biopsy (EBUS-TBCNB) as a novel approach for mediastinal lymph node sampling in 4 patients with mediastinal lymphadenopathy [13]. These first EBUS-TBCNB revealed encouraging results but further studies are necessary.

Patients with severe respiratory failure are at high risk for bronchoscopic procedural complications. An alternative diagnostic approach, transoesophageal bronchoscopic ultrasound guided fine needle

aspiration (EUS-B-FNA) was described in 16 patients with severe respiratory insufficiency and central lesions suspicious for lung cancer [14]. EUS-B-FNA showed a diagnostic yield of 81% with no severe side effects, thus demonstrating an overall acceptable safety profile in this patient group with high morbidity.

Take home messages

- RNB is a promising tool to reach small peripheral lesions.
- nCLE is a safe and effective diagnostic modality in addition to navigation bronchoscopy, causing sampling area readjustment in 35% of cases.
- Microwave ablation therapy seems to be a safe, tissue-sparing alternative therapy for malignant lung nodules and pulmonary oligometastatic nodules smaller than 30 mm.
- EBUS-TBCNB is currently being explored as a novel approach for mediastinal lymph node sampling.

Interstitial Lung Disease (ILD)

Transbronchial cryobiopsy (TBCB) has become a relevant diagnostic tool to obtain histology in patients with interstitial lung disease (ILD). In 2020, the COLDICE trial showcased TBCB as a safe alternative to surgical diagnostic biopsy, as there was high histopathologic agreement between these two approaches [15; 16]. In the COLDICE cohort, the main factor predicting histopathologic agreement was the number of TBCB samples. In a multicenter study by Hetzel et al. reported at this year's ERS, 127 ILD patients underwent TBCB with 4.8 ± 1.3 biopsies, total area of 51 ± 29 mm², and approximate freezing time of 7 seconds [17]. The authors described a significant correlation of the total area of all histological specimens per patient and total area per biopsy with the confidence level of histological diagnosis. Contrary to the findings in the COLDICE trial, the number of biopsies did not have a significant impact on the yield.

Another approach for performing TBCB in ILD patients was presented in the FROSTBITE study that evaluated the feasibility and safety of a novel smaller sheath cryoprobe and demonstrated an acceptable risk profile with low complication rates [18].

In ILD, computed tomography scans or lung biopsies are often indeterminate in early disease. Use of polarisation-sensitive optical coherence tomography (OCT) may help to distinguish between different ILD patterns. OCT, using infrared light similarly to a radial probe, has the ability to assess larger lung volumes than biopsies, with higher visual acuity than computer tomography through lengthwise recording of the wall lining of multiple bronchial trees, showing loss of aerated space and increase of collagen with a 10 µm resolution and 2-3 mm depth. In a study from Amsterdam, collagen present in

OCT showed 87% concordance with biopsies in patients with different ILDs and controls [19]. OCT showed a 100% sensitivity and specificity for diagnosis of usual interstitial pneumonia in another recent study with 27 patients [20].

Take home messages

- TBCB has become implemented as standardised diagnostic tool in ILD with an acceptable safety profile. Larger sample size improves diagnostic confidence regardless of sample number.
- OCT assesses collagen deposition and loss of aerated space in large lung volumes, with an 87% concordance with biopsies and may help to distinguish different ILD patterns.

Obstructive Lung Disease

In patients with severe asthma, bronchial thermoplasty (BT) improves asthma control, quality of life and exacerbation frequency for up to 10 years, with few adverse effects such as mild-to-moderate bronchiectasis in 7% after treatment [21]. In the randomised controlled TASMA trial, airway smooth muscle (ASM) reduction was confirmed as a mechanism of action with long-term altered airway remodelling [22]. One trial presented at the ERS congress 2021 evaluated the use of OCT to assess airway remodelling following BT in 15 patients with severe asthma treated in TASMA trial [22; 23]. Following BT, high intensity OCT showed reduced size of proximal larger airways reflecting changes in airway extracellular matrix content [23]. As an alternative diagnostic tool to assess airway pathology in patients with asthma, the feasibility, safety and efficacy of mucosal cryobiopsies were compared to endobronchial forceps biopsies in 48 patients. Mucosal cryobiopsies were safe and yielded biopsies that were larger and better preserved compared with forceps biopsies [24]. The cryotechnique seems to be a promising tool for future in vivo studies of airway pathology.

In patients with advanced chronic obstructive pulmonary disease (COPD) and emphysema, surgical or endoscopic lung volume reduction (ELVR) is an established guideline-endorsed treatment option. As an endoscopic approach, the implantation of one-way valves presents a reversible, symptom-improving and disease-modifying therapeutic option for patients with complete interlobar fissures [25]. Data from the Lung Emphysema Registry (LE-R) in Germany confirmed that surgical lung volume reduction as well as endoscopic valve therapy led to significant improvements in various outcome parameters [26]. Another bronchoscopic method to achieve lung volume reduction and improvement of elastic recoil is endoscopic coil implantation. In a 2016 published randomised controlled trial, coil implantation was shown to lead to an improvement of median exercise tolerance though this was only modest and of uncertain clinical importance [27]. At ERS 2021, authors presented results from one

study that evaluated an improved coil-like device, Lung Volume Reduction Reverser (LVR-R System). In this pilot study, 15 COPD patients were treated bronchoscopically with the LVR-R System. Six months following intervention, no significant improvement in lung function parameters, exercise capacity or quality of life questionnaires was seen. However, a significant complication rate, mainly due to pneumonias, was noted [28].

