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Editor
Prof. Dr. Aykut ELİÇORA

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PREFACE

In daily cardiovascular surgery practice, understanding current techniques is of vital importance.With this in mind, we have compiled a book that examines contemporary topics from diverse perspectives, informed by the latest global developments, and we are pleased to present it to you, our esteemed readers. Titled "Current Studies in Thoracic Surgery," this book offers comprehensive information for those beginning their journey in the field of cardiovascular surgery. We hope it will serve as a valuable resource for our colleagues as they advance in this specialty. We extend our gratitude to all the authors who contributed to this work, and we express our appreciation to the BİDGE publishing house for their unwavering support.

PROF. DR. AYKUT ELİÇORA

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BÖLÜM 1

LEARNİNG CURVE AND COST-EFFECTİVENESS ANALYSİS İN ENDOBRONCHİAL ULTRASOUND (EBUS) AND ADVANCED INTERVENTİONAL BRONCHOSCOPY TECHNİQUES: A MİNİ-REVİEW

SUZAN TEMİZ BEKCE[1]

Introduction

Evaluating mediastinal lymph nodes is a clinical necessity for accurate staging, treatment planning, and response monitoring. Prior to the widespread adoption of endosonographic techniques, obtaining a tissue diagnosis was feasible only through surgical interventions such as parasternal mediastinotomy, extended cervical mediastinoscopy (ECM), video-assisted mediastinoscopy (VAM),

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and video-assisted thoracoscopic surgery (VATS) (Call et al., 2018; Dietrich et al., 2015).

In recent years, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has emerged as a prominent minimally invasive modality (Matache et al., 2025).

Nevertheless, contemporary literature continues to comprehensively investigate these techniques regarding their safety profiles, cost parameters—including procedure and hospitalization durations—and their relative impact on the pathological evaluation processes of obtained biopsy specimens (Joseph, 2018).

The aim of this book chapter is to examine the learning curves, physician competency thresholds, and the direct and indirect financial impacts on healthcare expenditures associated with EBUS techniques from 2007 to the present, in light of the available literature.

Data Sources and Literature Search Strategy

In the preparation of this book chapter, the PubMed, Scopus, and Web of Science databases were comprehensively searched covering the years 2007–2026. Keywords used in the literature search included *"Endobronchial Ultrasound"*, *"EBUS-TBNA"*, *"Navigational Bronchoscopy"*, *"Learning Curve"*, *"Competency Thresholds"*, and *"Cost-Effectiveness in Mediastinal Staging"*, alongside their respective Medical Subject Headings (MeSH) terms.

Although publications regarding EBUS were available in earlier years, 2007 was selected as the baseline year for the literature search primarily because the American College of Chest Physicians (ACCP) updated its lung cancer mediastinal staging guidelines in 2007, formally introducing EBUS-TBNA (specifically convex-probe EBUS) and EUS-FNA as "minimally invasive

endosonographic staging modalities" under official guideline recommendations (Detterbeck et al., 2007). Following this landmark publication, learning curves, physician competency thresholds, and the health economic impacts of endosonographic methods began to be systematically investigated in the literature.

The capacity to perform interventional procedures is inherently linked to a learning curve that depends on the operator's technical skill, expertise, and training (Singh et al., 2019). Various studies have demonstrated a wide variation in acquiring procedural proficiency, ranging from 10 to 100 procedures. The American College of Chest Physicians (ACCP) empirically recommends performing at least 50 supervised EBUS-TBNA procedures (Ernst et al., 2003). In contrast, single-center experiences have reported that competency can be attained after as few as 10 procedures (Groth et al., 2008). Relevant research and learning curve analyses continue to be actively conducted today.

Original research articles in English and multicenter clinical trials evaluating the learning curves, physician competency, and health economic financial impacts of EBUS techniques—either prospectively or retrospectively—were included in the review. Case reports, letters to the editor, meta-analyses, reviews, as well as unrelated pediatric and animal studies were excluded from the analysis scope.

Results

In the literature, 19 open-access articles regarding the subject were included in the review. The studies were evaluated in terms of learning curve data as well as direct or indirect cost analyses. A table was created for a more comprehensible comparison of the data (Table 1).

Nakajima et al. (2007) examined patients who developed lung metastases from extrapulmonary primary tumors and were candidates for resection (metastasectomy). When this study, conducted by an experienced team, was evaluated from a health economics perspective, it was demonstrated that performing the procedure on an outpatient basis under conscious sedation eliminated the need for cervical mediastinoscopy, which requires general anesthesia. Furthermore, it was reported that correctly identifying patients with mediastinal and hilar lymph node involvement prevented unnecessary major metastasectomy surgeries, thereby achieving indirect cost avoidance (Nakajima et al., 2007).

One of the most significant findings in the study by Rintoul et al. (2009) was that the success achieved was validated in a multicenter setting. The fact that the procedure yielded similar results across all participating centers demonstrated that EBUS-TBNA is a method with high reproducibility that can be easily learned and performed by physicians with a reasonable level of experience (Rintoul et al., 2009).

Harewood et al. (2010) investigated the impacts of mediastinal staging strategies on health economics using a decision-tree cost-minimization model in patients with suspected or proven non-small cell lung cancer (NSCLC). In this simulation model, which did not involve direct patient recruitment, the prevalence of mediastinal lymph node metastasis was varied between 0% and 50%, and the study was conducted assuming no risk of false positivity (100% specificity) in interventional biopsy methods, with details shown in the table (Table 1) (Harewood et al., 2010).

In the study conducted by Hergott et al. (2010), it was identified that more than 90% of the equipment failures in EBUS bronchoscopes resulted from insertion tube damage, moisture invasion into the insertion tube, U-cord damage, and breakage of the

image guide bundle. Examining these technical components: the insertion tube is the flexible shaft advanced into the patient's airway, housing the working channel through which the biopsy needle passes, as well as the optical and ultrasound transmission lines. Puncture or tearing of the working channel by the needle during EBUS-TBNA, or microscopic cracks forming on the outer sheath during reprocessing, leads to moisture invasion into internal components, resulting in severe image degradation and electronic malfunction. Furthermore, the U-cord—the flexible umbilical cable connecting the bronchoscope to the main processor—houses delicate signal transmission bundles that are highly susceptible to mechanical bending and structural damage. The study demonstrated that increased operator experience did not reduce the need for repairs; while the lowest costs were recorded in the first year, repair rates remained constant in subsequent years. This suggests that damage stems from the inherently delicate nature of the device, repetitive needle manipulation, and general operational wear and tear over time, rather than operator inexperience (Hergott et al., 2010).

It has been shown that the endobronchial ultrasound-guided miniforceps biopsy (EBUS-MFB) technique does not significantly prolong procedural time (2.25–2.75 minutes per biopsy), poses no additional risk of complications, and can be safely performed even at the fellow/resident level with a short learning curve of 10–14 cases, indicating that the method is highly suitable for practical and clinical integration (Chrissian et al., 2011).

In the ASTER clinical trial evaluating 241 patients with potentially resectable lung cancer, the clinical and economic superiority of the combined endosonography-guided staging protocol (EBUS-TBNA + EUS-FNA) over standard surgical staging was demonstrated. Over a six-month follow-up period, the mean cost per patient was £9,713 in the endosonography arm and £10,459 in the surgical arm; this approach exhibited a dominant cost-utility

profile with a net cost advantage of £746 per patient. To facilitate the clinical integration of this strategy, which significantly reduces the need for thoracotomy and surgical invasiveness, the establishment of combined EBUS/EUS training curricula for practitioners was recommended (Sharples et al., 2012).

