Original Article

Vein-first *vs.* artery-first robotic lobectomy outcomes in non-small cell lung cancer

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Background: Data remains limited as to whether the order of pulmonary vessel division during performance of a lobectomy for non-small cell lung cancer (NSCLC) affects survival outcomes. Some authors have suggested that ligation of the pulmonary veins should be conducted first in order to minimize the spread of tumor cells secondary to manipulation of the lung. This study examines whether there is a difference in outcomes between patients who undergo robotic lobectomies for NSCLC using a vein-first (V-first) *vs.* artery-first (A-first) technique.

Methods: A retrospective review of electronic medical record data was performed for patients who underwent robotic lobectomies from January 2013 to May 2019. Patients were separated into two groups based on the sequence in which the pulmonary vessels were divided: V-first or A-first. Baseline characteristics and postoperative events were recorded and compared between groups using Chi-squared and Student's *t*-tests. Kaplan-Meier survival curves for overall and recurrence-free survival were constructed and compared with log-rank tests.

Results: A total of 374 patients were identified: 94 V-first and 280 A-first patients. There was no significant difference between the V-first and A-first groups with regards to postoperative complications, length of stay, recurrence-free survival, or overall survival.

Conclusions: Our study suggests that choosing a V-first *vs.* A-first technique for a robotic lobectomy does not significantly impact overall survival or cancer recurrence for patients with NSCLC. Further studies are needed to evaluate whether the order of pulmonary vessel resection affects outcomes for patients with NSCLC.

Keywords: Robotic lobectomy; non-small cell lung cancer (NSCLC); artery-first (A-first); vein-first (V-first)

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Introduction

Lung cancer is the leading cause of death due to cancer in the United States, with non-small cell lung cancer (NSCLC) being most common (1). Many NSCLC tumors are now removed via robotic lobectomy, which has been shown to have comparable perioperative morbidity and mortality outcomes to that of video-assisted thoracoscopic surgery (VATS) lobectomy (2,3). Considerable care must be taken to decrease the risk of metastasis and recurrence following surgical resection of lung tumors. Some studies have shown that the surgical manipulation of tumors can promote the release of tumor cells into circulation (4,5). With respect

to lobectomies for NSCLC, ligation of the pulmonary vein prior to the artery may be a promising technique that can help mitigate these risks.

The decision of whether to ligate the artery or vein first during lobectomy has been debated, with some authors positing that early ligation of the vein can limit the spread of cancer cells secondary to manipulation of the lung tissue during surgery. In particular, circulating tumor cells can serve as a biomarker for prospective recurrence, making a technique that limits the circulation of these cells an important area of investigation (6,7). However, there is little evidence to guide whether a vein-first (V-first) approach to lobectomies is superior to an artery-first (A-first) approach with respect to short- or long-term outcomes. For thoracoscopic lobectomies, a prior study from Wei *et al.* demonstrated that patients who underwent V-first resections had higher rates of survival than patients who underwent A-first resections (8). This finding warrants further investigation in order to determine whether V-first approaches are truly superior. To our knowledge, there have been no prior studies examining V-first *vs.* A-first approaches among robotic lobectomies. Therefore, in this study, we aim to evaluate the short- and long-term outcomes of V-first *vs.* A-first approaches in patients who underwent robotic lobectomies for NSCLC. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1576/rc).

Highlight box

Key findings

- Our study suggests that choosing between a vein-first *vs.* artery-first technique for robotic lobectomy does not significantly impact overall survival or cancer recurrence in patients with non-small cell lung cancer (NSCLC).

What is known and what is new?

- Some authors suggest that early ligation of the vein can limit the spread of cancer cells secondary to manipulation of the lung tissue during surgery.
- Our study provides data for differences in outcomes between vein-first *vs.* artery-first robotic lobectomies.

What is the implication, and what should change now?

- Our data suggests that the order in which the pulmonary vessels are ligated during robotic lobectomy for NSCLC should be up to the discretion of the surgeon.

