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Adult Pulmonary Medicine: Thoracic Oncology

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ABSTRACT

The American Thoracic Society Core Curriculum updates clinicians annually in adult and pediatric pulmonary disease, medical critical care, and sleep medicine at the annual international conference. The 2021 Pulmonary Core Curriculum focuses on lung cancer and include risks and prevention, screening, nodules, therapeutics and associated pulmonary toxicities, and malignant pleural effusions. Although tobacco smoking remains the primary risk factor for developing lung cancer, exposure to other environmental and occupational substances, including asbestos, radon, and burned biomass, contribute to the

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global burden of disease. Randomized studies have demonstrated that routine screening of high-risk smokers with low-dose chest computed tomography results in detection at an earlier stage and reduction in lung cancer mortality. On the basis of these trials and other lung cancer risk tools, screening recommendations have been developed. When evaluating lung nodules, clinical and radiographic features are used to estimate the probability of cancer. Management guidelines take into account the nodule size and cancer risk estimates to provide recommendations at evaluation. Newer lung cancer therapies, including immune checkpoint inhibitors and molecular therapies, cause pulmonary toxicity more frequently than conventional chemotherapy. Treatment-related toxicity should be suspected in patients receiving these medications who present with respiratory symptoms. Evaluation is aimed at excluding other etiologies, and treatment is based on the severity of symptoms. Malignant pleural effusions can be debilitating. The diagnosis is made by using simple pleural drainage and/or pleural biopsies. Management depends on the clinical scenario and the patient's preferences and includes the use of serial thoracentesis, a tunneled pleural catheter, or pleurodesis.

Keywords:
lung cancer screening; lung nodule; malignant effusion; lung cancer treatment toxicity; lung cancer risks

LUNG CANCER RISK FACTORS AND PREVENTION

Oisin O'Corragain and Jamie Garfield

Lung cancer is the second most commonly diagnosed cancer and is the leading cause of cancer-related mortality worldwide. In 2020, there were 2.2 million new cases of lung cancer and 1.8 million lung cancer deaths, representing 11.4% of all cancer diagnoses and 18% of cancer deaths globally. Lung cancer is often detected at an advanced stage and has an estimated 5-year survival rate between 10% and 20% in most countries (1). Identification of risk factors and implementation of prevention strategies are key to decreasing the global impact of lung cancer.

Lung cancer incidence and mortality vary widely and largely reflect regional patterns of tobacco use. Approximately one-third of the global population used some form of tobacco in the year 2000. Rates of tobacco use decreased to 25% of the global population in 2015 and are projected to decline further to 20% in 2025 (2). In 2019, an estimated 50 million U.S. adults (20.8%) reported current tobacco use (3). Cigarette use has declined over the past decade, whereas electronic cigarette (e-cigarette) use has increased, with the highest prevalence of e-cigarette use being demonstrated among adolescents and young adults. In 2020, 3 million (19.6%) high school students reported current e-cigarette use (4). E-cigarette use has been strongly associated with cigarette smoking, including initiation of smoking in previous nonsmokers, raising concerns for increased tobacco use in a younger demographic (5).

Risk factors for lung cancer may be broadly divided into modifiable and nonmodifiable factors (Table 1). Tobacco smoking remains the leading risk factor for lung cancer, with current smoking status conferring relative risks of 6.99 and 7.33 for women and men, respectively (6). Exposure to radon is the leading cause of lung cancer among nonsmokers in North America (7). Other

Table 1. Lung cancer risk factors

Modifiable	Nonmodifiable
Tobacco use	Genetics and family history
Environmental or second-hand tobacco smoke	Prior radiation therapy
Diet and alcohol intake	Use of immunosuppressive medications
Environmental or occupational exposures	Chronic lung disease
Radon	Chronic obstructive pulmonary disease
Asbestos	Alpha-1 antitrypsin deficiency
Arsenic	Asthma
Beryllium	Fibrotic lung disease
Cadmium	Chronic infections
Silica	Mycobacteria
Vinyl chloride	*C. pneumoniae*
Nickel compounds	Human immunodeficiency virus
Chromium compounds	
Coal products	
Mustard gas	
Chloromethyl ethers	
Air pollution	
Wildfire exposure	
Biomass exposure	

Definition of abbreviation: *C. pneumoniae* = *Chlamydia pneumoniae*.

increasingly recognized risk factors for lung cancer include environmental factors, such as air pollution, wildfires, and biomass exposure. Particulate matter with a diameter less than 10 μm is associated with lung cancer incidence (hazard ratio, 1.22 per 10 $\mu g/m^3$) (8). Cumulative exposure to smoke and particulate matter with a diameter less than 2.5 μm in wildland firefighters are associated with an increased lifetime risk of lung cancer (relative risk, 1.08–1.43) (9). Use of solid fuels and biomass for heating and cooking are important factors in developing countries, conferring a 70% increased risk of lung cancer (10).