In a prospective database analysis conducted by Lee et al. (2012), it was determined that EBUS-TBNA (using 21G/22G needles) performed under general anesthesia in patients with non-small cell lung cancer (NSCLC) eliminated the need for more invasive cervical mediastinoscopy in 95% of cases (69/73). This was reported to significantly reduce operating room and surgical staging costs indirectly. It was emphasized that the success of the procedure was highly dependent on the operator's anatomical experience, and it was noted that all procedures were performed by thoracic surgeons (Lee et al., 2012).

When comparing diagnostic yield and reimbursement data between EBUS-TBNA (n=257) and blind FB-TBNA (n=37), Grove et al. (2012) found a significantly higher diagnostic yield in the EBUS-TBNA group. This was shown to significantly reduce the need for additional diagnostic surgical procedures (mediastinoscopy or VATS/thoracotomy). When the costs of surgical procedures were taken into account, the average total expenditure per patient was calculated as $1,542.44 in the EBUS-TBNA group and $2,613.53 in the blind TBNA group; the use of EBUS was reported to provide a net cost savings averaging $1,071.09 per patient (Grove et al., 2012).

While Usluer and Kaya (2014) did not directly evaluate the EBUS-TBNA procedure from a financial or monetary perspective in their study. However, they emphasized the importance of experience through learning thresholds set at 37 cases for diagnostic accuracy and 50 cases for procedural speed/competency, summarizing the situation concisely with the phrase "practice makes perfect" (Usluer & Kaya, 2014).

In the study conducted by Kalluri et al. (2015), no specific evaluation was made regarding operator competency or the learning curve, nor was a detailed prospective clinical intervention protocol presented. The study was built upon a decision-analytic cost model (simulation) based on a retrospective review of 95 cases. The authors demonstrated that the cost savings achieved by adding Rapid On-Site Evaluation (ROSE) to the EBUS-TBNA process stemmed primarily from avoiding unnecessary and repetitive lymph node samplings, preventing additional interventional procedures (such as transbronchial lung biopsy and mucosal biopsy), and eliminating the need for repeat procedures, rather than an increase in diagnostic yield alone (Kalluri et al., 2015).

it was determined that trainee involvement in EBUS-TBNA procedures did not affect tissue sample quality. However, trainee participation was found to prolong procedural duration and reduce diagnostic yield, which subsequently delayed diagnostic and therapeutic processes by increasing the patients' need for additional investigations (Nguyen et al., 2017).

Ong et al. (2018) noted that simulation training in EBUS-TBNA did not provide a distinct superiority in terms of diagnostic yield, major complication rates, or cost parameters, and that its clinical contribution remains uncertain as CUSUM analysis demonstrated performance fluctuations over time in the simulation group. In light of these findings, it can be stated that a continuous and modular apprenticeship model conducted under expert supervision (direct clinical experience) maintains its fundamental role in acquiring EBUS-TBNA competency, rather than one-time simulation courses (Ong et al., 2018).

In a large-scale database analysis conducted by Verdial et al. (2020), it was stated that EBUS-TBNA has the potential to provide cost savings compared to mediastinoscopy. In addition to the cost

factor, the study reported a significantly lower risk of developing vocal cord paralysis in the EBUS group (Verdial et al., 2020).

In a prospective multicenter study conducted across France (EValuation of EBUS-TBNA In PEripherally Located Bronchial and Mediastinal Lesions (EVIEPEB Study)), Chouaid et al (2019). demonstrated that following a standardized training program, EBUS-TBNA eliminated the need for invasive mediastinoscopy in 80% of patients, presenting an overall sensitivity of 89.3% and a specificity of 100%. Furthermore, even under general anesthesia conditions, EBUS-TBNA offered a safe and highly precise staging strategy while generating an average cost savings of €1,450 per patient (Chouaid et al., 2019).

Parallel to technological advancements in interventional pulmonology, research evaluating mediastinal lesions through Cryo-EBUS performed alongside or in addition to conventional EBUS-TBNA has increasingly gained traction in the literature. In their study evaluating the concurrent application and outcomes of both EBUS-TBNA and Cryo-EBUS, Perelló Roselló et al. (2025) highlighted that the diagnostic yield of Cryo-EBUS is directly associated with operator experience. While the diagnostic success rate of operators during their initial 15 cases was 53.3%, this rate significantly increased to 84.7% after surpassing the 15-case learning threshold ($p = 0.001$). Due to cryoprobe equipment costs, device depreciation, and prolonged procedural time, Cryo-EBUS is initially more costly than performing EBUS-TBNA alone. However, in cases where EBUS-TBNA alone proves non-diagnostic over the long term, patients often require repeat sampling, secondary diagnostic procedures, or significantly more expensive and invasive surgical mediastinoscopy. Demonstrating that combining Cryo-EBUS with EBUS-TBNA increases the overall diagnostic yield to 86% (and to 93.3% in malignant cases), this approach reduces the

necessity for costly secondary interventions, thereby lowering total diagnostic pathway costs (Perelló Roselló et al., 2025).

Similarly, Corcione et al. (2025) reported a high standalone diagnostic yield of 95.1% for Cryo-EBUS in their retrospective study, noting that this high accuracy yields indirect cost savings compared to standard EBUS-TBNA by eliminating the need for repeat sampling and surgical mediastinoscopy. Nevertheless, methodological differences exist between the two studies: while Perelló Roselló et al. (2025) defined a distinct 15-case learning curve utilizing a 22G needle tunneling technique, Corcione et al. (2025) emphasized the operator experience required for 19G needle pathway creation and demonstrated that the superiority of Cryo-EBUS is particularly pronounced in diagnosing lymphomas and granulomatous diseases, as well as serving as a rescue modality (100% rescue yield) following non-diagnostic EBUS-TBNA procedures (Corcione et al., 2025; Perelló Roselló et al., 2025).

Beyond the 40-case learning curve threshold in EBUS-TBNA, diagnostic accuracy increased from 72% to 90%, while mean procedure time decreased to 14 minutes and per-case costs fell from $829 to $244 (Turan et al., 2025). Despite higher initial expenditures related to equipment repair and secondary surgical procedures during early cases, overall mean per-patient costs were found to be comparable between EBUS ($477) and conventional methods ($467) (Turan et al., 2025).

An evaluation of the initial two-year implementation of EBUS-TBNA at an academic center in India demonstrated an overall diagnostic yield of 62.5% (Jalandra et al., 2025). Learning curve analysis revealed a statistically significant increase in diagnostic yield after the first 6 months before reaching a plateau ($p = 0.01$), whereas the difference between Year 1 (57.4%) and Year 2 (64.9%) was not statistically significant. Although direct cost calculations were not performed, it was emphasized that EBUS-TBNA provides

a clear financial advantage over surgery in resource-limited settings by eliminating the routine requirement for general anesthesia and inpatient admission (Jalandra et al., 2025).

An investigation into the learning curves of 4 pulmonologists without formal Interventional Pulmonology (IP) fellowship training across their first 70 EBUS-TBNA cases at a Canadian academic center demonstrated that diagnostic yield rose from 76.5% in the first quartile to 93.4% in the fourth quartile, while mean procedure time decreased from 56.7 minutes to 48.8 minutes (and further to 32.9 minutes in 2023 data) (Tyker et al., 2026). While direct monetary cost analyses were not conducted, the safe implementation of EBUS-TBNA outside dedicated IP centers significantly improved healthcare accessibility and resource optimization by preventing patients from traveling distances exceeding 200 km or undergoing invasive surgical staging (Tyker et al., 2026).

