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Randomized Clinical Trial

Minimally invasive lung surgery with an intraoperative completely or partially tubeless protocol: randomized clinical trial

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Abstract

Background: Thoracic surgery is an invasive procedure and there has been a move towards minimally invasive approaches. This includes video-assisted thoracoscopic surgery. Non-intubated video-assisted thoracoscopic surgery without endotracheal intubation has been developed with a view to avoiding complications associated with intubation including tracheal injury, vocal cord injury and lung impairment due to mechanical ventilation. This study aims to compare outcomes from non-intubated 'completely tubeless' *versus* intubated 'partially tubeless' minimally invasive thoracic surgery.

Methods: A single-institution, prospective randomized clinical trial was conducted comparing patients who underwent minimally invasive lung completely tubeless *versus* partially tubeless surgery, both with enhanced recovery. The primary outcome was the short-term postoperative complication rate. Binary logistic regression analysis was performed to determine the significant predictors of severe mediastinal shift and receiver operating characteristic (ROC) curve plots were drawn.

Results: Among the 348 patients, 174 patients were assigned to the completely tubeless group and 174 patients were assigned to the partially tubeless group. There was no difference in postoperative complications including pulmonary complications, supraventricular arrhythmia, acute myocardial infarction, acute cerebral stroke, venous thromboembolism and urinary retention. The completely tubeless protocol was associated with a higher proportion of early mobilization (66.7% *versus* 55.7%, $P = 0.047$), a shorter median duration of drainage (1.0 *versus* 2.0 days, $P = 0.002$), and a shorter median duration of postoperative hospital stay (2.0 *versus* 3.0 days, $P = 0.001$). The completely tubeless group had less of a difference in white blood cell count before and after the operation ($P = 0.042$). Binary logistic regression analysis revealed that weight was a significant predictor of mediastinal shift in the completely tubeless group.

Conclusion: Under enhanced recovery after surgery protocols, there is no difference in postoperative complications in patients undergoing completely or partially tubeless surgery. However, patients having completely tubeless surgery have shorter durations of postoperative drainage, shorter durations of hospital stay, milder systemic inflammatory reactions, and better immune protection than patients who undergo lung resection with a partially tubeless protocol. The severity of mediastinal shift may be mainly related to body-weight.

Registration number: NCT05269784 (http://www.clinicaltrials.gov).

Introduction

Thoracic surgery is considered an invasive and traumatic procedure for patients. Minimally invasive surgeries, including video-assisted thoracoscopic surgery (VATS), have significantly expanded the scope of surgical treatment. Enhanced recovery after surgery (ERAS) was first reported in the late 1990s[1] and studies have focused on the implementation of ERAS strategies after thoracic surgery[2]. Minimally invasive VATS surgery lends itself to ERAS[3,4] and can minimize surgical trauma, improve quality of life, and decrease financial burden.

VATS without endotracheal intubation was developed after the first report of nodule removal was published, after which a range of thoracoscopic procedures performed under anaesthesia without endotracheal intubation were reported[5–9]. A new subset of VATS, non-intubated VATS (NI-VATS), has been created[10]. The non-intubated approach may have several advantages, such as avoiding complications associated with general anaesthesia and intubation, including tracheal injury, vocal cord injury, lung impairment due to mechanical ventilation, intubation-associated discomfort, and alveolar barotrauma. Patients who undergo NI-VATS may have faster postoperative recovery, lower complication rates, and reduced stress hormones[11,12]. However, NI-VATS needs careful management by experienced anaesthetists, as risk of severe mediastinal shift requires urgent conversion to intubation. Rapid recovery after minimally invasive thoracic surgery under general anaesthesia with intubation combined with regional blockade is still observed, especially when an ERAS protocol is implemented. Modern anaesthesia via a video double-lumen endotracheal

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tube and total intravenous anaesthesia with bispectral index monitoring reduces anaesthetic drug use and the concentration of end-tidal anaesthetics. This can lead to faster recovery from anaesthesia[13–15].

The aim of this study was to determine the difference between minimally invasive lung surgery followed by ERAS with an intraoperative completely tubeless protocol (no endotracheal intubation, no routine placement of a transurethral catheter, and removal of a single chest tube after surgery as soon as possible) and minimally invasive lung surgery followed by ERAS with an intraoperative partially tubeless protocol (no routine placement of a transurethral catheter, and removal of a single chest tube after surgery as soon as possible).