Methods

Study design

This was a retrospective study using the electronic medical record of all patients who underwent robotic lobectomy procedures for NSCLC at the University of Alabama at Birmingham (UAB) from January 2013 through May 2019. A total of 374 patients from two surgeons were included, while bilobectomies (n=11) and cases that involved conversion from robotic to open lobectomy were excluded (n=16) (*Figure 1*). Robotic lobectomy was performed with a completely portal technique using four robotic arms and an assistant port. The camera port was typically located in the 7th or 8th intercostal space. Our technique has been described previously (9). Operative reports were reviewed, and all cases were then separated into either the V-first or A-first group, based on the sequence in which the pulmonary vessels were divided. The V-first group included patients who underwent division of the vein first followed by the artery (vein-artery), along with cases that also involved division of another vein after the artery (vein-artery-vein). The A-first group included cases in which the arteries were divided first followed by the vein (artery-vein) and cases where an additional artery was divided after the vein (artery-vein-artery). Order of division of the vessels was made at the discretion of the operating surgeon on each individual case; there was no set protocol or policy with regards to order of division of vessels. Mediastinal lymph node dissection was performed prior to division of vessels and the performance of lobectomy in all cases. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and informed consent was obtained from the patients included in this study. Institutional Review Board approval was obtained for this study through University of Alabama at Birmingham (protocol No. 300001851).

Data collection

Various baseline characteristics were collected for each patient, including demographics (age, gender, and race) and clinical characteristics (comorbidities, Zubrod score, etc.). Pathologic stage was determined according to the Eighth Edition of the American Joint Committee on Cancer staging manual (10). Peri-operative (procedure time) and post-operative (events, recurrence, mortality, etc.) data were also collected. Follow-up clinic notes up until June

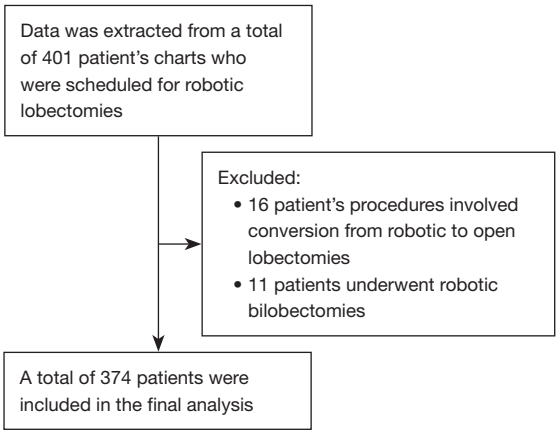

Figure 1 Criteria for exclusion from final analysis.

2020 were used to determine recurrence among patients. Recurrence was defined as a new abnormality or lesion(s) seen on computed tomography (CT) scan, confirmed by positron emission tomography (PET)-CT scan, repeat CT scan (to document growth), and/or biopsy. The UAB tumor registry data was used to calculate follow-up duration for each patient, with the last update of the registry being in June 2022. Primary outcomes included overall survival and recurrence-free survival, while secondary outcomes included postoperative complication rates and hospital length-of-stay.

Statistical analysis

Mean or median values were calculated for continuous variables while counts and percentages were calculated for categorical variables. Median values were used for time-related continuous variables. Patient characteristics and perioperative events and outcomes were compared between the two groups using Chi-squared and Student's *t*-tests, as appropriate. Kaplan-Meier survival curves for recurrence-free survival and overall survival were constructed and compared with log-rank tests. We developed a multivariable Cox proportional hazards regression model to assess factors predicting mortality, and another to predict recurrence. All statistical analyses were performed using SAS software (Version 9.4, SAS Institute Inc., Cary, NC, USA). A P value of less than 0.05 was considered statistically significant.

Results

A total of 401 patients underwent a robotic lobectomy for NSCLC during the study period. As described in *Figure 1*, 27 patients were excluded from the analysis. Of the remaining 374 patients, 94 were identified to be in the V-first group and 280 were in the A-first group. In the V-first group, 2 (2.1%) patients had an additional vein divided after the artery (vein-artery-vein), while the A-first group included 106 (37.3%) patients who had an additional artery divided after the vein (artery-vein-artery).