Table 1: Comprehensive Chronological Analysis of Learning Curves and Cost-Effectiveness in EBUS and Advanced Interventional Bronchoscopy

Publication Year & Source	Modality / Technology (& Setting / Anesthesia)	Sample Size (n) & Study Design	Learning Curve / Competency Threshold	Cost-Effectiveness Analysis
2007 Nakajima et al.	EBUS-TBNA (22G) Outpatient/Sedation	n=43 (60 LN stations) Prospective Clinical Study	Quantitative threshold not specified (Performed by experienced thoracic surgery team).	Indirect: Eliminates the need for cervical mediastinoscopy and inpatient hospitalization, yielding indirect budget savings.
2009 Rintoul et al.	EBUS-TBNA (22G) Outpatient/Sedation	N=109 (127 LN stations) Multicenter Prospective Study	Quantitative threshold not specified; demonstrates high learnability and reproducibility across multiple centers.	Indirect: Prevents surgical staging in 71% of patients, providing substantial indirect cost avoidance.
2010	EBUS-TBNA, EUS-FNA, Combined	Not applicable	Quantitative threshold not specified (Economic Decision Model based on prospective clinical trial literature data).	Direct & Indirect: Base-case least costly: EUS-FNA ($18,603) vs Combined EBUS+EUS ($18,753).

Harewood et al.	(EBUS+EUS), Mediastinoscopy *Setting:* Outpatient / Inpatient mix (Medicare Model) Anesthesia: Not specified for endoscopic arms (Standard outpatient procedural reimbursement model)			• CT-Negative (<32.9% LN risk): EUS alone is most economical. • CT-Positive (>32.9% LN risk): Combined EBUS+EUS is most cost-effective (93% sensitivity), avoiding costly thoracotomies. Mediastinoscopy ($20,157) and blind TBNA ($21,136) generated highest overall costs.
2010 Hergott et al.	Linear EBUS-TBNA vs. Flexible Bronchoscopy Outpatient / Conscious sedation	n = 949 EBUS n = 2,767 Flexible bronchoscopies	Process-Based Evaluation: Operator experience did not reduce repair frequency over time. >90% of repairs stemmed from scope complexity and mechanical wear (moisture invasion, insertion tube damage).	Direct: Repair cost per procedure: EBUS $116.00 CAD (Canadian Dollar) vs. Flexible Bronchoscopy $24.32 CAD (EBUS repair is 4.8 times more expensive).
2011 Chrissian et al.	EBUS-TBNA (22G) vs. EBUS-Miniforceps Biopsy (MFB) vs. Combined (EBUS-TBNA + MFB) Setting: Outpatient / Moderate Sedation (Transoral, no endotracheal tube)	n = 50 patients (74 LN stations)	Trainees/Pulmonology fellows achieved proficiency after 10–14 supervised cases. MFB did not significantly prolong procedure duration (2.25–2.75 min/biopsy).	Indirect Cost Avoidance: Direct financial cost analysis was not performed. However, achieving a 97% combined diagnostic yield (and 100% in lymphoma) avoids costly invasive surgical interventions (mediastinoscopy/thoracoscopy) and repeat diagnostic steps, particularly in high-risk patients.
2012 Sharples et al. (ASTER Trial)	Combined Endosonography (EBUS-TBNA + EUS-FNA) vs. Surgery Setting: Outpatient / Moderate Sedation	n=241 Multicenter Randomized Controlled Trial	Structured dual-technique training recommended for single-operator (chest physician) combined EBUS/EUS execution.	Direct Cost & Cost-Utility: 6-Month mean cost: Endosonography strategy £9,713 vs. Surgical staging £10,459 (Net saving: £746 per patient).
2012 Lee et al.	Linear EBUS-TBNA (21G/22G Needle) Setting: Operating Room / General Anesthesia with Laryngeal Mask Airway (LMA)	N=73 (140 LN stations) Prospective Observational	Operator-dependent (No numerical threshold specified).	Indirect: Obviated the need for cervical mediastinoscopy in 95% (69/73) of NSCLC patients, avoiding OR & surgical staging costs.
2012 Grove et al.	Linear EBUS-TBNA vs. "Blind" FB-TBNA Setting: Academic Hospital / Outpatient Bronchoscopy Suite	n = 294 patients Prospective Comparative Study	Quantitative threshold not reported (Single expert operator).	Direct: Mean total cost including subsequent surgery: EBUS-TBNA $1,542 vs. Blind TBNA $2,613 (Net saving of $1,071 per patient).
2014	Linear EBUS-TBNA	n=160	Diagnostic Accuracy Threshold: 37 cases.	Direct financial/cost analysis was not performed.

Usluer & Kaya	Setting: Outpatient / Conscious sedation	Prospective Cumulative Sum Analysis (CUSUM) Analysis	Procedural Speed/Competency: 50 cases.	
2016 Kalluri et al.	EBUS-TBNA + Rapid On-Site Evaluation (ROSE) Cost-Model Moderate/conscious sedation in an outpatient procedural suite.	n = 95 patients (retrospective chart review used to populate the model) Decision-analytic economic model (Decision-Tree Cost Model)	Not Assessed / No Specific Data: Learning curve was not measured or primary to this simulation model. • Operator Role: Retrospective evaluation was conducted directly by an expert cytopathologist. • Per Patient Savings: - Lung Cancer: $63 CAD ($51.04 USD) - Sarcoidosis: $544 CAD ($440.65 USD) • Provincial Annual Savings (Alberta): - Lung Cancer: $50,000 CAD ($40,501 USD) - Sarcoidosis: $109,000 CAD ($88,337 USD) • Mechanism: ROSE avoids unnecessary additional lymph node sampling and extra tissue biopsies (TBB/mucosal).	Direct: ROSE implementation avoids redundant biopsies, saving $63 CAD in lung cancer and $544 CAD in sarcoidosis per patient. • Per Patient Savings: - Lung Cancer: $63 CAD ($51.04 USD) - Sarcoidosis: $544 CAD ($440.65 USD) • Provincial Annual Savings (Alberta): - Lung Cancer: $50,000 CAD ($40,501 USD) - Sarcoidosis: $109,000 CAD ($88,337 USD) • Mechanism: ROSE avoids unnecessary additional lymph node sampling and extra tissue biopsies (Transbronchial Biopsy/ mucosal).
2017 Nguyen et al.	Linear EBUS-TBNA Moderate/conscious sedation	N=220 Retrospectively Analyzed Cohort	Competency Threshold: 10–50 cases; performance improvements persist beyond 200 cases.	• Indirect Cost & Resource Utilization Impact: - Procedure Duration: Significantly longer with trainees (16.0 vs. 13.7 min, p=0.002). - Anesthetic Consumption: Significantly higher topical lidocaine dose (322.3 vs. 304.2 mg, p=0.045). - Diagnostic Efficiency: Lower yield increases potential costs associated with repeat procedures or secondary diagnostic workups
2018 Ong et al.	Linear EBUS-TBNA Conscious Sedation or Moderate/Deep Sedation	n = 608 total procedures (n = 331 Pre-Simulation vs. n = 277 Post-Simulation group) Retrospective Cohort Study with CUSUM analysis	Simulation did not shorten the clinical learning curve or improve diagnostic yield (88.2% vs. 84.5%, p = 0.179). CUSUM analysis revealed an unexpected upward slope (underperformance) after initial success in the post-simulation cohort, demonstrating that simulation cannot replace direct clinical exposure	Scope repair costs decreased from SGD 413.88 to SGD 182.79 per procedure (a 55.8% reduction / SGD 231.09 savings), and scope damage rates dropped (2.7% vs. 0.7%). However, this reduction was not statistically significant (p = 0.268).
2019 Verdial et al.	EBUS-TBNA vs. Cervical Mediastinoscopy inpatient or outpatient claims during the study period	N=30.570 (EBUS-TBNA: 15.097, Mediastinocopy: 15.473) Retrospective study	Not evaluated	Unadjusted mean cost of EBUS was $2,211 lower ($6,816 vs. $9,023; $P < .001$). After multivariable adjustment, EBUS remained $1,650 less expensive (95% CI: $1,525–$1,776). Primary cost drivers were same-day hospitalizations and concomitant bronchoscopic procedures
2019	Linear EBUS-TBNA	n = 394 total patients enrolled (n = 231 in Step 1	Threshold: ≥9/10 consecutive informative biopsies.	Direct: • EBUS (Local/Sedation): €120 • EBUS (General Anesthesia): €840

