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Research Article

Robotic Lobectomy for Non-Small Cell Lung Cancer: Technical Aspects and Long-Term Outcomes

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Abstract

Robotic Portal (RPL) and Robotic-Assisted (RAL) lobectomy are becoming increasingly common surgical treatment for lung resection in a community and academic settings. The improved optics, increased dexterity of the instruments, and better ergonomics are only few of the numerous advantages what make this constantly evolving technology unique. Over the years the increased robotic experience demonstrated that RPL and RAL are a feasible, safe, and oncologically sound surgical treatment for early-stage Non-Small Cell Lung Cancer (NSCLC). In this study, we provide general and technical update on the current use of robotic lobectomy and report on the long-term, cancer related outcomes following this novel minimally invasive approach.

Keywords: Robotic lobectomy; Lung cancer; Minimally invasive; Lung resection

Introduction

Lobectomy is currently the gold standard for surgical treatment of non-small cell lung cancer (NSCLC). Since it was firstly described at the Toronto General Hospital in 1932 [1], the surgical technique of lobectomy has dramatically evolved.

Large body of literature has demonstrated Robotic Portal Lobectomy (RPL) and Robotic-Assisted Lobectomy (RAL) to be safe alternatives to VATS and traditional open lobectomy, delivering outstanding intra-operative and short-term post-operative outcomes [2-6]. Despite the profound improvements that have taken place throughout the years and the increasing utilization of robotic systems worldwide, the controversy about the application of RL in thoracic surgery is still open.

The aim of this study is to provide more accurate view on the current use of robotic lobectomy and deliver an update on the long-term, cancer related outcomes following this novel minimally invasive approach.

Robotic nomenclature

In order to allow accurate communication among scientists and surgeons, but also to ensure proper outcome comparison, the American Association of Thoracic Surgeons Writing Committee proposed recently a definition and nomenclature for robotic thoracic surgery [6]. According to the consensus statement, Robotic Portal (RP) operation is defined as an operation that use ports only and the port incision(s) is/are not generally enlarged at any time during the operation to be larger than the trocars in them except for the removal of a specimen. Robotic operations that include a utility incision are defined as Robotic-Assisted (RA) procedures. For more precise description of the various procedures the Committee described the following four step system:

- First Letter=R for robot
- Second Letter=P for portal or A for assist
- Third letter=type of procedure (for the purpose of this paper - L as lobectomy)
- Fourth letter–the number of robotic arms used

Preoperative evaluation and patient selection

The preoperative assessment of patients undergoing RPL/RAL is similar to the evaluation used for planning a conventional open or VATS lobectomy. There is no difference in the type and number of preoperative studies required. No additional cost should be expected when robotic lobectomy is being anticipated. In addition, considering that the minimally invasive approach results in a better functional outcome, patients considered marginal or unfit for thoracotomy may still be considered for robotic lobectomy [7].

Oncological work up

Oncological work up and clinical staging is achieved in all patients *via* Computer Tomography (CT) of the chest with integrated whole-body Positron Emission Tomography (PET). In addition, staging could be complemented using mediastinoscopy, endobronchial ultrasound Fine-Needle Aspiration biopsy (EBUS-FNA) and/or esophageal ultrasound-guided fine needle aspiration biopsy. Those studies are appropriate in selected group of patients with suggested N2 or N1 disease as well as in individuals with synchronous tumors in different sides of the chest or those with tumors larger than 5 cm (even if clinically node negative). A brain MRI should be considered if there

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is concern for metastatic brain involvement such as in symptomatic patients or patients or with large central adenocarcinomas. Also, dedicated CT scan with Intravenous contrast (IV) or alternatively MRI could be performed if concern exists for vascular or vertebral/ nerve invasion, respectively.

There are few relative contraindications that should be considered when performing robotic lobectomy. Below each one of the listed relative contraindications we have added web links to technical videos demonstrating the various surgical procedures:

 Relative contraindications (based on the surgeons experience):

- Vascular invasion
- Extensive mediastinal and/or esophageal invasion
- Locally invasive T4 lesions
- Pancoast tumors
- Massive tumors with diameter >10 cm
- Need for airway reconstruction
- Chest wall invasion
- Hilar nodal disease

In certain cases, tumors with diameter >7 cm (T3), centrally located and/or tumors crossing fissures could also be considered for RPL/RAL based on the adequate patient selection and surgeons experience. Those patients should not be considered early in surgeon's learning curve. In cases, where chest wall resection is indicated, the robotic console could be used for the parenchymal portion of the resection. Hennon et al. [8] has previously shown that VATS chest wall resection has been safe and decreases the extent of the necessary reconstruction. However, to date there are no large published series of combined robotic lung-chest resection, so that the exact benefits of such minimally invasive chest wall resection remain unclear.

