Review

Sleeve Lobectomy: Current Indications and Future Directions

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Sleeve lobectomy was initially conceived as an alternative to pneumonectomy for patients with low-grade, centrally located lesions and limited cardiopulmonary reserve. Over the last several decades, advances in patient selection criteria and surgical techniques have allowed sleeve lobectomy to evolve from a compromise to pneumonectomy to first line intervention for centrally located lesions of all grades. Although more challenging than pneumonectomy, long-term outcomes and cost-effective measures favor sleeve lobectomy. The use of sleeve lobectomy has been expanded for locally advanced disease, and results remain superior to alternative procedures. Current literature has also shown evidence supporting the use of neoadjuvant treatment and minimally invasive techniques. It is likely that future results will continue to improve making sleeve lobectomy an even more attractive treatment option for qualifying patients. (Ann Thorac Cardiovasc Surg 2010; 16: 310–318)

Key words: sleeve lobectomy, pneumonectomy, lung cancer, lymph node, chemotherapy

Overview and History

The incidence of lung cancer has steadily increased over the last century. Each year more than 1.3 million people will be diagnosed with lung cancer, making it the world's most common malignancy.¹⁾ Despite advances in chemotherapy, surgery has remained the cornerstone of therapy. Pulmonary resections vary widely in the amount of airway and parenchyma surgically removed. Among the most

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Note: The work described took place at the University of Pennsylvania.

Support: Doris Duke Clinical Research Foundation research grant to Jarrod D. Predina

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extensive pulmonary resections is the pneumonectomy.

The first documented pneumonectomy was completed in multiple stages in 1895 by Macewen for a patient with tuberculous empyema.²⁾ A one-stage pneumonectomy was not successfully completed until 1933, when Graham and Singer completed a left en bloc pneumonectomy for a patient with lung cancer.²⁾ Since the pioneering days of pneumonectomy, the field of thoracic surgery has made tremendous advances, but pneumonectomy remains associated with high rates of complications, especially for patients with decreased pulmonary reserve. With these considerations in mind, bronchoplastic procedures were introduced as alternatives to pneumonectomy for patients with disease involving proximal bronchi.³⁾

Bronchoplastic procedures involve resections of the airway distal to the tracheal carina. Accompanying lung parenchyma may or may not be involved. The most common bronchoplastic resections are sleeve resections, which are circumferential airway resections that require remaining airways to be joined by end-to-end anastomosis (Fig. 1). As a consequence, lung parenchyma can be preserved for gas exchange. The first documented bronchial sleeve resection was completed in 1947 by Price Thomas for a patient with pulmonary carcinoid located in the right

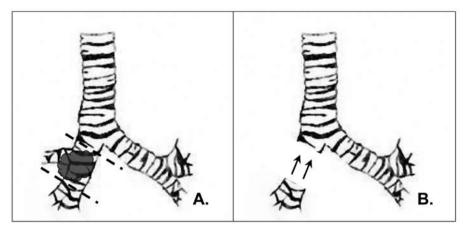


Fig. 1. Pictorial depiction of sleeve lobectomy for right upper lobe tumor invading bronchus intermedius. A. Right upper lobe sleeve lobectomy with circumferential resections sketched.
B. Resected right upper lobe bronchus and a portion of bronchus intermedius with arrows representing anastomosis formation.

mainstem bronchus.

The patient returned to active flying duty in the Royal Air Force, a feat that would not have been possible if a pneumonectomy was performed.⁴⁾ In 1952, Allison performed the first successful right upper lobe sleeve lobectomy for a patient with bronchogenic carcinoma, marking the first sleeve lobectomy performed for a high-grade thoracic malignancy.⁵⁾ Although initial indications for sleeve resections were for lung parenchyma-sparing purposes,⁶⁾ sleeve lobectomy has become accepted for anatomically suitable tumors, regardless of pulmonary function.

