



Robotic versus thoracoscopic combined anatomic subsegmentectomy for early-stage lung cancer: early results of a cohort study

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Background: Combined anatomic subsegmentectomy performed by video-assisted thoracic surgery or robot-assisted thoracic surgery is an emerging minimally invasive surgical technique for patients with early-stage non-small cell lung cancer (NSCLC). However, the early results of these two methods have barely been studied.

Methods: A retrospective analysis of medical records from Shanghai Ruijin Hospital between July 2017 and August 2021 included 62 patients, 32 of whom underwent video-assisted combined anatomic pulmonary subsegmentectomy and 30 underwent robot-assisted combined anatomic pulmonary subsegmentectomy. Perioperative outcomes were compared.

Results: Sixty-two patients with comparable baseline characteristics were included in this study. No significant difference was found in the length of postoperative hospital stay, operation duration, intraoperative blood loss and the rate of overall complications between the robot-assisted and video-assisted groups. A higher cost was observed in the robot-assisted group compared to the video-assisted group. There were more N1 lymph nodes and N1 stations dissected in the robot-assisted group compared with the video-assisted group; the same results were observed with regard to the number of N2 lymph nodes and N2 stations dissected.

Conclusions: It is safe and feasible for the patients with early-stage NSCLC to be treated with combined anatomic subsegmentectomy performed via robot-assisted or video-assisted thoracic surgery. The robotic approach may contribute to the potential improvements in N1 and N2 lymph node retrieval.

Keywords: Combined anatomic subsegmentectomy (CAS); retrospective analysis; robotic; video-assisted thoracic surgery (VATS)

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Introduction

For small pulmonary lesions, especially those with ground-glass opacity, as long as sufficient margins and staging of lymph node are fully acquired, a sublobar resection can be regarded as an option to lobectomy (1,2). Many

recent studies have shown that sublobar resection results in equivalent oncologic outcomes in patients with stage I non-small cell lung cancer (NSCLC) (3-6). Recently, a phase III randomized trial (JCOG0802/WJOG4607L) (7) demonstrated that patients obtain more benefits from

segmentectomy than lobectomy in terms of overall survival and post-surgery pulmonary function, which suggests that segmentectomy may be considered as the standard treatment for early-stage peripheral NSCLC.

As for intersegmental pulmonary nodules located between adjacent segments or at the edge of the diseased segments, single segmental resection is arduous to ensure a safe margin (8,9). Intersegmental pulmonary nodules resected by extended segmental resection is essentially a wedge resection with the added potential problem of insufficient margins (10). To solve this, combined anatomic subsegmentectomy (CAS) is performed to ensure a safe incisional margin by placing intersegmental nodules in the central area of the adjacent involved subsegments. The advantages of CAS are that it can offer a better margin for intersegmental nodules (10-12) and result in the retention of more lung parenchyma (9), since the removal of two subsegments is essentially equivalent to the removal of a lung segment.

However, hilar dissection in anatomical segmentectomies or CAS via video-assisted thoracic surgery (VATS) can be technically more complicated than lobectomy (13). With the increasing use of robotic surgery for sublobectomy, robotic systems are more likely to promote segmental lung resection because robotic-assisted thoracic surgery (RATS) has shown superiority over conventional VATS, with its use of three-dimensional vision, greater flexibility, and better assistance for surgeons (14). RATS also has disadvantages, such as unsatisfactory tactile feedback and higher costs (15,16).

To the best of our knowledge, there is no evidence to confirm if RATS CAS could provide the same perioperative and oncological results as VATS CAS, although there have been a few reports on the application of thoracoscopic and robotic surgery for subsegmental lung resection (9,12,17). Herein, we collected and presented the perioperative outcomes of 30 patients who underwent RATS CAS and 32 patients who underwent VATS CAS. The aim of our study was to retrospectively analyze and compare oncological safety, early results, and the costs of CAS using the RATS and VATS methods in early NSCLC. We present the following article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-1895/rc>).

