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Safety and efficacy of transbronchial cryobiopsy for elderly lung cancer patients

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Abstract

Background The increasing prevalence of lung cancer in the elderly population necessitates a closer evaluation of diagnostic and therapeutic approaches. This study aimed to compare the safety and diagnostic efficacy of transbronchial lung cryobiopsy (TBLC) between patients ≥ 80 years and younger patients.

Methods A retrospective review was conducted of 96 patients diagnosed with peripheral lung cancer who underwent TBLC between April 2021 and October 2023. The patients were categorized into two groups: the elderly group (age ≥ 80 years, $n = 20$) and younger group (age < 80 years; $n = 76$). Data regarding the biopsy yield, complications, and feasibility of molecular analyses were collected and analyzed.

Results The diagnostic yield of TBLC was comparable between the elderly and younger groups (95% vs. 89.5%, $p = 0.679$). Biomarker testing, including programmed death-ligand 1 expression and genetic mutations, were feasible in all cases diagnosed with cancer using TBLC samples. No significant differences were observed in major complications such as pneumothorax or bleeding.

Conclusions TBLC was found to be a safe and effective diagnostic tool for peripheral lung cancer in elderly patients and provided adequate samples for molecular testing. Since the complication rates did not significantly differ between the two age groups, age alone should not be considered a contraindication for the procedure.

Keywords Cryobiopsy, Bronchoscopy, Peripheral lung cancer, Elderly patients, Biopsy yield, Complications, Molecular analysis

Background

Lung cancer remains one of the leading causes of death worldwide, particularly affecting older populations [1]. The well-documented increasing incidence of lung cancer with age is a significant health concern for the elderly. In older adults, therapeutic options, such as surgery, radiation, and chemotherapy, have proven to be effective; however, these interventions are associated with an increased risk due to the presence of comorbidities and reduced physiological reserves [1]. It is encouraging to see that recent advances in chemotherapies, including immune checkpoint inhibitors (ICIs) and treatments based on specific genetic mutations, have expanded the

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therapeutic options for elderly patients with lung cancer. These advances offer important alternatives that can be tailored to an individual's biomarker profile, which is a promising step forward.

Cryobiopsy, a relatively novel bronchoscopic technique, has gained prominence in recent years due to its capacity to procure larger and higher-quality tissue samples with fewer crush artifacts than those from traditional forceps biopsies [2]. This method has demonstrated promising diagnostic yields in a range of pulmonary diseases, including peripheral lung cancer. However, the procedure is not without inherent risks and higher rates of complications, such as bleeding and pneumothorax, than those of conventional methods due to the required freezing and tearing of the tissue during sample collection [3]. Although cryobiopsy's utility in younger populations is well-documented, there is a paucity of data on its safety and effectiveness in elderly patients. Given the demographic shift towards an aging population and increasing incidence of lung cancer among the elderly, it is crucial to evaluate the safety and utility of cryobiopsy in this vulnerable group. This study aimed to compare the outcomes of transbronchial lung cryobiopsy (TBLC) between patients aged ≥ 80 years and those aged < 80 years diagnosed with peripheral lung cancer.

Methods

Patients

This retrospective study was conducted at Fujita Health University Hospital and included 96 patients who underwent TBLC between April 2021 and October 2023. The patients were divided into the elderly group (≥ 80 years old; $n=20$) and the younger group (< 80 years old; $n=76$). The median age was significantly higher in the elderly group than in the younger group (82, range: 80–85 years versus 73.5, range: 43–79 years; $p<0.001$). These patients presented with peripheral lung lesions not visible through direct bronchoscopy that were subsequently diagnosed as primary lung cancer through histopathological examination. Along with TBLC, other biopsy methods, such as forceps biopsy, were also performed as necessary. Patients with central lung lesions or incomplete clinical data were excluded from the study. Use of antiplatelet or anticoagulant medications was discontinued prior to the procedure.

