

International Consensus on Severe Lung Cancer—The Second Edition

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Background: Following the 2021 first International Consensus on Severe Lung Cancer, global attention to patients with PS 2–4 has grown significantly. Recent advances in novel therapies, interventional techniques, and supportive care, along with emerging real world data, have expanded treatment opportunities for this population. To incorporate these advances, we have updated the consensus.

Methods: A multidisciplinary panel comprising experts from oncology, radiation oncology, thoracic surgery, radiology, interventional medicine, respiratory medicine, critical care medicine, and nursing. After being presented with a comprehensive review of the current evidence pertaining to severe lung cancer and thorough discussions, the panel reached a consensus on 11 recommendations, each with over 70% expert agreement.

Results: The 11 consensus points focused on definition and causes (n=2), assessment and general strategies (n=4), and specific treatment modalities (n=5) were updated or newly developed. This updated consensus emphasizes dynamic and precise detection, robust life support, flexible application of novel therapies, and MDT guided treatment adjustment based on PS dynamics. Early rehabilitation and comprehensive supportive care are integral to disease management.

Conclusions: This consensus updates the definition, diagnostic evaluation, and treatment strategies, providing a practical framework for clinicians based on current evidence and multidisciplinary expert consensus. Prospective trials focusing specifically on patients with severe lung cancer are urgently needed.

Keywords: Severe lung cancer; performance status (PS); Delphi method; multidisciplinary team (MDT); consensus

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Introduction

According to GLOBOCAN 2022, lung cancer is the leading cause of cancer morbidity and mortality worldwide (1). The majority of clinical studies in lung cancer have enrolled only patients with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) score of 0–1, and there has been limited inclusion of those with a PS score of 2, with those with a PS score of 3 or 4 rarely being included. Due to the lack of high-quality evidence, best supportive care (BSC) is recommended for patients with a PS score of 3 to 4 in almost all current guidelines. In the real world, however, approximately 25% of patients with lung cancer present with a PS score of 3 or 4 at initial diagnosis (2) or attain scores between 3 and 4 during the course of treatment. Certain patients with high PS scores can benefit

from individualized anticancer treatment and additional life support strategies. For this reason, the Lung Cancer Research Team at the Guangzhou Institute of Respiratory Health, First Affiliated Hospital of Guangzhou Medical University, pioneered the concept of advanced severe lung cancer in 2017 (3) and further refined it in a featured article in 2019 (4). In 2021, 87 experts from China and other countries jointly formulated the first edition of the *International Consensus on Severe Lung Cancer*, which introduced the concept of severe lung cancer. This is defined as a condition in which a patient with cancer has a PS score of 2–4 at certain stages due to various acute or chronic comorbidities and/or treatment-related adverse events (TRAEs) but also a high probability of achieving survival benefits and/or improvement in PS score following

life support interventions and anticancer treatments guided by precision diagnostics and dynamic monitoring.

The first edition of the consensus has drawn attention to this patient population both domestically and internationally, spurring continuous exploration in this field. In recent years, an increasing number of clinical studies have included patients with a PS score of 2, while some real-world studies have broadened eligibility to include those with PS scores of 3–4. The ongoing development and approval of novel therapies have increased the number of antineoplastic drugs and regimens suitable for patients with advanced lung cancer. Furthermore, clinical medical technologies have advanced in diagnosis, monitoring, and treatment.

Therefore, a multidisciplinary expert panel collaborated to revise and update the *International Consensus on Severe Lung Cancer*, providing a reference for fellow professionals in the field.

Highlight box

Key findings

- This second edition refines the term “severe lung cancer” to refer to patients with Eastern Cooperative Oncology Group (ECOG) performance status (PS) 2–4 who may achieve survival or PS improvement via individualized treatment. It emphasizes precision diagnostics, life support, multidisciplinary team (MDT) collaboration, and adaptive therapies.

What was recommended and what is new?

- The first edition introduced the concept of severe lung cancer, emphasized the reversibility and fluctuation of PS, and recommended MDT-guided individualized multimodal treatment.
- This edition refines the definition of severe lung cancer, incorporates new assessment methods and advanced diagnostic techniques, and expands treatment options to include several novel therapies.

What is the implication, and what should change now?

- There should be a shift from palliative to active management for patients with a PS score of 2–4.
- MDT-guided precision medicine with continuous monitoring should be implemented.
- Early rehabilitation and comprehensive supportive care should be prioritized.
- Prospective evidence on novel therapies for patients with severe disease should be generated.
- Guidelines should be updated to reflect severe lung cancer care pathways.

Methods

This consensus was developed by an expert panel comprising a multidisciplinary team (MDT) with extensive experience and specialized knowledge in oncology, radiation oncology, thoracic surgery, radiology, interventional medicine, respiratory medicine, critical care medicine, and nursing. Experts were selected according to professional position, regional distribution, and clinical experience in managing severe lung cancer. The Preliminary Consensus Expert Panel (PCEP) was divided into eight subgroups, each responsible for updating content on a specific topic. Based on the population, intervention, comparison, and outcome framework, a systematic literature search was conducted across multiple databases, including PubMed, Embase, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), and Wanfang Med Online, from January 2000 to July 2024. The keywords used in the search included “lung cancer”, “poor performance status”, “poor lung function”, “comorbidities”, “complications”, “comorbidity”, “cardiopulmonary exercise testing”, “cardiorespiratory fitness”, “Charlson Comorbidity Index”, “Elixhauser Comorbidity Index”, “large airway obstruction”, “malignant central airway obstruction”, “adverse events”, “chemotherapy”, “radiotherapy”, “emergency radiotherapy”, “surgery”, “salvage surgery”, “interventional therapy”, “bronchoscopy”, “bronchial arterial”, “thermal ablation”, “epidermal growth factor receptor”, “anaplastic lymphoma kinase”, “antiangiogenic therapy”, “immune checkpoint inhibitors”, “antibody-drug conjugate”, “supportive treatment”, “extracorporeal membrane oxygenation”, “mechanical ventilation”, “nutritional support”, “anticoagulant therapy”, and “nursing care”. The findings were graded according to the Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009) (5). The expert panel discussed the update strategy for each topic based on the search results, with revisions made independently by the respective subgroups. Each recommendation required more than 70% panel agreement to be included in the final manuscript. Eleven experts including Chengzhi Zhou, Xinqing Lin, Qian Chu, Yuchao Dong, Min Li, Tangfeng Lv, Gen Lin, Ling Sang, Panwen Tian, Yang Xia, and Zhanhong Xie drafted the document. The first draft was then circulated to PCEP and underwent multiple rounds of editing, resulting in a preliminary consensus of 11 recommendations. Experts

who had not participated in the initial consensus process were subsequently invited to review and further modify the document. After repeated revisions, the final consensus document was completed.

In contrast to the first edition, the *International Consensus on Severe Lung Cancer—Second Edition* includes the definition of severe lung cancer and updated diagnostic and therapeutic strategies, including the application of new diagnostic and treatment techniques, based on emerging evidence. Additionally, the new edition incorporates new content on the assessment of severe lung cancer, timely acquisition of pathological specimen, and rehabilitation and care strategies. These updates aim to advance clinical practice and enhance the clinical relevance and practical value of the consensus.

Consensus 1: the concept of severe lung cancer

Severe lung cancer is considered to be a condition in which a patient has a PS score of 2–4 but also has a high probability of achieving survival benefits and/or improvement in PS score following individualized diagnosis and treatment.

Etiology

Three major factors contribute to the development of severe lung cancer: (I) TRAEs (e.g., lung injury), which may arise due to a variety of lung cancer therapies; (II) acute or chronic comorbidities affecting various organ systems, such as chronic obstructive pulmonary disease (COPD); and (III) cancer-related complications, including malignant effusions and paraneoplastic syndromes.

Targeted populations

Severe lung cancer includes not only patients with PS scores between 2 and 4 at certain stages but also those who have the potential to achieve survival benefits and/or improvement in PS score through various approaches and individualized multimodal treatments.

Value of diagnosis and treatment

The value of diagnosis and treatment for severe lung cancer depends on the integration of dynamic and precise detection, life support measures, and anticancer therapies.

Consensus 2: common causes

A cross-sectional study reported (6) that treatment-related adverse reactions (46.0%), severe cancer-related complications (45.6%), and acute exacerbations of chronic comorbidities (8.4%) may be the three major factors that contribute to severe lung cancer. These findings represent a change from the first edition of the consensus (level of evidence: 1a).

TRAEs

Surgery, radiotherapy, chemotherapy, targeted therapy [including antibody-drug conjugates (ADCs)], antiangiogenic therapy, and immunotherapy are all associated with serious adverse events (SAEs) that may lead to a decline in PS. However, prompt management of these events may lead to PS improvement.

Postoperative lung injury

A meta-analysis reported that the incidence of lung injury after thoracic surgery is 4.3% and that patients with lung injury have a mortality of up to 26.5% and a significantly reduced 1-year survival rate compared to those without lung injury (7).

Cerebral radiation necrosis

A retrospective study found that the rate of cerebral radiation necrosis was 4.7–9.2% in patients with metastatic brain tumors treated with stereotactic radiosurgery (SRS) at radiation doses of 18–30 Gy (8). With brachytherapy, the reported cerebral radiation necrosis rate was between 25% and 50% (9).

Chemotherapy- and/or immunotherapy-induced bone marrow suppression and comorbidities

Neutropenia is a common hematologic toxicity induced by chemotherapeutic agents. Prolonged neutropenia is associated with a significantly increased risk of infection (10). The reported mortality rate of patients with lung cancer and febrile neutropenia is 11.2% (11).

Bleeding caused by antiangiogenic agents

In a meta-analysis involving 12,617 patients with various solid tumors, the incidence of all-grade hemorrhage with bevacizumab was 30.4% and that of grades 3–5 was 3.5%. The risk of fatal hemorrhage was only 0.8%, but was

significantly higher in patients with lung cancer (relative risk =5.02) (12).

Tyrosine kinase inhibitor (TKI)-associated interstitial lung disease (ILD)

A meta-analysis found that the incidences of all-grade and high-grade (grade ≥ 3) ILD associated with epidermal growth factor receptor (EGFR)-TKIs (EGFR-TKIs) were 1.6% and 0.9%, respectively, with a mortality rate of 13.0% (13). In another meta-analysis, the incidences of all-grade and high-grade (grade ≥ 3) pneumonitis (including ILD) associated with anaplastic lymphoma kinase (ALK)-TKIs were 2.14% and 1.33%, respectively (14).

Checkpoint inhibitor pneumonitis (CIP)

The reported incidence of CIP in clinical studies is 3–5%, with a mortality rate of 18.2–22.7% among affected patients (15–17). The severity of CIP is positively correlated with PS score (18).

ADC-related adverse reactions

Common adverse reactions to ADCs included fatigue, hematologic toxicities, nausea/vomiting, lung injury, ocular toxicities, and peripheral neuropathy (19). A recent meta-analysis revealed that TRAEs occur in 91% of ADC-treated patients, with approximately 46% experiencing grade ≥ 3 events. Although most studies indicate that ADCs are generally well tolerated, their safety profiles vary across agents, with SAEs leading to treatment interruption or, in rare cases, treatment-related mortality (20).

Cancer-related emergencies

Cancer-related emergencies include malignant effusions, airway obstruction, venous thromboembolism (VTE), nervous system metastases, and paraneoplastic syndrome. Timely management of these conditions can improve patients' quality of life and PS scores (21).

Malignant effusions

Malignant pleural and pericardial effusions are the most common oncologic emergencies related to lung cancer. Pleural effusion occurs in 40% of patients with lung cancer, and malignant pleural effusion is an adverse prognostic factor (22,23), with PS score worsening markedly as the severity of pleural effusion increases (24). A high PS score is also a risk factor for poor prognosis in patients with pleural

effusion (25). Over one-third of malignant pericardial effusions are caused by lung cancer (26,27), and pericardial effusion is a risk factor for decreased survival in patients with lung cancer (28,29). Furthermore, patients with malignant pericardial effusion and a PS score ≥ 2 exhibit a worse prognosis (30).

Airway stenosis

Tracheal or proximal bronchial stenoses occur as complications in 20–30% of lung cancers, resulting in dyspnea, a poor PS score, and poor prognosis (21,31). Relief of airway obstruction can rapidly improve clinical condition, enhance quality of life, and lower PS scores (32,33).

VTE

Cancer is a risk factor for VTE, with a hazard ratio (HR) of 4.7 (34). VTE, including pulmonary embolism and lower extremity deep vein thrombosis, occurs in approximately 13.9% of patients with lung cancer (35) and is also a cause of death in these patients (36).

Paraneoplastic syndromes

Paraneoplastic syndromes can occur in patients with cancer, particularly those with lung cancer. They may affect the nervous, cutaneous, and musculoskeletal systems (37), leading to severe disability, irreversible PS deterioration, compromised quality of life, and reduced survival.

Acute and chronic comorbidities

Among patients with lung cancer, 87.3% have at least one comorbidity and 15.3% have severe comorbidity scores (38). Nieder *et al.* reported that those with lung cancer without comorbidities have lower PS scores (39). Another study also showed a positive correlation between the simplified comorbidity score and PS score (40), while other research suggests that patients with lung cancer and comorbidities have significantly lower survival rates than do those without comorbidities (41).

Heart failure (HF)

The incidence of HF in patients with lung cancer increases each year (42,43). HF elevates the risk of death in all patients with lung cancer (HR =1.85), and among those with early-stage disease, HF is associated with a reduced likelihood of surgery and an increased risk of postoperative complications (44).

COPD

COPD is a risk factor for lung cancer and is present in 40–70% of patients with lung cancer (45,46). One study reported that 50.2% of patients with non-small cell lung cancer (NSCLC) have coexisting COPD (47). Among patients with lung cancer and COPD, one-third are ineligible for surgery due to poor pulmonary function and other related factors (48). A meta-analysis of 29 studies reported that COPD is associated with a lower survival rate and increased postoperative pulmonary complications in patients with lung cancer (49).

ILD

Extensive epidemiological evidence supports the correlation between ILD and lung cancer. Patients with ILD have a 3.5- to 7.3-fold higher risk of developing lung cancer compared to the general population. Fifteen percent of patients with ILD may die from lung cancer, and the ILD incidence upon the diagnosis of lung cancer varies from 2.4% to 10.9% (50). The 5-year survival rate is significantly lower in patients with stage IA lung cancer and ILD than it is in those without ILD (54.2% *vs.* 88.3%; $P < 0.0001$) (51). Moreover, lung cancer develops in over 50% of patients with idiopathic pulmonary fibrosis (IPF) over the course of the disease (52). The coexistence of lung cancer is associated with increased mortality in this population (53). Studies have shown that patients with IPF undergoing lung cancer surgery face a significantly increased risk of postoperative acute exacerbation, with an incidence of approximately 20% and a mortality rate of up to 50% (54–57). In patients with lung cancer and ILD, various anticancer treatments may induce acute exacerbation of ILD (50).

Obesity

In individuals with obesity, the presence of adipose tissue around the rib cage, abdomen, and visceral cavity reduces lung volume and impairs airway stability (58,59). Moreover, patients with obesity exhibit impaired postoperative cough function and sputum clearance, as well as difficulty turning in bed, which contribute to significantly increased rates of perioperative complications and postoperative mortality compared to those without obesity (60,61).

Coronavirus disease 2019 (COVID-19) and other infections

Severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2) infection may pose risks across the continuum of care for patients with lung cancer. A meta-analysis showed that patients with lung cancer and COVID-19 have a two-fold higher risk of mortality compared to those without COVID-19 [HR =2.00, 95% confidence interval (CI): 1.52–2.63] (62). Patients with lung cancer and COVID-19 are prone to fluctuations in PS and progression to severe illness, which, if not promptly managed, may lead to death and disrupt overall disease management.

Consensus 3: value of diagnosis and treatment in severe lung cancer

The term “severe lung cancer” differs from “end-stage lung cancer” in that it emphasizes the clinical value of treatment and the potential for survival benefit. Patients in this category typically present with a transient worsening of condition, reflected by an elevated PS score relative to baseline, but may achieve partial or complete recovery following appropriate treatment, with survival often exceeding 3 months from the onset of the severe condition. Therefore, severe lung cancer is characterized not only by a PS score of 2–4 but also by the reversibility or fluctuation in PS. Furthermore, individualized treatment can provide survival benefits in this population (grade of recommendation: B; level of evidence: 2a).

Reversibility of PS score

The reversibility of PS score in patients with lung cancer reflects their ability to recover to baseline or near-baseline levels following prompt targeted treatment (*Figure 1A,1B*), with survival exceeding 3 months from the onset of the severe condition. In one study, 79% of patients with NSCLC treated with first-line gefitinib showed PS improvement. Notably, 68% of these patients improved from a PS score of 3–4 to one of 0–1 (63). In a retrospective study evaluating chemotherapy in patients with advanced NSCLC and a PS score ≥ 2 , 45.26% of patients exhibited improved PS scores (64). For patients with massive pleural and pericardial effusions, drainage can provide rapid symptom relief (25,65,66). Meanwhile, for patients with major airway obstruction, prompt and effective local bronchoscopic treatment can immediately alleviate the symptoms of airway obstruction (32,33). Therefore, the reversibility of PS depends on addressing the immediate

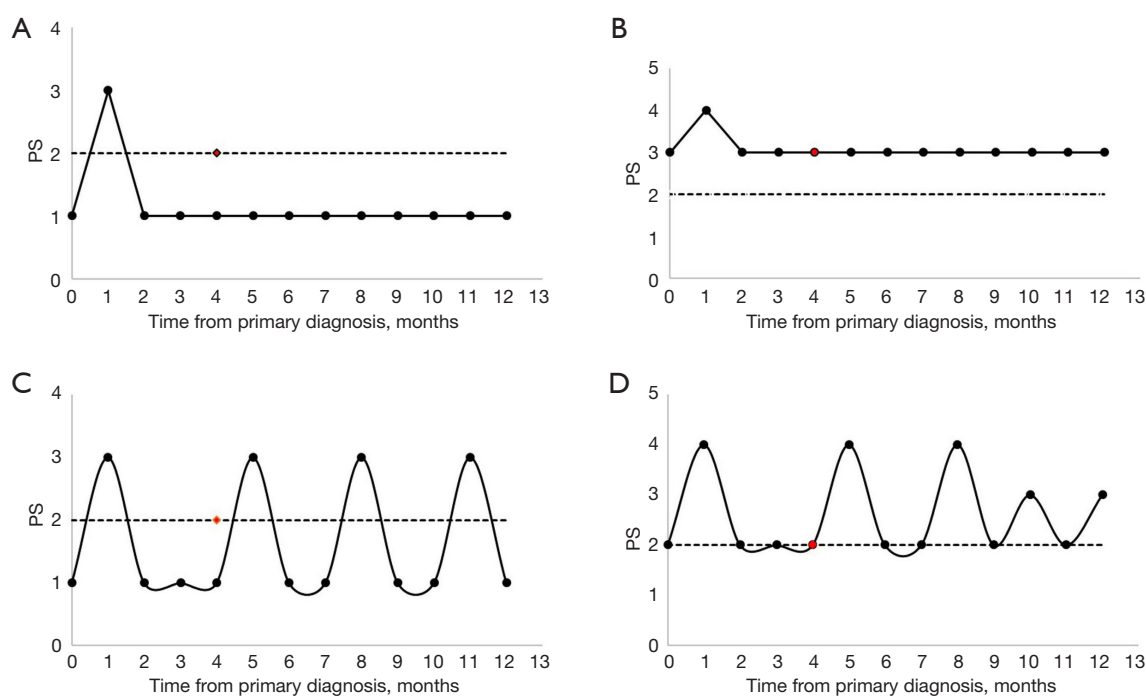


Figure 1 Schematic diagrams illustrating the fluctuation and reversibility of Eastern Cooperative Oncology Group PS. (A,B) Schematic diagrams showing PS improvement after treatment, illustrating reversibility; (C,D) Schematic diagrams showing PS fluctuation. PS, performance status.

causes of deterioration (67).

Fluctuation in PS score

In patients with lung cancer and chronic comorbidities or malignant pleural/pericardial effusions, relapse or exacerbation of the underlying disease may lead to fluctuations in PS. Timely intervention to reverse PS deterioration can help patients achieve long-term survival despite such fluctuations (*Figure 1C,1D*). One study that included 882 patients with lung cancer demonstrated that PS was adversely associated with increasing severity of comorbidities (68). In a study analyzing the clinical characteristics of patients with NSCLC and a PS score ≥ 2 , active respiratory support and management of comorbidities involving vital organ systems resulted in PS improvement in 91.7% of patients (3). In another study of 70 patients with lung cancer and a PS score of 2–3, 40% had underlying pulmonary disease, and treatment with anlotinib plus S-1 led to improved and fluctuating PS scores over the treatment course (69).

