




ERS International Congress, Madrid, 2019: highlights from the Clinical Techniques, Imaging and Endoscopy Assembly

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ABSTRACT This manuscript summarises the highlights from Assembly 14, “Clinical techniques, imaging and endoscopy”, which were presented at the 2019 European Respiratory Society (ERS) International Congress in Madrid, Spain. Novel diagnostic approaches and innovative therapeutic strategies in patients with lung cancer, interstitial lung disease, obstructive airway disorders and infectious diseases are discussed. The authors from the different Assembly 14 subgroups focus on the key take-home messages given new study results, and place them in the context of current knowledge in these areas.

At the 2019 ERS International Congress, encouraging results of numerous trials in the field of interventional pulmonology, imaging and ultrasound were presented. Key topics included novel diagnostic and therapeutic approaches in patients with lung cancer, interstitial lung disease, obstructive airway disorders and infectious diseases.



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This article summarises some of the developments in interventional pulmonology, imaging techniques and ultrasound presented at the 2019 #ERSCongress. Key topics included novel diagnostic and therapeutic approaches in various lung diseases. <https://bit.ly/2XYF6Fn>

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Group 14.01: Interventional Pulmonology

Lung cancer

One of the biggest challenges that interventional pulmonologists face is how to safely diagnose small, peripheral lung nodules. The number of patients with peripheral pulmonary nodules (PPNs) that require tissue confirmation is rapidly increasing with the use of computerised chest tomography (CT) and the implementation of lung cancer screening programmes. Navigation to the target lesion is key. At the ERS International Congress, several different methods to reach PPNs were presented.

One novel technique to sample peripheral nodules is bronchoscopic transparenchymal nodule access (BTPNA) where, at the chosen point of entry, a hole is created in the central airway, then dilated to create a new transbronchial pathway to reach a lung nodule [1]. To identify the point of entry, virtual navigation bronchoscopy (VNB) is used to create a 3D reconstruction of the airways, aligning it with the bronchoscopic image and suggesting the path to follow to reach the target peripheral lesion or the point of entry prior to BTPNA [2]. In a multicentre study, 106 patients underwent VNB or BTPNA or combined methods to obtain biopsy samples [3]. Results showed that the combination of VNB and BTPNA provides safe and effective access to the PPNs in the lungs. However, the data related to BTPNA are still very limited and further prospective trials are required to evaluate the safety and efficacy of this approach.

Another approach to PPNs is the use of radial endobronchial ultrasound probes (r-EBUS), which provide 360° ultrasound images in the peripheral airways. When introducing the EBUS probe into a peripheral lesion, the snowstorm-like whitish ultrasound image is replaced by a solid mass indicating the location of the lesion. Another navigation system is electromagnetic navigation bronchoscopy (ENB), which combines virtual bronchoscopy imaging with an electromagnetic field and a locatable guide to reach the PPN. ENB has been shown to be a promising bronchoscopy tool for accessing PPNs; however, the overall diagnostic yield remains ~70%, and is even lower in lesions <2 cm [4]. At the ERS International Congress, a study was presented that considered whether cone beam CT (CBCT) guidance with live 3D fluoroscopic navigation could be of added value in combination with ENB and r-EBUS. The procedure started with ENB and r-EBUS navigation alone, after which verification of navigation accuracy was performed using CBCT imaging. If CBCT imaging showed an inaccurate position of the catheter, subsequent repositioning and consecutive navigation was performed using CBCT guidance and live 3D lesion and pathway augmentation on fluoroscopy. The results demonstrated that a small repositioning with CBCT was needed to obtain 58% navigation success for nodules with a mean nodule size of 11.5 mm. When combined with live 3D CBCT, this resulted in navigation success of 88% [5]. This trial demonstrates that CBCT may be helpful as a guiding tool to reach small lung nodules. However, the availability of CBCT in most institutions is limited and therefore it remains questionable whether this approach will be widely used.

