ERS International Congress 2022: highlights from the Thoracic Oncology Assembly

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The annual #ERSCongress 2022 highlighted all recent advances in thoracic oncology, from lung cancer prevention to advanced-stage treatment. This article provides an overview of the thoracic oncology highlights presented. https://bit.ly/43oRrTS

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Abstract

Thoracic malignancies are associated with a substantial public health burden. Lung cancer is the leading cause of cancer-related mortality worldwide, with significant impact on patients' quality of life. Following 2 years of virtual European Respiratory Society (ERS) Congresses due to the COVID-19 pandemic, the 2022 hybrid ERS Congress in Barcelona, Spain allowed peers from all over the world to meet again and present their work. Thoracic oncology experts presented best practices and latest developments in lung cancer screening, lung cancer diagnosis and management. Early lung cancer diagnosis, subsequent pros and cons of aggressive management, identification and management of systemic treatments' side-effects, and the application of artificial intelligence and biomarkers across all aspects of the thoracic oncology pathway were among the areas that triggered specific interest and will be summarised here.

Introduction

Thoracic oncology has noted numerous exciting advances over the past few years, following a previous period of slower progress. In non-small cell lung cancer (NSCLC), the use of immunotherapy and targeted therapies has been ambitiously extended from metastatic disease to early and locally advanced stages. In small cell lung cancer (SCLC) and mesothelioma, the introduction of immunotherapy has demonstrated improved overall survival. Novel radiotherapy techniques have also revolutionised treatment options in lung cancer with more accurate targeting and minimal side-effects. Minimal invasive thoracic surgery has gained grounds with the use of video-assisted thoracic surgery (VATS) and most recently robotic-assisted thoracic surgery, with a view to reducing hospital stay and post-operative complications and improving clinical outcomes. Over the last years, particular emphasis has been given to early lung cancer detection, lung cancer screening (LCS) and management of screening findings. Low-dose chest computed tomography (LDCT) in high-risk populations is a novel early diagnostic tool to ensure lung cancer diagnosis shifts to an earlier stage where radical treatment is feasible. Artificial intelligence (AI) underpins all the recent advances and appears to have a promising role in standardisation, quality improvement and clinical time management.

The European Respiratory Society (ERS) International Congress 2022 highlighted all recent advances in thoracic oncology, from lung cancer prevention to advanced-stage treatment. All 19 scientific sessions in thoracic oncology (including symposia, state of the art, pro–con debates, hot topics, oral and thematic poster sessions, and workshops) were well attended. They provided a clear overview of the current state and, through meaningful panel and audience engagement in discussions, they identified future research needs to optimise thoracic oncology patient care.

In this article, we will provide an overview of the thoracic oncology highlights presented at the ERS International Congress 2022.

ERS guideline on various aspects of quality in lung cancer care

This ERS guideline was presented in the 2022 ERS Congress and was dedicated to the provision of good quality recommendations in lung cancer care [1]. A multidisciplinary panel of lung cancer experts has worked closely with patients and ERS methodologists to deliver high quality recommendations. Their initiative extended further to create a starting point for future quality improvement research in lung cancer care with ongoing patient input. Eight PICO (Patient/Population, Intervention, Comparison, Outcome) questions were developed and covered various aspects of lung cancer care, with subsequent recommendations as shown in table 1. The ERS Task Force panel is convinced that the implementation of these ERS guidelines will ensure high quality patient-centred lung cancer care.

Lung cancer: from screening to early diagnosis

Lung cancer screening

LCS in high-risk populations using LDCT reduces lung cancer mortality by 20–24% [3, 4] and all-cause mortality by 6.7% [3]. The US Preventive Services Task Force recommended annual LCS for individuals between 50 and 80 years old, smokers with a 20-pack-year smoking history or ex-smokers within the past 15 years [5]. Even though these seem straightforward inclusion criteria and they possibly constitute an accessible way to identify high-risk individuals and invite them to LCS, several studies demonstrated that there are better ways to identify individuals that would benefit from LCS. The use of risk prediction models for lung cancer has been suggested as a better strategy to select individuals for LCS than using age and smoking history alone. Risk prediction models have a higher sensitivity and specificity than age and smoking criteria *per se* [6–9]. These risk prediction models include other risk factors for lung cancer such as respiratory comorbidities (COPD, presence of emphysema, occupational lung disease) or family history of lung cancer [7, 8, 10, 11]. The implementation of LCS is gaining ground in various countries and therefore the inclusion criteria as a standalone *versus* risk stratification models are expected to create a dilemma in delivery and implementation of LCS programmes.

