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REVIEW ARTICLE

Robotic esophagectomy with function-preserving radical mediastinal lymphadenectomy for esophageal cancer

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Abstract

Radical lymphadenectomy is the critical component of surgery for esophageal cancer. However, lymphadenectomy significantly contributes to postoperative morbidity, particularly in terms of pulmonary complications following esophagectomy. Function-preserving mediastinal lymphadenectomy seeks to balance the procedure's necessary radicality and optimal functional outcomes. This approach emphasizes the preservation of the thoracic duct, tracheobronchial vascularity, and the pulmonary and recurrent laryngeal branches of the vagus nerve. Preservation of the thoracic duct is facilitated by indocyanine green fluorescence. Compared to the conventional technique of thoracic duct identification using anatomical landmarks, indocyanine green fluorescence lymphangiography offers real-time feedback, making it particularly advantageous in cases with complex anatomy or when the thoracic duct is challenging to visualize using conventional methods. Preservation of pulmonary branches of the right vagus during subcarinal lymphadenectomy and left recurrent laryngeal nerve during left paratracheal node dissection are technically challenging. The description of two types of left recurrent laryngeal nerve node dissection and technical tips for nerve function preservation are outlined in this review. Intraoperative neuromonitoring is a useful adjunct for nerve-sparing mediastinal lymphadenectomy. As ischemia to the respiratory tract impairs respiratory protective mechanisms, preservation of the tracheobronchial blood supply is critical. Preoperative imaging to detect bronchial artery anatomical variations and intraoperative assessment of perfusion using laser doppler flowmetry and indocyanine green fluorescence angiography are useful strategies to minimize tracheobronchial ischemia. Function-preserving mediastinal lymphadenectomy has the potential to improve short- and long-term outcomes after esophagectomy for esophageal cancer.

KEYWORDS
esophagectomy, esophageal cancer, lymphadenectomy, robotic, thoracic duct

1 | INTRODUCTION

Surgery is a fundamental component of multidisciplinary treatment for esophageal cancer. The primary objective of surgical management is to achieve an en-bloc resection of the esophagus and its associated lymph nodes. Lymphadenectomy provides crucial insights into the lymphatic spread of esophageal cancer, particularly in its two major histopathological types: squamous cell carcinoma (SCC) and adenocarcinoma (EAC).[1,2] Furthermore, radical lymph node dissection enhances the yield of lymph nodes and improves the accuracy of pathological staging. Although the impact of radical lymphadenectomy on survival remains debated, data indicate that standard surgery results in high loco-regional recurrence rates (30–40%) and poor 5-year overall survival (OS) rates (20–30%), whereas radical surgery achieves better 5-year OS rates (40–50%).[3–5]

Nevertheless, the widespread adoption of radical lymphadenectomy is hindered by the increased morbidity associated with the procedure, particularly pulmonary complications. Postoperative pneumonia rates following extended lymphadenectomy for esophageal tumors can be as high as 60%.[6] Minimally invasive esophagectomy, especially the robotic approach, has improved short-term postoperative outcomes.[7] However, pulmonary complications remain an important cause of postoperative morbidity following esophagectomy with radical lymphadenectomy. This review focuses on "function-preserving mediastinal lymphadenectomy," a technique that aims for radical lymphadenectomy without significantly impairing respiratory function in patients undergoing robotic esophagectomy. This approach involves preserving the thoracic duct, tracheobronchial vascularity, and the vagus nerve's pulmonary and recurrent laryngeal branches. Each of these elements will be discussed in detail under separate subheadings.

2 | THORACIC DUCT PRESERVATION

The thoracic duct (TD), the largest lymphatic vessel in the body, originates from the cisterna chyli at the L2 vertebral level.[8] It carries approximately 1.38 mL/kg of lymph per hour, collecting lymph from the entire body except for the right hemithorax, right upper limb, and right side of the head and neck. In radical lymphadenectomy for esophageal cancer, the TD is often excised due to its multiple lymphatic connections with the esophagus.[9,10] Murakami et al.[11] in a cadaver study identified three types of lymphatic channels associated with the esophagus and the TD (Figure 1):

1. Direct lymphatic drainage of the esophagus: This type involves direct drainage from the esophagus to the TD and is predominantly located at the 1st–3rd and 6th–8th thoracic vertebrae levels.