Methods

Patient eligibility

The inclusion criteria were as follows: lung lesions that were suitable for VATS, including benign and malignant lesions diagnosed using CT (enhanced or non-enhanced) or pathological results; age 18–80 years and BMI less than 30 kg/m^2; Karnfsky score greater than or equal to 80 and cardiopulmonary function, liver function, and renal function allowing minimally invasive surgery[16]; normal cognitive function and ability to cooperate with the rehabilitation training[17,18]; and agreement with the protocol of the clinical trial and signing of the consent form.

The exclusion criteria were as follows: BMI greater than or equal to 30 kg/m^2; severe chronic obstructive pulmonary disease or pulmonary infection; ASA classification greater than or equal to III and New York Heart Association classification greater than or equal to III; coagulation dysfunction, hypoxaemia, hypercapnia, or hepatorenal insufficiency; refusal of randomization; and inability to cooperate with the rehabilitation training or tolerate the minimally invasive surgery due to any other reasons.

Pretreatment workup

This study was approved by the Ethics Committee of The Second Hospital of Shandong University (KYLL-2021 (TRIAL) P-098) and was registered in ClinicalTrials.gov (NCT05269784). All procedures involving human participants in this study were performed in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was obtained from all patients. The work was fully compliant with the CONSORT criteria and the work is reported in line with the CONSORT criteria[19].

Randomization and allocation

Randomization was performed by a statistician at the Evidence-Based Medicine Centre of The Second Hospital of Shandong University using the envelope method. Once the informed consent form was signed, the patient was assigned to the group listed in the sequentially numbered envelope[20]. No patients were blinded in this randomized clinical trial, in accordance with the management protocol.

Study interventions

Control group (partially tubeless group)

The patients who were randomly assigned to the control group (partially tubeless group) underwent standard VATS and perioperative management is described in the 'ERAS Protocol' (available as *Supplementary material*). An endobronchial double-lumen tube or single-lumen tube with a blocker was used during surgery. Details can be found in the 'Anaesthesia Protocol' (available as *Supplementary material*).

Completely tubeless group

The patients who were randomly assigned to the experimental group (completely tubeless group) underwent standard VATS and perioperative management is described in the 'ERAS Protocol' (available as *Supplementary material*). NI-VATS was performed by experienced anaesthetists with spontaneous ventilation[21], with further details available from the consensus document by He *et al.*[16]. Further details can be found in the 'Anaesthesia Protocol' (available as *Supplementary material*).

Assessment of mediastinal shift

Mediastinal shift caused by an open pneumothorax can negatively impact the safety of NI-VATS. Mediastinal shift was divided into three categories by the study team for evaluation. The study team conducted an exploratory analysis on clinical factors that could influence mediastinal shift and attempted to identify key factors affecting the occurrence of mediastinal shift. The three items of mediastinal shift (see the 'Grading of mediastinal shift', available as *Supplementary material*) were as follows:

First, the visual field shift range (see 'Range of shift in visual field', available as *Supplementary material*), which is the range of shift of central structures in the field of view (the same doctor holds the thoracoscope on the same surgical team); when the shift range is less than or equal to one-third of the distance from the centre to the edge of the field of view regardless of the direction of shift, it is scored as 1, when the shift range is between greater than one-third and two-thirds of the distance from the centre to the edge of the field of view, it is scored as 2, and, when the shift range is greater than two-thirds of the distance from the centre to the edge of the field of view, it is scored as 3.

Second, the diaphragm displacement range (see 'Diaphragm displacement range 1' and 'Diaphragm displacement range 2', available as *Supplementary material*); when the range of displacement of the diaphragm apex spans a certain number of vertebrae in the patient, the score corresponds to that number (for example, when the diaphragm apex displacement spans two vertebrae in the patient, it is scored as 2).

Third, the surgical operation impact; when the surgeon considers the mediastinal shift to be slight, causing minimal interference with the surgical operation or no impact at all, it is scored as 1, when the surgeon observes mediastinal shift, but the surgery can still proceed safely, it is scored as 2, and, when the surgeon deems the mediastinal shift to be severe, making the surgery difficult and significantly compromising surgical safety, it is scored as 3.

