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Thoracoscopic resection of lung masses is associated with excellent survival to discharge and good long-term outcomes

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OBJECTIVE
To report and evaluate risk factors for conversion and perioperative and long-term outcomes in dogs undergoing thoracoscopic lung lobectomy for resection of lung masses.

ANIMALS
61 client-owned dogs.

METHODS
This retrospective cohort study (June 11, 2008, to February 14, 2020) of data collected from medical records included signalment, results of diagnostic imaging, surgical technique, surgical and anesthesia time, mass location and size, hospitalization time, histopathologic findings, and long-term outcome. Follow-up was obtained from medical records and telephone contact with owners or referring veterinarians.

RESULTS
Histopathology results were available for 60 of 61 tumors. Fifty-seven (95%) were considered primary lung tumors, of which 46 (81%) were carcinomas. Clean surgical margins were achieved in 46 of 52 (88%) dogs. Conversion from thoracoscopy to thoracoscopic-assisted or open surgery occurred in 16 of 61 (26%) dogs. Larger tumor diameter (≥ 5 cm) and lymphadenopathy detected by preoperative CT scan were significantly associated with increased risk of conversion. There was no association between conversion and patient weight, body condition score, and tumor location. All 61 dogs survived to discharge, and 56 of 57 were alive 1 month postoperatively. Median overall survival time was 311 days (95% CI, 224 to 570 days). Tracheobronchial lymphadenopathy on preoperative CT scans was associated with shorter postoperative survival ($P < .001$). Patient age, tumor diameter, adjuvant chemotherapy following surgery, and incomplete margins were not associated with survival time.

CLINICAL RELEVANCE
Dogs had high survival to discharge and good long-term prognosis following thoracoscopic lung lobectomy. However, larger tumor size and tracheobronchial lymphadenopathy may increase the likelihood of conversion.

Keywords: tumors, lung, conversions, thoracoscopy, minimally invasive

Thoracoscopic lung lobectomy (TLL) has been described in canine patients in a number of studies to date for resection of primary or metastatic pulmonary masses,[1–4] for treatment of spontaneous pneumothorax,[5,6] and for treatment of pulmonary consolidation with or without foreign body migration.[7,8] While reports describing the technical aspects of TLL and data from smaller cohorts of patients are helpful in establishing any new procedure, results from larger studies are necessary to establish the evidence base that any given procedure is at least as effective as an open thoracotomy. While previous studies of TLL have provided data on intraoperative complications and

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conversion rates,[1–3] very little data exist evaluating longer-term oncological outcomes in dogs undergoing TLL for treatment of primary lung tumors or other types of pulmonary neoplasia. One small study reported that oncological outcomes were equivalent to those of open surgery, but this study included a cohort of only 9 dogs that underwent TLL.[3] In that study, the 1- and 2-year survival rates were 62% and 42% for those dogs undergoing TLL and 64% and 56% for dogs undergoing thoracotomy.

The aims of this study were to report the perioperative and long-term outcomes of a large cohort of dogs with lung masses undergoing TLL at centers experienced with minimally invasive procedures. A secondary aim was to evaluate risk factors for conversion in this case population.

Methods

Animals

The medical records of canine patients with pulmonary masses that had been surgically managed by TLL between June 2008 and February 2020 at 1 of 4 veterinary medical teaching hospitals and 1 private practice were evaluated. Dogs were excluded from the study if a pulmonary mass was not diagnosed and thoracoscopic treatment was initiated for a different pathology. Data from dogs in which a total thoracoscopic approach was attempted but the procedure was converted to a thoracoscopic-assisted approach or a thoracotomy were retained in the study. This study included some data from a small cohort of patients for which short-term outcomes were previously published.[2]

Diagnostic evaluation

Data collected from medical records included signalment, clinical signs exhibited, results of diagnostic imaging, anesthesia and surgical technique employed, mass location and size, the number and reason for conversion to an assisted or open procedure, perioperative complications, hospitalization time, histopathologic findings, and long-term outcome. Patient follow-up was obtained from medical records and telephone contact with owners or referring veterinarians.