Take home messages

- Clinical applications of OCT to visualise extracellular matrix composition and collagen deposition in patients with severe asthma are emerging.
- Extracellular matrix collagen content is reduced in OCT measurements after bronchial thermoplasty.
- Data from the “Lung Emphysema Registry” emphasizes the efficacy of surgical lung volume reduction and endoscopic valve therapy in patients with advanced emphysema.

Pleural disease

Malignant effusions are accompanied by considerable symptoms and morbidity. Recently, early definite interventional treatment was shown to be beneficial in malignancies both responsive and unresponsive to anticancer therapy [29]. However, talc pleurodesis and indwelling pleural catheters (IPC) require up to six days of inpatient stay with a pleurodesis rate of 51-92% [30-33]. To reduce inpatient stay in 313 patients to a median of two days with comparable pleurodesis success rates, the SIMPLE trial used ultrasonographic controls [34]. Currently, a retrospective study performed in Cambridge combined a day-only case setting with thoracoscopy, IPC, talc poudrage, suction, and daily drains. Admission was required in only 13% of 45 patients, because of air leak and unrelated pneumonia, whilst mean rate of pleurodesis success was 78% [35].

Intrapleural enzyme therapy (IET) with tissue plasminogen activator and deoxyribonuclease has been established as a therapeutic option in pleural infection. Complications of infectious pleural effusion treatments with IET were assessed by the RETROLYSIS study [36]. In 1833 patients, pleural bleeding occurred in only 4.1%, independent of IET dose. Bleeding risk was doubled with concurrent systemic anticoagulation treatment.

Persistent air leak may present a challenge in the clinical routine. Zhang et al. reported a combination of targeted body positioning with thrombin injection and suction drainage to assist pleural adherence in 20 predominantly male patients after spontaneous pneumothorax or bullous reputeure. Air leak remission was seen after 1.3 ± 1 days, with 5% recurrence, and without serious adverse events [37].

Take home messages

- To minimise interventional burden for a quality-of-life intervention, shifting malignant effusion pleurodesis to day-case treatment showed acceptable efficacy and safety, with a low admission rate.
- In pleural empyema and septated pleural effusion, IET resulted in 4% pleural bleed risk independently of IET dose. Full anticoagulation doubled risk to 8%.

Group 14.02: imaging

Coronavirus disease 2019

Coronavirus disease 2019 (COVID-19), a highly infectious respiratory disease caused by SARS-CoV-2, has completely changed our lives. Over the past two years much has been learned about its clinical and radiologic manifestations. Imaging, especially with computed tomography (CT), has established its role not only in diagnosing and assessing disease extent, but has also shown promise in assessing short-term outcomes. In a late-breaking abstract presented at ERS 2021, the prognostic value of chest CT findings in older and multimorbid COVID-19 patients was evaluated [38]. In this study, which included 380 hospitalized patients aged 60 years or older (mean 78 years), ground-glass opacities (GGO) (85%) and consolidations (41%) were the most common CT findings, but pleural effusion (23%) and pulmonary nodules (12%) were more prevalent than previously reported in younger cohorts [39; 40]. Patients were also grouped in 5 different clusters according to the prevalence of GGO and pleural effusions. At multivariate analysis, only cluster “LH” (i.e., low GGO, high pleural effusion prevalence) was an independent predictor for mortality. This study suggests that pleural effusions may have an important prognostic factor in older patients with COVID-19.

Although the radiologic signs of the disease have been extensively reported in the literature, the long-term health consequences remain largely unknown. This year, Tomassetti et al. presented an interim analysis from the ongoing PCOILS study (Prevalence and Characteristics of Post-COVID-19 Interstitial Lung Syndrome) [41]. In this multicenter prospective study, 550 patients underwent high-resolution chest CT (HRCT) 6 months after being hospitalised due to COVID-19. Out of 550 subjects, 212 (38.6%) showed no CT abnormalities, 147 (26.7%) had interstitial abnormalities affecting < 5% of the lung and 191 (34.7%) had interstitial abnormalities affecting > 5% of the lung volume. All patients presenting

with interstitial abnormalities affecting > 5% of the lung at 6 months then undergo follow-up CT at 12 and 18 months. In this subgroup of patients, 133 (24.2%) had fibrotic interstitial abnormalities, which were diffuse in 98 cases (17.8%) and from these, the majority of patients (61, 11%) had a CT pattern resembling fibrotic NSIP / organising pneumonia; 31 (5.8%) had a pattern which was indeterminate for UIP and only 6 patients (1.1%) had a UIP pattern (definite UIP or probable UIP). Also, 58 patients (10.5%) had interstitial abnormalities without fibrotic-like features. The potential progression of the observed fibrotic changes has to be further elucidated in subsequent analysis.

