Title
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Journal
Clinics in Perinatology, 44(4)

ISSN
0095-5108

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Publication Date
2017-12-01

DOI
10.1016/j.clp.2017.08.003

Peer reviewed

HHS Public Access

Author manuscript

Clin Perinatol. Author manuscript; available in PMC 2018 May 24.

Published in final edited form as:

Clin Perinatol. 2017 December ; 44(4): 781–794. doi:10.1016/j.clp.2017.08.003.

Thoracoscopic Lobectomy for Congenital Lung Lesions

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Abstract

Congenital lung lesions (CLL) comprise a heterogeneous group of developmental and histologic entities often diagnosed on screening prenatal ultrasound. While large lesions can produce hemodynamic compromise and fetal nonimmue hydrops or neonatal respiratory distress, most fetuses with CLL proceed to uncomplicated term delivery and are asymptomatic at birth. The risk of developing malignancy and infectious complications drives the decision to prophylactically resect CLL in asymptomatic patients. Since first described in 2003, thoracoscopic lobectomy for CLL has been shown to provide decreased hospital length of stay and decreased time of tube thoracostomy when compared to open resection, without increased risk of perioperative morbidity. Additionally, recent advances in minimally invasive instrumentation promise to address some of the remaining challenges of thoracoscopic surgery in small infants and neonates. We describe our approach to minimally invasive lobectomy in children with CLL, post-operative care and management of procedure-specific complications.

Keywords

Congenital; lung; lesion; malformation; thoracoscopic; resection; lobectomy; CPAM; cystic; adenomatoid; pulmonary; sequestration; airway; minimally; invasive; neonatal

Introduction

Congenital lung lesions (CLL) comprise a heterogeneous collection of rare developmental parenchymal lung abnormalities present in utero and at birth, including congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestration (intralobar and extralobar), bronchial atresia, and congenital lobar emphysema. Additionally, pleuropulmonary blastoma (PPB), mediastinal teratoma and bronchogenic cysts can mimic CLL on fetal ultrasonography, post-natal radiograph, and post-natal contrast-enhanced CT or MRI. CLL are often diagnosed on prenatal ultrasound and have overlapping radiologic features. Thus, definitive diagnosis relies on histopathologic analysis of resected tissue[1]. Given the heterogeneity of CLL, it is not surprising that these lesions carry unpredictable

and vastly different clinical outcomes if left untreated. On one hand, CLL can produce mediastinal shift, polyhydramnios and fetal nonimmune hydrops in 5-30% of cases[2,3], requiring prenatal intervention to avoid fetal demise. On the other hand, approximately one-in-five cases are diagnosed outside of the neonatal period incidentally, or due to infection or pneumothorax[4]. Finally, in utero behavior of CLL is variable, with an early proliferative phase producing a peak in size around 25 weeks' gestation, often followed by size regression in the third trimester. In a case series of 600 CLL, 68% of pulmonary sequestration and 15% of CPAM underwent marked spontaneous regression before birth[2]. Accordingly, the rarity of CLL, heterogeneity in lesion pathology for prenatally diagnosed lung lesions, and an unpredictable and widely variable natural history make the development of evidence-based treatment algorithms difficult. Thus, while the development of hydrops mandates prenatal intervention, and symptomatic neonates clearly benefit from resection, optimal treatment of the asymptomatic CLL is less clear, and is determined on a case-by-case basis with the guidance of case-series and expert opinion.

In patients who warrant surgical intervention, formal lobectomy is recommended over segmental resection[5,6]. Case reports and series have demonstrated precursors to mucinous bronchioloalveolar carcinoma harbored in CPAM type 1[7,8], and pleuropulmonary blastoma can be indistinguishable from CPAM type 4, resulting in inadequate surgical margins and risk of recurrence with segmental resection[9]. Additionally, determining lesion margins both preoperatively on CT scan and intraoperatively is difficult, resulting in a high risk of incomplete resection with non-anatomic resection[4,5]. Traditionally, lobectomy occurred as an open surgical procedure through posterolateral thoracotomy. However, Albanese, et al. first described a completely thoracoscopic minimally invasive lobectomy in 2003[10]. Subsequent case series and a meta-analysis have shown the thoracoscopic technique to provide improved or equivalent complication rates, decreased hospital length of stay, and decreased time of tube thoracostomy when compared to open techniques[11–15]. The focus of this article is on the indications, surgical approach, technical considerations, post-operative care and outcomes of thoracoscopic resection of CLL, in particular CPAM.