Procedures

All patients had intravenous access for infusion, and their oxygen saturation (SpO2) was continuously monitored via pulse oximetry, with supplemental oxygen administered through a nasal cannula to maintain SpO2 of > 90%. Electrocardiograms were continuously monitored, and blood pressure was measured every 5 min during the procedure. Before sedation, 2% lidocaine was applied topically to the upper airways. For sedation, patients aged ≤ 70 years received an initial intravenous dose of midazolam at 0.075 mg/kg before the procedure, with additional doses of 0.0375 mg administered every 20 min as needed. For patients aged ≥ 71 years, the starting dose of midazolam was 0.05 mg/kg, with supplementary doses of 0.025 mg/kg given every 20 min as necessary [4, 5]. In addition, all patients received intramuscular pethidine hydrochloride. In some cases, intravenous dexmedetomidine hydrochloride was added at the operator's discretion. Throughout the procedure, 1% lidocaine was administered intrabronchially. A radial endobronchial ultrasound (R-EBUS) probe (UM-S20-17 S, Olympus, Tokyo, Japan) was used to perform all bronchoscopies. Operators chose between various bronchoscopes, including thin or medium scopes (BF-P260F, BF-P290, or BF-260, Olympus), with or without a small guide-sheath kit (K-201, Olympus), or thick scopes (BF-1T260 or BF-1TQ290, Olympus), with or without a large guide-sheath kit (K-203, Olympus). For hemostasis, another bronchoscope was selected regardless of the model. A 7.5–8.5-mm inner-diameter tracheal tube (Portex Uncuffed Ivory PVC, Oral/Nasal Tracheal Tube; Smiths Medical, Minneapolis, MN, USA.) was used to intubate the patients. Endobronchial balloons (Fogarty® catheter, E-080–4 F; Edwards Lifesciences, Irvine, CA, USA.) were used for bronchial occlusion and hemostasis in all patients. A deflated balloon catheter was introduced through the suction channel of the tracheal tube and placed in the bronchus segment or subsegment targeted for TBLC [6]. The main scope was inserted through the tube and positioned near the target bronchus, with bronchial branch tracing and fluoroscopy used as guides [5, 7]. An R-EBUS probe, with or without a guide sheath, was advanced through the working channel, and findings were classified as within, adjacent to, or invisible depending on the positional relationship between the probe and target peripheral lung lesion [8]. A flexible cryoprobe (1.1-mm, 1.7-mm, or 1.9-mm diameter) connected to an ERBECRYO 2 system (Erbe Elektromedizin GmbH, Tübingen, Germany) was used to perform cryobiopsy, and prior to this, biopsy sampling with forceps (FB233D, 1.5-mm or FB231D, 1.9-mm), brushes, or aspiration needles was conducted on the basis of the operator's assessment. The selection of cryoprobe size was determined by the operator without predefined criteria. The cryoprobe tip was frozen for 3–5 s, after which both the probe and bronchoscope were swiftly removed together. After removal, the endobronchial balloon was inflated prophylactically with 2–3 mL of a contrast-saline mixture to control bleeding. An auxiliary scope was then advanced through the tracheal tube to monitor for hemorrhage. The attached cryobiopsy specimen was immersed in saline, thawed, and released. After 2–3 min, the balloon was deflated to

assess for continued bleeding, and an epinephrine–saline mixture was administered if necessary. The process was repeated to collect multiple TBLC specimens, with a median of three biopsies per procedure [6, 9, 10].

Data Collection

Data were retrospectively collected from medical records and included patient demographics, lesion characteristics, procedural details, and outcomes. Specific attention was given to the diagnostic yield of TBLC, rate of procedural complications, and adequacy of biopsy samples for further molecular, including programmed death-ligand 1 (PD-L1) expression, and genetic analysis. All cases included in this study were confirmed to be primary lung cancer through histopathological examination. Bleeding complications were categorized according to the criteria proposed by the Nashville Working Group for standardized definitions of bleeding after transbronchial lung biopsy [11]. In all cases, prophylactic intubation and balloon occlusion were performed, and adrenaline was administered at the operator's discretion.