Chouaid et al. (EValuation of EBUS-TBNA In PEripherally Located Bronchial and Mediastinal Lesions (EVIEPEB Study))	vs. Cervical Mediastinoscopy EBUS-TBNA: Flexible setting depending on center practice — Day-hospital with brief general anesthesia, outpatient with IV sedation or a combination of both. Mediastinoscopy: Always performed under General Anesthesia and required Inpatient Hospitalization.	training; n = 163 in Step 2 cost-effectiveness study) Multicenter Prospective Study	Certified operators had 33.3 ± 31 prior cases vs. 5.3 ± 4.3 cases for non-certified operators.	• Mediastinoscopy: €2,300 EBUS strategy achieved an expected savings of €1,450 per patient and avoided mediastinoscopy in 80% of patients.
2025 Perelló Roselló et al.	EBUS-Guided Transbronchial Cryobiopsy (Cryo-EBUS) (1.1 mm cryoprobe, 3–5 sec freeze time) vs. EBUS-TBNA (22G needle) vs. Combined (EBUS-TBNA + Cryo-EBUS) Bronchoscopy Suite / Outpatient; General AnesthesiaGeneral Anesthesia.	n=100 Prospective Analysis	Breakpoint: 15 cases (Diagnostic yield: 53.3% in cases 1–15 □ 84.7% in cases 16–100).	Indirect: High combined yield (86%) eliminates re-biopsy rates, providing clear financial advantages.
2025 Corcione et al.	EBUS-Guided Transbronchial Cryobiopsy (Cryo-EBUS / TMC) (1.1 mm cryoprobe, 4 sec freeze time) vs. EBUS-TBNA (19G/21G needle). Operating Room / Outpatient & Inpatient mix. Deep Sedation with Laryngeal Mask Airway (LMA)	n=41 Retrospective Study	Not quantitatively defined (technique requires operator experience for 19G needle tract creation).	Indirect: Removes the need for repeat biopsies and mediastinoscopy, conferring indirect savings over EBUS-TBNA alone.
2025 Turan et al	EBUS-TBNA (22 G) vs. Conventional Procedures (Mediastinoscopy 94%, VATS 4%, Thoracotomy 2%)	n = 200 (100 EBUS vs. 100 Conventional) Retrospective Cohort Study	Diagnostic accuracy significantly increased from 72% (cases 1–40) to 90% (cases 41–100, p=0.03). Procedure duration dropped from 30 to 14 minutes (p=0.01).	Direct Procedure Cost: EBUS ($222) vs. Conventional ($467) (p=0.001). Pre-learning phase (Cases 1–40): Average cost spiked to $829 per case due to re-interventions and scope repairs ($20,000 total). Post-learning phase (Cases 41–100): Total cost per case dropped to $244. Net total cost

				per patient averaged $477 (EBUS) vs. $467 (Conventional).
2025 Jalandra et al	EBUS-TBNA (22 G) Conscious Sedation	n = 144 Retrospective Cohort Study	Overall diagnostic yield was 62.5%. Yield improved from Year 1 (57.4%) to Year 2 (64.9%, p=0.46). A statistically significant yield increase occurred from the first 6 months to the subsequent 6 months (p=0.01), plateauing thereafter.	No direct micro-costing or formal economic modeling performed. Contextual Note: Emphasizes EBUS as a cost-reducing alternative to surgical staging in resource-limited settings by avoiding general anesthesia and inpatient hospitalization.
2026 Tyker et al	EBUS-TBNA (Various needle gauges: 20G, 21G, 22G, 25G). Conscious Sedation	n = 280 Retrospective Cohort Study	Proficiency Achieved Within 51–70 Cases: Diagnostic yield increased across quartiles from 76.5% (1st quartile) to 93.4% (4th quartile). All 4 physicians achieved a yield ≥ 89.5% by the 4th quartile. Procedure time decreased from 56.7 min (1st quartile) to 48.8 min (4th quartile) and further to 32.9 min.	No formal micro-costing or monetary analysis performed.
EBUS-TBNA: Endobronchial Ultrasound-Transbronchial Needle Aspiration EUS-FNA: Endoscopic Ultrasound-guided Fine Needle Aspiration CUSUM: Cumulative Sum Analysis ROSE: Rapid On-Site Evaluation EVIEPEB Study: EValuation of EBUS-TBNA In PEripherally Located Bronchial and Mediastinal Lesion EBUS-TMC: Endobronchial Ultrasound-guided Transbronchial Mediastinal Cryobiopsy LMA: Laryngeal Mask Airway NSCLC: Non-Small Cell Lung Cancer OR: Operating Room EBB: Endobronchial Biopsy				
Currencies: £: British Pound Sterling (GBP); $: United States Dollar (USD); $ CAD: Canadian Dollar; $ AUD: Australian Dollar; €: Euro (EUR); SGD: Singapore Dollar.				

Conclusion

In conclusion, the available literature spanning nearly two decades indicates that EBUS techniques—ranging from conventional EBUS-TBNA to advanced modalities such as Cryo-EBUS and miniforceps biopsy—offer a valuable, minimally invasive alternative to traditional surgical staging in the evaluation of mediastinal lesions. Although procedural competency relies on an operator learning curve that varies across institutional contexts and technical approaches, surpassing established proficiency thresholds has been shown to enhance diagnostic accuracy. The high diagnostic yield of EBUS methods can generate indirect cost savings by reducing the necessity for repeat tissue sampling, unnecessary hospitalizations, and invasive surgical procedures such as

mediastinoscopy. However, because healthcare reimbursement systems, institutional resources, and training curricula differ substantially on a global scale, further standardized, multicenter studies are required to more precisely define optimal learning pathways and long-term cost-effectiveness across diverse clinical settings.

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BÖLÜM 2

PROGNOSTIC FACTORS IN STAGE IV NON-SMALL CELL LUNG CANCER: CLINICAL, PATHOLOGICAL, AND MOLECULAR PREDICTORS

MURAT SARIÇAM[1]

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, accounting for approximately one in five cancer deaths annually (Mountain, 1997). Non-small cell lung cancer (NSCLC) represents nearly 85% of all lung cancer diagnoses, and a significant proportion of patients present with metastatic disease at the time of diagnosis. Advanced stage at presentation contributes substantially to poor survival outcomes, with five-year survival rates for stage IV NSCLC remaining below 10% despite therapeutic advances.

Prognosis in stage IV NSCLC is notably heterogeneous. While some patients experience prolonged survival with modern systemic therapies, others demonstrate rapid disease progression and limited treatment benefit. Identifying prognostic factors is therefore critical for risk stratification, therapeutic decision-making, patient counseling, and clinical trial design. Prognostic indicators encompass a broad range of variables, including patient-related characteristics, tumor burden and distribution, histopathological features, molecular biomarkers, systemic inflammatory markers, and treatment-associated factors.

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This article reviews current evidence regarding prognostic factors in stage IV NSCLC, emphasizing their clinical relevance and integration into predictive models.

Performance Status

Performance status (PS) is among the most robust and consistently validated prognostic factors in advanced NSCLC. The Eastern Cooperative Oncology Group (ECOG) PS scale is widely used to assess functional capacity and predict treatment tolerance. Patients with ECOG PS scores of 0–1 demonstrate significantly improved overall survival compared with those with PS ≥2 (O'Connell et al., 1986). Poor PS reflects diminished physiological reserve, increased comorbidity burden, and reduced capacity to tolerate systemic therapy.