Complications and conversion

Complications were recorded for each procedure and classified using the Veterinary Cooperative Oncology Group–Common Terminology Criteria for Adverse Events scheme recently described.[9] Conversion was classified as either conversion to a thoracoscopic-assisted approach or an open thoracotomy along with the reason conversion was pursued. Conversions were graded from Grades 1 to 4 on the basis of a previously published classification system.[10]

Statistical analysis

Summary statistics were calculated. Continuous variables were assessed for normal distribution using a combined test of skewness and kurtosis. Logistic regression was used to identify variables associated with conversion to open lung lobectomy (variables tested included institution, caudal tumor location, body weight, body condition score, maximum tumor diameter, and presence of enlarged lymph nodes on CT) and incomplete histopathological margins (variables tested included institution, caudal tumor location, maximum tumor diameter, enlarged lymph nodes, and conversion to open). Univariable tests were performed, and variables with $P < .15$ on Wald tests were evaluated for inclusion in the final model using a forward selection approach. Final multivariable models included variables with $P < .05$ on Wald tests or those identified as confounders on the main effects. Survival times were estimated using the Kaplan-Meier product limit method, and log-rank tests were used to evaluate unadjusted associations between survival and tumor diameter ≥ 5 cm, incomplete margins, chemotherapy, and enlarged lymph nodes on CT scan. All tests were 2 sided, and $P < .05$ was considered statistically significant. All analyses were performed with a commercially available statistical software program (Stata Statistical Software, version 16.1; StataCorp LLC.)

Results

Animals

Sixty-one dogs met the inclusion criteria for the study and were recruited from 4 veterinary medical teaching hospitals and 1 private specialty practice, all of which had extensive experience in veterinary minimally invasive procedures.

Signalment

Breeds included Labrador Retrievers (n = 9), mixed-breed dogs (9), Bernese Mountain Dogs (7), Golden Retrievers (7), German Shepherd Dogs (4), Cocker Spaniels (4), Doberman Pinschers (4), Australian Shepherds (2), Boxers (2), Standard Poodles (2), and 1 each of 11 other breeds. Mean age was 10.6 ± 2.0 years old (range, 6 to 15 years old). Mean body weight was 31.1 ± 10.3 kg (range, 12.6 to 54.6 kg). Median body condition score was 6 (range, 4 to 8). Thirty of 61 (49.2%) dogs were spayed females, 24 (39.4%) were castrated males, and 7 (11.5%) were intact males.

Clinical signs

In 32 of 61 (52.4%) dogs, the finding of a lung mass was an incidental finding not associated with clinical signs but detected during a diagnostic evaluation for other reasons. Preoperative clinical signs in dogs that were symptomatic included coughing (25/61 [40.9%]), dyspnea (3/61 [4.9%]), sneezing (2/61 [3.3%]), wheezing (1/61 [1.6%]), and panting (1/61 [1.6%]).

Diagnostic imaging

Thoracic radiographs were available for evaluation in 57 of 61 dogs and revealed thoracic masses in all cases. One dog had evidence of pulmonary consolidation in 1 lung lobe. Evaluation with abdominal ultrasonography was performed preoperatively in 36 of 61 dogs. Significant findings during ultrasonography included splenic nodules (n = 10), nonspecific hepatomegaly (4), adrenomegaly (4), renal cyst (1), prostatomegaly (1), and liver nodules (1). Computed tomography was performed preoperatively in 58 of 61 dogs.