Table 1 Baseline characteristics and variables of patients

	Elderly (≥80) (*n*=20)	Younger (<80) (*n*=76)	*p* value*
Age, median (range)	82 (80–85)	73.5 (43–79)	<0.001**
Gender, n (%)			0.637
Male	13	45	
Female	7	31	
Body mass index, mean (SD)	22.2 (0.73)	22.3 (0.37)	0.905†
Smoking history, n (%)			
Current	2	18	0.351
Former	9	32	
Never	9	25	
Performance status, n (%)			0.041‡
0–1	18	76	
≥2	2	0	
Charlson Comorbidity Index, n (%)			0.002
0	3	43	
1–2	10	23	
≥3	7	10	
Comorbidity, n (%)			
Chronic lung disease	5 (25)	7 (9.2)	0.057
Cerebrovascular disease	3 (15)	2 (2.6)	0.059‡
Diabetes	5 (25)	15 (19.7)	0.606
Dementia	0	2 (2.6)	1.00‡
Cardiovascular	4 (20)	7 (9.2)	0.232‡
Previous cancer	5 (25)	22 (28.9)	0.726
Use of drugs, n (%)			
Antithrombotic agents	7 (35)	11 (14.4)	0.036
Immunosuppressant	1 (5)	7 (9.2)	1.000‡
Pulmonary function test, mean (SD) (*n*=71)			
FEV1	2.22 (0.14)	2.18 (0.08)	0.789†
%FEV1	120.3 (6.54)	116.4 (1.48)	0.294†
FEV1/FVC	74.1 (2.55)	71.0 (2.69)	0.099†
FVC	3.07 (0.19)	3.10 (0.11)	0.868†
%FVC	115.3 (5.51)	113.1 (3.21)	0.728†

*Pearson chi-square P value except as noted. **From Wilcoxon Rank Sum Test. †From t-test. ‡From Fisher's exact test

Abbreviations: FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity

Statistical analysis

Continuous variables are summarized as medians and ranges, and categorical variables are expressed as frequencies and percentages. The Mann–Whitney U-test for non-normally distributed continuous variables and the t-test for normally distributed continuous variables were used for comparisons between the elderly and younger groups. The chi-squared test was performed for categorical variables when all expected cell frequencies were ≥5, ensuring the validity of the test. However, when any expected cell frequency was <5, Fisher's exact test was performed due to its accuracy in handling small sample sizes. Values of $p<0.05$ were accepted as indicative of statistical significance. JMP Pro 17 (JMP Statistical Discovery LLC, Cary, NC, USA) was used to perform all statistical analyses.

Results

The sex distribution and body mass index (BMI) values were similar between the two groups, but the median age was significantly higher in the elderly group than in the younger group (82, range: 80–85 years versus 73.5, range: 43–79 years; $p<0.001$). Regarding performance status (PS), significantly more patients in the elderly group had a PS of ≥2 ($p=0.041$). The Charlson Comorbidity Index was higher in the elderly group, with more patients having a score of ≥3 ($p=0.002$). In terms of comorbidities, chronic lung disease ($p=0.057$) and cerebrovascular disease ($p=0.059$) were more frequent in the elderly group, but these differences were not statistically significant. Use of antithrombotic agents was significantly higher in the elderly group than in the younger group (35% vs. 14.4%, $p=0.036$). Pulmonary function tests, including forced expiratory volume in 1 s, forced vital capacity, and their percentages, were not significantly different between the two groups (Table 1, presented at the end of this document).

Lesion characteristics, such as size and lobar location, were similar between the groups, and the number of biopsy specimens obtained also did not differ significantly. The median number of cryobiopsies obtained per procedure was 3 (range: 1–4) in both groups. In cases where both cryobiopsy and forceps biopsy were

performed, the median number of forceps biopsies obtained per procedure was 6 (range: 3–12) in the elderly group and 6 (range: 2–14) in the younger group. Regarding the sedation, the elderly group received a lower dose of midazolam on average (7.41 mg vs. 8.23 mg, $p=0.267$), although the difference was not statistically significant. A significantly lower proportion of patients in the elderly group received dexmedetomidine (25% vs. 64.5%, $p=0.001$) (Table 2).

In terms of diagnostic yield for histopathological diagnosis from bronchoscopic samples, there was no significant difference between the elderly and younger groups (95% vs. 89.5%, $p=0.679$). In both groups, approximately half of the patients underwent cryobiopsy in combination with forceps biopsy (45% in the elderly group and 47.4% in the younger group); however, no cases were diagnosed using forceps biopsy alone. Both groups primarily had adenocarcinoma as the most frequent histological diagnosis. With regard to the treatment strategy, radiation therapy tends to be selected over surgery for elderly patients. However, 16 (80%) patients in the elderly group underwent cancer treatment, including surgery in 7 of the 16 cases (Table 3).

