CHEST

State of the Art
Interventional Pulmonology

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Interventional pulmonology (IP) has evolved over the past decade from an obscure subspecialty in pulmonary medicine to a recognized discipline offering advanced consultative and procedural services to patients with thoracic malignancy, anatomic airway disease, and pleural disease. Innovative interventions are now also available for diseases not traditionally treated procedurally, such as asthma and emphysema. The IP field has established certification examinations and training standards for IP training programs in an effort to enhance training quality and ensure competency. Validating new technology and proving its cost-effectiveness and effect on patient outcomes present the biggest challenge to IP as the health-care environment marches toward value-based health care. High-quality research is now thriving in IP and promises to elevate its practice into patient-centric evidence-based care.

CHEST 2020; 157(3):724-736

KEY WORDS: bronchoscopy; interventional pulmonology; lung biopsy; lung neoplasm

More than 10 years have passed since the initial publication on the state of the art in interventional pulmonology (IP) in this journal.[1] Much has changed in this past decade. IP is now a well-recognized subspecialty of pulmonary medicine with a focus on advancing the care of patients with thoracic malignancy, airway disease, and pleural disease via minimally invasive techniques and innovative approaches.[2] IP training programs grew at an exponential rate to reach more than 40 available annual training positions; to ensure quality training, the IP community standardized fellowship training and accreditation and created a board examination for certification.[3-6] Innovations in IP have led to the development of therapeutic options for benign and malignant disease. Novel minimally invasive procedural interventions for asthma and COPD have been approved by the Food and Drug Administration

ABBREVIATIONS: AABIP = American Association for Bronchology and Interventional Pulmonology; APC = argon plasma coagulation; BLVR = bronchoscopic lung volume reduction; BTPNA = bronchoscopic transparenchymal nodule access; CAO = central airway obstruction; CBCT = cone-beam CT; DNase = deoxyribonuclease; DPLD = diffuse parenchymal lung disease; EBUS = endobronchial ultrasound; EC = electrocautery; EM = electromagnetic; ENB = electromagnetic navigation bronchoscopy; ETTNA = electromagnetic guidance transthoracic needle aspiration; FDA = Food and Drug Administration; IP = interventional pulmonology; IPC = indwelling pleural catheter; PT = percutaneous tracheostomy; R-EBUS = radial EBUS; RFA = radiofrequency ablation; SLB = surgical lung biopsy; TBNA = transbronchial needle aspiration; tPA = tissue plasminogen activator

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FUNDING/SUPPORT: The authors have reported to *CHEST* that no funding was received for this study.

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DOI: https://doi.org/10.1016/j.chest.2019.10.013

(FDA) in the United States. Navigation and robotic-assisted bronchoscopy are in various phases of development and promise to enhance the reach to peripheral lung targets for diagnosis and ablative treatment. Clinical trials examining the management of pleural infections and malignancy have driven real change in daily clinical practice. In this review, we aim to summarize recent developments, evolving technologies, and future challenges in IP.

Therapeutic Bronchoscopy

Therapeutic bronchoscopy is indicated for the relief of central airway obstruction (CAO) located in large airways (trachea, mainstem bronchi, and bronchus intermedius). The goal is to provide relief of symptoms or, occasionally, a lasting cure for early localized cancers (carcinoma in situ) or benign lesions. The main cause of CAO is malignancy (primary lung cancer or metastases from extrathoracic cancers), but other nonmalignant conditions can be seen (inflammatory, infectious or sequelae of artificial airways). Patients often present initially with cough and exertional dyspnea, then progress with increasing severity of obstruction to resting dyspnea; stridor; hemoptysis; postobstructive infections; and, ultimately, asphyxiation.[7]

The specific intervention in the airways is tailored to the type of airway lesion, generally divided into exophytic growth (intrinsic), extrinsic compression from adjacent growths, or a combination of both diseases. Mechanical debridement and ablative therapy are most appropriate for exophytic lesions, whereas bronchoplasty and stent placement are best suited for extrinsic compression. Rigid bronchoscopy is preferred over flexible bronchoscopy for therapeutic procedures because the rigid bronchoscope has a larger diameter that allows for effective suctioning and the removal of large pieces of tissue, there is also the ability to ventilate through the scope, and the barrel of the scope is useful in coring out tissue and dilating stenoses. Most bronchoscopists use a combination of rigid and flexible bronchoscopic techniques in which the flexible scope is used through the rigid scope for better visualization of distal lesions or easier articulation in curved or tortuous airways.

Ablative Therapy: Laser, Electrocautery, Argon Plasma Coagulation, Cryotherapy

Ablative therapy in the airway consists of both hot (laser, electrocautery [EC], and argon plasma coagulation [APC]) and cold (cryotherapy) modalities. The ideal lesion for ablative therapy is intraluminal and short (< 4 cm) and has confirmed aeration in lung areas distal to it (on the basis of CT scanning or bronchoscopic visualization). Although heat therapy can be used to vaporize the tumor, it is used more commonly to coagulate the tumor before mechanical resection to control bleeding. The neodymium:yttrium-aluminum-garnet laser was introduced in 1980s and has been the main heat modality used in the airways.[8] However, its use has decreased over the past decade in favor of other modalities. EC is a modality that uses an electric probe to conduct an electric current to heat the target tissue directly. EC is perceived as an alternative that is cheaper and easier to use than is laser and that also can be combined with accessories such as an EC knife and EC snare to provide effective ways to cut webs or snare polypoid lesions, respectively.[9-11] APC is an alternative noncontact electrocoagulation technique in which a high-frequency current meets with argon gas at the tip of probe to generate a plasma jet that heats tissue. APC is predominantly a coagulation technique because its depth of effect is limited to 1 to 3 mm. With all heat modalities, there is the concern for airway ignition when performed under high oxygen conditions. Thus, decreasing the F_{IO_2} to $< 40\%$ is recommended when heat ablative modalities are used.[9,12]

