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Short-Term Outcomes of Conventional versus VATS Lobectomy in Surgical Treatment of NSCLC

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ABSTRACT
Background: A major cause of cancer-related death is non-small-cell lung cancer (NSCLC). As only 20 % of NSCLC cases are typically discovered while the illness is potentially curable & resectable, resulting in poor 5-year survival rate.
Objective: To compare between conventional versus VATS lobectomy in surgical treatment of NSCLC.
Patients and Methods: This prospective randomized open label clinical trial involved 100 patients aged >18 years old sex diagnosed with NSCLS at Benha university. Randomly, cases were classified into 2 equal groups by computer generator into group A (n=50): underwent open thoracotomy, and group B (n=50): underwent VATS. All patients were subjected to full history taking, general examination such as vital signs and laboratory investigations were recorded.
Results: Group A had significant increased duration of operation, prolonged air leak, & atelectasis than group B (P value <0.001, 027, 0.030 respectively). Pneumonia, hemothorax, AF, cerebrovascular accident and wound infection were insignificantly different between both groups. Group B had significant lower ICU stay & hospital stay than group A. Bleeding, readmission, recurrence, and mortality were insignificantly different between both groups. Group B had significant higher mean survival rate than group A.
Conclusion: Open lobectomy was accompanied with a reduced survival rate and more comorbidities than VATS lobectomy. These findings imply showed that for treating NSCLC at an early stage, VATS is a safe & efficient method.
Keywords: Conventional, VATS, Open thoracotomy, Surgical treatment, NSCLC.

INTRODUCTION

A major cause of cancer-related death is non-small-cell lung cancer (NSCLC). As only 20 % of NSCLC cases are typically discovered while the illness is potentially curable & resectable, resulting in poor 5-year survival rate [(1)]. The spread of screening programmes of lung cancer in the past 2 decades which have lowered mortality in high-risk persons through early diagnosis, has increased the number of small nodules and, consequently, the number of small incisions that surgeons must deal with & perform [(2)]. Video technology utilization & rib spreading avoidance are characteristics of minimally invasive thoracoscopic surgery. In comparison with open thoracotomy, this minimally invasive surgical method has demonstrated positive perioperative outcomes, including decreased occurrences of pain, cardiac arrhythmias, & pneumonia [(3)].

For NSCLC treatment, it has been demonstrated that Video-assisted thoracic surgery lobectomy (VATS-L) is a safe & effective substitute to conventional thoracotomy. With more experience and improved technology, the applicability of VATS has substantially grown [(4)]. Since VATS is safe & successful, it has been established and is approved for the excision of a clinical stage I NSCLC (early-stage). In earlier studies, VATS lung resection was associated with superior short-term results, including shorter hospital stays, fewer adverse events, and lower morbidity & mortality rates compared to thoracotomy [(5)]. In spite of its generally acknowledged benefits, thoracic surgeons had not accepted VATS as a successful technique until recently. As these minimally invasive treatments were perceived to be more technically difficult and less ontologically appropriate in terms of long-term survival & acceptable outcomes, open surgery and large pulmonary resection were favoured for lung cancer treatment for a long time [(6)]. Nevertheless, VATS-L is still regarded as a difficult treatment with intraoperative complications risk so severe that they necessitate emergency or urgent thoracotomy for care [(7)].

Regarding 5-year overall survival & systemic recurrence for selected patients with early-stage NSCLC, VATS was revealed to be superior to open thoracotomy according to a recent meta-analysis. The thoracic community's adoption of VATS has been gradual, despite numerous retrospective observational studies reporting superior short- & long-term outcomes. Globally, only a small percentage of pulmonary resections are conducted utilizing VATS at now [(8)]. To compare VATS to open thoracotomy, there is a shortage of strong clinical evidence in the form of large randomized controlled studies & publication bias cannot be ruled out in the great majority of published retrospective research studies. This study aimed to compare between conventional versus VATS lobectomy in surgical treatment of NSCLC.

PATIENTS AND METHODS

This retrospective randomized open label clinical trial involved 100 patients aged >18 years old of both sex diagnosed with NSCLS.