For the multi-gene panel testing, Oncomine Dx® Target Test (Thermo Fisher Scientific Inc., Waltham, MA, USA) and the AMOY Dx® Pan Lung Cancer PCR panel (Amoy Diagnostics Co., Ltd., Xiamen, China) were used based on the discretion of the attending physician. Multigene panel testing was successfully performed on all 19 elderly patients diagnosed via bronchoscopy (using

Table 2 Lesion characteristics and bronchoscopy data

	Elderly (≥80) (*n*=20)	Younger (<80) (*n*=76)	*p* value*
Lesion size, median (range), mm	29.7 (15.8-140.3)	31.5 (10.9-102.9)	0.729**
Lobar location, n (%)			0.730†
Upper	10 (50)	30 (39.5)	
Middle/Lingular	2 (10)	10 (13.2)	
Lower	8 (40)	36 (47.3)	
Diameter of the Cryoprobe, n (%)			0.834
1.1 mm	14 (70)	55 (72.4)	
1.7 /1.9 mm	6 (30)	21 (27.6)	
Number of cryobiopsy specimens, median (range)	3 (1–4)	3 (1–4)	0.527*
Procedures, n (%)			0.850
Cryobiopsy alone	11 (55)	40 (52.7)	
Combined with forceps biopsy	9 (45)	36 (47.3)	
Sedation, n (%)			0.001
Midazolam and pethidine	15 (75)	26 (34.2)	
Midazolam, pethidine and dexmedetomidine	5 (25)	50 (65.8)	
Dose of midazolam, mean (SD), mg	7.41	8.23	0.267‡
Dose of lidocaine, mean (SD), mg	398.5	413.6	0.452‡

*Pearson chi-square P value except as noted. **From Wilcoxon Rank Sum Test. †From Fisher's exact test. ‡From t-test

Table 3 Diagnosis and initial treatment

	Elderly (≥80) (*n*=20)	Younger (<80) (*n*=76)	*P* value*
Histological diagnoses, n (%)			0.649
Adenocarcinoma	17 (85)	67 (88.2)	
Squamous cell carcinoma	3 (15)	7 (9.2)	
NSCLC-NOS	0 (0)	2 (2.6)	
Diagnostic yield, n (%)	19 (95.0)	68 (89.5)	0.679
Cryobiopsy alone	11/11	37/40	
Combined with forceps biopsy	8/9	31/36	
Diagnosis via cryobiopsy only	2	2	
Diagnosis via both methods	6	29	
Stage, n			0.393
I/II/III/IV/unknown	9/3/3/4/1	33/7/15/21/0	
Initial treatment, n (%)			0.042
Surgery	7 (35)	40 (52.6)	
Radiation	5 (25)	7 (9.2)	
Chemotherapy	4 (20)	24 (31.6)	
Best supportive care	4 (20)	5 (6.6)	

* Fisher's exact test P value

Abbreviations: NSCLC-NOS, Non-Small Cell Lung Cancer - Not Otherwise Specified, Immunohistochemistry (IHC) was performed with PD-L1 IHC 22C3 pharmDx (Dako/Agilent, Tokyo, Japan). PD-L1 expression testing was not conducted in 2 elderly cases and 14 younger cases. In all remaining cases where bronchoscopic samples were submitted, PD-L1 testing was successfully evaluated, with 62 younger patients and 18 elderly patients assessed. Among the younger group, 32 patients were PD-L1 negative (Tumor Proportion Score (TPS) < 1%), 17 were low-positive (TPS 1–49%), and 13 were high-positive (TPS ≥ 50%). In the elderly group, six patients were PD-L1 negative, nine were low-positive, and three were high-positive (Fig. 1)