Indications

Sleeve lobectomy is most commonly indicated for lesions involving main or lobar bronchi.⁷⁾ These lesions typically are benign to low-grade malignant neoplasms and stenoses.⁵⁾ Carcinoid tumors account for more than 80% of the low-grade neoplasms, followed by mucoepidermoid tumors, fibrous histiocytomas, hamartomas and adenoid cystic carinomas.⁵⁾ The majority of stenoses involve traumatic or post-infectious etiologies. Sleeve lobectomy for bronchogenic carcinomas is less common, and accounts for fewer than 10% of operable cases of lung cancers. In addition to anatomic location, a sleeve lobectomy has a role when the bronchial resection margin is at risk or in the case of peribronchial lymph node involvement.⁵⁾

Sleeve lobectomy is also indicated for patients with impaired cardiopulmonary function.⁸⁾ General indications for sleeve resection as a lung parenchyma conserving procedure

include FEV_1 <50% predicted value and maximum voluntary ventilation <50% predicted value.⁵⁾

Any lobe can be a potential site for sleeve lobectomy, however, the most common location is the right upper lobe.^{8,9)} The explanation lies in the anatomy of the right mainstem bronchus and its anatomic relation to the long bronchus intermedius.^{5,7)} The left upper lobe is the second most common site for sleeve lobectomy. A left upper lobe sleeve resection is technically more challenging due to presence of the aorta and left recurrent nerve.^{5,7)}

Contraindications

Patients with advanced lung cancer, specifically T4 disease are typically poor candidates for sleeve lobectomy. Involvement of the pleura, superior vena cava, atria, or transverse aortic arch are contraindications. Relative contraindications include invasion of the pericardium phrenic nerve, vagus nerve, and diaphragm. The presence of N2 does not contraindicate sleeve lobectomy, but significantly impairs long term outcomes due to systemic recurrences.

Patient Selection

Flexible bronchoscopy is the single most important diagnostic step in identifying potential candidates for sleeve lobectomy.⁵⁾ The key finding is intraluminal tumor extension from segmental bronchi to the lobar or main bronchial orifice.⁷⁾ Bronchoscopy also allows for tissue biopsy, which is particularly important if a malignancy is

suspected.¹⁰⁾ Mucosal biopsy both proximal and distal to the lesion should be attempted to assess tumor extension.¹⁰⁾ Detection of decreased bronchial wall motion during respiration may be a sign of peribronchial tumor infiltration, and this requires further radiographic evaluation to assess for tumor extent.¹⁴⁾

Radiographic studies play a supplemental role to bronchoscopy in identifying potential surgical candidates. Computed tomography (CT) allows for better appreciation of disease size, extent, and location relative to mediastinal and thoracic structures.⁷⁾ Magnetic resonance imaging (MRI) can help reconcile ambiguous CT findings. If suspicious mediastinal lymph nodes are identified, further investigation via PET or mediastinoscopy is warranted as N2 disease may indicate the need for pneumonectomy.^{10,13,15)} General pre-operative considerations for other pulmonary resections should also be considered for sleeve lobectomy candidates.

Surgical Technique

Approach for sleeve lobectomy is through a standard posterolateral thoracotomy or a muscle-sparing anterolateral incision. Once the chest has been opened, pre-operative assessment should be confirmed by palpation of the hilum, lung parenchyma, pleural surfaces, lymph nodes, and other surrounding structures. If no contraindications are encountered, mobilization of the lobe should follow.

This process begins at the hilum with careful dissection of the pulmonary artery and its lobar branches. Dissection should be carried out with consideration for the bronchial vessels which will supply the remaining distal lung parenchyma. Once lobar arterial supply has been adequately identified and transected, corresponding pulmonary veins should similarly be divided. Incomplete fissures should be divided at this time as well.

Airway dissection should be completed only after other hilar structures have been divided. The majority of anastomotic complications result from disruption of mucosal blood flow, thus careful consideration should be given to the bronchial blood supply which is located within the peribronchial tissue. Unnecessary lymph node dissection should be avoided as this may also compromise bronchial blood supply. The presence of a single right bronchial artery makes these considerations particularly important when performing sleeve lobectomies in the right thorax. With a sharp knife, the proximal bronchi should be circumferentially divided close to the origin of the main bronchus to preserve the bronchial artery supply. Distal bronchotomy should be made in a similar fashion

at the level of the segmental bronchi, which is the location of rich pulmonary and systemic anastomoses.

