Interventional Pulmonology for Lung (and other) Cancer

Hsienchang Thomas Chiu, MD
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Hsienchang Thomas Chiu, MD, has no financial interests or other relationships with commercial concerns related directly or indirectly to this presentation. He will not be discussing off-label drug uses.

Dr. Chiu is an Assistant Professor of Internal Medicine, Division of Pulmonary and Critical Care Medicine. His interests are in interventional pulmonology for both cancer and non-cancer related airway and pleural diseases.

Introduction

Lung cancer is one of the most commonly diagnosed cancers globally, accounting for 12.4% of new cancer cases. It is also a cancer associated with a high degree of morbidity and mortality, accounting for 29% of cancer deaths. In the year 2002, there were 1.35 million new cases of lung cancer world wide, and 1.18 million people succumbed to the disease[1]. Both expected survival and optimal treatment strategy depend the stage of presentation and the host factors. When patients present with suspected lung cancer, timely diagnosis and accurate staging is crucial in the selection of treatment modality. When disease progresses and complications from cancer arise, palliative measures are needed to minimize the effects of morbidity as definitive treatment continues. Likewise, when other cancers metastasize to the thorax, their presence causes similar morbidities. Many techniques have been developed to address these issues, and this collection of procedures formed the core of interventional pulmonology.

Interventional pulmonology is a discipline of pulmonary medicine with emphasis on procedures to diagnose and manage various disease processes that arise in the lungs and the pleural spaces. It seeks to achieve these goals in a minimally invasive manner. It develops from the philosophy that if there is a clinical problem it could be addressed through an intervention, and if current tools and methodology are inadequate new tools and techniques could be developed to achieve the goals. The repertoire of interventional pulmonology has applications for both benign and malignant disease – today's grand round will focus on its role in malignant diseases.

Diagnosis and Staging of Lung Cancer

When facing lung cancer, the recognition of disease, the tissue confirmation of disease, and the staging of disease are all of great importance in selecting the appropriate modality of treatment. As in most cancers, lung cancer is usually silent in the early stages, and discovery usually occur as incidental radiographic findings or when disease becomes advanced enough to be symptomatic. In the 1960s and 1980s, several screening studies

Several screening strategies have been studied. Neither CXR screening alone nor CXR plus sputum cytology confer mortality benefits back in the 1960s. This screening method has been repeated in the 1980s in four separate studies from Johns Hopkins

Once again, while more cancers were detected, no survival benefit was detected. However, this does lead to recognition of radiographic occult lung cancer, which is early central lung cancer that is not yet visible on CXR and CT. ROLC could be

detected on sputum cytology and endobronchial inspection. ROLC are squamous carcinoma of the lung. Natural history of the pulmonary SCC

Radiographic occult lung cancer and enhanced visual recognition

Lung cancer is often silent in its early stages, and disease is often not recognized until it has progressed to advanced stages. Several large screening studies in the 1960s [2] [3] and the 1980s [4], [5], [6], [7], [8] utilizing CXR and sputum cytology resulted in diagnoses of more lung cancer cases but with no improvement in survival. They also led to recognition of radiographic occult lung cancer (ROLC) – lung cancers detected by sputum cytology but undetectable by radiographic means. These cancers are predominantly squamous cell carcinoma. They are thought to progress through the following sequence: hyperplasia -> metaplasia -> mild/moderate/severe dysplasia -> carcinoma in situ -> invasive bronchiogenic squamous cell carcinoma. While dysplasia sometimes regress, the rate of progression from CIS to actual cancer has been estimated as high as 87.5% [9]. Upon bronchoscopic airway inspection, they could be detected endobronchially – sometimes. While actual carcinomas are usually detectable, carcinoma in situ detection is much more difficult utilizing conventional white light bronchoscopy – only 29% [10]. This led to development of autofluorescence bronchoscopy to assist in the search for these precancerous lesions.