Methods

Patients population

We conducted a retrospective study of 62 consecutive

patients who underwent minimally invasive CAS using the RATS or VATS approach for early-stage NSCLC at Shanghai Ruijin Hospital between July 2017 and August 2021. Retrospective analysis of the data was performed using a system approved by the Investigation Review Board of Ruijin Hospital (KY201996), including appropriate patient identification of those enrolled for the purpose of privacy protection. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Investigation Review Board of Ruijin Hospital (No. KY201996). Because of its retrospective nature, informed patient consent was not required. CAS is defined as the removal of two or more subsegments during surgery, usually when the small pulmonary nodules involve two or more adjacent segments. In this study, we systematically reviewed the clinical data of 62 patients who underwent successful CAS. Some of these patients entered clinical experiments NCT03192904 or NCT03134534 at the department. As described in an earlier study (12), patients were required to meet the following eligibility criteria to receive CAS for early-stage lung cancer in the series: (I) nodules ≤ 2 cm in size with 50% or more ground-glass appearance on computed tomography (CT); (II) strongly suspected stage I NSCLC; (III) pulmonary lesions involving two or more adjacent segments; and (IV) patient performance status ≤ 1 or sufficient organ function. All patients made a choice for their surgical approach based on their own preference. Seven cases were excluded from this study due to the intraoperative change of surgical plan (*Figure 1*). Hook-wire localization assisted by CT angiography and bronchography (Xudong, China) was optionally applied based on patient's condition.

Operative preparations and postoperative treatment protocols were similar for RATS CAS and VATS CAS. The clinical data of baseline characteristics, perioperative results, and pathological outcomes were collected from the electronic medical records of each patient. The perioperative period corresponds to the entire process surrounding the operation, including the periods before, during, and after the surgery. Specifically, this begins from the time that the surgical treatment was confirmed (approximately 5–7 days before surgery) until the treatment related to the surgery was completed (7–12 days after surgery). The follow-up period to determine mortality outcomes was approximately 30 days via telephone. The percent forced expiratory volume in 1 second (%FEV1) was divided into three categories: $\geq 80\%$, 50–80%, and $< 50\%$, based on the Global Initiative for Chronic Obstructive Disease classification of

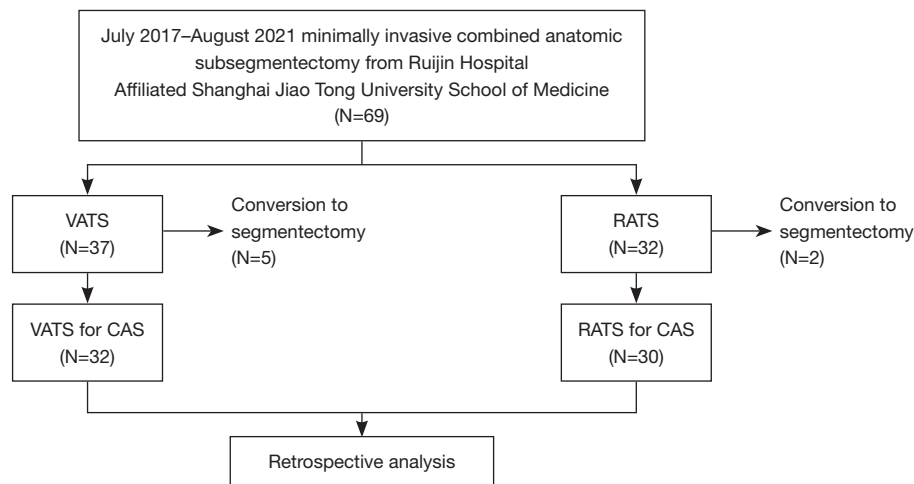
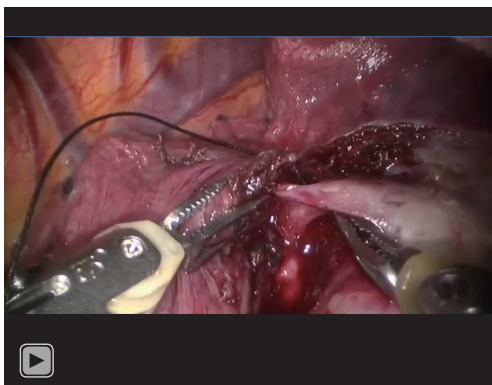


Figure 1 Patients' flow in this study. VATS, video-assisted thoracic surgery; RATS, robot-assisted thoracic surgery; CAS, combined anatomic subsegmentectomy; N, number.