Another important topic discussed at the ERS International Congress 2019 was the use of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), which increasingly represents the first-line approach for mediastinal staging in lung cancer patients [6]. There is a lot of discussion about the needle size and its relation to diagnostic yield. A randomised study in 500 subjects found no significant difference between the 19G and 21G needles in a final diagnosis of benign, malignant and non-diagnostic samples ($p=0.928$). The sensitivity was 77% and specificity was 100% for both needles. Both needles were safe with complication rates of 3.2% (19G) and 3.6% (21G) [7]. A new, even smaller histological 25G core needle was evaluated in a small group of patients ($n=20$), which showed no complications and a sensitivity, specificity and positive predictive value of 90%, 100% and 100%, respectively [8]. Summarising these trials, it seems that the needle size seems to play a less important role in the diagnostic yield of EBUS-TBNA. Combining EBUS-TBNA with elastography images can provide additional information about the lymph nodes. When comparing EBUS-elastography ($n=215$) with EBUS ($n=285$), EBUS-elastography showed a lower number of non-diagnostic samples (1.9% *versus* 18%; $p=0.001$) and a higher rate of malignant results (54% *versus* 12%; $p=0.005$). Using EBUS-elastography, lymph nodes with a blue pattern had the probability of malignant infiltration of 92% ($p=0.004$). Furthermore, malignant lymph nodes presented with less colour dispersion, a higher ratio of blue pixels and a higher strain ratio [9].

The performance of EBUS-TBNA is also crucial for the diagnosis of centrally located lung tumours without endobronchial abnormalities [10, 11]. In one international multicentre analysis presented at the congress, the feasibility and diagnostic yield of EBUS-TBNA for centrally located intrapulmonary tumours were retrospectively evaluated. In 159 patients with centrally located tumours, EBUS-TBNA's feasibility to sample the intrapulmonary lesion was found to be 91%. The diagnostic yield was 86% and mutational analysis was successful in 86% of cases [12]. This trial confirms the satisfying results of earlier studies that evaluated the efficacy of EBUS-TBNA for the diagnosis of centrally located tumours [10], but also demonstrates that these EBUS-TBNA samples are mostly suitable for molecular analysis.

Take-home messages

- Transparenchymal nodule access may present another method to diagnose peripheral pulmonary lesions.
- EBUS-TBNA plays a crucial role in the diagnosis and staging of lung cancer. It is the gold standard in mediastinal staging, where the diagnostic yield is independent of needle size. Furthermore, EBUS-TBNA plays an important role in the diagnosis of centrally located tumours.

Obstructive airway diseases

In the last decade, several bronchoscopic treatments have been evaluated for patients suffering from severe COPD and asthma. Careful patient selection with the aim of delivering personalised treatment with a high probability of success is a priority.

COPD and emphysema

In selected COPD patients, endoscopic valve therapy is an established treatment that significantly reduces hyperinflation resulting in clinical improvement [13].

Patients presenting with complete fissures and thus, an absence of collateral ventilation are most likely to benefit. At the ERS International Congress, multiple studies investigated patient and target lobe selection for valve therapy to increase treatment success and prevent inappropriate treatments. Comparing quantitative CT fissure analysis with invasive catheter-based Chartis (Pulmonx Inc., Redwood City, CA, USA) measurement showed an additional benefit with use of the Chartis procedure [14]. For the left major fissure, a fissure completeness of >95% on CT had a positive predictive value of 91%, whereas a fissure completeness \leq 83% had a sensitivity of 100%. For the right major fissure, a fissure completeness of >95% had a 74% positive predictive value, with a sensitivity of 100% when the fissure completeness was \leq 90%. The results of this trial support the clinical decision on which fissure integrity an additional Chartis measurement is appropriate.

Another trial focused on identifying the best target lobe for valve placement by using the lower lobar ventilation (V') and perfusion (Q') quantification to select the target lobe [15]. This was associated with larger improvements in pulmonary function tests (PFTs) compared with a planar V'/Q' scan, which is reliant upon fissures analysed on CT. The authors also found a significantly improved V'/Q' quantitation of the contralateral non-targeted upper lobe that was positively associated with improved forced expiratory volume in 1 s (FEV_1), though the exact mechanism of this is unclear.

Another technique to potentially improve identification of the optimal lobar target for valve implantation may be endoscopic measurement of the lobar oxygen uptake [16]. In 21 patients, it was shown to be feasible to perform 49 measurements using a customised gas measurement set-up after lobar balloon occlusion. A slower decrease in oxygen uptake was significantly correlated with a higher lobar destruction score and was linked with lower arterial and venous vascular volume within the target lobes. This proves what can be expected from a pathophysiological point of view. However, it still remains unclear whether routine measurement of oxygen uptake will facilitate patient selection or whether CT, which reflects the highest lobar destruction score, is sufficient. Another therapeutic approach to reduce hyperinflation in emphysema patients is bronchoscopic thermal vapour ablation (BTVA). A randomised controlled trial, the STEP-UP (Sequential Segmental Treatment of Emphysema with Upper Lobe Predominance) trial, has already demonstrated the efficacy of this novel approach, which induces an inflammatory reaction in the most emphysematous, destroyed lung segments, thus reducing hyperinflation [17]. A multicentre BTVA post-market registry study presented at the ERS International Congress 2019 showed similar safety data for BTVA compared with the safety profile seen in the STEP-UP trial [18]. COPD exacerbations and pneumonia were the most frequently reported adverse events.