Consensus 4: assessment of severe lung cancer

The ECOG PS score serves as a core assessment measure for severe lung cancer. In addition to PS, cardiopulmonary function (grade of recommendation: A; level of evidence: 1a) and comorbidities (grade of recommendation: B; level of evidence: 1b) should be assessed to enable a comprehensive evaluation of functional status and guide treatment strategies.

ECOG PS assessment

PS score ≥ 2 as a prognostic factor for patients with lung cancer

A systematic review and meta-analysis of 39 studies comprehensively evaluated predictors of mortality within 3–24 months in patients with advanced cancer. The findings indicated that a PS score >1 was a predictor of mortality, whereas a PS score of 0–1 or 1 alone showed no statistically significant association with mortality (70). A single-center retrospective study of 251 hospitalized patients with lung cancer showed that a PS score ≥ 2 was associated with a

significantly higher 30-day mortality than was a PS score of 0–1 (27.5% *vs.* 14.8%; $P=0.028$) (71). Another retrospective analysis involving 378 patients with small-cell lung cancer (SCLC) identified a PS score ≥ 2 as the most significant prognostic factor for both limited- and extensive-stage SCLC (72).

PS score ≥ 2 as a prognostic factor for lung cancer treatment

PS score assessment is also crucial for treatment selection and prognosis prediction in lung cancer. Several clinical studies have demonstrated a close association between PS and outcomes in patients with lung cancer receiving various anticancer treatments, including surgery (73), radiotherapy (74,75), interventional therapy (76,77), chemotherapy (78–80), targeted therapy (79,81–83), and immunotherapy (84,85). The bulk of these studies used a PS score of 2 as the threshold and concluded that a PS score of 2 or ≥ 2 can serve as a prognostic factor for lung cancer treatment.

Assessment of cardiopulmonary function

Anticancer therapies including surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy may impair cardiopulmonary function in patients with lung cancer (86). To balance the risks and benefits of lung cancer treatment, it is essential to assess the cardiopulmonary function of patients with severe lung cancer.

Since PS scores are generally patient-reported and susceptible to subjective influences, they may not accurately reflect a patient's true functional status (86). Therefore, objective assessment tools, such as cardiopulmonary exercise testing (CPET), cardiorespiratory fitness (CRF), 6-minute walk test (6MWT), and frailty index based on laboratory test (FI-Lab), should be incorporated to comprehensively evaluate cardiopulmonary function (86–91).

Assessment of comorbidities

A cross-sectional study using data from the China Urban Employees' Basic Medical Insurance (UEBMI) database and the Hospital Information System (HIS) database of Beijing Cancer Hospital found that 32.2% of patients with lung cancer had at least one comorbidity (92). Aside from secondary cancers, the most common comorbidities were chronic respiratory diseases (e.g., COPD) and cardiovascular diseases (e.g., hypertension), which is consistent with findings from the UK Office for National

Statistics (ONS) (92,93). Moreover, the presence of comorbidities was significantly associated with an increased risk of 31-day readmission and in-hospital mortality among patients with lung cancer (92).

Several comorbidity assessment tools, such as the Charlson Comorbidity Index (CCI), age-adjusted CCI, and Elixhauser Comorbidity Index (ECI), have demonstrated close associations with prognosis in patients with lung cancer (70,80,94–99). Nevertheless, there remains an ongoing debate regarding which index provides the most accurate prognostic value (100,101).

Consensus 5: basic diagnosis and treatment approaches for severe lung cancer

The value of diagnosis and treatment in severe lung cancer depends on the integration of clinical techniques across four key areas: (I) timely acquisition of pathological specimens, which can help establish an early and accurate diagnosis of lung cancer, including pathological classification; (II) precision detection and dynamic monitoring, which can aid in promptly identifying populations likely to benefit from treatment; (III) powerful life support measures, which can create the conditions for the administration of various anticancer therapies; (IV) individualized treatment strategies that balance efficacy and toxicity through the flexible application of available therapeutic options (grade of recommendation: A; level of evidence: 2).

Timely acquisition of pathological specimens

Timely acquisition of pathological specimens is critical for informing treatment decisions in patients with severe lung cancer who lack a confirmed pathological diagnosis. Delays in diagnosis can negatively impact prognosis and are associated with increased mortality (102,103). Pathological specimen acquisition and subtyping are essential for the treatment of patients with severe lung cancer. Given the critical condition of these patients, routine biopsy procedures carry a high risk; therefore, life support measures, real-time bedside imaging, and multidisciplinary technical support should be applied as appropriate to facilitate specimen collection. The details of the biopsy methods are summarized in *Table 1*.

Precision detection and dynamic monitoring

Precision detection in lung cancer begins with the

Table 1 Principal methods for the timely acquisition of pathological specimens

Specimen type	Biopsy method	Applicable lesions or specimen types
Tissue specimens	Bronchoscopy	Large airway masses or tumors causing airway stenosis via compression
	CT-guided percutaneous biopsy	Lesions located deep within the organ (use is recommended with caution due to stringent requirements for patient positioning and ECOG PS score)
	Ultrasound-guided biopsy (bedside if necessary)	Peripheral lung masses, subpleural and pleural lesions, subcutaneous nodules, superficial lymph nodes, superficial organs (e.g., liver)
	Minimally invasive procedure	Bone metastases and bedside dissection of superficial lymph nodes
Body fluid specimens	Bronchoscopy, if necessary	Sputum or bronchoalveolar lavage fluid
	Lumbar puncture	Cerebrospinal fluid
	Thoracentesis/paracentesis/pericardiocentesis	Pleural effusion, ascites, and pericardial effusion

CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status.

detection of driver mutations. Tissue specimens should be collected for testing whenever possible. However, in cases where tissue specimens are unavailable or insufficient for genotyping, fluid biopsy [e.g., peripheral blood, malignant effusions, sputum, and circulating tumor DNA (ctDNA)] serves as a viable alternative. For critically ill patients, a rapid polymerase chain reaction assay may initially be used to detect common mutations and can be followed by next-generation sequencing (NGS) for comprehensive profiling.

Given the high heterogeneity of tumors, biopsy specimens typically reflect only localized lesions. Moreover, anticancer therapies may alter a patient's genetic profile and tumor characteristics over time. Relying solely on the test results obtained at initial diagnosis to guide subsequent treatment may introduce bias (104,105). Therefore, dynamic monitoring of the pathological and genetic profiles of patients is warranted throughout the course of treatment.

Patients with severe lung cancer require vital sign monitoring and targeted evaluations so that underlying causes can be identified. If treatment-related lung injury is suspected, tests involving computed tomography (CT), KL-6, cytokine, bronchoalveolar lavage fluid (BALF), etc., should be performed. For patients with coexisting COPD, dynamic assessments of lung function and peripheral blood eosinophil count are necessary. In cases of suspected pulmonary infection, pathogen testing should be conducted, and NGS can also be incorporated if indicated.

Life support and symptomatic treatments

The treatment of severe lung cancer requires a multimodal,

comprehensive approach that spans the entire disease course and may involve multiple organ systems. Life support interventions including noninvasive or invasive ventilation, hepatic or renal replacement therapy, and extracorporeal membrane oxygenation (ECMO) should be provided based on the patient's condition. Symptomatic supportive care for individual organs (including fluid management, nutritional, metabolic support, etc.) is also essential. In addition, complications should be closely monitored during treatment and preventive interventions implemented in timely fashion.

Anticancer therapies

Anticancer therapies, such as surgery, chemotherapy, radiotherapy, interventional therapy, targeted therapy (including ADCs), antiangiogenic therapy, and immunotherapy, should be applied flexibly. Treatment regimens that balance efficacy and toxicity (safety) should be prioritized to improve patients' quality of life.

Consensus 6: specific diagnosis and treatment strategies for severe lung cancer

The diagnosis and treatment of patients with severe lung cancer should be personalized, including but not limited to MDT management, concurrent management of cancer and comorbidities or complications, PS score-guided treatment escalation and de-escalation, precision detection with dynamic monitoring, and combination therapy that maximizes efficacy and minimizes toxicity.

MDT management

The management of severe lung cancer is complicated by its multifaceted etiology, diagnostic complexity, limited evidence-based guidance, and the need for comprehensive care across multiple organ systems, thereby necessitating MDT involvement. A meta-analysis of 59 cancer studies showed that patients managed by an MDT have a longer overall survival (OS) compared with control patients (HR =0.67, 95% CI: 0.62–0.71; $I^2=84\%$) (106). The National Comprehensive Cancer Network (NCCN) guidelines clearly recommend that for the full-course management of lung cancer—from diagnosis to treatment—an MDT-centered approach integrating the best available evidence and individual patient data facilitates the development of optimal treatment strategies. This approach enhances therapeutic outcomes while reducing the risk of complications and disease progression. The *Chinese Expert Consensus on the Multidisciplinary Team Diagnosis and Treatment of Lung Cancer* states that the management of lung cancer from diagnosis to treatment should be based on a comprehensive assessment of clinical stage, interindividual variability, pathological characteristics, tumor heterogeneity, and disease progression. The diagnosis and treatment plan should be developed under MDT guidance to balance the therapeutic benefits against potential risks. MDT-based individualized and systematic treatments can improve both the survival and quality of life of patients with severe lung cancer.

Concurrent management of patients with cancer and comorbidities or complications

In the concurrent management of patients with cancer and comorbidities or complications, there is a strong need to address other acute and chronic conditions, such as respiratory diseases (e.g., COPD, ILD, and pulmonary infections), cardiovascular diseases, chronic kidney disease, and diabetes, alongside lung cancer treatment. These comorbidities or complications directly affect the patient's PS score, a key determinant in treatment selection. Patients with lung cancer often have one or more comorbidities. One study found that among patients who died from lung cancer in England between 2001 and 2017, 19.0% had one comorbidity at the time of death and 8.8% had two or more comorbidities (93). Another retrospective study conducted in China reported that among 10,175 patients with cancer, 32.2% had at least one comorbidity, with the proportions of patients with 1, 2, and ≥ 3 comorbidities being 21.7%,

8.3%, and 2.2%, respectively (92). These comorbidities may adversely affect the diagnosis and treatment of lung cancer (107), and thus their management should not be overlooked.

Precision detection and dynamic monitoring

Tumor biomarker testing

The molecular targets for lung cancer treatment include *EGFR*, *ALK* fusion, *ROS1* fusion, *KRAS*, *HER-2*, *BRAF V600*, *RET* fusion, *MET* amplification, *MET* exon 14 skipping mutations, and *NTRK* fusion. Targeted therapies should be selected for patients with severe lung cancer based on the identified driver mutations. In cases of drug resistance, repeat testing is recommended. When tissue specimens are unavailable, ctDNA analysis serves as a viable alternative. The efficacy of immune checkpoint inhibitors (ICIs) is associated with PD-L1 expression, mismatch repair/microsatellite instability status, tumor mutation burden, *POLE/POLD1* mutations, tumor-infiltrating lymphocytes (TILs), tumor neoantigens, and the tumor microenvironment.

Adverse reaction monitoring

Adverse reactions should be monitored at baseline and throughout the course of treatment to facilitate early identification and treatment. Patients with pre-existing lung diseases are more susceptible to treatment-induced lung injury. In the event of serious adverse reactions, active treatment should be accompanied by continuous monitoring of both treatment-related complications and the progression of adverse reactions.

Comorbidity-related tests

Comorbidity assessment parameters vary depending on the nature and type of the condition. Organ-specific parameters should be used, and specialist consultation is recommended to ensure appropriate guidance.

PS score-based treatment escalation and de-escalation

PS score-based escalation and de-escalation strategies entail the adjustment of anticancer treatment regimens according to the patient's PS score and the efficacy and toxicity profiles of guideline-recommended agents. For critically ill patients, treatment may begin with a low-toxicity, high-efficacy regimen or a combination therapy that is not the standard first-line treatment; once the patient's condition

improves, therapy can be switched to a more tolerable standard anticancer regimen based on the patient's status, in an approach known as a “de-escalation strategy”. Patients with severe lung cancer often present with poor PS scores in stages that fluctuate and are reversible. Therefore, it is essential to identify the causes of poor PS in these patients and actively manage comorbidities and complications. An initial low-toxicity, high-efficacy regimen may be used, followed by a more intensive anticancer therapy once the PS score improves. Recently, Professor Yilong Wu proposed the concept of adaptive treatment in the full-course management of lung cancer (108). This approach involves adapting the original standard of care to different treatment scenarios, with the goal of optimizing efficacy while maintaining tolerability. In a phase II clinical study, simplified chemotherapy improved both the PS score and quality of life in patients with poor PS scores (PS ≥ 2) (109).

Optimized combination treatment for maximizing efficacy and minimizing toxicity

Different antineoplastic drugs exhibit distinct mechanisms of action. Appropriate combination treatment can enhance therapeutic efficacy while reducing adverse effects. Deng *et al.* introduced the concept of “chemo-reform”, which involves the addition of chemotherapy to immunotherapy, with the dose and duration of chemotherapy adjusted to reduce chemotherapy-related toxicity while enhancing the efficacy of immunotherapy (110,111). This strategy may be suitable for patients with poor PS scores. The selection of combination regimens should be based on the patient's condition and a comprehensive evaluation of each regimen's benefits applied to optimize efficacy and minimize adverse reactions.

Consensus 7: surgical indications, principles, and perioperative considerations for severe lung cancer

Patients with lung cancer who develop critical illness due to brain or bone metastases or who experience complications such as hyperpyrexia, active bleeding, hemothorax, or empyema secondary to obstructive pneumonia may benefit from surgical treatment (grade of recommendation: B; level of evidence: 2b). The primary goal of preoperative MDT assessment in patients with severe lung cancer is to determine whether surgical treatment can address the cause of the severe condition. Preoperative assessments

may include cardiopulmonary function assessments conducted prior to the onset of critical illness (grade of recommendation: B; level of evidence: 2a). The selection of surgical and anesthetic approaches for patients with severe lung cancer should follow the principle of addressing the primary cause and minimizing trauma. Nonintubated video-assisted thoracic surgery (NIVATS) has been shown to facilitate postoperative recovery (112) (grade of recommendation: A; level of evidence: 1b). Intraoperative noninvasive brain monitoring can help prevent complications such as postoperative stroke or cognitive dysfunction in these patients (grade of recommendation: A; level of evidence: 1b). Additionally, postoperative MDT management can better reverse the systemic stress response caused by severe lung cancer (grade of recommendation: B; level of evidence: 2b).

Surgical indications in selected cases of severe lung cancer

Brain metastases from lung cancer

A solitary brain metastasis may cause critical illness in patients with lung cancer. Surgical resection of the lesion can rapidly reduce the risk and improve prognosis. In cases of multiple brain metastases, surgical resection of the dominant lesion can relieve local compression, lower intracranial pressure, and reduce tumor burden and edema, thereby improving PS score and survival. For patients with severe lung cancer who present with brain metastases as the initial clinical manifestation, surgical resection of the brain metastases can facilitate rapid diagnosis and guide subsequent treatment of the primary lesion (113-116).

Bone metastases from lung cancer

In patients with severe lung cancer, bone metastases may cause complications such as pathological fractures, compression, paraplegia, and secondary infections, which adversely affect prognosis and may even be life-threatening. Surgical treatment of metastases in weight-bearing bones, such as the spine, can rapidly restore neurological function or mobility, significantly alleviate pain, and improve PS scores (117,118).

Emergency surgery for severe complications

Patients with lung cancer may develop critical illness due to complications such as hyperpyrexia, infection, tumor necrosis, active bleeding, hemothorax, and empyema secondary to obstructive pneumonia. When medical or interventional treatments are ineffective, rescue surgery,

despite its high risk, may be necessary to manage life-threatening acute events and enable subsequent tumor-specific therapies. These surgeries include pneumonectomy, bilobectomy, lobectomy, and segmentectomy (119-129).

Preoperative assessments

Critically ill patients with lung cancer may not be able to undergo complete the preoperative risk assessments recommended in other consensus statements. Even if a portion of routine assessments are performed, the results may not accurately reflect the patient's true surgical tolerance. Certain preoperative assessments, such as color echocardiography, blood gas analysis, nutritional evaluation, pharmacotherapy review, and 3D pulmonary reconstruction, can still be conducted. However, other examinations, including pulmonary function tests, coronary and vascular imaging, pulmonary ventilation/perfusion (V/Q) scans, and exercise capacity assessments, are typically difficult to perform in this population. Therefore, preoperative assessments in patients with severe lung cancer should be based on data obtained prior to the onset of critical illness. For patients with severe lung cancer and poor cardiopulmonary function, active surgical treatment may still be considered if it has the potential to improve their cardiopulmonary status.

Intraoperative safeguards and surgical principles

The selection of surgical and anesthetic approaches for patients with severe lung cancer should follow the principle of addressing the primary cause and minimizing trauma. NIVATS reduces the need for muscle relaxants and intrapulmonary shunting, improves the ventilation-perfusion ratio, and mitigates the physiological and immunological burden in patients with severe lung cancer (112). It may further lower the risk of postoperative complications in patients with poor PS scores related to surgery.

Intraoperative monitoring

Preoperative preparation is often limited in patients with severe lung cancer, particularly in terms of hemodynamic evaluation, and thus enhanced intraoperative monitoring may be necessary for these patients. Cerebrovascular autoregulation (CA) is a protective mechanism that maintains stable cerebral blood flow. Dysfunction of CA results in cerebral blood flow fluctuating with blood

pressure, placing brain tissue at risk of ischemic injury or hyperemic edema and increasing the likelihood of ischemic cognitive impairment and stroke (130-132). Real-time intraoperative monitoring of cerebral perfusion, individualized anesthesia management, and enhanced intraoperative monitoring of cerebral blood flow can help prevent postoperative stroke and cognitive impairment.

Postoperative support

Postoperative management of severe lung cancer requires intensified supportive care to alleviate systemic stress and MDT consultation for guiding subsequent treatment. Precision diagnostics and the appropriate use of antibiotics are essential for developing effective strategies in treating pulmonary infections. In cases of persistent pulmonary air leaks, nutritional support, digital chest drainage systems, and intrapleural administration of sclerosing agents are recommended. Pulmonary atelectasis should be addressed with postoperative rehabilitation and, when necessary, bronchoscopic suctioning. Cardiovascular events and acute exacerbation of ILD are severe postoperative complications requiring proactive prevention and treatment (133-135) in addition MDT-guided management.

Consensus 8: specific application of radiotherapy in severe lung cancer

Radiotherapy is indicated across all stages of lung cancer. In patients with severe lung cancer, radiotherapy serves three key roles: (I) radical radiotherapy for patients with early-stage severe lung cancer who cannot tolerate surgery; (II) combination of precision radiotherapy with antineoplastic drugs for patients with locally advanced severe lung cancer to achieve curative intent; and (III) palliative radiotherapy targeting special sites in advanced severe lung cancer to rapidly mitigate severe symptoms and the further enhancement of therapeutic benefit when combined with pharmacotherapies (grade of recommendation: B; level of evidence: 2a).

Radical radiotherapy for patients with early-stage severe lung cancer who cannot tolerate surgery

Radiotherapy is an effective treatment option for patients with early-stage lung cancer who cannot tolerate surgery due to various reasons, such as advanced age, poor pulmonary function, poor PS score, and severe systemic

comorbidities. The efficacy of stereotactic body radiation therapy (SBRT), also known as “stereotactic ablative radiotherapy” (SABR), is significantly superior to that of conventional fractionated radiotherapy, with a 3-year local control rate of 73–91% and a 3-year OS rate of 43–60%. Based on a rigorous assessment of organ-at-risk doses and patient tolerance, a biologically effective dose (BED) of ≥ 100 Gy is recommended for SBRT (136–138). For patients with early-stage central lung cancer and ILD, poor PS (PS score ≥ 2), and advanced age, SBRT may be considered for radical treatment following careful risk-benefit assessment, with a recommended dose of 50 Gy/5F (139,140). For patients with early-stage NSCLC ineligible for surgery, SABR in combination with immunotherapy may be considered, provided that thorough assessment and close monitoring for adverse reactions are in place (141).

Radiotherapy for patients with locally advanced severe lung cancer

Patients with and lung cancer and a poor PS score [2–4] or advanced age often cannot tolerate standard concurrent chemoradiotherapy followed by sequential immunotherapy. Hence, sequential chemoradiotherapy or radiotherapy alone followed by durvalumab consolidation therapy is recommended for these patients (142–145). Based on the results of the phase III LAURA study, consolidation osimertinib is recommended for patients with EGFR-mutant NSCLC following chemoradiotherapy (146,147).

In addition to sequential chemoradiotherapy, split-course concurrent chemoradiotherapy (148) or individualized hypofractionated regimens (42.0–49.0 Gy/13–16 F or 60 Gy/15 F) (149,150) may be considered for patients with locally advanced severe lung cancer who cannot tolerate concurrent chemoradiotherapy at conventional doses.