Tumors were located in the following lung lobes: left caudal (21/61 [34.4%]), right caudal (16/61 [26.2%]), right cranial (10/61 [16.4%]), left cranial (8/61 [13.1%]), right middle (5/61 [8.2%]), and both right middle and right cranial (1/61 [1.6%]). No tumors were located in the accessory lobe. Overall, 37 of 61 (60.7%) tumors were in the caudal lobes, and 24 of 61 (39.3%) were in the cranial or middle lobes. Median tumor maximum diameter was 4.2 cm (IQR, 2.5 to 5.5; range, 0.5 to 12.5 cm). Enlarged lymph nodes were observed on CT scans in 8 of 58 dogs for which data were available. Metastatic lesions were detected in 3 dogs within the same lung lobe as the primary tumor, and in 1 dog with a mass in the left cranial lobe, a small mass that was considered a possible metastatic lesion was detected in the right cranial lobe. Incidental bullae/blebs were detected in the lungs of 9 of 58 dogs on CT images.

Anesthesia and surgery

In 52 of 61 (85%) cases, one-lung ventilation (OLV) was used. The following devices were used to initiate OLV: endobronchial blockers (7 to 9 Fr size, Arndt Endobronchial Blocker; Cook Medical Inc) in 25 dogs, double-lumen endobronchial tubes (28 to 41 Fr sizes, Rusch Robert-Shaw Endobronchial Tube; Teleflex Medical Inc) in 13, EZ-blockers (Teleflex Medical Inc) in 12, and selective intubation with a large animal endotracheal tube (12 mm) in 5 dogs. In 29 of 52 (56%) cases, complications occurred with induction or maintenance of OLV, and in some dogs more than 1 modality for induction of OLV was attempted. The most common complications associated with OLV were intraoperative intermittent or permanent loss of OLV (n = 10), persistent ventilation of the right cranial lung lobe (7), requirement for tube repositioning (2), double-lumen endobronchial tube being too short (2), incomplete endobronchial blocker balloon filling (2), OLV device placed into contralateral main stem bronchus (1), endobronchial balloon prolapse (1), and EZ-blocker being too short (1).

Dogs were positioned depending on the location of their tumor in either left lateral recumbency (n = 38), right lateral recumbency (16), 45° oblique right sternal recumbency (3), 45° oblique left sternal recumbency (2), or dorsal recumbency (2). Dogs operated in dorsal recumbency had a paraxiphoid camera portal placed, whereas dogs operated in lateral or oblique lateral recumbency had an intercostal camera portal placed. Precise additional portal positions were variable and not described in detail due to the large number of combinations used by operating surgeons but generally followed previously described triangulation techniques for the different lung lobes.[11] A 3-port technique was used in 40 dogs, and a 4-port technique was used in 14 dogs. In 3 dogs that were converted, either 2 ports (n = 2) or a single port (1) was inserted prior to conversion to an open approach, and in 4 dogs, port numbers were not noted in the medical record. In all dogs, surgical technique mirrored the technique for TLL previously described in other studies and references.[1–3] In all dogs, surgical staplers were used to complete the lobectomy or lobectomies. Where staple type was noted in the record, EndoGIA (Medtronic Inc) cartridges were used in 51 dogs, whereas in 8 dogs that were converted, thoracoabdominal (TA) staplers were used. In 20 dogs a single EndoGIA cartridge was used, in 27 dogs 2 cartridges were used, and in the remainder of dogs conversion to an open approach precipitated use of a TA stapler or the number of cartridges used was not noted. In all cases, 3.5-mm leg length EndoGIA staplers were used in 60-mm (n = 56), 45-mm (14), or 30-mm (11) cartridge lengths. Lung lobes were retrieved either by insertion into a specimen retrieval bag (n = 43), through an Alexis wound retractor (Applied Medical Inc) placed into a small expansion of one of the port incisions (11), or through a thoracoscopic-assisted incision or intercostal thoracotomy after conversion (7).