Frozen histological evaluation of bronchial resection margins is recommended. Tumor-free margins of 5 mm for high-grade carcinomas and 3 mm margins for low-grade lesions are minimal requirements. If these margins cannot be obtained, a more complete pulmonary resection should be performed.⁵⁾ Carcinoma in situ and less severe forms of dysplasia at margins, however, do not require additional resection as these findings have not been associated with higher recurrence rate.⁵⁾

The remaining airways should be anastomosed in an end-to-end fashion. As long as the anastomosis can be completed under minimal tension and with minimal luminal size mismatch, there is no upper limit in regards to the maximal distance which can be anastomosed. Tension can be typically minimized releasing the inferior pulmonary ligament. In the event when further mobilization is necessary, an infrahilar pericardial release maybe performed by dividing the pericardium above the inferior border of the inferior pulmonary vein.⁹⁾ Most surgeons perform the anastamosis in an interrupted fashion, however, an uninterrupted technique is acceptable. Short and long-term results are comparable in both human series¹⁶⁾ and canine models.¹⁷⁾ When possible, the use of a layer-tolayer anastomosis should be utilized as it minimizes potential inconsistencies in luminal architecture.

Ideally, the anastomosis should be begun in the region most difficult to visualize. An Alternatively, the authors use sutures at both ends of the airway where the posterior membrane meets the bronchus to align the rings. Absorbable 4–0 sutures, with knots placed outside the bronchial lumen, should be used to decrease the rate of stricture and granuloma formation.⁹⁾

To account for discrepancies in bronchial lumen diameter, there are several techniques that can be utilized. One relatively simple approach is the application of space-suturing to stretch the smaller lumen to better approximate the larger. Other methods include the excision of a small wedge and plication of larger bronchus or telescoping techniques. Telescoping techniques should be reserved for scenarios in which significant mismatch exists among diameters between proximal and distal bronchii. The primary limitation in telescoping methods is the remaining shelf of bronchial tissue which is left protruding into the bronchial lumen. This tissue may necrose or serve as a focus for secretional retention or infection.

The anastomosis should be covered with pedicled tissue to prevent bronchopleural and bronchovascular fistula

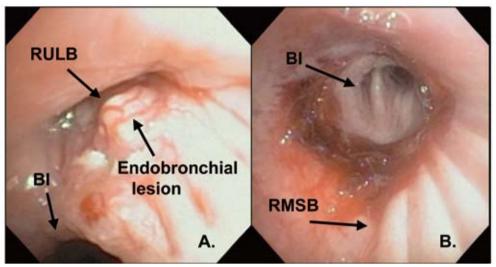


Fig. 2. Right upper lobe endobronchial lesion before and after right upper lobe sleeve lobectomy. **A.** Endobronchial NSCLC located in right upper lobe bronchus (RULB) immediately distal to take off from bronchus intermedius (BI). **B.** Anastomosis of right mainstem bronchus (RMSB) to bronchus intermedius. Notice consistency in luminal diameter and mucosal continuity.

formation. The use of pedicled tissue is also thought to aide in the formation of systemic bloodflow to the anastomosis. Easily mobilized pedicled tissues include intercostal muscle flaps or pericardial fat pads. Alternate options include the thymus, omentum, and pleura. Before closing the chest, surveillance flexible bronchoscopy should be performed to evaluate for luminal continuity at the anastomosis (Fig. 2). Even the slightest mucosal inconsistencies predispose for stricture formation. All residual secretions and blood should also be removed from the airway at the time of bronchoscopy.

Video Assisted Thoracic Surgery (VATS)

Sleeve lobectomy, and bronchoplastic procedures in general, have traditionally been performed through a posterolateral thoracotomy. Until recently sleeve resection has been viewed as an absolute contraindication to VATS lobectomy, despite numerous advantages associated with minimally invasive procedures. The first documented VATS sleeve lobectomy was reported by Santambrogio and colleagues in 2002 for a 15 year-old female with low-grade mucoepidermoid carcinoma of the left lower lobe bronchus. VATS was chosen over an open approach in this individual because of the potential for improved cosmetic outcomes without the sacrifice of outcome.

The only VATS sleeve lobectomy series to date was described by Mahtabifard and colleagues in 2008. 18)

Their technique mirrors that of open procedures; dissection begins at the hilum, followed by identification and transection of the pulmonary vessels, and finally bronchial resection and anastomosis. Of the 13 patients reported, four (31%) had complications including atrial fibrillation, anastomotic stricture, reintubation, and bronchial tear requiring takeback. They reported no deaths at 30 days. Long term results, however, were not discussed. Although Mahtabifard and colleagues reported results comparable to those observed with more traditional approaches, they suggest the use of VATS sleeve lobectomy to surgeons with adequate experience with minimally invasive techniques.

