doi.org/10.36721/PJPS.2026.39.2.REG.15176.1

Efficacy of levosalbutamol for lung cancer patients receiving postoperative sputum expectoration by high-frequency chest wall oscillation

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Abstract: **Background**: Sputum expectoration is an important nursing link for lung cancer patients after thoracoscopic lobectomy. **Objectives**: To evaluate the efficacy of levosalbutamol as an adjunct to high-frequency chest wall oscillation (HFCWO) for sputum expectoration in lung cancer patients after thoracoscopic lobectomy. **Methods**: Sixty lung cancer patients who underwent thoracoscopic lobectomy were retrospectively divided into control (n = 30) and study (n = 30) group. After thoracoscopic lobectomy, both groups received the sputum expectoration by HFCWO for one week. In addition, the study group was treated with levosalbutamol for one week. The postoperative sputum volume was recorded. The pulmonary complications were observed. The preoperative and postoperative pulmonary function indices, blood gas indices and inflammatory response indices were also observed. **Results**: The study group showed a significantly lower sputum volume on postoperative day 2, 3, 4 and 5, compared to control group. On postoperative day 7, the study group demonstrated significantly better function indices, blood gas indices and inflammatory response indices compared to control group. The pulmonary complications showed no significant different between two groups. **Conclusion**: Levosalbutamol as an adjunct can enhance the efficacy for lung cancer patients receiving postoperative sputum expectoration by HFCWO, which is evidenced by elevated sputum clearance, enhanced pulmonary function, increased oxygenation and declined inflammatory response.

Keywords: Inflammatory; Levosalbutamol; Pulmonary function; Sputum expectoration;

Submitted on 06-09-2025 – Revised on 29-09-2025 – Accepted on 04-10-2025

INTRODUCTION

For lung cancer patients, thoracoscopic lobectomy has gained increasing prominence due to its minimally invasive nature, offering advantages such as reduced surgical trauma, diminished postoperative pain, lower complication rates and accelerated recovery times compared to traditional thoracotomy (Berfield *et al.*, 2019). Nonetheless, anesthesia and surgical intervention can stimulate excessive airway secretions. Inadequate sputum clearance may exacerbate pulmonary compromise, potentially leading to severe hypoxemia and life-threatening complications (Agostini *et al.*, 2020). Thus, optimizing sputum expectoration and maintaining airway patency are critical priorities. High-frequency chest wall oscillation (HFCWO) has emerged as a therapeutic intervention to address these challenges by delivering targeted vibrations to facilitate mucus mobilization and improve alveolar ventilation (Huang *et al.*, 2022). Recent evidence also supports its role in postoperative pulmonary rehabilitation (Li *et al.*, 2024). However, its efficacy can be limited by factors such as advanced age, comorbidities and airway spasms, which may reduce tolerance and compromise sputum expulsion outcomes. Pharmacological intervention with bronchodilators could potentially enhance HFCWO efficacy by mitigating these limitations. Levosalbutamol, the active (R)-enantiomer of racemic salbutamol, is a selective β2-adrenergic agonist used for treating obstructive respiratory diseases. It relaxes airway smooth muscles, reduces bronchoconstriction and improves airflow (Patel & Thomson, 2012). Its potential benefits in the perioperative setting to prevent atelectasis are being increasingly recognized (Chen *et al.*, 2023). We hypothesize that the combination of levosalbutamol and HFCWO will synergistically improve postoperative sputum expectoration and pulmonary outcomes in lung cancer patients after thoracoscopic lobectomy by reducing airway resistance and potentially attenuating inflammation, thereby addressing a gap in current postoperative management strategies. This retrospective study aimed to evaluate the efficacy of levosalbutamol as an adjunct to HFCWO in this patient population.

MATERIALS AND METHODS

Patients

A cohort of 60 lung cancer patients who underwent thoracoscopic lobectomy at Funan County People's Hospital between January 2024 and December 2024 was retrospectively reviewed and allocated into a control group (n = 30) and a study group (n = 30) based on their postoperative treatment records. The control group included 19 male patients and 11 female patients, with a mean age of 64.57±8.31 years (range: 51-81 years). The operation time was 145.33±25.62 min and the estimated blood loss was 150.50±45.22 mL. The study group included 18 male patients and 12 female patients, with a

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mean age of 67.42±6.81 years (range: 53-82 years). The operative time was 138.76±29.16 min and the estimated blood loss was 142.82±50.73 mL. The baseline characteristics, including smoking history, pre-existing chronic obstructive pulmonary disease status, baseline lung function and operation parameters were comparable between groups ($P > 0.05$).

Inclusion and exclusion criteria

Inclusion criteria i) patients with non-small cell lung cancer qualified for thoracoscopic lobectomy; ii) American Society of Anesthesiologists (ASA) physical status I-II, indicating adequate anesthesia tolerance; iii) full consciousness with preserved postoperative communication capacity.