Take home messages

- Pleural effusions may be an important poor prognostic factor in older patients hospitalised with COVID-19
- At six-month follow-up after hospitalisation from COVID-19 infection, almost 25% of patients had fibrotic interstitial lung abnormalities on a follow-up CT

Interstitial Lung Diseases

Interstitial lung diseases (ILDs) encompass a variety of disorders with a wide range of causes, clinical manifestations and radiological and pathological features. Although HRCT plays an absolutely central role in the diagnostic process of these entities, chest radiograph is commonly the first indicator of the presence of an ILD. At ERS 2021, Nishikiori et al. [5] presented a validation study of an artificial intelligence (AI) software to detect chronic fibrosing ILDs in chest radiographs [42]. In 1280 consecutive patients who had chest radiography and chest CT on the same day, 352 patients (27.5%) had chronic fibrosing ILD, 618 (48.3%) had abnormal radiologic findings other than fibrosing ILD and 310 (24.2%) had normal chest radiographs. Area under receiver operating characteristics curve (AUC) was 0.872 for CF-ILD patients versus other radiologic abnormalities and 0.946 for CF-ILD versus no abnormal findings.

Recent evidence suggests that small airways disease may be a feature of idiopathic pulmonary fibrosis (IPF) [43]. In a late-breaking abstract presented at the congress, a multistage convolutional neural network to perform airway segmentation from CT volume was applied to 31 IPF patients [44]. This software showed that in comparison with “stable IPF” patients, “progressive” disease is characterized by larger increases in median airway sizes and larger declines in lung volumes.

Take home messages

- Artificial intelligence software can detect chronic fibrosing ILDs in chest radiographs

- Airway measurements with AI may have a role as a surrogate marker for IPF progression

Lung cancer screening

Lung cancer is the leading cause of cancer-related death in the world [45]. Randomised controlled trials such as the National Lung Screening Trial (NLST) [46] or the Netherlands-Leuven Longkanker Screenings Onderzoek (NELSON) trial [47] have shown a significant reduction in lung cancer specific mortality with low-dose chest CT screening. In the United States, previous U.S. Preventive Services Taskforce (USPSTF) guidelines recommended screening for asymptomatic adults aged 55-80 years who had a ≥ 30 pack-year smoking history and were smokers or had quit smoking within the previous 15 years [48]. One Australian study presented at the congress aimed to identify the proportion of newly diagnosed lung cancer patients who would have been eligible for screening according to USPSTF criteria [49]. During the study period, 175 patients were diagnosed with lung cancer and only 43% (75/175) would have qualified for screening in the preceding 12 months, capturing 54% of non-small cell lung cancers and 100% of small cell lung cancers. Also only 40% (70/175) of patients would have been eligible for screening in the preceding 5 years. It would be interesting to re-analyse the data according to the recently updated and wider USPSTF criteria which now include a lower age limit (50-80 years-old) and a minimum smoking history of ≥ 20 pack-years [50].

Audelan et al. [51] evaluated whether a deep-learning system trained to detect lung nodules from LDCT could detect malignant lesions one year prior to diagnosis by radiologists. This system was tested in 1179 examinations from NLST in which 2 CT scans were available one year apart. Among the 177 biopsy-proven malignant nodules, the algorithm detected 172 regions of interest within 3 cm of their ground-truth (97% sensitivity). Missed malignant nodules were all located close to the mediastinum. On CT images obtained 1 year prior to diagnosis, 20 nodules were not visible and the system was able to detect 97% of the visible nodules (152/157). However, this system also provided a large number of false positive nodules (mean 12 new candidate nodules per scan).

Take home messages

- A significant proportion of newly diagnosed cancer patients may not be eligible for lung cancer screening according to most widely used criteria
- Deep-learning based systems may detect malignant pulmonary nodules one year prior to their detection by radiologists

Chronic obstructive pulmonary disease

Asthma and COPD are two prevalent chronic lung diseases characterised by airflow limitation. While treatment differs between these entities, they often present with clinical similarities. HRCT is the main imaging tool for evaluation of emphysema and airways disease. One study presented at the congress aimed to determine if a machine learning approach using quantitative CT-derived features could differentiate COPD and asthma [52]. Using airway and parenchymal-related CT features, the algorithm could discriminate between asthma and COPD patients with 87% sensitivity, 71% specificity and 80% accuracy.

Another study tried to investigate the relationship between 129-xenon (¹²⁹Xe) MRI and pulmonary function test (PFT) metrics in patients with asthma and/or COPD [53]. Worsening disease severity as assessed by spirometry and TLCO was associated with increased ventilation defect percentage (VDP) and mean acinar dimensions (LmD) and with decreased red blood cell to tissue-plasma ratio (RBC/TP), RBC/gas and TP/gas ratios. ¹²⁹Xe MRI ventilation metrics also correlated moderately with spirometry, RV/TLC, TLCO and lung clearance index (LCI), but not with oscillometry. Moreover, a significant proportion of patients with normal spirometry had elevated VDP due to the high sensitivity of ¹²⁹Xe MRI in detecting ventilation abnormalities.