Patient characteristics are summarized in *Table 1*. For the entire cohort 58.0% of patients were female, 54.8% were between the ages 65–79 years, and 84.5% were Caucasian. There were no significant differences between the two groups with respect to gender, age, or race. Within the cohort, the most common comorbidities were hypertension (67.1%), obesity (36.1%), and chronic obstructive pulmonary disease (34.95%), with no significant differences between the V-first or A-first groups. Approximately 1/3 (32.9%) of patients in this cohort had undergone prior cardiothoracic surgery; 12.3% of patients received pre-operative chemotherapy, while 8.02% received pre-operative radiation therapy, with no significant differences between the groups. Of note, a V-first technique appeared to be used more often for patients with tumors ≤2 cm in size than an A-first technique (50.0% *vs.* 29.2%, P=0.007). Also, patients in the V-first group appeared to have a lower mean predicted forced expiratory volume in the first second (FEV_1) compared to the A-first group (78 *vs.* 84, P=0.011).

Operative and tumor characteristics are described in *Table 2*. In this cohort, adenocarcinoma was the most common histology (65.8%) and the majority of patients (70.9%) were Stage 1. There were no significant differences in histology or pathologic stage between the groups. The rate of R0 resection was similar between both groups (V-first: 97.9% *vs.* A-first: 98.9%, P=0.440) The patients who underwent A-first operations had a greater mean number of nodes removed (21 *vs.* 17; P<0.001). The V-first group was more likely to have undergone right upper lobectomy (54.3% *vs.* 36.4%; P=0.019) or right middle lobectomy (20.2% *vs.* 2.9%; P<0.001) when compared to the A-first group. On the other hand, the A-first group was more likely to have undergone left upper lobectomy (23.2% *vs.* 2.1%; P<0.001).

As shown in *Table 3*, there were no significant differences with respect to postoperative complications, length of stay, or 30- and 90-day mortality between the two groups. The most common post-operative complications were urinary retention (16.3%), prolonged air leak (12.6%), and atrial arrhythmia requiring treatment (8.6%). Interestingly, the incidence of atrial arrhythmia was over twice as high in

Table 1 Baseline characteristics of vein-first and artery-first robotic lobectomy groups

Baseline characteristics	Vein-first, n=94	Artery-first, n=280	All, n=374	P value
Age, years				
18–44	2 (2.13)	6 (2.14)	8 (2.14)	0.993
45–64	30 (31.91)	91 (32.50)	121 (32.35)	0.931
65–79	49 (52.13)	156 (55.71)	205 (54.81)	0.684
80+	13 (13.83)	27 (9.64)	40 (10.70)	0.283
Gender				
Female	62 (65.96)	155 (55.36)	217 (58.02)	0.243
Male	32 (34.04)	125 (44.64)	157 (41.98)	0.170
Race				
Caucasian	80 (85.11)	236 (84.29)	316 (84.49)	0.940
Black/African American	14 (14.89)	41 (14.64)	55 (14.71)	0.956
Hispanic or Latino Ethnicity	0 (0.00)	3 (1.07)	3 (0.80)	0.316
Comorbidities				
Obesity (BMI ≥30 kg/m^2)	38 (40.43)	97 (34.64)	135 (36.10)	0.419
Hypertension	59 (62.77)	192 (68.57)	251 (67.11)	0.552
Congestive heart failure	3 (3.19)	11 (3.93)	14 (3.74)	0.749
Coronary artery disease	16 (17.02)	63 (22.50)	79 (21.12)	0.317
Pulmonary hypertension	1 (1.06)	3 (1.07)	4 (1.07)	0.995
Interstitial fibrosis	2 (2.13)	3 (1.07)	5 (1.34)	0.443
Prior stroke or TIA	9 (9.57)	18 (6.43)	27 (7.22)	0.326
Diabetes	18 (19.15)	59 (21.07)	77(20.59)	0.722
COPD (n=329)	30 (31.91)	85 (30.36)	115 (34.95)	0.276
Preoperative chemotherapy	14 (14.89)	32 (11.43)	46 (12.30)	0.407
Preoperative thoracic radiation	7 (7.45)	23 (8.21)	30 (8.02)	0.820
Prior cardiothoracic surgery	31 (32.98)	92 (32.86)	123 (32.89)	0.986
Smoking status				
Former smoker	50 (53.19)	151 (53.93)	201 (53.74)	0.933
Current smoker	22 (23.40)	64 (22.86)	86 (23.00)	0.924
Never smoked	22 (23.40)	65 (23.21)	87 (23.26)	0.974
Zubrod score (n=329)				
0	16 (22.22)	56 (21.79)	72 (21.88)	0.945
1	44 (61.11)	163 (63.42)	207 (62.92)	0.827
2	9 (12.50)	32 (12.45)	41 (12.46)	0.992
3	3 (4.17)	6 (2.33)	9 (2.74)	0.406