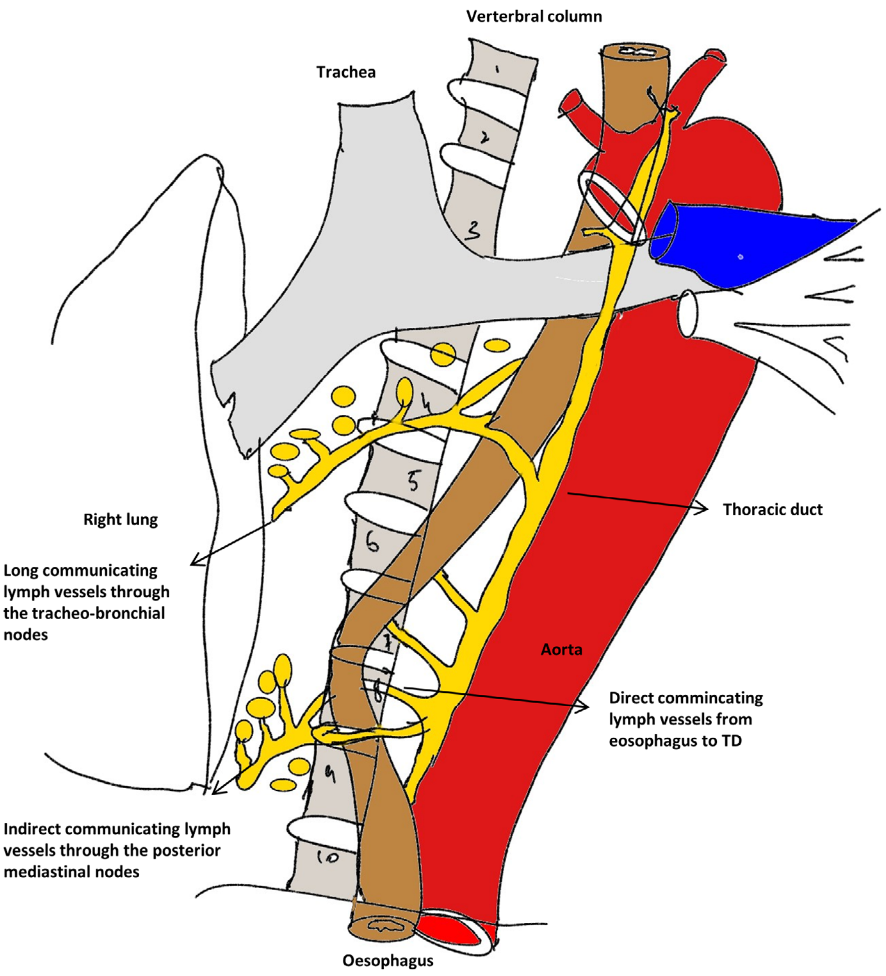

FIGURE 1 Pictorial depiction of different types of lymphatic channels associated with esophagus and thoracic duct.

2. Common lymphatic drainage around the esophagus: These are large collector ducts that primarily drain the tracheobronchial nodes to the TD at the level of the 4th–6th thoracic vertebrae. Half of them communicate with the direct esophageal drainage channels.
3. Indirect drainage channels: These channels stem from large posterior mediastinal lymph nodes surrounding the esophagus at the levels of the 6th–8th thoracic vertebrae.

A thin fascial structure covering the TD and surrounding adipose tissue contains TD lymph nodes. TD lymph node positivity ranges from 6% to 15% and increases with the tumor stage.

2.1 | Oncological outcomes of TD resection in esophageal cancer

The impact of routine TD resection on survival and prognosis remains contentious. Earlier studies indicated that routine TD resection increased the yield of resected lymph nodes, but recent research has shown mixed results regarding its effect on survival outcomes. Udagawa et al.[10] studied 778 patients undergoing radical three-field lymphadenectomy for SCC of the thoracic esophagus. They found no metastatic lymph nodes in either TD resected or TD preserved groups for Tis or T1a tumors. For T1b/T2 and T3/T4 tumors, the number of lymph nodes retrieved was higher in the TD resected group (2.2 vs. 10 for T1b/T2 and 6.5 vs. 11.5 for T3/T4). However, this increased lymph node yield did not translate to improve 5-year OS, 50% versus 44.9% for T1b/T2 tumors and 25.2% versus 33.3% for T3/T4 tumors in TD resected and TD preserved groups, respectively.[10] Matsuda et al.[12] found that the incidence of TD lymph node metastasis was higher in upper thoracic tumors (40%) compared to the middle (31%) and lower thoracic tumors (25%). Interestingly, 5-year recurrence-free survival (RFS) was 90% in the TDR group compared to 67.3% in the TDP group for clinical stage I tumors, though this difference was not statistically significant ($p=0.055$). Also, no survival difference was observed in clinical stages II and III esophageal tumors.[12] The same authors investigated the prognostic significance of TD lymph node metastasis in 232 patients with esophageal SCC who underwent transthoracic esophagectomy. Their study revealed that TD lymph node metastasis was an independent predictor of reduced recurrence-free survival and overall survival in multivariate analysis. The survival outcomes for patients with TD lymph node metastasis were comparable to those with metastasis to non-regional lymph nodes, highlighting the adverse impact of TD lymph node involvement on prognosis.[13] The oncological outcomes of TDR versus TDP explored in several studies are summarized in Table 1.[14–17]

2.2 | Physiological outcomes of TD resection in esophageal cancer

Given that the TD carries 75% of the lymph volume of the body, its resection can lead to significant hemodynamic and nutritional alterations. Imamura et al.[18] reported increased postoperative fluid requirements following TD resection, with the TD resection group requiring 9.10 ± 2.35 mL/kg body weight, compared to 6.05 ± 2.22 mL/kg in the TD preservation group. They also observed abnormal lymphatic pathways developing near the kidneys 1-year post-TD resection. Similarly, Anand et al. reported that the median fluid requirement on the first postoperative day was higher in the TD resection group (3310 mL vs. 2875 mL), although this difference was not statistically significant ($p=0.059$).[19] Interestingly, the TD resection group exhibited persistent tachycardia on postoperative day three (median pulse rate of 111/min vs. 95/min in the TD preservation group, $p=0.043$), likely due to significant volume depletion. Other parameters, such as mean postoperative blood pressure and urine output, showed no significant differences.[19] Fujisawa et al. reported on the nutritional outcomes of TD resection in 174 patients with esophageal malignancy, focusing on total body weight, body mass index, and fat mass 1 year after surgery.[20] The TD resection group had significantly lower total body weight (51.11 ± 8.32 kg vs. 55.32 ± 8.77 kg, $p=0.017$), body mass index (18.71 ± 2.44 kg/m^2 vs. 20.14 ± 2.48 kg/m^2 in TD preservation, $p=0.002$), and fat mass (6.96 ± 3.99 kg vs. 10.34 ± 4.89 kg in TDP, $p<0.001$) compared to TD preservation group. However, the two groups had no difference in the skeletal mass.[20] Nishimura et al.[21] investigated the long-term effects of TD resection on body composition in 217 patients over 5 years following esophagectomy with radical lymphadenectomy. Adipose tissue loss was significantly higher in the TD resection group at 1 and 3 years, but muscle mass loss was comparable. The difference in adipose tissue loss between the two groups decreased over the 5-year follow-up.[21]