Indications/Contraindications

As mentioned above, the clinical presentation of antenatally diagnosed CLL varies widely, from fetal nonimmune hydrops to asymptomatic term live birth extending into childhood. Large lesions can produce mediastinal shift, cardiac compression and obstruction of the vena cava, resulting in profound hemodynamic alterations and development of hydrops in the fetus. Lesions can be risk-stratified according to the cystic adenomatoid volume ratio (CVR), which normalizes lesion volume to head circumference and predicts an 80% risk of hydrops for CVR > 1.6[16,17]. Fetuses with CVR > 1.6 should be monitored with weekly ultrasound exams, as hydrops is associated with near 100% fetal mortality if left untreated[3,18]. Treatment strategies include maternal betamethasone administration, as well as invasive techniques such as fetal lobectomy via maternal laparotomy and hysterotomy, thoracoamniotic shunting, radiofrequency or laser ablation, or percutaneous ultrasound-guided sclerotherapy[19]. Steroid administration is especially effective in treating microcystic lesions producing nonimmune hydrops, with survival rates to delivery as high as 92%[20–22].

Given the effectiveness of prenatal steroids in the treatment of hydrops, there are now fewer clinical scenarios where invasive fetal intervention is indicated.

Most fetuses with a prenatal diagnosis of CLL proceed to live birth without the development of hydrops. Of these neonates, roughly one-quarter will be symptomatic at birth with abnormal breathing and respiratory distress, with large lesions portending higher risk[2,23]. Symptomatic neonates should proceed to surgical resection, which may be facilitated by ex utero intrapartum therapy (EXIT) or support with extracorporeal membrane oxygenation (ECMO) in rare cases of severe distress[1,2].

The timing and necessity of surgical resection of CLL in asymptomatic neonates is a source of controversy. Roughly 10-30% of asymptomatic neonates will develop an infection within the first year of life[4,24], and the presence of infectious symptoms correlates with higher rates of intra- and post-operative complications and longer hospitalizations[4,25]. Additionally, early surgical resection offers the theoretical advantage of compensatory lung growth[26,27]. However, in a long-term prospective study, there was no correlation between age at operation and eventual pulmonary function or exercise capacity following lobectomy[28]. Finally, some authors advocate early resection due to the risk of malignancy; namely, difficulty in distinguishing CPAM from PPB, and the observation that CPAM type 1 can harbor precursors to mucinous bronchioloalveolar carcinoma that can undergo malignant transformation later in life[8]. Our institution has developed a protocol for asymptomatic neonates with CLL, which includes chest computed tomography (CT) scan at six months of age to allow for better evaluation of the location of the lesion, and lobectomy at 6-9 months of age for those with higher risk of future respiratory infections (radiographic findings of predominantly large cysts).

After determining the need for and timing of surgical resection for CLL, it is important to consider whether a thoracoscopic approach is feasible for resection. While case series and a meta-analysis have shown no difference in thoracoscopic complication rates compared to open resection[11–14], case series demonstrate conversion rates as high as 33-50%[11,29] with early experience. The primary risk factor for conversion to open thoracotomy is the presence of preoperative respiratory symptoms and infection[11,29,30], which can produce intrathoracic adhesions and a potentially more difficult dissection. Resection should be performed after resolution of the acute infection and inflammation. Once infection subsides, an initial thoracoscopic approach appears safe, as a recent case series of lung resections in the setting of CLL and preoperative infection found no difference in complication rates between open and thoracoscopic approaches[31]. Additional risk factors for intraoperative conversion to thoracotomy may include procedures performed early in the surgeon's learning curve[29], with one case series demonstrating an early conversion rate of 27% reduced to 8% with increased surgeon experience[30], and patient age, as another series found a higher rate of conversion in patients less than five months of age at lobectomy[14]. However, multiple series have shown no difference in complication or conversion rates based on patient age or size[32–34].

SURGICAL CONSIDERATIONS

Preoperative Planning

Most CLL are diagnosed prenatally, with surgical timing and planning dependent on the presence or absence of respiratory distress or altered breathing at birth. Lesions with CVR greater than 0.84 are at increased risk for respiratory symptoms at birth[23], and some authors advocate delivery at a quaternary care center for lesions with CVR >1.0[35]. This facilitates resection during EXIT procedure or ECMO support as a bridge to resection. In the absence of severe respiratory distress, a thorough postnatal preoperative workup should be performed, which includes advanced cross-sectional imaging with contrast-enhanced chest CT scan[1]. This allows increased definition of the lung lesion and its location relative to surrounding anatomic structures, which may help narrow the differential diagnosis.