After adding up the scores of the three items, when the total score is less than or equal to 4.5 points, it is classified as mild, when the total score is greater than 4.5, but less than or equal to 6.5, it is classified as moderate, and, when the total score is greater than 6.5 points, it is classified as severe (see the 'Grading of mediastinal shift', available as *Supplementary material*). The clinical factors that were included in the analysis were sex, age, height, weight, BMI, oxygen partial pressure of preoperative arterial blood gas analysis, and carbon dioxide partial pressure of preoperative arterial blood gas analysis. The three items and total score were subjected to binary logistic regression analysis and receiver operating characteristic (ROC) curve plotting (*Fig. 1*).

Withdrawal from the trial

Patients were withdrawn from the trial as follows: when withdrawal was requested by the patient or a family member;

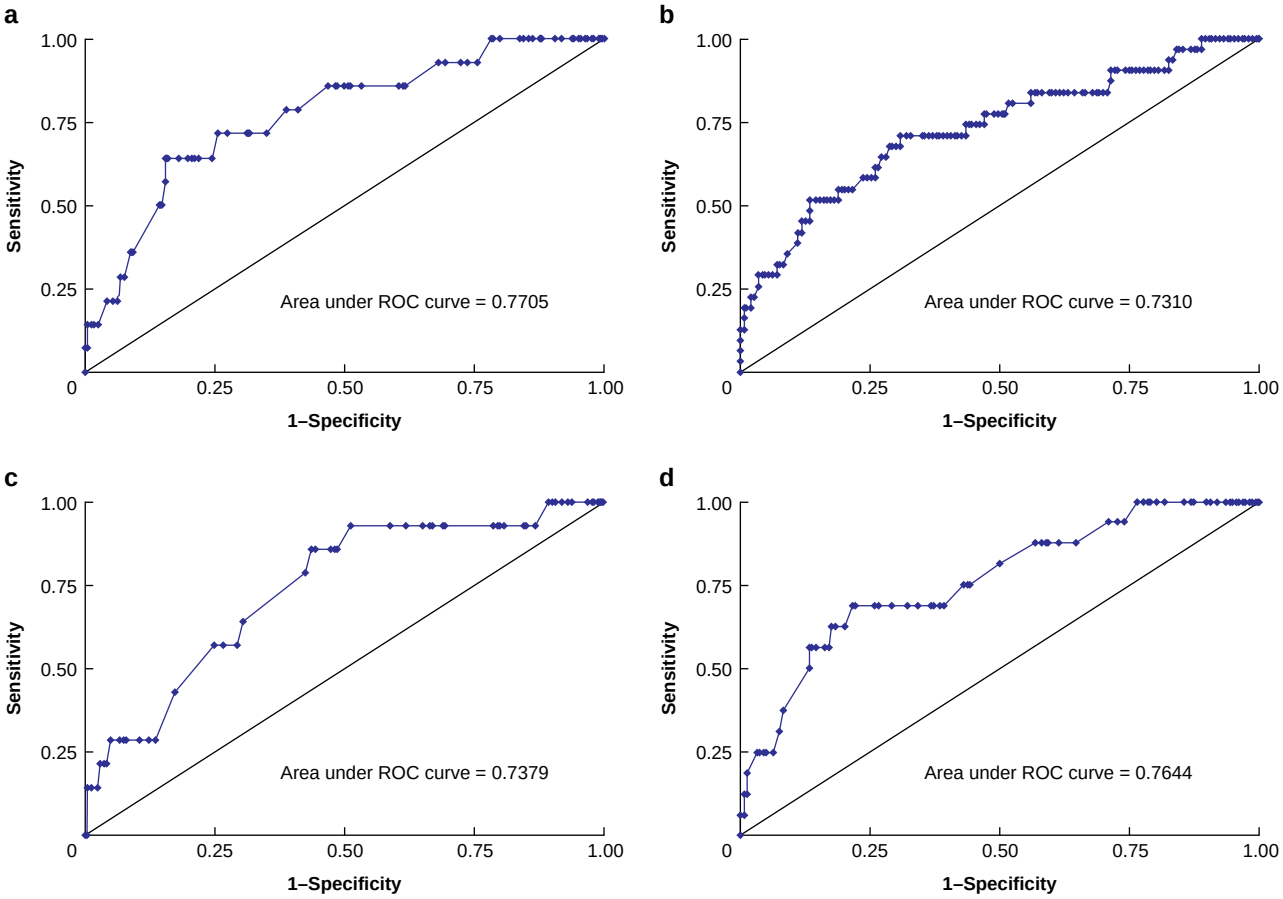

Fig. 1 Receiver operating characteristic (ROC) curves for factors impacting mediastinal shift
a visual field shift range. **b** diaphragm displacement range. **c** surgical operation impact. **d** total mediastinal shift score.

when there was poor compliance with the training protocol; or when severe complications, such as heart disease or stroke, occurred.