In white light bronchoscopy, the light source illuminates the airway with the full spectrum of visible light and observes reflected, back-scattered, and absorbed light. White light also induces tissue fluorescence, but its intensity is low and easily overwhelmed by reflected and back-scattered light. In autofluorescence bronchoscopy, a 442 nm wavelength blue laser light source is used, and the resultant fluorescence image is captured and filtered and the intensities of the red and green fluorescence are measured. In dysplastic and cancerous lesions, there is a slight decrease in the red and a marked decrease in the green fluorescence; therefore the lesion appears red in a green background. Recent studies utilizing fibered confocal fluorescence microscopy revealed the main fluorophores from airway AF are located in the subepithelial elastin network, and decreases in AF represents a disruption in the basement membrane matrix [11].

How well does it work? In one study involving patients with proven or highly suspicious for lung cancer, using AFB in conjunction with WLB increased the sensitivity from 25% to 67% [12]. However, a study of patients with history of smoking related cancer but no known residual disease revealed no increase in detection of CIS or severe dysplasia (Kurie, Lee et al. 1998). The differences in the two studies may be the result of different study population versus differences in pathology interpretation. However, AFB has one major weakness in its low specificity – many non-malignant causes, including suction artifact and prior biopsy sites would show up with increased R/G ratio – any disruption in the basement membrane matrix would do. As such, routine bronchoscopic surveillance with AFB is not recommended outside of research protocols.

Another approach to improve the bronchoscopic airway inspection involves the use of narrow band imaging to highlight the subepithelial vascular pattern. As many other bronchoscopic technologies, narrow band imaging was first developed for and validated in GI endoscopy in demonstrating vascular pattern changes in precancerous colonic polyps and Barrett's esophagitis. Narrow band imaging refers to use of selected spectrums of the light source in order to enhance the contrast in hemoglobin-containing structures – namely, vessels. Conventional bronchoscopy utilizes white light that is composed of red (600-700 nm), green (500-600 nm), and blue (400 – 500 nm) filters. NBI bronchoscopy utilizes blue 1 (400-430 nm), blue 2 (420-470 nm), and green (560-590 nm) filters for its light source. This optimizes the absorptive spectrum for hemoglobin, which is near the 415 nm wave length. Under NBI visualization, the blood vessels appear in dark blue that is sharply contrasted with the pink background of the bronchial mucosa. The original study from Japan utilizes NBI light source in conjunction with a high magnification videobronchoscope that when combined with a high definition monitor that enlarge mucosal details by 110 fold [13]. This combination allows for observation of dotted, complex, and tortuous vessel network that are recognized evidence of neoangiogenesis. In the United States, however, the NBI bronchoscope that is commercially available only offers improved resolution and limited magnification. In a pilot study seeking validation of the technology, NBI bronchoscopy was able to detect in 23% of its study patients dysplasia and carcinoma not detected by WLB alone [14]. Additional data needed in order to fully validate the technology. From personal experience, NBI does highlight the highly abnormal vascular patterns in areas clearly identified as abnormal in WLB, but lacking higher magnification I have never seen abnormal vascular pattern in places where WLB is normal.

One salient take home message from the various bronchoscopic surveillance studies is that while we could identify precancerous lesions and attempts to treat them, there is no proven mortality benefit at this point. In 44% of patients, synchronous and metachronous lesions were noted in the airways, supporting field cancerization theory [15]. As even the smallest bronchoscope could only reach the 5th to 6th generation bronchi, there are large portions of the tracheobronchial tree that could not be examined visually. Furthermore, detailed examination of additional generation of bronchi increases the procedure time exponentially and complete examination down to the 6th generation is exceeding difficult. This presents a great challenge to bronchoscopic inspection as means of cancer screening.