A different mechanism of action in the treatment of COPD is to stop cholinergic hyperactivity. Targeted lung denervation (TLD), a novel endoscopic treatment, aims to target cholinergic hyperactivity by disrupting the parasympathetic pulmonary nerves. A double-blind, randomised, sham-controlled study, AIRFLOW-2, was performed in 82 moderate-to-severe COPD patients to look at 1-year safety data [19]. TLD demonstrated a significantly lower rate of severe COPD exacerbations (TLD 12% versus sham 32%; $p=0.039$) and respiratory serious adverse events (TLD 15% versus sham 37%; $p=0.042$). Furthermore, the TLD arm had a lower rate of re-hospitalisation (TLD 20% versus sham 70%; $p=0.069$). The results of this randomised sham-controlled trial suggest that in future there may be an endoscopic approach for patients with a predominant obstructive ventilatory disorder but only slight-to-moderate hyperinflation.

The mechanism of action of TLD was further investigated in a sub-study of AIRFLOW-2 [20]. The hypothesis was that by disrupting the pulmonary nerves, neuronal acetylcholine release would be decreased with subsequent reduction in airway inflammation. Surprisingly, in AIRFLOW-2, predefined inflammatory markers were unchanged. However, when the group looked at changes in gene expression on bronchial epithelial brushes taken 3 months after both procedures, TLD-treated patients had evidence of altered gene expression that signals reduction in airways inflammation.

Chronic bronchitis

A novel treatment for chronic bronchitis is metered cryospray (MCS) to treat airway metaplasia and excessive mucus secretion in chronic bronchitis. Delivering liquid dinitrogen to the airways aims to ablate abnormal epithelium, reduce chronic airway inflammation and promote regeneration of a healthy mucosal lining. In a prospective, single-arm safety and feasibility study in 35 patients with COPD (Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages II–III) and mucus overproduction, MCS was associated with clinically significant improvements in health-related quality of life and 6-min walk distance (by 28 m) 9 months after treatment [21]. This result is encouraging; further studies should be performed to evaluate the safety and efficacy of MCS.

Asthma

Bronchial thermoplasty (BT) is a bronchoscopic treatment for severe uncontrolled asthma. BT targets airway remodelling using radiofrequency energy. Early studies showed that BT reduces exacerbations and improves Asthma Quality of Life Questionnaire (AQLQ) scores [22]. The BT Global Registry collects data on subjects treated with BT in a prospective, multicentre study [23]. This real-world study demonstrates sustained improvement in clinical outcomes and a reduction in asthma medication usage 2 years after BT in 157 subjects. That BT significantly reduces the airway smooth muscle (ASM) has been shown in early, relatively small uncontrolled studies and was confirmed by the results of the randomised controlled TASMA (Targets of Bronchial Thermoplasty in Severe Asthma) trial presented at the ERS International Congress 2019, which showed a reduction from 10% before BT to 4.6% after BT ($p=0.01$) in 27 patients [24]. To create a bigger sample size to investigate airway remodelling responses to BT, data were pooled for 99 patients from seven centres [25]. Again, a reduction in ASM mass in 99 patients occurred 6 weeks after BT (16% before BT to 4.4% after BT; $p\leq 0.0001$). The reticular basement membrane thickness reduced within 6 weeks (6.8 μm before BT to 5.8 μm after BT; $p=0.024$). These effects persisted beyond 1 year after treatment. However, the observed improvements in airway remodelling parameters did not translate to improvements in clinical outcomes (exacerbation rate, AQLQ and lung function).

Take-home messages

- Endoscopic lung volume reduction is an established treatment. Current studies focus on precise patient selection. Additional Chartis measurement, a decrease of lobar oxygen uptake or attention to lobar perfusion are some of the predictors to be investigated.
- TLD may be an endoscopic approach for patients with a predominant obstructive ventilatory disorder but only slight-to-moderate hyperinflation.
- MCS may be a novel endoscopic treatment that reduces hypersecretion in patients with chronic bronchitis. Further studies are warranted.