Take home messages

- Machine learning using CT imaging-derived features may have a role in distinguishing patients with COPD and asthma
- ¹²⁹Xe MRI-derived metrics correlate moderately with COPD and asthma disease severity as assessed by PFT

Group 14.03: ultrasound

Coronavirus disease 2019

The continued presence of the global SARS-CoV-19 pandemic encourages physicians to seek out ways of improving bedside evaluation, aiding in clinical assessment, diagnosis and prognostication for patients admitted with COVID-19. As predicted in the 2020 ERS highlights, the past year has led multiple researchers to explore the clinical utility of lung ultrasound in these patients [54].

The diagnostic accuracy of lung ultrasound for detection of peripheral changes in COVID-19 pneumonia was assessed by Smargiassi et. al. [55], using a scoring system proposed by Soladati et. al.

[56] in which 14 thoracic zones are scored from 0 to 3 based primarily on alterations of the pleural line. Sixteen patients with confirmed COVID-19 pneumonia were subject to both an HRCT-scan and a lung ultrasound examination within 48 hours. While lung ultrasound showed encouraging results for identification of any peripheral alterations (sensitivity 92.1% and specificity 90%), the accuracy for identification of severe pneumonic changes were lower (sensitivity 70.1% and specificity 84%). Overall, these findings are impressive when considering that a recent Cochrane meta-analysis reported a pooled sensitivity and specificity of 86.4% and 54.6%, respectively, for lung ultrasound's ability to diagnose COVID-19 [57].

The utility of lung ultrasound in predicting clinical deterioration in patients admitted with COVID-19 was appraised by two studies at the ERS congress 2021. Bielosludtseva et. al. examined 20 patients with severe COVID-19 pneumonia and found that a lung ultrasound score (LUS) >18 and presence of triangular subpleural hypoechoic lesions were associated with disease progression [58]. Utilising the same scoring system as Pierrakos et. al, a study on 18 patients found that a lung ultrasound examination within 72 hours of admission to a dedicated COVID-19 ward could not predict clinical deterioration, but noted that if ultrasound is performed daily, a sudden increase in score may herald significant disease progression [59].

An international multicenter study by Pierrakos et. al. appraised the prognostic value of a global LUS-aeration score on 55 invasively ventilated patients with COVID-19 [60]. Twelve thoracic zones were evaluated, each receiving a score between 0 and 3: Normal aeration (0 points), B-lines covering <50% of the pleural line (1 point), B-lines covering >50% of the pleural line (2 points) or present consolidation, suggesting complete or near-complete loss of aeration (3 points). The authors concluded that a global LUS-aeration score of ≤ 13 aided in predicting successful liberation from a ventilator ($p < 0.01$) and a score of > 17 was associated with higher mortality at 28 days ($p = 0.01$).

Take home messages

- While some studies report promising overall diagnostic accuracy of lung ultrasound in suspected COVID-19, the authors of a recent Cochrane meta-analysis conclude that due to the disappointing specificity, the role of lung ultrasound should be to rule out COVID-19 pneumonia, rather than confirming it.
- In patients with COVID-19, ultrasound may be of value in prognostication for invasively ventilated patients and to detect peripheral pneumonia.
- Evidence is sparse for prognostic value in patients referred to dedicated COVID-19 wards not requiring intensive care. Study populations are generally small, and studies utilise different scoring systems, complicating comparison of results.

Diaphragm

As the principal respiratory muscle, it is no surprise that ultrasound assessment of the diaphragm is receiving increasing scientific attention. Indeed, a reliable sonographic evaluation of excursion, thickness and thickening might spare the patient an invasive diaphragmatic pressure measurement [61]. While initial research on this topic was aimed at appraising diaphragmatic dysfunction in intubated patients, the proposed utility of diaphragmatic ultrasound has since expanded as highlighted by this years' congress where multiple studies appraised its value in distinct settings and conditions.

Gabrysz-Forget and colleagues evaluated 111 patients with cystic fibrosis establishing a normal lower range of diaphragmatic thickening fraction at 30% and revealing that it was significantly correlated to the disease markers transthyretin, CRP, FEV₁ and grip strength. Encouragingly, their findings suggest that the diaphragm measurement may be an even better marker of dyspnoea level than FEV₁ ($p=0.03$) [62]. Their findings establish a basis for future studies evaluating diaphragmatic activity as a marker of prognosis and efficacy of interventions in cystic fibrosis

In patients with acute exacerbation of COPD, readmissions are common. This encouraged Kharat et. al. to examine whether diaphragmatic ultrasound was predictive of re-hospitalisation. Twenty-eight patients with exacerbation of COPD were enrolled, and the authors reported that a diaphragmatic thickening fraction above 48% at discharge was highly predictive of re-hospitalisation within 30 days (sensitivity 100% and specificity 76%) [63].

Take home messages

- Diaphragmatic ultrasound is a promising surrogate marker of disease severity and a possible alternative to invasive evaluation of diaphragmatic function in several pathologies, but evidence is heterogenous and reference values as well as standardised scanning protocols are still needed, limiting clinical applicability.