Beyond the visible range – quest for the peripheral lesions

Shifting gears, we now address the challenge presented by pulmonary nodules. By definition, they are less than 3cm in diameter and are completely surrounded by lung parenchyma. They may or may not be connected to an airway, and they could be located either centrally or peripherally. The prevalence of pulmonary nodules varies greatly depending on the method of detection, the study population, and definition of a pulmonary nodule. When pulmonary nodule referred

to coin lesions identified by CXR back in the 1950s, prevalence was 0.2% [16]. When low dose rate chest CT were used in screening studies during the 1990s and the 2000s, prevalence varies from 8% to as high as 51% in region where incidence of infectious granulomatous disease such as histoplasmosis are very high [17], [18], [19]. When nodules are discovered, management is triaged into either radiographic surveillance, attempts at biopsy, and surgical resection, depending on exact size, appearance, and likelihood of neoplastic disease in the patient in question. The lower limit of feasibility in biopsying a nodule through any modality is around 7 to 8mm in size. While relatively safe, endobronchial biopsy utilizing conventional bronchoscopy with fluoroscopic guidance is limited as nodules below 2cm in size are rather unlikely to be successfully sampled unless there is a clear open bronchus sign. CT-guided transcutaneous needle aspiration, while having fairly high success rate in sampling nodules 1cm or above, does carry with it a much higher rate of pneumothorax when compared to bronchoscopy (15 to 30% depends on location and surrounding lung parenchyma versus 1 to 2%) as the needle have to puncture the parietal and the visceral pleurae on its way to the lesion. Surgical resection, being the most definitive of treatment options, has its own morbidity and mortality that may be unacceptably high in patients who have significant cardiopulmonary and other co-morbidities. Better sampling methods were needed.

Several techniques were developed to meet this need. The first of which is the use of radial probe endobronchial ultrasound to help confirm the correct branch of airway has been selected to insert sampling tools. Utilizing the rotating radial ultrasound employed in EUS, the small and semi-rigid probe, ~ 2mm in size, is directed to the airway in question and advanced until its ultrasound image change from echogenicity of normal air-filled bronchus/lung to that of a solid lesion. Once lesion is detected, sampling tools are sent to the same location to obtain tissue. While providing real time feedback, this method is severely limited by the semi-rigid nature of the radial probe, which makes travel into the certain parts of the lung exceedingly difficult. Furthermore, locating the suspected lesion is often a game of trial and error, and if there is no airway directly nearby, the technique does not work. In a study targeting lesions 3cm or less in size, radial probe EBUS technique increased the diagnostic yield to 70% - provided that the lesion is accessible by the probe [20].

Another technology was developed to meet the challenge, the electromagnetic navigational system. Combining an eight-way steerable probe equipped with a magnet tip with an electromagnetic field generator/detection board placed beneath the patient, the three-dimensional location of the probe is superimposed on a virtual lung that is reconstructed from CT images of the patient. Target is pre-selected during the planning phase and it is projected in the virtual lung along with the reconstructed airways, and once the bronchoscope is maneuvered as to its closest point of approach to the target the steerable probe takes over with navigating the remaining distance, using its eight-axis of rotation to make turns impossible to make with the bronchoscope, and direct a thin extended working channel to the target area, which is left in place to guide biopsy tools.

Although rather complicated, ENB is a very powerful technique allowing endobronchial access to places that could not be previously reached with any degree of precision – diagnostic yield of nodules greater than 2cm nodules increased to 74% [21] and 50% for smaller nodules [22]. In a study combining ENB with radial probe EBUS going after lesions primarily 2 to 3cm in size, diagnostic yield of 69% for radial probe EBUS, 59% for ENB, and 88% for combined technique was reported [23]. However, in the same study, pneumothorax rate of 5 to 8% were reported, up from the previously reported rate of 3.5%. The widely variant diagnostic yield and complication rate aptly highlighted the difficulty of systemic analysis of a procedure that is highly dependent upon operate skill and with greater variability of difficulty from lesion to lesion due to size, location, and other patient characteristics.