Tuberculosis

The diagnosis of tuberculosis (TB) is challenging and often requires multiple, time-consuming tests with subsequent costs. Pleural TB is one of the most frequent causes of pleural exudates. In patients with exudative pleural effusion and normal lung parenchyma with suspected pleural TB, thoracoscopic pleural biopsy is advised. One trial presented at the ERS International Congress 2019 investigated the use of the new Xpert MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) on thoracoscopic pleural biopsies [26]. In this study, 134 out of 198 patients who underwent thoracoscopic pleural biopsy were diagnosed with TB. The sensitivity of the Xpert MTB/RIF assay was higher compared with biopsy culture (52.2% versus 41%) and had the same specificity (100%). In addition, the Xpert MTB/RIF assay also provides the status of drug resistance, suggesting the potential value of this new technique in the diagnosis and management of pleural TB. Although this trial demonstrates the utility of the Xpert MTB/RIF assay on thoracoscopic pleural biopsies, we would recommend using this assay in addition to biopsy culture, as the culture provides testing for all drug resistances.

Similarly, EBUS-TBNA combined with Xpert MTB/RIF assay was shown to have a positive result in 42 (75%) out of 56 patients compared with TB culture (52%) [27]. Nevertheless, it remains important to send

specimens for culture as well to diagnose other drugs' resistance and detect rifampicin resistance missed by the Xpert MTB/RIF assay.

Take-home message

- The use of the Xpert MTB/RIF on thoracoscopic pleural biopsies or on EBUS-TBNA specimens has an additional value in the diagnosis of TB.

Bronchial fistula

Bronchial fistula (BF) after pneumonectomy is a serious complication, associated with high mortality. Diagnostic methods to gain information about the size of the BF prior to the placement of an occluder is needed for successful treatment. Novel BF diagnostic methods and treatments were discussed at the ERS International Congress 2019.

In one trial, eight out of 13 patients with a BF following pneumonectomy underwent a BF measurement using a sizing balloon under fluoroscopy, with subsequent successful occluder installation [28]. In the remaining five patients, where BF size was measured with fibrobronchoscopy and CT scans, the occluders chosen needed re-instillation. This suggests that BF measurement with a sizing balloon might be the recommended technique. Although this study result is encouraging, we would like to point out that measurement with a balloon can be quite subjective and there is also the risk of fistula enlargement. Therefore, further studies would be desirable. Bronchopleural fistula (BPF) presents another management challenge. Selective bronchography can provide information about the presence and number of BPF. When retrospectively compared with CT in 27 patients, selective bronchography demonstrated BPF in 81.5% versus 55.5% on CT [29]. For BPF management, ventricular septal defect occluders can be used safely and successfully [30].

Take-home message

- Selective bronchography provides to identify BPF.

Interstitial lung diseases

Transbronchial cryobiopsy (TBCB) for the diagnosis of interstitial lung diseases (ILDs) was again a key topic at the ERS International congress 2019. TBCB is a promising alternative to surgical biopsy and has the advantage of acquiring larger alveolar tissue samples of a higher quality compared with traditional forceps biopsies. Recently, an Australian accuracy study, the COLDICE (Cryobiopsy versus Open Lung biopsy in the Diagnosis of Interstitial Lung disease allianCE) trial) showed high levels of diagnostic agreement between TBCB and surgical lung biopsy (histopathological agreement was 70.8%; diagnostic agreement at multidisciplinary discussion was 76.9%) [31]. The TBCB expert statement suggested a standardised approach for bronchoscopic TBCB and encouraged the need for further randomised studies concerning diagnostic yield, safety and technical aspects [32].

A large study involving 278 patients with ILD investigated the prognostic significance of a multidisciplinary diagnosis of idiopathic pulmonary fibrosis (IPF) versus non-IPF obtained with cryobiopsy [33]. In patients without a typical usual interstitial pneumonia (UIP) pattern on high-resolution CT (HRCT), cryobiopsy was informative in 83% (IPF in 43%, non-IPF in 52%). Results demonstrated a significant prognostic separation between multidisciplinary IPF diagnosis and non-IPF similar to the pathological distinction between UIP and non-UIP cases. This supports the meaningfulness of cryobiopsies in patients with ILD.

To simplify the procedural aspects of TBCB, a prospective study with 84 patients was conducted performing radial EBUS to guide biopsy under conscious sedation without intubation [34]. This was found to be safe and efficient with a diagnostic yield of 79.8%. However, we still recommend to use either an endotracheal tube or a rigid bronchoscope, so that TBCB is performed safely.