Medical work up

Once a tumor has been deemed resectable, all patients undergo the same standard preoperative evaluation independent of the selected surgical approach: conventional open, VATS or robotic lobectomy:

 Pulmonary function testing including measurement of diffusion capacity (DLCO) and spirometry

 Cardiac stress test (intended for patients with history of cardiac disease or high suspicion for cardiac disease and patients with significant smoking history)

Certain individuals who are border line in terms of overall health and/or respiratory parameters are recommended to undergo exercise testing to determine maximal oxygen consumption (VO2 max):

 15 mL/kg*min are considered moderate risk,

 10 to 15 mL/kg*min are high risk

 <10 mL/kg*min are prohibitive risk

From a respiratory point of view, the same criteria used for VATS apply for RL as well. Predicted postoperative forced expiratory volume (FEV1) or DLCO <40% of predicted is considered safe with acceptable morbidity and mortality [9].

Perioperative phase and conduct of operation

Equipment: Da Vinci system® (Sunnyvale, CA, USA) is the only FDA approved robotic system that is considered eligible to perform advanced thoracic surgery. The robotic console significantly evolved over the years introducing four different generations (Standard, S, Si and Xi) with improvements of wide variety of technological features.

All four generations share the same general concept: the operating surgeon sits at a console some distance from the patient, who is positioned on an operating table in close proximity to the robotic unit with its 4 "operating" arms. Fine proprietary endowrist instruments are attached to the arms allowing wide range of high-precision motions. Those motions are initiated and controlled by the surgeon's hand movements, *via* "master" instruments located at the console. The master instruments sense the surgeon's hand movements and translate them electronically into scaled-down micromovements to manipulate the small surgical instruments.

A 6-Hz motion filter filters out any hand tremor. The operation is controlled via binocular screen located at the surgeon's consol. The image comes from a highly maneuverable high-definition digital camera (endoscope) attached to one of the robot arms. In addition, the console is provided with foot pedals that allow the surgeon to engage and disengage different instrument arms, reposition the console master controls without the instruments themselves moving, and activate the various instruments. A second optional console could be linked to the system in for tandem surgery and/or training.

Despite the outstanding quality of visualization when robotic system is used it is important to mention the difference in viewing angle between open, VATS and robotic lobectomy. During a conventional lobectomy, the surgeon has two views of the hilum: the anterior or posterior direction. In VATS or RL the camera approaches the hilum from an inferior direction. The relationships between the various anatomic structures do not change, however the perception and visibility need to be adjusted. As a consequence, the different viewing angle could affect the interpretation of the anatomy, especially at the beginning of the surgeon's learning curve.

Patient positioning and port placement: Similarly to conventional and VATS lobectomy, in RPL/RAL single lung ventilation is accomplished by placement of the double lumen endotracheal tube prior to positioning the patient. When robotic lobectomy is anticipated, it is important to check the ability to tolerate single lung ventilation prior to placing the drapes, as repositioning the tube will be extremely difficult once the robot is docked. As with all lobectomies, the intubated patient is positioned in lateral decubitus position.

Depending on the da Vinci generation, the placement of the robotic ports might vary. Independent on the type of console we recommend marking the location of the scapula, the spinous processes the entire length of the patients back and number the intercostal spaces. For most resections, we place the ports in the 8th or 9th intercostal space, although some surgeons may choose to place their ports in the 7th intercostal space for upper and middle lobectomies. Once the chest has been entered, CO_2 is insufflated (range, 5 mmHg-8 mmHg) in order to depress the diaphragm, push the lung, enlarge the chest cavity and guarantee a good exposition of hilar structures.

As any surgical procedure, in RL there are different techniques that have been described. Louie et al. [10] and Anderson et al. [11]

described a three-arm robotic lobectomy with a utility port. Park et al. [12] reported a three arms technique with two thoracoscopic ports and a 4 cm utility incision. Gharagozloo et al. [13] reported a hybrid technique with three robotic arms, (positioned at the 8th, camera, 6th and 5th intercostal space), in this case the surgeon used a robotic approach for hilar structures dissection, then the platform was removed and he returned to the operating table to complete the operation. Jang et al. [14] used a utility incision at the fifth intercostal space. Ninan and Dylewski [15] reported a three arms technique using the same intercostal space for all ports (the 5th or 6th) and a utility port over the 11th rib. Veronesi et al. [16] reported the safety of a 4-arm robotic assisted (not completely portal) lobectomy (using a 3-cm to 4-cm access incision as used by VATS surgeons) in 54 patients. Cerfolio et al. [17] described four arms robotic lobectomy without utility incision as well.