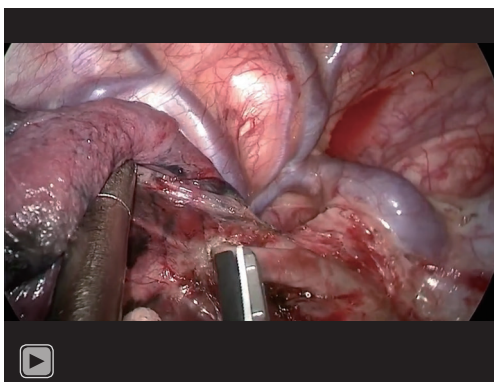
Video 1 Robot-assisted combined anatomic subsegmentectomy performed by using the da Vinci robot.

airflow limitation severity in chronic obstructive pulmonary disease. Clavien–Dindo classifications were used to describe perioperative complications. The 8th edition of the Tumor Node Metastasis (TNM) classification was applied to evaluate the pathological stages of the patients. Since the postoperative pathological N outcomes of all patients in this study were pN0, N upstaging was no longer mentioned. Regarding the cost analysis, the finance department was responsible for calculating of total cost for every patient, representing both the total direct and indirect costs. Direct cost refers to any item used for patient care, including all disposable items during operation, staplers, laboratory tests, imaging tests, and medications. Indirect cost refers to extra cost during in-hospital stay, comprised of overhead costs

and amortization of capital equipment, which includes the cost of purchasing and maintaining these surgical platforms, specifically the videoscope or the da Vinci robot.

Operative techniques

RATS CAS was performed by using the da Vinci robot (Model S/Si; Intuitive Surgical, California, USA) equipped with 4 arms (*Video 1*) as we mentioned in the earlier studies (12,13). Meanwhile, videoscope guidance (Karl Storz, Tuttlingen, Germany) was applied during the VATS CAS procedure via 1 incision (*Video 2*). The main steps for both types of CAS were performed in a similar manner. The first step is dissection of the anatomical target structure at the segmental hilum with silk thread or staplers. Subsequently, the surgeons need to precisely identify inter-subsegmental planes. The surgeons should then accurately separate the intersegmental plane. Arteries and veins were clipped with Hem-o-Lok (Teleflex, Morrisville, NC) or stapled with a vascular stapler. Bronchus was subsequently isolated and stapled. The imaginary intersegmental plane was stapled after ventilating and deflating the remnant lung. All operations were performed by one general thoracic surgeon (H. L.), and clinical assessments were conducted according to National Comprehensive Cancer Network Guidelines. it was imperative to first confirm N0 status. N1 and N2 node resection and mapping is a routine of lung cancer surgery in this study, as well as No.12 and No.13 lymph nodes. and a minimum of three N2 stations should be sampled or



Video 2 Single port video-assisted combined anatomic subsegmentectomy.

Table 1 Patient characteristics

Characteristic	RATS (n=30)	VATS (n=32)	P value
Age, years	46.97±10.81	50.47±12.60	0.25
Gender			0.65
Male	12 (40.0)	11 (34.38)	
Female	18 (60.0)	21 (65.62)	
BMI	23.44±2.48	22.70±2.38	0.24
%FEV1			0.55
≥0.8	20 (66.67)	19 (59.28)	
0.5–0.8	10 (33.32)	13 (40.62)	
<0.5	0	0	
ASA score			0.42
1	8 (26.67)	6 (18.75)	
2	21 (70.0)	26 (81.25)	
3	1 (3.33)	0	
Tobacco use			0.46
Current smokers	3 (10.0)	1 (3.12)	
Abstained for at least 1 year	5 (16.67)	4 (12.5)	
Never	22 (73.33)	27 (84.38)	
Hook-wire localization	13 (43.33)	11 (32.35)	0.47
Tumor size (cm)	0.83±0.27	0.8±0.22	0.67

Mean ± standard deviation (SD) is used to describe continuous data, and n (%) is used to describe categorical data. RATS, robot-assisted thoracic surgery; VATS, video-assisted thoracic surgery; BMI, body mass index; %FEV1, percent forced expiratory volume in 1 second; ASA, American Society of Anesthesiologists.

a standardized lymph node dissection. If enlarged nodes (>1 cm) or positive margins were identified, a frozen section analysis was performed.

Statistical analysis

Statistical analysis was performed by the SPSS software (version 22.0; International Business Machines Corporation, Armonk, NY, USA). Given that the measured data had a normal distribution, homogeneity of variance was analyzed using *T*-tests or Wilcoxon rank sum tests, and reported as mean ± standard deviation. Categorical data were compared using the χ^2 tests or Fisher's exact tests and reported as n (%).