Conversion and perioperative complications

Conversion occurred in a total of 16 of 61 (26.2%) dogs, 12 of which were converted to an intercostal thoracotomy and 4 of which were converted to a thoracoscopic-assisted technique as previously described.[12] Reasons for conversion (more than 1 reason given for some cases) included the following: mass judged to be too large (n = 6), failure of or difficulty maintaining OLV (3), poor visualization (3), presence of adhesions (2), OLV not tolerated (1), surgical stapler unable to be opened in the thorax (1), intercostal artery bleed (1), or pus leaking from necrotic mass (1). Larger tumor diameter (OR, 1.65; 95% CI, 1.05 to 2.61; P = .029) and lymphadenopathy on CT scan (OR, 16.4; 95% CI, 1.21 to 220.57; P = .035) were significantly associated with conversion, adjusting for institution. Caudal tumor location, body weight, and body condition score were not associated with odds of conversion.

Intraoperative complications occurred in 10 of 61 (16%) dogs. Hemorrhage from intercostal arteries occurred in 2 dogs, 1 of which required conversion to thoracotomy to achieve hemostasis and 1 of which was managed thoracoscopically by placement of circumcostal ligatures. In 4 other dogs, excessive bleeding was noted as an intraoperative complication beyond the expected intraoperative hemorrhage, although none of the 61 dogs required a blood transfusion. In 3 dogs, intraoperative air leakage was detected. In 1 dog, air leakage from the EndoGIA staple line was detected and resolution followed conversion to a thoracoscopic-assisted approach and reinforcement with a TA stapler. In a second dog, leakage from an EndoGIA staple line was treated by placement of a resorbable self-locking loop device (Ligatie; Resorbable Devices Inc). In a third dog, an iatrogenic tear in the cranial lung lobe resulted in air leakage, which was managed by conversion to a thoracoscopically assisted approach with subsequent surgical stapling of the affected area. In 1 dog, during lung lobe extraction, rupture of the mass occurred, with leakage of purulent material into the thorax. This complication was successfully managed by copious saline lavage of the thorax and surgical drain placement.

Postoperative complications occurred in 5 of 61 (8%) dogs. These included postoperative air leakage in 2 dogs. One was a low-grade and self-resolving air leak that required no specific treatment. The second case was the dog in which a resorbable self-locking loop device had been placed. The dog developed a pneumothorax 7 days postoperatively, and reexploration of the thorax revealed a broken Ligatie with air leakage from the site. Two dogs developed aspiration pneumonia postoperatively that resolved with medical management, and 1 dog developed a surgical site infection that resolved with antibiotic treatment.

Anesthesia and surgery time for all completed procedures was a median of 225 (range, 100 to 382) and 105 (range, 65 to 185) minutes, respectively, for nonconverted cases. For converted cases, median anesthesia and surgery time was 240 (range, 90 to 425) and 135 (range, 50 to 293) minutes. In some cases, anesthesia time included time for a preoperative CT scan under the same anesthetic episode.

Histopathology

Among 60 tumors for which histopathology was available, 57 (95%) were considered primary lung tumors and 3 were not. These included 46 carcinomas, 8 histiocytic sarcomas, 1 liposarcoma, 1 granuloma, and 2 osteosarcoma. One dog had thymoma and carcinoma, 1 dog had carcinoma and histiocytic sarcoma, and 2 dogs had an endocrine tumor and carcinoma. Among 52 dogs for which data were available, histopathological margins were clean in 45 (86.55%) dogs and incomplete in 7 (13.5%). Diagnoses for the incomplete cases were carcinoma in 6 and histiocytic sarcoma in 1. Institution, caudal tumor location, maximum tumor diameter, body condition score, body weight, and conversion were not associated with incomplete histopathological margins.

Lymph nodes were harvested at the time of surgery in 16 dogs, 7 of which occurred in nonconverted cases and 9 of which occurred in converted cases. Lymph nodes extirpated included the right tracheobronchial lymph node (n = 6), left tracheobronchial lymph node (1), and sternal lymph node (1). Histopathology revealed metastatic disease in 5 dogs and benign disease in 8 dogs. Benign changes included lymphoid hyperplasia, anthracosis, and sinus histiocytosis.