Exclusion criteria: Broncho-angioplasty or bronchoplasty, sleeve lobectomy, substantial anatomical resection with pneumonectomy or small lung resections, as well as patients who received lobectomy for a condition other than NSCLC. Also,

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VATS cases that once dissection had begun, had to be changed to traditional surgery.

Randomly, cases were equally divided into 2 groups by computer generator into group A (n=50) underwent open thoracotomy, and group B (n=50) underwent VATS.

All patients were subjected to full history taking (age, sex, comorbidities, past surgical history and medication), general examination such as vital sign (temperature, RR, HR, SBP & DBP) and laboratory investigations were recorded.

Surgical technique:

Open lobectomy: In a lateral decubitus position, the patient was placed, and one lung ventilation was employed. An incision laterally or postero-laterally was done in the 4th or 5th intercostal space. During the thoracotomy, no or one neighboring rib was excised. To widen the intercostal gaps and open the incision, a rib retractor was utilised. Botallo ligament, Hillal & carinal lymph nodes were dissected for the resection of the left lung, for right lung resection, a full mediastinal lymphadenectomy was done.

VATS lobectomy: 2 or 3 trocars were inserted for the thoracoscope & equipment during VATS lobectomy. Then, in the 5th intercostal space along the posterior axillary line or in the 4th intercostal space along the anterior axillary line, access thoracotomy of 4-8 cm was performed, and added 1, 2, or more access ports. Pulmonary arteries & bronchi dissection is conducted identically to open lobectomy, and the absence of fissures or minor adhesions are not contraindications for VATS resection. Similar to open lobectomy procedures, mediastinal lymph node dissection was done in NSCLC cases. No rib spreader was used. Via the anterior utility port, and in a plastic bag, the lobe removed was placed and put into the patient's chest before being recovered intact.

Selection of approach: After exploratory video-assisted thoracoscopy, each surgeon made an individual judgement regarding whether to use an open approach or VATS. However, our department's requirements have been standardized for VATS. To perform lung resection, the following conditions must be met:

1. The tumour had to be at least 2 cm away from the interlobar carina, located on the periphery, & never within the lobar bronchi.
2. A relative contraindication for VATS is pleural adhesions even though they only pose a significant hurdle when they are extensive & dense; nevertheless, they may usually be entirely eliminated.
3. Tumours up to 6 cm in our study were efficiently removed, however, the optimal size of a tumour is 4 cm as there are normally no issues if the tumour is located in a suitably peripheral area.
4. Currently, the existence of an open fissure is debatable. The minor fissure on the right side does not impede upper, middle, or lower lobectomies, nor does the fused major fissure impede upper or lower lobectomies in which the bronchus must be excised prior reaching to the artery. The primary fissure on the left side must be opened. However, if the fissure is fused, the lobar bronchus can be performed first, as on the right side.

Intraoperative & postoperative outcomes were assessed including duration of chest tube, estimated blood loss, operative time, morbidity, death, length of stay, & specific consequences incidence.

Visual analogue scale (VAS) pain ratings varied from severe pain (7 - 10), moderate (4 – 6) & mild (0 – 3). All patients received standard pre-operative evaluations, which included contrast-enhanced thoracic and abdominal computed tomography (CT) scans, positron emission tomography-CT (PET-CT) scans, brain CT scans, and cardiac & pulmonary function tests (PFTs). PET-CT scan hyperactivity, or endobronchial ultrasound transbronchial needle aspiration (EBUS-FNA) in cases of enlarged mediastinal lymph nodes on CT, mediastinoscopy biopsies were performed prior to surgery.

Ethical consent: Written consent was obtained from the patient or relatives of the patients. The study was approved by The Ethics Committee of Benha Faculty of Medicine. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduction of this study.

Statistical analysis:

SPSS v 26 for statistical analysis (IBM Inc., Armonk, NY, USA). To compare 2 groups: Quantitative variables were provided as means and SD, unpaired Student's t-test was used. To analyse qualitative variables Chi-square & Fisher's exact tests where necessary were used. While, frequency and percentage (%) counts were used to provide quantitative data. Significant results were defined as having a two-tailed P value of ≤ 0.05. Overall survival rate was shown on a Kaplan-Meier curve.