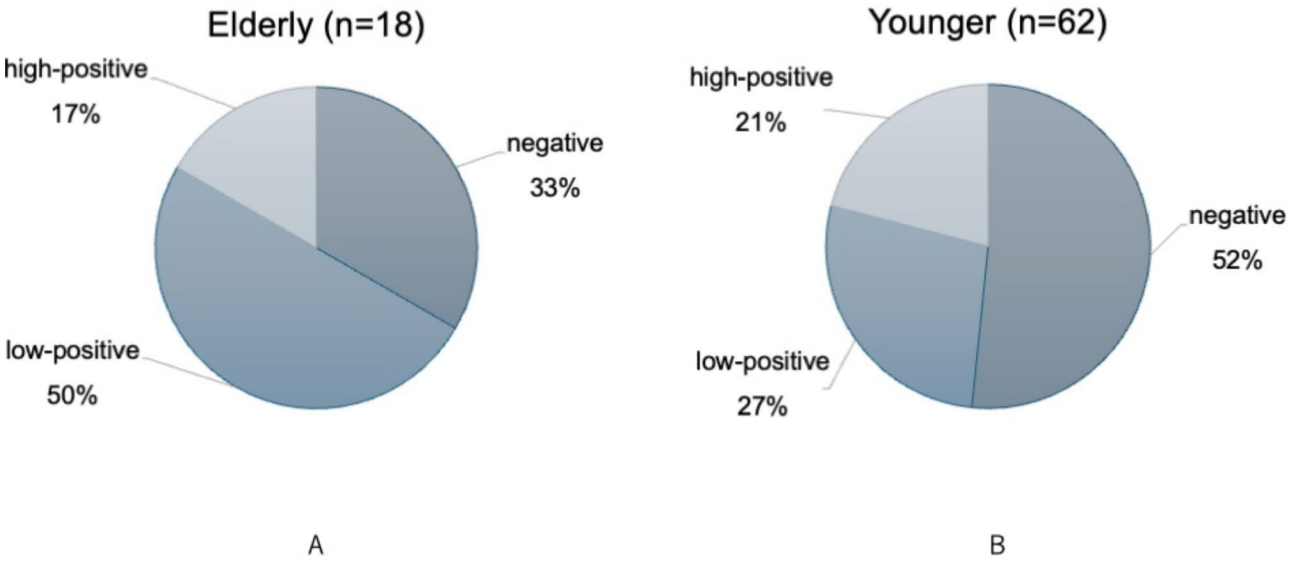

Fig. 1 Comparison of the PD-L1 results of transbronchial lung cryobiopsy samples between the elderly group (≥ 80 years old) (**A**) and younger group (< 80 years old) (**B**) using three cutoffs, negative (tumor cells of < 1%), low-positive (TPS1 − 49%), and high-positive (TPS ≥ 50%) (*n* = 80)

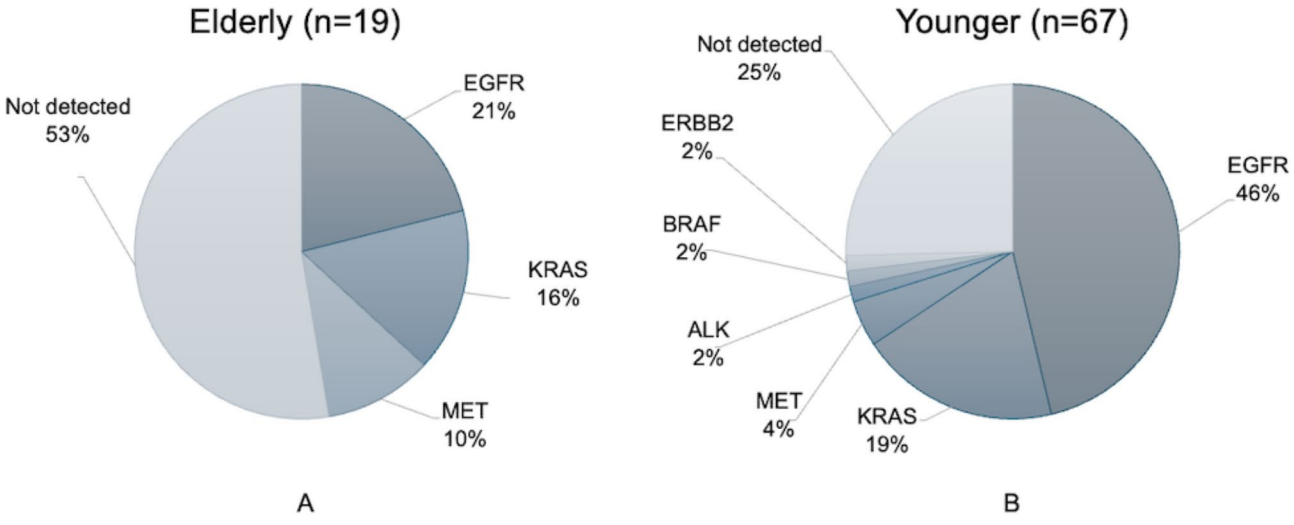

Fig. 2 Molecular characterization of transbronchial lung cryobiopsy samples between the elderly group (**A**) and younger group (**B**). Frequencies are expressed as the percentage of positive samples for each molecular alteration relative to the total number of patients with an informative molecular result (*n* = 86)