Lung cancer prevention should focus on modifiable risk factors with exposure mitigation and abstinence. Occupational and household carcinogens, including radon and asbestos, should be avoided. Chemoprevention agents including glucocorticoids, myoinositol, prostacyclin analogs, thiazolidinediones, beta carotene, and aspirin have not been effective in preventing carcinogenesis (11). Genetic mutations that confer risk and biomarkers that predict the response to targeted agents are of growing importance.

Comprehensive tobacco control and cessation strategies impact lung cancer risk

(12). Countries with tobacco demand-reduction measures have seen the greatest decline in tobacco prevalence. These measures include monitoring use and prevention, tobacco-free policies, evidence-based cessation therapies, advertising bans, and tobacco taxes (1). Even in countries where tobacco demand-reduction measures are advanced, tobacco use remains high in marginalized groups, which include those with lower socioeconomic status, coexistent substance use disorder or mental health disorders, and minority ethnicity. Risk factor identification and mitigation are especially important in these high-risk groups.

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LUNG CANCER SCREENING

Sahil Patel and Janelle V. Baptiste

Patients with lung cancer are frequently asymptomatic in the early stages of the disease when a surgical cure is most likely. Screening is therefore currently the best strategy for early detection of lung cancer. In 2011, the NLST (National Lung Screening Trial) demonstrated that screening with low-dose computed tomography (LDCT) resulted in a 20% relative reduction in lung cancer death (1). Nine years later, the Dutch-Belgian NELSON (Nederlands–Leuvens Longkanker Screenings Onderzoek) trial (2) confirmed the results of the NLST. At 10-year follow-up, lung cancer mortality was 24% lower in men and 33% lower in women who underwent LDCT than in those who had no screening (2). The use of nodule volume measurements and doubling time resulted in a higher sensitivity (93.5% vs. 92.5%) and specificity (98.3% vs. 73.4%) for detecting lung cancer than in the NLST (2).

These trials provided evidence supporting the development of several lung cancer screening guidelines (3–5). In 2021, the U.S. Preventive Services Task Force provided updated guidance, recommending screening in adults aged 50 to 80 years with a 20 pack-year smoking history (3). This differs from the 30 pack-years used in the NLST and expands its previous screening criteria. In contrast, the National Comprehensive Cancer Network offers an alternative guideline that targets adults with additional risk factors for lung cancer and combines this with a shorter smoking history requirement and expanded age criteria (Table 2) (6).

There is a critical gap in knowledge about how best to identify and select individuals at high risk for lung cancer and refer them for lung cancer screening. Several lung cancer risk prediction models have been developed to address this knowledge gap and the limitations of existing guidelines (7). One such model, the Prostate, Lung, Colorectal, and Ovarian Model 2012 (PLCOm2012) estimates 6-year lung cancer risk of ever-smokers aged 55–74 years by using several risk factors. When compared against NLST eligibility criteria, the PLCOm2012 significantly improved sensitivity and had a significantly higher positive predictive value without compromising specificity (8). Other models include the Bach model, Lung Cancer Risk Assessment Tool, and Lung Cancer Death Risk Assessment Tool, each with an online risk calculator (9). Several organizations incorporate one or more of these models in their screening guidelines. National Comprehensive Cancer Network guidelines now recommend screening smokers who have a PLCOm2012 6-year risk of 1.3% or greater. More prospective studies are needed to determine the effectiveness and the feasibility of implementing a risk-based screening program (7).

The use of artificial intelligence to develop algorithms capable of identifying LDCT features that may be specific to lung cancer is emerging as a promising tool for improving lung cancer screening. Coupling artificial intelligence with radiomics or integrating artificial intelligence into analysis of genomic, plasma biomarker, biopsy staining pattern, and other patient-derived data are currently under investigation (10).

