



Review Article

Advances in lung cancer surgery

Mark W. Hennon^{1,2}, Sai Yendamuri^{1,2*}

Departments of Thoracic Surgery, Roswell Park Cancer Institute, ¹Surgery, State University of New York, Buffalo, NY, USA

E-mail: sai.yendamuri@roswellpark.org

*Corresponding author

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Abstract

The last few years have witnessed an explosion of the use of minimally invasive techniques for the detection, diagnosis, and treatment of all stages of lung cancer. The use of these techniques has improved the risk–benefit ratio of surgery and has made it more acceptable to patients considering lung surgery. They have also facilitated the delivery of multi-modality therapy to patients with advanced lung cancer. This review article summarizes current surgical techniques that represent the “cutting edge” of thoracic surgery for lung cancer.

Keywords: Lung cancer; outcomes, thoracoscopy

INTRODUCTION

This is an exciting time for those involved in surgically treating patients with non-small-cell lung cancer (NSCLC). New techniques and technology are continuously being developed and refined for the diagnosis, staging, resection, and palliation of NSCLC. As treatment algorithms for patients with NSCLC become increasingly complex, these new techniques and tools allow for the optimization of treatment planning, which is driven by accurate clinical and surgical staging. The tools available for the surgical approach to undiagnosed pulmonary nodules are expanding as well. Advancements in minimally invasive approaches to lung surgery have decreased the morbidity traditionally associated with anatomic lung resection and expanded indications for thoracoscopic resection. With these improved techniques, patients with more advanced stage lung cancer can be considered for thoracoscopic resection safely with the potential for decreased post-operative morbidity,

which may increase their chances completing adjuvant therapy. Finally, unresectable patients who are not candidates for anatomic lobectomy or pneumonectomy have more palliative options for effectively treating their disease. This review article attempts to summarize investigations that represent the frontiers of thoracic surgery for lung cancer.

Advances in diagnostic techniques for lung cancer

Important enhancements for diagnosis include endobronchial ultrasound (EBUS) and navigational bronchoscopy, a clinical are a shared by pulmonologists and thoracic surgeons. As these advances in these areas are described in another article in this series, they will not be discussed here.

Intraoperative ultrasound for localizing lung nodules

Localizing pulmonary nodules when performing thoracoscopic resection can be difficult depending on the size and location of the lesion. Traditionally, the gold standard for locating embedded, peripheral pulmonary nodules has been by manual palpation, which requires thoracotomy. Manual palpation is not feasible thoracoscopically and is an inherent limitation. When approaching a potentially challenging nodule thoracoscopically, other options for increasing the yield include image-guided needle localization, fiducial marker placement, or India ink staining through means such as navigational bronchoscopy. Potential drawbacks for these approaches include the need for

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additional pre-operative procedure time, risk for pneumothorax, needle migration or dislodgement when isolating the operative lung, and non-specific ink staining in the targeted lung region.

Intraoperative ultrasonography during video-assisted thoracoscopic surgery (VATS) has become a viable option for detecting pulmonary nodules at the time of surgery. Utilizing an articulating laparoscopic 10-mm ultrasound probe (B-K Medical, Herlev, Denmark) and conductive gel applied topically to the lung surface, lesions not visible by traditional VATS techniques can be identified and localized. Once identified, the lesion can be removed with standard wedge resection techniques. Reports describing the usefulness of intraoperative ultrasound are increasing.^[1-3] A previously reported series of 54 consecutive patients who underwent transthoracic ultrasonography-assisted VATS for localization and resection of 65 lung nodules revealed that 16 of 65 nodules diagnosed pre-operatively by computed tomography were not visible or palpable by VATS alone. Intraoperative ultrasound was able to locate and identify 15/16 of these nodules.^[3] Potential drawbacks to the technology are minimal and include an operator learning curve, but risk to the patient is minimal, and the potential for enhanced localization of lung nodules may prevent unnecessary thoracotomy in many cases.

Advances in surgical staging of lung cancer

Accurate surgical staging of mediastinal lymph nodes remains critical in the management of NSCLC. In addition to avoid futile surgery, accurate surgical staging helps select patients who will benefit from neoadjuvant treatment and allow for accurate comparison of different clinical studies. Restaging after neoadjuvant treatment is critical in determining who may benefit from surgical resection. Traditionally, mediastinoscopy has been the gold standard for surgical staging of NSCLC. Non-surgical techniques for staging that include EBUS with transbronchial needle aspiration exist, and continue to undergo validation. Evolving techniques for the surgical staging of NSCLC, including video-assisted mediastinal lymphadenectomy (VAMLA) and transcervical extended mediastinal lymphadenectomy (TEMLA) have further advanced staging effectiveness and accuracy in patients with NSCLC.