Moreover, proton therapy also represents a viable treatment option for patients with locally advanced severe lung cancer who are in poor physical condition, have impaired cardiopulmonary function, and lack driver gene mutations (151).

Palliative radiotherapy for patients with advanced severe lung cancer

The standard of care for advanced lung cancer involves a multimodal approach primarily based on systemic therapy. For severe lung cancer with poor PS scores, radiotherapy

offers two key benefits: (I) palliative treatment of local lesions to relieve symptoms and improve PS scores and (II) increasing the control rate of local lesions and improving survival when systemic treatment is effective.

Radiotherapy for brain metastases can control lesions, relieve symptoms, and prolong survival. For patients with NSCLC and ≤ 10 brain metastases, SRS alone is the preferred local treatment. When a lesion is located near a critical organ, fractionated SRS may be considered to further reduce side effects (152,153). Whole-brain radiotherapy (WBRT) is recommended for patients with SCLC. For those with oligometastases, SRS can supplement WBRT to improve the local control rate (154,155). For patients with brain metastases and a PS score of 2–3, individualized radiotherapy for brain metastases in combination with systemic therapy can better prolong OS (75). For those with brain metastases and a PS score of 4, radiotherapy for brain metastases is not recommended, and systemic BSC is instead advised (74). In patients with leptomeningeal metastases, WBRT is recommended for symptom relief and may provide survival benefits in selected cases (156). Local high-dose radiotherapy may be considered for patients with mass-like leptomeningeal metastases that are visible on imaging.

Palliative radiotherapy for other sites includes but is not limited to (I) bone metastases; (II) hemoptysis; and (III) superior vena cava syndrome (SVCS). (I) For patients with bone metastases, radiotherapy helps relieve localized pain and reduce the incidence of bone-related events such as pathological fractures and paraplegia. Among those with bone metastases and a PS score > 2 , radiotherapy in combination with immunotherapy and bone-targeted therapy may help prolong OS and progression-free survival (PFS) (157). (II) Regarding hemoptysis, for patients with central lung cancer and uncontrolled hemoptysis, palliative radiotherapy helps control bleeding after the bleeding site has been identified through endoscopy or imaging. The most commonly prescribed fractionations are 20 Gy/5 F, 30 Gy/10 F, and 8 Gy/F (158). (III) Finally, SVCS is often a complication of SCLC, which typically presents as a centrally located mass. In this scenario, hypofractionated radiotherapy is recommended for achieving rapid decompression and relieving symptoms.

For patients with advanced severe lung cancer who respond to systemic therapy (159–161), palliative radiotherapy for both primary and metastatic lesions may prolong survival.

Table 2 Common respiratory interventional techniques for severe lung cancer and their corresponding indications (162-174)

Respiratory interventional technique	Indications
Airway debridement	
Bronchoscopic removal with forceps	Intraluminal tumor tissue, granulation tissue, necrotic debris, and limited granulation tissue hyperplasia following airway stenting
High-frequency electrocautery	Resection of malignant tumors and pedunculated lesions
Laser therapy	Tumor tissue removal
Argon plasma coagulation	Tumor tissue removal and local hemostasis
Cryotherapy	Removal of tumor tissue and recurrent proliferative lesions
Photodynamic therapy (169)	Tumor tissue within the airway lumen
Endobronchial brachytherapy	Tumor tissue within the airway lumen
Mechanical dilation	
Balloon dilation	Malignant airway stenosis
Rigid bronchoscopic dilation	Malignant airway stenosis
Bronchoscopic intratumoral injection of antineoplastic drugs (170)	Tumors unresponsive to conventional treatments and accompanied by malignant airway stenosis
Local ablative therapy for peripheral lung cancer (radiofrequency ablation, microwave ablation, and cryoablation) (171-174)	Cardiopulmonary insufficiency, multiple primary tumors, unresectable disease or postoperative recurrence, and nonresponse to anticancer therapies
Airway stenting	
Silicon stents	Airway stenosis unresponsive to conservative treatment and ineligibility for silicon stenting, active bleeding requiring local compression hemostasis, and lung cancer-induced tracheal fistulas requiring closure
Metal stents	Malignant airway stenosis requiring emergency airway opening, airway stenosis unresponsive to conservative treatment and ineligibility for silicone stenting, active bleeding requiring local compression hemostasis, and lung cancer-induced tracheal fistulas requiring closure
Bronchoscopic instillation of fibrin glue, cyanoacrylate glue, growth factors, and autologous platelet-rich plasma	Lung cancer-related tracheal fistula

Consensus 9: specific application of interventional techniques in severe lung cancer

Appropriate interventional techniques can rapidly alleviate or control clinical symptoms, improve PS, create opportunities for other anticancer therapies, and potentially achieve a cure in selected patients with severe lung cancer. Interventional approaches for lung tumors include airway, chest wall, and vascular routes (162-165) (grade of recommendation: B; level of evidence: 2a).

Application of airway interventions in severe lung cancer

Common airway interventional techniques and methods for severe lung cancer

Advances in minimally invasive endoscopic techniques such as high frequency electrosurgery, laser therapy, cryotherapy, balloon dilation, and airway stenting have made respiratory interventional therapy an important therapeutic modality for managing patients' severe lung cancer (e.g., those with malignant airway stenosis, massive hemoptysis, or tracheal

fistula). Common respiratory interventional techniques for patients with severe lung cancer and their corresponding indications are summarized in *Table 2*.

Severe lung cancer caused by malignant severe airway stenosis can be improved by airway interventions

Malignant central airway stenosis involves the narrowing of the trachea, carina, mainstem bronchi, or bronchus intermedius caused by primary or metastatic malignancies. When tumor-related obstruction or compression leads to a greater than 50% luminal narrowing, patients may develop severe dyspnea, which can progress to asphyxia and death (175-177). Selection of the optimal bronchoscopic ablation technique should be based on the specific clinical scenario. High-frequency electrocoagulation plays an important role in mitigating malignant central airway stenosis. Removing neoplastic endobronchial tissue with a high-frequency electrocautery snare can rapidly reduce tumor bulk and is a cost-effective means to preventing respiratory failure. Thermal ablation is best suited for patients with small intraluminal tumors (<4 cm in length) and preserved distal lung ventilation confirmed by CT scans or bronchoscopy (163).

Among all available methods, only bronchoscopic thermal ablation therapies (APC, high-frequency electrocautery, and laser therapy) provide immediate relief of large airway obstruction caused by malignant tumors. For more diffuse lung tumor lesions, transbronchial cryobiopsy (TBCB) has been employed to obtain a greater volume of pathological tissues (167).

Severe lung cancer caused by hemoptysis can be improved by airway interventions

Hemoptysis is a common symptom of lung cancer. When the amount of acute bleeding from the lower respiratory tract caused by lung cancer exceeds 100 mL in a single episode, it is classified as massive airway hemorrhage (178), which may lead to airway obstruction and become life-threatening. For patients whose symptoms cannot be relieved by conventional treatments, airway intervention may be considered to control bleeding. For cases in which hemoptysis causes asphyxia and other life-threatening conditions (179), bronchoscopy can be used to accomplish the following: (I) identify the bleeding site and guide vascular intervention; (II) assist with endotracheal intubation, argon plasma coagulation (APC) treatment, or balloon occlusion; and (III) when necessary, place silicone or covered metal stents to control bleeding and save the patient's life.

Severe lung cancer caused by airway fistula can be improved by airway interventions

An airway fistula is an abnormal tract formed along the airway wall due to disruption of its integrity (180). Lung cancer may cause esophagorespiratory, bronchopleural, tracheomediastinal, and tracheal or bronchial anastomotic fistulas, resulting in secondary pulmonary infections, hemoptysis, dyspnea, and other symptoms. Bronchoscopic placement of stents (silicone or covered metal stents), occluders, or silicone plugs can be performed to seal the fistula and alleviate symptoms. In some patients with severe lung cancer and bronchial fistulas, silicone stents may achieve better sealing and a longer duration of fistula closure than may metal stents, provided there is good apposition between the stent and the surrounding airway wall (180).

In summary, endoscopic treatment of airway complications of malignant tumors requires the development of safe and effective individualized plans and the capacity to manage complications.

Application of percutaneous interventions in severe lung cancer

A portion of patients with peripheral lung cancer are of advanced age, frail, and have poor pulmonary function, rendering them intolerant to bronchoscopic biopsy and treatment. In such cases, percutaneous lung biopsy is a feasible and safe diagnostic method (181,182). There is a growing body of evidence supporting the use of percutaneous ablation techniques, including radiofrequency ablation, microwave ablation, and cryoablation, as safer debulking options for patients with early-stage lung cancer who cannot tolerate surgery (183-185). Tumor control can also be achieved in patients with early-stage lung cancer and underlying diseases such as COPD and IPF through percutaneous interventions (186-188). In patients with advanced lung cancer, combining systemic therapy with percutaneous ablation may improve survival as compared to systemic therapy alone; however, evidence supporting the use this type of combination treatment in patients with severe lung cancer is currently lacking (164,189).

Application of vascular interventions in severe lung cancer

As interventional oncology continues to evolve, vascular interventions are being more widely adopted in clinical practice and have become an integral part of lung cancer

diagnosis and treatment. In patients with severe lung cancer, this technique is primarily used to treat lung cancer-related massive hemoptysis and SVCS.

Vascular interventions for lung cancer-related massive hemoptysis

Bronchial artery embolization (BAE) has become the first-line treatment for lung cancer-related massive hemoptysis when conservative treatment fails (190,191). The immediate bleeding control rate for lung cancer-related hemoptysis is 77–82%. However, the hemoptysis recurrence rate after BAE is as high as 23.8%, and median hemoptysis-free survival is only 61 days (179,192). To enhance efficacy, bronchial arterial chemoembolization (BACE) may be performed by an initial infusion of chemotherapeutic agents directly into the bronchial artery during BAE, followed by embolization. This approach increases the intratumoral drug concentration, promotes more effective tumor killing, and inhibits neovascularization, thereby prolonging hemoptysis-free survival. Preliminary evidence suggests that BACE can effectively prolong hemoptysis-free survival in patients with lung cancer with hemoptysis, achieving favorable treatment outcomes (193–195). If pulmonary artery lesions are detected on imaging and hemoptysis persists after BAE, pulmonary artery bleeding should be considered. Pulmonary angiography is recommended for obtaining a definitive diagnosis, and pulmonary artery embolization should be performed if indicated (196,197). For patients with asphyxiating massive hemoptysis and unstable vital signs, concurrent vascular and airway interventions may be necessary. In such cases, airway intervention is performed first to establish a secure artificial airway and is followed by bronchoscopic clearance and endoscopic hemostasis. Once the patient's condition stabilizes, vascular intervention can be initiated.

Vascular interventions for SVCS

The incidence of SVCS is 2–4% in patients with lung cancer and up to 10% in those with SCLC (198). SVCS is a potentially fatal condition that necessitates prompt active intervention for the rapid alleviation of symptoms and the facilitation of subsequent treatment. For patients with severe acute symptoms, contraindications to radiotherapy or chemotherapy, or poor response to such treatments, vascular interventions (including stent placement and balloon dilation) can rapidly alleviate obstruction and improve quality of life. In recent years, these techniques have become the preferred treatment options for patients

with SVCS (199–201).

Consensus 10: specific application of antineoplastic drugs in severe lung cancer

Not all patients with severe lung cancer are unsuitable for pharmacotherapies. The key is to achieve optimal outcomes with minimal toxicity through precision medicine. Current pharmacotherapies for lung cancer include chemotherapy, targeted therapy, anti-angiogenic therapies, immunotherapy, and ADCs.

For patients with advanced NSCLC and a PS score of 2, platinum-based doublet chemotherapy may be considered, provided tolerability is carefully evaluated (grade of recommendation: A; level of evidence: 1a). For those with a PS score >2, individualized treatment strategies should be developed using an MDT approach (grade of recommendation: B; level of evidence: 2b). In SCLC patients, single-agent or reduced-dose chemotherapy should be used with caution (grade of recommendation: A; level of evidence: 1a). For patients with a PS score ≥ 2 and sensitizing EGFR mutations or ALK fusions, single-agent targeted therapy is recommended (grade of recommendation: A; level of evidence: 1b). For those with rare targets, corresponding targeted agents may be considered as treatment options (grade of recommendation: D; level of evidence: 5). Evidence supporting the use of anti-angiogenic therapies in patients with a PS score ≥ 2 is limited, and the clinical benefit appears modest (grade of recommendation: B; level of evidence: 2b). While patients with a PS score ≥ 2 derive less benefit from immunotherapy than those with a PS score <2, immunotherapy still offers a survival benefit in both first- and subsequent-line settings (grade of recommendation: B; level of evidence: 1b). Currently, there is insufficient evidence to support the use of ADCs in patients with a PS score ≥ 2 , and safety concerns should be prioritized when considering these treatments.

Chemotherapy

Platinum-based doublet chemotherapy may be considered following a thorough safety assessment for patients with advanced NSCLC and a PS score of 2.

A meta-analysis of 12 clinical studies involving patients with NSCLC and a PS score of 2 reported that platinum-based doublet chemotherapy results in a significantly longer survival than does single-agent chemotherapy (HR = 0.71, 95% CI: 0.61–0.81) (202). Another meta-analysis

also confirmed that doublet chemotherapy significantly improves OS (HR =0.72, 95% CI: 0.61–0.84; $P<0.0001$) and 1-year survival rate but increases grade 3–4 hematologic toxicities as compared to single-agent chemotherapy (203). A meta-analysis of 10 clinical studies found that compared to pemetrexed alone, pemetrexed in combination with platinum-based therapy improves both PFS (HR =0.46; $P<0.001$) and OS (HR =0.62; $P=0.001$) in patients with NSCLC and a PS score of 2 (204). Another recent study also reported the promising efficacy of carboplatin plus nab-paclitaxel in patients with NSCLC and a PS score of 2 (median PFS: 5.2 months; median OS: 14 months) (205). Taken together, these findings indicate that platinum-based doublet chemotherapy may be considered for patients with advanced NSCLC and a PS score of 2 following a thorough assessment of tolerability.

Development of individualized treatment strategies by an MDT is recommended for patients with advanced NSCLC and a PS score of 3–4

A phase II randomized controlled study comparing gemcitabine (standard dose) with cisplatin (low dose) in patients with advanced NSCLC and a PS score 2–3 (75.9% with a PS score of 3) found that low-dose combination chemotherapy was superior to single-agent chemotherapy (median PFS: 5.6 *vs.* 3.8 months; median OS: 6.8 *vs.* 4.3 months) and resulted in a low incidence of adverse reactions (206). In another prospective, single-arm phase II clinical study (ImPACt) that evaluated weekly paclitaxel administration in 46 patients with NSCLC (87% with a PS score of 3–4), the median PFS and median OS were 3.3 months (95% CI: 2.36–5.6) and 6.8 months (95% CI: 2.47–8.8), respectively (109).

A retrospective observational study (MOON-OSS) enrolled 221 patients with EGFR/ALK-negative, PD-L1 <50%, stage IIIB–IV NSCLC who received first-line single-agent chemotherapy. Of these patients, 46.6% had a PS score ≥ 2 and a median of two severe comorbidities. The single-agent treatment consisted of oral metronomic vinorelbine (MetV; 78.6%), gemcitabine (10%), oral standard vinorelbine (8.2%), and other agents (3.2%). The median PFS and OS were 4.5–5 months and 9–10.5 months, respectively, and the incidence of grade 3–4 toxicities was less frequent with MetV (78).

In summary, evidence supporting the use of chemotherapy in patients with lung cancer and a PS score of 3–4 remains scarce, with most studies being retrospective in nature and lacking large-scale prospective clinical trials.

In clinical practice, individualized treatment strategies should be developed through an MDT approach following comprehensive assessment.

Single-agent or reduced-dose chemotherapy may be used with caution for patients with advanced SCLC and a PS score of 3–4

For patients with extensive-stage SCLC (ES-SCLC) and a PS score of 3–4 due to tumor burden the guideline-recommended treatment options are similar to those for patients with PS 0–2. However, chemotherapy regimens, such as single-agent or reduced-dose combination therapy, should be selected with caution based on a comprehensive assessment. A retrospective study involving older adult patients with ES-SCLC and a PS score of ≥ 2 who had received first-line etoposide plus carboplatin therapy compared the treatment efficacy in patients with a baseline PS score of 2 ($n=8$) to that in patients with a PS score of 3–4 ($n=25$). In the PS 2 and PS ≥ 3 groups, the objective response rate (ORR) was 71.1% and 72.0%, the median PFS was 4.6 months and 3.1 months, and the median OS was 7.7 months and 5.1 months, respectively; the PS score improved to 0–1 posttreatment in 65.8% and 48.0% of the patients in the two groups, respectively (207). Another retrospective study found that chemotherapy significantly prolonged survival in patients with SCLC and a PS score of 3–4 as compared to BSC (208).

Targeted therapy

Clinical evidence for use of EGFR-TKIs in patients with advanced EGFR-mutant NSCLC with PS ≥ 2

Research has shown that gefitinib provides good efficacy and tolerability in patients with advanced EGFR-mutant NSCLC and PS ≥ 2 (209). A retrospective study in very older adults (≥ 85 years old) patients with advanced NSCLC found that the OS tended to be longer in the gefitinib group than in the BSC group for patients with a PS score of 3–4 (4.6 *vs.* 2.3 months; $P=0.060$) (210). In a small prospective study involving patients with EGFR-mutant NSCLC and PS ≥ 2 who received first-line osimertinib (a third-generation EGFR-TKI), the ORR was 56.3%, the median PFS was 10.5 months, and the PS score improved in 50% of patients (211). In a retrospective study of patients with a PS score of 2 and ≥ 3 treated with osimertinib, the reported median PFS was 14.5 months and 3.0 months, while the median OS was 18.1 and 5.0 months, respectively (212). Osimertinib is an effective second-line treatment for patients

with T790M-positive NSCLC and poor PS who are resistant to EGFR-TKIs (ORR: 53.1%; disease control rate: 75%; median PFS: 5.1 months; median OS: 10.0 months) (213). In retrospective analysis of osimertinib in patients with T790M-positive NSCLC and a PS score of ≥ 2 , osimertinib yielded an ORR of 53%, a PS score improvement rate of 63%, a median PFS of 8.2 months, and good tolerability (214). In a similar phase II clinical study involving 18 patients with T790M-positive NSCLC and PS ≥ 2 who were resistant to first- or second-generation EGFR-TKIs, osimertinib also demonstrated favorable efficacy (median PFS: 7.0 months; median OS: 12.7 months), with PS improvement observed in 72% of patients (214). The most common adverse reactions to osimertinib included rash (42%), diarrhea (36%), and perionychia (36%). Despite a minimal risk of interstitial pneumonitis (211,213), the drug was generally well tolerated in most patients.

For patients with advanced EGFR-mutant NSCLC and PS ≥ 2 , EGFR-TKI monotherapy remains the preferred option. Currently, there is a lack of evidence to support the use of EGFR-TKIs in combination with other therapies.

Clinical evidence for ALK-TKIs in patients with advanced NSCLC and a PS score ≥ 2 (grade of recommendation: A; level of evidence: 1b)

A case series (N=5) reported the robust efficacy of crizotinib for treating patients with advanced ALK-rearranged NSCLC and PS ≥ 2 (215). A large retrospective study including 441 patients with ALK-rearranged NSCLC (97 with PS ≥ 2) found that those with poor PS scores derived significant benefit from ALK-TKIs (72.2% of patients received crizotinib treatment, with a median PFS of 9.3 months and a median OS of 17.9 months) (216). However, multivariate analysis reported that a PS score ≥ 3 was significantly associated with poor outcomes (median OS of 20.6 months for PS 2 and 8.6 months for PS 3–4) (216). Another phase II clinical study reported that alectinib treatment in patients with advanced ALK-rearranged NSCLC and a PS score ≥ 2 resulted in an ORR of 70%, a median PFS of 16.2 months, a 3-year OS rate of 42%, and a PS improvement rate of 83.3% (217,218). In another study, grade ≥ 3 AEs occurred in 15.7% of alectinib-treated patients with PS ≥ 2 (compared to 9% in those with PS ≤ 1). Among those affected, 72.1% recovered or improved after treatment. The most common grade 3 AEs were anemia, decreased appetite, ILD, and constipation (219).

Therefore, ALK-TKIs are recommended for patients with advanced ALK-rearranged NSCLC and a PS score ≥ 2 .