cryobiopsy alone or in combination with forceps biopsy) and on 67 of the 68 younger patients, with one case not submitted for testing. In cases where both cryobiopsy and forceps biopsy were performed, it is possible that both types of specimens contributed to the testing. In the younger group, epidermal growth factor receptor (EGFR) mutations were detected in 31 patients, Kirsten rat sarcoma virus (KRAS) mutations in 13, mesenchymal-epithelial transition (MET) in 3. In the elderly group, mutations of EGFR in 4 patients, KRAS in 3, and MET in 2 were found (Fig. 2).

Table 4 Complications

		Elderly (≥80) (*n*=20)	Younger (<80) (*n*=76)	*P* value*
All, n (%)		3 (15)	10 (13.2)	1.00
Bleeding, n (%)		2 (10)	4 (5.3)	0.601
	Grade 3	2	4	
	Grade 4	0	0	
Pneumothorax, n (%)		1 (5)	2 (2.6)	0.508
	Follow-up only	1	1	
	Chest tube insertion	0	1	
Lung abscess, n (%)		0 (0)	1 (1.3)	
Agitation, n (%)		0 (0)	2 (2.6)	
Difficulty in extubation, n (%)		0 (0)	1 (1.3)	

*From Fisher's exact test

Complications were comparable between the two groups. Grade 3 bleeding requiring interruption of the procedure and hemostatic intervention within 20 min occurred in 10% of elderly patients and 5.3% of younger patients (p=0.601) and there were no significant Grade 4 bleeding events [intensive care unit (ICU) admissions, transfusions, embolizations, or resuscitations] observed in either group. All instances of Grade 3 or higher bleeding observed in this study occurred during the use of a 1.1 mm probe. Pneumothorax occurred in 5% of elderly patients and 2.6% of younger patients (p=0.508) and one elderly patient developed a minor pneumothorax, which was managed conservatively without further intervention. No significant differences were observed in the incidence of overall complications. Difficulty with extubating an 8.0-mm endotracheal tube was encountered in one patient in the younger group, and after the procedure, the patient developed laryngeal edema and required ICU admission. The patient was treated with steroids but required a tracheostomy due to persistent airway obstruction. The patient was discharged from the ICU after 6 days, and after a 1.5-month recovery period, the patient underwent surgery for lung cancer; the tracheostomy was then successfully closed after surgery (Table 4).

Discussion

Bronchoscopy remains an important diagnostic and therapeutic procedure for lung diseases, including in elderly patients. Although bronchoscopy is generally considered a relatively safe procedure, cases of mortality have been reported [12] and have traditionally been approached with caution in elderly patients due to the perceived increased risk of complications, such as bleeding, pneumothorax, and anesthesia-related issues [13]. Although age alone should not be considered a contraindication for bronchoscopy, as emphasized by the British Thoracic Society guidelines, elderly patients often present with comorbidities that may increase the risk of complications [14], and several studies have explored this issue. Studies have produced mixed results regarding the safety of bronchoscopy in elderly populations. For example, Haga et al. conducted a prospective multicenter study and found that the rates of complications, such as bleeding, oxygen desaturation, and pneumonia, were significantly higher in patients aged≥80 years than in younger patients [13]. Another study involving patients aged≥80 years also found that the complication rate was significantly higher in this group than in younger patients, and mortality was also significantly higher in octogenarians [15]. Conversely, several studies have shown that complication rates, including pneumothorax, bleeding, and infection, are comparable between elderly and younger patients undergoing bronchoscopy [16–18]. Mineshita et al. reported that even in lung cancer patients aged≥85 years, bronchoscopy was performed without serious complications, and many cases led to treatment decisions [19]. In elderly populations undergoing bronchoscopy, several studies, including those referenced earlier, have reported the safe and effective use of moderate to deep sedation with agents, such as benzodiazepines and opioids, as recommended by guidelines, although the choice of drugs and dosage should be adjusted on the basis of age and comorbidities [14, 17, 18]. Tanc et al. noted that even with the use of deep sedation, including propofol, ketamine, and midazolam, no significant differences in adverse events or recovery time were observed between elderly and younger patients [20]. In the present study, we found that the complication rate, including grade of ≥3 bleeding, did not differ significantly between patients aged≥80 and those<80 years. These findings are consistent with the view that bronchoscopy, including TBLC, can be safely performed in elderly patients after appropriate patient selection and procedural planning.