Cryotherapy started as a modality to destroy tissue by rapidly freezing it to a very cold temperature ($< -40^{\circ}C$). However, it gradually fell out of favor because it required repeated freeze and thaw cycles on the target lesion and had delayed effects, making it unsuitable for rapid relief of CAO. Instead, a new application of cryotherapy emerged. Cryoadhesion is a technique in which the cold temperature of the probe is used to adhere to the tissue, with the probe then being abruptly withdrawn, thereby retrieving the attached tissue. This technique can be used to remove luminal tumor tissue (cryocanalization), blood clots, mucous plugs, or foreign objects.[13,14]

The data on the efficacy of ablative therapy in the airways is limited but, overall, show a high success rate in achieving luminal patency ($> 90\%$), relief of shortness of breath and a low rate of complications.[15-17] Figure 1 illustrates a typical case of therapeutic bronchoscopy in CAO.

Other modalities, such as brachytherapy and photodynamic therapy, have a delayed therapeutic effect and often are not suitable for situations in which immediate relief of airway obstruction is desired. Both modalities now are used less commonly because of cost, burdensome procedural steps, and unfavorable adverse

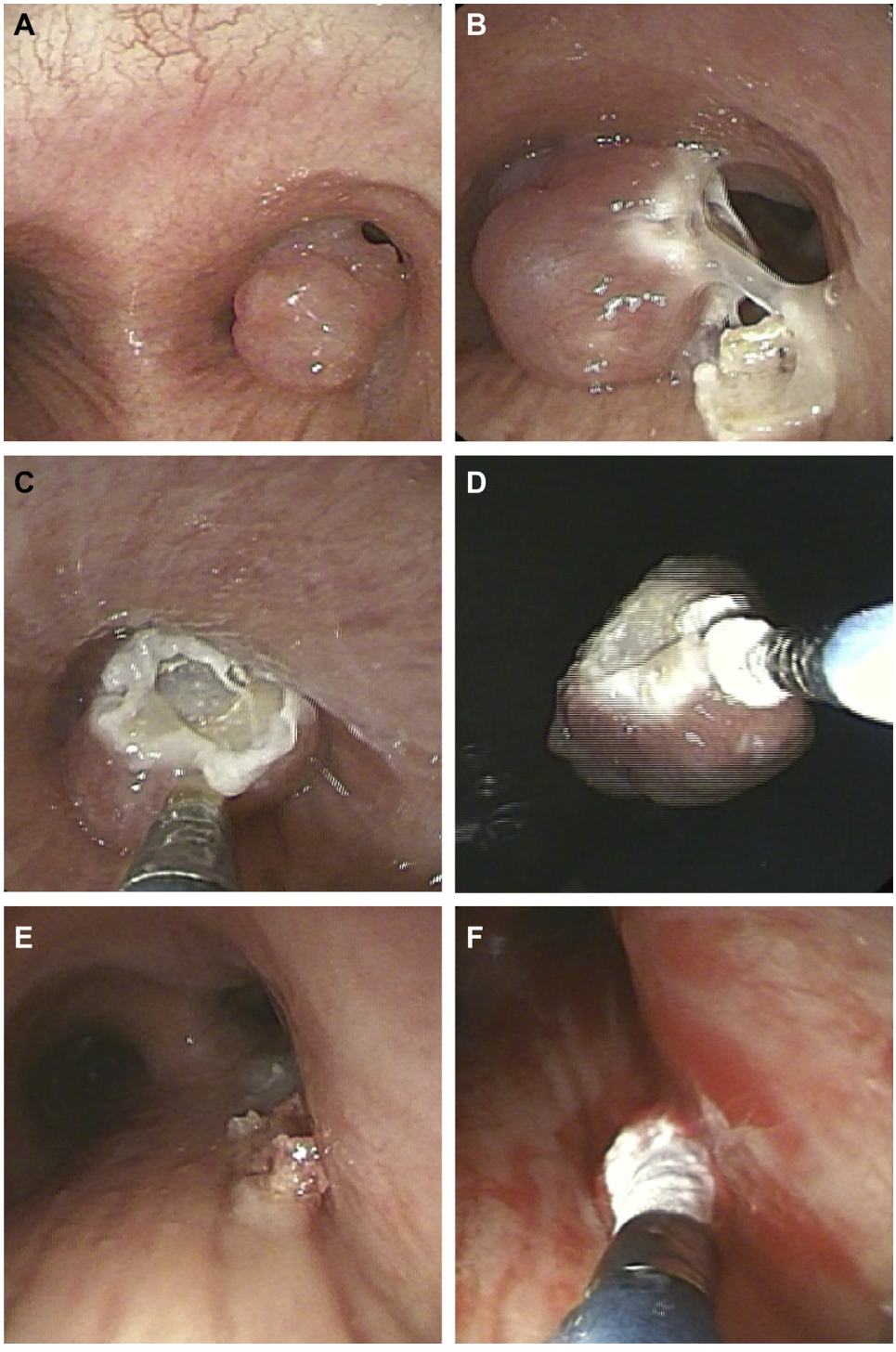

Figure 1 – *Therapeutic bronchoscopy procedure images. A, A large, right mainstem bronchial mass. B, An electrocautery snare was first applied to the mass and then detached the mass from its base. C and D, A cryotherapy probe then was used to adhere to and remove the mass. E and F, The residual base of the mass was treated with touch cryotherapy.*

event profiles (prolonged skin photosensitivity and fatal hemoptysis in photodynamic therapy and massive hemoptysis, radiation bronchitis, and airway stenosis in brachytherapy).[18]