The arguments favoring TD resection are increased lymph node yield and radicality of surgery, the potential for better survival in early-stage tumors where neoadjuvant chemoradiotherapy is not used, and reduced incidence of chyle leak. However, TD preservation is supported by better hemodynamic parameters in the immediate postoperative period and superior short- and long-term nutritional outcomes without adversely affecting oncological outcomes. Hence, despite its limitations, the available evidence does not support routine TD resection in the era of neoadjuvant chemoradiotherapy. TD resection is indicated only when the tumor is directly infiltrating TD, bulky posterior mediastinal nodes necessitating TD resection to ensure complete clearance and intraoperative suspicion of TD injury.

2.3 | Operative strategies for the preservation of thoracic duct

Conventionally, TD is identified intraoperatively using anatomical landmarks. In the infracarinal region, the TD is located between descending thoracic aorta and azygous vein (Figure 2). At the level of the fourth and fifth thoracic vertebrae, the TD crosses to the left side of the esophagus, where it is more prone to injury. Further superiorly, the TD assumes a course more to the left of the esophagus and ascends in the left part of the thoracic inlet (Figure 2). With the advent

TABLE 1 Summary of data depicting incidence of metastasis to thoracic duct (TD), oncological outcomes of TD resection and its comparison with TD preservation group.

Author, year	Study groups	Number of patients	Incidence of TD lymph node metastases	Number of dissected lymph nodes	Postoperative morbidity	Survival outcomes
Yoshida et al., 2019[15]	TDP TDR	392 145	10%	19.2 ± 9.5 21.2 ± 8.7 $p = 0.034$	Overall morbidity (33.9 vs. 43.4, p-0.04) and pulmonary morbidity (12.2 vs. 26.9, $p < 0.01$) higher in TDR group.	No significant difference in 1-, 3-, and 5-year OS rates between two groups.
Oshikiri et al., 2019[16]	TDP TDR	122 122	8%	22 ± 11 25 ± 10 $p = 0.005$	Chylothorax (0 vs. 2.5%, $p = 0.04$) and left recurrent laryngeal nerve palsy (12.9% vs. 29.8%, $p = 0.018$) were significantly higher in the TDR group.	No significant difference in 5-year OS and DFS rates between two groups.
Matsuda et al., 2016[13]	TDP TDR	89 167	11%	20.02 ± 8.16 27.93 ± 11.75 $p \leq 0.001$	Pneumonia—20% Anastomotic leakage—15% Chylothorax —1% No significant difference in complication rate between two groups.	The 5-year DFS in clinical Stage I patients was higher in the TDR group, nearing statistical significance (90.3% vs. 67.3%, $p = 0.055$). Other stages have no difference in survival rates.
Tanaka et al., 2021[17]	TDP TDR	642 642	NR	23.55 ± 12.32 26.35 ± 11.01 $p \leq 0.0001$	NR	The 5-year OS and DFS significantly higher in the TDR group.
Oshikiri et al., 2023[18]	TDP TDR	1638 1638	NR	21 30 $p \leq 0.0001$	NR	No significant difference in 5-year OS and cancer specific survival rates between two groups.

Abbreviations: DFS, disease free survival; NR, not reported; OS, overall survival; TD, thoracic duct; TDLN, thoracic duct lymph node; TDP, thoracic duct preservation; TDR, thoracic duct resection.

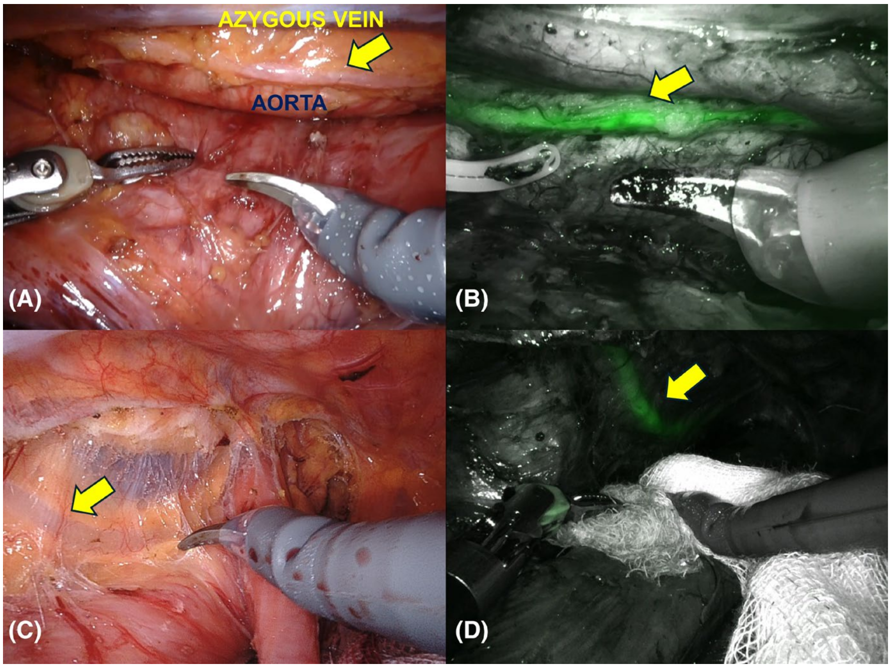

FIGURE 2 Anatomical location of thoracic duct. (A) In the infracarinal region, the thoracic duct (arrow) is located between the descending thoracic aorta and the azygous vein. (B) Indocyanine green fluorescence facilitates the identification of the thoracic duct (arrow) in difficult cases. (C) In the supracarinal region, the thoracic duct (arrow) moves to the left of the esophagus. (D) Identification of thoracic duct (arrow) facilitated by indocyanine green fluorescence.