Performance status remains a key component of prognostic nomograms and survival prediction models in immunotherapy-treated populations (Nomogram to Predict Survival in NSCLC Patients Treated with Nivolumab, 2019).

Demographic and Host Factors

Age and sex also influence prognosis in stage IV NSCLC. Advanced age is frequently associated with poorer outcomes, particularly when accompanied by comorbid conditions that limit treatment options. Female sex has been associated with improved survival compared with male sex, potentially due to biological differences, hormonal factors, and smoking patterns (Predictors of Survival in Patients with Non-Small Cell Lung Cancer, 2013).

Nutritional status is an additional host-related prognostic factor. Weight loss, low body mass index, and cancer cachexia correlate with inferior survival outcomes and reduced treatment tolerance, underscoring the importance of systemic host condition in advanced disease.

Metastatic Burden and Distribution

The extent and location of metastatic disease strongly influence prognosis in stage IV NSCLC. Patients with a limited number of metastatic sites exhibit improved survival compared with those with widespread dissemination. Oligometastatic disease, typically defined as one to five metastatic lesions, is associated with more favorable outcomes and may be amenable to aggressive local therapies (Prognostic Factors of Oligometastatic NSCLC Meta-Analysis, 2018).

Specific metastatic sites confer differential prognostic impact. Brain and liver metastases are consistently associated with worse survival, reflecting both biological aggressiveness and therapeutic challenges (Kuang et al., 2025). Bone metastases also predict poorer outcomes, particularly when complicated by skeletal-related events such as fractures or spinal cord compression (Prediction of Overall Survival of NSCLC with Bone Metastasis).

Histological Subtype

Histological classification remains an important prognostic variable in NSCLC. Adenocarcinoma generally confers a more favorable prognosis compared with squamous cell carcinoma in the metastatic setting. This difference is partly attributable to the higher prevalence of actionable molecular alterations in adenocarcinoma, enabling targeted therapeutic approaches.

Squamous cell carcinoma has historically been associated with inferior survival outcomes; however, the advent of immune checkpoint inhibitors has narrowed this gap. Histology nonetheless remains an essential stratification factor in prognostic modeling and clinical trial design.

Molecular and Serum Biomarkers

Molecular profiling has transformed prognostic assessment in advanced NSCLC. Epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements identify patient subsets with improved survival when treated with targeted tyrosine kinase inhibitors (TKIs). In EGFR-mutant stage IV NSCLC, absence of brain or liver metastases, younger age, and adenocarcinoma histology are associated with prolonged survival (Kuang et al., 2025).

Serum biomarkers including carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and cytokeratin-19 fragment (CYFRA 21-1) have demonstrated independent prognostic value. Elevated levels of these markers typically correlate with increased tumor burden and poorer outcomes.

Proteomic assays such as the VeriStrat test further illustrate the prognostic potential of serum-based molecular signatures, particularly in predicting benefit from EGFR-directed therapies.

Systemic Inflammatory Markers

Systemic inflammation plays a central role in tumor progression and immune evasion. Inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are easily obtainable and reproducible prognostic markers. Elevated NLR and PLR are consistently associated with reduced overall survival in stage IV NSCLC (Prognostic Model Integrating Histology, Systemic Inflammation, 2025).

These markers reflect both tumor-induced inflammation and host immune competence, offering additional prognostic insight beyond traditional clinical factors.

Treatment-Related Prognostic Factors

Therapeutic interventions significantly influence survival outcomes in metastatic NSCLC. Patients receiving systemic therapy—including chemotherapy, targeted agents, or immunotherapy—demonstrate improved survival compared with untreated individuals. Combination chemo-immunotherapy regimens have shown superior outcomes in selected patient populations (Establishment and Validation of a Survival Prediction Model for Stage IV NSCLC, 2025).

Local therapies such as radiotherapy may also confer prognostic benefit in selected patients, particularly those with limited metastatic burden or dominant thoracic disease. High-dose thoracic radiotherapy has been associated with improved survival in some stage IV NSCLC cohorts (Radiotherapy and Survival in Stage IV NSCLC).

Prognostic Models and Nomograms

Multivariable prognostic models integrating clinical, pathological, and laboratory parameters have been developed to provide individualized survival estimates. Nomograms incorporating performance status, tumor burden, and inflammatory markers demonstrate improved predictive accuracy compared with single-factor assessments. However, many models require external validation and prospective evaluation before widespread clinical adoption.

Conclusion

Prognosis in stage IV non-small cell lung cancer is influenced by a complex interplay of patient-related, tumor-related, molecular, and treatment-associated factors. Performance status, metastatic distribution, histology, molecular alterations, and systemic inflammation remain key determinants of survival. Continued refinement and validation of integrated prognostic models will

enhance personalized treatment strategies and improve outcomes for patients with advanced NSCLC.

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BÖLÜM 3

PATIENT SAFETY IN PLEURAL PROCEDURES: PREVENTION, EARLY RECOGNITION, AND MANAGEMENT OF COMPLICATIONS

BURCU ANCIN[1]

Introduction

Pleural procedures encompass a range of interventions, including thoracentesis, small-bore pleural catheter or chest tube insertion, indwelling pleural catheter placement, image-guided pleural biopsy, and medical thoracoscopy. A substantial proportion of these procedures are performed at the bedside, often in patients with limited respiratory reserve. Although complications are relatively uncommon, wrong-side procedures, organ injury, hemothorax, tension pneumothorax, and sedation-related respiratory depression may result in severe or even life-threatening consequences. Patient safety therefore depends on establishing an appropriate indication, confirming the correct side, ensuring the availability of an experienced team and a suitable procedural environment, and initiating the necessary rescue intervention without delay when a complication occurs (Asciak et al., 2023; Corcoran et al., 2015).

The foundation of a safe approach is the reduction of preventable risks before the procedure, recognition of early warning signs during the intervention, and systematic management of clinical deterioration after the procedure. Inadequate imaging, incomplete preparation, rushed decision-making, poorly defined drain-management instructions, and insufficient handover may contribute

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to preventable safety events (Asciak et al., 2023; Corcoran et al., 2015). Although pneumothorax, bleeding, re-expansion pulmonary edema, infection, and drain dysfunction arise through different mechanisms, their incidence and clinical consequences may be reduced through shared safety measures, including appropriate imaging, meticulous technique, close monitoring, and prompt intervention (Asciak et al., 2023; Corcoran et al., 2015).

System-Based Approach to Safe Pleural Procedures

Patient safety in pleural procedures begins when the indication is established. The expected clinical benefit should be clearly defined, and a less invasive alternative should be considered whenever the same objective can be achieved without an intervention of comparable complexity. Elective procedures may be postponed to allow completion of the necessary preparations or correction of modifiable risk factors. In contrast, delaying intervention may pose a greater risk in conditions such as sepsis secondary to pleural infection, tension pneumothorax, or progressive respiratory failure attributable to pleural disease (Asciak et al., 2023; Roberts et al., 2023).

Procedural competence should not be assessed solely on the basis of the number of procedures performed. The ability to interpret thoracic ultrasonography, maintain sterile technique, use procedural equipment safely, recognize early signs of complications, and seek timely assistance when required should also be included in competency assessment. Simulation-based training, direct observation, and structured feedback should be used, while clinical competence should be verified using objective criteria and reassessed when necessary (Asciak et al., 2023; Hassan et al., 2026; Holden, 2021).

A pre-procedure safety checklist should be completed. This assessment should include confirmation of patient identity and the side of the procedure, the clinical indication, current imaging findings, antithrombotic therapy, allergies, the calculated maximum

dose of local anesthetic, the sedation and monitoring plan, required specimens, and the availability of rescue equipment. During the handover of a patient with a pleural drain, the drain size and external length, the volume and characteristics of the drainage, the status of the underwater seal system, and the plans for clamping, suction, and flushing should be communicated both verbally and in writing (Asciak et al., 2023; Corcoran et al., 2015).