Transcervical extended mediastinal lymphadenectomy

Recent advances in surgical staging with video-assisted mediastinoscopy and TEMLA now afford the thoracic surgeon with more effective surgical tools, but at a potential cost (mildly increased risk for recurrent laryngeal nerve injury with TEMLA). With TEMLA, mediastinal lymph nodes are completely dissected out, from all lymph node stations, providing the most thorough, accurate means of staging. Due to the increased complexity of the procedure and potential for

complications, indications may vary from one institution to another.^[4] In the largest reported series of patients undergoing TEMLA ($N = 698$) for staging of NSCLC, sensitivity for detecting N2/3 disease was found to be 96.2%. In 445 patients who subsequently went on to thoracotomy, omitted N2 disease was found in only seven cases (1.6%). Negative predictive value was 98.7%. Overall morbidity of the procedure was reported to be 6.6%, with recurrent laryngeal nerve palsy occurring in 16 (2.3%) patients. No life-threatening intraoperative complications were reported. Of five deaths in the series, none were attributed to the TEMLA procedure itself.^[5]

We reserve TEMLA for patients' at high risk for having mediastinal lymph node involvement. Those with larger tumors, hilar nodal involvement based on imaging, separate primary tumors in bilateral lungs, and those patients having undergone neoadjuvant treatment prior to planned resection. It is in the subset of patients where TEMLA has demonstrated its strength. Reports comparing TEMLA for the restaging of patients who have undergone neoadjuvant chemotherapy or chemoradiation demonstrate it to be superior to standard restaging with mediastinoscopy, EBUS, and/or PET/CT imaging.^[6] Moving forward, the technology and techniques for surgical staging will only be further refined, and will continue to be used in a complimentary fashion. For example, EBUS offers the potential to initially diagnose and stage suspected N2 disease, sparing the patient from a mediastinal dissection, which will be critical in the future after undergoing neoadjuvant treatment.

Advances in surgical treatment of non-small-cell lung cancer

Expanding indications for video-assisted thoracoscopic surgery

Well accepted for the surgical resection of early stage NSCLC, indications for thoracoscopic approaches to more advanced cases of NSCLC are expanding as experience grows. Increasingly, complex resections are now being performed thoracoscopically with preliminary perioperative outcomes indicating both safety and feasibility.^[7] VATS techniques and results for single institution series have been reported for patients with locally advanced NSCLC requiring pneumonectomy as well.^[8] Thoracoscopic chest wall resection has been described and is being safely performed in the hands of experienced VATS surgeons. Long-term results are still not available and the role of minimally invasive approaches for extensive chest wall resections is still not well defined.

Improved technology and instrumentation now allow for equivalent and sometimes superior surgical retraction and exposure that can mimic that of an open operation. Low profile 5 mm instruments allow for multiple working instruments through one 10 mm incision. Tools that allow

for division of bony structures that have been adopted from other surgical subspecialties allow for thoracoscopic chest wall resection for NSCLC.

Robotic-assisted lung resection

Another recent advance in the surgical management of NSCLC has been the incorporation of robotic-assisted surgical technology over the past decade, specifically the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California). Though not widely accepted or incorporated for all general thoracic procedures, there has been an increasing level of interest in determining whether the advantages realized for robotic assistance in other surgical specialties will translate to robotic-assisted lung resection for NSCLC.

By overcoming some of the perceived limitations of traditional thoracoscopic resection, namely 2-dimensional imaging, unsteady camera platforms, and limited maneuverability of instruments used through non-rib spreading incisions, robotic-assisted lung resection may serve to enhance current minimally invasive resection outcomes. Though reports are limited to those coming out of selected number of centers, early results indicate that robotic assistance is both feasible and safe.^[9] A recent multi-institutional retrospective review of patients undergoing robotic lobectomy for NSCLC demonstrated that robotic lobectomy for early stage NSCLC can be performed with low morbidity and mortality. Long-term stage-specific survival is acceptable and consistent with results for patients undergoing resection via traditional thoracotomy or VATS.^[10]

Single incision thoracoscopic surgery

Though VATS has been well documented to reduce perioperative morbidity for lung resection, further advances in minimally invasive approaches may improve how well lung resection is tolerated. By limiting the number of incisions required to perform a resection to a single access incision, the potential to reduce perioperative morbidity now exists. Reports of single incision resection for wedge resection, anatomic lobectomy, and even single incision VATS pneumonectomy have been described.^[11-13] Recently reported was a case involving bilateral VATS performed without violating the chest wall by approaching each space through a single cervical incision.^[14] Though technically feasible, proposed benefits of this approach have not yet been validated.

Technical advances that have made it possible to perform lung resections through a single incision include low profile 5 mm thoracoscopic instruments (Sontek, Columbus, Ohio), adjustable tip camera technology (Olympus) available in 10 mm and 5 mm diameters, and adjustable tip endoscopic stapler technology.