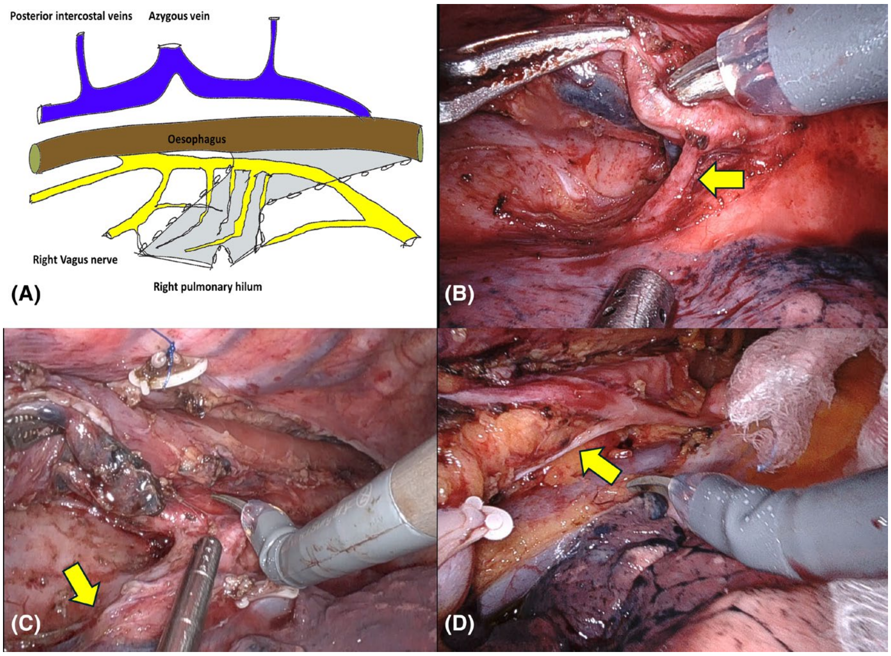

FIGURE 3 Nerve-sparing lymphadenectomy. (A) Pictorial depiction of pulmonary branches of right vagus. (B) Division of right vagus beyond caudal pulmonary branches (arrow) during subcarinal lymphadenectomy. (C) Completion of subcarinal lymphadenectomy with preservation of pulmonary branches of vagus (arrow). (D) Completion of right paratracheal lymphadenectomy with preservation of pulmonary branches of vagus (arrow).

of fluorescence-guided surgery, the usefulness of indocyanine green (ICG) fluorescence for TD identification has been documented in recent studies.[22] Administering ICG into the groin nodes under sonographic guidance has shown more consistent outcomes than traditional subcutaneous injections in the dorsum of the foot. Vecchiato et al.[23] successfully demonstrated TD in all 19 patients undergoing minimally invasive oesophagectomy after a mean of 52.7 min from ultrasound-guided percutaneous injection of 0.5 mg/kg body weight of ICG in the inguinal nodes. Also, authors could successfully identify and clip the cut edges of TD in two patients where TD was resected for oncological purposes. Retrospective analyses have shown a significant decrease in the incidence of chylothorax in patients undergoing minimally invasive oesophagectomy with the application of ICG compared to those without it (12.2% vs. 0%).[24,25] This underscores the importance of incorporating ICG fluorescence into surgical protocols to reduce the risk of TD injury. ICG fluorescence lymphangiography offers real-time feedback, making it particularly advantageous in cases with complex anatomy or when the TD is challenging to visualize using conventional methods. However, determining the optimal dosage of ICG remains variable across studies, ranging from 0.2 to 0.5 mg/kg.[25] Standardizing the dosage would achieve consistent outcomes with TD preservation in minimally invasive esophagectomy.

3 | NERVE-SPARING MEDIASTINAL LYMPHADENECTOMY

Complications arising from nerve damage represent the primary constraint in performing radical lymphadenectomy for esophageal cancer. The recurrent laryngeal nerves (RLN) and the pulmonary branches of the vagus nerve are particularly susceptible to injury during RLN and subcarinal lymph node dissection. Such nerve damage can lead to a range of pulmonary complications, including hoarseness, dyspnea, aspiration, atelectasis, pneumonia, and acute respiratory distress syndrome. These issues can pose immediate life-threatening risks postoperatively or result in chronic pulmonary conditions. Thus, ensuring the preservation of nerve function is essential during radical lymphadenectomy.

3.1 | Anatomy and physiology of pulmonary and recurrent laryngeal branches of the vagus nerve

The vagus nerve, the longest cranial nerve, originates from the dorsolateral sulcus of the medulla oblongata and descends into the thorax through the thoracic inlet in the posterior mediastinum.[26] In the thorax, both vagus nerves branch out to provide the esophageal, tracheal, and pulmonary branches and the recurrent laryngeal nerves. These branches are crucial for various autonomic functions, including regulating the heart rate, gastrointestinal peristalsis, and other vital reflexes.[27]