Mechanical Debridement and Bronchoplasty

Mechanical debridement of endobronchial lesions can be achieved with flexible forceps, large rigid forceps, the beveled tip of the rigid scope, cryoavulsion or with the

use of a microdebrider. Debridement with flexible forceps is most effective for smaller lesions in the distal airways because it could be quite time-consuming for larger airway masses. Debridement with the beveled tip of the rigid scope is used in the central airways for lesions that are short with a clear distal lumen, although caution must be exercised to avoid damage to the airway wall.[19]

The microdebrider uses disposable rotating blades that can shave and suction protuberant tissue. Advantages to this method include its rapid action and the ability to debride and suction tissue at the same time. The main limitations are the rigid shaft and short length of the blades, which limit their maneuverability and access beyond the trachea and proximal mainstem bronchi.[20]

Bronchoplasty, or bronchial dilatation, can be achieved with the barrel of the rigid scope or with balloons inserted via the flexible scopes. It is most commonly used for dilatation of stenotic airways or disruption of webs related to nonmalignant causes of airway diseases. This method generally leads to immediate relief of the stenosis, but results are usually short-lived. Mucosal tears and minor bleeding are expected and common. Rupture of airways and vessels may occur if proper techniques are not followed.[21]

Another technique commonly used for concentric benign tracheal stenoses incorporates the use a neodymium:yttrium-aluminum-garnet laser or EC to produce radial cuts in the stenotic web. This technique is then followed by bronchoplasty. This combined approach can result in mucosal sparing and potentially more durable results.[22]

Airway Stents

Reports of endoscopically implantable stents for the airways date back to 1914.[23] The implantation of the first dedicated silicone stent in the airway was reported by Dumon in 1990.[24] There are currently three types of stents available: metallic (uncovered or partially covered), silicone, and hybrid (silicon and metallic elements). Airway stents are commonly used to treat patients with CAO due to extrinsic compression from a variety of malignant and benign disorders.[7] Stents are effective and lead to relief of symptoms in CAO in $>$ 90% of patients (Fig 2).[25] However, effects may not be durable, and complications are not uncommon, especially when stents are placed for benign disorders or remain in place for an extended time.[17] Complications with airways stents include migration, tumor overgrowth, infections, granulation tissue formation, and mucous plugs.[26,27]

Bare metallic stents can embed quickly in normal mucosa and become difficult to remove, so they can cause complications with consequences more dire than those of the original airway disease. Therefore, it is not advisable to place them for benign disorders for which life expectancy is long; the FDA issued a black box warning cautioning against the use of metallic stents in patients with benign tracheal disorders.[28]

First generations of biodegradable stents, three-dimensional printed tailored stents, and drug-coated or drug-delivering stents currently are being evaluated and have been used in small series. These options promise to move IP into a personalized medicine approach in which stents are tailored to an individual patient's airway anatomy.[29-31]

Diagnostic Bronchoscopy

Endobronchial Ultrasound

Convex endobronchial ultrasound (EBUS) was first used in the airway in 2003 and has rapidly become the gold standard for mediastinal sampling.[32] EBUS provides a sonographic view that is parallel to the long axis of the bronchoscope and allows for real-time visualization during transbronchial needle aspiration (TBNA) of mediastinal and hilar lymph nodes and masses adjacent to the airways (Fig 3). Since its introduction, the evidence has been mounting for the superior performance of this technology in sampling mediastinal and hilar lymph nodes and has led it largely to replace conventional TBNA and, to some extent, mediastinoscopy.

Multiple studies have illustrated that EBUS-TBNA has a pooled sensitivity of roughly 90% and specificity of 100% in the staging of non-small cell lung cancer.[33] The 2013 CHEST lung cancer guidelines recommended EBUS-TBNA over surgical staging as the initial test for mediastinal staging of known or suspected lung cancer.[33] EBUS-TBNA also has a similarly high yield for intrathoracic lymph nodal metastases from extrathoracic malignancies.

Of equal importance, the EBUS-TBNA technique also has been well proven to obtain tissue samples that are adequate to perform molecular profiling for targeted therapies in lung cancer, with adequacy rates for testing that exceed 95%.[34] A 2016 CHEST guideline statement summarized best conditions and optimal technical