Surgical technique: We perform robotic portal lobectomy using total of 5 ports placed in the 8th or 9th intercostal space. Figures 1-4 demonstrate our suggested port placement for left and right RPL for the last two console generations Si and Xi: Once the thoracic cavity has been entered, the pleura surface is carefully inspected in order to confirm the absence of metastasis. The next step during our performance of robotic lobectomy is the dissection of the mediastinal Lymph Nodes (LN). This step is used for exposing the hilum structures and also later for oncologic staging.

Right mediastinum:

- Anterior retraction of the lung
- Division the inferior pulmonary ligament
- Remove LN stations 9 and 8
- Medial/anterior retraction of the lower lobe in order to access LN station 7
- Inferior retraction of the upper lobe in order to access LN 2R and 4R
- Avoid dissection too far superior in order to prevent injury to the right recurrent laryngeal nerve that loops around the subclavian artery

Left mediastinum

- Anterior retraction of the lung
- Divide the inferior pulmonary ligament
- Remove LN stations 9 and 8
- Access LN station 7 in the space between the inferior pulmonary vein and lower lobe bronchus, lateral to the esophagus. During the dissection the vagus should be retracted toward the aorta and the esophagus
- Inferior traction of the left upper lobe in order to access LN stations 5 and 6
- In contrast with the right chest, 2L LN cannot be accesses because of the aortic arch, 4L LN station is accessible for dissection
- Careful dissection in the aorto-pulmonary window in order to avoid injury to the left recurrent laryngeal nerve

Once the initial mediastinal LN dissection has been completed, we proceed with the formal pulmonary lobectomy as follow:

Right chest:

Upper lobe:

- Expose the hilum by lateral and posterior retraction of the Right Upper Lobe (RUL)
- Identify the bifurcation between the right upper and middle lobar veins and dissect it off the underlying pulmonary artery
- Encircle the superior pulmonary vein with a vessel loop and divide the truncus branch
- Anterior reflection of RUL in order to demonstrate the bifurcation of the right main stem bronchus
- Encircle and divide the RUL bronchus
- Once the bronchus and the vein are divided, the specimen should be handled with maximal caution in order to avoid tear in the remaining pulmonary artery
- After removing the N1 LN, expose the posterior segmental artery to the RUL, encircle and divide the vessel
- Verify that there are no additional branches of the pulmonary artery attached and divide the fissure in order to free the specimen.

Middle lobe:

- Expose the hilum of the Right Middle Lobe (RML) by lateral and posterior retraction of the RML
- Identify the bifurcation between the right upper and middle lobar veins and dissect it off the underlying pulmonary artery
- Encircle the right middle pulmonary vein and divide it
- Divide the fissure between the RML and Right Lower Lobe (RLL) from anterior to posterior without injuring segmental arteries to the RLL
- Identify and isolate the RML bronchus and dissect the Level 11 LN
- When the posterior dissection of the fissure is continued, one should identify the one or two middle lobar segmental arteries that should be isolated and divided
- Complete the division of the fissure

Lower lobe:

- Division of the inferior pulmonary ligament to the level of the inferior pulmonary vein
- Dissection of the bifurcation of the right superior and inferior pulmonary vein and identification of the RML vein branch/ branches
- Encircle and divide the right inferior pulmonary vein
- Dissect, identify and ligate the superior segmental artery
- The Right Lower Lobe (RLL) bronchus is isolated, taking care to visualize the right middle lobar bronchus crossing from left to right. The surrounding lymph nodes are dissected and the bronchus divided

Left chest:

Upper lobe:

- Expose the hilum by lateral and posterior retraction of the Left Upper Lobe (LUL)
- Identify and dissect the bifurcation of the superior and inferior pulmonary veins
- Divide the fissure if not complete
- Posterior reflection of the lung and establishing of a subadventitial plane. The lingual branches are encountered and divided in the fissure
- Dissect, isolate and divide the posterior segmental artery followed by transection of the lingular artery
- Isolation and division of the superior pulmonary vein
- Next structure to be encircled and divided is the left upper lobar bronchus
- Anterior retraction of the LUL with dissection and removal of the level 10 lymph nodes