Ultrasound for guiding pleurodesis

Recurrent malignant pleural effusion is most often observed in relation to mesothelioma, lung or breast cancer. Even though new treatments such as indwelling pleural catheters with or without concomitant talc pleurodesis are options, talc pleurodesis through a chest tube remains the most common definitive treatment. While successful in obtaining effusion control in four out of five instances, the procedure requires an initial hospital admission until adherence of pleural membranes

is confirmed. In a recently published ambitious randomised controlled trial, Psallidas and colleagues noted that the current recommendations on removal of the chest tube by the British Thoracic Society, suggest awaiting daily fluid volume drainage of less than 250 mL and lung re-expansion confirmed radiologically, however these are not based on strong evidence [64]. The authors hypothesized that integration of thoracic ultrasound before and after pleurodesis could shorten the length of hospital stay without compromising pleurodesis success.

The results were eloquently summarised by the study's second author, M. Hassan, in an oral presentation at this year's ERS conference. 313 patients requiring talc pleurodesis were included and randomised 1:1 to standard care or integrated thoracic ultrasound. The length of hospital stay was significantly shorter in the thoracic ultrasound group compared to standard care ($p < 0.001$). Furthermore, the ultrasound approach was non-inferior to standard care in relation to pleurodesis failure (34.6% vs. 32.2% of patients).

These results raise the question of whether thoracic ultrasound should be considered a standard approach in patients undergoing pleurodesis for recurrent malignant pleural effusion.

Take home messages

- The current recommendation for removal of a chest tube following talc pleurodesis for malignant pleural effusion is based on sparse evidence.
- Integration of thoracic ultrasound prior to and following talc pleurodesis reduces length of hospital stay and is non-inferior to standard care in terms of pleurodesis failure.

Pulmonary embolism

Computed tomography pulmonary angiography (CTPA) is considered the diagnostic gold standard in suspected pulmonary embolism (PE). But the procedure is time consuming, expensive and exposes the patient to radiation. Furthermore, the increasing availability of radiation-based diagnostics lowers the threshold for referral. Indeed, only 20-30% of patients referred for CTPA in Europe are diagnosed with pulmonary embolism. As such, in the hope of improving selection of patients for irradiating imaging, researchers often appraise the diagnostic accuracy of ultrasound in suspected pulmonary embolism, and this year was no exception.

A small study by Abdelkader and colleagues examined the diagnostic accuracy of ultrasonographic detection of hypoechoic rounded or wedge-shaped pleural consolidations in 30 haemodynamically stable patients with moderate to high pretest probability of PE [65]. To further increase diagnostic accuracy, the consolidations had to be hypoperfused, gauged by absence of colour doppler signals. The authors report a sensitivity of 61% and specificity of 91.6%, hinting that this approach may be of value in ruling in suspicion of pulmonary embolism, possibly limiting the need for CTPA.

A comprehensive review and meta-analysis by Falster et. al. compiled not only studies on diagnostic accuracy of lung ultrasound, but also on deep venous, cardiac and multi-organ ultrasound [66]. The study, analysing 70 unique publications, found that several single organ ultrasound findings such as detection of a deep venous thrombus, the McConnell's sign or detection of at least two hypoechoic pleural based lesions exhibit specificities above 95%, hinting a high utility in confirming suspected pulmonary embolism. Furthermore, meta-analysis of a multi-organ ultrasound examination devoid of right ventricular strain or thrombi, hypoechoic pleural based lesions and deep venous thrombi yielded a sensitivity of 90%, correlating with a high negative predictive value in patients with low or moderate pre-test probability.

Take home messages

- More than 70 descriptive studies have assessed the diagnostic accuracy of ultrasound in suspected pulmonary embolism.
- Several single organ and multi-organ findings are highly predictive of pulmonary embolism while a normal ultrasound investigation of the lungs, heart and deep veins of the legs may be of value in dismissing suspicion in patients with low to moderate pre-test probability.
- No randomised controlled studies on the subject have been conducted.

References

- [1] Myers R, Herth F, Lam S, et al. Transbronchial microwave ablation: feasibility and safety assessment in a porcine model. *Eur Respir J* 2021; 58: Suppl. 65, PA2462.
- [2] Zhong CH, Fan MY, Xu H, et al. Feasibility and safety of radiofrequency ablation guided by bronchoscopic transparenchymal nodule access in canines. *Respiration*. 2021; 100(11): 1097-1104. doi: 10.1159/000516506.
- [3] Chan JWY, Lau RWH, Ngai JCL, et al. Transbronchial microwave ablation of lung nodules with electromagnetic navigation bronchoscopy guidance—a novel technique and initial experience with 30 cases. *Transl Lung Cancer Res*. 2021; 10(4): 1608-1622. doi: 10.21037/tlcr-20-1231.
- [4] Lau K, Lau R, Baranowski R, Ng C. Late Breaking Abstract - Bronchoscopic microwave ablation of peripheral lung tumors. *Eur Respir J* 2021; 58: Suppl. 65, 1571.
- [5] Kalchiem-Dekel O, Connolly JG, Lin IH, et al. Shape-Sensing Robotic-Assisted Bronchoscopy in the Diagnosis of Pulmonary Parenchymal Lesions. *Chest* 2022; 161(2) :572-582. doi: 10.1016/j.chest.2021.07.2169.
- [6] Chen AC, Pastis NJ Jr, Mahajan AK, et al. Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study (BENEFIT). *Chest* 2021; 159(2): 845-852. doi: 10.1016/j.chest.2020.08.2047.
- [7] Kramer T, Wijmans L, de Bruin M, van Leeuwen T, Radonic T, Bonta P, Annema JT. Bronchoscopic needle-based confocal laser endomicroscopy (nCLE) as a real-time detection tool for peripheral lung cancer. *Thorax* 2021. doi: 10.1136/thoraxjnl-2021-216885.
- [8] Manley C, Kramer T, Kumar R, et al. Late Breaking Abstract - Needle based confocal laser endomicroscopy for the diagnosis of peripheral lung nodules by robotic navigational bronchoscopy. *Eur Respir J* 2021; 58: Suppl. 65.
- [9] Huizen LV, Daniels J, Radonic T, et al. Instant on-site histological feedback on bronchoscopic biopsies using higher harmonic generation microscopy. *Eur Respir J* 2021; 58: Suppl. 65, OA4319.