RESULTS

In this study, 127 patients were assessed for eligibility, 19 patients did not match the criteria & 8 patients declined to take part in the research. The remaining 100 cases were randomly allocated equally into 2 groups. All patients were followed-up and analyzed statistically (Figure 1).

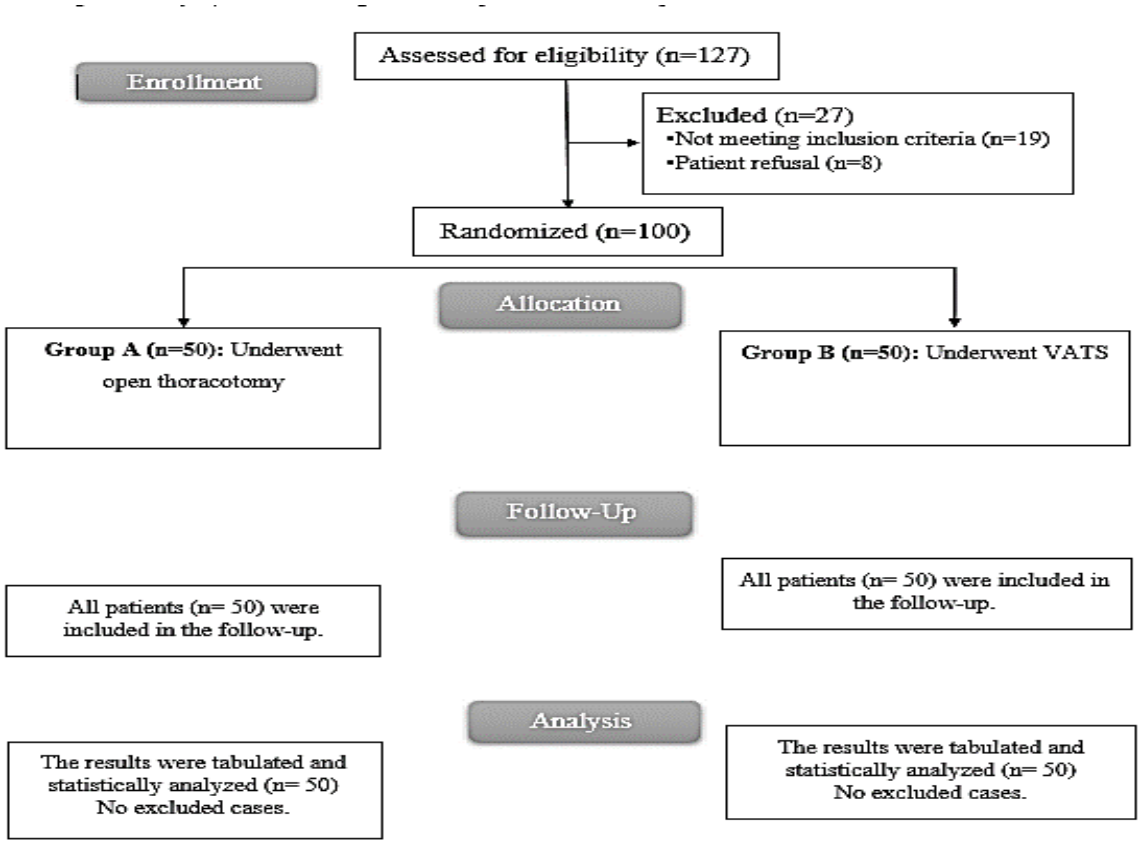

Figure (1): Flow chart of the enrolled patients in the studied groups.

Age, sex, BMI, smoking, DM, hypertension, CVD and COPD were insignificantly different between both groups. Group A had significant increased duration of operation than group B (P value <0.001) (Table 1).