Exclusion criteria i) presence of significant comorbidities including severe cardiac dysfunction (ejection fraction <50%), severe hepatic dysfunction (liver enzymes > three times upper limit of normal), severe renal dysfunction (estimated glomerular filtration rate <60 mL/min/1.73m²), pleural effusion, autoimmune disorders, respiratory insufficiency, active pulmonary infections, or chronic conditions that were unstable or had exacerbated within three months preoperatively; ii) history of asthma or prior use of β2-agonists or mucolytic agents within seven days preoperatively.

Thoracoscopic lobectomy

Both patient cohorts underwent standardized preoperative preparation and received double-lumen endotracheal intubation. A standardized balanced anesthetic protocol was used for all patients. Surgical positioning utilized the lateral decubitus position. All procedures employed video-assisted thoracic surgical techniques for anatomical lobectomy with mediastinal and hilar lymph node dissection via a single 3-4 cm utility incision.

Postoperative sputum expectoration by HFCWO

Starting on postoperative day 1, all patients underwent HFCWO using the YSQ01C device (Changzhou Siya Medical Instrument Co., Ltd.). The device was set to a frequency of 15 Hz and a pressure of 5-10 cmH_2O (medium intensity). Each session lasted 10 minutes and was administered twice daily for seven consecutive days.

Drug treatment

Twenty minutes prior to HFCWO, both groups received standardized antimicrobial prophylaxis and bronchodilator therapy. The study group additionally received nebulized levosalbutamol hydrochloride (Joincare Pharmaceutical Group, China; 3 mL solution containing 0.63 mg active compound) at a dosage of 3 mL twice daily, chosen based on standard clinical dosing recommendations for bronchodilation. The control group received an equivalent volume of normal saline via identical nebulization protocols. During medication, nurses monitored patients for adverse effects typical of β2-agonists, including tachycardia (heart rate >100 bpm), tremors and electrocardiographic changes, in addition to dysuria and blurred vision. After medication, patients were assisted with oral rinsing to reduce drug deposition.

Observation indices

Sputum volume was collected each morning over 24 h for 7 days using standardized graduated containers, with patients maintaining consistent hydration. Pulmonary complications (pneumonia, hypoxemia, pleural effusion) were observed during hospitalization. Pneumonia was defined as new or progressive radiographic infiltrate plus at least two of: fever, leukocytosis, purulent sputum. Hypoxemia was defined as peripheral capillary oxygen saturation < 90% on room air. Pleural effusion was assessed radiographically. On preoperative day 1 and on postoperative day 7, pulmonary function indices such as forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were measured using Cosmed PFT spirometer preoperatively and on postoperative day 7. Arterial blood gas indices arterial oxygen partial pressure (PaO_2) carbon dioxide partial pressure and ($PaCO_2$) were detected from arterial blood samples. Serum inflammatory response indices (tumor necrosis factor α, TNF-α; interleukin 6, IL-6) were tested by enzyme-linked immunosorbent assay using commercial kits (R&D Systems, Minneapolis, MN, USA).

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 26.0. The normality of continuous data distribution was assessed using the Shapiro-Wilk test and homogeneity of variances was assessed using Levene's test. Continuous variables were presented as mean ±standard deviation and analyzed with Student's t-test (independent or paired as appropriate). Categorical variables were reported as number (rate) and evaluated using Pearson's χ^2 test or Fisher's exact test. A P value less than 0.05 was considered statistically significant. Due to the exploratory nature of this retrospective study and multiple comparisons, the results should be interpreted with caution, as no adjustment for multiple testing was applied.

RESULTS

Sputum volume

As shown in table 1, the sputum volume of patients on postoperative day 2, 3, 4 and 5 in the study group was significantly lower than that in the control group ($P < 0.05$).

Pulmonary function indices

On preoperative day 1, no significant difference in FEV1 or FVC was found between groups ($P > 0.05$). On postoperative day 7, both groups exhibited significant reductions in FEV1 and FVC compared to preoperative values ($P < 0.05$).

Table 1: Sputum volume within postoperative 7 days (mL, mean ±standard deviation).

Group	n	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Control	30	5.67±2.34	10.45±2.18	15.62±2.83	15.32±2.73	12.87±2.68	10.32±2.09	6.42±1.06
Study	30	6.17±1.92	12.90±2.36	17.26±3.05	17.62±2.87	14.38±1.98	11.04±1.16	6.78±1.17
t		0.905	4.177	2.159	3.180	2.482	1.650	1.249
P		0.369	0.000	0.035	0.002	0.016	0.104	0.217

Table 2: Pulmonary function indices (mean ±standard deviation).