Clinical evidence for targeted therapy in patients with advanced NSCLC harboring rare driver mutations and a PS score ≥ 2 (grade of recommendation: D; level of evidence: 5)

For patients with advanced NSCLC harboring rare driver mutations, evidence is lacking on whether those with poor PS can benefit from targeted therapies. However, according to the expert consensus, high-efficacy and low-toxicity targeted therapies are recommended for patients with advanced NSCLC harboring rare driver mutations and a PS score ≥ 2 . Inhibitors for ROS1 fusion-positive NSCLC include crizotinib, entrectinib, unecritinib, repotrectinib, and taletrectinib; those for MET exon 14 skipping-positive NSCLC include crizotinib, savolitinib, glumetinib, bozitinib, tepotinib, and capmatinib; those for NTRK fusion-positive NSCLC include entrectinib and larotrectinib; those for BRAF V600-mutant NSCLC include dabrafenib in combination with trametinib and encorafenib in combination with binimetinib; those for RET inhibitors include pralsetinib and selpercatinib; and those for EGFR exon 20 insertion-mutant NSCLC include sunvozertinib.

Therefore, for patients with PS ≥ 2 and advanced NSCLC harboring rare driver mutations (including ROS1 fusion, MET exon 14 skipping mutation, NTRK fusion, BRAF V600 mutation, RET fusion, and EGFR exon 20 insertion mutation), the corresponding targeted agents are recommended.

Antiangiogenic therapy

Antiangiogenic agents mainly include small-molecule multitarget TKIs and macromolecular antibody-based drugs.

VEGF-targeting TKIs have demonstrated efficacy in the second- and later-line treatment of severe NSCLC. A retrospective study of 206 patients with NSCLC who received anlotinib as second- or later-line treatment reported that the median PFS was 4 months in patients with a PS score ≤ 1 and 3 months in those with a PS score ≥ 2 , with an incidence of grade 3 TRAEs of 14% (220).

For patients with PS ≥ 2 , it remains uncertain whether combining antiangiogenic therapy with chemotherapy offers additional benefit. A retrospective study suggested that patients with PS ≥ 2 derived more benefit from anlotinib plus S-1 than did anlotinib alone (69).

Evidence supporting the use of antiangiogenic agents in patients with a PS score ≥ 2 is limited, with preliminary data indicating modest efficacy. A phase II single-arm study

investigating the combination of erlotinib and bevacizumab as first-line treatment demonstrated limited survival benefit in patients with a PS score ≥ 2 and no EGFR mutations. The regimen was therefore not recommended for this population (221). In the subgroup analysis of the NEJ051 study, second-line treatment with ramucirumab plus docetaxel demonstrated significantly inferior efficacy in patients with a PS score ≥ 2 than in those with a PS score 0–1 (median PFS: 1.4 *vs.* 4.2 months; median OS: 4.2 *vs.* 12.4 months), suggesting that this second-line regimen should be used with caution in patients with severe lung cancer (222).

Immunotherapy

The selection of immunotherapeutic agents and regimens for patients with severe NSCLC should be based on a comprehensive assessment of PS, comorbidities, age, and other relevant factors to maximize therapeutic benefit. Although studies evaluating immunotherapy in patients with severe lung cancer remain limited, emerging evidence from multiple clinical studies, in conjunction with the first version of the consensus, supports immunotherapy as a potentially feasible treatment option for patients with PS ≥ 2 .

Immunotherapy for severe NSCLC

A real-world study involving 1,395 patients with NSCLC and PS ≥ 2 reported that first-line treatment with ICIs was associated with improved prognosis as compared to no treatment, irrespective of PD-L1 expression. For patients with PD-L1 expression $< 50\%$, an improved median OS was observed for pembrolizumab plus chemotherapy as compared to pembrolizumab alone (223). A phase III randomized controlled study including 453 patients (age ≥ 70 years) with NSCLC and a PS score ≥ 2 or 0–1 ineligible for platinum-containing chemotherapy demonstrated that irrespective of PD-L1 expression, atezolizumab monotherapy, as compared with single-agent chemotherapy, was associated with an improved OS (10.3 *vs.* 9.2 months; HR = 0.78) and 2-year survival rate (24% *vs.* 12%) (224). In contrast, a French multicenter academic randomized phase III trial comparing first-line dual immune checkpoint inhibition with platinum-based chemotherapy in patients aged ≥ 70 years or with a PS score of 2 failed to demonstrate an OS benefit in the overall population; subgroup analyses suggested a survival benefit restricted to elderly patients with PS 0–1, with no benefit observed in patients with PS 2, although the trial was prematurely discontinued for futility, limiting the statistical power of these findings (225).

Additionally, the underlying cause of poor PS score correlated with the clinical outcomes of ICIs. Patients with a comorbidity-induced PS score of 2 had significantly better survival outcomes than did those with a disease burden-induced PS score of 2 (226). The lung immuno-oncology prognostic score (LIPS, which incorporates the neutrophil-to-lymphocyte ratio and the pretreatment use of steroids) serves as a prognostic factor for the efficacy of first-line ICIs in patients with NSCLC and a PS score of 2. Patients with low LIPS scores can achieve better survival benefits (227), but there is a lack of evidence concerning the use of ICIs as later-line treatment in patients with severe lung cancer.

A meta-analysis of 5,357 patients with NSCLC treated with first-line pembrolizumab reported that the incidence of immune-related adverse reactions is 21.2% in patients with a PS score ≥ 2 and 35% in those with a PS score of 0–1 (228). The IPSOS study revealed that patients with NSCLC who were ineligible for platinum-based doublet chemotherapy had higher quality-of-life scores and that atezolizumab monotherapy, compared to single-agent chemotherapy, resulted in a lower incidence of grade 3–4 TRAEs (16% *vs.* 33%) (224). In contrast, the CheckMate 817 trial reported a higher toxicity burden with first-line nivolumab plus ipilimumab in patients with ECOG PS 2, with grade 3–4 TRAEs occurring in 27.3% of patients and treatment discontinuation in 14.4% (229). Taken together, these data suggest that ICI monotherapy represents a reasonable option for many patients with severe lung cancer, whereas dual immunotherapy should be considered in highly selected cases and applied under close clinical supervision.

Immunotherapy for severe SCLC

Clinical studies of immunotherapy in patients with severe SCLC are limited and have predominantly been conducted in the first-line treatment setting. In a real-world study comparing first-line immunotherapy plus chemotherapy to chemotherapy alone for patients with ES-SCLC, the combination group had a significantly longer median OS ($P < 0.0001$). In the PS 2–3 subgroup, immunotherapy plus chemotherapy tended to provide better survival than did chemotherapy alone (median OS: 315 *vs.* 124 days; $P = 0.13$) (230). Another retrospective analysis demonstrated that among patients with ES-SCLC receiving first-line immunotherapy plus chemotherapy, the overall incidence of TRAEs was similar between the PS 0–1 and PS 2–3 groups, but patients with a PS score of 2–3 experienced higher rates of treatment delays and incidence of hospitalization due to

AEs (231). Therefore, a more active treatment strategy may be considered for patients with ES-SCLC.

ADCs

The efficacy of ADCs in patients with lung cancer and a PS score ≥ 2 warrants further clinical validation. Currently, the evidence base is limited to case reports and small series. In a 52-year-old female patient with NSCLC harboring a HER2 exon 20 insertion mutation and a PS score of 3 who had undergone multiple lines of treatment, trastuzumab deruxtecan (T-DXd) treatment resulted in a significant reduction in tumor size and improvement in PS score from 3 to 1, with no disease progression observed at 6 months (232). Another male patient with advanced HER2-mutant NSCLC and a PS score of 3–4 who had undergone multiple lines of treatment achieved partial response after WBRT and T-DXd treatment, with a PFS of nearly 9 months and an improvement in PS score from 3–4 to 1 (233). ADCs, through their unique mechanism of action, may represent a promising treatment option for patients with lung cancer, particularly those with poor PS. However, the efficacy and safety of ADCs in such patients still require further validation and should not be used as a routine treatment.

Consensus 11: specific application of life support and symptomatic treatments in severe lung cancer

For patients with severe lung cancer, particularly those newly diagnosed, life support interventions and symptomatic treatments such as respiratory support, other organ support, nutritional support, anti-infective therapy, and anticoagulation therapy can act as a bridge to pathological and molecular diagnoses. These interventions may sustain patients until anticancer therapies take effect, improve PS, and enable successful weaning from life support and transition to standard of care (grade of recommendation: A; level of evidence: 1b). Moreover, attention should be paid to the rehabilitation of patients with severe lung cancer through comprehensive management measures including aerobic exercise, breathing training, airway clearance techniques, and patient education (grade of recommendation: A; level of evidence: 1b). It is recommended that a thorough assessment be conducted prior to initiating care for patients with severe lung cancer and that demand-oriented supportive care escalation and de-escalation strategies be adopted across different stages of the

disease (grade of recommendation: A; level of evidence: 1b).

Appropriate respiratory support

In patients with severe lung cancer, high flow oxygen therapy (HFNC) can better maintain oxygenation and alleviate respiratory distress. It is better tolerated than is noninvasive ventilation (NIV) (234–237). If hypoxemia and respiratory distress persist despite conventional oxygen therapy and HFNC, NIV should be initiated as early as possible to reduce the rate of endotracheal intubation (238–240). In cases for whom HFNC or NIV fails, invasive mechanical ventilation (IMV) should be instituted without delay to gain an opportunity for rescue treatment, but this should be preceded by thorough communication with the patient and his/her family and the provision of informed consent.

Currently, there is no established consensus on IMV strategies for patients with severe lung cancer. In cases of acute respiratory failure, a ventilation approach similar to the lung protective strategy used for acute respiratory distress syndrome (ARDS) should be adopted (241). In recent years, several case reports have documented patients with severe lung cancer and severe respiratory failure who achieved satisfactory outcomes following comprehensive anticancer therapies and symptomatic treatment supported by ECMO (242–245).

Supportive care for other vital organs

Patients with severe lung cancer should undergo prompt evaluation of organ function so that potential causes and triggers can be actively eliminated or mitigated, and early symptomatic supportive care should be provided for vital organs (e.g., the heart, liver, kidneys, and brain). In cases of suspected immune-related myocarditis, close monitoring of cardiac conduction is required, and implantation of a temporary pacemaker may be necessary. Attention should be also paid to correcting the electrolyte imbalance and strengthening fluid management to prevent hypovolemia or fluid overload. For critically ill patients with multiple organ failure, intra-aortic balloon counterpulsation and liver or kidney with the patient's family replacement therapy may be necessary after communication with the patient and his/her family and the provision of informed consent.

Nutritional support

Patients with severe lung cancer should be assessed for the

presence or risk of malnutrition. Nutritional assessments that can be used include the Nutritional Risk Screening 2002 (NRS-2002), Patient-Generated Subjective Global Assessment (PG-SGA), and the Global Leadership Initiative on Malnutrition (GLIM) criteria.

According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines (246), patients should receive dietary counseling and, if able to eat, be encouraged to consume adequate energy (25–30 Cal/kg) and protein [1.0–1.5 g/(kg·d)], with nutritional supplements provided if necessary. Enteral nutrition is preferred for patients who have difficulty eating. When enteral nutrition cannot sufficiently meet nutritional requirements or is contraindicated, parenteral nutrition should be used. Micronutrient supplementation should be considered, and individualized nutritional prescriptions are recommended.

Active anti-infective therapy

A prospective cohort study found that among patients with solid tumors admitted to the intensive care unit for acute respiratory failure, bacterial infection accounted for 36.1% of cases, viral infection for 5.5%, fungal infection for 4.3%, and extrapulmonary sepsis for 11.7% (247). The spectrum of pathogens causing infections in patients with lung cancer varies across regions and hospitals in China. In general, common pathogens include *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, and *Haemophilus influenzae* (248–250). For viral infections in patients with lung cancer, pathogens of concern include SARS-CoV-2, influenza virus, adenovirus, parainfluenza virus, rhinovirus, respiratory syncytial virus, human bocavirus, and human metapneumovirus (251). Patients with lung cancer are generally at high risk for invasive fungal infections, especially invasive pulmonary aspergillosis (IPA). In a large retrospective cohort study, 11.7% of patients with lung cancer developed IPA, with a higher risk observed in those receiving chemotherapy and immunotherapy (252). A single-center retrospective study reported high short-term mortality in severe lung cancer patients with IPA who had advanced age, organ failure, or hypoproteinemia (253).

The *NCCN Clinical Practice Guidelines in Oncology: Prevention and Treatment of Cancer-Related Infections* (version 3, 2024) recommend stratifying patients with cancer according to infection risk and implementing appropriate anti-infective prophylaxis and treatment measures based

on risk level. Prophylaxis against bacterial, fungal, and viral infections should be considered for intermediate- and high-risk patients (254).

In patients with severe lung cancer and infection, empiric antimicrobial therapy should be initiated immediately after etiological specimens have been collected. For immunocompromised individuals, delays in appropriate antimicrobial therapy increase the risk of secondary complications and infection-related death (255).

Improvement of coagulation status

Among patients with lung cancer and pulmonary embolism, those who do not receive anticoagulation therapy have a higher mortality rate than those who do (256). Patients with VTE or risk factors for VTE should receive active anticoagulant therapy. Regarding anticoagulation strategies (257–259), full-dose anticoagulation is recommended for patients with cancer-related VTE and a platelet count exceeding $50 \times 10^9/L$, and half-dose anticoagulation is advised for those with platelet counts between $25 \times 10^9/L$ and $50 \times 10^9/L$, but anticoagulation is not recommended for patients with platelet counts below $25 \times 10^9/L$.

Rehabilitation in severe lung cancer

Rehabilitation in severe lung cancer involves the implementation of assessment-based comprehensive management measures, including aerobic exercise, breathing training, airway clearance techniques, and patient education (Figure 2). The research on severe lung cancer has focused on its etiology, treatment, and full-course management (Figure 3). Several studies have shown that preoperative respiratory rehabilitation exercises improve postoperative atelectasis and reduce postoperative complications in patients with lung cancer and COPD (238,239,260). Rehabilitation exercises can also help improve the quality of life of patients after surgery (261). In patients with advanced lung cancer, exercise training can improve their physical performance, anxiety, and depression (262,263). Respiratory rehabilitation exercises include exercise training, education, nutritional support, and psychological support (264) and thus require multidisciplinary collaboration.

Patients with lung cancer are prone to cardiovascular events (265). Aerobic physical training can improve ejection fraction, exercise tolerance, quality of life, and skeletal muscle metabolism in patients with HF. Exercise-based cardiac rehabilitation carries a grade IA recommendation

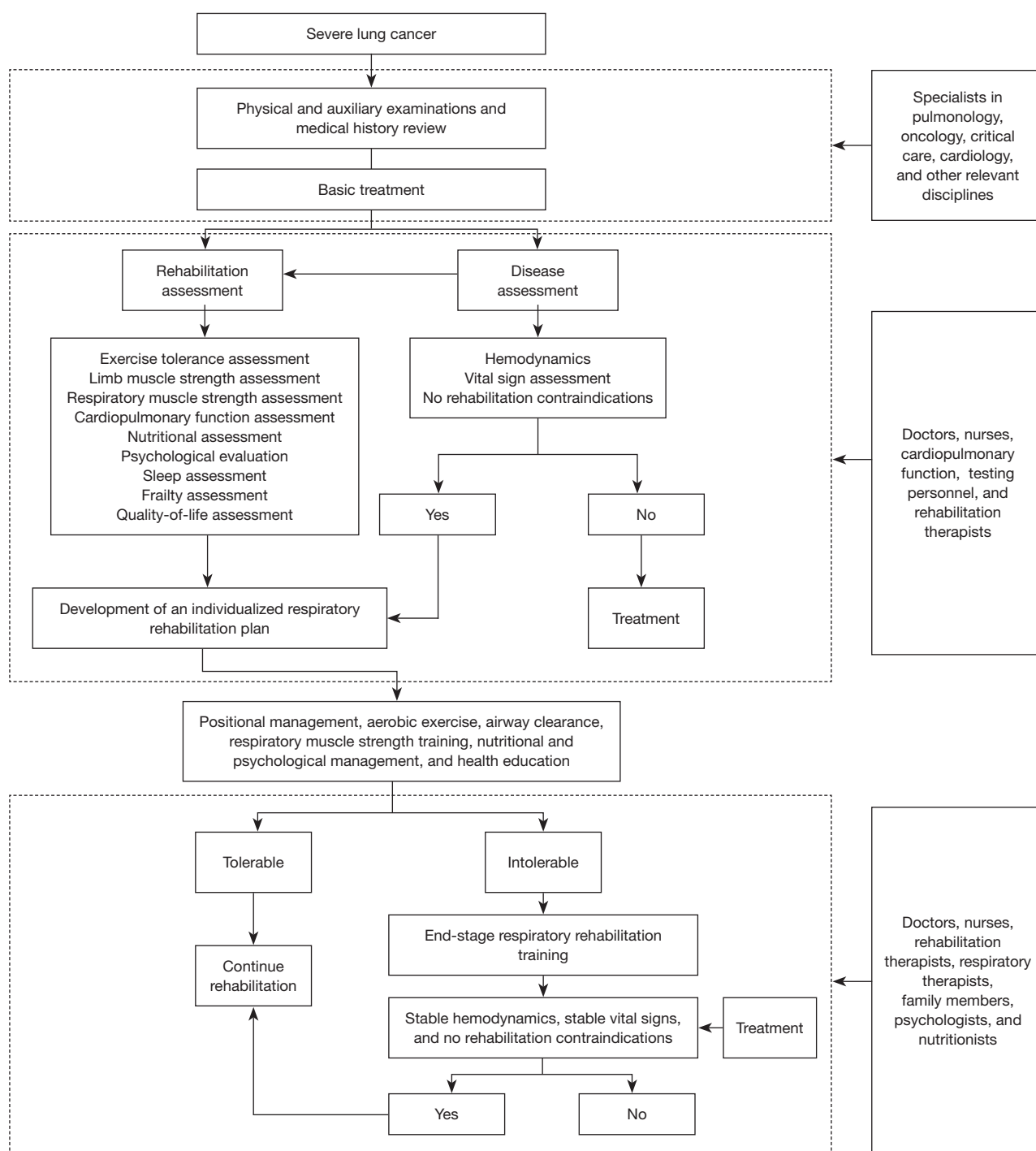


Figure 2 Assessment and treatment workflow for rehabilitation in patients with severe lung cancer.

in the relevant guidelines (266,267). Inspiratory muscle training is an effective and feasible rehabilitation modality for HF in patients with lung cancer and can improve inspiratory muscle fatigue (268).

For patients with severe lung cancer, an individualized rehabilitation strategy should be developed based on multimodal treatment and the patient's condition. Patients with advanced lung cancer and a PS score ≥ 2 may undergo

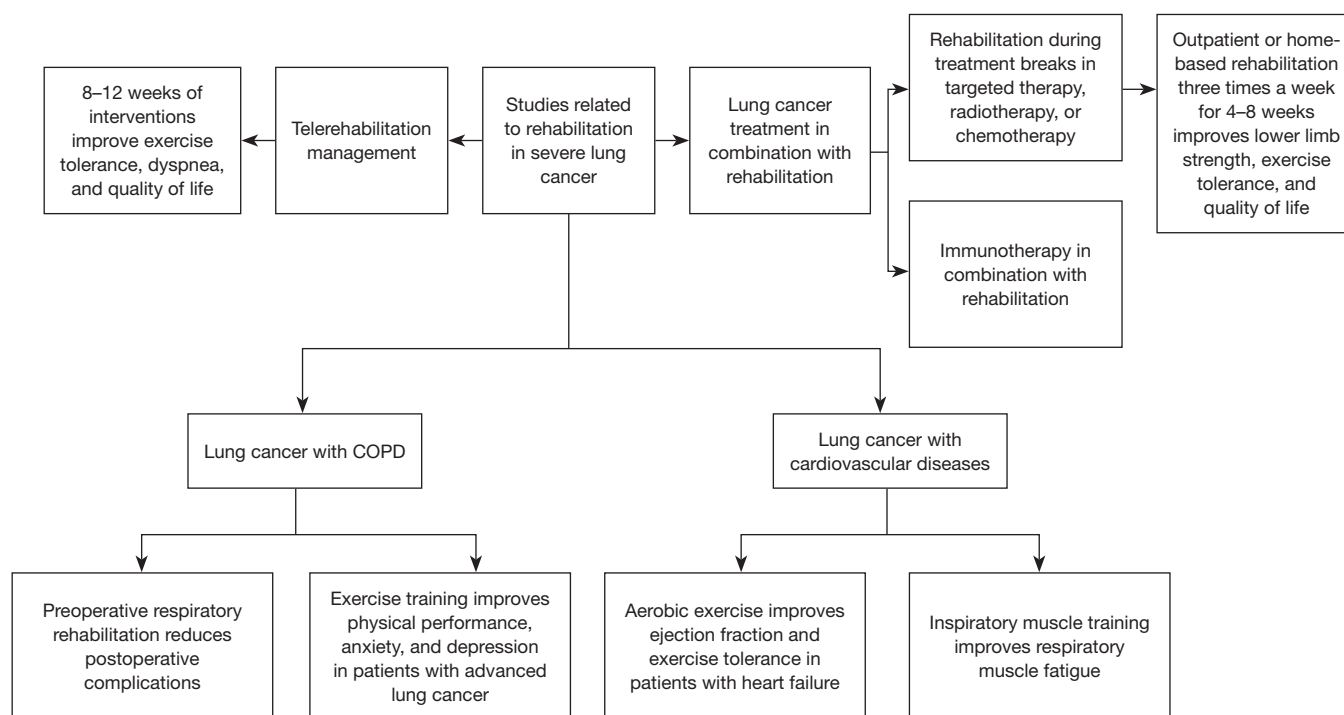


Figure 3 Advances in research on rehabilitation in severe lung cancer. COPD, chronic obstructive pulmonary disease.

outpatient or home-based rehabilitation three times a week for 4–8 weeks under the guidance of a rehabilitation MDT during treatment breaks in targeted therapy, radiotherapy, or chemotherapy. Respiratory rehabilitation includes aerobic exercise, resistance training, and breathing training. The 6MWD, Modified Borg Scale (for dyspnea symptoms), and quality-of-life questionnaire can be applied before and after rehabilitation. Respiratory rehabilitation improves patients' lower-limb strength, exercise tolerance, and quality of life (269–275). However, the research on respiratory rehabilitation during immunotherapy for lung cancer is limited. Nonetheless, a few studies on patients with melanoma receiving immunotherapy have indicated that multimodal rehabilitation can enhance clinical efficacy and reduce immunotoxicity (276,277). Evidence-based studies on respiratory rehabilitation in patients with advanced lung cancer and PS ≥ 3 remain limited. However, initiating prehabilitation from the time of diagnosis is feasible. Early rehabilitation appears to reduce time spent in the hospital and may improve treatment outcomes and long-term survival (278).