Table (1): Baseline characteristics and risk factors of the studied group

		Group A (n=50)	Group B (n=50)	P value
Age		48 ± 16.11	48.4 ± 14.46	0.912
Sex	**Male**	27 (54%)	30 (60%)	0.545
	Female	23 (46%)	20 (40%)	
BMI (kg/m^2)		28 ± 2.28	27.6 ± 2.5	0.335
Smoking		14 (28%)	19 (38%)	0.288
DM		26 (52%)	19 (38%)	0.159
Hypertension		17 (34%)	22 (44%)	0.305
CVD		23 (46%)	17 (34%)	0.221
COPD		19 (38%)	14 (28%)	0.288
Duration of operation (min)		147.8 ± 19.95	133.1 ± 8.83	<0.001*

Data are presented as mean ± SD or frequency (%), DM: diabetes mellitus, CVD: cardiovascular disease, COPD: chronic obstructive pulmonary disease, *: significant as P value ≤0.05.

Tumor characteristics (histological types, side and site) showed no significant difference between groups (Table 2).

Table (2): Tumor characteristics of the studied group

		Group A (n=50)	Group B (n=50)	P value
Histology types	**Squamous cell carcinoma**	17 (34%)	20 (40%)	0.933
	Adenocarcinoma	26 (52%)	24 (48%)	
	Adeno-squamous carcinoma	5 (10%)	4 (8%)	
	Others	2 (4%)	2 (4%)	
Side	**Left**	21 (42%)	19 (38%)	0.683
	Right	29 (58%)	31 (62%)	
Site	**Upper lobe**	21 (42%)	20 (40%)	0.704
	Lower lobe	24 (48%)	27 (54%)	
	Middle lobe	5 (10%)	3 (6%)	

Data are presented as frequency (%)

Group A had significant increased prolonged air leak & Atelectasis than group B (P value =0.027 & 0.030 respectively). There was insignificant difference between both groups as regards pneumonia, hemothorax, AF, cerebrovascular accident & wound infection (Table 3).

Table (3): Complications of the studied group

	Group A (n=50)	Group B (n=50)	P value
Prolonged air leak	10(20%)	2 (4%)	0.027 *
Atelectasis	8 (16%)	1(2%)	0.030 *
Pneumonia	5 (10%)	1 (2%)	0.204
Hemothorax	4 (8%)	2 (4%)	0.677
AF	3 (6%)	1 (2%)	0.617
Cerebrovascular accident	1 (2%)	0 (0.0%)	1.00
Wound infection	4 (8%)	0 (0.0%)	0.117

Data are presented as frequency, AF: atrial fibrillation

Group B had significant lower mean ICU stay than group A (3.28 ± 1.09 versus 3.78± 1.28 days). Group B had significant lower mean hospital stay than group A (2.1 ± 0.79 versus 3.9 ± 0.83 days) (P value < 0.001). There was insignificant difference between both groups as regards bleeding, readmission, recurrence, and mortality (Table 4).

Table (4): Outcomes of the studied group

	Group A (n=50)	Group B (n=50)	P value
Chest tube duration	2.9 ±0.7	1.50 ±0.5	<0.001 *
Intensive care unit stay	3.78± 1.28 (2-3)	3.28 ± 1.09 (1-2)	<0.001 *
Hospital stay (days)	3.9 ± 0.83 (4-5)	2.1 ± 0.79 (2-3)	<0.001 *
Bleeding	1 (2%)	3 (6%)	0.617
Readmission	5 (10%)	1(2%)	0.204
Recurrence	2(4%)	0(0.0%)	0.494
Mortality	3(6%)	1(2%)	0.617

There was insignificant difference between both groups in mean survival time (Table 5 & figure 2)

Table (5): Mean and median 30-days survival time between the studied groups

	Mean	SE	95% CI for the mean	P value
Group A	29.640	0.356	28.941 to 30.339	0.317
Group B	30.000	0.000	30.000 to 30.000	