New data consider the use of biomarkers in LCS with a view to improving the sensitivity of LCS eligibility criteria (age, smoking status) and taking a step further to inform risk stratification of incidental pulmonary nodules should they be found in LCS [12]. Several biomarkers [13–18] have been studied in LCS; however, there is no consensus with regards to their routine use in LCS programmes, mainly due to the lack of acceptable clinical validation.

Several genomic and epigenomic-transcriptomic biomarkers were investigated for their role in early lung cancer detection and potential inclusion in LCS [19]. It was demonstrated that circulating microRNA-21 levels distinguish patients diagnosed early with lung cancer from healthy population [20] and in the two retrospective validation studies from Italy (MILD trial), microRNA signature classifier decreased the likelihood of false positive results in patients submitted to LDCT [21, 22]. Recently, the BioMILD trial demonstrated that in individuals with indeterminate or positive results in LDCT, the addition of circulating microRNA signature classifier improved clinical decisions, in particular with regard to LDCT intervals screening [23]. Moreover, the detection of DNA methylation of specific genes may help for the risk stratification in LCS, namely *SHOX2* and *RASSF1A* genes [24].

Biomarkers have not been used in Europe to complement LCS inclusion criteria. An e-mail survey of key opinion leaders from several European countries highlighted the challenges and variability of LCS implementation [25]. Among the 23 responding countries, only one had implemented a LCS programme, while three were anticipating implementation in 2022 and 11 participated in feasibility projects at the time of the survey. The primary barriers among respondents were associated costs, radiology services' capacity, radiologists' job planning to accommodate the additional workload, public opinion and concern regarding acceptance of such a programme by primary care physicians and radiologists.

A pilot LCS project in Vojvodina, Serbia [26] showed these challenges in a pragmatic setting. Response rates to the LCS programme were low, particularly among younger, unemployed males. Participants had a relatively low perception of lung cancer risk, despite a smoking prevalence of 84% among the screened

TABLE 1 Summary of PICO (Patient/Population, Intervention, Comparison, Outcome) questions and recommendations in the European Respiratory Society guideline on various aspects of quality in lung cancer care

PICO question	Recommendation	Strength
PICO 1: In patients with lung cancer (or those suspected of having lung cancer), should shorter rather than longer cancer care time intervals be used (*e.g.* time from diagnosis to treatment)?	Minimise delay in initiation of first treatment.	Conditional
PICO 2: In patients with lung cancer (or those suspected of having lung cancer), should a multidisciplinary team (MDT) or certain disciplines be involved during lung cancer care rather than no involvement of an MDT or certain disciplines?	Integrate MDTs and/or multidisciplinary consultation in the management of patients with (suspected) lung cancer.	Conditional
PICO 3: In patients with lung cancer (or those suspected of having lung cancer), should guidelines or standard operating procedures (SOPs) for lung cancer care be implemented or adhered to rather than non-implementation of or non-adherence to these guidelines or SOPs?	Methodologically robust, evidence-based guidelines and SOPs should be implemented and adhered to (based on informed consent by the patient).	Conditional
PICO 4: Should patients with lung cancer (or those suspected of having lung cancer) receive lung cancer-specific diagnostic or therapeutic procedures in hospitals/from professionals with higher volumes of activity/with a higher grade of specialisation for these procedures rather than receiving them in hospitals/from professionals with lower volumes of activity/with lower grade of specialisation for these procedures?	Perform lung cancer surgery in lung cancer services and by surgeons specialised in thoracic surgery with high institutional volumes of pulmonary resections.	Strong
	Perform procedures other than lung cancer surgery in lung cancer services and by professionals specialised in these procedures with high institutional volumes of these procedures.	Conditional
PICO 5: Should patients with lung cancer (or those suspected of having lung cancer) obtain pathological confirmation of tumours or subtyping of lung cancers rather than no pathological confirmation of tumours or subtyping of lung cancers?	Seek pathological confirmation where it determines management.	Strong
	Further subtype lung cancers through application of the World Health Organization Classification of Tumours [2].	Good practice statement
	Perform molecular characterisation for actionable targets or response to treatment.	Good practice statement
PICO 6: In patients with lung cancer (or those suspected of having lung cancer), should palliative care or its delivery by specialists be integrated into lung cancer care already early during the course of the disease rather than no integration of palliative care or no palliative care delivery by specialists?	Integrate palliative care at an early stage into lung cancer care pathways, based on patient symptom load and well linked to routine tumour-specific management.	Conditional
PICO 7: In patients with lung cancer (or those suspected of having lung cancer), should quality improvement measures be applied in lung cancer care rather than no application of these methods in lung cancer care?	Utilise national clinical lung cancer registries involving quality indicators to provide feedback for future lung cancer guidelines and to inform lung cancer services.	Conditional
	Refer lung cancer patients to services with ready access to multiple lung cancer specialist facilities.	Conditional
PICO 8: In patients with lung cancer (or those suspected of having lung cancer), should patient decision tools be involved in the decision-making and decision-sharing process rather than not involving them?	Use patient decision tools as a measure to improve patient involvement in decision making.	Conditional