Despite the progress made in establishing lung cancer screening with LDCT, the uptake in clinical practice has been slow and inconsistent, and patient adherence has been low (11). Improving integration into practice will require education and changes in clinical practice patterns. Combining smoking cessation interventions with annual LDCT may further increase the benefit of screening. Identifying the best strategies to incorporate smoking cessation is an active area of investigation (12).

Table 2. Eligibility criteria for lung cancer screening in asymptomatic patients

	Age (*yr*)	Smoking History (*Pack-Years*)	Years since Quitting Smoking	Other
NLST	55–74	⩾30	⩽15	The NLST excluded patients with symptoms suggesting lung cancer (hemoptysis, weight loss), patients who had a prior history of lung cancer or other threatening cancers in the previous 5 yr, patients with recent pneumonia, and those who had undergone a chest CT scan in the past 18 mo.
NELSON	55–74	⩾15	<10	
AATS				
Tier 1	55–79	⩾30	–	Additional risk factor*
Tier 2	⩾ 50	⩾ 20	–	Lung cancer survivor for >5 yr
CHEST	55–77	⩾30	<15	–
ACS	55–74	⩾30	<15	–
CMS	55–77	⩾30	<15	–
NCCN				
Group 1	55–77	⩾30	<15	
Group 2	⩾50	⩾20	–	⩾1 additional risk factor†
USPSTF				
2013	55–80	⩾30	<15	Discontinue screening when the individual exceeds the upper age criterion, has not smoked for >15 yr, has a comorbidity that substantially limits the life expectancy, or is unable or unwilling to have curative surgery.
2021	50–80	⩾20	<15	

Definition of abbreviations: AATS = American Association for Thoracic Surgery; ACS = American Cancer Society; CHEST = American College of Chest Physicians; CMS = Centers for Medicare and Medicaid Services; CT = computed tomography; NCCN = National Comprehensive Cancer Network; NELSON = Nederlands–Leuvens Longkanker Screenings Onderzoek; NLST = National Lung Screening Trial; USPSTF = U.S. Preventive Services Task Force.
Adapted by permission from Reference 6. One pack-year indicates having smoked an average of one pack of cigarettes per day for 1 year.
*Additional risk factors for lung cancer defined by NCCN include cancer history, lung disease history, family history of lung cancer, radon exposure, and occupational exposure.
†Additional risk factors for lung cancer defined by the AATS include chronic obstructive pulmonary disease, environmental and occupational exposures, any prior cancer or thoracic radiation, and genetic or family history.

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CURRENT APPROACH TO LUNG NODULES

Ngoc-Tram Ha and Van K. Holden

Approximately 1.5 million incidental pulmonary nodules are detected in the United States annually (1). Pulmonary nodules can be benign or malignant; therefore, risk stratification is essential in their evaluation and management.

The likelihood of malignancy can be determined on the basis of clinical and radiographic characteristics, including size, location, density, margins, and presence of calcification. Smooth, well-defined margins and popcorn-like calcifications are characteristics of benign nodules, whereas irregular margins and spiculation are associated with malignancy. Other important features include morphologic patterns, wall thickness, and growth rates. Although the doubling time of most malignant nodules ranges from 20 to 400 days, subsolid malignant nodules double between 400 and 800 days (2).

Current risk stratification models categorize nodules into low, intermediate, and high malignancy risk on the basis of the clinician pretest probability of malignancy (pCA) (Table 3) . Use of these models can guide follow-up and management, but careful selection and application of available calculators are required. Models may not have been validated outside of the original patient population and may apply only to solid nodules (3).

Recent studies have focused on molecular biomarkers to further risk-stratify nodules, but additional clinical utility studies are

Table 3. Models to estimate the probability of malignancy in patients with pulmonary nodules