Table 1 (*continued*)

Table 1 (*continued*)

Baseline characteristics	Vein-first, n=94	Artery-first, n=280	All, n=374	P value
Tumor size (cm) (n=329)				
≤2	36 (50.00)	75 (29.18)	111 (33.74)	0.007
>2, ≤3	17 (23.61)	79 (30.74)	96 (29.18)	0.322
>3, ≤5	17 (23.61)	77 (29.96)	94 (28.57)	0.373
>5, ≤7	2 (2.78)	20 (7.78)	22 (6.69)	0.147
>7	0	6 (2.33)	6 (1.82)	0.195
Pulmonary function testing				
FEV_1 (mean, % predicted) (n=367)	78	84	83	0.011
DLCO (mean, % predicted) (n=360)	72	76	75	0.087

The total number of patients for Zubrod score and tumor size was 329. For these items, the V-first group had 72 patients, while the A-first group had 257 patients. Data are presented as N (%) or mean, % predicted. BMI, body mass index; TIA, transient ischemic attack; COPD, chronic obstructive pulmonary disease; cm, centimeters; FEV_1, forced expiratory volume in 1 second; DLCO, diffusing capacity of lungs for carbon monoxide; V-first, vein-first; A-first, artery-first.

the A-first group (10.0%) as in the V-first group (4.3%), although this difference did not reach statistical significance (P=0.100). Among the whole cohort, median length of stay from admission to discharge was 2 [interquartile range (IQR) 2–4] days.

The median postoperative follow-up duration with respect to overall survival was 67 (IQR 45–87) months. A total of 8 patients were lost to follow-up with respect to recurrence evaluation, 1 in the V-first group and 7 in the A-first group. Out of the 366 patients who were not lost to follow-up, recurrence occurred in 66 (18.0%) patients, while 59 (16.1%) patients died. *Figure 2* depicts the recurrence-free survival curves and *Figure 3* depicts the overall survival curves for the two groups. According to comparison through log-rank tests, there was no significant difference between the V-first and A-first groups with respect to both recurrence-free (P=0.941) and overall survival (P=0.202). Multivariable Cox regression analysis showed that whether the vein or artery was ligated first did not predict recurrence or death (*Tables 4*,*5*).

Discussion

The results of this study suggest that a V-first *vs.* A-first robotic lobectomy technique does not significantly impact the overall survival or cancer recurrence in patients with NSCLC. We found no significant difference in overall and recurrence-free survival between our two groups. Furthermore, both groups also did not significantly differ in the incidence of postoperative complications or in length of hospital stay. Interestingly, we found that technique selection was influenced by tumor size and location. In particular, a V-first technique was performed more often for small tumors (≤2 cm), along with those located in the right upper and middle lobes. On the other hand, an A-first technique was more often performed for patients who underwent left upper lobectomies.

To our knowledge, the impact of the sequence of vessel ligation has not been investigated in patients who have undergone robotic lobectomies. We found that ligation of the pulmonary vein prior to the artery did not appear to significantly impact the recurrence or overall survival of patients with NSCLC who underwent robotic lobectomies. These findings are consistent with the study of open lobectomies by Refaely *et al.*, along with the study of VATS lobectomy by He *et al.* (5,11). Given that VATS lobectomy is considered more similar to robotic lobectomy, the findings of He *et al.* may be more comparable to our study. In the retrospective study by He *et al.*, it was found that the order of vessel ligation during VATS lobectomy did not affect long-term survival of patients, which is consistent with our findings (11). Despite this, we do find our results to be surprising, as a large proportion of the literature continues to show favor of V-first techniques (9,12). However, since robotic lobectomy is inherently a minimally invasive procedure, it is possible that minimization of tumor

Table 2 Operative and tumor characteristics of vein-first and artery-first robotic lobectomy groups