Postoperative Care

Bronchotomy and anastomosis during sleeve resection disrupt normal mucociliary clearance and create breaks in the mucosal barrier. These alterations ultimately set up for secretion retention and air trapping. Sufficient pain control, typically a via spinal or an epidural route, allows for effective deep inspiration and adequate coughing which can help to minimize these morbidities. Hest physiotherapy, postural drainage, incentive spirometry, and bronchodilators also play roles, especially during the first week following the procedure. In our unit, all patients are encouraged to sleep with the non-operative hemithorax in the decubitus position. In the event of inadequate sputum clearance, bed-side bronchoscopy is

recommended. Airway secretions should be suctioned under direct visualization in order to avoid potential trauma to the anastomosis. Other indications for bronchoscopy include a coarse wheeze at the anastomosis, loss of volume on chest x-ray, or lobar consolidation.¹⁰⁾

Outcomes Following Sleeve Lobectomy

Overall survival following sleeve lobectomy for patients with Non-small Cell Lung Cancer (NSCLC) ranges from 39%–53% at 5 years and 28%–34% at 10 years. 6,11,13,15,20–23) In a series of 217 patients reported on by Bagen et al. in 2005, 5-year survival rates were recorded as high as 72%; however, the report was limited to patients who underwent right upper lobe sleeve lobectomy which has been suggested to be less challenging than sleeve lobectomies for other lobes.²⁴⁾ Sleeve lobectomy for pulmonary carcinoid is extremely well tolerated with 5 and 10 year survivals range from 100% and 92%-100%, respectively. 12,22) Documented factors decreasing long-term survival following a sleeve lobectomy include incomplete resection and increasing nodal involvement. 13,21,22,25) Literature commenting on outcomes involving squamous cell histology, age at resection, and induction radiotherapy remain unclear.12,13)

Complications following sleeve lobectomy arise in 15%-38% of patients (Table 1 and Table 2). Common complications include sputum retention and secondary atelectasis, bronchovascular and bronchopulmonary fistula, and anastomotic failure (stricture and breakdown).79 Bronchovascular fistula, bronchopulmonary fistula, and anastomotic failure can result from disruption of the bronchial blood flow during airway dissection or excessive tension at the anastomotic site. Bronchovascular fistula occur in less than 2% of cases of sleeve lobectomy and are almost always fatal complications.⁷⁾ Bronchopulmonary fistula formation is slightly more common, occurring in 5% of sleeve lobectomies. 12,13,20-22,25,26) Death from bronchopulmonary fistula follows in approximately 40% of the patients. Anastomotic stricture or breakdown occurs in 1%-4% of patients undergoing sleeve lobectomy. 13,21,22,25)

Post-operative, or 30 days, mortality for sleeve lobectomy is approximately 5% in recent reports (Table 1 and Table 2). Commonly documented causes of early mortality include bronchopleural fistula, bronchovascular fistula, cardiac complications, pneumonia or empyema, and pulmonary embolism. Rarer causes include renal failure, acute respiratory distress syndrome, hemothorax, and respiratory failure.

Sleeve lobectomy was initially described as an alternative to pneumonectomy for patients with impaired cardiopulmonary reserve. Today sleeve lobectomy has replaced pneumonectomy as the procedure of choice for the majority of centrally located lesions, including high grade carcinoma. 6,15,27) Current series support this transition as sleeve lobectomy is associated with superior five year survival rates, decreased operative mortality, and comparable complication rates when compared to pneumonectomy (Table 3). Locoregional recurrence rates are also comparable among sleeve lobectomy and pneumonectomy with rates ranging from 4%-22% and 8%-35%, respectively.6, 15, 24) Interestingly, in a series of 249 patients reported by Kim and colleagues in 2005, the locoregional recurrences with sleeve lobectomy occurred in 32.6% of patients versus 8.5% in pneumonectomy. There was, however, no significant difference in overall survival at 5 years. 11) A recent meta-analysis including 1606 patients (860 sleeve lobectomies and 746 pneumonectomies) found sleeve lobectomy to be more cost effective and associated with higher quality of life when compared to pneumonectomy.²⁸⁾ Similarly, in 2008 Balduyck et al. reported lower rates of dyspnea burden, general and thoracic pain, and shoulder dysfunction in those undergoing sleeve lobectomy.²⁹⁾