Patient positioning

Proper patient positioning for thoracoscopic lung resections allows optimal ergonomics for the operating surgeon, excellent visualization of the hemithorax and pulmonary hilum, and protects the patient from pressure- or stretch-induced injury. To achieve this, patients are first placed on the operating table supine, to allow for safe induction of general anesthesia with optimal oropharyngeal access for the anesthesiologist. After induction of anesthesia, intubation should proceed to allow for single lung ventilation. This can be achieved through mainstem intubation with or without the use of a fiberoptic bronchoscope; other techniques include insertion of a bronchial block, or simultaneous mainstem intubation with two endotracheal tubes[36]. The method for single lung ventilation depends on the expertise of the pediatric anesthesiologist and the size and age of the patient. Double lumen endotracheal tubes are used for older patients. Once the airway is secure, we place the patient in the lateral decubitus position. Care is taken to position the head, neck, arms, hips and legs in neutral positions with all pressure points protected by padding. The surgeon and the assistant stand on the same side of the table, facing the patient’s anterior chest and abdomen, with the thoracoscopic monitor placed opposite the operating surgeon, as demonstrated in Figure 1.

Surgical approach

The authors prefer a completely thoracoscopic approach and formal lobectomy for treatment of CLL. Three trocars are inserted to accommodate the camera and two working instruments. A 12-mm port allows passage of an EndoGIA stapler (Covidien, Medtronic, Mineeapolis, MN), as well as removal of the complete resected lobe for thorough histopathologic analysis. Variations to this approach include a hybrid-procedure that utilizes a mini thoracotomy for direct manipulation and removal of the specimen, as well as pulverization of the resected specimen to facilitate removal[37]. We find the 12-mm port enables specimen retrieval, while maintaining the benefits of minimally invasive approaches, including improved cosmesis and shorter hospital length of stay[11].

Most authors recommend formal lobectomy rather than wedge resection for treatment of CLL[1]. Retrospective case series have demonstrated contrast-enhanced CT has low sensitivity for identification of multiple lesions within the same lobe[5], leaving local approaches prone to incomplete resection and residual disease. Accordingly, a meta-analysis showed a 15%

risk of incomplete resection with non-anatomic resections[4], compared to 0% with lobectomy. Additionally, case reports of early occurrence of PPB after local CLL resection[9] likely reflect incomplete resection, rather than malignant transformation, illustrating the difficulty in obtaining a definitive preoperative diagnosis and the danger of obtaining inadequate surgical margins. Finally, children who undergo formal lobectomy have good pulmonary functional outcomes, with most patients achieving normal exercise capacity and pulmonary function[28]. However, formal lobectomy is not always feasible; lesions in multiple lobes may necessitate local resection.

Surgical procedure

The following description of the surgical procedure focuses on younger patients less than one year of age at our institution. After induction of anesthesia, sterile preparation and draping of the entire hemithorax of interest, and administration of prophylactic antibiotics, the surgical procedure begins. Access to the thoracic cavity is achieved by placement of three to four thoracoscopic trocars, as shown in Figure 2. After instillation of subcutaneous bupivacaine, the authors first place a Veress needle with a Step radially-expanding sheath (Covidien, Medtronic, Minnesota, MN) anteroinferior to the inferior angle of the scapula and insufflate the chest with 4 torr CO2 insufflation at 1.0 L/min to create pneumothorax and collapse the lung completely. The Veress needle is removed, and a 5-mm port is placed through the sheath to facilitate a 4-mm, 30-degree telescope. Two, 5-mm working ports are then placed along the mid-anterior axillary line. A fourth port may be placed to allow improved retraction and hilar exposure for lesions with large cystic components, as shown in Figure 2A. These ports allow the use of 3 mm, 20 cm monopolar hook cautery, atraumatic grasper, Maryland dissector and curved scissors (Karl Storz, Tuttlingen, Germany); as well as the 5-mm Ligasure coagulating system (Covidien, Medtronic, Minneapolis, MN) or the 3-mm JustRight Vessel Sealing System (JustRight Surgical, Boulder, CO). Placement of the 5mm port in the anterior axillary line occurs at the level of the fissure, to allow dissection along this plane, and enlargement of this port to 12mm facilitates use of the EndoGIA stapler, if used, to divide the bronchus and the fissure if incomplete. Rothenberg also describes recent use of a 5-mm stapler (JustRight Surgical, Boulder, CO) that may facilitate stapling in small neonates[37]. Other techniques include a hybrid procedure, including a mini-posterolateral thoracotomy in the fifth intercostal space, using a muscle-sparing approach and two to three 3-5mm trocars[38].