Telerehabilitation is safe, feasible, and effective for patients with lung cancer, with 8–12 weeks of interventions leading to improvements in exercise tolerance, dyspnea, and

quality of life. Mobile health-based remote management allows for the monitoring of patient activities via respiratory rehabilitation applications and wearable devices (279–283).

Supportive care for severe lung cancer

Comprehensive assessment of patients

For patients with severe lung cancer, a comprehensive assessment (including functional status, psychological status, comorbidities, social support, and nutritional status) should be conducted by an MDT composed of specialists, specialized nurses, rehabilitation therapists, nutritionists, pharmacists, and psychological counselors. Patient-reported outcome measures are evidence-based tools and/or instruments, typically in the form of interviews or questionnaires, that are used to assess patient-reported outcomes, including symptoms, functional status, and psychological and emotional well-being (284).

Escalation and de-escalation strategies for supportive care

Individualized demand-oriented care can improve the functional status, quality of life, and prognosis of patients with severe lung cancer (285,286). These patients typically

have high and diverse care needs. A care escalation strategy involves the implementation of life support and symptomatic treatments (e.g., observations, respiratory support, complication prevention, pain care, airway care, fluid management, nutritional management) to help maintain function and promote recovery. Once the patient's PS improves, a de-escalation strategy should be implemented. Patient empowerment and education should be provided to help meet their ongoing care needs, and the focus should shift to enhancing activities of daily living and self-management capabilities, implementing tertiary prevention measures, and preventing disease recurrence (e.g., medication guidance, rehabilitation exercises, complication prevention, and continuing care).

Questions to be further discussed and considered

Question 1: Do you agree that the newly refined definition of severe lung cancer (PS score of 2–4 with potential for survival benefit) better reflects the reversible nature of this condition compared to end-stage lung cancer?

Expert opinion: Dr. Alfonso Fiorelli

Yes. Severe lung cancer and end-stage lung cancer are different clinical entities. Severe lung cancer represents a reversible clinical condition. Acute co-morbidities or complications related to lung cancer spread are responsible for poor PS. Active therapies or endoscopic procedures may result in recovery of PS and improvement of survival. By contrast, end-stage lung cancer is an irreversible clinical condition where BSC remains the only option.

Expert opinion: Dr. Baptiste Abbar

Yes, because this refined definition acknowledges that poor PS may be reversible with adapted antitumor treatment, particularly in treatment-naïve patients with small-cell lung cancer. It better distinguishes patients who may still benefit from active treatment from those receiving purely palliative care.

Expert opinion: Dr. Francesco Petrella

Yes. Recent clinical trials indicate that patients with poor PS (ECOG 2–4) due to lung cancer, particularly when the impairment is cancer-related rather than from irreversible comorbidities, can experience meaningful improvements in survival and PS with modern systemic therapies. These

outcomes are notably superior to historical controls, underscoring the potential reversibility of severe lung cancer.

Expert opinion: Dr. Kim Styrvoky

Yes. The revised definition, with emphasis on PS change as a result of cancer-directed therapy, best reflects current treatment strategies. This framework suggests the potential reversibility of PS when functional impairment is driven by tumor burden rather than fixed comorbid conditions.

Expert opinion: Dr. Marcin Braun

Yes, I agree.

Expert opinion: Dr. Mariano Provencio

Yes. The refined definition, focusing on patients with PS 2–4 who retain potential for survival benefit, better captures the dynamic and potentially reversible nature of functional impairment. It clearly differentiates these patients from those with true end-stage disease, where deterioration is irreversible.

Expert opinion: Dr. Rajat Thawani

I agree with the spirit of this definition. But I think a big exception is that the decline should be considered from the lung cancer and reversible to avoid over-treating patients.

Expert opinion: Dr. Rossana Berardi

Yes.

Expert opinion: Dr. Satoshi Watanabe

This is acceptable, as it has not changed substantially from the previous definition.

Expert opinion: Dr. Taichiro Goto

Yes, I strongly agree. The newly refined definition more accurately captures the reversible and dynamic nature of this clinical condition. Unlike end-stage lung cancer, severe lung cancer often reflects a transient deterioration caused by acute complications, comorbidities, or TRAEs.

Expert opinion: Dr. Takeo Nakada

I agree with the proposal, but with some conditions. In patients with PS4, physical function is often severely compromised, making it difficult to regard their condition as truly “reversible”. Moreover, using the term “reversible” may create unrealistic expectations and could potentially delay the initiation of appropriate palliative care.

Expert opinion: Dr. Yoshinobu Ichiki

Yes. Severe lung cancer is a common case encountered in daily clinical practice. Unlike terminal lung cancer, appropriate treatment of cancer-related symptoms, complications, and TRAEs can be expected to improve overall condition and extend survival.

Expert opinion: Dr. Yuichi Saito

Yes, I agree with the concept.

Expert opinion: Dr. Piergiorgio Solli

I fully endorse the transition toward the “severe lung cancer” definition. In daily practice, we frequently encounter patients with poor PS driven by acute, reversible complications. Labeling these cases as “end-stage” is clinically inaccurate and dangerous, as it often leads to therapeutic nihilism. This new definition provides a much-needed framework to distinguish between patients who require aggressive stabilization and those who truly need exclusive palliative care.

Question 2: Do you believe that novel therapies like ADCs and targeted agents offer meaningful clinical benefits for severe patients with lung cancer with poor PS (PS score ≥ 2)?

Expert opinion: Dr. Alfonso Fiorelli

Yes. Patients with severe lung cancer are often considered unsuitable for traditional chemotherapy. ADCs and targeted agents present a favorable toxicity profile and are new therapeutic options for these subsets of patients. Tumor shrinkage may improve clinical symptoms with recovery of PS. However, these benefits are more evident when poor PS is due to tumor extension rather than comorbidities, and careful patient selection remains crucial.

Expert opinion: Dr. Baptiste Abbar

Yes, for targeted therapies that have demonstrated meaningful efficacy in patients with poor PS [2–4], whereas for ADCs, clinical benefit in this population still needs to be confirmed in dedicated prospective studies.

Expert opinion: Dr. Francesco Petrella

Yes. Novel therapies such as ADCs and targeted agents offer meaningful clinical benefits for patients with severe lung cancer who have poor PS in biomarker-selected populations. Trastuzumab deruxtecan, for example, achieved ORRs up to 53% in HER2 IHC 3+ NSCLC. For patients

with poor PS, careful selection is critical, as toxicity remains a concern.

Expert opinion: Dr. Kim Styrvoky

Yes. Targeted agents and novel therapies may be better tolerated in patients with poor PS or severe lung cancer and, in selected patients, can result in meaningful clinical benefit.

Expert opinion: Dr. Marcin Braun

Yes/No—it highly depends on the type of therapy and patient characteristics other than PS alone.

Expert opinion: Dr. Mariano Provencio

Yes. Novel therapies such as ADCs and targeted agents can provide meaningful clinical benefit in selected patients with poor PS, particularly when functional decline is disease-driven rather than comorbidity-driven. Their favorable efficacy-to-toxicity ratios make them especially relevant in this population.

Expert opinion: Dr. Rajat Thawani

Again, as above. Targeted therapies can offer meaningful benefit in patients with PS >2 in most cases. ADCs, on the other hand, are not as dramatic with responses, and also have a significant risk of toxicities, which makes their use in PS >2 less appealing.

Expert opinion: Dr. Rossana Berardi

Yes, in selected cases.

Expert opinion: Dr. Satoshi Watanabe

I certainly agree. However, this should be demonstrated in a prospective clinical trial, preferably a randomized study.

Expert opinion: Dr. Taichiro Goto

Yes, I do. Novel therapies often provide rapid tumor control with relatively favorable toxicity profiles, which is particularly important in patients whose poor PS is tumor-driven. When guided by appropriate biomarker testing, these therapies can lead to symptom relief, PS improvement, and survival benefit.

Expert opinion: Dr. Takeo Nakada

I agree with the statement. The clinical condition of patients with PS2 and PS4 differs substantially, and the potential benefit of these therapies is likely to be quite limited in those with PS4. For such patients, it is essential to

integrate appropriate palliative care alongside any treatment considerations.

Expert opinion: Dr. Yoshinobu Ichiki

Yes. ADCs combine molecularly targeted drugs with cytotoxic anticancer drugs. Because molecularly targeted drugs primarily target cancer-specific molecules, they are thought to have less impact on normal cells, potentially reducing adverse events. While careful consideration is required, we believe they have the potential to provide clinical benefits to patients with severe lung cancer.

Expert opinion: Dr. Yuichi Saito

I believe whether such therapies are meaningful clinically varies depending on the case.

Expert opinion: Dr. Piergiorgio Solli

This is a crucial point. While we have established evidence for TKIs in oncogene-addicted patients with poor PS, the data for ADCs is still maturing, though highly promising. A “safety-first” approach is paramount. We must be exceptionally vigilant regarding specific side effects, such as ILD, which can be fatal in a patient with compromised respiratory reserve. The goal is to offer these therapies as a calculated intervention for patients whose profile suggests a realistic chance of improvement.

Question 3: Do you agree that dynamic PS monitoring should be an essential component in guiding treatment escalation and de-escalation strategies for patients with severe lung cancer?

Expert opinion: Dr. Alfonso Fiorelli

Yes. Escalation or de-escalation strategies are the two sides of the same coin, and the choice depends on PS of patient. PS is affected by several factors and requires a weekly assessment. Patients with good PS may be candidates for escalation of treatment. By contrast, when PS declines, de-escalation remains the strategy of choice to reduce toxicity.

Expert opinion: Dr. Baptiste Abbar

Yes, I agree that dynamic PS monitoring is crucial throughout the oncologic management of these patients to guide timely treatment escalation and de-escalation.

Expert opinion: Dr. Francesco Petrella

Yes. Dynamic monitoring enables more accurate, timely, and patient-centered decision-making. It allows clinicians

to detect clinically meaningful changes that may warrant adjustment of therapy. Traditional tools like ECOG PS are limited by subjectivity and infrequent assessment, often failing to capture rapid fluctuations in functional status.

Expert opinion: Dr. Kim Styrvoky

Yes. PS should be assessed at every clinical encounter, and treatment recommendations should be individualized based on both treatment response and changes in PS over time.

Expert opinion: Dr. Marcin Braun

Yes, I definitely agree.

Expert opinion: Dr. Mariano Provencio

Yes. Dynamic PS monitoring should be an essential component of care, as PS is not static and may improve or worsen with treatment response or supportive interventions. Regular reassessment enables more appropriate treatment escalation, de-escalation, or discontinuation.

Expert opinion: Dr. Rajat Thawani

Yes. Dynamic PS monitoring should be done to advance therapy, and consider aggressive supportive care or hospice referral.

Expert opinion: Dr. Rossana Berardi

Yes, together with clinical benefit including other parameters (lab exams, weight...)

Expert opinion: Dr. Satoshi Watanabe

I agree. Treatment escalation or de-escalation should be considered based on the patient's PS.

Expert opinion: Dr. Taichiro Goto

Yes, dynamic PS monitoring is essential. PS in severe lung cancer is not static but fluctuates over time. Continuous assessment is crucial for identifying patients who may benefit from treatment escalation once their condition improves, as well as for timely de-escalation to avoid overtreatment.

Expert opinion: Dr. Takeo Nakada

Yes, I agree.

Expert opinion: Dr. Yoshinobu Ichiki

Yes. Compared to end-stage lung cancer, intensive treatment is expected to improve overall condition, and this population is considered to have high therapeutic

value. Identifying biomarkers to appropriately detect this population is important, and dynamic PS monitoring is considered one promising biomarker.

Expert opinion: Dr. Yuichi Saito

Yes, I do.

Expert opinion: Dr. Piergiorgio Solli

I strongly agree. A single, static assessment of PS at admission is often a poor predictor of a patient's true therapeutic potential. By adopting dynamic monitoring, we can implement a "test-of-treatment" strategy, reassessing the patient's fitness within 24 to 72 hours. This allows us to safely navigate the balance between treatment escalation and de-escalation, ensuring decisions align with the patient's real-time physiological status.

Question 4: Do you think that early rehabilitation interventions should be systematically integrated into the comprehensive management of patients with severe lung cancer?

Expert opinion: Dr. Alfonso Fiorelli

Yes. Physical, respiratory, and functional assistance are likely to preserve PS and improve tolerance to therapies, making rehabilitation interventions crucial. Timely rehabilitation helps to overcome sarcopenia, respiratory failure and to reinforce functional independence, which then allows escalation treatment.

Expert opinion: Dr. Baptiste Abbar

Yes, as the early involvement of the different supportive care professionals is essential for the comprehensive management of patients with severe lung cancer.

Expert opinion: Dr. Francesco Petrella

Yes. Early rehabilitation has demonstrated moderate benefits in improving health-related quality of life, functional capacity, and symptom burden for patients with severe lung cancer. These interventions are safe, feasible, and can be tailored to individual needs, supporting their use across the disease continuum.

Expert opinion: Dr. Kim Styrvoky

Yes. Patients with severe lung cancer should receive multidisciplinary care aimed at optimizing physical function, including early rehabilitation interventions to improve or

preserve PS.

Expert opinion: Dr. Marcin Braun

Yes.

Expert opinion: Dr. Mariano Provencio

Yes. Early and systematic integration of rehabilitation interventions (physical, nutritional, and psychosocial) is critical. These measures can improve functional status, treatment tolerance, and quality of life, and may directly influence eligibility for and benefit from anticancer therapies.

Expert opinion: Dr. Rajat Thawani

Early rehabilitation should be integrated, because a major component of "severe" status is deconditioning and modifiable symptoms, like physical therapy/occupational therapy (PT/OT), respiratory therapy, and even psychotherapy to avoid depression and apathy.

Expert opinion: Dr. Rossana Berardi

Yes.

Expert opinion: Dr. Satoshi Watanabe

If rehabilitation is expected to improve a patient's general condition or PS, it may be considered; however, it is not necessarily indicated for all patients.

Expert opinion: Dr. Taichiro Goto

Yes, early rehabilitation should be systematically integrated. Such interventions can improve functional capacity, reduce complications, enhance tolerance to anticancer therapies, and facilitate recovery of PS. It should be considered a standard component of multidisciplinary care rather than an adjunctive strategy.

Expert opinion: Dr. Takeo Nakada

Yes, I agree. However, in reality, the shortage of rehabilitation specialists and institutional limitations make it challenging to systematically implement early rehabilitation for all patients.

Expert opinion: Dr. Yoshinobu Ichiki

Yes. We believe that maintaining and increasing muscle strength through early rehabilitation is essential to maintaining and improving PS. Multidisciplinary collaboration and individualized comprehensive treatment

are extremely important in the treatment of severe lung cancer.

Expert opinion: Dr. Yuichi Saito

Yes, I think so.

Expert opinion: Dr. Piergiorgio Solli

Rehabilitation is frequently undervalued, so its systematic inclusion here is a significant strength. For a patient with severe lung cancer, “rehab” is a fundamental physiological intervention. Early rehabilitation is essential to maintain enough functional reserve to tolerate systemic therapy. I would argue that a patient’s engagement with early rehab should be considered a functional “test of fitness” for treatment escalation.

Question 5: Do you believe that MDT management is crucial for developing individualized treatment strategies for patients with severe lung cancer across different healthcare systems?

Expert opinion: Dr. Alfonso Fiorelli

Yes. MDT plays a crucial role as it allows defining an optimized treatment based on current international guidelines. Multiple specialists review all clinical data and molecular biomarkers to plan a personalized treatment. The use of telemedicine guarantees standardization of treatment also for patients living in remote areas.

Expert opinion: Dr. Baptiste Abbar

Yes, MDT discussion is essential to develop individualized treatment strategies, as clinical guidelines cannot capture all real-world situations and must be adapted to each patient’s specific context.

Expert opinion: Dr. Francesco Petrella

Yes. MDTs facilitate the integration of diverse expertise, allowing for comprehensive assessment and tailored management, particularly in complex cases requiring multimodality therapy. This approach optimizes diagnostic accuracy, staging, and treatment selection, and ensures adherence to guideline-concordant care.

Expert opinion: Dr. Kim Styrvoky

Yes. Given current advances in lung cancer care, MDT management is essential to ensure patients receive state-of-the-art, guideline-recommended therapies and appropriate consideration for clinical trial enrollment.

Expert opinion: Dr. Marcin Braun

Yes.

Expert opinion: Dr. Mariano Provencio

Yes. MDT management is crucial to develop individualized treatment strategies for patients with severe lung cancer. Coordinated input from oncology, pulmonology, radiation oncology, supportive care, rehabilitation, and other specialties is essential to address clinical complexity and ensure consistent, patient-centered care.

Expert opinion: Dr. Rajat Thawani

Absolutely. And in lower resource settings, tele-MDT should be considered.

Expert opinion: Dr. Rossana Berardi

Yes.

Expert opinion: Dr. Satoshi Watanabe

Multidisciplinary assessment of patients with lung cancer is essential for determining appropriate treatment strategies. This need is even greater in patients with severe lung cancer.

Expert opinion: Dr. Taichiro Goto

Yes, MDT management is crucial. Given the complexity of these cases—often involving comorbidities, organ dysfunction, and rapidly changing clinical status—collaboration among multiple specialties is indispensable. MDT-based decision-making enhances both quality of care and patient outcomes.

Expert opinion: Dr. Takeo Nakada

Yes, I agree. At the same time, I believe that the effective implementation of MDT requires addressing various challenges, including the time and cost involved, as well as the availability of medical resources and personnel.

Expert opinion: Dr. Yoshinobu Ichiki

Yes. It is important that medical professionals from various specialties work together as a team to pursue the best clinical practice. In the treatment of severe lung cancer, the collaboration of surgeons, medical oncologists, radiation oncologists, nurses, and social workers is essential to improve treatment outcomes and quality of life.

Expert opinion: Dr. Yuichi Saito

Yes, I think that MDT management is critically important

for developing individualized treatment strategies, however it is still unclear what type of professional staff should join into the MDT management.

Expert opinion: Dr. Piergiorgio Solli

I am firmly convinced that MDT management is the absolute cornerstone of success. The complexity of these cases makes individualized strategy impossible without synergistic collaboration. MDT isn't a luxury—it's a necessity for high-quality, patient-centered care globally. This represents the most effective way to reduce mortality and ensure individualized strategies in this complex population.

Conclusions

The *International Consensus on Severe Lung Cancer: The Second Edition* reaffirms and refines the concept of severe lung cancer. This updated consensus underscores the critical importance of dynamic and precise detection, robust life support strategies, and the flexible application of novel therapeutic modalities, including targeted therapies, ADCs, immunotherapy, and advanced interventional techniques. Central to this framework is an MDT that guides treatment intensity adjustment in response to the patient's evolving clinical status. The integration of structured rehabilitation and comprehensive supportive care from the outset is emphasized as a pillar of management to improve functional status and quality of life.

Moving forward, prospective clinical trials focusing specifically on the population of patients with severe lung cancer are urgently needed to generate high-level evidence. It is imperative to disseminate and implement these consensus recommendations globally to standardize care pathways, with the ultimate aim of improving survival outcomes and the quality of life for patients with severe lung cancer.