Model	Study Population	Number of Subjects	Prevalence of Malignancy	Nodule Size (*mm*)	Variables
Mayo Clinic (1997)	Incidental new PN detected with CXR	629	23%	4–30	Age, smoking history, history of extrathoracic cancer ⩾5 yr, nodule diameter, nodule spiculation, upper lobe location
VA (2007)	PNs seen at CXR and confirmed at CT and/or FDG-PET	375	54%	7–30	Age, smoking history, time since quitting smoking, nodule diameter
Herder (2005)	Patients referred for FDG-PET	106	57%	<30	Mayo Clinic model and FDG-PET avidity intensity (none, faint, moderate, intense)
BIMC (2015)	PN diagnosis with biopsy, or deemed benign if stable at imaging for ⩾2 yr	343	58%	4–30	Age, smoking, history of previous malignancy, nodule diameter, edges, nodule location, volume doubling time, minimum focal density, enhancement at contrast-enhanced CT, FDG-PET avidity

Definition of abbreviations: BIMC = Bayesian Inference Malignancy Calculator; CT = computed tomography; CXR = chest X-ray; FDG-PET = fluorodeoxyglucose–positron emission tomography; PN = pulmonary nodule; VA = Department of Veterans Affairs.
Data are from Reference 3.

needed (4). A bronchial genomic classifier demonstrated a 91% negative predictive value in current or former smokers with an intermediate pCA and inconclusive bronchoscopic biopsy results (5). Thus, a negative classifier result can down-classify the risk, resulting in less invasive procedures for benign lesions (6). An integrated plasma proteomic classifier (two plasma proteins and five clinical risk factors) has been evaluated in patients with undiagnosed 8- to 30-mm lung nodules and a low-to-moderate pCA of ⩽50% (7). A "likely benign" result accurately identified patients with benign nodules for up to 2 years of follow-up (8).

The Fleischner Society, the American College of Chest Physicians, the British Thoracic Society, and others have proposed guidelines on the management of incidentally identified pulmonary nodules (Table 4) (9–11). Lung-RADS from the American College of Radiology provides recommendations for screen-detected nodules (12), which the British Thoracic Society recommendations also address (10). On the basis of Fleischner Society guidelines, solid nodules measuring 6–8 mm are followed by computed tomography (CT) for 2 years, and subsolid nodules ⩾6 mm are followed by CT for 5 years. A partly solid nodule with a solid component ⩾6 mm is highly suspicious for malignancy. A repeat CT examination at 3 months, positron emission tomography (PET)-CT, or tissue sampling can be considered for a solitary pulmonary nodule >8 mm (9), depending on the pCA.

American College of Chest Physicians guidelines give further direction on the invasive management of solid, indeterminate nodules >8 mm on the basis of the pCA and patient preference. For patients with a pCA of 5–65%, functional imaging with PET should be considered. Nonsurgical biopsy is suggested when the pCA and findings of imaging tests are discordant, the pCA is 10–60%, a benign diagnosis requiring specific medical

Table 4. Management of incidentally detected pulmonary nodules

	CHEST 2013	BTS 2015	Fleischner Society 2017
Solitary solid nodules			
No follow-up	≤4 mm in patients with no risk factors for lung cancer	<5 mm or <80 mm^3	<6 mm or <100 mm^3
CT surveillance	No risk factors:	Indications:	6–8 mm or 100–250 mm^3
	>4 mm to 6 mm: 12 mo	≥5 mm to <8 mm or ≥80 mm^3 to <300 mm^3	Low risk: 6–12 mo, then consider at 18–21 mo
	>6 mm to 8 mm: 6–12 mo, then again at 18–24 mo	≥8 mm or ≥ 300 mm^3 and pCA < 10% using the Brock model	High risk: 6–12 mo, then again at 18–21 mo
	1+ risk factors:	5–6 mm	
	≤4 mm: 12 mo	CT at 12 mo, then management based on volume doubling time	
	>4 mm to 6 mm: 12 mo, then again at 18–24 mo	≥6 mm or ≥80 mm^3	
	>6 mm to 8 mm: 3–6 mo, then at 9–12 mo and at 24 mo	CT at 3 mo, then management based on volume doubling time	
CT at 3 mo, PET-CT, or tissue sampling	>8 mm	≥8 mm or ≥ 300 mm^3 and pCA ≥ 10% using the Brock model	>8 mm or >250 mm^3
	<5% pCA: CT at 3–6, 9–12, and 18–24 mo	PET-CT and risk assess using Herder model	
	5–65% pCA: PET	<10% pCA: CT surveillance	
	>65% pCA: surgical diagnosis	10–70% pCA: biopsy	
	Note there are additional recommendations on when to obtain nonsurgical or surgical biopsy.	>70% pCA: excision or nonsurgical treatment	
Solitary pure ground-glass nodules			
No follow-up	≤5 mm	<5 mm	<6 mm or <100 mm^3

Table 4. *Continued*.