Lower lobe:

- Division of the inferior pulmonary ligament to the level of the inferior pulmonary vein with consecutive posterior reflection of the lobe
- Dissection the bifurcation of the left superior and inferior pulmonary veins
- Anterior reflection of the lung followed by identification, isolation and division of the superior segmental artery
- Consider division of the common trunk to left lower lobe basilar segments as long as this does not compromise the middle lobar segmental vessels
- Divide the fissure if not complete in order to expose the pulmonary artery
- Division of the arterial branches followed by posterior reflection of the lung
- Division of the inferior pulmonary vein
- Isolate the LLL bronchus, dissect the surrounding LN and divide the bronchus

Short-and long term outcomes

Perioperative and postoperative morbidity and mortality: Robotic Lobectomy has been shown to be a safe procedure with very low morbidity and mortality. Cerfolio et al. [18] published recently a multi-institutional study representing the largest series on robotic lobectomy to date. A total of 1339 patients underwent robotic lobectomy in four institutions in the United States and Europe. The reported 30-day and 90-day operative mortality was 0.2% and 0.5%, respectively. The estimated major morbidity in this retrospective review was 8%. Another international study led by the thoracic group at Memorial Sloan Kettering has also previously demonstrated 30-day mortality rate of 0.25%, a 90-day mortality rate of 0.5%, and a major morbidity rate of 9.6% in patients undergoing robotic anatomic pulmonary resection (lobectomy and segmentectomy) [19]. The reported conversion rate to thoracotomy varies widely from 1%-9% depending on the source and experience of the surgeons [18,20,21]. According to the largest published series on robotic lobectomy, conversions occurred in 116 patients (9%) and in 24 (2%) the indication was bleeding [18]. Park et al. [19] converted to thoracotomy in 27 out of 325 patients or 8% of the cases. Those numbers are consistent with the largest series of VATS lobectomies, where the conversion rate varies from 2.5% to 17.5% [22-24].

Robotic lobectomy is equivocal to VATS in regards to blood loss, blood transfusion, air leak, chest tube duration, length of stay, and mortality when compared to traditional open technique [9,20,25]. Cerfolio et al. [26] reported median blood loss of 50 cc per lobectomy. Vascular injury is rare event, and when it does occur, it can occasionally be repaired without converting to a thoracotomy [26]. In a propensity-matched analysis, Oh et al. [27] demonstrated comparative analysis of perioperative clinical outcomes from elective RL, VATS, and Open Lobectomy (OL). When comparing total of 2775 patients in each group, the Operative Time (OR) time needed to perform RL (275.5 ± 94.6 min) was slightly longer but statistically significant when compared to OL (235.3 min ± 93.5 min) or VATS respectively (247.6 min ± 86.8 min). Considering the data of this study spans over 4 years (from 2011-2015) one could assume that the prolonged OR time is based on evolving technology (transition from one generation console to another) and the learning curve of the surgeons. In a multicenter retrospective study including 325 patients, Park et al. [19] reported that both conversion rates (11% [17/150] *vs.* 5.7% [10/175]) and median operative times (210 minutes *vs.* 195 minutes) were lower after the first 50 cases at each center. Cerfolio et al. [18] included 1339 patients from four high volume centers with median operative time of 136 min (38-411) - almost twice faster than the data provided in the propensity matched analysis.

Hospital length of stay is another important metric when assessing the performance of an advanced surgical procedure. Robotic lobectomy does not prolong the hospital stay of the patients and it has significantly improved over the years. Oh et al. [27] reported median Hospital Length of Stay (HOS LOS) of 5 days for RL, 6 days for VATS and 7 days for OL. Park et al. [19] reported median length of stay of 5 days (range, 2 to 28 days) when reviewing the data of 325 consecutive patients from November 2002 through May 2010 [19]. The international multi-institutional study from Cerfolio et al. [18] reported a HOS LOS as low as 3 days (1 to 86). An overview of the various perioperative and postoperative outcomes are demonstrated in Table 1.

The lymph nodes: Lymph nodes are well known predictors of oncologic outcome and survival. Appropriate lymph node dissection is important not only for accurate staging, but also for therapeutic purposes. If robotic lobectomy is used as a surgical technique to conduct oncologic procedures, it is important to assess how RL perform during a lymph node dissection.