Adapted from [1].

population and the known relationship between lung cancer and smoking. Smoking cessation counselling was offered as part of this programme, but concerningly the uptake of counselling was only 1.3%. Despite the low uptake, most of these few individuals succeeded in smoking cessation. Over half of the lung cancers were detected at stage I or II, underlining the value of screening.

The lack of primary care education for LCS referral guidelines [27] may have a negative impact in LCS, resulting in up to 30% of providers never ordering LDCT scans for eligible individuals [28]. Among the few providers ordering LDCT scans, 80.9% stated that they only order 1–3 per month [28].

Incidental findings during LCS can be a cause of concern, creating anxiety and unsettlement for participants. Although the majority (71%) of findings are benign [29], there will be an increasing diagnosis of interstitial lung abnormalities, emphysema, bronchiectasis, consolidation, pleural effusion/pleural plaques, diaphragmatic abnormalities, cardiovascular diseases, and mediastinal, thyroid, breast, adrenal and kidney lesions [30]. Unlike the other cancer screening programmes currently in progress, LDCT provides much more information than required for lung cancer detection and LDCT is suboptimal for diagnosis and evaluation of many soft tissue abnormalities. Therefore, it is fundamental to have guidance for proper management of participants. Recently, the American College of Radiology published a quick reference guide for incidental findings in LCS [31], making recommendations for imaging follow-up, for referrals to a specific specialisation and the requirement for other complementary diagnostic tests [31].

Despite these challenges, it is well established that the implementation of LCS and the widespread application of imaging investigations have resulted in an increased diagnosis of pulmonary nodules in clinical practice, leading to an early detection of lung cancer and reducing mortality.

Methods for early lung cancer detection

Liquid biopsies may be used for the early detection of lung cancer [19]. Exhaled volatile organic compounds (VOCs) are biomarkers of interest in the noninvasive detection of lung cancer, and validated models to distinguish subjects with lung cancer from those without lung cancer are needed. Using an electronic nose (aeroNose®) to detect VOCs, a multicentre, prospective study [32] developed a prediction model using exhaled breath from 160 patients with NSCLC and 216 controls, and a blinded cohort of 199 subjects for validation. Using exhaled breath data alone, the training cohort sensitivity was 93%, specificity 54%, positive predictive value 60% and negative predictive value 91%; the blinded validation cohort results were 88%, 48%, 52% and 87% respectively. The addition of clinical variables such as age and pack-years smoked to the exhaled breath data improved sensitivity in the training and validation cohorts to 95%, and negative predictive value to 93% and 94% respectively. Specificity was low in both cohorts at 51% and 49% respectively, partly due to methodological aims to maximise sensitivity and reduce the risk of false negatives [32].