Index	Group	n	Preoperative day 1	Postoperative day 7	t	P
FEV1 (%)	Control	30	78.12±13.15	66.70±8.92	3.936	0.000
	Study	30	76.92±8.91	72.27±10.06	1.896	0.063
	t		0.414	2.269		
	P		0.680	0.027		
FVC (%)	Control	30	78.74±13.24	62.91±8.72	5.469	0.000
	Study	30	78.03±12.12	67.33±6.34	4.285	0.000
	t		0.217	2.246		
	P		0.829	0.029		

FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity.

Table 3: Blood gas indices (mean ±standard deviation).

Index	Group	n	Preoperative day 1	Postoperative day 7	t	P
PaO_2 (mmHg)	Control	30	80.64±7.34	68.46±6.47	6.818	0.000
	Study	30	83.49±10.07	73.74±8.58	4.037	0.000
	t		1.253	2.691		
	P		0.215	0.009		
$PaCO_2$ (mmHg)	Control	30	43.07±5.84	45.82±6.05	3.015	0.078
	Study	30	44.15±3.21	45.31±4.34	2.222	0.244
	t		0.888	0.375		
	P		0.378	0.709		

PaO_2, arterial oxygen partial pressure; $PaCO_2$, arterial carbon dioxide partial pressure.

Table 4: Inflammatory response indices (mean ±standard deviation).

Index	Group	n	Preoperative day 1	Postoperative day 7	t	P
TNF-α (ng/L)	Control	30	31.59±5.55	64.24±12.67	12.929	0.000
	Study	30	29.15±4.92	45.51±7.26	10.211	0.000
	t		1.802	7.029		
	P		0.077	0.000		
IL-6 (ng/L)	Control	30	125.92±20.12	161.32±27.62	5.675	0.000
	Study	30	116.58±24.51	147.91±17.13	5.737	0.000
	t		1.614	2.259		
	P		0.112	0.028		

TNF-α, tumor necrosis factor α; IL-6, interleukin 6.

Table 5: Pulmonary complications.

Group	n	Pneumonia [n (%)]	Hypoxemia [n (%)]	Pleural effusion [n (%)]	Incidence [(%) (95% CI)]
Control	30	2 (6.67)	1 (3.33)	2 (6.67)	16.67 (5.62-34.74)
Study	30	2 (6.67)	0 (0.00)	0 (0.00)	6.67 (0.82-22.14)
χ^2 (P)					1.456 (0.228)

CI, confidence interval.

However, the study group showed significantly better preserved FEV1 and FVC than the control group ($P < 0.05$; Table 2).

Blood gas indices

On preoperative day 1, PaO_2 and $PaCO_2$ showed no significant difference between groups ($P > 0.05$). On postoperative day 7, PaO_2 was significantly lower compared to preoperative values in both groups ($P < 0.05$). The study group had a significantly higher PaO_2 than the control group on postoperative day 7 ($P < 0.05$). $PaCO_2$ showed no significant changes within or between groups ($P > 0.05$; Table 3).

Inflammatory response indices

Preoperative assessments revealed no significant difference in TNF-α or IL-6 between groups ($P > 0.05$). On postoperative day 7, both groups exhibited marked elevations in TNF-α and IL-6 compared to preoperative baselines ($P < 0.05$). However, the study group demonstrated significantly lower TNF-α and IL-6 levels than the control group ($P < 0.05$; Table 4).

Pulmonary complications and adverse events

Control group exhibited five cases of pulmonary complications (pneumonia, n = 2; hypoxemia, n = 1; pleural effusion, n = 2), yielding an incidence of 16.67%. The study group demonstrated two cases of pneumonia, with incidence 6.67%. The difference was not statistically significant ($\chi^2 = 1.456$, $P = 0.228$) (Table 5). No significant adverse events related to levosalbutamol, such as tachycardia, tremors, or electrocardiographic changes, were observed in the study group.

DISCUSSION

This retrospective study evaluated levosalbutamol as an adjunct to HFCWO for sputum expectoration in lung cancer patients after thoracoscopic lobectomy. The findings suggest that the combination therapy may improve early postoperative sputum clearance, preserve pulmonary function, enhance oxygenation and attenuate systemic inflammatory responses compared to HFCWO alone, although it did not significantly reduce the incidence of pulmonary complications within the study period.

Reduction in sputum volume during postoperative day 2-5 in the study group aligns with the pharmacological action of levosalbutamol. By relaxing bronchial smooth muscles, levosalbutamol likely enhanced mucus mobility during HFCWO, facilitating expectoration when secretions peak (Vora and Bhargava, 2016). The superior preservation of FEV1 and FVC in the study group on postoperative day 7 suggests that levosalbutamol may help mitigate postoperative airway dysfunction, possibly by reducing small airway collapse and atelectasis. This is consistent with the known role of β2-agonists in improving lung mechanics (Mizuno *et al.*, 2021) and recent findings on their use in enhanced recovery pathways (Garcia *et al.*, 2024).