From a technical point of view, LN dissection in RL is facilitated by the great precision of the wristed instruments available at the console. It has been demonstrated that the use of RL results in upstaging of early stage lung cancers (clinical T1a, T1b, and T2a). In the retrospective data from Cerfolio et al. [18], 10.9% of all patients were upstaged: 6.6% were upstaged owing to hilar (pN1) disease and 4.3% were upstaged owing to mediastinal (pN2) disease. Compared with prior series, this rate of overall nodal upstaging was similar to VATS (8% to 12%), but lower than thoracotomy (20% to 25%) [15]. other investigators have demonstrated a comparable number of

Table 1: Comparable overview of selected perioperative and postoperative outcomes (robotic lobectomy, VATS, open/conventional lobectomy). *The reported 4612 patients are review of the National Data Bank with median conversion rate 8.1% (2.5 to 24%).

Author/Year	Cerfolio [18]	Park [19]	Adams [20]			Ccrfolio [21]		Oh [27]		
Type of operation	robotic	robotic	robotic	VATS	open	robotic	open	robotic	VATS	open
Total number of patients	1339	325	116	4612	5913	106	318	2775	2951	2775
30 day operative mortality	0.20%	0.30%	0	1%	2.20%	0	0.03	1.30%	1.40%	2.20%
90 day operative mortality	0.50%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Complications										
None	76%	75%	N/A	N/A	N/A	73%	62%	65.40%	62.40%	56.80%
Minor	16%	7%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Major	8%	12%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Operative Time, min	136 (38-411)	206 (110-383)	241 ± 64.9	179.8 ± 84.2	175.5 ± 84.2	132 ± 60	90 ± 48	275 ± 94.6	247.6 ± 86.8	235 ± 93.5
EBL	50 (10-1000)	N/A	N/A	N/A	N/A	30 ± 26	90 ± 22			
Conversion to thoracotomy, total n (%)	116 (9%)	27 (8.3%)	4 (3.3%)	8.1%*	N/A	13 (9.3%)	N/A	179 (6.5%)	387 (13.1%)	N/A
Length of stay	3 (1-86)	5 (2-28)	4.7± 3.1	5.3+7.1	7.3± 7.6	2 (1-7)	4 (1-67)	7 ± 5.7	7.3 ± 7.5	8.9 ± 5.9

lymph nodes dissected during robotic and VATS lobectomy [13]. In an international study the number of dissected LN varied from 10 to 19 depending on the institution (median number of removed LN=13) [26]. The authors did describe that they performed a formal complete thoracic lymphadenectomy and not "only" lymph node sampling. As result they demonstrated better intra-operative staging during resection and more liberal discovery of N2 disease, which led to the use of adjuvant chemotherapy in 76% of these patients, which eventually translated in improved survival rates.

Overall and stage specific long-term survival: Park and colleagues, descried an overall and stage-specific survivals in RL that are consistent both with the largest recent series of VATS lobectomies [19,23,24] and the data used for the seventh edition of the lung cancer staging system, which was largely derived from conventional open surgery [28]. Onaitis et al. [23] reported 2-year overall survival of 80% and stage-specific survivals of 85% for stage I and 77% for stages II and higher in a cohort of 500 patients undergoing VATS lobectomy for clinical early-stage disease. Goldstraw et al. [28] reported 5-year overall survivals of 73% and 58% for stages IA and IB, respectively, and 46% and 36% for stages IIA and IIB. In a retrospective review of 325 patients undergoing robotic lobectomy, 76% of the patients (248/325) had pathologic stage I disease (IA, 176; IB, 72), and in 68 (21%) patients the severity of disease was upstaged [19]. The authors

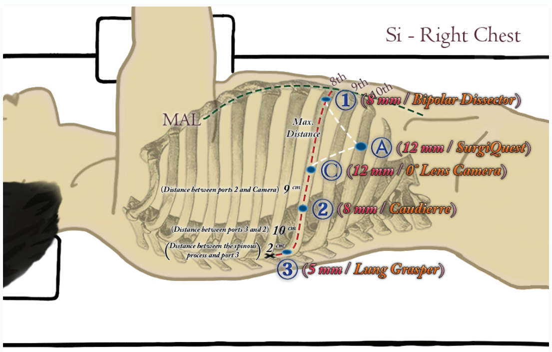

Figure 1: Working port placement for right portal lobectomy (RPL-4) using SI console.