Also utilizing three-dimensional reconstruction of CT-images, a third technology was developed to address the same difficulty of sampling peripheral lesions bronchoscopically. CT-assisted bronchoscopy system, like ENB, also takes the radiographic data to provide three-dimensional airway reconstruction. However, instead of utilizing an electromagnetic system to guide a steerable probe to target, CT-assisted bronchoscopy focus primary on the visual feedback of the bronchoscopist. Once a target is selected on the CT image during the planning phase, the software-based system automatically calculate three varying paths through the bronchial tree that lead to the closest point of approach to the target. Furthermore, during the procedure the virtual image is displayed adjacent to the actual bronchoscopic image, and utilizing pattern recognition software the system could synchronize the virtual image with the actual image during each turns in the airway to ensure the bronchoscopist stays on the correct path. Once the bronchoscope reached as far as it could approach, the target is also projected virtually in the reconstructed image to assist transbronchial sampling of out of reach targets. The system has been commercially available only for about a year and validation studies are still in progress. It has the advantage over ENB in that it uses exactly the same tools and the same skill sets as in conventional bronchoscopy, and its disadvantage is that conventional bronchoscopes are larger and less maneuverable than the steerable probe used in ENB. Which technology will prevail remains to be seen.

Mediastinal and hilar lymph node staging

Once lung cancer is diagnosed, proper staging is vitally important in both prognosis as well as guiding treatment modality. When lung cancer progresses, it does so in one of four ways: 1) local invasion, 2) lymphatic dissemination, 3) hematogenous metastasis, and 4) lepidic spread. Of these, local invasion is demonstrated radiographically and surgically. Hematogenous metastasis is usually demonstrated radiographically, and could be confirmed via percutaneous biopsy if in doubt. Lepidic growth is demonstrated both on histology of the diagnostic material and radiographic findings. Lymph node involvement, however, presents a unique challenge.

Lymphatic drainage of the lungs empties into chains of lymph nodes that start intraparenchymally before extending to the hila and finally the mediastinum. The mediastinum is separated from the lungs by the pleurae. As lung cancer progresses along the lymphatic route it becomes increasing difficult to eradicate. In non-small cell lung cancer, when there is local-regional lymph node involvement, defined as nodal involvement no greater than the hilar lymph nodes, 5 year survival rate drops from 42% without to 29% (accounting for all tumor sizes and local extension and without metastatic involvement). When lymph node involvement progresses past the confines of the pleurae and extends into the mediastinum, 5 year survival further decreases to 16%. When lymph node involvement extends past the mid-line or outside of the thorax, 5 year survival drops to 7% [24]. Currently, disease with only local-regional lymph node involvement and no distant metastasis could be treated with surgical resection followed by adjuvant chemotherapy, while disease with mediastinal lymph node involvement are only treated with surgical resection if neoadjuvant chemotherapy could eradicate lymph node involvement, which is uncommon. Therefore, timely and accurate lymph node staging is crucial in the management of lung cancer.

Traditionally, lymph node staging is based either clinically or pathologically – clinically based on available radiographic data, and pathologically based on surgically sampled lymph nodes. Clinical staging based simply on CT and PET scans are non-invasive but their sensitivity and specificity is only 76.9%/55.3% for CT and 80.0%/70.1% for PET scan [25]. With significant false positive and false negative rate, relying upon clinical staging alone will incorrectly deny patients to potentially curative local regional control (surgery versus stereotactic radiation therapy) and also subject patient with advanced disease to unnecessary surgery. Surgical staging, while serving as the gold standard in terms of diagnostic accuracy, does have certain drawbacks. Surgical staging is performed as cervical mediastinal exploration, anterior mediastinotomy (Chamberlain's procedure), video-assisted thoracoscopic surgery, and open thoracotomy. CME allows for sampling of lymph nodes anterior to and next to the trachea. Chamberlain's procedure allows for sampling of the paraaortic and subaortic (the AP window nodes). VATS and thoracotomy allows for sampling of subcarinal and the ipsilateral hilar nodes of the targeted hemithorax. Each procedure has areas of lymph nodes that could not be sampled, and each procedure has its own set of associated morbidity and mortality risks.

