Editorial

Robotic-assisted lobectomy for locally advanced N2 non-small cell lung cancer

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In their surgical technique article, "*Three-arm robot-assisted thoracoscopic surgery for locally advanced N2 non-small cell lung cancer*", Cheng *et al.* describe their approach to robotic lobectomy (RATS) in a patient with a clinical T1N2M0 adenocarcinoma (1). They underscore several advantages of a robotic approach and provide an excellent illustrative video. Minimally invasive approaches to pulmonary resection, including robotic approaches, are generally preferred due to decreased morbidity, length of stay (LOS), and quicker recovery. While initially there were concerns regarding oncologic outcomes, several studies have reported equivalent outcomes to open lobectomy with decreased chest tube duration, pain, postoperative complications, and LOS (2-4). However, the use of minimally-invasive approaches for locally-advanced disease, especially after induction therapy, is more controversial and the data more limited.

Robotic *vs.* thoracoscopic *vs.* open approaches

While a robotic approach provides the surgeon with improved dexterity and visualization, it remains unclear whether this directly affects patient outcomes. Several authors have reported at least equivalent long-term survival when comparing thoracoscopic (VATS) and open lobectomy (3,4) and that experienced thoracic surgeons can safely perform RATS lobectomy with no significant differences in morbidity or mortality (5-7). Tchouta *et al.* found a shorter LOS and decreased mortality at high-volume centers analyzing data from 8,253 robotic lobectomies in the Healthcare Cost and Utilization Project National Inpatient Sample (8). While Yang *et al.* found that minimally-invasive approaches were associated with shorter LOS and improved 2-year survival, they were also associated with increased 30-day readmissions in the National Cancer Database (30,040 lobectomies for stage I lung carcinoma including 7,824 VATS and 2,025 RATS) (9).

Liang *et al.* analyzed 7,438 patients undergoing lobectomy or segmentectomy in a meta-analysis of 14 studies comparing RATS versus VATS and found a lower rate of conversion to thoracotomy (10.3% *vs.* 11.9%) and decreased 30-day mortality (0.7% *vs.* 1.1%) with RATS (10). There were no significant differences in OR times, postoperative complications, chest tube duration, or LOS. Louie *et al.* found that operative times were longer for RATS but nodal upstaging, complications, hospital stay, and 30-day mortality were equivalent in a study analyzing data from the STS General Thoracic Surgery Database (1,220 robotic and 12,378 VATS lobectomies) (11). Paul *et al.* found an increased risk of iatrogenic bleeding complications with RATS of 5.0% versus 2.0% evaluating 37,595 thoracoscopic and 2,498 robotic lobectomies in the Nationwide Inpatient Sample (12). Kent *et al.* analyzed a cohort of 33,095 patients (20,238 open, 12,427 VATS, and 430 RATS) from multiple state inpatient databases and found a decreased LOS, complication rates, and mortality (0.2% *vs.* 1.1%) with RATS although this was not significant (13).

Data is more limited for locally advanced disease, especially after neoadjuvant therapy, and the use of minimally-invasive approaches after induction therapy remains more controversial, especially after radiation. Although studies, including a series of 43 patients undergoing VATS resection by Huang *et al.*, have shown that locally advanced disease can be approached minimally-invasively with similar perioperative outcomes and survival even after neoadjuvant treatment, the approach has not been widely adopted (14), and many minimally-invasive thoracic surgeons continue to perform thoracotomies for advanced, central lung cancers or following neoadjuvant chemoradiation.

Park *et al.* evaluated patients undergoing resection for stage II and IIIA non-small cell lung carcinoma after induction chemotherapy including 397 undergoing thoracotomy, 17 robotic, and 14 VATS (15). A complete R0 resection was achieved in 97%. The minimally-invasive group had a shorter LOS but a 26% conversion rate to thoracotomy. Glover *et al.* evaluated 256 patients undergoing robotic lobectomy including 52 cN1 or cN2 patients with 7 patients undergoing induction chemotherapy and 6 patients undergoing neoadjuvant chemoradiation (16). They found higher rates of recurrent laryngeal nerve injury, tracheal/bronchial injury, and pulmonary embolus after induction chemotherapy with or without radiation. The largest study to date is a multicenter trial by Veronesi *et al.* evaluating patients with clinically evident (72 patients) or occult (151 patients) N2 non-small cell lung cancer (NSCLC) (17). Almost half of the patients with clinical N2 disease (34/72) underwent neoadjuvant treatment. The authors concluded that a robotic approach was safe and effective in patients with locally advanced disease with an overall survival similar to published open thoracotomy studies.