One concern in ILD patients is possible concomitant pulmonary hypertension (PH), which may increase the bleeding risk when performing cryobiopsy. It is known that PH with a pulmonary artery systolic pressure (PASP) >40 mmHg is a relative contraindication for TBCB due to risk of bleeding and worsening of hypoxaemia. When retrospectively reviewed, 23 out of 150 ILD patients undergoing cryobiopsy were identified as having PH (PASP >40 mmHg) [35]. These patients were pre-optimised and cryobiopsy only performed with a PASP <45 mmHg under general anaesthesia. Compared to patients with PAPS <40 mmHg, there was no significant difference in complications such as bleeding, pneumothorax, worsening

hypoxaemia and mortality. Another relative contraindication is a forced vital capacity (FVC) <50% predicted. In a retrospective study including 151 subjects, a higher risk of pneumothorax (27.9 *versus* 14.4%; $p < 0.05$) was found in patients with a FVC <50%. The risk of bleeding and mortality was no different [36]. This result demonstrates that cryobiopsy in patients with significantly reduced lung function should still be performed with caution after weighing the benefit–risk profile in experienced centres.

Take-home messages

- TBCB is a valuable diagnostic tool for patients with ILD.
- A standardised approach for bronchoscopic TBCB is crucial to reduce risks and complications. Cryobiopsy should only be performed with caution after weighing the benefit–risk profile, particularly in ILD patients with significant reduced lung function or PH.

Group 14.02: Imaging

ILDs

Multiple papers relating to updates on IPF imaging were presented at the ERS International Congress 2019.

Magnetic resonance imaging (MRI) has been emerging as an imaging method to assess ILDs. One of the trials presented compared lung T1 weight sequences in patients with IPF and healthy volunteers acquired during inspiration, expiration and tidal breathing. Results revealed that free breathing lung MRI can visualise the changes in both regional and global lung T1 signals, which might offer a radiation-free assessment of lung scarring [37]. In this trial, the number of patients and healthy subjects was still very low ($n=26$), so that further trials are needed that evaluate the usefulness of MRI in ILD patients.

More specifically, previous studies have shown that hyperpolarised gas diffusion-weighted (DW) MRI provides a noninvasive, quantitative assessment of microstructural acinar changes in the lung [38]. However, the utility of 129-xenon diffusion imaging has not been studied previously in ILDs; it was evaluated in a prospective, multicentre trial for the first time and presented at the congress. In the study, diffusion restriction quantified by an apparent diffusion coefficient (ADC) provided information about lung microstructure down to the alveolar level, which was then correlated with diffusing capacity of the lung for carbon monoxide, transfer coefficient of the lung for carbon monoxide and CT fibrosis score on hyperpolarised helium DW [39]. The authors demonstrated that ADC correlates with the diffusion capacity; furthermore, the 129Xe DW-MRI could potentially differentiate changes in the airway microstructure in ILD subtypes. Findings on hyperpolarised 129-Xe MR spectroscopy were also presented, where the ratio of 129-Xe uptake in the red blood cells compared with tissue/plasma was shown to be a more sensitive marker for the longitudinal change in IPF and hypersensitivity pneumonitis patients compared with PFTs [40].

To highlight an interesting lecture: a randomised, double-blind, placebo-controlled positron emission tomography (PET) imaging study confirmed target engagement in the lungs of patients with IPF following a single dose of a novel inhaled $\alpha v \beta 6$ integrin inhibitor, an attractive therapeutic target for IPF, which works by modulating the fibrogenic mechanisms in mouse and human lung cells and tissue. Higher levels of $\alpha v \beta 6$ were seen in IPF compared with healthy subjects, where PET was used to demonstrate the target engagement in the lung, which corresponded to fibrotic areas seen on HRCT [41]. This is a promising study result, as it is the first time a target-specific radioligand has been used to assess target engagement in the lung.

Take-home message

- Hyperpolarised gas DW MRI may play a role in ILD, as it potentially differentiates changes in the airway microstructure in ILD subtypes and provides a sensitive marker for the longitudinal change in IPF.

PH

Cardiac MRI (cMRI) metrics are proposed end-points for pulmonary arterial hypertension (PAH) trials. At the congress, the results of the RESPIRE Study were presented, assessing the repeatability and sensitivity to change of right ventricle (RV) analysis methods using cMRI in PAH. In the trial, 44 PAH patients (27 of whom underwent initiation or escalation of therapy) received cMRI at baseline and then two cMRIs within 24 h at 6-month follow-up. Interobserver, intraobserver and interscan repeatability were assessed and found to be excellent. The RV end-systolic volume (RVESV) and RV ejection fraction (RVEF) were sensitive markers of the change of metrics with PAH therapy [42]. RVESV decreased and RVEF increased significantly following initiation or escalation of therapy. This study demonstrated that cMRI metrics may be used to control and guide therapy in PAH patients.