Operative and tumor characteristics	Vein-first, n=94	Artery-first, n=280	All, n=374	P value
Procedure time (median minutes)	157	133	137	0.061
Removed lobe				
Right upper	51 (54.26)	102 (36.43)	153 (40.91)	0.019
Right middle	19 (20.21)	8 (2.86)	27 (7.22)	<0.001
Right lower	12 (12.77)	61 (21.79)	73 (19.52)	0.087
Left upper	2 (2.13)	65 (23.21)	67 (17.91)	<0.001
Left lower	10 (10.64)	44 (15.71)	54 (14.44)	0.262
Pathologic stage				
0	1 (1.06)	3 (1.07)	4 (1.07)	0.995
IA1	30 (31.91)	79 (28.21)	109 (29.14)	0.565
IA2	18 (19.15)	52 (18.57)	70 (18.72)	0.869
IA3	4 (4.26)	5 (1.79)	9 (2.41)	0.182
IB	19 (20.21)	58 (20.71)	77 (20.59)	0.926
IIA	3 (3.19)	17 (6.07)	20 (5.35)	0.296
IIB	15 (15.96)	32 (11.43)	47(12.57)	0.284
III	4 (4.26)	31 (11.07)	35 (9.36)	0.062
IV	0	3 (1.07)	3 (0.80)	0.316
Cancer histology				
Adenocarcinoma	61 (64.89)	185 (66.07)	246 (65.78)	0.903
Squamous cell	17 (18.09)	67 (23.93)	84 (22.46)	0.301
Neuroendocrine	14 (14.89)	24 (8.57)	38 (10.16)	0.096
Large cell	0	1 (0.36)	1 (0.27)	0.562
Mixed	2 (2.13)	3 (1.07)	5 (1.34)	0.443

Data are presented as median or N (%).

cell manipulation with this method therefore makes the sequence of vessel ligation not a significant factor in patient outcomes. Specifically, lobectomy via open thoracotomy has been shown to result in increased circulating tumor cells in the pulmonary venous drainage (13-15). Thus, in more invasive techniques that involve greater manipulation of the lung, the sequence of vessel ligation may play a greater role in outcomes. Furthermore, a study by Duan *et al.* suggests that the timing of V-first ligation, early versus late, may play a role in outcomes as well (16). This study found that ligating the vein immediately during VATS lobectomy (early ligation group) resulted in decreased dissemination of circulating tumor cells when compared to ligating the vein later once the artery, bronchus, and pulmonary fissure were partially or completely exposed (late ligation group) (16). This finding also introduces the possibility that even with a V-first technique, the timing of vein ligation may also play a role in tumor cell dissemination and therefore recurrence and survival.

The decision about whether or not to ligate the vein first during lobectomy for non-small lung cancer is often dictated by the particular anatomy of the specific patient. That said, certain trends with regards to vessel to be divided first do exist. For instance, we found that V-first ligation was more likely in patients undergoing right upper and middle lobectomy. In both of these instances, it is often simpler to ligate the vein prior to the artery given the relative location of the vessels. We believe that this is due to

Table 3 Postoperative events for vein-first and artery-first robotic lobectomy groups