Lymph node dissection

Initially, there were concerns that thoracoscopic lobectomy would compromise nodal staging. However, VATS mediastinal lymph node dissection (MLND) has been reported to be equivalent to open node dissection in several studies, and RATS MLND may actually have potential advantages in nodal evaluation (2). Wilson *et al.* found nodal upstaging in 5.2%, 7.1%, and 5.7% after VATS and 7.4%, 8.8%, and 11.5% after RATS for T1a, T1b, and T2a tumors respectively in a study evaluating 302 patients in the STS Database (18). The authors concluded that nodal upstaging after robotic resection was similar to open node dissection and superior to VATS. Disease-free and overall survival were comparable to previous VATS studies.

In contrast, Louie *et al.* found no difference in nodal upstaging after evaluating 12,378 VATS and 1,220 robotic lobectomies in the STS General Thoracic Surgery Database (11). Yang *et al.* also found no significant difference in nodal upstaging for patients undergoing lobectomy for stage I lung carcinomas in the National Cancer Database (9), and Liang *et al.* reported no difference in the number of lymph node stations or lymph nodes retrieved (10). Rajaram *et al.* found that a smaller number of lymph nodes were removed and more than 12 lymph nodes were obtained less frequently with RATS after evaluating 62,206 patients in the National Cancer Database (19).

Induction therapy

Treatment of locally advanced N2 disease (stage IIIA) remains a challenging and controversial area. However, the case presented by Cheng *et al.* may not be representative of the more common neoadjuvant treatment approaches for stage IIIA disease or fully demonstrate the potential benefits of the robot for dissection of hilar adhesions after induction chemotherapy or chemoradiation (1). According to the most recent NCCN (National Comprehensive Cancer Network) guidelines, stage IIIA (T1N2) non-small cell lung carcinoma should be treated with either definitive or induction chemotherapy with or without radiation followed by surgery. The ESMO (European Society of Medical Oncology) guidelines recommend induction chemotherapy with or with radiation followed by surgery or resection followed by adjuvant chemotherapy but only for biopsy-confirmed single station N2 disease. The surgical technique article by Cheng *et al.* does not describe the final pathology from the patient's individual nodal stations (pT1N2M0). However, the patient appears to have enlarged 2R, 4R, and 10R lymph nodes on imaging consistent with multistation disease (1), and the ESMO guidelines recommend concurrent definitive chemoradiation for multistation N2 disease.

The authors state that the patient refused EBUS-FNA or induction therapy due to fear of disease progression. However, they state in the discussion that patients with stage III disease usually have systemic treatment prior to surgery. It is unclear why this patient was chosen to illustrate their robotic approach to locally advanced N2 disease when the overall treatment was not consistent with the standard treatment or society guidelines. In addition, it is unclear why this patient was enrolled in their randomized study comparing RATS and open surgery in stage II–IIIA NSCLC if they did not undergo standard treatment.

A minimally-invasive or robotic approach may be beneficial in patients undergoing resection after induction treatment, and improved visualization, dexterity, and bipolar dissection can be helpful with hilar scarring due to radiation. Some authors have even suggested that minimally invasive approaches may be associated with improved long-term survival due to decreased immunologic and stress responses (20). More rapid recovery from thoracoscopic lobectomy may also allow earlier treatment with adjuvant chemotherapy. In the ANITA trial, only 60% of patients were able to complete 3 cycles of adjuvant chemotherapy (21). Petersen *et al.* found a decrease in delayed or reduced chemotherapy doses with 61% of patients receiving greater than 75% of chemotherapy doses after VATS compared to only 40% after open lobectomy (22). In clinical trials evaluating adjuvant chemotherapy after lung cancer resection, approximately half of all patients actually received the planned chemotherapy dose.