Several pulmonary branches offshoot from the right vagus nerve from the right subclavian artery to the right main bronchus (Figure 3). These branches descend over the trachea and are embedded in the loose connective tissue anterior to it. Among these branches, the inferior one courses dorsal to the pre-tracheal lymph nodes, forming the anterior pulmonary plexus superior to the right pulmonary artery. Continuing downward, the right vagus nerve provides superior branches to supply the right upper lobe and inferior branches that innervate the right middle and lower lobes. Further, along its course, the right vagus nerve gives rise to multiple branches that coalesce to form the posterior pulmonary plexus, which contributes significantly, up to 77%, to the nerve supply of the right lung.[28] Conversely, on the left side of the thorax, the anterior pulmonary plexus is formed anterior to the left pulmonary artery by two to four branches originating from the left vagus nerve. The left posterior pulmonary plexus, formed by an average of 12 nerve fibers from the left vagus nerve, is primarily responsible for supplying the left lung, accounting for up to 74% of its nerve innervation.[29]

Sympathetic nerve fibers originate from the thoracic T1–T4 nerve roots, with distinct pathways on each thorax side. On the right side, these fibers travel medially along the right bronchial artery to reach the right main bronchus. Conversely, on the left side, fibers from the left sympathetic trunk traverse either dorsal or ventral to the aortic arch before joining the left bronchial artery. Within the thoracic cavity, micro ganglia, primarily situated along the posterior wall of the trachea and bronchi, receive these nerve fibers from both the pulmonary plexus and the sympathetic chains. Neurons within these ganglia predominantly innervate the sub-mucosal glands and smooth muscle of the airway, regulating their functions. The parasympathetic system governs mucus production and bronchoconstriction, which are crucial for airway protection. The sympathetic system regulates bronchodilation. Furthermore, non-cholinergic and non-adrenergic inhibitory mechanisms, mediated by vasoactive intestinal polypeptide (VIP) and nitric oxide, contribute significantly to bronchodilation, underscoring the complexity of respiratory regulation.[30]

The right and left recurrent laryngeal nerves (RLN) emerge as significant branches of the vagus nerve within the thorax, with distinct pathways on each side. On the right, the RLN loops around the right subclavian artery, while on the left, it wraps around the arch of the aorta before ascending along the trachea-esophageal groove into the neck.[31] Notably, the left RLN closely follows the course of the esophagus and trachea, posing technical challenges for its preservation. Apart from providing esophageal and tracheal branches, the RLN supplies all intrinsic muscles of the larynx except the cricothyroid muscle.[32] While most laryngeal muscles receive unilateral RLN innervation, the interarytenoid muscles are supplied by both RLNs. This extensive neural network enables the RLN to regulate vocal cord adduction and abduction, control the laryngeal inlet, facilitate vocal cord tension for phonation, and receive sensory input from the vocal cords. Additionally, the RLNs play a role in the relaxation of the upper esophageal sphincter, underscoring their multifaceted involvement in respiratory and swallowing regulation.[33]

3.2 | Operative strategies for sparing pulmonary branches of the vagus

The operative strategies aimed at minimizing pulmonary complications through preservation of the pulmonary nerve plexus are based on a nuanced understanding of the distribution of nerve supply to the lungs at various levels. This includes the superior margin of the main bronchus, the inferior margin of the main bronchus, and beyond the terminal pulmonary branches.

When the vagal nerve is severed at the superior margin of the main bronchus, it results in a substantial loss of nerve supply to the lungs.[34,35] This loss ranges from 68% to 100% in the right lung and 48–72% in the left lung. Specifically, the superior lobe of the right lung may experience a loss of 55–98%, while the middle and inferior lobes could lose 64–100% of their nerve supply. In the left lung, the superior lobe may lose 0–6%, while the inferior lobe could lose 86–100% of its nerve supply. Similarly, severing the vagal nerve at the inferior margin of the main bronchus leads to a significant loss of nerve supply to the lungs. This loss ranges from 16% to 64% in the right lung and 0–45% in the left lung. Notably, the superior lobe of the right lung may experience no loss, while the middle and inferior lobes could lose 20–78% of their nerve supply. In the left lung, both the superior and inferior lobes may experience minimal to moderate losses.[34,35]

However, during the subcarinal lymphadenectomy, if the vagus nerve is severed distal to the terminal pulmonary branch, the loss of nerve supply is minimal in both lungs, ranging from 0% to 5% in the right lung and 0–9% in the left lung.[34] To perform a nerve-sparing subcarinal lymphadenectomy effectively, it is essential to follow a meticulous dissection protocol, ensuring the preservation of critical neural structures while removing the lymph nodes in the subcarinal region.[36] Begin by carefully dissecting the lymph nodes in the subcarinal region and along the main bronchi away from the pericardium. This establishes a clear plane for further dissection. Proceed cranially within the same plane to separate the lymphatic tissues from the right bronchi. This step ensures that the field is prepared for the exposure of the vagus nerve and its branches. Expose the right vagus nerve along with its esophageal and pulmonary branches. The goal is to visualize these structures clearly to avoid inadvertent damage. Cut the esophageal branches and the right vagus nerve distal to the last large pulmonary branch (Figure 3). This is done carefully to ensure that the pulmonary branches, crucial for maintaining nerve supply to the lungs, are preserved. On the left side, the preservation is generally more straightforward due to the anatomical positioning of the pulmonary branches, which are typically located away from the main dissection field. Recognize the typical locations of the caudal-most pulmonary branch, ranging from 5 to 26 mm below the right main bronchus and 1–37 mm below the left main bronchus.[34,35] By adhering to these principles, minimizing the loss of nerve supply to the lungs during a subcarinal lymphadenectomy while effectively removing the targeted lymph nodes is possible.