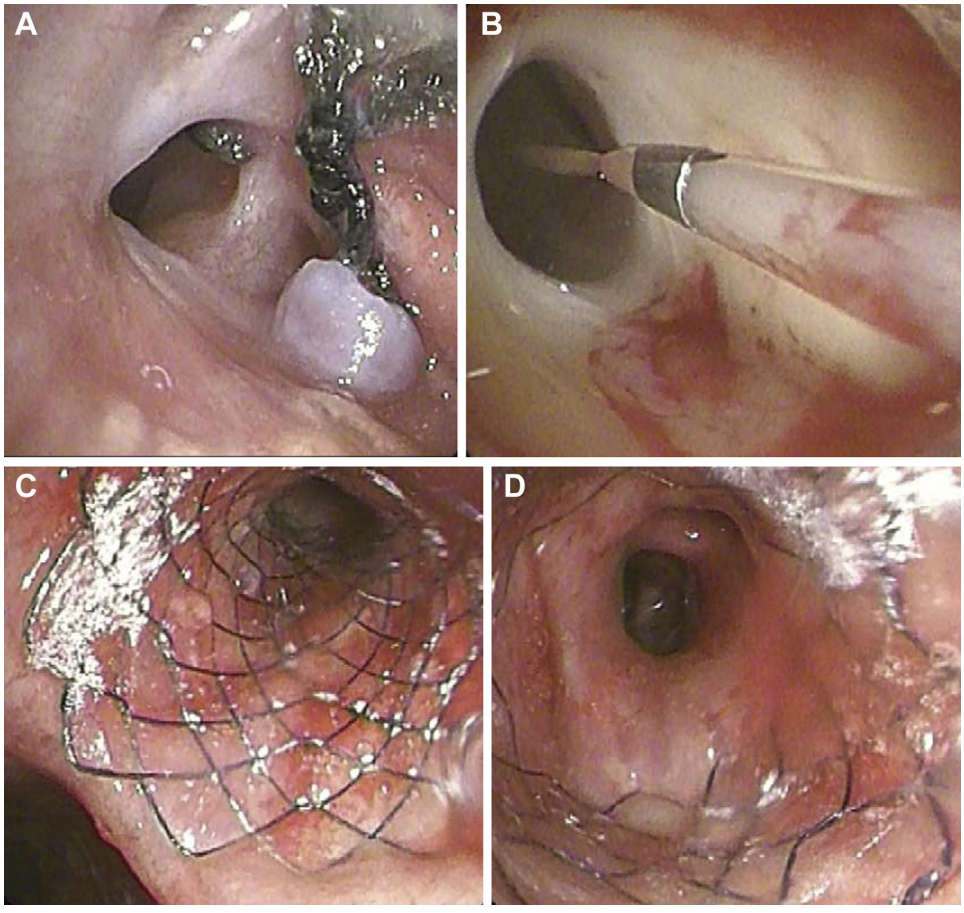

Figure 2 – *Images of airway stent placement in a patient with a lung transplant. A, A complex mixed lesion identified in the right mainstem bronchus. B, Bronchoplasty with a balloon. C, Proximal view of hybrid stent placed in the right mainstem bronchus. D, Distal view of airway stent with patency of distal airways.*

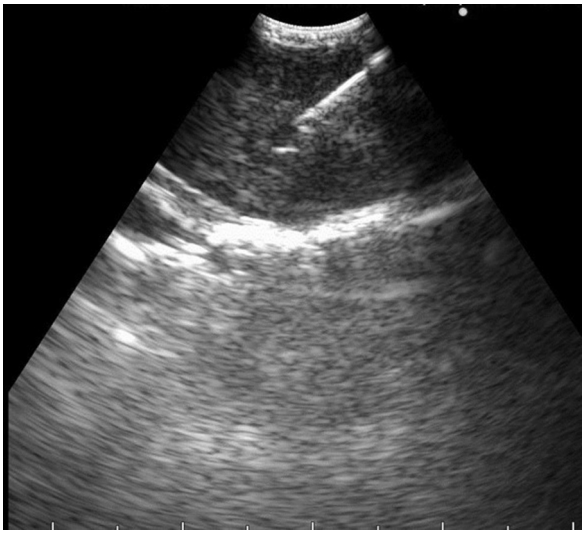

Figure 3 – *Endobronchial ultrasound-guided transbronchial needle aspiration image of the left interlobar lymph node (station 11L). A needle is visible within the lymph node, which is surrounded by lung tissue.*

performance to achieve maximal diagnostic yield and adequate tissue for various tests.[35] Other studies have shown that although the sensitivity of EBUS-TBNA for pulmonary sarcoidosis is relatively high,[36] it is lower for the diagnosis of lymphoma (sensitivity of 55%).[37]

Peripheral Bronchoscopy

Substantial effort has been made toward advancing the diagnostic yield of bronchoscopy for peripheral pulmonary lesions. A 2012 meta-analysis inclusive of more than 3,000 patients suggested that the diagnostic yield of guided bronchoscopy for peripheral lesions was approximately 70% regardless of the method used.[38] However, more recent data, including a prospective study of more than 600 patients undergoing guided bronchoscopy for peripheral lesions, revealed that procedures were nondiagnostic in more than 40% of patients.[39] Therefore, efforts continue to determine the true diagnostic yield of advanced guided procedures and

the optimal application of these techniques to improve diagnostic yields in the periphery.

Ultrathin bronchoscopy is the use of smaller bronchoscopes to facilitate improved access to the lung periphery. Oki and colleagues[40] performed a prospective randomized controlled trial comparing the use of a 4-mm-outer-diameter thin bronchoscope and guide sheath with an ultrathin 3-mm-outer-diameter bronchoscope with a 1.7-mm working channel for the diagnosis of peripheral pulmonary lesions. Both arms used radial EBUS (R-EBUS) and virtual bronchoscopic navigation, and the authors demonstrated a statistically significant increase in the diagnostic yield with use of the 3-mm bronchoscope (74% vs 59%; $P = .044$), as well as increased peripheral reach by approximately one generation of bronchus.[40]

R-EBUS uses a small, radial scanning ultrasound probe that is inserted through the bronchoscope's working channel and into the lung parenchyma. One contribution of this technology has been the discovery that successful biopsies in the periphery are contingent on overcoming multiple variables. A large retrospective study demonstrated that despite successful R-EBUS confirmation of peripheral lesions in 446 of 467 (96%) of patients, the diagnostic yield in this population was 69%.[41] This disconnect between localization and successful biopsy may be explained by anatomic relationships in the periphery. A concentric ultrasonographic view indicates that the peripheral lesion surrounds the bronchus, whereas an eccentric view indicates that the lesion is positioned adjacent to the bronchus (Fig 4). When a concentric view is obtained, the diagnostic yield of procedures with use of R-EBUS exceeds 80%, compared with diagnostic yields of approximately 40% when an eccentric view is obtained.[42]

Electromagnetic (EM) navigation bronchoscopy (ENB) describes image guidance systems that manipulate thin-section CT images to create virtual airway reconstructions that are used as maps during bronchoscopy. ENB systems also incorporate sensors that are tracked within an EM field during procedures. The patient's airway reconstructions and sensors are aligned using automated or manual registration algorithms, and the bronchoscopist is provided with a pathway to peripheral lesions, as well the ability to follow the location within the EM field. Experience using ENB systems has enhanced the understanding of the lung periphery during procedures, most notably the dynamic nature of the lung with respiration. One study quantified movement of peripheral lesions between full inspiration at CT scanning and end-exhalation during tidal volume breathing in which peripheral lesions moved approximately 24 mm in the lower lobes and 11 mm in the upper lobes, although the clinical effect of this remains unclear.[41] A recent multicenter registry revealed a 12-month diagnostic yield of ENB of 73%.[43]