Indeterminate pulmonary nodules: the ongoing challenge of (non)aggressive management

Despite specific guidelines for the management of pulmonary nodules identified incidentally or during LCS [33–35], aggressive management is still a matter of debate, mainly affected by the physician's behaviour and experience as well as patient preference. High suspicion of malignancy based on personalised risk stratification and good functional performance status calls for an aggressive approach, *i.e.* surgical removal without prior histological confirmation. Cautiousness is advised in pure ground glass opacities with smooth margins and no bubble lucency as they have been proved to be benign. Long-term follow-up of persistent sub-solid nodules (SSNs) until growth of a solid component could be a safe choice and preferable to an aggressive approach, as SSNs are unlikely to develop into a deadly cancer within 10 years of follow-up. They are instead associated with concurrent deadly comorbidities, including more aggressive intraindividual lung cancer.

Novel interventional pulmonology approaches in the diagnosis and management of lung cancer

A significant number of pulmonary nodules detected in LDCT will be biopsied to obtain material for early diagnosis, as delays in lung cancer diagnosis and further management can have an impact upon prognosis [36]. In this direction, interventional pulmonology is a dynamically evolving field that has revolutionised the minimally invasive diagnostic and therapeutic approach for lung nodules and mediastinal lesions [37].

The implementation of multiple guidance modalities during bronchoscopy investigation for peripheral lung lesions increases the diagnostic yield [38]. Recently, a large prospective multinational cohort demonstrated that electromagnetic navigational bronchoscopy had low complications and a 67.8% diagnostic yield, allowing histological diagnosis, staging and dye marking for surgery or radiotherapy in a single procedure [39].

During the 2022 ERS Congress, a first-in-human single-centre, prospective, single-arm treat-and-resect study was presented that examined the safety and feasibility of bronchoscopic radiofrequency ablation at escalating doses [40]. In selected patients with bronchoscopically accessible peripheral tumours considered suitable for lobectomy, the tumour was localised with radial endobronchial ultrasound, the radiofrequency catheter introduced *via* guide sheath and position confirmed with cone beam computed tomography before balloon occlusion and treatment. One serious adverse event occurred in the first patient treated, with coughing causing heated hypertonic saline escape and lung injury. This was prevented in subsequent patients through neuromuscular blockade and limited saline volumes, and the first subject recovered with no sequelae demonstrated on imaging before proceeding to lobectomy as planned. At resection 7 days post-ablation, uniform necrosis was achieved in the ablation zone with variable tumour proportion ablation as expected given the dose-escalation design. Further studies are planned for this promising technology, with improved targeting, and increasing energy levels to refine the dose–response relationship.

Surgery and alternative options in early lung cancer treatment

To date, surgical resection *via* VATS lobectomy is the standard of care for early stages of lung cancer. However, the indication of sublobar resection for malignant peripheral small-sized lesions (⩽2 cm) with no lymph node involvement has recently gained grounds [41]. A recent phase 3 trial showed that patients with clinical stage IA NSCLC who underwent segmentectomy had a significantly higher 5-year overall survival when compared to the lobectomy group [42]. Furthermore, the relapse-free survival was nearly identical between the two groups [42].

Stereotactic radiotherapy is an alternative for early-stage lung cancer treatment; however, patients that are unsuitable for any of the above options should still be offered an alternative. Percutaneous ablation is an alternative, and it has acceptable rates of local complications and long-term control.

The role of artificial intelligence in lung cancer diagnosis and management

AI has been emerging in most medical specialties over the last decade. It involves the use of computers to perform tasks previously performed by humans. Machine learning and deep learning are subclasses of AI. Machine learning is used to create algorithms solving problems without being explicitly programmed. Deep learning allows the algorithm to learn and adapt to new analysed data structures by using a complex structure of algorithms. Figure 1 shows the relationship between AI, machine learning and deep learning in thoracic oncology.

The application of AI-assisted diagnostic systems to clinical work has turned a new page in lung cancer diagnosis. In the field of thoracic oncology, AI can be used for radiological evaluations, pathological analysis, exhaled breath analysis or clinical prediction models [43–45].