Results

Patient characteristics

A total of 62 patients who underwent CAS via RATS (n=30) or VATS (n=32) met the selection criteria and were enrolled in this study. The patients' demographic and clinical characteristics are summarized in *Table 1*. The RATS and VATS cohorts were comparable in terms of age, gender, body mass index, %FEV1, American Society of Anesthesiologists (ASA) score, smoking history, and approximate tumor size. No significant differences were observed in the baseline characteristics of the patients.

Types of CAS

The types of CAS performed by RATS or VATS are shown in *Table 2*. The nodules are more commonly located on the right lung; specifically, 19 patients (63.33%) in the RATS group, and 22 patients (68.75%) in VATS group underwent right-sided CAS. Of all the cases, S²b + S³a was the most common CAS performed in both lung lobes, followed by S¹a + S². There was no significant difference in nodule location (P=0.65) or the type of CAS performed (P=0.19).

Perioperative results

The perioperative results are summarized in *Table 3*. There were no in-hospital and 30-day mortalities. There was no significant difference between RATS and VATS in the operative duration (127.23±22.99 vs. 128.13±35.42 min; P=0.91), intraoperative blood loss [50 mL [interquartile range (IQR), 30–100 mL] vs. 100 mL (IQR, 50–100 mL);

Table 2 Types and locations of resected subsegments

Surgery category	RATS (n=30)	VATS (n=32)	P value
Location of nodules			0.65
Right	19 (63.33)	22 (68.75)	
Left	11 (36.67)	10 (31.25)	
Type of CAS			0.19
Right lung			
S ¹ + S ² a	0	2	
S ¹ + S ³ b	2	1	
S ¹ a + S ²	4	4	
S ¹ a + S ² a	1	4	
S ¹ b + S ³	0	3	
S ¹ b + S ³ b	0	1	
S ² + S ³ a	0	1	
S ² b + S ³ a	6	5	
S ⁶ + S ⁸ a	2	0	
S ⁶ b + S*	1	0	
S ⁶ b + S ⁸ a	1	1	
S ⁸ a + S ⁹	2	0	
Left lung			
S ¹⁺² + S ³ c	3	0	
S ¹⁺² a + b + S ³ c	0	2	
S ¹⁺² a + S ³	2	1	
S ¹⁺² c + S ³ a	0	2	
S ¹⁺² c + S ⁴	1	3	
S ⁶ + S ¹⁰ a + S*	1	0	
S ⁶ + S ⁸ a	1	0	
S ⁶ b + S ⁷⁺⁸	1	0	
S ⁶ b + S ⁸ a	1	1	
S ⁹ b + S ¹⁰	1	0	
S ⁹ b + S ¹⁰ c	0	1	

N (%) is used to describe categoric data. RATS, robot-assisted thoracic surgery; VATS, video-assisted thoracic surgery; CAS, combined anatomic subsegmentectomy; S*, subsuperior segment.

P=0.70), and the rate of overall complications (23.33% *vs.* 29.41%; P=0.58). Furthermore, no significant difference was found in length of hospital stay [4 days (IQR, 3.5–5 days) *vs.* 3.75 days (IQR, 3–4.75 days); P=0.71] and mean duration

Table 3 Perioperative results

Characteristic	RATS (n=30)	VATS (n=32)	P value
Operative duration, min	127.23±22.99	128.13±35.42	0.91
Blood loss, median [IQR], mL	50 [30–100]	100 [50–100]	0.70
30-day morbidity	7 (23.33)	10 (29.41)	0.58
Clavien I–II	6	8	–
Atrial fibrillation	1	2	–
Air leak	1	1	–
Pleural effusion	1	0	–
Wound infection	0	1	–
Pneumonia	3	4	–
Clavien III–IV	1	2	–
Air leak	0	1	–
Pleural effusion	0	1	–
Pneumonia	1	0	–
Readmission, n (%)	1	0	–
In-hospital mortality	0	0	–
30-day mortality	0	0	–
Duration of drainage, median (IQR), d	2.5 (2.0–3.0)	2 (2.0–3.0)	0.12
PLOS, median (IQR), d	4 (3.5–5.0)	3.75 (3.0–4.75)	0.71

Mean ± SD is used to describe continuous data, and n (%) is used to describe categoric data. RATS, robot-assisted thoracic surgery; VATS, video-assisted thoracic surgery; IQR, interquartile range; PLOS, postoperative length of stay.

of drainage [2.5 days (IQR, 2–3 days) *vs.* 2 days (IQR, 2–3 days); P=0.12]. One readmission occurred in the RATS group because of multiple small discrete lung nodules distributed throughout both lungs, resulting in a second surgery.