	CHEST 2013	BTS 2015	Fleischner Society 2017
CT surveillance	>5 mm	⩾5 mm	⩾6 mm or >100 mm^3
	Annual CT for at least 3 yr (early follow-up at 3 mo may be indicated if >10 mm, followed by biopsy and/or surgery if nodule persists)	3 mo, then assess risk by using the Brock model <10% pCA: CT at 1, 2, and 4 yr >10% pCA: repeat CT, biopsy, or resection or nonsurgical treatment	6–12 mo, then CT every 2 yr until 5 yr
Solitary partly solid nodules	–	Management is the same as pure ground-glass nodules	–
CT surveillance	⩽8 mm with >50% ground glass: 3, 12, and 24 mo, followed by annual CT for an additional 1–3 yr	–	⩾6 mm or >100 mm^3 3–6 mo, then annual CT for 5 yr if solid component remains <6 mm
FDG-PET, nonsurgical biopsy, and/or surgical resection	8–15 mm with >50% ground glass: (may consider CT at 3 mo) >15 mm with >50% ground glass	–	Persistent nodules with solid components ⩾6 mm

Definition of abbreviations: BTS = British Thoracic Society; CHEST = American College of Chest Physicians; CT = computed tomography; CXR = chest X-ray; FDG-PET = fluorodeoxyglucose–positron emission tomography; pCA = probability of malignancy.
Data are from References 9–11.

treatment is suspected, or the patient desires proof of a malignant diagnosis before surgery. Surgical intervention is recommended when the pCA is >65%, the nodule is intensely hypermetabolic on PET images, the nonsurgical biopsy results are suspicious for malignancy, or the patient prefers undergoing a definitive diagnostic procedure. The risks and benefits of management strategies are discussed with the patient, and their preferences are elicited for shared decision-making regarding the optimal approach (11). The patient's candidacy for surgery and the feasibility of nonsurgical biopsies (e.g., percutaneous vs. bronchoscopic) are also considered, depending on the availability of resources and expertise. Robotically assisted bronchoscopy is an evolving technology, and additional studies evaluating its diagnostic yield and clinical impact are needed.

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LUNG CANCER THERAPEUTICS AND PULMONARY TOXICITIES

Codi Fitzgerald and Guang-Shing Cheng

The approach to lung cancer treatment is determined by a variety of factors, including tumor histology, stage, and patient comorbidities. Surgical resection is preferred for early-stage non–small cell lung cancer (NSCLC); stereotactic radiotherapy may be considered for poor surgical candidates (1, 2).

Treatment of advanced-stage NSCLC is often multimodal and may include chemoradiation, targeted therapies, and immunotherapy (1). Clinicians should have a high index of suspicion for treatment-related pulmonary toxicity in patients presenting with nonspecific symptoms of dyspnea, cough, fever, and exercise intolerance. This is particularly true for newer chemotherapeutic agents commonly associated with pulmonary toxicity.

Table 5. Pulmonary toxicities of lung cancer therapies

Therapeutic Class	Patterns of Toxicity
ICIs: anti–PD-1 (pembrolizumab, nivolumab), anti–PD-L1 (durvalumab, avelumab, atezolizumab), anti–CTLA-4 (ipilimumab)	• Interstitial pneumonitis • Organizing pneumonia • Acute fibrinous organizing pneumonia • Radiation recall pneumonitis • Alveolar hemorrhage • Pleural effusions
TKIs: EGFR (erlotinib, gefitinib, afatinib), ALK (crizotinib, alectinib), BRAF (dabrafenib), MEK1 (trametinib)	• Interstitial pneumonitis • Organizing pneumonia • Diffuse alveolar damage • Alveolar hemorrhage • Pleural effusions • Obliterative bronchiolitis
Conventional chemotherapy: gemcitabine, paclitaxel, docetaxel, pemetrexed	• Interstitial pneumonitis • Organizing pneumonia • Diffuse alveolar damage • Alveolar hemorrhage • Acute eosinophilic pneumonia • Noncardiac pulmonary edema • Radiation recall pneumonitis • Pulmonary fibrosis • Pulmonary arterial hypertension

Definition of abbreviations: ALK = anaplastic lymphoma kinase; EGFR = epidermal growth factor receptor; ICI = immune checkpoint inhibitor; TKI = tyrosine kinase inhibitor.