EM guidance has been applied to transthoracic approaches. This approach has been used previously for liver biopsies and more recently has been applied to the lung. A feasibility study in which EM guidance transthoracic needle aspiration (ETTNA) was performed using EM guidance for peripheral lesions in 24 patients achieved a diagnosis in 20 of the 24 (83%) patients, with a pneumothorax rate of 21%, and 2 patients (8%) required tube thoracostomy.[42] The combined approach of mediastinal staging by using EBUS-TBNA, ENB, and ETTNA in suspected cases of early stage lung cancer

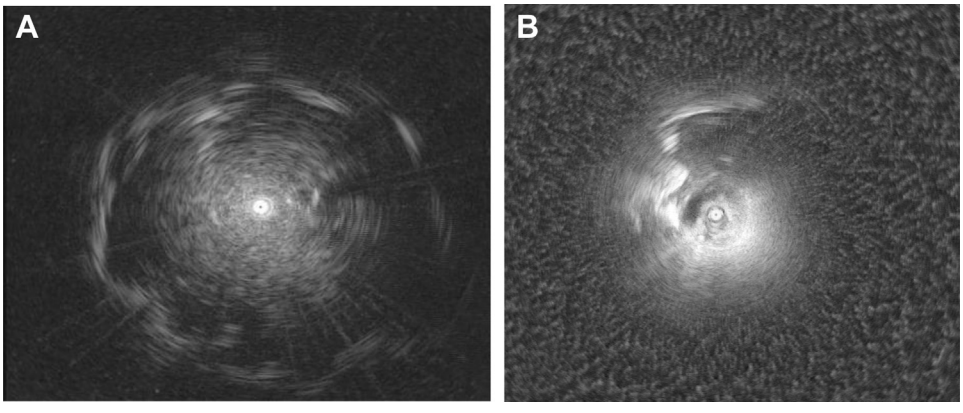

Figure 4 – *Radial endobronchial ultrasonographic images of lung nodules. A, A concentric view indicates that the peripheral lesion surrounds the bronchus. B, An eccentric view indicates that the lesion is positioned adjacent to the bronchus.*

currently is being investigated in a prospective, large, multicenter study.

Bronchoscopic transparenchymal nodule access (BTPNA) is a procedure in which navigational software is used to construct a direct pathway from a proximal bronchus through lung parenchyma to access peripheral lesions. Once the pathway has been constructed, the bronchoscopist uses a needle and dilation balloon to tunnel through pulmonary parenchyma to the peripheral lesion. A feasibility study in using BTPNA in 12 patients undergoing planned resection for possible early stage lung cancer obtained a diagnosis in 10 (83%), and subsequent evaluation of the resected lung did not show any immediate complications.[44] Additional studies of BTPNA are ongoing and are warranted to validate the safety and efficacy of this approach.

Cone-beam CT (CBCT) scanning, a compact CT scanning system with a moving C-arm, can be used intraprocedurally during bronchoscopy to provide real-time confirmation of biopsy device location. A prospective study of bronchoscopy with a thin bronchoscope, R-EBUS, and CBCT scanning in 20 patients showed that post-CBCT scanning maneuvers (redirecting sampling tools to the lesion based on CBCT images) increased the diagnostic yield from 50% to 70%; the mean estimated effective dose of radiation to patients from CBCT scanning ranged from 8.6 to 23 mSv.[45] The body of evidence about CBCT scanning is slim but promising; its added value and safety need to be confirmed with larger prospective studies. However, adoption of CBCT scanning may be low given its cost and lack of availability in most endoscopy suites.

Pleural Interventions

Pleural procedures ranging from pleural ultrasound to medical thoracoscopy remained an active area for research and clinical development in the past decade. Indwelling pleural catheters (IPCs) have gained tremendous popularity and have been declared by evidence-based guidelines to be as acceptable as chemical pleurodesis for the management of symptomatic malignant pleural effusions.[46] When comparing IPCs and pleurodesis via talc slurry, two multicenter, open-label, randomized controlled trials demonstrated that IPCs effectively relieved dyspnea and decreased hospital stay and need for future procedures.[47,48]

Early data showed that the use of an IPC can lead to spontaneous pleurodesis, albeit often delayed, in up to 50% of patients.[47,49] Early spontaneous pleurodesis with an IPC decreases supply cost and risks of catheter failure and infection and achieves the patient's freedom from a catheter.[50] Hence, there have been efforts to understand factors that promote the rate of spontaneous pleurodesis. In a multicenter, randomized, single-blinded trial, patients who underwent daily drainage had a 24% increase in the spontaneous pleurodesis rate, occurring 36 days earlier when compared with every-other day drainage.[51] In a similar effort, the IPC-PLUS study evaluated the addition of talc slurry through an IPC compared with use of an IPC alone; the authors demonstrated a 20% improvement in the pleurodesis rate with talc slurry through an IPC within the first 5 weeks, without any additional adverse events in the outpatient setting.[52]

Pleural infections (empyema or complex parapneumonic effusion) are commonly encountered in clinical practice. The mainstay of therapy used to consist of antibiotics, drainage of the infected pleural space with tube thoracostomy, and possibly surgical decortication. The landmark Multi-Centre Intrapleural Sepsis Trial 2 demonstrated that twice-a-day intrapleural sequential administration of tissue plasminogen activator (tPA) and deoxyribonuclease (DNase) improved fluid drainage in infected pleural effusions, reduced surgical referrals, and decreased hospital stay.[53] More recent studies aiming at reducing the complexity of the treatment regimen have showed that concurrent instillation of tPA and DNase could be as safe and as effective.[54,55] A 2017 observational trial showed that starting with a reduced dose of intrapleural tPA (5 mg) and DNase (5 mg) in treating pleural infection is feasible,[56] although prospective comparative trials are needed to confirm whether these modified schedules of administrations can be validated.