The lobar dissection begins with mobilization of the lung, releasing the inferior pulmonary ligament and any pleuropulmonary adhesions. In cases of intralobar bronchopulmonary sequestration, the systemic vascular supply is identified, ligated and divided. Once the lung is free, attention is turned to the hilum. The branches of the superior or inferior pulmonary vein are dissected free, but not divided in order to avoid vascular congestion, as shown in Figure 3. We then complete the fissure with the LigaSure prior to dissecting the pulmonary arterial supply, as demonstrated in Figure 4. Once isolated, the arterial branches to the particular lobe, seen in Figure 5, and then the vein are sealed and divided with the LigaSure. Middle lobectomies proceed first with completion of the fissures to allow identification of the branches of both the pulmonary vein and artery, followed by isolation and division of segmental branches using the LigaSure. Other strategies for sealing and dividing vessels

include endoscopic clips and use of the stapler, though these approaches are sometimes limited by patient size in small infants and neonates. Placement of traction silk sutures around vessels prior to division may facilitate exposure and aid in safe division, especially in infants less than 15 kg[39]. Finally, to divide the bronchus, we enlarge one of the 5-mm working ports to 12-mm to facilitate an EndoGIA stapler. If necessary, the fissure can also be completed with the stapler. In cases where the hemithorax is too small to facilitate a 12-mm port and stapler, we divide the bronchus sharply and oversew the bronchial stump using interrupted sutures. The specimen is removed intact through the 12-mm incision, which may need to be enlarged slightly to allow specimen removal. A thoracostomy tube is inserted through the most inferior port site and the lung is re-expanded under direct visualization. Port site incisions are then closed in two layers, using absorbable suture.

Complications & Management

Thoracoscopic resection of CLL can incur both intraoperative and post-operative complications. However, multiple case series have demonstrated a low incidence of overall morbidity, as described in Table 1, and no difference in complication rates between minimally invasive and open approaches to resection[11,13–15]. In their meta-analysis, Nasr, et al. found a 21% rate of overall morbidity, and a 16% rate of respiratory complications, most-commonly post-operative pneumonia[12]. The most frequently described intraoperative complications include hemorrhage requiring transfusion, bronchial injury requiring repair, phrenic nerve injury, and incomplete resection of the lesion. Common post-operative complications include pneumonia, persistent air leak/pneumothorax, and need for blood transfusion.

Additionally, while not a true complication, the most common unanticipated intraoperative event is conversion to an open procedure. Various centers report different rates of conversion, ranging from 1-50%[11,29,37,40]. As mentioned above, one established risk factor for conversion is the presence of preoperative infectious symptoms, and conversion rates are lower in asymptomatic patients[11,29]. Other factors that may increase the risk for conversion are procedures done early in the surgeon learning curve[29,30], and patient age less than five months[14], though multiple series have demonstrated high rates of thoracoscopic success in small neonates[32,33]. In general, the surgeon should consider conversion to an open procedure when unable to safely visualize, dissect, delineate and divide hilar structures. Specific barriers to safe hilar dissection include pleural adhesions, aberrant hilar anatomy, incomplete fissure, and hemorrhage.

Specific Complications

Intraoperative

- **Hemorrhage**: Sources of bleeding during thoracoscopic dissection include intercostal vascular injury, inflammatory pleural adhesions, and injury to hilar vessels. While not immediately life-threatening, bleeding from inflammatory adhesions can result in acute blood loss anemia requiring blood transfusion, and can prevent visualization of hilar structures, resulting in conversion to an open procedure. The meticulous use of electrocautery and the LigaSure can reduce oozing from these adhesions. Following basic surgical principles, hilar vessels

should be identified and controlled circumferentially prior to attempts at division. Incidental injury to these vessels incurred during dissection or division can produce life-threatening hemorrhage. Methods for controlling a vascular injury include local pressure, suture repair, and ligation, and these injuries often require emergent conversion to thoracotomy.

- **Bronchial injury**: Though rare, thermal injury, staple injury or laceration to an adjacent or incorrectly identified bronchus or bronchiole can lead to major morbidity, including complementary lobectomy[34]. If identified intraoperatively, successful primary suture repair has been described after conversion to an open procedure[38]. Missed injuries result in prolonged air-leak, and often necessitate re-operation for bronchial or bronchiolar repair.
- **Incomplete resection:** The risk of incomplete resection is dependent on the surgical approach, with non-anatomic resections demonstrating a 15% risk, compared to 0% with formal lobectomy[4]. This may be due to the observed low sensitivity of contrast-enhanced CT scan for identifying secondary lesions in the affected lobe[5]. In cases of residual disease identified on post-operative pathology, re-operation should be considered to gain clear margins, or to perform formal lobectomy. If residual disease is missed, cases thought to be CLL can manifest PPB[9], and CPAM type 1 can undergo eventual malignant transformation into bronchioloalveolar carcinoma[7,8].