Sample size calculation

The data for calculating the sample size were obtained from published research[22,23] and were also based on the following assumption. For the postoperative complication rate, a minimum 13% absolute risk reduction from a 27% complication rate was set. Postoperative complications (during hospitalization, less than or equal to 7 days after surgery) included postoperative pulmonary complications (PPCs), supraventricular arrhythmia, acute myocardial infarction, acute cerebral stroke, venous thromboembolism, urinary irritation, and acute urinary retention. In accordance with 1 : 1 randomization, a significance level of $\alpha = 0.05$ (bilateral) and a test efficiency of $1 - \beta = 80\%$ were assumed. At least 157 patients were required for each group, assuming a 10% dropout rate, with a final sample size of 348 patients required.

Outcome measures and statistical analysis

The primary outcome was the postoperative complication rate. The secondary outcome measures were postoperative short-term effects (including feeding time, ambulation time, duration of drainage, duration of postoperative hospital stay, readmission rate, and postoperative laboratory examination), health-related quality of life (HRQoL; an HRQoL scale was used for evaluation during surveillance), progression-free survival, and overall survival for patients who underwent VATS for lung cancer resection. Continuous variables that did not follow a normal distribution are presented as median (interquartile range (i.q.r.)/range) and binary variables are presented as *n* (%). The data were evaluated using Student's *t* test (data matching a normal distribution), non-parametric statistics (Wilcoxon rank sum test), the chi-squared test, or Fisher's exact test, as appropriate. Binary logistic regression analysis was used to reveal the predictors of severe mediastinal shift. Statistical analysis and graph generation were performed using Stata 12.0 (StataCorp LP, College Station, TX, USA) and the significance level was set at 0.05.

Results

From April 2021 to June 2023, 348 patients were ultimately enrolled in this study; 174 patients were assigned to the completely tubeless group and 174 patients were assigned to the partially tubeless group. The treatment protocol was completed for the enrolled patients. The patient characteristics were balanced between the two groups (*Table 1*).

As shown in *Table 2*, 128 patients (73.6%) in the completely tubeless group were able to drink water 2 h after returning to the general ward and 116 patients (66.7%) in the completely tubeless group were able to ambulate moderately on the day of surgery with the guidance and help of medical staff and a

Table 1 Patient characteristics

	Completely tubeless group (*n* = 174)	Partially tubeless group (*n* = 174)	*P*
Age (years), median (i.q.r.) (range)	56 (50–64) (18–79)	58 (50–66) (22–80)	0.270
Sex			0.670
Male	82 (47.1)	77 (44.3)	
Female	92 (52.9)	97 (55.7)	
Smoking status			0.890
Ever	32 (18.4)	34 (19.5)	
Never	142 (81.6)	140 (20.5)	
Co-morbidity			0.920
Hypertension	30	35	
Diabetes mellitus	18	20	
Heart disease	14	11	
Brain vascular disease	11	13	
COPD	6	5	
Pathological type			0.720
Malignant tumour	156	153	
Adenocarcinoma	117	120	
Squamous cell carcinoma	36	30	
Other	3	3	
Benign tumour	18	21	
Hamartoma	6	4	
Granuloma or inflammation	8	12	
Sclerosing pneumocytoma	2	2	
Pulmonary bulla	2	3	
Pulmonary function			
FEV1 (l), median (i.q.r.) (range)	2.27 (1.91–2.79) (1.01–4.81)	2.25 (1.68–2.680) (1.07–4.88)	0.260
MVV (l), median (i.q.r.) (range)	90.6 (78.4–102.2) (64.3–117.4)	89.8 (77.9–103.1) (64.3–116.9)	0.430
Surgical procedure			0.063
Lobectomy	75	93	
Segmentectomy	45	45	
Wedge resection	54	36	
Operating time (min), median (i.q.r.) (range)	60 (45–89) (25–240)	60 (45–88) (20–240)	0.150
Intraoperative blood loss (ml), median (i.q.r.) (range)	50 (40–60) (20–450)	50 (40–60) (20–400)	0.940
VATS surgery converted to open surgery	4 (2.3)	6 (3.5)	0.750