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References

- Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2024;74:229-63.
- Maclay JD, Farley JM, McCowan C, et al. Obtaining tissue diagnosis in lung cancer patients with poor performance status and its influence on treatment and survival. *Respir Med* 2017;124:30-5.
- Qin YY, Zhang DH, Lin XQ, et al. Clinical analysis of 36 cases of advanced non-small cell lung cancer (NSCLC) with performance status (PS) scores between 2 and 4. *Zhonghua Zhong Liu Za Zhi* 2017;39:855-61.
- Xie ZH, Zhou CZ, Qin YY, et al. Diagnosis and treatment strategies for advanced severe lung cancer. *Chin J Pract Intern Med* 2019;39:4.
- Centre for Evidence-Based Medicine. Oxford Centre for Evidence-Based Medicine: Levels of Evidence (March 2009). (October 8, 2024). Available online: <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009>
- Wang F, Xie X, Wang L, et al. Real-world data on severe lung cancer: a multicenter retrospective study. *Transl Lung Cancer Res* 2023;12:460-70.
- Serpa Neto A, Hemmes SN, Barbas CS, et al. Incidence of mortality and morbidity related to postoperative lung injury in patients who have undergone abdominal or thoracic surgery: a systematic review and meta-analysis. *Lancet Respir Med* 2014;2:1007-15.
- Ali FS, Arevalo O, Zorofchian S, et al. Cerebral Radiation Necrosis: Incidence, Pathogenesis, Diagnostic Challenges, and Future Opportunities. *Curr Oncol Rep* 2019;21:66.
- Rahmathulla G, Marko NF, Weil RJ. Cerebral radiation necrosis: a review of the pathobiology, diagnosis and management considerations. *J Clin Neurosci* 2013;20:485-502.
- Li Y, Klippel Z, Shih X, et al. Relationship between severity and duration of chemotherapy-induced neutropenia and risk of infection among patients with nonmyeloid malignancies. *Support Care Cancer* 2016;24:4377-83.
- Cupp J, Culakova E, Poniewierski MS, et al. Analysis of Factors Associated With In-hospital Mortality in Lung Cancer Chemotherapy Patients With Neutropenia. *Clin Lung Cancer* 2018;19:e163-9.
- Hapani S, Sher A, Chu D, et al. Increased risk of serious hemorrhage with bevacizumab in cancer patients: a meta-analysis. *Oncology* 2010;79:27-38.
- Qi WX, Sun YJ, Shen Z, et al. Risk of interstitial lung disease associated with EGFR-TKIs in advanced non-small-cell lung cancer: a meta-analysis of 24 phase III clinical trials. *J Chemother* 2015;27:40-51.
- Suh CH, Kim KW, Pyo J, et al. The incidence of ALK inhibitor-related pneumonitis in advanced non-small-cell lung cancer patients: A systematic review and meta-analysis. *Lung Cancer* 2019;132:79-86.
- Suresh K, Voong KR, Shankar B, et al. Pneumonitis in Non-Small Cell Lung Cancer Patients Receiving Immune Checkpoint Immunotherapy: Incidence and Risk Factors. *J Thorac Oncol* 2018;13:1930-9.
- Cho JY, Kim J, Lee JS, et al. Characteristics, incidence, and risk factors of immune checkpoint inhibitor-related pneumonitis in patients with non-small cell lung cancer. *Lung Cancer* 2018;125:150-6.
- Tone M, Izumo T, Awano N, et al. High mortality and poor treatment efficacy of immune checkpoint inhibitors

- in patients with severe grade checkpoint inhibitor pneumonitis in non-small cell lung cancer. *Thorac Cancer* 2019;10:2006-12.
18. Lin X, Deng H, Chen L, et al. Clinical types of checkpoint inhibitor-related pneumonitis in lung cancer patients: a multicenter experience. *Transl Lung Cancer Res* 2021;10:415-29.
 19. Tan HN, Morcillo MA, Lopez J, et al. Treatment-related adverse events of antibody drug-conjugates in clinical trials. *J Hematol Oncol* 2025;18:71.
 20. Zhu Y, Liu K, Wang K, et al. Treatment-related adverse events of antibody-drug conjugates in clinical trials: A systematic review and meta-analysis. *Cancer* 2023;129:283-95.
 21. Gompelmann D, Eberhardt R, Herth FJ. Advanced malignant lung disease: what the specialist can offer. *Respiration* 2011;82:111-23.
 22. Porcel JM, Gasol A, Bielsa S, et al. Clinical features and survival of lung cancer patients with pleural effusions. *Respirology* 2015;20:654-9.
 23. Porcel JM. Malignant pleural effusions because of lung cancer. *Curr Opin Pulm Med* 2016;22:356-61.
 24. Ryu JS, Ryu HJ, Lee SN, et al. Prognostic impact of minimal pleural effusion in non-small-cell lung cancer. *J Clin Oncol* 2014;32:960-7.
 25. Yoneda KY, Mathur PN, Gasparini S. The evolving role of interventional pulmonary in the interdisciplinary approach to the staging and management of lung cancer. Part III: diagnosis and management of malignant pleural effusions. *Clin Lung Cancer* 2007;8:535-47.
 26. Tsang TS, Seward JB, Barnes ME, et al. Outcomes of primary and secondary treatment of pericardial effusion in patients with malignancy. *Mayo Clin Proc* 2000;75:248-53.
 27. Gornik HL, Gerhard-Herman M, Beckman JA. Abnormal cytology predicts poor prognosis in cancer patients with pericardial effusion. *J Clin Oncol* 2005;23:5211-6.
 28. Rousseau-Bussac G, Crequit P, Alifano M, et al. Management of malignant pericardial effusion in lung cancer. *Rev Mal Respir* 2014;31:746-53.
 29. Hu ZG, Hu K, Li WX, et al. Prognostic factors and nomogram for cancer-specific death in non small cell lung cancer with malignant pericardial effusion. *PLoS One* 2019;14:e0217007.
 30. Di Liso E, Menichetti A, Dieci MV, et al. Neoplastic Pericardial Effusion: A Monocentric Retrospective Study. *J Palliat Med* 2019;22:691-5.
 31. Guibert N, Mazieres J, Marquette CH, et al. Integration of interventional bronchoscopy in the management of lung cancer. *Eur Respir Rev* 2015;24:378-91.
 32. Chen Y, Zhou Z, Feng J, et al. Use of Hybrid Stent in Management of Complex Malignant Airway Stenosis and Fistulas. *Zhongguo Fei Ai Za Zhi* 2020;23:472-8.
 33. Skowronek J, Młynarczyk W, Piorunek T. Brachytherapy in the treatment of lung and tracheal cancer: current indications, methods, results. *Przegl Lek* 2006;63:664-73.
 34. Walker AJ, Card TR, West J, et al. Incidence of venous thromboembolism in patients with cancer - a cohort study using linked United Kingdom databases. *Eur J Cancer* 2013;49:1404-13.
 35. Connolly GC, Dalal M, Lin J, et al. Incidence and predictors of venous thromboembolism (VTE) among ambulatory patients with lung cancer. *Lung Cancer* 2012;78:253-8.
 36. Khorana AA, Francis CW, Culakova E, et al. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. *J Thromb Haemost* 2007;5:632-4.
 37. Giometto B, Grisold W, Vitaliani R, et al. Paraneoplastic neurologic syndrome in the PNS Euronetwork database: a European study from 20 centers. *Arch Neurol* 2010;67:330-5.
 38. Grose D, Morrison DS, Devereux G, et al. Comorbidities in lung cancer: prevalence, severity and links with socioeconomic status and treatment. *Postgrad Med J* 2014;90:305-10.
 39. Nieder C, Engljähringer K, Angelo K. Impact of comorbidity on survival after palliative radiotherapy. *Strahlenther Onkol* 2014;190:1149-53.
 40. Alexander M, Evans SM, Stirling RG, et al. The Influence of Comorbidity and the Simplified Comorbidity Score on Overall Survival in Non-Small Cell Lung Cancer-A Prospective Cohort Study. *J Thorac Oncol* 2016;11:748-57.
 41. Grose D, Morrison DS, Devereux G, et al. The impact of comorbidity upon determinants of outcome in patients with lung cancer. *Lung Cancer* 2015;87:186-92.
 42. Ameri P, Canepa M, Anker MS, et al. Cancer diagnosis in patients with heart failure: epidemiology, clinical implications and gaps in knowledge. *Eur J Heart Fail* 2018;20:879-87.
 43. de Boer RA, Meijers WC, van der Meer P, et al. Cancer and heart disease: associations and relations. *Eur J Heart Fail* 2019;21:1515-25.
 44. Kravchenko J, Berry M, Arbeeve K, et al. Cardiovascular comorbidities and survival of lung cancer patients: Medicare data based analysis. *Lung Cancer* 2015;88:85-93.

45. Loganathan RS, Stover DE, Shi W, et al. Prevalence of COPD in women compared to men around the time of diagnosis of primary lung cancer. *Chest* 2006;129:1305-12.
46. Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. *Lancet* 2007;370:741-50.
47. Lee SJ, Lee J, Park YS, et al. Impact of chronic obstructive pulmonary disease on the mortality of patients with non-small-cell lung cancer. *J Thorac Oncol* 2014;9:812-7.
48. Hashimoto N, Matsuzaki A, Okada Y, et al. Clinical impact of prevalence and severity of COPD on the decision-making process for therapeutic management of lung cancer patients. *BMC Pulm Med* 2014;14:14.
49. Lin H, Lu Y, Lin L, et al. Does chronic obstructive pulmonary disease relate to poor prognosis in patients with lung cancer?: A meta-analysis. *Medicine (Baltimore)* 2019;98:e14837.
50. Naccache JM, Gibiot Q, Monnet I, et al. Lung cancer and interstitial lung disease: a literature review. *J Thorac Dis* 2018;10:3829-44.
51. Saito Y, Kawai Y, Takahashi N, et al. Survival after surgery for pathologic stage IA non-small cell lung cancer associated with idiopathic pulmonary fibrosis. *Ann Thorac Surg* 2011;92:1812-7.
52. Tomassetti S, Gurioli C, Ryu JH, et al. The impact of lung cancer on survival of idiopathic pulmonary fibrosis. *Chest* 2015;147:157-64.
53. Raghu G, Amatto VC, Behr J, et al. Comorbidities in idiopathic pulmonary fibrosis patients: a systematic literature review. *Eur Respir J* 2015;46:1113-30.
54. Hyzy R, Huang S, Myers J, et al. Acute exacerbation of idiopathic pulmonary fibrosis. *Chest* 2007;132:1652-8.
55. Hoshikawa Y, Kondo T. Perioperative lung injury: acute exacerbation of idiopathic pulmonary fibrosis and acute interstitial pneumonia after pulmonary resection. *Nihon Geka Gakkai Zasshi* 2004;105:757-62.
56. Kumar P, Goldstraw P, Yamada K, et al. Pulmonary fibrosis and lung cancer: risk and benefit analysis of pulmonary resection. *J Thorac Cardiovasc Surg* 2003;125:1321-7.
57. Miyamoto A, Kishi K, Yoshimura K. A nationwide survey concerning lung surgery for lung cancer associated with idiopathic interstitial pneumonia. *Nihon Kokyuki Gakkai Zasshi* 2011;49:148-50.
58. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol* (1985) 2010;108:206-11.
59. Zerah F, Harf A, Perlemuter L, et al. Effects of obesity on respiratory resistance. *Chest* 1993;103:1470-6.
60. Bamgbade OA, Rutter TW, Nafiu OO, et al. Postoperative complications in obese and nonobese patients. *World J Surg* 2007;31:556-60; discussion 561.
61. De Jong A, Verzilli D, Chanques G, et al. Preoperative risk and perioperative management of obese patients. *Rev Mal Respir* 2019;36:985-1001.
62. Oldani S, Petrelli F, Dognini G, et al. COVID-19 and Lung Cancer Survival: An Updated Systematic Review and Meta-Analysis. *Cancers (Basel)* 2022;14:5706.
63. Inoue A, Kobayashi K, Usui K, et al. First-line gefitinib for patients with advanced non-small-cell lung cancer harboring epidermal growth factor receptor mutations without indication for chemotherapy. *J Clin Oncol* 2009;27:1394-400.
64. Kancharla H, Gundu N, Pathak N, et al. Cytotoxic chemotherapy in advanced non-small cell lung cancer with poor performance status: A retrospective analysis from routine clinical practice. *Curr Probl Cancer* 2020;44:100550.
65. Celermajer DS, Boyer MJ, Bailey BP, et al. Pericardiocentesis for symptomatic malignant pericardial effusion: a study of 36 patients. *Med J Aust* 1991;154:19-22.
66. Martinoni A, Cipolla CM, Civelli M, et al. Intrapericardial treatment of neoplastic pericardial effusions. *Herz* 2000;25:787-93.
67. Lewis MA, Hendrickson AW, Moynihan TJ. Oncologic emergencies: Pathophysiology, presentation, diagnosis, and treatment. *CA Cancer J Clin* 2011;61:287-314.
68. Grose D, Devereux G, Brown L, et al. Variation in comorbidity and clinical management in patients newly diagnosed with lung cancer in four Scottish centers. *J Thorac Oncol* 2011;6:500-9.
69. Xie XH, Wang F, Lin XQ, et al. Anlotinib Plus S-1 for Patients with EGFR Mutation-Negative Advanced Squamous Cell Lung Cancer with PS Scores of 2-3 After Progression of Second-Line or Later-Line Treatment. *Cancer Manag Res* 2020;12:12709-14.
70. Owusuaa C, Dijkland SA, Nieboer D, et al. Predictors of Mortality in Patients with Advanced Cancer-A Systematic Review and Meta-Analysis. *Cancers (Basel)* 2022;14:328.
71. Leonetti A, Peroni M, Agnetti V, et al. Thirty-day mortality in hospitalised patients with lung cancer: incidence and predictors. *BMJ Support Palliat Care* 2023;spcare-2023-004558.
72. Tas F, Ozturk A, Erturk K. Prognostic significance of body mass index and serum albumin as the indicators of

- nutritional status in small cell lung cancer. *Postgrad Med* 2024;136:208-17.
73. Goldsmith I, Chesterfield-Thomas G, Toghill H. Pre-treatment optimization with pulmonary rehabilitation in lung cancer: Making the inoperable patients operable. *EClinicalMedicine* 2021;31:100663.
 74. Karlsson AT, Hjermstad MJ, Aass N, et al. Overall Survival after Radiotherapy for Brain Metastases According to ECOG Status-A Prospective Study of 294 NSCLC Patients. *Cancers (Basel)* 2024;16:1486.
 75. Holub K, Louvel G. Poor performance status and brain metastases treatment: who may benefit from the stereotactic radiotherapy? *J Neurooncol* 2021;152:383-93.
 76. Xing Y, Lv X, Zeng D, et al. Clinical Study of Airway Stent Implantation in the Treatment of Patients with Malignant Central Airway Obstruction. *Evid Based Complement Alternat Med* 2022;2022:6933793.
 77. Yang XG, Wu G, Li ZW, et al. Efficacy for artery chemoembolization combined with radiofrequency ablation in the treatment of advanced non-small cell lung cancer. *Zhonghua Yi Xue Za Zhi* 2016;96:539-43.
 78. Camerini A, Del Conte A, Pezzuto A, et al. Selection Criteria and Treatment Outcome for Advanced Non-Small Cell Lung Cancer (NSCLC) Patients Unfit for Platinum-Based First-Line Therapy: Results of the MOON-OSS Observational Trial. *Cancers (Basel)* 2022;14:6074.
 79. M SG, Mohapatra PR, Bhuniya S, et al. Impact of Comorbidity Scores on the Overall Survival of Patients With Advanced Non-small Cell Lung Cancer: A Real-World Experience From Eastern India. *Cureus* 2022;14:e30589.
 80. Gendarme S, Zebachi S, Corre R, et al. Predictors of three-month mortality and severe chemotherapy-related adverse events in patients aged 70 years and older with metastatic non-small-cell lung cancer: A secondary analysis of ESOGIA-GFPC-GECP 08-02 study. *J Geriatr Oncol* 2024;15:101506.
 81. Okuma Y, Shintani Y, Sekine I, et al. Efficacy of Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitors in Metastatic Non-Small Cell Lung Cancer Patients with Poor Performance Status and Epidermal Growth Factor Receptor Mutations: Findings from the Japanese Lung Cancer Registry Database. *Clin Lung Cancer* 2024;25:336-346.e2.
 82. Chang CY, Chen CY, Chang SC, et al. Efficacy and Prognosis of First-Line EGFR-Tyrosine Kinase Inhibitor Treatment in Older Adults Including Poor Performance Status Patients with EGFR-Mutated Non-Small-Cell Lung Cancer. *Cancer Manag Res* 2021;13:7187-201.
 83. Panda GS, Noronha V, Patil V, et al. Clinical outcomes of ROS1-positive non-small cell lung cancer with limited access to ROS1-tyrosine kinase inhibitors (TKIs): experience from an Indian tertiary referral centre. *Ecancermedicalscience* 2024;18:1654.
 84. Matsuo N, Azuma K, Murotani K, et al. Prognostic effect of cachexia in patients with non-small cell lung cancer receiving immune checkpoint inhibitors. *Thorac Cancer* 2023;14:1362-7.
 85. Lobefaro R, Viscardi G, Di Liello R, et al. Immunotherapy in advanced Non-Small Cell Lung Cancer patients with poor performance status: The role of clinical-pathological variables and inflammatory biomarkers. *Lung Cancer* 2021;152:165-73.
 86. Ha D, Mazzone PJ, Ries AL, et al. The Utility of Exercise Testing in Patients with Lung Cancer. *J Thorac Oncol* 2016;11:1397-410.
 87. Jain A, Philip B, Begum M, et al. Risk Stratification for Lung Cancer Patients. *Cureus* 2022;14:e30643.
 88. Arbee-Kalidas N, Moutlana HJ, Moodley Y, et al. The association between cardiopulmonary exercise testing and postoperative outcomes in patients with lung cancer undergoing lung resection surgery: A systematic review and meta-analysis. *PLoS One* 2023;18:e0295430.
 89. Wang K, She Q, Li M, et al. Prognostic significance of frailty status in patients with primary lung cancer. *BMC Geriatr* 2023;23:46.
 90. Ezzatvar Y, Ramírez-Vélez R, Sáez de Asteasu ML, et al. Cardiorespiratory fitness and all-cause mortality in adults diagnosed with cancer systematic review and meta-analysis. *Scand J Med Sci Sports* 2021;31:1745-52.
 91. Kasymjanova G, Correa JA, Kreisman H, et al. Prognostic value of the six-minute walk in advanced non-small cell lung cancer. *J Thorac Oncol* 2009;4:602-7.
 92. Zhu D, Ding R, Ma Y, et al. Comorbidity in lung cancer patients and its association with hospital readmission and fatality in China. *BMC Cancer* 2021;21:557.
 93. Henson LA, Chukwusa E, Ng Yin Ling C, et al. Lung cancer deaths (England 2001-2017)-comorbidities: a national population-based analysis. *BMJ Support Palliat Care* 2021;bmjspcare-2021-003107.
 94. Mellemegaard A, Lüchtenborg M, Iachina M, et al. Role of comorbidity on survival after radiotherapy and chemotherapy for nonsurgically treated lung cancer. *J Thorac Oncol* 2015;10:272-9.
 95. Fink CA, Weykamp F, Adeberg S, et al. Comorbidity in limited disease small-cell lung cancer: Age-adjusted