Postoperative

- **Persistent air leak/Pneumothorax:** Most case series report rates of persistent air leak and pneumothorax less than 10%[12,33,34]. Air leaks can originate at the bronchial staple/suture line, a transected bronchiole or a missed injury to an adjacent bronchus. Small air leaks will often resolve with continued thoracostomy drainage. However, if the lung fails to fully expand or the air leak does not resolve, reoperation may be necessary to identify and address bronchial or bronchiolar injury.
- **Pneumonia:** Approximately 5-10% of patients develop post-operative pneumonia following thoracoscopic lung resection[12]. Initial treatment is with intravenous antibiotics, while obtaining imaging to assess for undrained pleural effusions that may become infected. Any undrained collections should be drained, and development of purulent drainage may require reoperation and chest washout.

Post-operative Care

Generally, neonates and infants do well after thoracoscopic resection of CLL. Following completion of the case, patients without preoperative respiratory distress are usually extubated in the operating room. The thoracostomy tube is maintained in place until there is no air leak and no pneumothorax on chest radiograph, usually 1-3 days[11,12,15,38]. Patients may restart normal oral intake after recovery from general anesthesia[10]. Post-operative pain control is most often achieved with a combination of oral and intravenous analgesics, with

the rare need for regional analgesia through placement of an epidural. In the uncomplicated case, neonates and infants are ready to return home within two to eight days[11,30,34]. In a large case series including 97 thoracoscopic lung resections, Rothenberg reported an average post-operative hospital length of stay of 2.4 days[38].

Outcomes

In addition to the low rates of major perioperative morbidity described above and in Table 1, long-term functional outcomes are excellent following lobectomy in children. In a combined prospective and retrospective analysis of 15 children undergoing lobectomy for CLL before 1 year of age, Beres, et al. showed normal forced vital capacity in 93%, normal forced expiratory volume in 1 second in 86%, and normal diffusion capacity in 100% of children at 5 years of age or older[26]. Additionally, Naito, et al. demonstrated excellent long-term pulmonary function and exercise capacity in children undergoing lobectomy, with no correlation between age at lobectomy and exercise capacity or pulmonary function results[28]. However, both of these series included children who underwent open thoracotomy, and no study has examined long-term pulmonary function in patients undergoing thoracoscopic lobectomy exclusively.

Summary

Congenital lung lesions comprise a heterogeneous group of developmental and histologic entities and are often diagnosed on screening prenatal ultrasound. While large lesions can produce hemodynamic compromise and fetal nonimmue hydrops or neonatal respiratory distress, most fetuses with CLL proceed to uncomplicated term vaginal delivery and are asymptomatic at birth. The potential risk for developing malignancy and infectious complications drives the decision to resect CLL in asymptomatic patients. Accordingly, prophylactic surgery should entail minimal morbidity and excellent long-term outcomes. Since first described in 2003[10], thoracoscopic lobectomy for CLL has been shown to provide decreased hospital length of stay and decreased time of tube thoracostomy when compared to open resection, without increased risk of perioperative morbidity[11–15]. Additionally, most children exhibit normal long-term pulmonary function following resection[26,28]. The surgical technique continues to evolve, with outcomes improving as surgeons gain more experience[30,37]. Recent advances in minimally invasive instrumentation, including the development of a 5-mm endoscopic stapler, promise to address some of the remaining challenges of thoracoscopic surgery in small infants and neonates[37].

Best Practices

1. Steroid administration is first line treatment for fetal nonimmune hydrops in fetuses with CLL.
2. Chest CT scan is the best imaging study for evaluating CLL postnatally.
3. Thoracoscopic lobectomy for treatment of CLL can be done safely with minimal intraoperative and postoperative complications within the first year of life.

4. No clear consensus exists on the treatment algorithm for asymptomatic patients with CLL, who are at low risk for infection and have no clear radiographic features concerning for malignancy.