In search of a less invasive mean to sample the intrathoracic lymph nodes, convex probe endobronchial ultrasound bronchoscopy, or simply EBUS bronchoscopy, was developed. Mounting a linear array ultrasound probe at the tip of the bronchoscope, the working channel of the bronchoscope is angled so when the transbronchial needle catheter is extended it will pass in front of the field of ultrasound. This allows for extremely precise locating and sampling of nearly all the mediastinal and hilar lymph nodes immediately adjacent to the tracheobronchial tree, leaving only the aorto-pulmonary window, the pre-vascular, the paraesophageal, and the pulmonary ligament lymph nodes out of reach.

EBUS bronchoscopy is minimally invasive. Its complication rate of pneumothorax is around 0.05 to 0.1%, and its complication rate of post-procedure hemorrhage is unknown as none has been reported. It is most easily performed under general anesthesia, so complication rate from general anesthesia should be included in the risk assessment for an EBUS bronchoscopy. EBUS has very high sensitivity and specificity in detecting lung cancer involvement in the lymph nodes – 92.3% and 100% respectively, with a negative predictive value of 97.4% in one of the few studies where every EBUS lymph node sampling was followed by a surgical sampling to determine its false negative rate [25].

Pulmonary Complications from Malignancy

In addition to providing tissue diagnosis and staging information, interventional pulmonology also provides means of symptom alleviation when disease progresses. When lung and other cancers develop intrathoracically, the disease process could affect one of five compartments – the parenchyma, the airways, the vasculature, the lymphatics, and the pleural spaces. While some morbidity is caused by tumor's retained and often unregulated endocrine, paracrine, and exocrine functions, others adversely affect the patient simply through mass effect. Interventional pulmonology mainly focuses on morbidities of the airways and the pleural spaces.

Airway complications from malignancy

When lung cancer progresses or other cancers metastasized to the lungs, airway compromised could occur in one of several ways – direct endoluminal tumor growth/invasion, extrinsic compression through mass effect, and submucosal tumor infiltration causing both hyperemia and lymphedema. Oftentimes, a combination of the above would be present when cancer is advanced. Resultant airway narrowing will cause bronchial obstruction and atelectasis of lung parenchymal distal to the obstruction. If the obstructed area is sufficiently large and patient does not have adequate pulmonary reserve to compensate for the loss, dyspnea and hypoxia could occur. Post-obstructive pneumonia could easily develop in such settings. If the tumor invades into a nearby pulmonary vasculature, fatal hemoptysis could occur with very little warning. If there is significant amount of tumor neoangiogenesis, significant but non-life threatening hemoptysis could occur. Furthermore, if tumor erodes through the lumens of esophagus and trachea, tracheoesophageal fistula could occur and cause recurrent aspiration events.

Tracheobronchial obstruction and treatment modalities

Tracheobronchial obstruction from tumor is a medical emergency if it involves one of the major airways. As airway lumen narrows, patient is usually not symptomatic until there is more than 50% of reduction in the luminal diameter. At

that stage, laminar airflow is disrupted and patient becomes rather symptomatic. The tachypneic response to dyspnea merely results in worsening turbulent flow and results in a downward spiral. Also, when the airway diameter narrows by 50% the cross sectional area is reduced to 25% of the original, and the obstruction will soon progress to complete obstruction. Tracheal obstructions are always emergencies, as they could quickly lead to respiratory failure and death.

Once airway obstruction is complete and the post-obstructive atelectasis develops, patient actually may experience some relief in his/her symptoms, provided that the patient has enough pulmonary reserve to be able to compensate for the loss of the affected region, and that hypoxic vasoconstrictive response is not blunted by vasodilators such as calcium channel blockers or nitrates. Post-obstructive pneumonia could sometimes occur, although more commonly continued production of bronchial and alveolar secretions mere results in "drowned lung" appearance. Once the airway obstruction is complete, the lung parenchyma will not likely regain aeration after 6 to 8 weeks of complete obstruction even if obstruction is subsequently removed.