Table 1. Safety checklist for pleural procedures

Stage	**Check question**	**Action/safety threshold**
Preparation	Are the patient's identity, procedural side, and indication consistent with the current imaging findings?	If any discrepancy is identified, the procedure should not be initiated; the imaging findings and procedural plan should be reassessed.
Risk assessment	Have antithrombotic therapies, bleeding history, respiratory reserve, tolerance of positioning, and allergies been evaluated?	The urgency of the procedure should be determined, and an individualized plan should be developed according to medication use, renal function, and the risks of bleeding and thrombosis.
Final verification	Have the procedure, side, team roles, maximum local anesthetic dose, sedation and monitoring plan, and rescue equipment been confirmed?	The sterile procedure should not begin until all essential safety elements have been verified.
Procedure	Are the closed system and sterility being maintained, does the ultrasonographic target remain valid, and is communication with the patient continuing?	Drainage should be stopped and the patient reassessed if pain, chest pressure or tightness, persistent cough, dyspnea, hypoxemia, or hypotension develops.
Handover	Have the volume and characteristics of the drainage, collected specimens, drain size and external length, and the plans for suction, clamping, and flushing been documented?	Verbal and written handover should be completed together, and the monitoring plan and thresholds for clinical deterioration should be clearly specified.

Source: Prepared by the author based on Asciak et al. (2023) and Corcoran et al. (2015).

Pre-procedure Assessment and Preparation

Patient identity and the side of the procedure should be confirmed by reconciling the identification wristband, the patient's

own statement whenever possible, the physical examination, and current imaging. Thoracic ultrasonography should be repeated with the patient in the intended procedural position; if the position changes, the target should be reassessed before needle entry. Computed tomography may provide additional planning information in patients with loculated collections, prior thoracic surgery or pleurodesis, or substantially distorted anatomy (Asciak et al., 2023; Boccatonda et al., 2024; Hassan et al., 2026).

Respiratory reserve, oxygen requirement, hemodynamic status, level of consciousness, ability to control coughing, tolerance of the required position, and use of positive-pressure ventilation should be assessed before the procedure. A single functioning lung, pulmonary hypertension, fibrotic or bullous lung disease, and extensive pleural adhesions do not uniformly preclude intervention; however, these features should prompt an individualized risk-benefit assessment, senior operator involvement, appropriate image guidance, and enhanced monitoring. Puncture through infected skin should be avoided, and clinicians should recognize that deep sedation may obscure pain, cough, dyspnea, and other early warning symptoms (Asciak et al., 2023).

Bleeding risk should not be reduced to the international normalized ratio or platelet count alone. A history of abnormal bleeding, hepatic and renal function, hematologic disorders, anticoagulant or antiplatelet therapy, procedural invasiveness, and clinical urgency should be considered together. Ultrasound-guided thoracentesis is a low-bleeding-risk procedure, and observational studies have reported low event rates in selected patients with uncorrected coagulation abnormalities. These findings should not be extrapolated indiscriminately to higher-risk procedures. For elective interventions, medication-specific interruption intervals, renal function, and thrombotic risk should be addressed according to an institutional antithrombotic protocol (Cantey et al., 2016; Pathak et al., 2017; Puchalski, Argento, Murphy, Araujo, & Pisani, 2013).

Informed consent should cover the purpose of the procedure, reasonable alternatives, the likelihood of achieving the intended clinical objective, and risks specific to the patient and the planned intervention. Pneumothorax, the possible need for chest tube placement, bleeding, organ injury, re-expansion pulmonary edema, infection, and—when an indwelling pleural catheter is planned—the practical burden of home care should be discussed. Patients should be instructed to report pain, chest tightness, dyspnea, dizziness, or persistent severe coughing immediately (Asciak et al., 2023).

The ultrasound machine, sterile probe cover and gel, appropriate needle or catheter, closed drainage system, specimen containers, sutures, and dressing materials should be prepared before starting. Oxygen, suction equipment, intravenous access, emergency medications, and airway equipment should be immediately available, and the total planned dose of local anesthetic should be calculated in advance. When intravenous sedation is used, a trained clinician should be assigned to monitoring; continuous pulse oximetry, regular blood pressure assessment, and capnography when clinically appropriate should be used. The additive respiratory-depressant effects of sedative and analgesic agents should be anticipated, and explicit post-sedation recovery criteria should be defined (Asciak et al., 2023).

Ultrasonography and Technical Safety

Thoracic ultrasonography is a dynamic safety tool rather than a single static image. The pleural fluid pocket, adjacent atelectatic lung, diaphragm, liver, and spleen should be observed through several respiratory cycles, allowing estimation of the skin-to-pleura distance and a safe depth of needle advancement. Color Doppler may help identify intercostal vessels, particularly when an atypical or posterior access route is being considered (Boccatonda et al., 2024; Hassan et al., 2026; Roebker et al., 2023).

Ultrasound assistance or real-time ultrasound guidance improves procedural success and reduces pneumothorax compared

with a landmark-only approach. When a site is marked before the procedure, the patient should remain in the same position and the intervention should follow without unnecessary delay. Real-time guidance is preferable for small, deep, or loculated collections. Entering immediately above the superior border of a rib reduces exposure to the main neurovascular bundle but does not eliminate vascular risk, particularly in posterior interspaces; excessive depth should therefore be avoided. The planned tract should remain clear of aerated lung, solid organs, thick pleural nodules, and visible vessels (Boccatonda et al., 2024; Cavanna et al., 2014; Hassan et al., 2026; Perazzo et al., 2014; Roebker et al., 2023).

Thoracentesis: Prevention and Management of Complications

For therapeutic thoracentesis, a small-bore plastic catheter should be used, the drainage circuit should remain closed, and fluid should be removed slowly by manual aspiration or gravity drainage. A maximum of approximately 1.5 L in a single attempt remains a conservative practical limit rather than an absolute physiologic threshold. Drainage should be stopped immediately if persistent cough, chest pressure or pain, worsening dyspnea, hypoxemia, or hypotension develops. Vacuum bottles and uncontrolled wall suction should be avoided. Regardless of the volume removed, patient symptoms take priority over complete radiographic evacuation of the pleural space (Asciak et al., 2023; Sagar et al., 2020).

Post-thoracentesis pneumothorax may result from direct visceral pleural injury, entry of atmospheric air through the drainage system, or failure of the lung to re-expand. New pleuritic pain, dyspnea, oxygen desaturation, and unilateral reduction in breath sounds should prompt immediate assessment; loss of lung sliding on ultrasonography may support the diagnosis. A small, stable, asymptomatic pneumothorax can often be managed with observation and serial clinical or imaging assessment, whereas a symptomatic, enlarging, hemodynamically significant pneumothorax—or one occurring during positive-pressure ventilation—generally requires

pleural drainage. Imaging should not delay immediate decompression when tension physiology is present (Cantey et al., 2016; Shostak et al., 2013; Williams & Lerner, 2021).

A basilar air-fluid level after drainage, together with failure of the lung to re-expand, may represent pneumothorax ex vacuo due to a non-expandable lung. Patients are often clinically stable, and routine application of suction or insertion of an additional drain usually provides no benefit. Previous imaging, pleural thickening, the pattern of lung volume loss, pleural pressure behavior when available, and the characteristic radiographic distribution help distinguish this condition from an active air leak (Hu et al., 2020; Saha et al., 2020).