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Key Points

- Most congenital lung lesions are diagnosed on prenatal ultrasound.
- The majority of fetuses with congenital lung lesions proceed to uncomplicated term delivery.
- Thoracoscopic lobectomy is safe, well-tolerated and results in shorter length of hospital stay compared to open resection.
- Symptomatic neonates should undergo resection shortly after birth.
- Asymptomatic neonates can be observed, and undergo prophylactic resection at 6 months of life or later.
- Perioperative morbidity rates are low, with pneumonia and persistent air-leak the most common complications.
- Children who undergo resection demonstrate normal long-term pulmonary function.

Synopsis

Congenital lung lesions (CLL) comprise a heterogeneous group of developmental and histologic entities often diagnosed on screening prenatal ultrasound. Most fetuses with CLL are asymptomatic at birth, however the risk of malignancy and infection drives the decision to prophylactically resect these lesions. We describe our approach to minimally invasive lobectomy in children with CLL, post-operative care and management of procedure-specific complications.

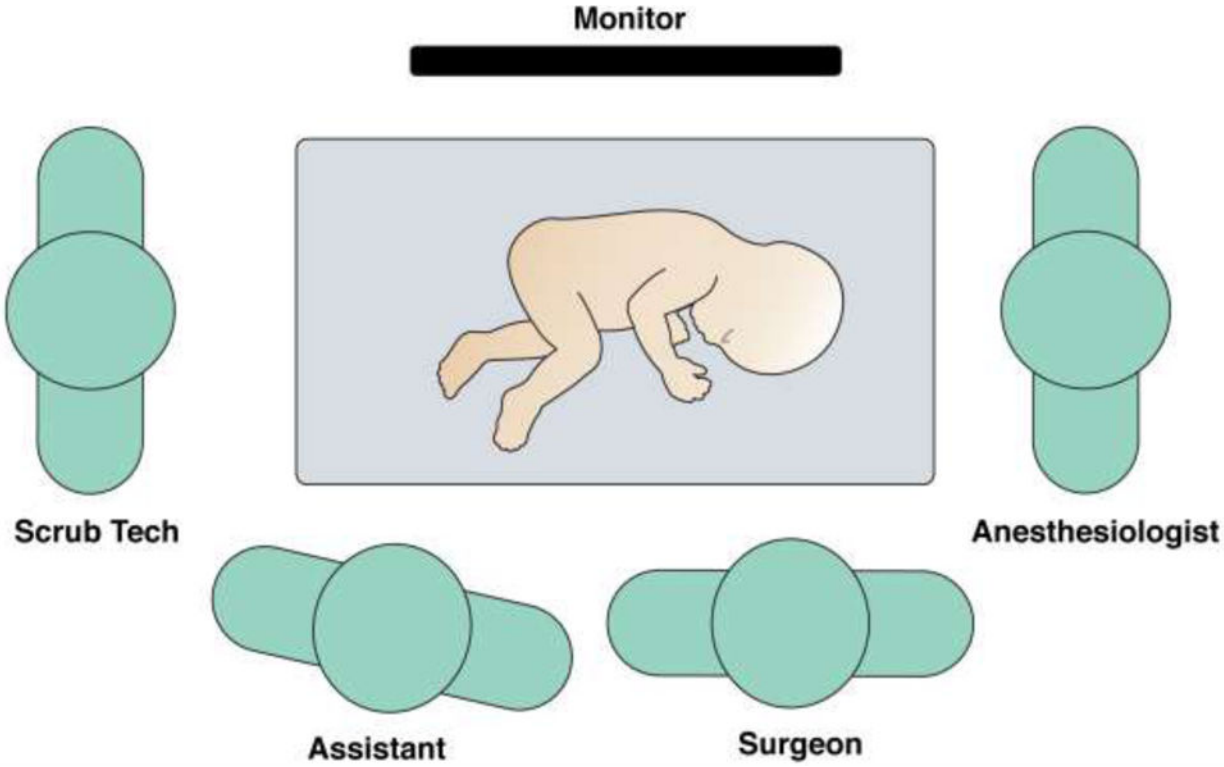

Figure 1.
Patient and room positioning for a right-sided lobectomy. The patient is placed in the lateral decubitus position, facing the surgeon and assistant. The thorax is aligned between the surgeon and the monitor.