Values are *n* or *n* (%) unless otherwise indicated. i.q.r., interquartile range; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1.0 s; MVV, maximum voluntary ventilation; VATS, video-assisted thoracoscopic surgery.

Table 2 Postoperative recovery

	Completely tubeless group (*n* = 174)	Partially tubeless group (*n* = 174)	*P*
Tolerating water p.o. 2h RTW	128 (73.6)	106 (60.9)	0.016
Semi-fluid diet within 3 h after RTW	103 (59.2)	93 (53.4)	0.331
Postoperative moderate ambulation on the day of surgery	116 (66.7)	97 (55.7)	0.047
Duration of drainage (days), median (i.q.r.) (range)	1 (1–2) (1–4)	2 (1–2) (1–7)	0.002
Duration of postoperative hospital stay (days), median (i.q.r.) (range)	2 (2–3) (1–6)	3 (2–3) (1–8)	0.001
Readmission within 14 days after surgery	2 (1.2)	1 (0.6)	0.500

Values are *n* (%) unless otherwise indicated. RTW, return to ward; i.q.r., interquartile range.

family member. The differences in these two characteristics were significant between the completely tubeless group and the partially tubeless group (73.6% *versus* 60.9% respectively ($P = 0.016$) with regard to being able to drink water 2 h after returning to the general ward, and 66.7% *versus* 55.7% respectively ($P = 0.047$) with regard to being able to ambulate moderately on the day of surgery with the guidance and help of medical staff and a family member). A total of 103 patients (59.2%) in the completely tubeless group and 93 patients (53.4%) in the partially tubeless group were able to initiate a semi-fluid diet within 3 h after returning to the general ward ($P = 0.331$). The duration of drainage in the completely tubeless group was significantly shorter than that in the partially tubeless group (median of 1 (i.q.r. 1–2) *versus* 2 (i.q.r. 1–2) days, $P = 0.002$). The duration of postoperative hospital stay was significantly shorter in the completely tubeless group (median of 2 (i.q.r. 2–3) days) than in the partially tubeless group (median of 3 (i.q.r. 2–3) days, $P = 0.001$). The readmission rate within 14 days after surgery was similar: 1.2% (2 patients) in the completely tubeless group and 0.6% (1 patient) in the partially tubeless group ($P = 0.500$).

Postoperative blood samples were collected and tested 2 days after surgery (*Table 3*) unless the patients were discharged from the hospital on the first day after surgery (19 patients in the completely tubeless group). The difference in the change in white blood cell count from before the operation to after the operation was lower in the completely tubeless group ($P = 0.042$). The differences in the changes in median percentage of neutrophil granulocytes, median albumin level, and median prealbumin level from before the operation to after the operation between the completely tubeless group and the partially tubeless group were not significant ($P = 0.068$, $P = 0.592$, and $P = 0.915$ respectively). Postoperative C-reactive protein

Table 3 Laboratory data for blood

	Completely tubeless group ($n = 174$)		Partially tubeless group ($n = 174$)		P
White blood cells (10^9), median (i.q.r.) (range)	Preoperative 5.31 (4.45–6.36) (2.85–12.72)	Postoperative 10.51 (8.64–12.81) (5.24–18.84)	Preoperative 5.1 (4.39–6.27) (2.07–12.82)	Postoperative 11.13 (9.45–13.01) (5.46–23.71)	0.042
NEUT%, median (i.q.r.) (range)	Preoperative 57.75 (51.43–64.98) (32.1–85.6)	Postoperative 80.15 (74.8–83.88) (55.1–91.7)	Preoperative 56.65 (51.05–64.48) (31.9–88)	Postoperative 80.95 (77.83–84) (58.5–91.7)	0.068
Postoperative CRP (mg/l), median (i.q.r.) (range)	72.1 (42.7–121.2) (8.3–202)		85.25 (53.98–132.78) (5.1–200)		0.108
Albumin (g/l), median (i.q.r.) (range)	Preoperative 42.9 (40.78–46.13) (29.6–51.5)	Postoperative 39.0 (36.23–41.2) (29.1–48.3)	Preoperative 42.5 (40.53–44.7) (33.1–51.9)	Postoperative 38.1 (36.1–40.6) (26.5–48.1)	0.592
Prealbumin (mg/dl), median (i.q.r.) (range)	Preoperative 23.8 (20.9–26.5) (5.9–36.2)	Postoperative 16.7 (14.13–19.5) (5.6–32.0)	Preoperative 23.25 (20.6–25.96) (13.3–35.4)	Postoperative 15.9 (13.95–18.6) (7.8–28.7)	0.915