Postoperative events	Vein-first, n=94	Artery-first, n=280	All, n=374	P value
Unexpected return to operating room	1 (1.06)	10 (3.57)	11 (2.94)	0.220
Reintubation	2 (2.13)	1 (0.36)	3 (0.80)	0.097
Recurrent laryngeal nerve paresis	0	2 (0.71)	2 (0.53)	0.413
Urinary tract infection	3 (3.19)	5 (1.79)	8 (2.14)	0.420
Air leak >5 days	9 (9.57)	38 (13.57)	47 (12.57)	0.344
Atelectasis requiring bronchoscopy	1 (1.06)	6 (2.14)	7 (1.87)	0.508
Pleural effusion requiring drainage	1 (1.06)	2 (0.71)	3 (0.80)	0.743
Pneumonia	1 (1.06)	10 (3.57)	11 (2.94)	0.219
Acute respiratory distress syndrome	0	2 (0.71)	2 (0.53)	0.413
Respiratory failure	3 (3.19)	5 (1.79)	8 (2.14)	0.420
Pneumothorax	5 (5.32)	24 (8.57)	29 (7.75)	0.327
Initial ventilatory support >48 h	0	2 (0.71)	2 (0.53)	0.413
Tracheostomy	0	1 (0.36)	1 (0.27)	0.562
Atrial arrhythmia requiring treatment	4 (4.26)	28 (10.00)	32 (8.56)	0.100
Ileus	0	3 (1.07)	3 (0.80)	0.316
Postop packed RBCs	1 (1.06)	5 (1.79)	6 (1.60)	0.633
Urinary retention	16 (17.02)	45 (16.07)	61 (16.31)	0.844
Sepsis	0	2 (0.71)	2 (0.53)	0.413
Other infection requiring IV antibiotics	0	9 (3.21)	9 (2.41)	0.082
Delirium	1 (1.06)	8 (2.86)	9 (2.41)	0.332
Other neurological event	1 (1.06)	0	1 (0.27)	0.084
Renal failure (RIFLE criteria)	2 (2.13)	2 (0.71)	4 (1.07)	0.251
Chylothorax requiring medical intervention	0	7 (2.50)	7 (1.87)	0.125
Other events requiring OR w/general anesthesia	1 (1.06)	6 (2.14)	7 (1.87)	0.508
Unexpected admission to ICU	1 (1.06)	13 (4.64)	14 (3.74)	0.121
Postoperative length of stay (median days)	2	3	2	0.890
Recurrence (n=366)	16 (17.20)	50 (18.32)	66 (18.03)	0.662
30-day mortality	2 (2.13)	3 (1.07)	5 (1.34)	0.353
90-day mortality	2 (2.13)	5 (1.79)	7 (1.87)	0.280

The total number of patients for which recurrence data was available was 366. For this item, the V-first group had 93 patients, while the A-first group had 273 patients. Data are presented as N (%), or median. RBCs, red blood cells; IV, intravenous; RIFLE criteria, Risk, Injury, Failure, Loss of kidney function, End-stage kidney disease criteria; OR, operating room; ICU, intensive care unit; V-first, vein-first; A-first, artery-first.

the position of the vein relative to the arteries (for instance, the middle lobe vein is peripheral/medial to the artery in patients). In certain instances, such as when a posterior ascending artery is easily accessible after dividing the right upper lobe bronchus, or when a right middle lobe artery is traveling in a complete oblique fissure, it can be easier to ligate the artery first when doing the respective lobectomy. However the more common anatomic configuration is

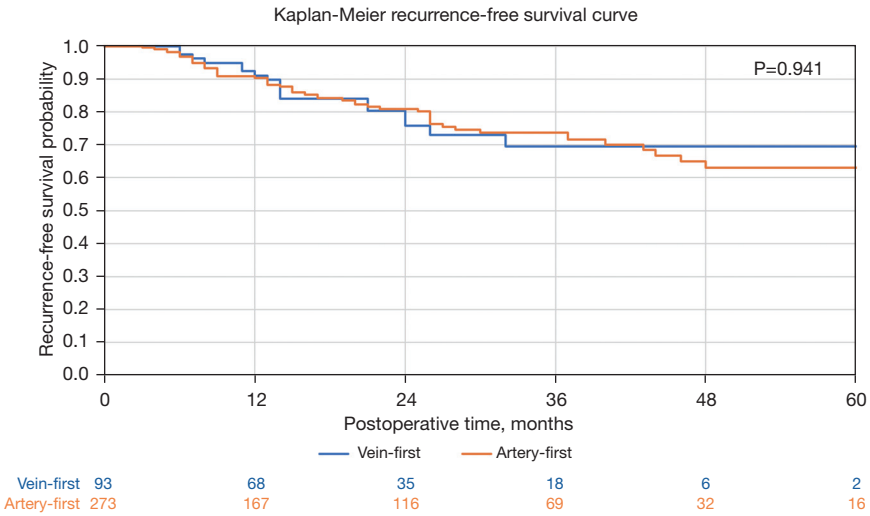

Figure 2 Kaplan-Meier recurrence-free survival curve for vein-first and artery-first robotic lobectomy groups.