Medical thoracoscopy or pleuroscopy has a diagnostic yield $>$ 95% when used to evaluate lymphocytic exudative effusions without a clear cause (Fig 5).[57] Since its introduction, the procedure has evolved such that it now is performed with the patient under moderate sedation and as an outpatient treatment with excellent outcome.[58,59] Narrow-band imaging and tissue autofluorescence have been used in pleuroscopy to assess the pleura for targeted biopsy quickly.[60,61] Techniques to facilitate larger pleural biopsies by using a diathermy knife, hybrid knife, and cryobiopsy have been described.[62-64] None of the mentioned techniques have yet been validated with comparative trials to assess their added clinical value.

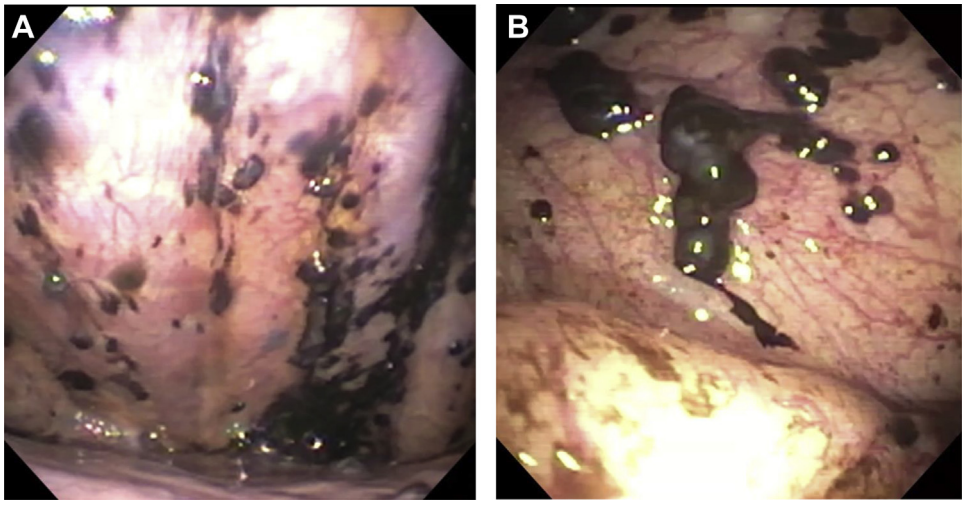

Figure 5 – *Medical thoracoscopy images obtained in a patient with recurrent exudative pleural effusion with negative cytologic findings. A, View of thoracic cavity with abnormal nodules on the parietal pleura. B, Close-up of abnormal parietal nodules; biopsy results revealed metastatic melanoma.*

Percutaneous Tracheostomy

Dilatational percutaneous tracheostomy (PT) has become the technique of choice for performing tracheostomy in patients in the ICU. Advantages of PT over surgical tracheostomy include simpler technique, smaller incision, less tissue trauma, lower incidence of wound infection, lower incidence of peristomal bleeding, decreased morbidity from patient transfer, and cost-effectiveness. A meta-analysis comparing complications of PT with those of surgical tracheostomy in patients who are critically ill confirmed that both techniques led to similar outcomes, with a trend toward fewer complications with PT and more cost-effectiveness.[65] Another potential advantage of PT is that it can be performed by physicians from multiple different subspecialties, including those without traditional surgical training, in a safe and effective manner and may improve patient access and decrease time to tracheostomy.[66] Preparation, performance, and postoperative management for PT are provided best by a multidisciplinary team, which has been shown to improve quality of care by decreasing the incidence of tracheostomy complications and improving time to tracheostomy, duration of procedure, and postprocedural ICU stay.[67]

New Developments and Concepts

Robotics

Robotic-assisted bronchoscopic platforms are currently under investigation for peripheral lesion biopsy. These systems attempt to offer extended distal access and enhanced articulation and stability of peripheral sampling instruments. Two separate systems have demonstrated the safety and feasibility of performing peripheral lesion biopsy in a small cohort of patients.[68,69] One additional study showed that the reach of a robotic endoscopic system in human cadaveric lungs was greater than that of a conventional thin bronchoscope of identical caliber (4.2 mm).[70] Additional studies are currently underway to explore further the usefulness of these systems for peripheral lesion biopsy.[71] Given its high cost, robotic bronchoscopy's added value in clinical practice needs to be validated rigorously before it becomes mainstream.

Endobronchial Intratumoral Chemotherapy

Endobronchial intratumoral chemotherapy is an intervention aimed at improving or maintaining airway patency in patients with malignant airway obstruction, with the potential to eliminate the need for airway stent placement and its associated complications. In a recent pilot study using a microneedle injection catheter designed to optimize drug delivery in the airway wall after airway recanalization, the injection of paclitaxel was both feasible and safe; none of the patients who received the drug injection had evidence of restenosis during subsequent procedures or a clinical need for an airway stent.[72] Additional studies are needed to assess the long-term effects of endobronchial intratumoral chemotherapy.

Ablation

Bronchoscopic ablation of early stage lung cancer long has been described as the holy grail of bronchoscopy because of the appeal of diagnosing, staging, and treating

biopsy-proven early stage lung cancer in one procedural setting. Limited experience with bronchoscopic radiofrequency ablation (RFA) exists, focusing mainly on feasibility and safety.[73,74] A longer-term study that treated 20 patients with nonsurgical early stage lung cancer with bronchoscopic RFA illustrated a local control rate of 82.6%, median progression-free survival of 35 months, and 5-year overall survival of 61.5%; three patients required hospitalization for acute ablation-related reaction (fever, chest pain), and all improved with conservative treatment.[75]

Bronchoscopic microwave ablation also has been proposed as a potential means to treat early stage lung cancer. Bronchoscopic microwave ablation therapy has potential advantages over RFA, such as decreased treatment time and less susceptibility to the thermodilution generated by the heat sink effect of the circulation in adjacent vasculature.[76] Limited experience has been reported using bronchoscopic microwave therapy, and a pilot study was halted secondary to safety concerns (NCT03603652), which highlights the critical importance of rigorous protocol design and implementation. Ultimately, the efficacy of bronchoscopic ablation of early stage nonoperable lung cancer must be proven in longitudinal studies (at least 5 years) demonstrating noninferiority in survival compared with that of the current gold standard of stereotactic body radiation therapy.