Long-term outcome

All 61 (100%) dogs survived to discharge and 56 of 57 (98.2%) that were available for follow-up were alive 1 month postoperatively. Median (range) for hospitalization time in days was 3 days (1 to 7 days) and in postoperative hours was 48 hours (24 to 240 hours).

Among 55 dogs with available data, 21 dogs had chemotherapy postoperatively, most commonly CCNU, vinorelbine, carboplatin, or a combination of the drugs. Dogs with incomplete margins were not more likely to receive chemotherapy compared to dogs with complete margins ($P > .99$). At the time of data collection, 44 dogs had died and 17 were alive or lost to follow-up.

Median overall survival time was 311 days (95% CI, 224 to 570 days). Lymphadenopathy on CT images was associated with increased hazard of death ($P < .001$). Unadjusted median survival time for 8 dogs with enlarged thoracic lymph nodes identified on thoracic CT was 60 days (95% CI, 7 to 300) compared to 365 days (95% CI, 240 to 720) in 50 dogs without enlarged nodes. Dog age, tumor diameter, administration of chemotherapy, and incomplete margins were not associated with hazard of death.

Discussion

This study reported the perioperative and long-term outcomes of the largest cohort of dogs reported in the literature to date that underwent TLL for management of lung masses. Thoracoscopic treatment of thoracic disorders remains in its infancy in veterinary medicine, with outcomes of only relatively small numbers of patients reported in the veterinary literature despite the equipment and expertise having been available to veterinary surgeons for many years now. The reasons for this may be multifactorial but may be related to challenges in training minimally invasive thoracic surgeons or the paucity of trained anesthesiologists available to help induce and monitor OLV that is essential to performing TLL successfully in dogs. This study attempted to provide more robust data on essential perioperative and long-term outcomes to strengthen the evidence base for use of TLL in dogs with pulmonary neoplasia. It is essential to establish that minimally invasive thoracic procedures are providing oncological outcomes that are at least as good as those reported for open thoracic approaches and that perioperative morbidity is no greater than the current standard of care.

Short-term outcomes of TLL in this cohort of dogs were very good, with all dogs being discharged from the hospitals where they were operated and 98% of dogs being alive at 1 month postoperatively. The rates of intraoperative complications (16%) and postoperative complications (8%) compare favorably with the complication rates reported for lung lobectomy performed through open thoracotomy.[13–17] Intraoperative complications were mostly related to hemorrhage and air leakage. Care needs to be taken to avoid intercostal artery hemorrhage by cannula placement away from the caudal margin of ribs in the intercostal spaces. Air leakage occurred due to either iatrogenic damage to the lung from instrument exchanges and manipulation or once from a staple line failure. Great care needs to be taken during thoracoscopic procedures to avoid damage to the delicate surface of the lung, and the fulcrum effect of the instrumentation sometimes masks just how much force is being exerted on tissues during manipulation. A recent large retrospective study[16] of dogs that underwent open thoracotomy for resection of primary lung tumors reported a 5.9% perioperative mortality (within 14 days postoperatively) and intraoperative and postoperative complications of 11.8% and 20.6%, respectively.

Conversion to an open approach did occur in almost a quarter of the dogs in the study, which was a higher rate than in previous publications. This conversion rate may reflect the early part of the learning curve in some centers. Further experience may result in the conversion rate decreasing over time. In 4 of the cases, conversion to a thoracoscopic-assisted approach was performed and therefore those patients may still have benefited from the advantages a less invasive approach may have afforded them.[12] In humans, conversion rates for TLL for treatment of lung cancer were 9.6% in 1 metanalysis of 20 studies.[18] While this number is lower than that reported in our study in dogs, it is still higher than for a lot of other minimally invasive techniques and reflects the complexity of the procedure in both dogs and people. In general, 4 main causes of conversion have been reported in humans: intraoperative complications, technical problems, anatomical problems, and oncological conditions.[19] More specifically, in people > 73% of conversions are caused by just 3 reasons: vascular injury, difficulty dissecting the lymph nodes, and adhesions.[18]