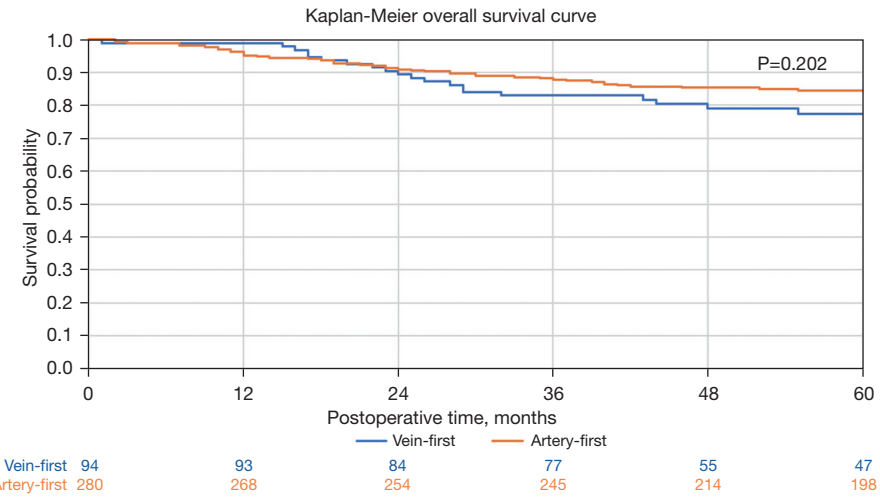

Figure 3 Kaplan-Meier overall survival curve for vein-first and artery-first robotic lobectomy groups.

such that the vein is ligated first in these operations. On the other hand, left upper lobectomy was more commonly performed in an A-first manner in our study. This is because the apicoposterior artery is often easily isolated and ligated with the lung retracted in an anterior fashion during the initial hilar/mediastinal nodal dissection. In the absence of evidence suggesting that the order of vessel division impacts oncologic outcomes, it is reasonable to state that these decisions can and should be based on convenience, safety, surgeon experience and comfort level, and ease, rather than biased towards a V-first approach to provide a hypothetical benefit of reducing circulating tumor cells.

There are some limitations to this study. First, the data used in the study was collected from a single institution, which could have introduced bias based on institutional or surgeon preference regarding operative technique. This limits the generalizability of our findings. Furthermore, the sample size was small, and due to the retrospective nature of this study, the size of the A-first group ended up being almost triple the size of the V-first group. Also, the retrospective nature of chart review could have introduced some errors in data collection. Thus, prospective studies with larger sample sizes are needed to further assess the impact of the sequence of vessel ligation during robotic

Table 4 Multivariable Cox regression analysis for predicting recurrence

Variables	Hazard ratio (95% CI)	P value
Vein *vs.* artery	0.79 (0.39, 1.61)	0.5226
Age at time of surgery	1.02 (0.98, 1.05)	0.3349
Female *vs.* male	1.61 (0.90, 2.88)	0.1059
Histology		
Large cell *vs.* adenocarcinoma	14.38 (1.56, 132.88)	0.0188
Mixed *vs.* adenocarcinoma	N.A.	0.9966
Neuroendocrine *vs.* adenocarcinoma	1.71 (0.60, 4.84)	0.312
Squamous cell *vs.* adenocarcinoma	1.81 (0.95, 3.42)	0.0692
Stage		
II, III, or IV, unknown *vs.* 0 or I	N.A.	0.9823
Location		
Left lower *vs.* right upper	2.08 (0.96, 4.48)	0.0626
Left upper *vs.* right upper	0.49 (0.14, 1.71)	0.2595
Right lower *vs.* right upper	2.53 (1.25, 5.12)	0.0099
Right middle *vs.* right upper	2.49 (0.85, 7.23)	0.0947
Smoking status		
Current smoker *vs.* never smoked	2.21 (0.89, 5.47)	0.0875
Former smoker *vs.* never smoked	2.01 (0.95, 4.24)	0.0677
ECOG score		
1 *vs.* 0	1.30 (0.70, 2.42)	0.4045
2 *vs.* 0	0.89 (0.37, 2.14)	0.792
3 *vs.* 0	0.45 (0.06, 3.50)	0.4424

None of the 5 patients with mixed cancer experienced recurrence, making it impossible to estimate the hazard ratio and its corresponding 95% confidence interval. Additionally, none of the patients diagnosed with Stage II, III, or IV cancer had experienced recurrence, which prevented the estimation of the hazard ratio due to the absence of variation in the outcome. CI, confidence interval; N.A., not available; ECOG, Eastern Cooperative Oncology Group.