3.3 | Operative strategies for nerve-sparing recurrent laryngeal lymphadenectomy

The RLN lymph nodes are frequently involved in esophageal cancer, especially in SCC. Hence, RLN lymphadenectomy is a crucial part of esophagectomy for esophageal cancer. However, RLN lymph node dissection is technically challenging due to narrow anatomical space and the possibility of RLN damage-associated morbidity. As RLN palsy is strongly associated with severe pulmonary complications, various techniques have been described to safely perform RLN lymph node dissection, especially along the left RLN.[36–41] The methods for left RLN dissection can be broadly classified into two types:

1. Type I—Esophagus retracted posteriorly (towards vertebra) using a traction suture attached to the thoracic wall or retracted posteriorly with a thread through the thoracic wall. The fibro-fatty tissue containing the left RLN and the lymph nodes is separated from the trachea by dividing the branches of the tracheoesophageal arteries. The esophageal branches of the RLN are initially preserved, keeping the lymph nodes and RLN attached to the esophagus. After the tissue is dissected from the trachea, the esophageal branches of the RLN are divided, which separates the left RLN from the nodal tissue attached to the esophagus.
2. Type II—The esophageal branches of the RLN are divided at the beginning of the procedure. The esophagus is retracted laterally. The tissues, including the left RLN and lymph nodes, were maintained in the tracheoesophageal groove. The trachea is retracted to open the space between RLN and the trachea The RLN nodes, typically located in this space, are grasped with the surgeon's left-hand instrument and carefully dissected off the RLN and trachea (Figure 4).

In both types of RLN dissection, azygous vein and right bronchial artery are routinely divided to improve exposure to the left tracheoesophageal groove. In type I dissection, the esophageal suspension is critical, which can be achieved with (the Bascule technique) or without (mesenterization technique and its variations) esophageal transection.[40,42] While esophageal transection allows wide exposure due to better esophageal retraction, it may not be feasible when the tumor is located at the carina level. There is no level I evidence comparing two different types of dissection. While some studies reported decreased RLN palsy rate with type I dissection, others did not find any difference.[36–43] While type I dissection might be technically easier with a conventional minimally invasive approach, both approaches can be performed with relative ease with robot-assisted minimally invasive esophagectomy due to the unique advantages of the robotic platform. It is essential to remember that RLN is very sensitive, and apparently, intact nerves can be injured by clamping, stretching, compressing, ischemia, and thermal injury. If used during RLN dissection, thermal energy should be applied in pulses (the "Thermal Buzz technique") rather than continuously to prevent and decrease thermal injury to the nerve. One of the underreported mechanisms of RLN injury is the stretching of incompletely isolated left RLN during cervical esophageal mobilization. This can be avoided by completing the entire left RLN dissection from the aortic arch till the nerve enters the cricoid cartilage during the thoracic phase.

The standard technique for the right RLN dissection is to follow the right vagus cranially until the right subclavian artery, where the right RLN loops around it. Often, a tracheoesophageal artery crosses the right RLN at its origin, which needs to be securely controlled to avoid bleeding at the initial stage of dissection. The right RLN nodes located between the right RLN and trachea are dissected to the level of the inferior thyroid artery, which marks the upper extent of dissection (Figure 5).[36] The usefulness of intraoperative neuromonitoring (IONM) to prevent RLN injury has been evaluated in various studies. In a retrospective analysis, Takeda et al. reported that the incidence of grade 2 or higher RLN palsy was notably lower in the IONM group compared to the non-IONM group (6% vs. 21.2%).[44] Furthermore, recovery from RLN palsy within 6 months was significantly better in the IONM group, with 87.5% recovering in the IONM group versus 20% in the non-IONM group. During the procedure, intraoperative neural stimulation was performed using a probe stimulator, and the evoked electromyogram (EMG) responses from

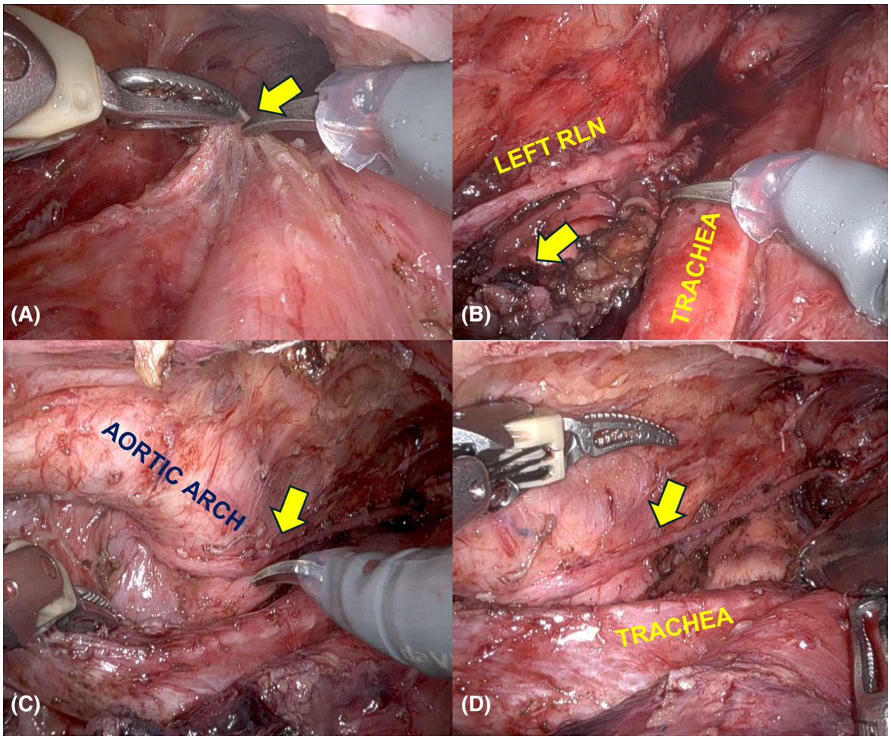

FIGURE 4 Left recurrent laryngeal nerve lymphadenectomy. (A) Esophageal branches of the left recurrent laryngeal nerve (arrow) are divided to isolate the nerve from esophagus. (B) Left recurrent laryngeal nerve lymph nodes (arrow) are typically located between the nerve and trachea. (C) The left recurrent laryngeal nerve (arrow) loops around the aortic arch. (D) Complete course of left recurrent laryngeal nerve (arrow) visualized after lymphadenectomy.