In this population of dogs, while all of these causes of conversion were reported, it appears that anatomical causes (tumors judged to be too large for resection) and technical problems with equipment and anesthesia/OLV-related problems appeared to predominate. This is perhaps not surprising given the relative inexperience of veterinarians with the TLL procedure, which might account for poor case selection decisions and challenges associated with using inappropriately sized human medical devices (such as staplers and OLV devices). Lack of experience with OLV or the lack of availability of experienced anesthesiologists to troubleshoot the use of OLV may also be an important factor. Importantly, of the 12 dogs in this study that underwent conversion, complication rates did not appear to be different between those that were converted to thoracoscopic-assisted procedures, those that were converted to open thoracotomy, and those that underwent successful TLL without conversion. These findings are mirrored in human video-assisted thoracoscopic surgery (VATS) lung lobectomy, in which VATS conversion cases had similar complication rates to open thoracotomy cases.[20]

The ability to achieve a complete margin of resection is one of the principal tenets of surgical oncology. It is essential that TLL can provide equivalent completeness of resection to that achieved with open approaches, and a previous study with smaller cohorts of patients and a control population suggested that this was the case.[2] In this study, a complete surgical resection was achieved in 86% of dogs. This compares favorably to data reported for primary lung tumor resection via open thoracotomy.[14–17] Cases selected for TLL may, however, have smaller lesions located further from the pulmonary hilus compared to dogs in which an open thoracotomy is selected, which may represent a significant bias in case selection. While techniques that seek to improve the percentage of cases in which clean margin resection is achieved should continue to be investigated, it is critical to establish that TLL is not falling short of the oncological standards achieved using open thoracotomy.

In this study, median survival of patients undergoing TLL was 311 days. Long-term outcomes of dogs undergoing TLL appear to be in line with those reported historically, with previous reports showing median survival times of 300 to 498 days.[14–17] No studies contain completely homogeneous populations of patients, and this study was no exception. Multiple histological types are reported here as well as in other studies and these data are grouped together, which is suboptimal for comparison purposes. Furthermore, this study lacked a control group of dogs with lung masses that would have been good candidates for TLL but were treated by open thoracotomy and therefore direct comparisons cannot and should not be drawn. A recent study[17] reported longer median survival times (716 days) for a cohort of 52 small dog breeds with primary pulmonary carcinomas. Given that patients treated by TLL in this and other studies tend to be limited to large breeds (median weight, 31 kg) due to the challenges associated with anesthesia, working space, and available stapling technologies, there might be a negative bias on median survival time when results from dogs treated by TLL are reported. While not directly comparable to any other study data, there is no reason from this study to suspect that long-term survival is affected by surgical approach (TLL vs open thoracotomy) in dogs with primary lung tumors. These findings have been confirmed in human patients with non–small cell lung cancer, which is the closest corollary to dogs with primary lung tumors. Mature data with long-term survival have been reported in the form of multiple meta-analyses and suggest that outcomes are similar when propensity-matched analysis is used to compare open and minimally invasive lung lobectomy for non–small cell lung cancer.[21,22]

There were very important limitations that need to be considered when evaluating the data presented in this study. Most importantly, the authors do not have access to data from a contemporary population of canine patients operated through an open thoracotomy and so no direct comparisons of outcomes can be made. The patients in this study were operated at 5 veterinary institutions all with variable surgeon experience levels and somewhat different diagnostic and surgical approaches, although similar techniques were used in all cases. Due to the retrospective nature of the study, not all data were available for evaluation and not every patient was available for follow-up.

In conclusion, TLL appears to provide a very safe and effective surgical option for removal of lung masses in canine patients that fit the selection criteria. A prospective randomized study would be required to provide higher-level evidence to compare open and minimally invasive approaches for lung lobectomy.

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