Besides MRI, the role of CT pulmonary angiography (CTPA)-derived right atrial area was emphasised. It is known that right atrial dilatation is associated with tricuspid valve regurgitation, which is a significant predictor of long-term mortality in PAH [43]. One trial from the UK reported that use of a simple CTPA-derived right atrial area measurement correlated well with mean right atrial pressure and can risk stratify patients with PAH [44]. Further studies are warranted to identify optimal CT prognostic thresholds.

Take-home messages

- MRI metrics (RVESV and RVEF) can be used to control and guide therapy in PAH patients.
- CTPA-derived right atrial area correlated well with mean right atrial pressure and thus can risk stratify patients with PAH.

Obstructive sleep apnoea

CT-derived right-to-left ventricular diameter measurement is a parameter that is used in patients with acute pulmonary embolism to identify those at high risk. New insights on this topic include the findings of a German group, which reported that RV dysfunction might be underestimated in severe obstructive sleep apnoea (OSA) when being evaluated by the RV/left ventricle (LV) diameter ratio assessment on CTPA [45]. In the trial, 197 patients with acute pulmonary embolism underwent CTPA to assess RV dysfunction by calculating the RV/LV diameter ratio. RV dilatation was significantly more frequent in OSA patients compared with subjects with an apnoea-hypopnea index of $<5\text{-h}^{-1}$. Furthermore, it could be observed that left-sided congestive heart failure (CHF) and signs of acute myocardial injury were significantly more frequent in patients with severe OSA. Thus, importantly, LV dilatation due to coexisting CHF in severe OSA might prevent the RV/LV diameter ratio being >1 even in the presence of clinically relevant RV enlargement.

Take-home message

- CTPA can be used to assess RV dysfunction by calculating the RV/LV diameter ratio in patients with pulmonary embolism. However, it is important to note that in patients with coexisting CHF, CTPA can underestimate an acute right heart dysfunction.

Obstructive airway disease and emphysema

CT is an established diagnostic technique to assess the presence, pattern and extent of emphysema. Besides visual assessment, various software platforms are available that provide emphysema quantification by densitometry. A Swedish pilot study reported that visual CT assessment of emphysema is reliable with a satisfactory inter- and intraobserver variability (Krippendorff alpha values ranging 0.80–0.85) [46]. However, when defining emphysema as an LAV950 (% low attenuation value below 950 Hounsfield Units) of $\geq 10\%$, a matched paired case-control study with 100 emphysema patients and 100 healthy controls, found the sensitivity of detecting emphysema to be only 27%. Thus, the quantitative measurement of LAV950 *via* the software used in this study was not able to distinguish between patients with or without visually detected mild emphysema [46]. Large-scale studies are needed to evaluate other quantitative emphysema analysis methods with different LAV thresholds and emphysema indices.

Besides quantitative emphysema analysis, CT allows evaluation of airway abnormalities that represent key pathophysiological features in COPD patients. One of the most interesting CT imaging-based modelling studies proved that there are fewer and smaller airways throughout each of the five lobes in COPD subjects compared with controls. This reduction in airways started relatively proximally in generation 5 airways. The reason for this finding remains unclear but may indicate an abnormal remodelling process in the larger airways [47]. These radiological trials allow characterisation of airway abnormalities and assist in our understanding about the pathophysiological processes in COPD and emphysema patients.

Another focus of research is COPD phenotyping, where CT imaging again plays an important role. Alveolar dimensions of quantitative emphysema subtypes (QES) were correlated with an ADC derived from hyperpolarised helium MRI in smokers with COPD and healthy subjects. Apical, diffuse, senile and vanishing lung QES were associated with a rise in mean ADC, suggesting an increase in mean alveolar volume compared with non-emphysematous lung, with particularly large escalations in the apical and vanishing lung QES. This novel QES approach may facilitate personalisation in COPD [48].