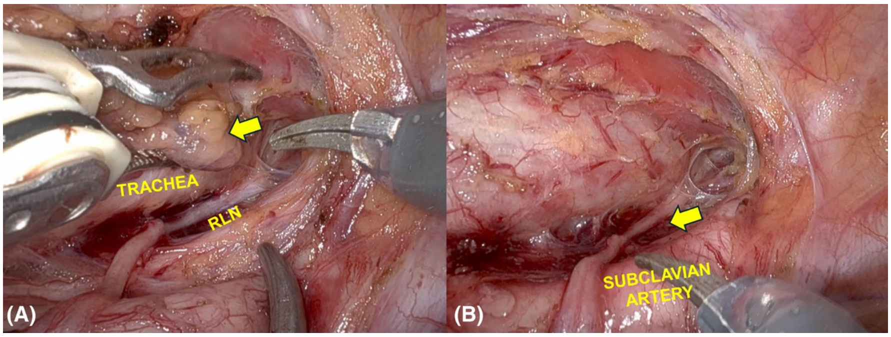

FIGURE 5 Right recurrent laryngeal nerve lymphadenectomy. (A) Right recurrent laryngeal nerve lymph nodes (arrow) are typically located between the nerve and trachea. (B) The right recurrent laryngeal nerve (arrow) loops around the subclavian artery.

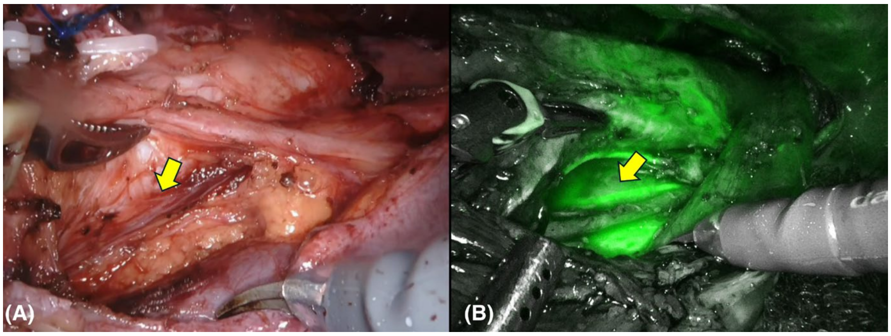

FIGURE 6 Preservation of tracheal vascularity. (A) Preserved lateral longitudinal anastomosis (arrow) after right paratracheal lymphadenectomy. (B) Lateral longitudinal anastomosis clearly visualized with indocyanine green fluorescence.

the laryngeal muscles were recorded.[44] A lack of or reduced EMG activity (<100 μV) suggested neural injury. A recent systematic review of 10 studies encompassing 949 patients reported that IONM significantly reduced the incidence of RLN palsy and pneumonia.[45] The retrospective nature of most of the included studies and the small sample size of the only randomized controlled trial precluded a definite conclusion. However, IONM is a useful adjunct for nerve-sparing lymphadenectomy.

4 | BRONCHIAL ARTERY PRESERVATION

Ischemia to the respiratory tract, mainly due to ligation or injury to the bronchial arteries during radical mediastinal lymphadenectomy, impairs respiratory protective mechanisms, leading to atelectasis and pneumonia.[46] Preserving bronchial arteries during radical mediastinal lymphadenectomy may reduce ischemia and postoperative lung complications.[47]

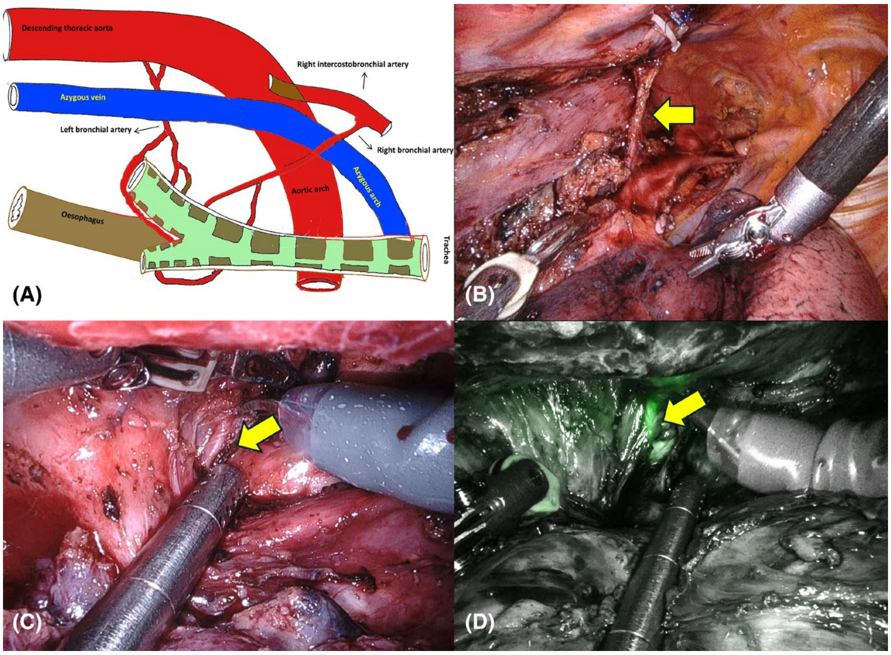

FIGURE 7 Bronchial artery anatomy. (A) Pictorial depiction of typical anatomy of bronchial arteries. (B) Typical course of the right bronchial artery that prevents adequate exposure for left paratracheal and recurrent laryngeal nerve lymphadenectomy. (C) Typical course of the left bronchial artery that can be easily preserved. (D) Visualization of the left bronchial artery using indocyanine green fluorescence.