Robotic technique

Cheng *et al.*, describe their robotic technique starting with port placement in the 7th or 8th intercostal space (1). While the ports shown in the provided figure appear to be in different interspaces, I generally try to place the majority of the ports in the same space to reduce the risk of injuring multiple intercostal nerves, potentially decreasing postoperative pain. With the introduction of the robotic stapler, placing the anterior-most port as inferior and anterior as possible is critical to provide the stapler with enough length to fully roticulate. Cheng *et al.* also utilize a 4th interspace utility incision. I use a completely portal technique for the dissection with CO_2 insufflation to 5–8 mmHg to displace the diaphragm improving exposure, especially for lower lobectomies. I also start with the lymph node dissection although I take down the inferior pulmonary ligament obtaining 9R lymph nodes and allowing the lower lobe to move superiorly to help fill the post-lobectomy space. I complete the subcarinal and right paratracheal lymph node dissection before the lobectomy allowing more time for hemostasis, packing each station with oxidized cellulose.

I also agree with the authors that flipping and manipulating the lung should be minimized to avoid air leaks. Gauze rolls can be used to manipulate the lung rather than directly grasping the parenchyma, maintain a bloodless field, and serve as a sponge to tamponade any significant bleeding, which is important when the surgeon is at the robotic console and not at the bedside. While the authors used a monopolar hook, I prefer the curved bipolar dissector. In their video, the energy setting seems a little high with arcing from the hook to the fenestrated grasper and metal suction. The bipolar is less likely to cause collateral thermal or electrical injury, especially close to nerves and vessels, with increased scarring after induction therapy.

Cheng *et al.* describe a posterior approach dividing the bronchus first followed by the fissure and then stapling the artery and vein together. Leaving the artery for last increases the risk that the artery could be avulsed especially with the lack of haptic feedback with the robot. While simultaneous stapling of the hilum has been described previously, stapling the artery and the vein together could theoretically increase the potential for developing an arteriovenous fistula. I generally prefer an anterior to posterior approach similar to a standard thoracoscopic approach and divide the pulmonary veins followed by the arteries, bronchus, and then the fissure last.

Cheng *et al.* advocate using a three-arm approach. Both Cerfolio and Veronesi have described a 4-arm robotic technique (23,24). I prefer the 4-arm approach allowing the surgeon to control the retraction of the lung and the direction of the dissection with less reliance on an experienced bedside assistant. While Veronesi uses a utility incision, I use a total of 4 robotic ports only and enlarge the anterior port to remove the specimen in a bag. Another important difference is that we use the da Vinci Xi robot while the authors use the da Vinci S. The Xi robot addresses many of the shortcomings of the S/Si robots for a lobectomy including decreased arm collisions, patient clearance adjustments to allow the robotic arms to work facing towards the diaphragm when taking down the inferior pulmonary ligament, the ability to move the camera to any robotic port improving visualization, and the availability of a robotic stapler.

Regardless of the specific approach used, complex thoracoscopic procedures are associated with a learning curve due to reduced tactile feedback, loss of degrees of freedom, and counterintuitive hand-eye coordination. Robotic surgery has overcome some of these challenges with three-dimensional imaging, improved dexterity with greater degrees of freedom, and better hand-eye coordination. Similar to VATS lobectomy, with a learning curve of approximately 50 cases (25), transitioning to a robotic approach is associated with a learning curve, and a robotic lobectomy should only be performed in patients with locally advanced disease by experienced surgeons, especially following neoadjuvant chemoradiation.

Conclusions

Robotic surgery has overcome some of the shortcomings of thoracoscopy by combining improved dexterity and visualization which could be especially useful with hilar scarring after induction therapy and may also improve MLND in these patients with known N2 disease. The robotic approach has been found in several studies, including one across multiple centers, to have at least equivalent outcomes to VATS and open thoracotomy. There is a significant learning curve, and robotic lobectomy in locally advanced N2 disease, especially after induction radiation, should only be attempted by experienced robotic, thoracic surgeons. There should also be a low threshold to convert to an open thoracotomy when needed due to dense hilar scarring. With increasing experience, more thoracic surgeons performing robotic surgery, and growing patient demand, further studies are needed to evaluate outcomes following RATS lobectomy, and we look forward to the results of the randomized trial Cheng *et al.* are performing comparing robotic to open resection for locally advanced stage II–IIIA disease.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

Ethical Statement: The author is 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.

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