In radiology, selected AI software, scan techniques and algorithms can be used to enhance image quality and automate volumetry. Radiology AI contributes to radiologists' reporting as concurrent or second reader. AI radiology applications also contribute to lung cancer imaging biobanks, estimate the malignancy risk of nodules, detect lung cancer with accuracy close to that of radiologists, and detect SSNs [46–48]. AI is also estimated to impact on clinical decision support systems, structured reporting and workflow.

For pathologists, AI can be helpful in analysing digital images of lung tissue biopsies. Using pathomics, quantitative features from digitised images can be converted into discrete data, allowing interaction with algorithms. Deep learning models can play an important role in the accurate pathology diagnosis of lung cancer: they can predict the status of some molecular markers on regular haematoxylin and eosin slides, as well as predict lung cancer subtypes. Al has also been trained to predict gene mutations and count the proportion score for PD-L1 expression [49–51].

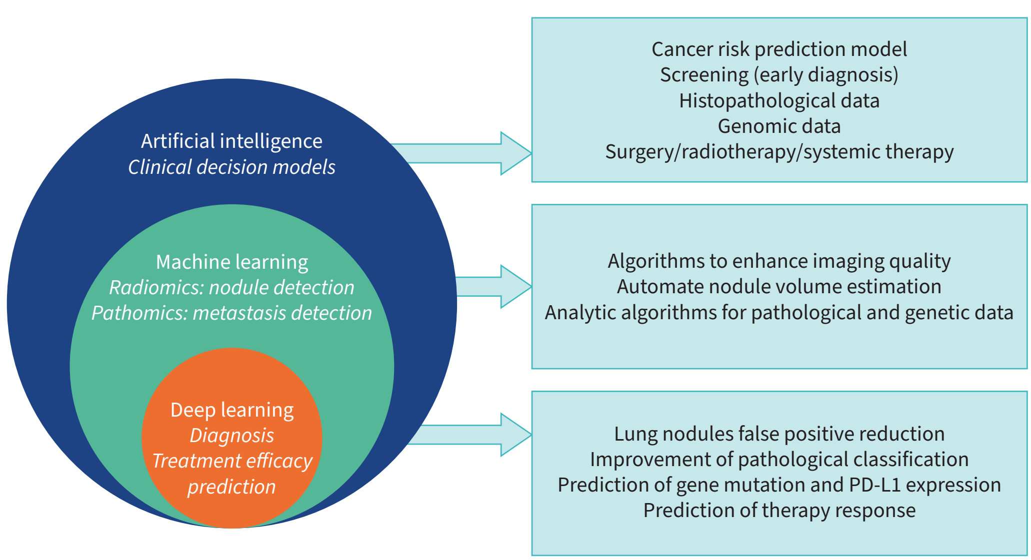

FIGURE 1 Relationship between artificial intelligence, machine learning and deep learning in thoracic oncology.

Pathomics can overall eliminate inter-observer variations and ensure precise lung cancer treatment. They also play an important role in next-generation sequencing in modern lung cancer treatment. AI can determine tumour cells and tumour DNA which are essential for successful next-generation sequencing testing.

However, there are limitations in complex pathology diagnosis, image data quality, data integration and cost of resources. Despite the increasing number of experienced pathologists involved in AI for lung cancer pathology image annotation, most AI advances in this area have not entered everyday clinical practice in lung cancer care.

In addition to pathology, AI can have an impact on lung cancer treatment response prediction. Radiomics signatures such as volume, shape and tumour heterogeneity predict treatment response in patients with lung cancer, offering an approach that could enhance clinical decision-making and forecast overall survival [52]. Determining in advance which patients are potential non-responders to treatment can allow for either an intensified treatment approach or a change in the treatment sequence or, conversely, avoid potentially harmful therapies that are not beneficial to the patient.

The moment of primary AI decisions is not yet in reach, but in the future, AI will be able to assist in clinical practice by combining clinical, radiological and pathological data.

Concluding remarks

Thoracic oncology, in particular lung cancer, has been on the main stage of the 2022 hybrid ERS Congress, where the best practices and latest developments have been presented. Significant progress is anticipated over the coming years with a view to improving overall survival, quality of life and patient experience. The annual ERS Congress will continue to play a key role in sharing new scientific data and best practices in thoracic oncology and provide a scientific hub to advance collaborations and initiatives.

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