The type of obstruction and the specific location of the obstruction will dictate what airway intervention could be performed and its likely efficacy. As airway intervention are almost always treating only "the tip of the iceberg" with no ability to affect underlying tumor, even successful reestablishment of airway needs to be followed with definitive treatments such as chemotherapy or radiation therapy to optimize the likelihood of future airway patency.

In lung cancer and other metastatic cancers whose spread is primarily endobronchial (breast, renal, thyroid, renal, and melanoma all have propensities toward endobronchial spread), tumor could be resected through combination of rigid and flexible bronchoscopic debulking following ablation and devitalization utilizing one of the many immediate ablative modalities to be discussed below. Unlike benign strictures, balloon dilation is rarely used in malignant diseases as obstruction occurs at sites where the airway luminal structure is already compromised, and uncontrolled dilation could result in airway perforation. In cases where the tumor is pedunculated, polypectomy snare could be used to remove the tumor in its entirety through transecting the stalk. In most other cases where the tumor is broad-based, modalities such as laser, electrocautery, and argon plasma coagulator could be used to achieve immediate ablative effect through thermoablation. The different modalities have different depths of penetration and area of effects, and selection is as much based on preference of the interventionalist as is based on the type of lesion and the desired approach.

In diseases that involve the lobar and segmental carina treatment is much more complicated, as frequently disease involvement spreads along the bronchovascular tree and affects distal bronchi as well. If disease extends distally and there is no open segment to open an obstructed airway to, immediate endobronchial ablation will not be successful.

If one does not need to achieve immediate ablative effect due to critical airway obstruction, several techniques with delayed effects could be used to treat much larger areas. Cryotherapy has been used quite successfully for such purposes, although there is usually the need to repeat bronchoscopy several days after treatment to remove necrotic debris as dead tissue sloughs off with successful cryotherapy treatment.

Photodynamic therapy (PDT) is another treatment modality with delayed action and a broad area of effect, which is ideal for treating cancers with circumferential involvement and limited luminal penetration. Patient is first pre-treated with a photosensitizing agent, which is injected intravenously and allowed to circulate through the system and then allowed to washout of the system in 48 to 72 hours (Moghissi and Dixon 2003). The photosensitizer is preferentially retained in areas where there are vascular and lymphatic congestion – such as sites with neoplastic involvement. A laser is used to generate the desired wavelength of light, which is transmitted into the target site via a cylindrical diffuser that is extended to the target area via the bronchoscope. When cells that retain photosensitizer are exposed to light of the appropriate wave length it undergoes type II photo-oxidation reaction and releases oxygen singlets that causes direct cytotoxicity. Additional delayed effects are achieved through vascular disruption and immunologic response due to inflammation from tissue necrosis [26]. In the United States, the FDA approved photosensitizer is Photofrin, which is a purified hematoporphyrin derivative, which has absorption peak at the 630 nm range (red). Endobronchially, depth of penetration of 630 nm light is approximately 5mm, which limits the effect of PDT and avoids overpenetration. While quite effective in treating tumors of the above specified characteristics – diffuse and shallow – PDT does have one serious drawback: after administration of Photofrin, patient suffers 4 to 6 weeks of photosensitivity as if they have porphyria cutanea tarda, and severe sunburn could result if they are exposed to sunlight. This drawback limits PDT's utility in places where sun exposure is constant.

Endobronchial brachytherapy is another treatment modality that has delayed reaction and a prolonged effect. After endobronchial placement of a brachytherapy catheter in the desired location and secured to the patient's nostril, patient is then moved to the treatment area and radiation source – usually iridium-192, which undergoes beta-decay – is advanced into the brachytherapy catheter to the desired depth until the desired radiation dose is delivered. Multiple catheters could be placed for multiple sites or treatment and for straddling the carina [27].