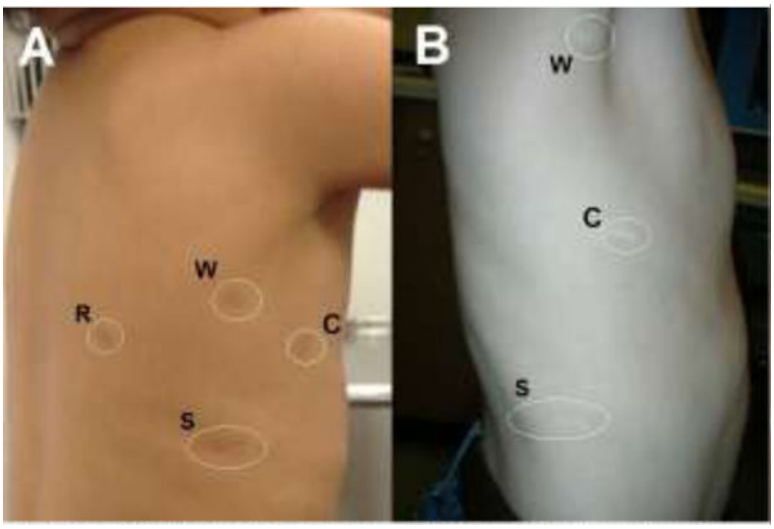

Figure 2.

A. Incisions illustrating port placement for a lower lobectomy. The camera is initially inserted through the incision antero-inferior to the tip of the scapula (W), then is moved to the mid-axillary (C) line to allow triangulation of the lower lobe. The inferior port is enlarged to 12 mm to facilitate the stapler and specimen retrieval (S). A fourth incision (R) can be made to assist in lung retraction for large cystic lesions.

B. Port placement for a right upper lobectomy. The initial incision (C) remains the camera port, while **a** working port (W) is placed cranially to allow triangulation of the lesion The inferior working port is again enlarged to 12mm (S).

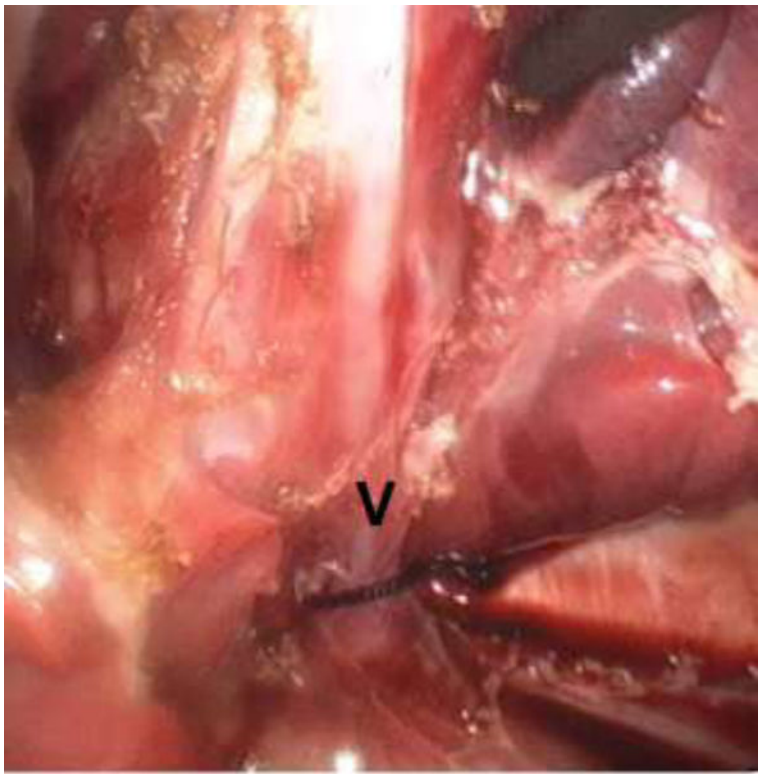

Figure 3.
The inferior pulmonary vein (V) is dissected circumferentially, and encircled with a silk tie. The tie can aid in the arterial dissection and can provide traction on the vein during division using the vessel sealing device