Pathologic results

The pathologic results of patients in the RATS and VATS groups are presented in *Table 4*. An R0 resection was achieved in all patients. The most common pathological type was adenocarcinoma (93.33% *vs.* 84.38%; P=0.44). There is no significant difference in the parenchymal margins, and the distribution of the T stage was statistically comparable between two groups. As for the pulmonary

Table 4 Pathological results

Characteristic	RATS (n=30)	VATS (n=32)	P value
Histology lung cancer			0.44
Adenocarcinoma	28 (93.33)	27 (84.38)	
Squamous-cell carcinoma	0	1 (3.12)	
Other	2 (6.67)	4 (12.5)	
R0 resection	30 (100.0)	32 (100.0)	–
Parenchymal margins, median (IQR), cm	2.15 (1.88–2.40)	2 (1.8–2.18)	0.30
pT stage lung cancer			0.13
Benign	1 (3.33)	3 (9.38)	
Tis	1 (3.33)	4 (12.5)	
T1a	21 (70.0)	23 (71.88)	
T1b	7 (23.34)	2(6.24)	
pN stage lung cancer			–
N0	30 (100.0)	32 (100.0)	
N1	0	0	
LN1 stations, median [IQR]	2.5 [1–3]	2 [1–2]	0.008
LN2 stations, median [IQR]	2 [1–3]	1 [0–2]	0.009
No. of LN1, median [IQR]	3 [2–5]	2 [1–2]	0.002
No. of LN2, median [IQR]	2 [1–3]	1 [0–2]	0.007

N (%) is used to describe categoric data. RATS, robot-assisted thoracic surgery; VATS, video-assisted thoracic surgery; IQR, interquartile range; LN, lymph node.

lymph node, there were more N1 lymph nodes [3 (IQR, 2–5) *vs.* 2 (IQR, 1–2); $P=0.002$] and N1 stations [2.5 (IQR, 1–3) *vs.* 2 (IQR, 1–2); $P=0.008$] dissected in the RATS group compared to the VATS group, and the same results were found for the number [2 (IQR, 1–3) *vs.* 1 (IQR, 0–2); $P=0.007$] and the stations [2 (IQR, 1–3) *vs.* 1 (IQR, 0–2); $P=0.009$] of N2 lymph nodes dissected.

Analysis of cost

The comparative cost analysis between the two surgical approaches is presented in *Table 5*. There was a significantly higher mean total cost (\$13,617.6±1,316.84

Table 5 Analysis of cost

Type of cost	RATS (n=30)	VATS (n=32)	P value
Total cost (\$)	13,617.6±1,316.84	9,253.13±1,926.99	<0.001
Direct cost (\$)	7,634.53±1,356.23	7,699.61±1,719.14	0.87
Indirect cost (\$)	5,983.07±176.67	1,553.52±943.52	<0.001

Mean ± SD is used to describe continuous data. RATS, robot-assisted thoracic surgery; VATS, video-assisted thoracic surgery.

vs. \$9,253.13±1,926.99; $P<0.001$) and mean indirect cost (\$5,983.07±176.67 *vs.* \$1,553.52±943.52; $P<0.001$) in the RATS CAS group compared to the VATS CAS group. Nevertheless, no significant difference was found in the mean of direct cost (\$7,634.53±1,356.23 *vs.* \$7,699.61±1,719.14; $P=0.87$) between the two groups.

Discussion

Rapid advances in minimally invasive thoracic surgery have resulted in the clinical application of robot-assisted systems, which has facilitated the development of anatomical pulmonary dissection. Previous research (18) has shown that robotic segmentectomies are safe, effective, and offer excellent perioperative results. Our team has recently conducted a multi-institutional retrospective analysis (13) comparing the early results of segmentectomy via robot-assisted and thoracoscopic-assisted thoracic surgery for the patients with early-stage lung cancer and reported comparable results and oncologic safety in the short term. Here, we report the first analysis to compare the short-term results of CAS using robotic and thoracoscopic approaches for patients with lung cancer at an early stage.