SE: standard error, CI: confidence interval

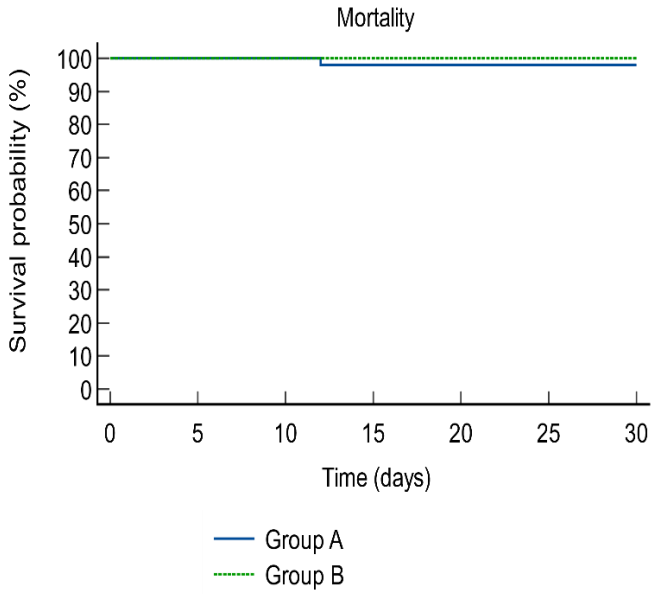

Figure (2): Kaplan Meier of overall survival rate of the studied groups.

The mean survival rate was significantly higher in group B compared to group A with hazard ratio (95%CI) (2.4769(1.0676 to 5.7466) (Table 6 & figure 3).

Table (6): Mean 5-year survival time.

Factor	Mean	SE	95% CI for the mean	P value
Group A	4.160	0.193	3.783 to 4.537	0.0347
Group B	4.620	0.144	4.338 to 4.902	

SE: standard error, CI: confidence interval

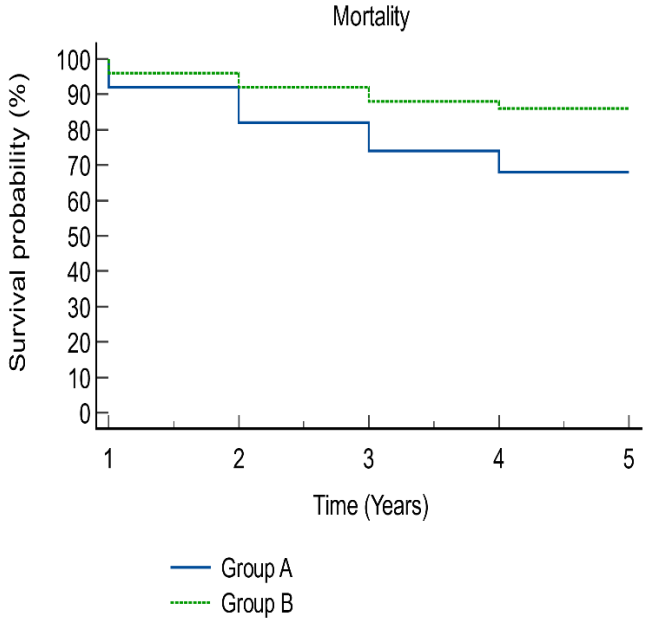

Figure (3): Kaplan Meier of overall survival rate of the studied groups

DISCUSSION

In 1993, The 1st successful lobectomy by use of VATS was done [9]. Subsequently, various benefits of this technique over conventional one has been demonstrated. There was exponential growth of VATS in popularity led it to become the most common access for lung cancer resection, largely on its own momentum on the promise of "better recovery," unsupported by any robust clinical trial evaluation. We aimed to compare between conventional versus VATS lobectomy in surgical treatment of NSCLC.

Our results stated that the mean duration of VATS was significantly lower than conventional method (147.8 ± 19.95 versus 133.1 ± 8.83 min). This comes in line with **Trivino *et al.*** [10] who determined in a clinical study that the VATS lobectomy mean duration was 117 min, compared to 171 min by lateral thoracotomy (P=0.001). Although, **Subroto *et al.*** [11] showed that the VATS lobectomy time was significantly longer than that of a conventional lobectomy (173 vs. 143 min). According to these findings, the length of operation must also be considered in addition to aggressiveness to the chest wall and the subsequent consequences on post-operative improvement after one approach or another.

Our findings revealed that VATS lobectomy provided shorter postoperative hospital stay, ICU stay, pain and fewer SAEs after discharge and readmissions, and less pain. This reduction in hospital stay length with VATS has been reported in previous studies and is due to reduced early withdrawal of pleural drainage or postoperative pain. This is congruent with the findings of **Li *et al.*** [12], who compared the long-term outcomes of VATS & open thoracotomy using a meta-analysis. Indicative of the microinvasive nature of VATS, the complication incidence following VATS for stage I lung cancer treatment was lower than the open lobectomy.