One limitation of CT in emphysema patients is its inability to provide functional information. To overcome this limitation, one study evaluated a CT-based full-scale airway network (FAN) flow model, which assesses ventilation in COPD patients [49]. Thereafter, pulmonary tissue density information was extracted from the CT and, in combination with PFT results, was used for patient-specific modelling. Afterwards, the ventilation

calculated in the FAN model was compared with the PFT data and the ventilation hyperpolarised Xenon-129 MRI and ventilation single-photon emission CT imaging. The results of this study revealed that the CT-based FAN model is able to provide ventilation images comparable with other functional imaging techniques.

Take-home message

- Quantitative and qualitative CT are increasingly taking a prominent role in the diagnostic process of emphysema and airway remodelling in COPD patients.

Bronchiectasis

The authors of one study developed a novel quantitative bronchiectasis scoring technique for CT (BEST-CT), which assessed the sensitivity of CT features in quantifying lung disease in bronchiectasis patients [50]. The scoring techniques include various parameters obtained by volumetric CT scans of patients with bronchiectasis and chronic *Pseudomonas* infection: consolidation/atelectasis, bronchiectasis with mucus plugging, bronchiectasis without mucus plugging, airway wall thickening, mucus plugging, ground-glass opacities (GGO), emphysema/bullae, healthy airways and healthy parenchyma. This novel quantitative bronchiectasis scoring technique might be helpful for phenotyping and to measure outcomes in clinical trials in patients with bronchiectasis.

Take-home message

- A quantitative BEST-CT supports phenotyping of patients with bronchiectasis.

Acute respiratory failure

A Dutch paper showed for the first time that confocal laser endomicroscopy (CLE) in patients with acute respiratory failure can be used to study the alveolar compartment for various causes of respiratory failure in mechanically ventilated patients [51]. The authors concluded that CLE imaging has the potential to distinguish between important causes of respiratory failure in critically ill patients in the intensive care unit.

Take-home message

- CLE may help identify the cause of the acute respiratory failure in critically ill patients.

Group 14.03: Ultrasound

ILDs

Technical developments have made ultrasound available in many institutions. As a result, researchers have and will continue to expand its use as a tool for diagnosis and disease monitoring. In one trial presented at the ERS International Congress 2019, sonographic patterns in IPF patients were correlated with peripheral fibrotic changes on HRCT, and another trial investigated whether ultrasound could be used to predict severity of IPF by using a 12-zone protocol [52, 53]. Both studies were small, with 16 and 31 patients, respectively, but concludes that sonographic patterns are positively correlated with HRCT; however, thoracic ultrasound could be misleading in cases with concomitant GGO and large cystic honeycomb. Ultrasound may not only be an important tool in the diagnosis and monitoring of ILD but may also be a valuable method for detecting complications following cryobiopsy in ILD patients. One study assessed the diagnostic accuracy of post-procedure ultrasound for diagnosing pneumothorax in ILD patients after TBCB [54]; the authors found a low sensitivity (20%, 95% CI 2.52–55.6%) compared to the literature [55], but a high specificity (100%, 95% CI 95–100). In this setting, ultrasound can identify patients in need of immediate treatment for pneumothorax but fails to identify many patients who develop pneumothorax later on post-procedure.

Take-home message

- Transthoracic ultrasound may present an additional tool in the diagnosis of ILD as the sonographic pattern correlates with fibrotic changes in CT.

Pneumonia

Thoracic ultrasound for the assessment of pneumonia has been explored for years. It is said to overcome many of the challenges and disadvantages of using conventional chest radiography or thoracic CT, e.g.

exposure to radiation, inter-rater reliability, and low image quality because of insufficient inspiration or supine one-image radiography. Ultrasound has been proven to have a high sensitivity, specificity and diagnostic accuracy for pneumonia in adults [56–58]. Evidence has been more sparse in the paediatric population. Three studies were presented on this topic at the ERS International Congress 2019.

One trial explored the prognostic role of air bronchograms (static, dynamic, and both static and dynamic in consolidated lung tissue) in the management of children admitted with pneumonia [59]. The authors adopted a grading system called the USINCHILD score. They found that in children with proven community-acquired pneumonia, a difference in USINCHILD score of <1 point within the first 48 h was associated with an increased risk of complicated pneumonia and longer hospitalisation.

In another trial, the authors hypothesised that thoracic ultrasound in children admitted with signs of acute bronchiolitis could predict the need for oxygen therapy [60]. The authors found a statistically significant difference between the ultrasound scores of the group that needed supplementary oxygen therapy and the group that did not need supplementary oxygen therapy.