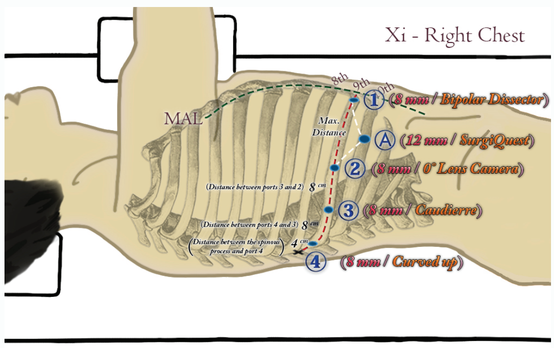

Figure 3: Working port placement for right portal lobectomy (RPL-4) using XI console.

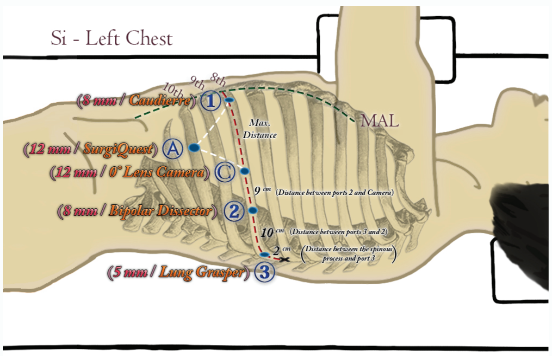

Figure 2: Working port placement for left portal lobectomy (RPL-4) using SI console.

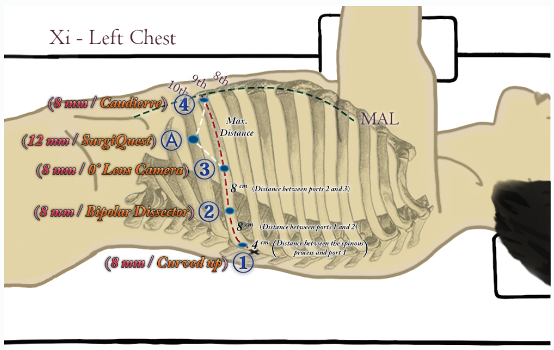

Figure 4: Working port placement for left portal lobectomy (RPL-4) using XI console.

reported a median tumor size of 2.2 cm (range, 0.7 cm to 10.2 cm), and the median number of lymph node stations dissected was 5 (range, 2 to 8). From the entire cohort, 61 (19%) patients had metastatic nodal disease, and 67 patients received adjuvant cytotoxic chemotherapy. After a median follow-up of 27 months, 32 (10%) patients had had recurrence, and 25 died of their disease. The majority (72%) of detected recurrences were distant (distant only, 17; locoregional+distant, 6), and 28% (9/32) were locoregional only. The overall 5-year survival for the group was 80% and stage specific survival at 5 years was as follow: 91% for stage IA, 88% of stage IB, 49% for stage II. According to the authors, the excellent 5-year survival in pathologic stage I (IA, 91%; IB, 88%) was likely related to the fact that the median tumor size was small (2.2 cm).

Cerfolio et al. [18] reported a favorable 5 year survival as well. Total of 1339 patients were followed for median of 30 months with 5-year overall survival of 77%. Tumor recurrence was observed in 128 patients (cumulative incidence=15%, 95% CI=13% to 18%) with a median disease-free interval of 16 months (range 1 to 82). Local recurrence was recorded in 26 patients (cumulative incidence=3%, 95% CI=2% to 5%). The 5 year stage specific survival was consistent with the data reported by thoracic group at Memorial Sloan Kettering: 83% for Stage IA, 77% for stage IB, 68% for Stage IIA, 70% for Stage IIB and 62% for Stage IIIA. There are several explanations for the improved survival rates. First, the minimally invasive approach is believed to be associated with reduction of cytokines and subsequent immunocompromized state when compared to a conventional thoracotomy. Flores et al. [29] demonstrated a lower systemic rate (solid organ metastases) of non-small cell lung cancer recurrence in patients who underwent resection via VATS when compared to those who had a thoracotomy when matched stage for stage. Second, the technical ease in performing lymphadenectomy during RL allows higher number LN to be obtained which leads to greater upstaging [30]. A better N1 as well as N2 lymph node dissection may lead better staging and a higher chance of adjuvant chemotherapy.

Conclusion

Robotic portal and robotic-assisted lobectomy are feasible, safe, and oncologically sound surgical treatment for early-stage NSC lung cancer. According to the available data, the technique is reproducible across multiple centers and delivers long term results consistent with the best seen with the established minimally invasive VATS. RL will continue to gain popularity, both in community and academic settings as a novel technology for lung resection.

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