- [10] Schumann C, Hetzel J, Babiak AJ, et al. Cryoprobe biopsy increases the diagnostic yield in endobronchial tumor lesions. *J Thorac Cardiovasc Surg* 2010; 140(2):417-21. doi: 10.1016/j.jtcvs.2009.12.028.
- [11] Herth FJ, Mayer M, Thiboutot J, et al. Safety and performance of transbronchial cryobiopsy for parenchymal lung lesions. *Chest*. 2021; 160(4): 1512-1519. doi: 10.1016/j.chest.2021.04.063.
- [12] Matsumoto Y, Nakai T, Tanaka M, et al. Diagnostic outcomes and safety of cryobiopsy added to conventional sampling methods. *Chest*. 2021; 160(5): 1890-1901. doi: 10.1016/j.chest.2021.05.015.
- [13] Gonuguntla HK, Md V, Ganapathy T, et al. Endobronchial Ultrasound-guided Transbronchial Cryo Nodal Biopsy (Ebus-tbcnb): A novel approach for mediastinal lymph-node sampling. *Eur Respir J* 2021; 58: Suppl. 65, PA2452.
- [14] Christiansen IS, Bodgter U, Nessar R, et al. Safety of EUS-B-FNA in patients with respiratory insufficiency. *Eur Respir J* 2021; 58: Suppl. 65, OA236.
- [15] Cooper WA, Mahar A, Myers JL, et al. Cryobiopsy for identification of usual interstitial pneumonia and other interstitial lung disease features. Further lessons from COLDICE, a prospective multicenter clinical trial. *Am J Respir Crit Care Med* 2021; 203(10): 1306-1313. doi: 10.1136/thoraxjnl-2021-216885.
- [16] Troy LK, Grainge C, Corte TJ, et al. Cryobiopsy versus Open Lung biopsy in the Diagnosis of Interstitial lung disease alliance (COLDICE) Investigators. Diagnostic accuracy of transbronchial lung cryobiopsy for interstitial lung disease diagnosis (COLDICE): a prospective, comparative study. *Lancet Respir Med*. 2020 Feb;8(2):171-181. doi: 10.1016/S2213-2600(19)30342-X.
- [17] Hetzel J, Wells A, Costabel U, et al. Histological confidence of transbronchial cryobiopsy in interstitial lung diseases is influenced by sample size. *Eur Respir J* 2021; 58: Suppl. 65, OA233.
- [18] Thiboutot J, Kapp C, Demaio A, et al. Safety of a sheath cryoprobe for transbronchial biopsy: Preliminary results of the FROSTEBITE Trial. *Eur Respir J* 2021; 58: Suppl. 65, PA2460.
- [19] Vaselli M, Kalverda KAM, Bonta P, et al. In vivo PS-OCT to detect fibrotic lung disease. *Eur Respir J* 2021; 58: Suppl. 65, OA234.

- [20] Nandy S, Raphaely RA, Muniappan A, et al. Diagnostic accuracy of endobronchial optical coherence tomography for the microscopic diagnosis of usual interstitial pneumonia. *Am J Respir Crit Care Med*. 2021; 204(10): 1164-1179. doi: 10.1164/rccm.202104-0847OC.
- [21] Chaudhuri R, Rubin A, Sumino K, et al. Safety and effectiveness of bronchial thermoplasty after 10 years in patients with persistent asthma (BT10+): a follow-up of three randomised controlled trials. *The Lancet Respiratory Medicine*. 2021; 9(5): 457-466. doi: 10.1016/S2213-2600(20)30408-2.
- [22] Goorsenberg AWM, d'Hooghe JNS, Srikanthan K, et al. Bronchial thermoplasty induced airway smooth muscle reduction and clinical response in severe asthma. The TASMA randomized trial. *Am J Respir Crit Care Med*. 2021; 203(2): 175-184. doi: 10.1164/rccm.201911-2298OC.
- [23] Wijsman P, Goorsenberg A, Elzen RVD, et al. Optical coherence tomography detected changes in airway remodeling after bronchial thermoplasty in severe asthma. *Eur Respir J* 2021; 58: Suppl. 65, OA231.
- [24] Hvidtfeldt M, Pulga A, Sverrild A, et al. Mucosal cryobiopsies – a new method for studying airway pathology in asthma. *Eur Respir J* 2021; 58: Suppl. 65, PA849.
- [25] Klooster K, Slebos DJ. Endobronchial valves for the treatment of advanced emphysema. *Chest*. 2021;159(5):1833-1842. doi: 10.1016/j.chest.2020.12.007.
- [26] Lenga P, Grah C, Ruwwe-Glösenkamp C, et al. Outcome of surgical and endoscopic lung volume reduction with valves in patients with severe lung emphysema: preliminary results from the national Lung Emphysema Registry (LE-R) in Germany. *Eur Respir J* 2021; 58: Suppl. 65, OA2635.
- [27] Sciurba FC, Criner GJ, Strange C, et al. Effect of Endobronchial Coils vs Usual Care on Exercise Tolerance in Patients With Severe Emphysema: The RENEW Randomized Clinical Trial. *JAMA* 2016 24-31; 315(20): 2178-89. doi: 10.1001/jama.2016.6261.
- [28] Kontogianni K, Brock J, Trudzinski F, Heussel CP, Herth FJ, Eberhardt R. Evaluation of the Lung Volume Reduction Reverser System (Lvr-r) in treating patients with severe emphysema. Feasibility and safety at 6 months follow up; preliminary results. *Eur Respir J* 2021; 58: Suppl. 65, PA3799.