Cryobiopsy has demonstrated a robust ability to obtain high-quality biopsy specimens, which has been particularly beneficial for diagnosing peripheral lung lesions [11]. In a multicenter study, cryobiopsy was performed for diagnosing both diffuse and localized respiratory diseases, including in patients aged≥75 years. This study proved that cryobiopsy was safe and effective, without a significant increase in complications [6]. In addition, cryobiopsy has been more effective than traditional biopsy methods in obtaining sufficient tissue for pathological diagnosis and biomarker analysis, such as molecular testing and PD-L1 expression analysis, which are crucial for guiding targeted lung-cancer treatments [21]. The selection of probe size was determined by the operators' decision in the present study; however, there was a tendency to prefer the 1.1 mm probe in both elderly and younger patients. The 1.1 mm probe, owing to its smaller diameter, is more flexible and can navigate sharp angles more effectively, potentially facilitating access to

peripheral lesions using thin scopes. Furthermore, the 1.1 mm probe provides tissue samples sufficient for lung cancer diagnosis, including next-generation sequencing [22]. These advantages may explain its preference in clinical practice. Compared with younger patients, the elderly population showed no significant differences in the rates of major complications, such as pneumothorax or bleeding, which reinforces the utility of cryobiopsy as a safe diagnostic tool even in patients aged > 75 years [6]. A previous report has suggested that the 1.1 mm probe is associated with significantly fewer bleeding complications compared to the 1.9 mm probe in TBLC [23]. However, in this study, all cases of Grade 3 or higher bleeding occurred with the use of the 1.1 mm probe. As the majority of cases in this study utilized the 1.1 mm probe and the overall number of bleeding complications was small, further evaluation is challenging. Adoption of cryobiopsy, especially when combined with R-EBUS and biomarker analysis, offers a comprehensive diagnostic approach in the elderly. Our study findings, consistent with those of previous studies, have shown that the complication rates for TBLC in the studied patients aged ≥ 80 years were not significantly different from those in younger patients. This finding indicates that age alone should not be considered a contraindication for performing TBLC in elderly patients.

Elderly patients often face unique challenges in treatment due to other factors, such as comorbidities, reduced physiological reserves, and polypharmacy. Therefore, a more individualized approach to treatment that balances efficacy with the risks of potential side effects is needed [24, 25]. Lindqvist et al. found that adherence to treatment guidelines improved overall survival in elderly NSCLC patients, especially those with performance status (PS) 0–2. However, nearly 10% of fit elderly patients were undertreated and could have benefitted from more intensive care [26]. Recent advances in chemotherapy for advanced lung cancer, particularly the development of immunotherapy and targeted therapies based on specific genetic mutations (e.g., EGFR, ALK), have provided new treatment options for elderly patients. These therapies have different adverse event profiles than those of traditional cytotoxic agents and have been shown to be effective and better tolerated in elderly populations [27, 28]. Moreover, studies on immune checkpoint inhibitors have demonstrated comparable safety and response rates in patients aged ≥ 75 years, supporting their use in this population [29]. In our study, TBLC provided adequate tissue for both histopathological diagnosis and biomarker testing, including PD-L1 expression and genetic mutations, enabling personalized treatment strategies. This result highlights the increasing importance of TBLC as a diagnostic tool in the era of personalized medicine in which targeted therapies offer less invasive and more tolerable treatment options for elderly patients.