In our study, there was no difference between both methods as regards atelectasis, pneumonia, hemothorax, AF, cerebrovascular accident, wound infection, bleeding and readmission except air leakage that was significantly lower in VATS group than in open thoracotomy.

VATS was related with reduced postoperative morbidity rates than thoracotomy according to several studies. VATS decreased intraoperative chest drain time, blood loss, & hospitalization duration. Furthermore, the complication incidence following VATS was lower than in the open lobectomy group, demonstrating the micro-invasive nature of VATS according to this meta-analysis. This mismatch may be attributable to the small sample size utilised to highlight the difference in complications. Moreover, **Lim *et al.*** [13] suggested that VATS lobectomy results in better physical function at 5 weeks, shorter postoperative hospital stay despite more air leaks and bleeding, fewer SAEs after discharge and readmissions, and less pain.

The mortality rate was insignificantly different between both groups. As in the broader series published [14], mortality rates ranged between 0.4% - 3.7%, however in our research, the 1st 30 days mortality rate following VATS group was extremely low (2%), with insignificant difference between the two groups. VATS did not increase the risk of death according to the prospective trial by **Villamizar *et al.*** [15], which is in line with our findings, as 30-days mortality rate after surgery was insignificantly different between the two groups. In the same line with our findings, the prospective trial by **Villamizar *et al.*** [7] found that VATS did not increase the risk of death as no differences between the two groups in the 1st 30 days mortality after surgery. In addition, **Trivino *et al.*** [10] performed a retrospective analytic research of patients stage I NSCLC receiving surgery and discovered that in cases with no complications, VATS shortened hospital stays. Mortality was insignificantly different. Similar to our findings, a previous meta-analysis [16] on stage I NSCLC cases who performed open lobectomy or VATS, evaluated the recurrence rate, survival & complications and reported that VATS was related with a lower risk of total complications and also a better 5-year survival than open surgery, which is consistent with other meta-analyses' findings [17-19]. There are numerous plausible factors for why VATS has a higher 5-year survival rate than open surgery. Lower cytokine release, which would reduce perioperative immunosuppression, is one probable explanation [20]. Another plausible explanation is that VATS patients may be able to tolerate postoperative chemotherapy better [21]. However, **Trivino *et al.*** [10] stated that there was insignificant difference in local recurrence, 5-year overall survival, and distant metastasis. Additionally, a prior meta-analysis [12] demonstrated that at 5 years overall survival, VATS considerably outperformed open lobectomy, although at 1.3 years there was insignificant difference between the two groups. This may be partially due to decreased invasiveness & surgical procedures improvement. The immunosuppressive cytokine effect may be diminished by the less invasive nature of VATS lobectomy.

Application of VATS remains disputed in spite of the benefits of anatomical lung resections using it in lung cancer treatment. According to the technique's defenders in a VATS lung resection, all oncological surgery principles are adhered, involving lymph node dissection & complete resection (R0).

Despite the fact that our study revealed that VATS is an effective & safe therapy option for stage I NSCLC patients, the procedure has a few drawbacks. VATS may be associated with greater expenses. Although **Burfriend *et al.*** [22] discovered in prior studies using prospectively gathered quality-of-life data and creating a quality-adjusted life-year for each patient, a cost and cost-utility analysis was undertaken. The total cost of thoracotomy was substantially higher than that of thoracoscopy (P=.0012; $12,119 versus $10,084,

respectively). Additionally, using data obtained from a national hospital claims database. **Swanson *et al.* [23]** demonstrated that VATS lobectomy hospital expenses were considerably lower than open lobectomy.

Our study had limitations as of relatively small sample size & is single centre study. Additionally, limitation that is common to most surgical trials is the inability to blind the participants when an incision is performed. For evaluation of long-term outcomes of both methods and for high risky patients, further cohort studies with larger population are required.

CONCLUSION

Open lobectomy was accompanied with a lower survival rate and more comorbidities than VATS lobectomy. These findings imply that VATS is an effective & safe method for treating NSCLC in its early stages.

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