New techniques for sublobar resection

Though anatomic lobectomy is the accepted gold standard for attempted curative resection for patients with early stage NSCLC, a large proportion of patients do not have the cardiopulmonary reserve to safely undergo anatomic lobectomy. Retrospective analysis of patients who have undergone wedge resection instead of lobectomy has shown increased local recurrence rate and reduced disease-free survival. A national, randomized, blinded multi-institutional trial evaluating lobectomy versus sublobar resection for small (<2 cm) peripheral tumors, has been plagued by slow patient accrual.

Anatomic segmentectomy offers the potential for lung sparing resection of small NSCLC with the aim of improved outcomes compared to simple wedge resection. Improved techniques for identifying the vascular and airway structures of segmental bronchi now make it feasible to safely perform sublobar anatomic resections thoracoscopically. Novel techniques that can aid the surgeon in identifying the segmental anatomy, including the use of selective intraoperative jet ventilation delivered through bronchofiberscopy have been described. The inflated segment to be resected is demarcated from the non-inflated adjacent lung that is to remain. In a series of 52 patients with peripheral T1 tumors smaller than 2 cm, all were able to be safely resected with segmentectomy, with no deaths, and an overall complication rate of 13.5%.^[15]

Sublobar resection with brachytherapy

For patients who are not candidates for anatomic lobar resection due to cardiopulmonary comorbidities, another option that exists and can allow for prolonged disease-free survival is the addition of intraoperative brachytherapy to sublobar resection. Results reported for sublobar resection compared to sublobar resection with intraoperative brachytherapy demonstrated a statistically significant decrease in local recurrence with the addition of brachytherapy to a sublobar resection. Brachytherapy mesh seeds, now come as pre-packaged, are easy to surgically implant at the time of VATS wedge resection, and are relatively safe. Results from a recent multi-center phase III randomized trial including 222 patients demonstrated that sublobar resection with brachytherapy can be performed safely in high-risk patient with no associated increase in morbidity at 30 days and 90 days compared to sublobar resection alone.^[16]

Awake thoracic surgery

Awake thoracoscopic surgery was first described in 2004 for the resection of solitary pulmonary nodules and has now been described for a variety of lung pathologies.^[17-20] By eliminating the need for general anesthesia, double lumen intubation, and the positive pressure ventilation, it has been hypothesized that in-operating room time could be reduced, with the potential for faster recovery. In a series of 60 patients randomized to two

treatments arms, the 30 patients treated with epidural anesthesia reported higher anesthesia satisfaction scores and hospital stay was reduced to 1 day. There were no mortalities.^[17] In another separately reported series, 46 patients with peripheral lung nodules were treated using 3-mm needlescopic video-assisted wedge resection without general anesthesia.^[18] Only two patients required conversion to general anesthesia. Indications have expanded to include metastasectomy, and awake thorascopic lobectomy without general anesthesia has been described.^[19,20] Awake thoracic surgery may now make it possible in certain scenarios for previously deemed non-surgical candidates to undergo resection with less morbidity.

New surgical techniques for advanced disease Lung suffusion

Long-term results for patients with incurable stage IV NSCLC are dismal. Surgery has traditionally been reserved for palliation of malignant pleural effusions with pleurodesis and treatment of airway obstruction secondary to tumor effects with such modalities as laser, endoscopic cryotherapy, and airway stenting with self-expanding stents.

Advances in systemic chemotherapy are being reported, but the systemic effects of treatment can still be morbid for patients. By performing regional chemotherapy with lung suffusion, select patients with tumor burden predominately located in one hemithorax are now being treated with early dose escalation protocols. Lung suffusion, performed by thorascopically isolating the superior and inferior pulmonary veins, while an interventional vascular occlusion balloon is placed in the main pulmonary artery, involves “draining” the target lung by first occluding the vascular balloon. The pulmonary veins are then snared down, and regional chemotherapy is infused into the lung for a pre-determined period of time and allowed to diffuse into the surrounding tissues. It is not a continuous infusion. After 30 min, the lung is reperfused, thus washing out the treated lung. Preliminary results of dose escalation studies have shown suffusion to be safe, with some remarkable responses the treated lung with less systemic effects.^[21]

CONCLUSION

Recent advances in surgical techniques and technology are expanding the options for surgical diagnosis, staging, and treatment of NSCLC while simultaneously improving the perioperative morbidity associated with these treatments.

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AUTHOR'S PROFILE

Dr. Mark Hennon, Assistant Professor of Thoracic Surgery at the Roswell Park Cancer Institute and Assistant Professor of Surgery at the State University of New York at Buffalo.

Dr. Sai Yendamuri, Associate Professor of Thoracic Surgery at the Roswell Park Cancer Institute and Associate Professor of Surgery at the State University of New York at Buffalo. In addition, he also serves as the Director of the Thoracic Surgery Research Laboratory at the Roswell Park Cancer Institute.



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