Both low dose rate (< 1 Gray/hour delivered over several days) and high dose rate (5 to 15 Gray/several minutes delivered in 2 to 6 fractions for a total of 30 to 60 Gray) protocols exist, and different institutions have their own preferred regimens. Overall symptom response for cough, dyspnea, and post-obstructive pneumonia ranges from 64 to 90%, while fatal complication rate from massive hemoptysis and bronchial necrosis ranges from to 3.6 to 4.7% [28], [29]. With endobronchial brachytherapy, there is approximately 1cm radius of effect from the radiation, and as such is slightly superior to the penetration of PDT. At the same

time, this increased penetration comes at the price of increased complication rates from fatal hemoptysis and bronchial necrosis. Furthermore, the application of radiation occurs after placement of the brachytherapy catheter, and unless the bronchoscopy lab is in close proximity to the radiation therapy treatment area the catheter could easily be dislodged during transportation.

Once airway has been re-established, endobronchial stent placement may be considered to maintain patency, especially if faster acting modality with more limited penetration and duration of effect (laser, APC, electrocautery, mechanical debulking) was selected. Endobronchial stents come in many varieties, ranging from silicone, bare metallic, covered metallic, and hybrid silicone with metallic supports. They come in various shapes, ranging from simple cylindrical to hourglass shaped to Y-shaped. They are designed for different airway configurations (Y-stents for the trachea anchored to bilateral main stems, cylinder for normal airway, hourglass for tight strictures). Decision to place a stent should not be taken lightly as stenting itself comes with its own sets of complications, ranging from something as simple as a vague chest discomfort to frequent cough to erosion into nearby vessel causing fatal hemoptysis.

One common cause of mortality in patients with advanced lung cancer is that of fatal hemoptysis. This could occur when the tumor erodes directly into pulmonary vasculature, or when treatment strategies compromised the vascular wall integrity. History of non-massive hemoptysis does not guarantee that a patient's hemoptysis will develop into massive hemoptyis in the near future. When truly massive hemoptysis occurs, very little could be done until an airway is immediately established, as patient could asphyxiate in a very short period of time. Once airway is secured, non-involved lung should be intentionally isolated and ventilated to ensure adequate oxygenation and ventilation. Then, several modalities have been described to control the bleeding. One utilizes rigid bronchoscope to quickly establish an airway and rapidly advance the rigid scope pass the lesions in order to suction out the accumulated blood in distal lesions as well as tamponading the source of bleeding. As distal airways are cleared, the bronchoscope is then slowly withdrawn while laser is applied to all the exposed tumor on the way out to cauterize any residual bleeding not stopped by the rigid tamponade.[30] Another technique utilizes the flexible bronchoscopy and the argon plasma coagulator catheter, which is quickly advanced to the bronchus where the bleeding is coming form and then using continuous stream cauterize the blood into a clot, to be left in place and gradually retracted and reabsorbed by the body in the coming days. [31] Other techniques involves placement endobronchial balloon blocker [32] and of injecting thrombin directly to the bleeding site.[33] Most of these measures are temporary, and definitive procedures such as IR-guided embolization of bleeding vessels should be pursued as soon as feasible.

Another catastrophic complication arising from cancer – more frequently with esophageal cancer – is the formation of a tracheoesophageal fistula. This usually happens to patients undergoing chemotherapy and radiation therapy for

advanced esophageal cancer and the tumor eroded through esophageal into the posterior membrane. As these patients tend to be extremely ill from cancer treatment they are rather poor candidates for any sort of surgical ligation with resection of the offending areas. A close-fitting tracheobronchial Y-stent could slow the rate of flow across the fistula and promotes healing, but the down side is that increased pressure by the stent against the mucosal surface and thereby creating more ischemic area. Oftentimes an esophageal stent also need to be placed in the esophagus to prevent the tracheal stent from eroding back into the esophagus.