i.q.r., interquartile range; NEUT%, percentage of neutrophil granulocytes; CRP, C-reactive protein.

Table 4 Cytokine detection

	Completely tubeless group ($n = 174$)	Partially tubeless group ($n = 174$)	P
IL-2 (pg/ml), median (i.q.r.) (range)	2.5 (1.6–2.5) (1.12–9.6)	1.77 (1.49–2.5) (1.1–4.95)	<0.001
IL-4 (pg/ml), median (i.q.r.) (range)	2.5 (2.5–2.62) (1.17–15.38)	2.5 (1.92–2.51) (0.5–6.71)	0.470
IL-6 (pg/ml), median (i.q.r.) (range)	42.2 (20.63–79.71) (3.64–2406)	56.01 (32.07–110.44) (3.85–1087)	0.007
IL-10 (pg/ml), median (i.q.r.) (range)	3.29 (2.5–4.76) (0.15–215)	4.03 (3.23–5.18) (1.61–91.06)	<0.001
IL-17A (pg/ml), median (i.q.r.) (range)	15 (3.81–15) (0–28.45)	7.59 (2.69–15) (0–199.77)	<0.001
Interferon-γ (pg/ml), median (i.q.r.) (range)	5 (2.14–5) (0.72–9.32)	2.14 (1.61–5) (0–75.94)	<0.001
TNF-α (pg/ml), median (i.q.r.) (range)	2.5 (2.05–2.5) (0.2–14.03)	2.27 (1.62–2.5) (0–11.71)	0.363

i.q.r., interquartile range; IL, interleukin; TNF-α, tumour necrosis factor-α.

levels were not significantly different between the two groups (median of 72.1 (i.q.r. 42.7–121.2) *versus* 85.25 (i.q.r. 53.98–132.78) mg/l for the completely tubeless group and the partially tubeless group respectively, $P = 0.108$).

Cytokine detection in postoperative blood samples was also performed 2 days after surgery (*Table 4*) unless the patients were discharged from the hospital on the first day after surgery (19 patients in the completely tubeless group). The levels of interleukin (IL) 2, IL-17A, and interferon-γ in the completely tubeless group were significantly higher than those in the partially tubeless group (median of 2.5 (i.q.r. 1.6–2.5) *versus* 1.77 (i.q.r. 1.49–2.5) pg/ml, $P < 0.001$, for IL-2; median of 15 (i.q.r. 3.81–15) *versus* 7.59 (i.q.r. 2.69–15) pg/ml, $P < 0.001$, for IL-17A; and median of 5 (i.q.r. 2.14–5) *versus* 2.14 (i.q.r. 1.61–5) pg/ml, $P < 0.001$ for interferon-γ). The levels of IL-6 and IL-10 in the completely tubeless group were significantly lower than those in the partially tubeless group (median of 42.2 (20.63–79.71) *versus* 56.01 (i.q.r. 32.07–110.44) pg/ml, $P = 0.007$, for IL-6; and median of 3.29 (i.q.r. 2.5–4.76) *versus* 4.03 (i.q.r. 3.23–5.18) pg/ml, $P < 0.001$, for IL-10). IL-4 and tumour necrosis factor-α levels did not significantly differ between the two groups (median of 2.5 (i.q.r. 2.5–2.62) *versus* 2.5 (i.q.r. 1.92–2.51) pg/ml for the completely tubeless group and the partially tubeless group respectively, $P = 0.470$, for IL-4; and median of 2.5 (i.q.r. 2.05–2.5) *versus* 2.27 (i.q.r. 1.62–2.5) pg/ml for the completely tubeless group and the partially tubeless group respectively, $P = 0.363$, for tumour necrosis factor-α).