SOUZA *et al.* [61] assessed the inter-operator agreement in thoracic ultrasound for pneumonia in children and achieved very important results. In the study, a novice and an experienced ultrasound operator scanned 23 children with suspected pneumonia. The results showed substantial inter-operator agreement for normal sonographic patterns and lung consolidation ($K=0.615$ and $K=0.635$, respectively), only moderate agreement for B-lines ($K=0.573$) but almost perfect agreement for pleural effusion ($K=0.868$). The authors concluded that even if scans are performed by operators with very different levels of experience, thoracic ultrasound has a high sensitivity, especially for consolidated lung tissue and pleural effusion.

Take-home message

- Ultrasound has a high sensitivity, specificity and diagnostic accuracy for pneumonia in adults. A number of trials have confirmed the usefulness of ultrasound in children with pneumonia. This is of value as the performance of ultrasound is superior to a chest radiography in children; moreover, radiation exposure is avoided.

Diaphragmatic dysfunction

One major topic was covered in several studies: assessment of the diaphragm, diaphragmatic function or correlation between diaphragm and peripheral muscle thickness. The diaphragm plays a major role in ventilation as the most important respiratory muscle. Because of this, research to assess its function in chronic, acute and critically ill patients still remains a hot topic.

Lower lung volume due to pleural effusion is not the only factor that causes dyspnoea, as only a very small increase in lung function is seen after thoracentesis. One trial presented on the ERS International Congress 2019 evaluated diaphragm function prior to and following thoracentesis in order to explore movement of the diaphragm in dyspnoeic patients with pleural effusion [62]. A midaxillary scan position in conventional B-mode (instead of M-mode, which is most often used for measuring diaphragm function) showed a significant increase in movement after thoracentesis to a level corresponding to the healthy side.

COPD patients are said to have reduced diaphragmatic movement. One of the studies presented at the congress explored whether it was possible to discriminate between severity in COPD patients (stage I–II and III–IV) by assessing the diaphragm with ultrasound in a stable period without respiratory distress [63]. A statistically significant difference in thickness between the groups during both inspiration and expiration was found, and both measurements correlated with the FEV_1/FVC ratio. The receiver operating characteristic curve on inspiratory measurement proved that a cut-off-point of 2.63 mm resulted in a sensitivity of 71.4% and a specificity of 100%. The authors concluded that ultrasound of the diaphragm could be used to assess severity in certain COPD subtypes, but also acknowledged that other already published studies did not demonstrate a link between COPD severity and diaphragm thickness and movement [64]. This hypothesis needs to be further explored.

Whereas in this trial COPD patients in a stable period were assessed, THABET *et al.* [65] assessed the correlation between diaphragmatic and peripheral muscle thickness in mechanically ventilated COPD patients. They measured the thickness of the diaphragm and two peripheral muscles on alternate days during mechanical ventilation until the end of mechanical ventilation and found that the change in diaphragmatic thickness differed significantly from changes in peripheral muscle thickness. They concluded that measuring peripheral muscles cannot predict changes in diaphragmatic thickness; however,

as a secondary outcome, they found that an early decrease in diaphragmatic thickness may be a sign of an extended hospital stay.

Take-home message

- Sonographic assessment of diaphragmatic function and muscle thickness may be useful to assess severity of COPD. However, the results of various trials are controversial, so further studies are needed.

Peripheral lung lesions

Ultrasound-guided transthoracic biopsies are also gaining substantial attention because the risk of pneumothorax is lower than CT-guided biopsies in peripheral lesions [66, 67]. Additionally, it is a procedure that can be performed by sufficiently trained pulmonologists, which minimises transfer of patients from one department or institution to another. A first prospective nationwide (French) study evaluated the diagnostic yield and complication rate after ultrasound-guided transthoracic lung biopsies performed by pulmonologists [68]. The results of this trial confirmed the work of previously published studies, [69] noting a high diagnostic yield (85.5%) and an acceptable complication rate (15%). The mean procedure time was short at 18.7 min, and the mean pain score was low (1.5 out of 10 on a numerical rating pain scale).

Take-home message

- Ultrasound-guided transthoracic biopsies for diagnosis of peripheral lung lesions have a high diagnostic yield and an acceptable complication rate.

Concluding remarks

This article summarises only some of the many exciting developments in interventional pulmonology, imaging techniques and ultrasound that were presented at the ERS International Congress 2019. The congress was the first to present in this new format, with its three independent Groups. This new Assembly is strongly committed to providing ERS members with high-quality activities during the congress. In order to do so, member input and feedback is highly desired. We encourage readers to participate in the forthcoming ERS International Congress and to follow-up on their personal topics of interest.

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