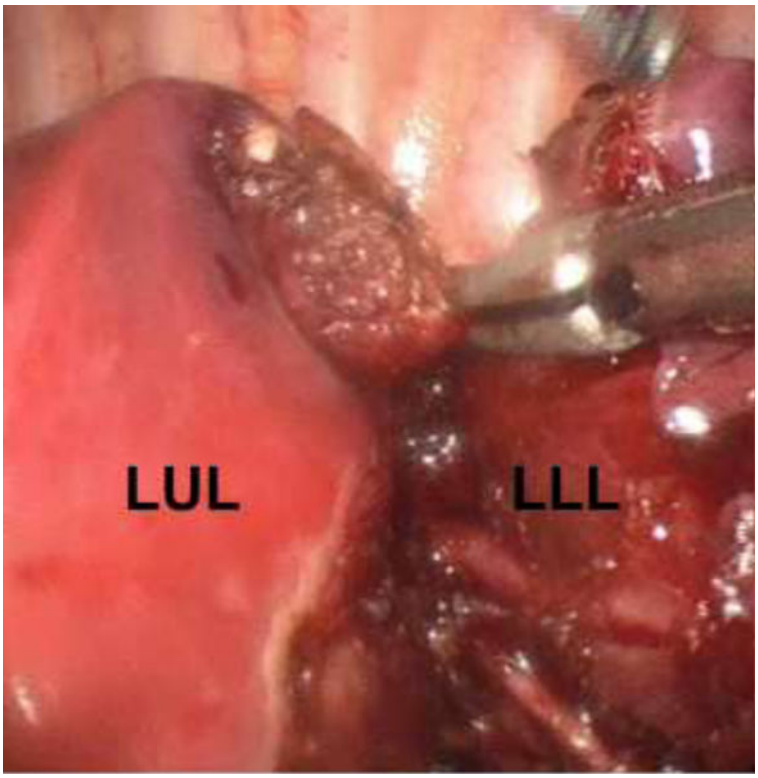

Figure 4.
The LigaSure is used to complete the oblique fissure of the left lung, isolating the left lower lobe (LLL) from the left upper lobe (LUL)

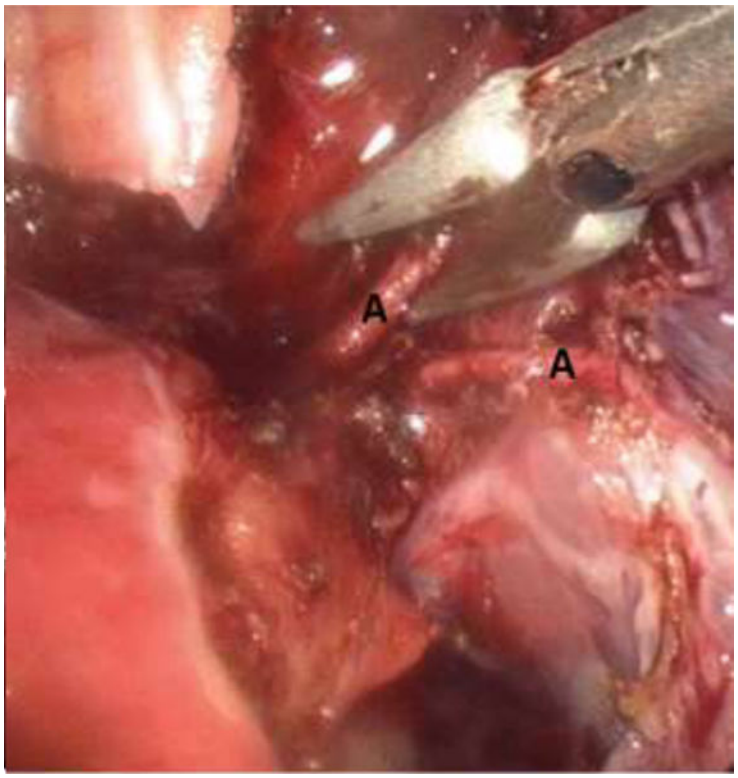

Figure 5.
The left lower lobe segmental arterial branches (A) are isolated and divided using the LigaSure.

Table 1

Perioperative Complications.

Author	n	Morbidity (%)	Infection (%)	Bleeding Transfusion (%)	Prolonged Tube Thoracostomy (%)	Pneumothorax (%)	Prolonged Intubation (%)	Phrenic Nerve Injury (%)	Chylochorus (%)	Bronchial Injury (%)
Albanese & Rothenberg (2007)	144	4 (2.8)	2 (1.4)	0	1 (0.7)	1 (0.7)	0	0	0	0
Seong et al. (2013)	50	1 (16)	0	1 (20)	6 (12)	0	0	0	1 (2.0)	0
Kunisaki et al. (2014)	40	15 (31)	0	11 (22)	2 (4.1)	0	0	2 (4.1)	1 (2.0)	0
Boubnova et al. (2011)	30	11 (37)	4 (13)	2 (6.7)	4 (13)	0	0	0	0	1 (3.3)
Kaneko et al (2010)	10	4 (25)	0	0	1 (6.3)	0	2 (13)	1 (6.3)	0	0
Rahman & Lakhoo (2009)	14	2 (14)	0	2 (14)	0	0	0	0	0	0
Diamond et al (2007)	12	4 (35)	3 (25)	0	0	1 (8.3)	0	0	0	0