The postoperative early complications are shown in *Table 5*. The incidence of PPCs was 9.8% in the completely tubeless group and 14.9% in the partially tubeless group ($P = 0.192$). The incidences of supraventricular arrhythmia, acute myocardial infarction, acute cerebral stroke, and venous thromboembolism were similar in both groups. No significant difference was observed in the frequency of urinary irritation or acute urinary retention between the two groups.

Table 5 Postoperative early complications

	Completely tubeless group ($n = 174$)	Partially tubeless group ($n = 174$)	P
Complications	21 (12.1)	35 (20.1)	0.057
PPCs	17 (9.8)	26 (14.9)	0.192
Pneumonia	7 (4.0)	11 (6.3)	0.469
Atelectasis	5 (2.9)	7 (4.0)	0.770
Air leak (≥3 days)	5 (2.9)	8 (4.6)	0.574
Bronchopleural fistula	0 (0.0)	0 (0.0)	1.000
Respiratory failure	0 (0.0)	0 (0.0)	1.000
Supraventricular arrhythmia	2 (1.1)	5 (2.9)	0.448
Acute myocardial infarction	0 (0.0)	0 (0.0)	1.000
Acute cerebral stroke	0 (0.0)	1 (0.6)	1.000
VTE	0 (0.0)	0 (0.0)	1.000
Urinary irritation	1 (0.6)	2 (1.2)	1.000
Acute urinary retention	1 (0.6)	1 (0.6)	1.000

Values are *n* (%). PPCs, postoperative pulmonary complications; VTE, venous thromboembolism, including deep-vein thrombosis and pulmonary thromboembolism.

Mediastinal shift

The results are shown in the 'Predictors of mediastinal shift' (available as *Supplementary material*). For the visual field shift range, sex (OR 0.21 (95% c.i. 0.05 to 0.88), $P = 0.033$) and weight (OR 1.14 (95% c.i. 1.06 to 1.24), $P = 0.001$) were significant predictors. For the diaphragm displacement range, height (OR 0.87 (95% c.i. 0.81 to 0.94), $P < 0.001$) and weight (OR 1.12 (95% c.i. 1.06 to 1.19), $P < 0.001$) were significant predictors. For the surgical operation impact, weight (OR 1.09

(95% c.i. 1.01 to 1.18), $P = 0.025$) was a significant predictor. For the total mediastinal shift score, sex (OR 0.16 (95% c.i. 0.04 to 0.65), $P = 0.011$) and weight (OR 1.14 (95% c.i. 1.06 to 1.24), $P = 0.001$) were significant predictors.

Discussion

In recent years, studies comparing intubated VATS and NI-VATS have shown that NI-VATS can reduce the rate of postoperative complications, shorten the duration of hospital stay, and decrease the perioperative mortality rate[11,15]. This indicates that NI-VATS is safe, effective, and feasible. However, studies on intubated uniportal VATS, including the combined use of visualized anaesthesia technology and an ERAS protocol, report shorter durations of hospital stay and better outcomes[24]. The aim of this study was to determine the difference between minimally invasive lung surgery followed by ERAS with a completely tubeless protocol and a partially tubeless protocol.

More patients are able to return to a normal diet earlier, as well as ambulating earlier, under an ERAS protocol than under traditional management. This study demonstrates that the completely tubeless protocol has significant advantages over the partially tubeless protocol, in terms of earlier ability to drink water and ambulation. An earlier return to a normal diet and mobilization may be beneficial for promoting lung inflation[25], significantly shortening the duration of drainage and the duration of postoperative hospital stay. The patients in the completely tubeless group did not have a higher readmission rate within 14 days after surgery, suggesting that this procedure is safe.

The biological impact was investigated in this study, as well as in other studies on organ surgeries followed by the implementation of an ERAS programme[26–28]. Laboratory data for blood, including the levels of several biomarkers, indicating the magnitude of surgical stress[29,30], were evaluated in this study. The white blood cell count of patients in the partially tubeless group increased more from before the operation to after the operation than did that of patients in the completely tubeless group. Other studies have confirmed that NI-VATS is associated with milder systemic inflammatory reactions with fewer pulmonary complications[10,31]. Regarding the serum albumin and prealbumin levels, changes were not significantly different between the two groups, which might be due to the adequate implementation of the ERAS protocol.