- Charlson comorbidity index and its association with overall survival following chemoradiotherapy. *Clin Transl Radiat Oncol* 2023;42:100665.
96. Dreyer J, Bremer M, Henkenberens C. Comorbidity indexing for prediction of the clinical outcome after stereotactic body radiation therapy in non-small cell lung cancer. *Radiat Oncol* 2018;13:213.
 97. Lee K, Kang S, Hwang J. Lung Cancer Patients' Characteristics and Comorbidities Using the Korean National Hospital Discharge In-depth Injury Survey Data. *J Epidemiol Glob Health* 2022;12:258-66.
 98. Murawski M, Walter J, Schwarzkopf L. Assessing the lung cancer comorbidity: An analysis of German claims data. *Lung Cancer* 2019;127:122-9.
 99. Yan M, Tjong M, Chan WC, et al. Dyspnea in patients with stage IV non-small cell lung cancer: a population-based analysis of disease burden and patterns of care. *J Thorac Dis* 2023;15:494-506.
 100. Pluchart H, Bailly S, Chanoine S, et al. Comparison of seven comorbidity scores on four-month survival of lung cancer patients. *BMC Med Res Methodol* 2023;23:256.
 101. Yang CC, Fong Y, Lin LC, et al. The age-adjusted Charlson comorbidity index is a better predictor of survival in operated lung cancer patients than the Charlson and Elixhauser comorbidity indices. *Eur J Cardiothorac Surg* 2018;53:235-40.
 102. Romine PE, Sun Q, Fedorenko C, et al. Impact of Diagnostic Delays on Lung Cancer Survival Outcomes: A Population Study of the US SEER-Medicare Database. *JCO Oncol Pract* 2022;18:e877-85.
 103. Tsai CH, Kung PT, Kuo WY, et al. Effect of time interval from diagnosis to treatment for non-small cell lung cancer on survival: a national cohort study in Taiwan. *BMJ Open* 2020;10:e034351.
 104. Keats JJ, Chesi M, Egan JB, et al. Clonal competition with alternating dominance in multiple myeloma. *Blood* 2012;120:1067-76.
 105. Almendro V, Marusyk A, Polyak K. Cellular heterogeneity and molecular evolution in cancer. *Annu Rev Pathol* 2013;8:277-302.
 106. Huang RS, Mihalache A, Nafees A, et al. The impact of multidisciplinary cancer conferences on overall survival: a meta-analysis. *J Natl Cancer Inst* 2024;116:356-69.
 107. Leduc C, Antoni D, Charloux A, et al. Comorbidities in the management of patients with lung cancer. *Eur Respir J* 2017;49:1601721.
 108. ZHANG JT, PAN Y, WANG BC, et al. Adaptive Treatment of Lung Cancer: Less or More?. *Journal of Evidence-Based Medicine* 2024;24:1-11.
 109. Pathak N, Garg R, Khurana S, et al. Improving the performance status in advanced non-small cell lung cancer patients with chemotherapy (ImPACt trial): a phase 2 study. *J Cancer Res Clin Oncol* 2023;149:6399-409.
 110. Deng H, Zhou C. From CheckMate 227 to CheckMate 9LA: rethinking the status of chemotherapy in the immunotherapy era-chemo-free or chemo-reform? *Transl Lung Cancer Res* 2021;10:1924-7.
 111. Deng H, Lin X, Xie X, et al. Immune Checkpoint Inhibitors Plus Single-Agent Chemotherapy for Advanced Non-Small-Cell Lung Cancer After Resistance to EGFR-TKI. *Front Oncol* 2021;11:700023.
 112. Liang H, Liu J, Wu S, et al. Nonintubated Spontaneous Ventilation Offers Better Short-term Outcome for Mediastinal Tumor Surgery. *Ann Thorac Surg* 2019;108:1045-51.
 113. Punchak M, Miranda SP, Gutierrez A, et al. Resecting the dominant lesion: Patient outcomes after surgery and radiosurgery vs stand-alone radiosurgery in the setting of multiple brain metastases. *Clin Neurol Neurosurg* 2021;211:107016.
 114. Piffko A, Asey B, Dührsen L, et al. Clinical determinants impacting overall survival of patients with operable brain metastases from non-small cell lung cancer. *Front Oncol* 2022;12:951805.
 115. Wang Q, Li J, Liang X, et al. Improved Survival With Surgical Treatment of Primary Lung Lesions in Non-Small Cell Lung Cancer With Brain Metastases: A Propensity-Matched Analysis of Surveillance, Epidemiology, and End Results Database. *Front Oncol* 2022;12:888999.
 116. Heßler N, Jünger ST, Meissner AK, et al. Recurrent brain metastases: the role of resection of in a comprehensive multidisciplinary treatment setting. *BMC Cancer* 2022;22:275.
 117. Chen Q, Chen X, Zhou L, et al. The emergence of new prognostic scores in lung cancer patients with spinal metastasis: A 12-year single-center retrospective study. *J Cancer* 2021;12:5644-53.
 118. Hu X, Huang W, Sun Z, et al. Predictive factors, preventive implications, and personalized surgical strategies for bone metastasis from lung cancer: population-based approach with a comprehensive cancer center-based study. *EPMA J* 2022;13:57-75.
 119. Lobinger D, Hiebinger A, Eicher F, et al. Rescue surgery in palliative indication as last therapeutic option for complicated advanced stage lung cancer. *Eur J Surg Oncol* 2023;49:107253.

120. Hino H, Nakahama K, Ogata M, et al. Emergent salvage surgery for massive hemoptysis after proton beam therapy for lung cancer: a case report. *Surg Case Rep* 2021;7:98.
121. Yagi Y, Kodama K, Momozane T, et al. Surgery to avoid fatal complications and secure radicality after definitive chemoradiotherapy for clinical T4N2M0 stage IIIB non-small cell lung cancer: a case report. *Surg Case Rep* 2020;6:16.
122. Suzuki S, Asakura K, Okui M, et al. Prognostic factors affecting survival in patients with non-small cell lung cancer treated with salvage surgery after drug therapy: a multi-institutional retrospective study. *World J Surg Oncol* 2023;21:290.
123. Motas N, Manolache V, Scarci M, et al. Salvage Surgery for Small-Cell Lung Cancer-A Literature Review. *Cancers (Basel)* 2023;15:2241.
124. Higuchi M, Watanabe M, Endo K, et al. Wine cup stoma anastomosis after extended sleeve lobectomy for central-type squamous cell lung cancer. *J Cardiothorac Surg* 2019;14:36.
125. Su C, Wang Y, Zhu X, et al. Recurrence of pulmonary sarcomatoid carcinoma presenting as haemothorax: a case report. *J Int Med Res* 2023;51:3000605231213533.
126. Kawamura T, Suzuki H, Kiyoshima M. Delayed postoperative bleeding following lobectomy caused by the sharp tip of a suture: a case report. *Surg Case Rep* 2020;6:261.
127. Negishi H, Tsubochi H, Maki M, et al. Incidental haemothorax after sublobar resection: did staple line scratch chest wall? *J Surg Case Rep* 2019;2019:rjz276.
128. Zhang G, Liu T, Liang C. Chylothorax and chylopericardial tamponade following lobectomy and lymphadenectomy: a rare presentation. *J Cardiothorac Surg* 2023;18:25.
129. Chen X, Miao Q, Yu Y, et al. Blunt Trauma-Induced Pericardial Tamponade After Video-Assisted Thoracoscopic Surgery. *Ann Thorac Surg* 2019;107:e381-3.
130. Ono M, Brady K, Easley RB, et al. Duration and magnitude of blood pressure below cerebral autoregulation threshold during cardiopulmonary bypass is associated with major morbidity and operative mortality. *J Thorac Cardiovasc Surg* 2014;147:483-9.
131. Ono M, Joshi B, Brady K, et al. Risks for impaired cerebral autoregulation during cardiopulmonary bypass and postoperative stroke. *Br J Anaesth* 2012;109:391-8.
132. Hori D, Brown C, Ono M, et al. Arterial pressure above the upper cerebral autoregulation limit during cardiopulmonary bypass is associated with postoperative delirium. *Br J Anaesth* 2014;113:1009-17.
133. Tran TN, Lee S, Kim HJ, et al. Treatment-related cardiovascular events in patients with non-small cell lung cancer: Evidence from real-world data with a competing risks approach. *Cancer* 2024;130:1303-15.
134. Endo S, Honda T, Kawahara T, et al. Profile of metastatic lung cancer patients susceptible to development of thromboembolism during immunotherapy. *Cancer Treat Res Commun* 2022;31:100547.
135. Kato T, Miyoshi S, Hamada C, et al. Associations between Comorbidities and Acute Exacerbation of Interstitial Lung Disease after Primary Lung Cancer Surgery. *Acta Med Okayama* 2023;77:301-9.
136. Videtic GMM, Donington J, Giuliani M, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. *Pract Radiat Oncol* 2017;7:295-301.
137. Guckenberger M, Andratschke N, Dieckmann K, et al. ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer. *Radiother Oncol* 2017;124:11-7.
138. Tandberg DJ, Tong BC, Ackerson BG, et al. Surgery versus stereotactic body radiation therapy for stage I non-small cell lung cancer: A comprehensive review. *Cancer* 2018;124:667-78.
139. Palma DA, Bahig H, Hope A, et al. Stereotactic Radiation Therapy in Early Non-Small Cell Lung Cancer and Interstitial Lung Disease: A Nonrandomized Clinical Trial. *JAMA Oncol* 2024;10:575-82.
140. Rulach R, McLoone P, Lumsden G, et al. Toxicity and Efficacy of Stereotactic Ablative Body Radiotherapy for Moderately Central Non-small Cell Lung Cancers Using 50 Gy in Five Fractions. *Clin Oncol (R Coll Radiol)* 2020;32:250-8.
141. Chang JY, Lin SH, Dong W, et al. Stereotactic ablative radiotherapy with or without immunotherapy for early-stage or isolated lung parenchymal recurrent node-negative non-small-cell lung cancer: an open-label, randomised, phase 2 trial. *Lancet* 2023;402:871-81.
142. Aupérin A, Le Péchoux C, Rolland E, et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. *J Clin Oncol* 2010;28:2181-90.
143. Curran WJ Jr, Paulus R, Langer CJ, et al. Sequential vs. concurrent chemoradiation for stage III non-small cell lung cancer: randomized phase III trial RTOG 9410. *J*

- Natl Cancer Inst 2011;103:1452-60.
144. Filippi ARR, García-Campelo MR, Paoli JB, et al. LBA62 Durvalumab after radiotherapy (RT) in patients with unresectable stage III NSCLC ineligible for chemotherapy (CT): Primary results from the DUART study. *Ann Oncol* 2023;34:S1302.
 145. Cheng Y, Spigel DR, Cho BC, et al. Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer. *N Engl J Med* 2024;391:1313-27.
 146. Nassar AH, Kim SY, Aredo JV, et al. Consolidation Osimertinib Versus Durvalumab Versus Observation After Concurrent Chemoradiation in Unresectable EGFR-Mutant NSCLC: A Multicenter Retrospective Cohort Study. *J Thorac Oncol* 2024;19:928-40.
 147. Lu S, Kato T, Dong X, et al. Osimertinib after Chemoradiotherapy in Stage III EGFR-Mutated NSCLC. *N Engl J Med* 2024;391:585-97.
 148. Zhou YM, Shin J, Jelinek M, et al. Four-Phase, Definitive Chemoradiation for a Real-World (Poor Risk and/or Elderly) Patient Population With Locally Advanced Non-small Cell Lung Cancer. *Cureus* 2022;14:e29423.
 149. Eze C, Guggenberger JE, Schmidt-Hegemann NS, et al. Pooled analysis on image-guided moderately hypofractionated thoracic irradiation in inoperable node-positive/recurrent patients with non-small cell lung cancer with poor prognostic factors and severely limited pulmonary function and reserve. *Cancer* 2022;128:2358-66.
 150. Iyengar P, Zhang-Velten E, Court L, et al. Accelerated Hypofractionated Image-Guided vs Conventional Radiotherapy for Patients With Stage II/III Non-Small Cell Lung Cancer and Poor Performance Status: A Randomized Clinical Trial. *JAMA Oncol* 2021;7:1497-505.
 151. Jin Y, Shimizu S, Li Y, et al. Proton therapy (PT) combined with concurrent chemotherapy for locally advanced non-small cell lung cancer with negative driver genes. *Radiat Oncol* 2023;18:189.
 152. Ernani V, Stinchcombe TE. Management of Brain Metastases in Non-Small-Cell Lung Cancer. *J Oncol Pract* 2019;15:563-70.
 153. Bi N, Ma Y, Xiao J, et al. A Phase II Trial of Concurrent Temozolomide and Hypofractionated Stereotactic Radiotherapy for Complex Brain Metastases. *Oncologist* 2019;24:e914-20.
 154. Sun H, Xu L, Wang Y, et al. Additional radiation boost to whole brain radiation therapy may improve the survival of patients with brain metastases in small cell lung cancer. *Radiat Oncol* 2018;13:250.
 155. Ni M, Jiang A, Liu W, et al. Whole brain radiation therapy plus focal boost may be a suitable strategy for brain metastases in SCLC patients: a multi-center study. *Radiat Oncol* 2020;15:70.
 156. Zhen J, Wen L, Lai M, et al. Whole brain radiotherapy (WBRT) for leptomeningeal metastasis from NSCLC in the era of targeted therapy: a retrospective study. *Radiat Oncol* 2020;15:185.
 157. De Felice M, Turitto G, Borrelli C, et al. Combination of immunotherapy, radiotherapy and denosumab as the best approach even for NSCLC poor prognosis patients: a case report with strong response, prolonged survival and a review of literature. *Curr Probl Cancer* 2023;47:100947.
 158. Sapienza LG, Ning MS, Jhingran A, et al. Short-course palliative radiation therapy leads to excellent bleeding control: A single centre retrospective study. *Clin Transl Radiat Oncol* 2019;14:40-6.
 159. Su S, Li T, Lu B, et al. Three-Dimensional Radiation Therapy to the Primary Tumor With Concurrent Chemotherapy in Patients With Stage IV Non-Small Cell Lung Cancer: Results of a Multicenter Phase 2 Study From PPRA-RTOG, China. *Int J Radiat Oncol Biol Phys* 2015;93:769-77.
 160. Gomez DR, Tang C, Zhang J, et al. Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non-Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study. *J Clin Oncol* 2019;37:1558-65.
 161. Gomez DR, Blumenschein GR Jr, Lee JJ, et al. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. *Lancet Oncol* 2016;17:1672-82.
 162. Stratakos G, Gerovasili V, Dimitropoulos C, et al. Survival and Quality of Life Benefit after Endoscopic Management of Malignant Central Airway Obstruction. *J Cancer* 2016;7:794-802.
 163. Mohan A, Shrestha P, Madan K, et al. A Prospective Outcome Assessment After Bronchoscopic Interventions for Malignant Central Airway Obstruction. *J Bronchology Interv Pulmonol* 2020;27:95-105.
 164. Uhlig J, Case MD, Blasberg JD, et al. Comparison of Survival Rates After a Combination of Local Treatment and Systemic Therapy vs Systemic Therapy Alone for Treatment of Stage IV Non-Small Cell Lung Cancer. *JAMA Netw Open* 2019;2:e199702.
 165. Guibert N, Roy P, Amari L, et al. Therapeutic bronchoscopy for malignant central airway obstruction:

- Introduction to the EpiGETIF registry. *Respirology* 2024;29:505-12.
166. Liu R, Shen Q, Lu H. The efficacy and safety of thermal ablation for patients with lung malignancy: a meta-analysis of 12 studies in China. *J Cardiothorac Surg* 2022;17:334.
 167. Jin F, Li Q, Li S, et al. Interventional Bronchoscopy for the Treatment of Malignant Central Airway Stenosis: An Expert Recommendation for China. *Respiration* 2019;97:484-94.
 168. Chhatre S, Vachani A, Allison RR, et al. Survival Outcomes with Photodynamic Therapy, Chemotherapy and Radiation in Patients with Stage III or Stage IV Non-Small Cell Lung Cancer. *Cancers (Basel)* 2021;13:803.
 169. Wang HW, Zou H, Jin FG. Chinese expert consensus on the clinical application of photodynamic therapy for respiratory tract tumors. *Chin J Lung Dis (Electronic Edition)* 2020;13:6-12.
 170. Zhou Y, Gao Y, Zhang N, et al. Clinical effects of cisplatin plus recombinant human endostatin (rh-endostatin) intratumoral injection on malignant central airway obstruction: a retrospective analysis of 319 cases. *J Thorac Dis* 2021;13:1100-5.
 171. Ablation Expert Committee of the Chinese Society of Clinical Oncology; Expert Group on Tumor Ablation Therapy of the Chinese Medical Doctors Association; Society of Tumor Ablation Therapy of the Chinese Anti-Cancer Association; Tumor Ablation Committee of the Chinese College of Interventionalists. Clinical practice guidelines: image-guided thermal ablation of primary and metastatic lung tumors (2021 edition). *Zhonghua Nei Ke Za Zhi* 2021;60:1088-105.
 172. Yang Q, Luo LC, Li FM, et al. Survival outcomes of radiofrequency ablation compared with surgery in patients with early-stage primary non-small-cell lung cancer: A meta-analysis. *Respir Investig* 2022;60:337-44.
 173. Steinfert DP, Antippa P, Rangamuwa K, et al. Safety and Feasibility of a Novel Externally Cooled Bronchoscopic Radiofrequency Ablation Catheter for Ablation of Peripheral Lung Tumours: A First-In-Human Dose Escalation Study. *Respiration* 2023;102:211-9.
 174. NCCN. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. Version 9.2024 — September 9, 2024.
 175. Wang HW, Jin FG. Expert consensus on the clinical application of rigid bronchoscopy. *Chin J Lung Dis (Electronic Edition)* 2022;15:6-10.
 176. Wang HW, Jin FG, Zhang N. Chinese expert consensus on the clinical application of airway metal stents. *Chin J Lung Dis (Electronic Edition)* 2021;14:5-10.
 177. Jin FG, Li SY, Wang HW. Expert consensus on interventional bronchoscopic diagnosis and treatment of malignant central airway stenosis. *Chin J Lung Dis (Electronic Edition)* 2017;10:647-54.
 178. Chinese Thoracic Society. Expert consensus on the prevention and treatment of massive bleeding associated with bronchoscopic diagnosis and treatment. *Chin J Tuberc Respir Dis* 2016;39:588-91.
 179. Garcia-Olivé I, Sanz-Santos J, Centeno C, et al. Results of bronchial artery embolization for the treatment of hemoptysis caused by neoplasm. *J Vasc Interv Radiol* 2014;25:221-8.
 180. Wang HW, Zou H, Li W, et al. Expert consensus on interventional diagnosis and treatment of secondary gastrorespiratory fistula (Second Edition). *J Clin Intern Med* 2021;38:573-6.
 181. Hsu WH, Tu CY, Chen HJ, et al. Dynamic flow US, color Doppler US, and power Doppler US in the assessment of vessel signals of thoracic lesions abutting pulsatile organs. *Acad Radiol* 2008;15:350-60.
 182. Lemieux S, Kim T, Pothier-Piccinin O, et al. Ultrasound-guided transthoracic needle biopsy of the lung: sensitivity and safety variables. *Eur Radiol* 2021;31:8272-81.
 183. Chan MV, Huo YR, Cao C, et al. Survival outcomes for surgical resection versus CT-guided percutaneous ablation for stage I non-small cell lung cancer (NSCLC): a systematic review and meta-analysis. *Eur Radiol* 2021;31:5421-33.
 184. Murphy MC, Wrobel MM, Fisher DA, et al. Update on Image-Guided Thermal Lung Ablation: Society Guidelines, Therapeutic Alternatives, and Postablation Imaging Findings. *AJR Am J Roentgenol* 2022;219:471-85.
 185. Genshaft SJ, Suh RD, Abtin F, et al. Society of Interventional Radiology Multidisciplinary Position Statement on Percutaneous Ablation of Non-small Cell Lung Cancer and Metastatic Disease to the Lungs: Endorsed by the Canadian Association for Interventional Radiology, the Cardiovascular and Interventional Radiological Society of Europe, and the Society of Interventional Oncology. *J Vasc Interv Radiol* 2021;32:1241.e1-1241.e12.
 186. Fintelmann FJ, Graur A, Oueidat K, et al. Ablation of Stage I-II Non-Small Cell Lung Cancer in Patients With Interstitial Lung Disease: A Multicenter Retrospective Study. *AJR Am J Roentgenol* 2024;222:e2330300.
 187. Rong Z, Ji Y, Dai F, et al. Effect of CT-guided microwave ablation for non-small cell lung cancer combined with