[29] Holling N, Patole S, Medford ARL, et al. Is systemic anticancer therapy associated with higher rates of malignant pleural effusion control in people with pharmacologically sensitive tumors? *Chest* 2021; 160(5): 1915-1924. doi: 10.1016/j.chest.2021.05.027.

[30] Bhatnagar R, Piotrowska HEG, Laskawiec-Szkonter M, et al. Effect of thoracoscopic talc poudrage vs talc slurry via chest tube on pleurodesis failure rate among patients with malignant pleural effusions: a randomized clinical trial. *JAMA*. 2020;323(1):60.

[31] Bhatnagar R, Keenan EK, Morley AJ, et al. Outpatient talc administration by indwelling pleural catheter for malignant effusion. *N Engl J Med*. 2018; 378(14): 1313-1322. doi: 10.1001/jama.2019.19997.

[32] Reddy C, Ernst A, Lamb C, et al. Rapid pleurodesis for malignant pleural effusions. *Chest* 2011; 139(6): 1419-1423. doi: 10.1378/chest.10-1868.

[33] Boujaoude Z, Bartter T, Abboud M, et al. Pleuroscopic pleurodesis combined with tunneled pleural catheter for management of malignant pleural effusion: a prospective observational study. *Bronchology Interv Pulmonol* 2015; 22(3): 237-43. doi: 10.1097/LBR.0000000000000186.

[34] Psallidas I, Hassan M, Yousuf A, et al. Role of thoracic ultrasonography in pleurodesis pathways for malignant pleural effusions (Simple): an open-label, randomised controlled trial. *Lancet Respir Med* 2022;10(2): 139-148. doi: 10.1016/S2213-2600(21)00353-2.

[35] Foo CT, Pulimood T, Knolle M, Marciniak SJ, Herre J. Day case rapid pleurodesis in malignant pleural effusion. *Eur Respir J* 2021; 58: Suppl. 65, OA 235.

[36] Bedawi E, Rahman N, Yarmus L, Akulian J. A multicentre study evaluating bleeding risk with intrapleural enzyme therapy in pleural infection (Retrolysis). *Eur Respir J* 2021; 58: Suppl. 65, OA239.

[37] Zhang H, Wang M, Zhang W, Ge C, Wang L. Efficacy and safety of position selection combined with intra-pleural thrombin injection in the treatment of postoperative persistent air leakage. *Eur Respir J* 2021; 58: Suppl. 65, OA238.

[38] Finamore P, Okoye C, Bellelli G, et al. Late Breaking Abstract - The prognostic value of computed tomography findings in COVID-19 older patients. *Eur Respir J* 2021; 58: Suppl. 65, OA1663.

- [39] Song F, Shi N, Shan F, et al. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. *Radiology*. 2020; 295(1): 210-7. doi: 10.1148/radiol.2020200274.
- [40] Chung M, Bernheim A, Mei X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology* 2020; 295(1):202-7. doi: 10.1148/radiol.2020200230.
- [41] Tomassetti S, Oggionni T, Barisione E, et al. A Multidisciplinary Multicenter Study Evaluating Risk Factors, Prevalence and Characteristics of Post-COvid-19 Interstitial Lung Syndrome (PCOILS). *Eur Respir J* 2021; 58: Suppl. 65, OA1567
- [42] Nishikiori H, Hirota K, Suzuki T, et al. Validation of the artificial intelligence software to detect chronic fibrosing interstitial lung diseases in chest X-ray. *Eur Respir J* 2021; 58: Suppl. 65, OA1211
- [43] Verleden SE, Tanabe N, McDonough JE, et al. Small airways pathology in idiopathic pulmonary fibrosis: a retrospective cohort study. *Lancet Respir Med* 2020; 8(6): 573-84. doi: 10.1016/S2213-2600(19)30356-X.
- [44] Roberts M, Kirov K, McLellan T, et al. Late Breaking Abstract - Fully automated airway measurement correlates with radiological disease progression in Idiopathic Pulmonary Fibrosis. *Eur Respir J* 2021; 58: Suppl. 65, OA3951
- [45] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; 71(3): 209-49. doi: 10.3322/caac.21660.
- [46] Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011; 365(5): 395-409. doi: 10.1056/NEJMoa1102873.
- [47] de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. *N Engl J Med* 2020; 382(6): 503-13. doi: 10.1056/NEJMoa1911793.
- [48] Moyer VA, Force USPST. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2014; 160(5): 330-8. doi: 10.7326/M13-2771.