Immune checkpoint inhibitors (ICIs) have emerged as first-line therapy for patients with advanced-stage lung cancer who do not have a molecular target for treatment. ICIs work by targeting cellular immune pathways that regulate tumor recognition and death (3, 4). ICI-related pneumonitis is a potentially life-threatening complication of therapy, with the time of onset ranging from days to months after the initiation of treatment (4). Molecular therapies, including tyrosine kinase inhibitors (TKIs), target oncogenic mutations in the EGFR (epidermal growth factor receptor), ALK (anaplastic lymphoma kinase), and RET (RET proto-oncogene) oncogenic proteins (1, 2). The TKIs are first-line therapies for patients who harbor these mutations, which

are more commonly identified in younger patients with adenocarcinoma and a limited smoking history (1). TKI-associated toxicities include acute pneumonitis, organizing pneumonia, and diffuse alveolar hemorrhage (5). In patients without molecular targets, conventional chemotherapy is offered (1, 2). Toxicities and the timing of onset vary by chemotherapeutic class (6). Common patterns of pulmonary toxicity are summarized in Table 5.

Stereotactic radiation therapy is used in both early- and advanced-stage NSCLC. Radiation-induced lung injury encompasses a spectrum of disease, including acute radiation pneumonitis and chronic fibrosis (7). Patients with lung cancer are at increased risk of radiation-induced lung injury compared with patients with other malignancies. Risk factors include the radiation dosage, underlying lung disease, and ongoing tobacco use (7). In addition, patients treated with chemoimmunotherapy are at risk of radiation recall pneumonitis manifesting as pulmonary infiltrates within the prior field of radiation (6, 7).

When pulmonary toxicity is suspected, CT of the chest should be performed. Patterns of radiographic injury are nonspecific and include ground-glass attenuation and reticular opacities (4). Bronchoscopy should be considered to exclude infection, alveolar hemorrhage, and cancer progression. Lymphocytosis or eosinophilia in bronchoalveolar lavage fluid may support a diagnosis of drug-induced toxicity; however, no definitive studies can confirm treatment-related pulmonary toxicity (6, 7).

Treatment of adverse pulmonary events is largely based on expert recommendations (4, 8). Asymptomatic patients may be observed clinically. For patients with new or worsening symptoms and imaging findings consistent with ICI-related pneumonitis, therapy is typically discontinued. Corticosteroids may be initiated (1–2 mg/kg/d) and tapered over 6 weeks (4, 8). If there is no improvement with corticosteroids or there is evidence of rapidly progressive respiratory failure, additional therapies such as infliximab, intravenous immunoglobulin, and mycophenolate may be considered (4, 8). Decisions about rechallenging a patient with a particular agent should occur on a case-by-case basis, with consideration given to the severity of the previous reaction and alternatives for treatment. In general, patients with severe pneumonitis should not be rechallenged.

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MALIGNANT PLEURAL EFFUSIONS

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Malignant pleural effusions (MPEs) affect nearly 15% of patients with cancer and are associated with a poor prognosis. Median survival ranges from 3 to 12 months, depending on the type of malignancy (1, 2). The diagnosis of MPE is usually confirmed by cytologic analysis of pleural fluid, which should be drained under ultrasound guidance (2). Cytologic analysis of the initial drainage has a sensitivity of close to 60% (3) for identification of MPE. This increases an additional 15% with a second sampling (2).

Once the diagnosis of MPE is confirmed, management is determined by symptoms (Figure 1). For asymptomatic patients, therapeutic pleural interventions should be avoided, as the risk of complications outweighs any clinical benefit (2). The initial management of symptomatic patients should start with a large-volume thoracentesis. This can provide evidence of symptomatic improvement with drainage and be used to assess for expandable lung when coupled with pleural manometry (2). Although using pleural manometry may not reduce procedural complications (4), it can help differentiate between fully expandable lung and both entrapped lung and trapped lung, for which treatment options are more limited.