- severe chronic obstructive pulmonary disease. *Am J Transl Res* 2021;13:13117-22.
188. Peng J, Bie Z, Li Y, et al. Safety and efficacy of CT-guided percutaneous microwave ablation for stage I non-small cell lung cancer in patients with comorbid idiopathic pulmonary fibrosis. *Eur Radiol* 2024;34:4708-15.
 189. Yang H, Li M, Mei T. Survival benefit of thermal ablation combined with chemotherapy for the treatment of stage IV nonsmall cell lung cancer: a propensity-matched analysis. *Int J Hyperthermia* 2022;39:348-57.
 190. Expert Panel on Thoracic Imaging; Olsen KM, Manouchehr-Pour S, et al. ACR Appropriateness Criteria® Hemoptysis. *J Am Coll Radiol* 2020;17:S148-59.
 191. Kettenbach J, Ittrich H, Gaubert JY, et al. CIRSE Standards of Practice on Bronchial Artery Embolisation. *Cardiovasc Intervent Radiol* 2022;45:721-32.
 192. Han K, Yoon KW, Kim JH, et al. Bronchial Artery Embolization for Hemoptysis in Primary Lung Cancer: A Retrospective Review of 84 Patients. *J Vasc Interv Radiol* 2019;30:428-34.
 193. Seki A, Shimono C. Transarterial chemoembolization for management of hemoptysis: initial experience in advanced primary lung cancer patients. *Jpn J Radiol* 2017;35:495-504.
 194. Xiaobing L, Meipan Y, Pengfei X, et al. Bronchial Artery Chemoembolization for Hemoptysis in Advanced Primary Lung Cancer. *Clin Lung Cancer* 2022;23:e203-9.
 195. Fu Z, Wang C, Wei W, et al. Efficacy and safety of drug-eluting beads bronchial arterial chemoembolization versus conventional bronchial arterial chemoembolization in lung cancer patients with hemoptysis. *Future Oncol* 2022;18:2805-15.
 196. Claudinot A, Douane F, Morla O, et al. Pulmonary Artery Embolization in the Management of Hemoptysis Related to Lung Tumors. *J Pers Med* 2023;13:1597.
 197. Marcelin C, Soussan J, Desmots F, et al. Outcomes of Pulmonary Artery Embolization and Stent Graft Placement for the Treatment of Hemoptysis Caused by Lung Tumors. *J Vasc Interv Radiol* 2018;29:975-80.
 198. Azizi AH, Shafi I, Shah N, et al. Superior Vena Cava Syndrome. *JACC Cardiovasc Interv* 2020;13:2896-910.
 199. Azizi AH, Shafi I, Zhao M, et al. Endovascular therapy for superior vena cava syndrome: A systematic review and meta-analysis. *EClinicalMedicine* 2021;37:100970.
 200. Wei S, Liu J, Li X, et al. A retrospective stenting study on superior vena cava syndrome caused by lung cancer. *Thorac Cancer* 2020;11:1835-9.
 201. Friedman T, Quencer KB, Kishore SA, et al. Malignant Venous Obstruction: Superior Vena Cava Syndrome and Beyond. *Semin Intervent Radiol* 2017;34:398-408.
 202. Mörtch C, Valachis A. Single-agent versus combination chemotherapy as first-line treatment for patients with advanced non-small cell lung cancer and performance status 2: a literature-based meta-analysis of randomized studies. *Lung Cancer* 2014;84:209-14.
 203. Luo L, Hu Q, Jiang JX, et al. Comparing single-agent with doublet chemotherapy in first-line treatment of advanced non-small cell lung cancer with performance status 2: a meta-analysis. *Asia Pac J Clin Oncol* 2015;11:253-61.
 204. Zinner R, Visseren-Grul C, Spigel DR, et al. Pemetrexed clinical studies in performance status 2 patients with non-small cell lung cancer (Review). *Int J Oncol* 2016;48:13-27.
 205. Nakashima K, Akamatsu H, Murakami H, et al. Carboplatin Plus Nab-paclitaxel in Performance Status 2 Patients With Advanced Non-small-cell Lung Cancer. *Anticancer Res* 2019;39:1463-8.
 206. Zwitter M, Kovac V, Rajer M, et al. Two schedules of chemotherapy for patients with non-small cell lung cancer in poor performance status: a phase II randomized trial. *Anticancer Drugs* 2010;21:662-8.
 27. Mamesaya N, Kodama H, Iida Y, et al. Efficacy and safety of carboplatin and etoposide in older extensive-stage small-cell lung cancer patients with a poor performance status. *Thorac Cancer* 2023;14:805-14.
 208. Bahij R, Jeppesen SS, Olsen KE, et al. Outcome of treatment in patients with small cell lung cancer in poor performance status. *Acta Oncol* 2019;58:1612-7.
 209. Okuma Y, Hosomi Y, Nagamata M, et al. Clinical outcomes after first-line EGFR inhibitor treatment for patients with NSCLC, EGFR mutation, and poor performance status. *Anticancer Res* 2013;33:5057-64.
 210. Kashiwabara K, Fujii S, Tsumura S, et al. Overall survival of super-elderly (85 years or older) advanced non-small cell lung cancer patients with active epidermal growth factor receptor mutations receiving first-line gefitinib therapy: a single-institute retrospective study. *J Cancer Res Clin Oncol* 2021;147:287-93.
 211. Igawa S, Fukui T, Kasajima M, et al. First-line osimertinib for poor performance status patients with EGFR mutation-positive non-small cell lung cancer: A prospective observational study. *Invest New Drugs* 2022;40:430-7.
 212. Takamizawa S, Okuma Y, Kato Y, et al. First-line osimertinib in EGFR mutation-positive non-small cell lung cancer patients with poor performance status. *Future Oncol* 2022;18:291-300.
 213. Tsubata Y, Watanabe K, Saito R, et al. Osimertinib in

- poor performance status patients with T790M-positive advanced non-small-cell lung cancer after progression of first- and second-generation EGFR-TKI treatments (NEJ032B). *Int J Clin Oncol* 2022;27:112-20.
214. Nakashima K, Kimura M, Akamatsu H, et al. Osimertinib for patients with EGFR T790M mutation-positive non-small-cell lung cancer and a poor performance status. *Jpn J Clin Oncol* 2019;49:671-5.
 215. Matsuo N, Sekine A, Kato T, et al. Promising Effect of Crizotinib on Anaplastic Lymphoma Kinase (ALK)-Positive Non-Small Cell Lung Cancer in an Elderly Patient with a Poor Performance Status: A Case Report and Literature Review. *Intern Med* 2016;55:507-9.
 216. Singh A, Kapoor A, Noronha V, et al. ALK-positive advanced non-small cell lung cancer patients with poor performance status: Outcomes in a real-world scenario. *Ecanermedalscience* 2022;16:1407.
 217. Iwama E, Goto Y, Murakami H, et al. Survival Analysis for Patients with ALK Rearrangement-Positive Non-Small Cell Lung Cancer and a Poor Performance Status Treated with Alectinib: Updated Results of Lung Oncology Group in Kyushu 1401. *Oncologist* 2020;25:306-e618.
 218. Iwama E, Goto Y, Murakami H, et al. Alectinib for Patients with ALK Rearrangement-Positive Non-Small Cell Lung Cancer and a Poor Performance Status (Lung Oncology Group in Kyushu 1401). *J Thorac Oncol* 2017;12:1161-6.
 219. Masuda N, Ohe Y, Gemma A, et al. Safety and effectiveness of alectinib in a real-world surveillance study in patients with ALK-positive non-small-cell lung cancer in Japan. *Cancer Sci* 2019;110:1401-7.
 220. Zhong Q, Liu Z. Efficacy and Safety of Anlotinib in Patients with Advanced Non-Small Cell Lung Cancer: A Real-World Study. *Cancer Manag Res* 2021;13:4115-28.
 221. Riggs H, Jalal SI, Baghdadi TA, et al. Erlotinib and bevacizumab in newly diagnosed performance status 2 or elderly patients with nonsquamous non-small-cell lung cancer, a phase II study of the Hoosier Oncology Group: LUN04-77. *Clin Lung Cancer* 2013;14:224-9.
 222. Yamaguchi O, Mori K, Takata S, et al. Extended ICI treatment after first-line chemoimmunotherapy could predict the clinical benefit of ramucirumab plus docetaxel in advanced non-small lung cancer: Post hoc analysis from NEJ051 (REACTIVE study). *Thorac Cancer* 2024;15:163-71.
 223. Veluswamy R, Hu L, Smith C, et al. Immunotherapy Outcomes in Individuals With Non-Small Cell Lung Cancer and Poor Performance Status. *JNCI Cancer Spectr* 2022;6:pkac013.
 224. Lee SM, Schulz C, Prabhaskar K, et al. First-line atezolizumab monotherapy versus single-agent chemotherapy in patients with non-small-cell lung cancer ineligible for treatment with a platinum-containing regimen (IPSOS): a phase 3, global, multicentre, open-label, randomised controlled study. *Lancet* 2023;402:451-63.
 225. Léna H, Greillier L, Cropet C, et al. Nivolumab plus ipilimumab versus carboplatin-based doublet as first-line treatment for patients with advanced non-small-cell lung cancer aged ≥ 70 years or with an ECOG performance status of 2 (GFPC 08-2015 ENERGY): a randomised, open-label, phase 3 study. *Lancet Respir Med* 2025;13:141-52.
 226. Facchinetti F, Mazzaschi G, Barbieri F, et al. First-line pembrolizumab in advanced non-small cell lung cancer patients with poor performance status. *Eur J Cancer* 2020;130:155-67.
 227. Banna GL, Tiseo M, Cortinovis DL, et al. Host immune-inflammatory markers to unravel the heterogeneous outcome and assessment of patients with PD-L1 $\geq 50\%$ metastatic non-small cell lung cancer and poor performance status receiving first-line immunotherapy. *Thorac Cancer* 2022;13:483-8.
 228. Facchinetti F, Di Maio M, Perrone F, et al. First-line immunotherapy in non-small cell lung cancer patients with poor performance status: a systematic review and meta-analysis. *Transl Lung Cancer Res* 2021;10:2917-36.
 229. Ready NE, Audigier-Valette C, Goldman JW, et al. First-line nivolumab plus ipilimumab for metastatic non-small cell lung cancer, including patients with ECOG performance status 2 and other special populations: CheckMate 817. *J Immunother Cancer* 2023;11:e006127.
 230. Sagie S, Maixner N, Stemmer A, et al. Real-world evidence for immunotherapy in the first line setting in small cell lung cancer. *Lung Cancer* 2022;172:136-41.
 231. Agarwal M, Liu A, Almquist D, et al. Chemoimmunotherapy in patients with extensive-stage small cell lung cancer and a poor performance status. *Cancer* 2023;129:3546-53.
 232. Kato Y, Kato Y, Minegishi Y, et al. Efficacy with Trastuzumab Deruxtecan for Non-Small-Cell Lung Cancer Harboring HER2 Exon 20 Insertion Mutation in a Patient with a Poor Performance Status: A Case Report. *Onco Targets Ther* 2021;14:5315-9.
 233. Xu J, He B, Wang Y, et al. Positive response to trastuzumab deruxtecan in a patient with HER2-mutant NSCLC after multiple lines therapy, including T-DM1: a

- case report. *Front Oncol* 2023;13:1268260.
234. Liu PP, Cui YH, Xu XZ, et al. Efficacy of three-dimensional conformal radiotherapy combined with high-flow oxygen therapy in chemotherapy of elderly patients with advanced lung cancer. *Oncol Prog* 2023;21:2155-8.
 235. Tu XH, Lei M, Chen YQ, et al. A propensity score matching study on the prophylactic use of high-flow nasal humidified oxygen therapy to reduce postoperative pulmonary complications in elderly patients with non-small cell lung cancer. *Chin J Clin Thorac Cardio Surg* 2024;31:1274-80.
 236. Gao AH, Cheng YW, Qin LJ. Efficacy of post-extubation high-flow nasal cannula oxygen therapy in intensive care unit patients with lung cancer. *Oncol Prog* 2023;21:877-80.
 237. Bai J. Application of Fisher & Paykel AIRVO2 high-flow oxygen therapy and non-invasive ventilation in patients with lung cancer and respiratory failure. *CMDI* 2023;29:101-3.
 238. Nava S, Ferrer M, Esquinas A, et al. Palliative use of non-invasive ventilation in end-of-life patients with solid tumours: a randomised feasibility trial. *Lancet Oncol* 2013;14:219-27.
 239. Girou E, Schortgen F, Delclaux C, et al. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA* 2000;284:2361-7.
 240. Kızılgöz D, Akın Kabalak P, Kavurgacı S, et al. The success of non-invasive mechanical ventilation in lung cancer patients with respiratory failure. *Int J Clin Pract* 2021;75:e14712.
 241. Demoule A, Antonelli M, Schellongowski P, et al. Respiratory Mechanics and Outcomes in Immunocompromised Patients With ARDS: A Secondary Analysis of the EFRAIM Study. *Chest* 2020;158:1947-57.
 242. Takizawa D, Ishida T, Nakano H, et al. A case of massive hemoptysis caused by lung cancer saved by V-V ECMO and hemostasis achieved by radiotherapy. *Int Cancer Conf J* 2024;13:54-7.
 243. Pan J, Zhou X, Xu Z, et al. Successful management of hemodynamic instability secondary to saddle pulmonary embolism-induced cardiac arrest using VA-ECMO in advanced malignancy with brain metastases. *J Cardiothorac Surg* 2022;17:296.
 244. Clapp N, Wu H, Marburger E, et al. Management of life-threatening malignant central airway obstruction: A novel approach of using extracorporeal membrane oxygenation with tumor debulking and stenting. *Respir Med Case Rep* 2022;39:101718.
 245. Kitazawa S, Kobayashi N, Ueda S, et al. Successful use of extracorporeal membrane oxygenation for airway-obstructing lung adenocarcinoma. *Thorac Cancer* 2020;11:3024-8.
 246. Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr* 2017;36:11-48.
 247. Benguerfi S, Dumas G, Soares M, et al. Etiologies and Outcome of Patients with Solid Tumors Admitted to ICU with Acute Respiratory Failure: A Secondary Analysis of the EFRAIM Study. *Respir Care* 2023;68:740-8.
 248. Ma YF, Yao LL, Liu L, et al. Pathogen distribution, antimicrobial resistance, and prevention strategies in lung cancer patients with infections. *J Public Health Prev Med* 2021;32:129-32.
 249. Jiang AM, Ma YY, Liu N, et al. Analysis of microbiological characteristics and prognostic factors of nosocomial infection in patients with lung cancer. *J Mod Oncol* 2022;30:1598-602.
 250. Liu PP, Xu XZ, Sun C, et al. Pathogen spectrum distribution and influencing factors of polymicrobial infections in patients with advanced lung cancer and infection. *J Trop Med* 2023;23:1699-703.
 251. Yao Y, Lu M, Liu Y, et al. The Effects and Management of Viral Pneumonia on Lung Cancer Patients. *Zhongguo Fei Ai Za Zhi* 2020;23:255-60.
 252. Kuo CW, Lin CY, Wei SH, et al. Navigating the challenges of invasive pulmonary aspergillosis in lung cancer treatment: a propensity score study. *Ther Adv Med Oncol* 2023;15:17588359231198454.
 253. Deng LJ, Wang HZ. Analysis of prognostic factors in severe lung cancer patients with invasive pulmonary aspergillosis. *Chin Med Herald* 2020;17:120-2.
 254. NCCN. NCCN Clinical Practice Guidelines in Oncology, Prevention and Treatment of Cancer-Related Infections Version 3.2024 — September 23, 2024.
 255. Evans SE, Ost DE. Pneumonia in the neutropenic cancer patient. *Curr Opin Pulm Med* 2015;21:260-71.
 256. Sun JM, Kim TS, Lee J, et al. Unsuspected pulmonary emboli in lung cancer patients: the impact on survival and the significance of anticoagulation therapy. *Lung Cancer* 2010;69:330-6.
 257. Key NS, Khorana AA, Kuderer NM, et al. Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update. *J Clin Oncol* 2020;38:496-520.
 258. Khorana AA, Noble S, Lee AYY, et al. Role of direct oral anticoagulants in the treatment of cancer-associated venous thromboembolism: guidance from the SSC of the ISTH. *J Thromb Haemost* 2018;16:1891-4.

259. Watson HG, Keeling DM, Laffan M, et al. Guideline on aspects of cancer-related venous thrombosis. *Br J Haematol* 2015;170:640-8.
260. Segura A, Pardo J, Jara C, et al. An epidemiological evaluation of the prevalence of malnutrition in Spanish patients with locally advanced or metastatic cancer. *Clin Nutr* 2005;24:801-14.
261. Hébuterne X, Lemarié E, Michallet M, et al. Prevalence of malnutrition and current use of nutrition support in patients with cancer. *JPEN J Parenter Enteral Nutr* 2014;38:196-204.
262. Mariani L, Lo Vullo S, Bozzetti F, et al. Weight loss in cancer patients: a plea for a better awareness of the issue. *Support Care Cancer* 2012;20:301-9.
263. Na BG, Han SS, Cho YA, et al. Nutritional Status of Patients with Cancer: A Prospective Cohort Study of 1,588 Hospitalized Patients. *Nutr Cancer* 2018;70:1228-36.
264. Kiss N. Nutrition support and dietary interventions for patients with lung cancer: current insights. *Lung Cancer (Auckl)* 2016;7:1-9.
265. Mitchell JDM, Laurie ML, Xia QX, et al. Rates of cardiovascular events are significantly different across cancer types. *European Heart Journal* 2021;42:ehab724.2877. doi: 10.1093/eurheartj/ehab724.2877.
266. Galenko V, Lelyavina TA, Bortsova MA, et al. Aerobic physical training improves skeletal muscle metabolism in heart failure patients. *European Heart Journal* 2020;41:ehaa946.1068. doi: 10.1093/ehjci/ehaa946.1068.
267. Bozkurt B, Fonarow GC, Goldberg LR, et al. Cardiac Rehabilitation for Patients With Heart Failure: JACC Expert Panel. *J Am Coll Cardiol* 2021;77:1454-69.
268. Marco E, Ramírez-Sarmiento AL, Coloma A, et al. High-intensity vs. sham inspiratory muscle training in patients with chronic heart failure: a prospective randomized trial. *Eur J Heart Fail* 2013;15:892-901.
269. Pagniez C, Olivier C, Olislagers A, et al. P1.06-040 Home-Based Pulmonary Rehabilitation in Advanced Non-Small Cell Lung Cancer Patients Treated by Oral Targeted Therapy: A Feasibility Study. *Journal of Thoracic Oncology* 2017;12:S690.
270. Hwang CL, Yu CJ, Shih JY, et al. Effects of exercise training on exercise capacity in patients with non-small cell lung cancer receiving targeted therapy. *Support Care Cancer* 2012;20:3169-77.
271. Borghetti P, Branz J, Volpi G, et al. Home-based pulmonary rehabilitation in patients undergoing (chemo)radiation therapy for unresectable lung cancer: a prospective explorative study. *Radiol Med* 2022;127:1322-32.
272. Do J, Lee SH, Kim SA, et al. The effects of inspiratory muscle training with pulmonary rehabilitation on NSCLC patients during radiation therapy: A pilot clinical study. *Thorac Cancer* 2023;14:1567-73.
273. Jastrzębski D, Maksymiak M, Kotorz S, et al. Pulmonary Rehabilitation in Advanced Lung Cancer Patients During Chemotherapy. *Adv Exp Med Biol* 2015;861:57-64.
274. Henke CC, Cabri J, Fricke L, et al. Strength and endurance training in the treatment of lung cancer patients in stages IIIA/IIIB/IV. *Support Care Cancer* 2014;22:95-101.
275. Rutkowska A, Rutkowski S, Wrzeciono A, et al. Short-Term Changes in Quality of Life in Patients with Advanced Lung Cancer during In-Hospital Exercise Training and Chemotherapy Treatment: A Randomized Controlled Trial. *J Clin Med* 2021;10:1761.
276. Mochalova AS, Koneva ES, Senchilov MO. Clinical efficacy of rehabilitation measures in patients with melanoma of the skin undergoing immunotherapy. *Vopr Kurortol Fizioter Lech Fiz Kult* 2022;99:26-30.
277. Mochalova AS, Koneva ES, Tsvetkova AV, et al. Comprehensive rehabilitation of immune-mediated adverse events in cancer patients receiving checkpoint inhibitor therapy. *Vopr Kurortol Fizioter Lech Fiz Kult* 2022;99:30-6.
278. Phillips I, Deans M, Walton A, et al. Early prehabilitation reduces admissions and time in hospital in patients with newly diagnosed lung cancer. *BMJ Support Palliat Care* 2024;15:125-9.
279. Fillon M. Virtual exercise regimens can help patients with cancer. *CA Cancer J Clin* 2021;71:457-8.
280. Cox NS, McDonald CF, Mahal A, et al. Telerehabilitation for chronic respiratory disease: a randomised controlled equivalence trial. *Thorax* 2022;77:643-51.
281. Ji W, Kwon H, Lee S, et al. Mobile Health Management Platform-Based Pulmonary Rehabilitation for Patients With Non-Small Cell Lung Cancer: Prospective Clinical Trial. *JMIR Mhealth Uhealth* 2019;7:e12645.
282. Ohri N, Kabarriti R, Bodner WR, et al. Continuous Activity Monitoring During Concurrent Chemoradiotherapy. *Int J Radiat Oncol Biol Phys* 2017;97:1061-5.
283. Burton M, Valet M, Caty G, et al. Telerehabilitation physical exercise for patients with lung cancer through the course of their disease: A systematic review. *J Telemed Telecare* 2024;30:756-80.
284. Di Maio M, Basch E, Denis F, et al. The role of patient-

- reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. *Ann Oncol* 2022;33:878-92.
285. Wang M, Sun Y, Zhang M, et al. Effects of high-quality nursing care on quality of life, survival, and recurrence in patients with advanced nonsmall cell lung cancer. *Medicine* (Baltimore) 2022;101:e30569.
286. Zeng SC. Effects of targeted nursing care on gastrointestinal function and quality of life in lung cancer patients undergoing concurrent chemoradiotherapy. *Hebei Med J* 2021;43:2067-9, 2073.

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