Table 5 Multivariable Cox regression analysis for predicting death

Variables	Hazard ratio (95% CI)	P value
Vein *vs.* artery	1.62 (0.81, 3.24)	0.1706
Age at time of surgery	1.01 (0.98, 1.05)	0.4472
Female *vs.* male	0.77 (0.42, 1.41)	0.4052
Histology		
Large cell *vs.* adenocarcinoma	N.A.	>0.99
Mixed *vs.* adenocarcinoma	0.63 (0.07, 5.84)	0.6875
Neuroendocrine *vs.* adenocarcinoma	2.82 (0.90, 8.89)	0.0763
Squamous cell *vs.* adenocarcinoma	1.02 (0.49, 2.09)	0.9655
Pathology		
II, III, or IV, unknown *vs.* 0 or I	N.A.	0.9773
Location		
Left lower *vs.* right upper	0.73 (0.21, 2.56)	0.619
Left upper *vs.* right upper	0.76 (0.41, 1.38)	0.3612
Right lower *vs.* right upper	7.12 (0.69, 73.16)	0.0986
Right middle *vs.* right upper	0.38 (0.10, 1.41)	0.1463
Smoking status		
Current smoker *vs.* never smoked	1.83 (0.64, 5.26)	0.2624
Former smoker *vs.* never smoked	2.29 (1.00, 5.25)	0.0512
ECOG score		
1 *vs.* 0	1.12 (0.59, 2.12)	0.7278
2 *vs.* 0	2.13 (0.77, 5.88)	0.146
3 *vs.* 0	2.90 (0.29, 28.51)	0.362

Only one patient was diagnosed with large cell cancer, resulting in an inability to estimate the hazard ratio and its corresponding 95% confidence interval. Out of the 69 patients who died during the study period, all had Stage II, III, or IV cancer, which led to the inability to estimate the hazard ratio due to a lack of variation in the outcome. CI, confidence interval; N.A., not available; ECOG, Eastern Cooperative Oncology Group.

lobectomy. In addition, the A-first and V-first groups were slightly different in terms of proportion of current *vs.* former smokers (more current smokers in the A-first group), size of tumor (higher percentage of tumors ≤2 cm in the V-first group), and the type of lobectomies performed (more right upper and middle lobectomies in the V-first group; more left upper lobectomies in the A-first group). This selection bias could impact the ability to detect a significantly different survival rate between the groups—however, the nature of these differences would be expected to negatively impact survival more in the A-first group and thus potentially make it more likely to detect a difference in favor of V-first lobectomy, as has been postulated by other studies. Finally, the fact that a significant proportion of

patients in the A-first group had the lobar vein divided prior to additional arteries (A-V-A rather than A-V) may have limited the ability to detect a survival difference between groups. That said, in the "real world", the order of division of vessels is often influenced by the necessities of anatomy and what is deemed safer or easier rather than an a priori decision to divide all arteries before the vein; our study reflects the application of a V-first versus A-first technique in actual clinical practice.

Ultimately, we found no significant difference in recurrence or overall survival among patients who underwent robotic lobectomies with V-first versus A-first techniques for the resection of NSCLC. This suggests that the order in which the pulmonary vessels are ligated should be up to the discretion of the surgeon. However, further investigation is necessary to evaluate whether the order of pulmonary vessel ligation affects the outcomes of patients with NSCLC who undergo robotic lobectomy.

Conclusions

We found no significant difference in overall survival or recurrence between the A-first and V-first approaches for robotic lobectomy among patients with NSCLC. We found some differences in technique based on size and location. Small tumors (≤2 cm) and those located in the right upper or middle lobes were more likely to be resected with removal of the vein first, while tumors in the left upper lobe were more likely to be resected with removal of the artery first. Further studies are needed to evaluate whether the order of pulmonary vessel resection affects outcomes for patients with NSCLC.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and informed consent was obtained from the patients included in this study. Institutional Review Board approval was obtained for this study through University of Alabama at Birmingham (protocol No. 300001851).

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