Cytokines are critical mediators that oversee and regulate immune and inflammatory responses via complex networks and their clinical significance is introduced from the perspective of their pro- and anti-inflammatory effects[32]. In this study, the postoperative IL-2 level in patients in the completely tubeless group was significantly higher than that in patients in the partially tubeless group; IL-2 is reported to increase T cell proliferation and activate B cells[33]. The postoperative IL-6 level in patients in the completely tubeless group was significantly lower than that in patients in the partially tubeless group; it is reported that, the greater the plasma IL-6 response, the longer the operative procedure[34]. The postoperative IL-10 level in patients in the completely tubeless group was significantly lower than that in patients in the partially tubeless group; IL-10 is an anti-inflammatory cytokine that inhibits monocytes/macrophages and Th1-type lymphocyte responses[32]. The postoperative IL-17A level in patients in the completely tubeless group was significantly lower than that in patients in the partially tubeless group; in a physiologically normal state, IL-17A is known to regulate the production of immunoglobulin A and antimicrobial proteins, which maintain barrier immunity in the body and aid in the protection from foreign pathogens[35]. Postoperative interferon-γ levels were significantly higher in patients in the completely tubeless group than in those in the partially tubeless group; interferon-γ is a proinflammatory cytokine that promotes Th1 immune responses/secretion of Th1-associated cytokines[32]. These significant differences, as well as those of other studies[36], may indicate that NI-VATS has a better immune protection effect, leading to better long-term outcomes for non-small cell lung cancer patients[37].

In this study, there were no significant differences between the completely tubeless group and the partially tubeless group regarding rates of PPCs, supraventricular arrhythmia, acute myocardial infarction, acute cerebral stroke, venous thromboembolism, urinary irritation, and acute urinary retention. In the majority of patients, intravenous anaesthesia with endotracheal intubation is safe and avoids airway injury, especially when combined with visualization-guided technology, bispectral index monitoring, and use of a relaxometer[15].

NI-VATS may have some potential benefits for patients; however, both surgeons and anaesthetists are concerned about the unexpected occurrence of intraoperative events, such as massive or fatal bleeding or respiratory and circulatory instability. A total of 8 of 174 patients (4.6%) in the completely tubeless group in this study converted to intubation (6 patients due to intraoperative bleeding management and 2 patients due to avoiding the adverse effects caused by severe mediastinal shift). According to a published study[38], the conversion rate is considered to be related to surgeon experience and patient age, BMI, and anatomical resection and adhesion[9,39]. Severe mediastinal shift due to significant respiratory movements, including movements of the diaphragm, could compromise surgical safety and is the main reason for conversion to intubation. However, there are no studies that elaborate on mediastinal shift[40]. The study team summarized the surgical data, suggested the grading of mediastinal shift (see the 'Grading of mediastinal shift', available as *Supplementary material*), and conducted binary logistic regression. Weight was found to be a significant predictor for all items and the cut-off value was 68.75 kg. This is somewhat different from the finding that BMI was not a significant predictor in this study. Patients who weigh less than 68.75 kg could have a mild to moderate mediastinal shift that surgeons can tolerate.

This study has several limitations. First, it was an open-label design, single-centre study. Second, the primary outcome was difficult to choose; the postoperative complication rate was chosen. Third, surveillance was required to assess some long-term results, such as patient quality of life and survival. The grading of mediastinal shift, first described in this study, requires adaptation and validation. Finally, the economic burden of NI-VATS was not explored in this study.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

The data are available from the corresponding author on reasonable request.

Author contributions

Yunpeng Zhao (Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Validation, Writing—original draft, Writing—review & editing), Lei Shan (Data curation, Methodology, Validation), Weiquan Zhang (Data curation, Investigation, Methodology), Peichao Li (Data curation, Investigation, Methodology), Ning Li (Data curation, Investigation, Methodology, Resources), He Zhang (Data curation, Investigation, Methodology, Resources), Chuanliang Peng (Investigation, Validation), Bo Cong (Resources, Supervision), and Xiaogang Zhao (Conceptualization, Funding acquisition, Resources, Supervision, Validation, Visualization)

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