Hemothorax is uncommon but potentially life-threatening. Expanding chest wall swelling, new or escalating pain, fresh blood in the drainage system, tachycardia, hypotension, or an otherwise unexplained fall in hemoglobin should trigger cessation of the procedure and immediate resuscitative measures, including intravenous access, blood sampling, and cross-matching. Computed tomography angiography is appropriate in a sufficiently stable patient, while ongoing hemorrhage may require transcatheter embolization or operative control. A catheter that may traverse a vessel or solid organ should be secured and must not be removed blindly; controlled withdrawal should be planned with interventional radiology and thoracic surgery (Williams & Lerner, 2021).

Re-expansion pulmonary edema typically presents within minutes to several hours after drainage with cough, dyspnea, hypoxemia, and unilateral alveolar opacities. Aspiration should be stopped, or a drain being used for pleural-fluid evacuation should be temporarily clamped, and oxygen should be administered while the need for ventilatory support is assessed. Management is supportive; diuretics are used by some clinicians, but evidence for their routine use is lacking (Asciak et al., 2023; Kasmani et al., 2010; Williams & Lerner, 2021).

Sharp or increasing pain and persistent coughing should be treated as warning symptoms rather than expected discomfort. A vasovagal reaction is managed by stopping the procedure and providing supportive care. Suspected local anesthetic systemic toxicity requires immediate airway and circulatory support and activation of a lipid emulsion protocol. In the rare event of suspected systemic air embolism, 100% oxygen, urgent critical care support, and immediate specialist assessment are required (Williams & Lerner, 2021).

Routine chest radiography is not necessary after every uncomplicated ultrasound-guided thoracentesis in an asymptomatic patient. Post-procedure imaging is indicated when symptoms develop, multiple passes were required, air was aspirated, the patient is receiving positive-pressure ventilation, the procedure was technically difficult, or another complication is suspected. Bedside ultrasonography may provide a rapid initial assessment when appropriate expertise is available. At discharge, patients should receive written instructions to seek urgent care for delayed dyspnea, chest pain, syncope, fever, or bleeding (Asciak et al., 2023).

Chest Tubes and Small-Bore Pleural Catheters

Chest tube malposition may involve an interlobar fissure, lung parenchyma, subcutaneous tissues, the subdiaphragmatic space, mediastinum, or a solid organ. The target should be defined with ultrasonography or computed tomography when required, and uncontrolled advancement of a trocar should be avoided. During a Seldinger insertion, the guidewire should advance without resistance, and the dilator should be inserted only far enough to traverse the chest wall rather than being advanced deeply into the thorax (Asciak et al., 2023; Kesieme et al., 2012; Kwiatt et al., 2014; Roebker et al., 2023).

Drain size should be selected according to the indication and the characteristics of the expected output. Small-bore drains are appropriate for most pleural effusions, pleural infections, and many

pneumothoraces and are generally better tolerated. A larger-bore drain should be considered in an unstable trauma patient, pneumothorax during mechanical ventilation or with a substantial air leak, and situations involving a large clot burden or very viscous material. The most proximal side hole should be confirmed to lie within the pleural cavity, the tube should be secured, the external length should be documented, and follow-up chest imaging should be obtained within a few hours to confirm position (Asciak et al., 2023; Hallifax et al., 2017; Porcel, 2018; Roebker et al., 2023).

At every clinical handover or nursing shift, the patient, insertion site, documented external length, tubing, connectors, stopcocks, underwater seal, air leak, and amount and character of drainage should be assessed. An abrupt reduction in output should prompt inspection of the entire system before catheter manipulation. If flushing is appropriate for the specific drain and indication, it should be performed gently with sterile saline according to a written prescription or protocol. Guidewires, sharp instruments, and high-pressure flushing should not be used to overcome resistance. Persistent residual collections are better managed by image-guided repositioning or catheter replacement than by blind manipulation (Roebker et al., 2023; Sorino et al., 2024).

With continuous bubbling, a pleural air leak should be distinguished from a leak within the drainage circuit. Routine clamping in a patient with pneumothorax, an ongoing air leak, or positive-pressure ventilation can precipitate tension pneumothorax. Routine stripping or milking of chest tubes is not recommended, and suction should be used only for a defined indication at a prescribed pressure. Clamping should be limited to situations in which the purpose and duration are explicit, the patient can be closely observed, and immediate intervention is available (Asciak et al., 2023; Porcel, 2018; Roebker et al., 2023; Sorino et al., 2024).

Progressive subcutaneous emphysema requires urgent assessment of drain patency, position, and the adequacy of pleural

decompression. If a catheter is accidentally dislodged, an occlusive dressing should be applied and the patient reassessed promptly; a tube should not be pushed back through an immature tract, and a new sterile insertion site should be used if drainage remains necessary. Analgesia, aseptic technique, and an occlusive dressing should also be provided during planned drain removal (Roebker et al., 2023).

Drain Safety and Intrapleural Therapy in Pleural Infection

In pleural infection, failure of source control is a central safety concern. Fever, sepsis physiology, daily drain output, catheter patency, inflammatory response, and residual loculations should be reviewed together. Antibiotic therapy, microbiologic sampling, additional or repositioned drainage, and timely surgical consultation should be coordinated rather than considered in isolation. A drain that appears correctly positioned on imaging may still fail to evacuate all septated compartments; inadequate clinical improvement should therefore prompt repeat imaging and reassessment for residual collections (Elsheikh et al., 2023; Roberts et al., 2023).

Combined intrapleural tissue plasminogen activator and deoxyribonuclease may improve drainage when an appropriately positioned chest tube has ceased to drain and a residual infected collection remains. Catheter position and bleeding risk should be reviewed before treatment, and therapeutic anticoagulation should be withheld when clinically feasible. The prescribed doses, dwell or clamping period, and reopening times should be documented clearly. Treatment should be stopped and the patient reassessed if fresh bloody drainage, escalating pain, hemodynamic change, or a fall in hemoglobin occurs (Akulian et al., 2022; Asciak et al., 2023; Roberts et al., 2023).

Safety of Indwelling Pleural Catheters

An indwelling pleural catheter can facilitate ambulatory symptom control in patients with recurrent pleural effusion, particularly malignant pleural effusion, but it transfers a substantial

component of care to the home. Patients and caregivers should demonstrate aseptic connection technique, controlled drainage, dressing care, and documentation before discharge. Drainage should be slowed or stopped if pain, persistent cough, dyspnea, or dizziness develops. Fever, erythema, purulent discharge, catheter damage, or an abrupt cessation of drainage in a symptomatic patient should prompt same-day contact with the clinical team (Asciak et al., 2023; Roberts et al., 2023).

A meta-analysis estimated the overall incidence of indwelling pleural catheter-related complications at approximately 20.3%, with infection and catheter malfunction among the most important problems. A functioning catheter does not always need to be removed when infection is clinically controlled and drainage remains adequate. Removal or exchange should be considered in uncontrolled sepsis, inadequate source control, progressive tunnel infection, or persistent catheter failure. Superficial cellulitis should be distinguished from deep pleural infection, and antibiotic selection should be integrated with culture results and assessment of drainage adequacy (Chalhoub et al., 2018; Lui et al., 2016; Wang et al., 2023).

When drainage decreases, the catheter course, valve, connectors, and possible kinking should be inspected, and residual fluid should be confirmed by ultrasonography. Depending on the clinical context, sterile saline flushing, specialist-supervised intrapleural fibrinolytic therapy, image-guided repositioning, or catheter replacement may be considered. During removal, the cuff should be dissected free without excessive traction, and the catheter should be inspected to confirm complete removal (Asciak et al., 2023; Chalhoub et al., 2018; Lui et al., 2016).