More than half of patients with MPE experience rapid fluid reaccumulation (i.e., within 1 mo) (5). Consequently, patients with a reasonable expected survival outcome should be evaluated for a definitive pleural procedure. This may

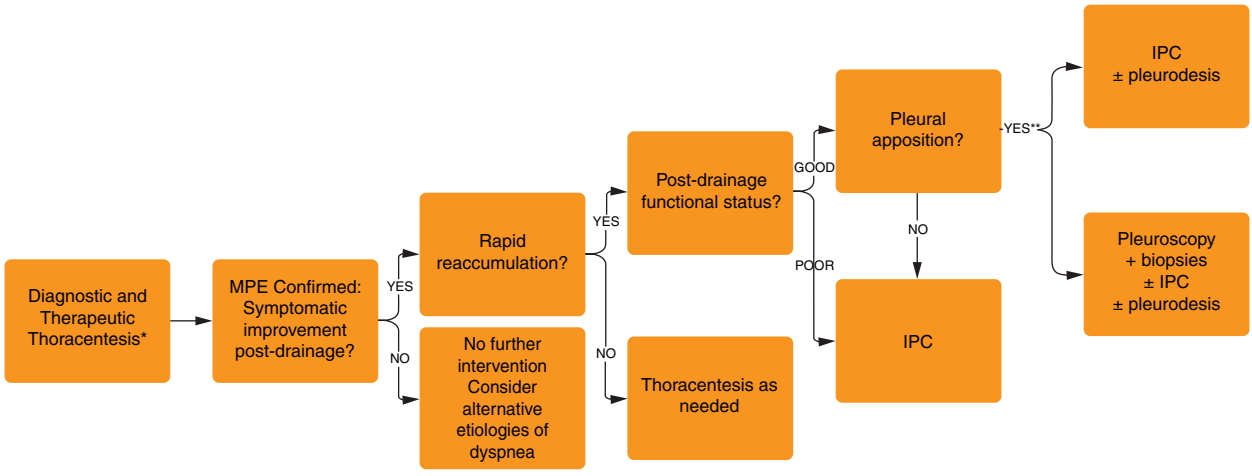

Figure 1. Treatment algorithm for malignant pleural effusion (MPE). *Consider pleural manometry and pleural fluid analysis: cell count and differential, chemistry (LDH [lactate dehydrogenase], protein, cholesterol, NT-proBNP [N-terminal pro b-type natriuretic peptide]), and cytology. Other pleural tests (e.g., flow cytometry, cultures, triglycerides) might be required, depending on the clinical scenario. **If the patient has a good performance status, expandable lung, and would prefer not to have a long-term indwelling pleural catheter (IPC), either IPC placement with daily drainage or IPC placement followed by talc pleurodesis can be considered.

reduce the total number of interventions required and may reduce the rate of procedural complications, improving symptoms and quality of life (5). Definitive procedures should be considered unless the prognosis is very poor, in which case repeat thoracentesis or management of dyspnea with opiates are reasonable options.

For patients with expandable lung, definitive treatment strategies include chemical and mechanical pleurodesis or indwelling pleural catheters (IPCs) (1). First-line treatment options are IPCs and chemical pleurodesis (6). IPCs are placed as an outpatient procedure, avoiding hospitalization for patients with a limited life expectancy, and they carry a lower risk of treatment failure. However, IPCs are associated with a higher risk of cellulitis and pleural space infection, at rates of 7.3% and 4.6%, respectively, than pleurodesis (2). Most cases of IPC-related infection can be treated with antibiotic therapy without removal of the catheter, reserving removal for those who do not improve with antibiotics. IPCs result in spontaneous pleurodesis in 16–65% of patients. Rates of pleurodesis can be increased with daily drainage or concomitant outpatient talc slurry pleurodesis through the existing IPC (7, 8). Chemical pleurodesis for management of MPE should be performed only in cases of fully expandable lung. The most effective pleurodesis agent is talc, which can be administered either via a poudrage (insufflation during thoracoscopy) or slurry (via an existing pleural drain).

For the 30% of patients with MPE and unexpandable lung, treatment options are limited (2). In this clinical scenario, IPCs are recommended, given the low risk of procedural complications (1). In patients with loculated MPE, IPCs are also preferred. For these patients, intrapleural fibrinolytics may help with drainage and improve symptoms, although this is at the expense of an increased bleeding risk and a higher cost (1, 2, 9). Future work is needed to better guide treatment for this specific patient population.

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