[49] Turner M, Smyth L, Taylor N, et al. Proportion of incident lung cancers that would have been eligible for a lung cancer screening program in Australia. *Eur Respir J* 2021; 58: Suppl. 65, PA2177

[50] Force USPST, Krist AH, Davidson KW, et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA* 2021;325(10):962-70. doi: 10.1001/jama.2021.1117.

[51] Audelan B, Lopez S, Fillard P, et al. Validation of lung nodule detection a year before diagnosis in NLST dataset based on a deep learning system. *Eur Respir J* 2021; 58: Suppl. 65, OA4317

[52] Kontogianni K, Moslemi A, Kirby M, et al. COPD and Asthma Differentiation using Quantitative CT Biomarkers by Hybrid Feature Selection and Machine Learning. *Eur Respir J* 2021; 58: Suppl. 65, PA1873

[53] Marshall H, Smith L, Biancardi A, et al. A comparison of ¹²⁹Xe MRI and advanced lung function testing in patients with asthma and /or COPD: The NOVELTY ADPro substudy. *Eur Respir J* 2021; 58: Suppl. 65, PA1872

[54] Pietersen PI, Klap B, Hersch N, Laursen CB, Walsh S, Annema J, Gompelmann D. ERS International Congress 2020: highlights from the Clinical Techniques, Imaging and Endoscopy assembly. *ERJ Open Res.* 2021 May 31;7(2):00118-2021. doi: 10.1183/23120541.00118-2021.

[55] Smargiassi A, Soldati G, Sofia C, et al. Lung ultrasound and high-resolution CT-scan of the chest for COVID-19 pneumonia. *Eur Respir J* 2021; 58: Suppl. 65, PA3542.

[56] Soldati G, Smargiassi A, Inchingolo R et al. Proposal for Interventional Standardization o the Use of Lung Ultrasound for Patients With COVID-19. *Journal of Ultrasound Medicine* 2002; 39: 1413-1319.

[57] Islam N, Ebrahimzadeh S, Salameh JP, et al. Thoracic imaging tests for the diagnosis of COVID-19. *Cochrane Database Syst Rev.* 2021 Mar 16;3(3):CD013639. doi: 10.1002/14651858.

[58] Bielosludtseva K, Fugol K, Krykhtina M, et al. The best predictor of COVID-19 pneumonia progression during lung ultrasound (LUS). *Eur Respir J* 2021; 58: Suppl. 65, PA514.

[59] Falster C, Jacobsen N, Wulff Madsen L, et al.. Lung ultrasound may be a valuable aid in decision making for patients admitted with COVID-19 disease. *Eur Clin Respir J*. 2021 Apr 7;8(1):1909521. doi: 10.1080/20018525.2021.1909521.

[60] Pierrakos C, Lieveid A, Pisani L, et al. Lung ultrasound aeration score for prognostication in invasively ventilated COVID-19 patients: multicenter observational study. *Eur Respir J* 2021; 58: Suppl. 65, OA4345.

[61] Vetrugno L, Guadagnin GM, Barbariol F, Langiano N, Zangrillo A, Bove T. Ultrasound Imaging for Diaphragm Dysfunction: A Narrative Literature Review. *J Cardiothorac Vasc Anesth*. 2019 Sep;33(9):2525-2536. doi: 10.1053/j.jvca.2019.01.003.

[62] Gabrysz-Forget F, Maynard-Paquette AC, Kharat A, et al. Ultrasound diaphragm in cystic fibrosis: a normative study. *Eur Respir J* 2021; 58: Suppl. 65, PA1069.

[63] Kharat A, Girard M, Dube BP. Ultrasound diaphragm activity as a marker of clinical status and prognosis in acute exacerbations of COPD. *Eur Respir J* 2021; 58: Suppl. 65, OA2559.

[64] Psallidas I, Hassan M, Yousuf A, et al. Role of thoracic ultrasonography in pleurodesis pathways for malignant pleural effusions (SIMPLE): an open-label, randomised controlled trial. *Lancet Respir Med*. 2022 Feb;10(2):139-148. doi: 10.1016/S2213-2600(21)00353-2.

[65] Abdelkader AAM, Zidan M, Eshmawey, et al. Study for evaluation of using transthoracic lung ultrasound in diagnosis of pulmonary embolism. *Eur Respir J* 2021; 58: Suppl. 65, PA3546.

[66] Falster C, Jacobsen N, Coman KE, Højlund M, Gaist TA, Posth S, Møller JE, Brabrand M, Laursen CB. Diagnostic accuracy of focused deep venous, lung, cardiac and multiorgan ultrasound in suspected pulmonary embolism: a systematic review and meta-analysis. *Thorax*. 2021 Sep 8:thoraxjnl-2021-216838. doi: 10.1136/thoraxjnl-2021-216838.

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