Bronchoscopic Lung Volume Reduction

During the past decade, several bronchoscopic therapeutic modalities have been tested in patients with severe emphysema to mimic the physiologic effects of surgical lung volume reduction in a less invasive fashion. Bronchoscopic lung volume reduction (BLVR) via valve placement is a technique that was approved in the United States by the FDA in 2018 (Fig 6). This approach involves placement of one-way valves in the most destructed lung lobe, allowing air and mucus to exit and blocking air entry to achieve lobar collapse. The biggest challenge to this approach is the network of collateral ventilation that may be connecting the target lobe to adjacent lobes, rendering anatomic airway blockage ineffective. Overcoming this obstacle requires assessing collateral ventilation via chest CT scanning (on the basis of the completeness of the fissures separating adjacent lobes) or bronchoscopic measurement of the airflow of the occluded bronchus of the target lobe. Several clinical

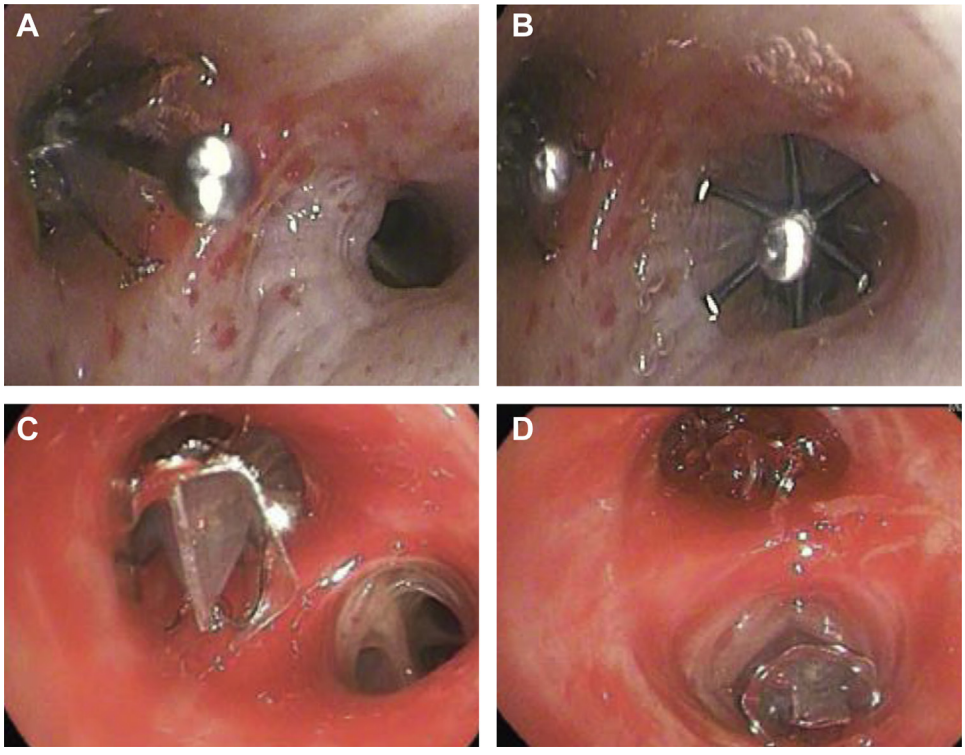

Figure 6 – *Images of bronchoscopic lung volume reduction with valves. A, Placement of Spiration valve (Olympus) in the apicoposterior segment of the left upper lobe (LUL). B, Placement of Spiration valve in the anterior segment of the LUL. C, Placement of Zephyr valve (Pulmonx) in the apicoposterior segment of the LUL. D, Placement of Zephyr valve in the anterior segment of the LUL.*

trials on BLVR with valves have demonstrated improvements in lung function, as well as overall improvement in quality of life and exercise tolerance.[77] However, these benefits came at the cost of a pneumothorax rate of 14.2% to 26.6%.[78]

Although BLVRs are approved in the treatment of patients with severe emphysema, caution should be exercised in careful patient selection and attentive postprocedural care. Realistic expectations should be set with physicians and patients because the benefits of this approach are variable in magnitude and durability is unknown.

Cryobiopsy

Cryobiopsy is a new technique in which the cryotherapy probe is extended into the periphery of the lung, cooled for a few seconds to cause lung tissue to adhere to its tip, and then removed along with the adherent tissue to obtain a large piece of lung tissue with minimal crush artifact. Cryobiopsy has shown benefit in establishing the diagnosis in diffuse parenchymal lung disease (DPLD) for which traditional transbronchial lung biopsy has performed poorly and surgical lung biopsy (SLB) has had a high complication rate. A specific pathologic diagnosis was obtained in 87% of a large cohort of patients with DPLD.[79] A recent study cast some doubt on the usefulness of cryobiopsy by comparing it with SLB performed sequentially in one procedure in 21 patients with DPLD; the study results showed poor concordance between the two modalities, with SLB being more frequently concordant with the final diagnosis as agreed on by a multidisciplinary team.[80] In addition to DPLD, reports on cryobiopsy usefulness in cancer, after lung transplant, and in immunocompromised hosts are emerging. Early experience with cryobiopsy was fraught with a high complication rate and even death.[81]