Nodal Status and Sleeve Lobectomy

Arguably the most controversial area involving sleeve lobectomy is the role of nodal status and long-term prognosis. In the case of N0 disease, sleeve lobectomy is generally accepted as safe and associated with outcomes equal to or better than those obtained with pneumonectomy. 11-13,20-22) The indications for sleeve lobectomy in the setting of nodal involvement become less clear. Although N1 and N2 disease outcomes are again similar to or better than those associated with pneumonectomy, several reports describe nodal disease negatively effecting survival when compared to N0 disease. 20,21) The majority of recent reports, however, describe no difference in survival amongst sleeve lobectomy candidates with N0 and N1 disease. 12,13,22,25) N2 disease does not contraindicate sleeve lobectomy, however few to no long term survivors are observed (Table 3). The lack of long-term survivors associated with N2 disease has been largely attributed to the increased rate of both local and distant recurrences, 40% and 21% respectively.^{21,22)}

Table 1. 5-year survival, postoperative complications, and 30-day mortality results after sleeve lobectomy for NSCLC

Author (Year)	# of Patients	5-Year Survival (%	%) Complications (%)	30-Day Mortality (%)	
Konstantinou et al (2009) ²⁶⁾	45	57 [*]	15	2	
Rea et al $(2007)^{25}$	93	39.7	Within 30 Days-17.9 After 30 Days-16.3	4.5	
Yidzeli et al (2007) ¹³⁾	218	53	22.9	4.1	
Mezzetti et al (2006) ²⁰⁾	38	43	10.8	3.6	
Terzi et al (2002) ¹²⁾	48**	38.8***	_	6**	
Fadel et al (2002) ^{22)****}	139	52	12.9	2.9	
Tronc et al (2000) ²¹⁾	184	52	Within 30 Days-14% After 30 Days-2	% 1.6	

^{*}survival at 4 years

Table 2. 5-year survival, 30 day mortality, and postoperative complications among NSCLC patients undergoing sleeve lobectomy or pneumonectomy

Author (Year) # of Patients	# of	Sleeve Lobectomy			Pneumonectomy			
		5-Year Survival (%)	30-Day Mortality (%)	Complications (%)	5-Year Survival (%)	30-Day Mortality (%)	Complications (%)	
Melloul et al (2008) (27)*	115		0	26		3	44	
Ma et al (2007) (6)	2,984**	50.3	3.5	31.3	30.6	5.7	31.6	
Bagan et al (2005) (24)***	217	72.5	4.5	28.8	51.2	12.6	29.9	
Ludwig et al (2005) (23)	310	39	4.3	38	27	4.9	26	
Kim et al (2005) (11)	249	53.7	6.1	51****	59.5	4.1	35****	
Deslauriers et al (2004) (15)	1,230	52	1.6		31	5.3		

^{*} includes only data of patients under 70 years age

Table 3. 5- and 10-year survival rates after sleeve lobectomy for NSCLC according to lymph node status

Author (Year)	# of Patients	5-Year Survival (%)			10-Year Survival (%)		
		N0	N1	N2	N0	N1	N2
Yildzeli et al (2007) (13)	218	57.1	67	0	40.5	19	0
Kim et al (2005) (11)	49	88	51	8	_	28	_
Terzi et al (2002)* (12)	160	57	33	19	33	22	0
Fadel et al (2002) (22)	139	55	68	0	39	19	0
Mezzetti et al (2002) (20)	83	61	39	9	50	26	0
Tronc et al (2000) (7)	184	63	48	8	43	27	0

^{*}Data includes survival from patients with diagnosis of NSCLC or pulmonary carcinoid

^{**} results from "contemporary phase" which was described by authors as era after routine of CT, use of mediastonoscopy, and advanced bronchoscopic techniques

^{***} survival excludes stage IV patients

^{****} data includes both NSCLC patients and pulmonary carcinoid patients

^{**} report is a meta analysis

^{***} includes only data involving right upper lobe sleeve lobectomies and right pneumonectomies with limited nodal involvment (N0, intralobar N1 and skip metastasis)

^{****} complications only include those which took place during the early postoperative period