Pleural complications from malignancy

In lung cancer and many other cancers disease progression could lead to pleural space involvement. This may take the form of pleural implantation by tumor, development of malignant pleural effusion, visceral pleural encasement resulting in lung entrapment, and thoracic duct obstruction resulting in chylothorax. A few interventions are available to address these issues in a minimally invasive manner.

Pleuroscopy for diagnosis

When pleural effusion develops in a cancer patient, pleural involvement may or may not be present. Cytology analysis of pleural effusion has diagnostic yield of 58 to 90%, depends on the type of cancer. [34] Repeating thoracentesis only adds another 5% to the yield whereas performing an unguided pleural biopsy adds another 7 to 12% diagnostic yield. Short of video-assisted thoracoscopic surgery and thoracotomy, pleuroscopy (medical thoracoscopy) has the next highest yield when it comes to detecting intrapleural cancer involvement, with diagnostic yield around 95%. In patient who are extremely ill and has extremely short life expectancy who is mostly bed ridden, repeating thoracentesis as needed once every few weeks may be all that is needed for palliation of symptoms.

Pleuroscopic and chest tube pleurodesis

When pleural effusion becomes symptomatic, a diagnostic and therapeutic thoracentesis should be performed in order establish whether if there is cancer involvement as well as determine whether if the lung would re-expand normally. If it does not, the possibility of lung entrapment or obstructing endobronchial lesion causing volume loss should be entertained. Assuming the lung re-expands normally, patient should be observed for recurrence of symptoms to determine rate of reaccumulation. If reaccumulation is fast, pleurodesis could be considered.

Pleurodesis simply introduces a noxious stimulus to the pleural space, with resultant inflammatory response that should ideally obliterate the potential space between the visceral and parietal pleurae. Chemical pleurodesis could be performed through a simple chest tube or even a small bore pigtail catheter, in both

inpatient and outpatient setting. Irritating chemical such as talc slurry, doxycycline, and bleomycin has been used to achieve pleural symphasis. Success rate ranges from 65 to 90%.[35] Talc poudrage through pleuroscopy could ensure direct visualization of applied talc, and the end result is similar to using talc slurry and slightly greater than 90% efficacy. Procedure is usually painful, and patient has a 2% chance of ARDS development as well as a procoagulable state due to the intense inflammation. Furthermore, as the procedure causes significant pleuritic pain, PCA is usually needed for pain control. Usually, pleural symphasis is achieved in 4 to 7 days, at which point chest tube could be removed. When chemical pleurodesis is not successful, mechnical pleurodesis through VATS could be attempted. Rate of success is also very high, greater than 90%.

An alternative to chemical or mechanical pleurodesis is the placement of a cuffed, tunneled intrapleural catheter. Such a catheter could provide drainage on daily basis if needed. Its placement is fairly simple, takes approximately 30 minutes with local lidocaine only. Once the catheter is in place, daily drainage will eventually causes a gradual pleural symphasis with 6 to 8 weeks amongst approximately 55% of the patients. If an intrapleural catheter has been placed, the exit site and the effusion must be observed for signs of infection, which could occur 2 to 8% of the time.

Summary

1. Interventional pulmonology techniques provide alternative to more invasive means of achieving diagnosis and staging, although each technique has its set of limitations that are yet to be overcome.
2. Combining different of diagnostic and treatment modalities is common in interventional pulmonology in order to achieve desired effects.
3. Central airway obstruction in lung (and other) cancer could be a life-threatening emergency and should be investigated as soon as possible.
4. Hemoptysis in cancer patients could be fatal and should be dealt with prompt upon presentation.
5. Prior history of scant hemoptysis is no guarantee that future hemoptysis episodes will not become massive.
6. Chemical pleurodesis and intrapleural catheter placement are two relatively non-invasive way to achieve pleural symphasis.

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