However, other clinicians have used safer techniques by using endotracheal tubes or rigid scopes, placing endobronchial blockers, using short freezing times of 3 to 5 s, using fluoroscopy, and maintaining a 1-cm safe distance from the pleura. Pneumothorax and severe bleeding are now estimated to occur at 9.5% and 1.1%, respectively.[82] A 2016 study investigating a minicryoprobe that can acquire samples through the working channel of a bronchoscope showed preservation of histologic quality with the promise of improved safety in an animal model, with human trials underway.[83]

In 2018, an international conference on transbronchial cryobiopsy published an expert statement on its safety and usefulness, including a call for the standardization of this procedure.[84] Although cryobiopsy has great potential, questions remain about optimal procedural technique, patient selection, and safety profile; additional studies are needed to understand its role fully. An American College of Chest Physicians evidence-based guideline has been recently published to help standardize the practice and techniques of cryobiopsy.[82]

Bronchial Thermoplasty

Bronchial thermoplasty is a bronchoscopic treatment for patients with severe persistent asthma who continue to have symptoms despite maximal medical treatment.[85] It deploys RFA energy to the airways to reduce their smooth muscle mass. RFA is delivered via a flexible basket during a series of three bronchoscopies separated by 2-week intervals. A pivotal randomized clinical trial did not show a change in FEV_1 or airway hyperresponsiveness but was able to demonstrate an improvement in quality of life and reduction in exacerbation rate, visits to the ED, and days lost from school or work.[86] A subsequent trial was able to confirm that these benefits are sustainable through 3 years from procedure performance (studies with longer follow-up are ongoing).[87] Bronchial thermoplasty has had low adoption in the medical community in the United States because of continued debate about its efficacy and denial of coverage by numerous insurers.

Training and Certification

IP practice encompasses advanced skills and requires interventions in potentially life-threatening situations. This complexity has made it clear that a dedicated year of training in consultative and procedural IP is required to prepare the learner for safe and effective clinical practice.

Although all pulmonologists learn about the evaluation and management of lung nodules and pleural disease, dedicated IP training increases this disease-specific knowledge base.[5] Furthermore, the number of advanced procedures offered by general pulmonary and critical care fellowship programs do not meet prior recommendations by the American Thoracic Society and American College of Chest Physicians, whereas IP fellowship programs far outreach these numbers. In addition to dedicated training, skills assessment tools have been developed and validated to distinguish novice vs intermediate vs expert skill levels appropriately in selected procedures such as EBUS and rigid bronchoscopy.[88,89] IP is not recognized as a distinct specialty by the American Board of Medical Specialties, but the American Association for Bronchology and

Interventional Pulmonology (AABIP) has developed and conducted annual certifying examinations in IP since 2013. Starting in 2017, completing 1 year of dedicated fellowship training in IP became a mandatory prerequisite for AABIP certification. That same year, the Association of Interventional Pulmonary Program Directors partnered with the AABIP, American Thoracic Society, American College of Chest Physicians, and Association of Pulmonary and Critical Care Medicine Program Directors to publish a consensus statement defining minimum training standards for IP fellowship programs.[3]

Challenges and Future Directions

IP, by the nature of its procedural focus, leads the way in innovation by challenging the status quo and seeking novel approaches to the diagnosis and treatment of ailments afflicting a typically vulnerable and frail patient population. With that privilege and enthusiasm comes a great responsibility. First, IP has the scientific and moral obligation to validate new technology. The 510(k) FDA clearance pathway allows new medical devices with no substantial data to be used in patients as long as the devices are shown to be substantially equivalent to a currently FDA-approved device. This option is a blessing and a curse. The blessings come from the acceleration of technology access for patients in need, but the perils come from the relaxed requirement for generation of data to prove safety and efficacy.

In addition, new technology can involve substantial capital cost and require careful evaluation of added value before adoption. Although it is exciting to have innovations in the field, it is incumbent on the IP community to take the lead on careful assessment of new technology in terms of long-term safety, clinical usefulness, and efficacy and cost-effectiveness.

Second, the ability to perform quality multicenter trials still is limited by the nature of IP, but a major step was taken with the establishment of the Interventional Pulmonary Outcome Group (IPOG), a cohesive evidenced-based group for systematic assessment of each new technology. Ideally, the community as a whole should come together to develop a universally accepted approach to document, store, and access all IP procedural data. Doing so will enable large-scale data mining for hypothesis generation, quality improvement, and practice-changing studies.

Finally, we must ensure the quality of training for the next generation of IP physicians. In addition to procedure competency, standardized curricula, and certification examinations, we must ensure that the training for and practice of IP are grounded in evidence-based medicine.

Summary

IP provides diagnostic and therapeutic options that span the spectrum of benign and malignant airway and pleural disorders. The constant innovations in diagnostic and treatment modalities have continued to energize the field and further push the boundary of pulmonary medicine.

IP has gained recognition and interest from the medical community and the public, and providers must strive to practice evidence-based medicine supported by high-quality research and best-practice guidelines. The future is both exciting and challenging.

Acknowledgments

Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following: M. M. W. has served as a consultant to Boston Scientific; Nuvaira Inc; Olympus Corporation; and Veracyte, Inc and has served as a reviewer on the Data Safety Monitoring Board for CSA Medical Inc. F. J. F. H. has served as a consultant to Broncus Medical, Inc; BTG plc; Olympus Corporation; Pulmonx Inc; and Uptake Medical and has received research funding from them. A. C. has served as a consultant to Auris Health, Inc; Boston Scientific; and Olympus Corporation and has received research funding from Auris Health, Inc; Boston Scientific; Olympus Corporation; and Veran Medical Technologies. G. C. has served as a consultant to Boston Scientific; Medtronic plc; Pinnacle Biologics, Inc; and Restor3D and has received research funding from Intuitive Surgical Inc and Pinnacle Biologics, Inc. L. Y. has served as a consultant to AstraZeneca; Boston Scientific; Olympus Corporation; Veracyte, Inc; and Veran Medical Technologies.

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