Neoadjuvant Therapy

The use of neoadiuvant radiation, either with or without chemotherapy, has traditionally been avoided due to concerns of damaging the bronchial blood supply and ultimately predisposing sleeve lobectomy candidates to anastomotic complications. Current literature, however, suggests that neoadjuvant treatment has minimal morbidity and mortality and should be administered 4 to 6 weeks prior to surgery. In 2009, Milman and colleagues reported a series of 64 patients who underwent sleeve lobectomy; 33% receiving neoadjuvant chemoradiation. In this report, neoadjuvant therapy consisted of platinum-based regimen with an average of 4,000 cGy of concurrent radiation (ranging from 2,000 to 6,100 cGy). The use of tissue reinforcement was not standardized, however, the authors advocate use when possible. There was no observable difference in complication rates, local recurrence rates, or 5-year survival among patients receiving therapy versus those who did not.30) These results may suggest that little to no delay in mucosal healing was observed. Similarly Yildizeli et al., in 2007, noted that induction chemoradiotherapy did not predispose patients receiving neoadjuvant therapy to postoperative complications.¹³⁾ Interestingly, Milman et al.'s report also describes increased distant recurrence rates among patients treated with neoadjuvant chemoradiotherapy versus resection alone, 52% and 12%, respectively. It is difficult to interpret these findings retrospectively as the results are likely confounded by advanced staging in the cohort of patients receiving neoadjuvant therapy. In contrast to the Milman and Yildizeli's accounts, Rea and colleagues noted safe use of neoadjuvant chemotherapy, but increased perioperative mortality and early bronchial complications associated with induction radiotherapy.²⁵⁾

Non-traditional forms of induction therapy have also been utilized as adjuvants to sleeve lobectomy. In 2008, DeArmond and colleagues reported the successful application of induction photodynamic therapy for a patient undergoing a right upper lobe sleeve lobectomy for an endobronchial non-small cell lung cancer.³¹⁾

Despite encouraging results with neoadjuvant therapies, thoracic surgeons should proceed with caution and exercise close monitoring throughout the post-operative period. Implementation of aggressive pulmonary therapy and frequent chest imaging should be the norm. If any indication of pulmonary collapse is observed, bronchoscopy should be performed immediately. Any hemoptysis may suggest a sentinel bleed of a bronchovascular fistula. Hemoptysis thus requires immediate bronchoscopy and a

possible completion pneumonectomy if an active bleed is located. If a clot is visualized, no effort should be made to remove the clot and immediate exploration should be performed. Lastly, all patients should undergo a diagnostic bronchoscopic evaluation prior to discharge to confirm anastomosis integrity.

Sleeve Lobectomy and Beyond

Sleeve lobectomy has become the standard of care for central or locally advanced NSCLC. When lesions also invade hilar and mediastinal vessels, vascular reconstruction may be required for oncologic resection. The most commonly involved vessels are the pulmonary arteries.⁶⁾ A sleeve resection with pulmonary artery arterioplasty, also known as a "Double sleeve" procedure, is the only alternative to pneumectomy for these patients. Results, however, supporting this procedure have been sparse. In 2007, Ma and colleagues performed a meta-analysis which compared double sleeve to pneumonectomy. This approach was found to be superior to pneumonectomy with regards to operative mortality with rates of 3.3% in double sleeve vs. 5.7% in pneumonectomy (p = 0.05).⁶⁾ Double sleeve was comparable to pneumonectomy when considering postoperative complications (32.4% versus 31.6%, respectively) and 5 year survivals (38.7% versus 30.6%, respectively). In 2001, Solli and colleagues also documented the use of sleeve lobectomy along with prosthetic replacement of the pulmonary artery and superior vena cava for a patient with locally advanced NSCLC of the right upper lobe bronchus.³²⁾

Another technique used to extend the positives of bronchoplasty in the setting of locally advanced disease is extended sleeve lobectomy. Extended sleeve lobectomy describes sleeve resection of more than one lobe in order to avoid pneumonectomy.³³⁾ In 2009, Chida and colleagues reported on a series of 23 patients who underwent an extended sleeve lobectomy. Fifteen of these patients underwent a lobectomy and resection of an additional segment. There were no operative mortalities documented, and the three year survival rate was 40%. Both the complication rate and the local relapse rate were found to be 8.7%. The authors concluded extended sleeve lobectomy as a safe and effective procedure as these results are similar to those achieved with sleeve lobectomy and pneumonectomy.

Conclusion

Sleeve lobectomy has evolved from a compromise to pneumonectomy in those with compromised pulmonary function, to first line intervention for centrally located lesions of all grades. Although more challenging than pneumonectomy, outcome and cost-effective measures favor sleeve lobectomy. The use of sleeve lobectomy has been expanded for locally advanced disease, and results remain superior to alternative procedures. With literature supporting the use of neoadjuvant treatment and VATS, it is likely that future results will continue to improve making sleeve lobectomy an even more attractive treatment option for qualifying patients.

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