Post-procedure Monitoring, Early Recognition, and Rescue

After the procedure, respiratory rate, oxygen saturation, pulse, blood pressure, pain, and level of consciousness should be compared with baseline values. The volume and appearance of removed fluid, specimens obtained, technical difficulties, and

adverse events should be documented, together with the drain's external length, connections, suction setting, and expected output. The intensity and duration of monitoring should reflect the procedure, sedative exposure, hemodynamic status, and individual complication risk; a statement that the procedure was "uneventful" cannot replace recorded observations and explicit instructions (Asciak et al., 2023; Williams & Lerner, 2021).

Clinical deterioration should trigger an airway-breathing-circulation approach: stop the procedure or drainage, call for assistance, administer oxygen, initiate monitoring, and secure intravenous access. Pneumothorax, hemothorax, re-expansion pulmonary edema, infection, and drainage-system failure should then be investigated rapidly. In a patient with a chest drain, the system should be traced systematically from the patient to the collection chamber. Hypotension with a new opacity should raise concern for hemothorax; hypoxemia with absent lung sliding suggests pneumothorax; and hypoxemia with new alveolar opacities after fluid removal is compatible with re-expansion pulmonary edema (Williams & Lerner, 2021).

Table 2. Early indicators and initial management of major complications

Complication	Early indicators	Immediate actions	Escalation
Pneumothorax	New dyspnea, pleuritic pain, hypoxemia, reduced or absent lung sliding	Stop drainage; provide oxygen and monitoring; assess with bedside ultrasonography and/or chest radiography	Immediate decompression for tension physiology; pleural drain for a symptomatic or enlarging pneumothorax and generally during positive-pressure ventilation
Pneumothorax ex vacuo	Basilar air-fluid level after drainage; failure of re-expansion; patient often clinically stable	Compare with previous imaging and the clinical course; assess for non-expandable lung	Avoid routine suction or an additional drain; manage the underlying pleural disease and symptoms
Hemothorax	Fresh blood, falling hemoglobin, tachycardia, hypotension, new pleural opacity	Stop the procedure; obtain intravenous access, blood count and cross-match; begin resuscitation	Computed tomography angiography if stable; embolization or surgery for ongoing bleeding; do not blindly remove a traversing catheter
Re-expansion pulmonary edema	Cough, dyspnea, hypoxemia, and new	Stop aspiration or clamp a drain used for fluid evacuation; administer	Critical care assessment; high-flow oxygen, noninvasive ventilation, or

Complication	Early indicators	Immediate actions	Escalation
	opacities within minutes to hours	oxygen and position upright when tolerated	intubation as required; treatment is supportive
Organ or vascular injury	Unexpected severe pain, hemorrhage, shock, or an atypical catheter course	Secure the catheter and do not remove it; initiate resuscitation and urgent imaging	Controlled withdrawal and repair with interventional radiology and/or surgery
Drain obstruction or migration	Abrupt loss of output, change in external length, persistent or recurrent collection	Inspect for kinks, stopcock or connection problems; reassess with bedside imaging	Prescribed sterile flushing when appropriate; image-guided repositioning or replacement
Infection	Fever, erythema, purulent discharge, sepsis, or residual loculations	Obtain cultures; start appropriate antibiotics; assess drain patency and source control	Additional drainage, catheter exchange or removal, intrapleural therapy, or surgery according to the clinical response
Sedation-related respiratory depression or local anesthetic systemic toxicity	Hypoventilation or reduced consciousness; neurologic symptoms, seizures, or arrhythmia	Stop causative drugs; support the airway, breathing, and circulation; administer oxygen	Use reversal agents when appropriate; activate a lipid emulsion protocol for local anesthetic toxicity; escalate to critical care

Source: Developed by the author based on Asciak et al. (2023), Roebker et al. (2023), and Williams and Lerner (2021).

Life-saving treatment should not await definitive diagnostic confirmation. Tension pneumothorax requires immediate decompression; active hemorrhage requires resuscitation and urgent interventional radiology or surgical control; re-expansion pulmonary edema requires oxygen and escalation of ventilatory support when needed; and sepsis requires cultures, antimicrobial therapy, and source control. When a catheter may be tamponading an injured organ or major vessel, it should be secured and left in place until a controlled removal and repair strategy has been agreed (Asciak et al., 2023; Roebker et al., 2023; Williams & Lerner, 2021).

Special Situations and High-Risk Patients

During positive-pressure ventilation, a small pleural air leak can enlarge rapidly and become hemodynamically significant. The target should be confirmed with real-time imaging when feasible, current ventilator pressures should be noted, and equipment for immediate decompression should be available. A post-procedure increase in peak airway pressure, reduction in delivered tidal volume, new hypotension, or hypoxemia requires urgent evaluation

for pneumothorax and drain malfunction (Asciak et al., 2023; Boccatonda et al., 2024; Hassan et al., 2026).

Obesity, chest wall deformity, edema, and inability to sit upright can make surface landmarks unreliable. Positioning should prioritize the safest needle path rather than simply the largest apparent fluid pocket, and needle length should be selected according to the measured skin-to-pleura distance. If the patient's position or the sonographic target changes, the procedure should pause and imaging should be repeated before further advancement (Asciak et al., 2023; Boccatonda et al., 2024; Hassan et al., 2026).

When bilateral drainage is contemplated, the cumulative dose of local anesthetic, overall fluid removal, physiologic reserve, and the possibility of bilateral complications should be considered. Same-session bilateral thoracentesis has been performed with complication rates comparable to unilateral procedures in selected patients, but a staged approach remains prudent when the patient is physiologically fragile or the first procedure produces pain, persistent cough, hypoxemia, hemodynamic instability, or another complication. In a large chronic effusion, the objective is safe symptom relief rather than complete radiographic evacuation (Asciak et al., 2023; Puchalski, Argento, Murphy, Araujo, Oliva, et al., 2013).

In patients with agitation, delirium, dementia, or severe anxiety, clear explanation, positioning support, and adequate local anesthesia should be prioritized. If sedation is necessary, the lowest effective dose should be titrated with appropriate monitoring. When cooperation and procedural safety cannot be achieved, the intervention should be deferred when clinically permissible or performed with anesthetic support (Asciak et al., 2023).

Life-saving drainage for tension pneumothorax or massive hemothorax should not be delayed while completing every element of elective preparation. Patient identity and the side of intervention should nevertheless be confirmed by the most reliable immediately

available method, resuscitation should proceed concurrently, and drain position should be imaged at the earliest safe opportunity. In a stable patient, urgency is not a justification for omitting current imaging or essential safety checks. After an emergency procedure, incomplete antithrombotic history, antimicrobial requirements, specimen handling, and the need for surgical escalation should be reviewed systematically and documented (Asciak et al., 2023; Roebker et al., 2023).

Specimens should be labeled at the bedside with patient identifiers, side, and collection time, and the requirements for microbiology, cytology, and biochemical analysis should be planned in advance. Pleural fluid intended for pH measurement should be collected anaerobically in an appropriate heparinized blood-gas syringe, protected from contamination with air or local anesthetic, and analyzed without avoidable delay (Elsheikh et al., 2023; Roberts et al., 2023).

Conclusion

Safety in pleural procedures depends on the combined application of an appropriate indication, reliable confirmation of the procedural side, dynamic ultrasonography, individualized risk assessment, a competent team, controlled drainage, and complete handover. Complications cannot be eliminated entirely, but early recognition and prompt rescue management can substantially reduce the likelihood of severe harm.

The most important practical principles are to image the patient in the actual procedural position; treat pain, persistent cough, and dyspnea as signals to stop and reassess; distinguish pneumothorax ex vacuo from an active air leak; exclude hemothorax when drainage becomes bloody; examine the entire drainage system before manipulating a catheter; avoid concurrent therapeutic anticoagulation with intrapleural tissue plasminogen activator and deoxyribonuclease whenever clinically feasible; and never remove blindly a catheter that may traverse an organ or major vessel.

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