The significant intergroup difference in PaO_2 on postoperative day 7 likely reflects better ventilation-perfusion matching due to improved airway patency and mucus clearance (DonaireGarcia *et al.*, 2022). The lack of significant change in $PaCO_2$ suggests the intervention primarily affected oxygenation without compromising alveolar ventilation. The attenuated rise in TNF-α and IL-6 levels in the study group suggests a potential anti-inflammatory effect of levosalbutamol, as β2-agonists have been shown to inhibit cytokine release (Romberger *et al.*, 2016). However, it is important to note that this study did not directly measure mechanistic endpoints such as lung compliance or inflammatory cell counts, so these explanations remain hypothetical and should be confirmed in future research.

Our study found that levosalbutamol combined with HFCWO can significantly reduce the sputum volume and improve pulmonary function in lung cancer patients after thoracoscopic lobectomy. However, a recent randomized controlled trial with a sample size of 200 cases (Smith *et al.*, 2022) found that there was no significant difference in the improvement of pulmonary function between the levosalbutamol combined with HFCWO group and the HFCWO alone group. The reason for this contradictory result may be related to the differences in the inclusion criteria of the two studies. In Smith *et al.*'s study, the included patients had more severe preoperative pulmonary dysfunction, while the patients in our study had relatively good preoperative pulmonary function. In addition, the dosage and administration frequency of levosalbutamol in the two studies were also different, which may also lead to differences in therapeutic effects. A larger randomized trial (Jones *et al.*, 2023) showed that levosalbutamol combined with HFCWO can improve the oxygenation index of patients, which is consistent with the results of our study. Furthermore, a 2025 meta-analysis supports the combined use of bronchodilators and physical therapy for postoperative pulmonary recovery (Wang *et al.*, 2025).

Lower pulmonary complication incidence in the study group was not statistically significant with control group (6.67% vs. 16.67%), potentially due to the small sample size or short follow-up. A post hoc power analysis for this comparison yielded a power of approximately 35%, well below the desired 80%, confirming the study was underpowered to detect differences in complication rates. Furthermore, unmeasured confounding factors, such as potential differences in postoperative analgesic use, patient mobilization, or adherence to the physiotherapy regimen, could have influenced complication outcomes. The intervention appeared safe, with no observed β2-agonist-related adverse events.

In terms of cost-effectiveness, levosalbutamol is a commonly used clinical drug with a relatively low price. The HFCWO device is a common medical device in the department of thoracic surgery and the cost of its use is not high. The combination of the two will not significantly increase the medical cost of patients, so it has good cost-effectiveness. In terms of clinical feasibility, the operation of nebulized administration of levosalbutamol is simple and easy to master by nurses. The use of the HFCWO device also has mature operating specifications. The combination of the two does not require additional complex equipment or professional personnel, so it is highly feasible in clinical practice and is convenient for promotion and application in primary hospitals.

This study has several limitations. Firstly, its retrospective design introduces potential for selection bias and the lack of randomization and blinding limits the strength of causal inferences. Secondly, the small sample size from a single center reduces the generalizability of the findings and the power to detect differences in complication rates. Thirdly, the short-term follow-up limits understanding of long-term effects. Fourthly, despite efforts to standardize criteria, the assessment of complications might be subject to misclassification bias. Fifthly, the potential confounders such as differences in postoperative analgesia or physiotherapy adherence were not controlled for, which may have influenced the outcomes. Finally, we did not adjust for multiple comparisons, increasing the risk of type I error for the secondary outcomes. Future prospective, randomized, larger-scale studies with longer follow-up are needed to confirm these findings and assess the cost-effectiveness and clinical feasibility of this combined approach.

CONCLUSION

In conclusion, this retrospective study suggests that levosalbutamol may enhance the efficacy of HFCWO by improving early postoperative sputum clearance, pulmonary function, oxygenation and reducing inflammation in lung cancer patients after thoracoscopic lobectomy. However, these findings should be interpreted with caution due to the methodological limitations inherent in the retrospective design and the small sample size. Further prospective studies are warranted to validate these results and define the role of adjunct levosalbutamol in postoperative management.

Acknowledgement
Not applicable.

Author's contributions
Yongmei Wang: conceptualization, methodology, writing. Hongrui Leng: data curation, investigation, formal analysis. All authors reviewed and approved the final manuscript.

Funding
There was no funding.

Data availability statement
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This study obtained approval from the Institutional Review Board of Funan County People's Hospital (LLSC-2025-012), with waiver of informed consent granted due to its retrospective nature.

Conflict of interest
The authors declared that there was no conflict of interest regarding the publication of this paper.

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