Chemotherapy has been shown to be effective in elderly patients with good PS, such as an Eastern Cooperative Oncology Group PS of 0–2, whereas poorer PS often leads to less favorable outcomes, indicating that PS is a more important factor than chronological age in determining the suitability of chemotherapy [26]. In addition to PS, The Geriatric Assessment (GA) is useful in guiding treatment decisions for elderly lung cancer patients. GA evaluates physical, cognitive, and social factors, offering a broader view of a patient's health beyond PS. This broad view helps identify frailty and comorbidities, leading to more personalized and appropriate treatment strategies for better outcomes in older patients [1, 24]. In early-stage NSCLC, lobectomy is generally the preferred option for fit older patients, though limited resection may be considered in certain cases [1, 24]. Ichinokawa et al. reported that surgical resection, including lobectomy, was safely performed in patients > 85 years old, with survival rates comparable to those 80–84 years old [30]. Importantly, surgical treatment should not be withheld on the basis of age alone but rather should be determined by the patient's overall health, comorbidities, and surgical fitness [25, 30, 31]. Radiotherapy with curative intent is an alternative, with stereotactic body radiotherapy the most likely preferred modality especially for unfit patients [32]. In our study, we found that the treatment strategies for elderly patients differed from those for younger patients. Although surgical treatment was more common in younger patients, radiation therapy was more frequently used in the elderly, probably reflecting concerns about the risks of surgery in older adults.

This study had several limitations. First, as a single-center retrospective study with a relatively small sample size, particularly in the elderly group ($n = 20$), the findings may not be generalizable to broader populations. Second, while balloon catheter hemostasis was performed for all cases as a standard procedure, additional measures such as diluted epinephrine application were employed at the operator's discretion. However, data on Grade 1 or 2 bleeding were not collected, which precluded the analysis of the incidence and characteristics of minor bleeding. Third, the frequent use of 1.1 mm probes and shorter freezing times could also be considered limitations. The preference for 1.1 mm probes was due to their flexibility and suitability for navigating peripheral lesions, but their predominant use may limit the generalizability of our findings to settings where larger probes are more commonly used. Similarly, while shorter freezing times did not compromise the tissue quality in this study, they may affect sample size or quality in other contexts. Forth, we did not perform a comprehensive GA on the elderly patients, which could have provided

additional insights into the appropriateness of the procedures and treatments in this population. Despite these limitations, our study findings should contribute valuable data on the safety and effectiveness of TBLC in diagnosing lung cancer in elderly patients, particularly in the context of molecular testing and personalized treatment approaches.

Conclusion

In conclusion, our study is the first to demonstrate that TBLC is as safe and effective in diagnosing peripheral lung cancer in patients ≥ 80 years old as it is in younger patients. Age alone should not be considered a contraindication for bronchoscopy or TBLC, and with appropriate patient selection, these procedures can be safely performed in elderly populations. The ability to provide adequate samples for molecular testing further supports TBLC's role in modern lung cancer diagnostics, particularly in the era of personalized medicine.

Abbreviations

BMI	Body mass index
EGFR	Epidermal growth factor receptor
GA	Geriatric Assessment
ICI	Immune checkpoint inhibitors
ICU	Intensive care unit
KRAS	Kirsten rat sarcoma
MET	Mesenchymal-epithelial transition
PS	Performance status
TBLC	Transbronchial lung cryobiopsy

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Author contributions

K.Y. and S.O. contributed to the conceptualization, methodology, investigation, writing, and bronchoscopic procedures. S.H., M.O., H.K., T.I., and T.H. were involved in investigation, writing, and bronchoscopic procedures. K.I. provided supervision, writing review, editing, and conceptualization. Y.O., Y.G., and N.H. contributed to supervision and writing review.

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Data availability

As new analyses are being conducted for potential publication, and due to pending approval from our ethics committee for data disclosure, the raw data supporting this study's findings cannot be made publicly available at this time. However, specific datasets or portions of the data may be available from the corresponding author upon reasonable request, subject to ethics approval.

Declarations

Ethics approval and consent to participate

Our institutional review board approved this study (approval number: HM23-206). Given that this study is a retrospective observational study, informed consent was not required. However, information related to the study was disclosed, and patients were given the opportunity to opt-out from participation, in accordance with institutional guidelines.

Consent for publication

Patients were given the opportunity to opt-out from publication, in accordance with institutional guidelines.

Competing interests

The authors declare no competing interests.

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