To the best of our knowledge, there are only a few publications (7,8,19,20) focusing on the application of VATS CAS and only our previous research (12) focusing on the use of robot-assisted systems for CAS. In this study, the short-term comparative results of RATS and VATS CAS for patients with lung cancer were prudently analyzed for the first time. Our outcomes demonstrated that for early NSCLC, RATS CAS offers perioperative results similar to those of VATS CAS. No significant difference was observed in operative duration, intraoperative blood loss, rate of overall complications, mean duration of drainage and length of in-hospital stay. Our experience also suggests that surgeons may be able to obtain plenty of benefits from arm 3 in the robotic system when performing CAS. Specifically, control of small bleeders using arm 3 is more

straightforward and convenient, leaving arms 1 and 2 available for operative procedures elsewhere (12).

Another significant finding was that RATS CAS might contribute to the potential improvement of N1 and N2 lymph node retrieval in early-stage NSCLC. Assessment of lymph nodes (LNs) includes the numbers of individual lymph nodes and stations dissected in sublobectomy for lung cancer (19,21). In this work, higher numbers of N1 and N2 LNs and stations were dissected in the RATS group. Our findings concur with those of recent studies (13,22-24). Li *et al.* (22) reported that RATS, compared with VATS, is associated with more lymph nodes stations examined and a higher number of LNs harvested. This could be attributed to the three-dimensional imaging, high-definition visualization, better maneuverability, and improved dexterity provided by the robot-assisted system, which endows the surgeon with better dissection capabilities for LNs around vessels and bronchi (23,24). Although all lymph nodes dissected from both groups of patients in our study were negative for metastasis, there may be a potential tendency to understage patients if adequate lymph node dissection is not performed. The sizes of the dissected lymph nodes are of great importance for precise and accurate pathological staging, as there may be latent neglected positive lymph node metastasis. The latest National Comprehensive Cancer Network guidelines also emphasize the importance of adequate lymph node dissection in sublobar resection. Extended segmental resection not only involves the removal of the affected and adjacent segments but also includes aggressive dissection of LNs surrounding the bronchi of the affected subsegment, as well as the hilum and mediastinum (25). However, in this study, the patient's survival benefit from the additional number of LNs and stations dissected from the RATS group may have been negligible. Dezube *et al.* (26) recently reported a correlation between the number of LNs harvested and long-term survival according to the National Cancer Database, and they found that, for lobectomy, the optimal number of LNs dissected is four, with no survival benefit when additional LN sampling was performed. Further studies, preferably randomized controlled trials, are required to clarify the clinical relevance between the improved LNs harvest and long-term survival in the RATS group.

One of the major concerns regarding the application of RATS is its economic viability. Some studies (27,28) have compared the cost of RATS and VATS and found that the cost of robotic surgery is consistently higher, while others reported no significant difference in cost (29). Musgrove

et al. (30) recently reported that the direct costs of robotic segmental resection and thoracoscopic segmental resection were comparable, although the total cost and indirect cost of the robot group were higher. Similar outcomes were observed in our study, with a significantly higher mean total cost and mean indirect cost in the RATS CAS group compared to the VATS CAS group. Additionally, no significant difference was observed in the mean direct cost between the groups. The Chinese's National Medical Insurance System can cover part of the cost comes from these two types of surgery in the perioperative period. However, no operation cost was covered in RATS CAS. This means the indirect cost of RATS CAS is approximately \$4,000 more than that of the VATS group, which mainly includes replenishment and depreciation of robot specifications.

This study has some limitations. First, the non-randomized retrospective design of this study may have created bias in patient selection. Second, the application of robotic systems is based on the patients' economic levels and preferences, which may also lead to selection bias. Furthermore, although the difference in N1 and N2 lymph node dissection may reveal the potential superiority of robotic systems in the dissection of pulmonary LN, to some extent, the caution of surgeons in identifying or labeling these pulmonary lymph nodes also affects the outcomes. Finally, the purpose of this retrospective study was to obtain perioperative results in the short term with a small number of patients treated; a longer follow-up and larger sample population is needed to compare the efficacy of these two methods. Nevertheless, this study provides highly encouraging results regarding the potential benefits of RATS for CAS.

In conclusion, the perioperative results of RATS and VATS CAS in patients with early-stage NSCLC were compared. RATS CAS may contribute to the potential improvements in N1 and N2 lymph node retrieval.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-1895/rc>

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Conflicts of interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-21-1895/coif>). The authors have no conflicts of interest to declare.

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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Investigation Review Board of Ruijin Hospital (No. KY201996). Because of its retrospective nature, informed patient consent was not required.

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