4.1 | Anatomy and physiology of arterial circulation of the bronchi and trachea

The primary blood supply to the trachea and bronchi originates from a network of segmental tracheoesophageal vessels.[48] These tracheoesophageal vessels are derived from several arterial sources, including the inferior thyroid arteries, the supreme intercostals, the subclavian, the internal mammary, and the bronchial arteries. Close to the tracheoesophageal groove, tracheoesophageal vessels bifurcate into primary tracheal and esophageal branches. The primary esophageal artery often emits smaller tracheal twigs called secondary tracheal arteries, which supply the posterior tracheal wall. Hence, esophagectomy itself reduces blood supply to the trachea by interrupting secondary tracheal arteries.

While the tracheal blood supply is primarily through primary and secondary tracheal arteries, there are critical vascular networks that ensure the adequacy of blood supply when the supply is interrupted from any of the arteries, contributing to segmental tracheoesophageal branches.[47,48] It includes:

(i) Lateral longitudinal anastomosis: It links the segmental primary tracheal vessels along the lateral walls of the trachea (Figure 6). The primary tracheal arteries exhibited a pattern of branching extending upwards and downwards across three or four interspaces along the lateral surface of the trachea. During this course, they established connections with the primary tracheal arteries originating from both superior and inferior directions. This intricate network resulted in a significant, albeit occasionally irregular, complete longitudinal tracheal anastomosis along the lateral wall of the trachea.

(ii) Transverse intercartilaginous arteries: These arteries unite the circulation between the right and left sides of the trachea, providing cross-communication and redundancy in the blood supply.

(iii) Anastomoses around the thyroid gland: The thyroid gland, particularly through the superior thyroid artery, contributes to the blood supply of the cervical trachea. Anastomoses between superior and inferior thyroid arteries around the thyroid gland ensure additional vascular support to the upper part of the trachea.

(iv) Subcarinal vascular network: It interconnects the upper thoracic trachea's circulation with the bronchial arteries, ensuring an extensive blood supply network in this region.

The extent to which these vascular networks are developed in an individual determines the severity of tracheobronchial ischemia following esophagectomy with radical lymphadenectomy. The ischemia to the respiratory mucosa may lead to ulceration and fistula formation in severe conditions.[49] Maruyama et al.[50] analyzed the incidence of tracheobronchial lesions (erosions, ulceration, and fistula) by regular bronchoscopy for the first 3 postoperative days in 305 patients who underwent transthoracic oesophagectomy with two-field or three-field mediastinal lymphadenectomy. While patients with erosion and ulcerations could be managed conservatively, fistula formation often requires revision of the gastric conduit and fistula take-down. Risk factors for tracheobronchial lesions include three-field lymphadenectomy with removal of 60 or more lymph nodes, presence of four or more metastatic lymph nodes and in patients with metastatic cervical or upper mediastinal lymph nodes. The authors reported that meticulous dissection around RLN nodes, proper preservation of the tracheal sheath, and regular measurement of the endotracheal cuff pressure may help decrease the incidence of tracheobronchial ischemic lesions.[50]

4.2 | Strategies for bronchial artery preservation and prevention of tracheobronchial ischemia

Fujita et al. reported that removing bronchial arteries in a canine study decreased the mean blood flow of the respiratory epithelium from 30 mL/100 gm/min to 20 mL/100 gm/min, highlighting the importance of these arteries in maintaining respiratory epithelium perfusion.[51]

The typical bronchial artery anatomy is the single right bronchial artery originating from the intercostal-bronchial trunk (short common trunk of the right bronchial and intercostal artery) and two left bronchial arteries arising directly from the descending thoracic aorta (Figure 7).[52] However, the typical anatomy is observed only in 50% of patients and variations in bronchial artery origin and its course are common. Hence, preoperative CT angiography is useful for identifying the origin and course of the bronchial artery. Wada et al. reported that the right and left bronchial arteries could be successfully evaluated in 97% and 86% of patients with CT angiography.[53] As the right bronchial artery is often sacrificed to facilitate supracarinal lymphadenectomy along RLN, preservation of the left bronchial artery is crucial, especially in the setting of neoadjuvant chemoradiation. Care should be taken while doing paratracheal and RLN dissection to avoid injury to the lateral longitudinal anastomosis along the tracheal wall. Also, while doing subcarinal lymph node dissection, the vascular network in the subcarinal region should be preserved to maintain communication between two bronchial vessels.

Two techniques have been documented for assessing tracheal blood flow during esophagectomy. The first technique is electrolytic regional blood flowmetry, which gauges tracheal mucosal blood flow via the hydrogen gas clearance method utilizing electrochemically produced hydrogen.[54] This technique allows for repeated measurements, though it is relatively invasive due to the needle-type probe used. The second technique is laser Doppler flowmetry, where a probe affixed to the endotracheal tube cuff evaluates tracheal blood flow.[55] This method also permits repeated measurements but is hindered by the influence of cuff pressure on tissue blood flow and the interference from mucus secretion from the tracheal mucosa. Conversely, a newer approach using ICG fluorescence imaging offers the benefits of being less invasive and easier to perform than the previous two methods. Sugimura et al.[56] reported that T1/2 (time from first fluorescence increase to half of the maximum) is a useful parameter to objectively document the tracheal vascularity using ICG fluorescence. Nevertheless, this technique is limited by its difficulty in being used repeatedly.

5 | SUMMARY AND FUTURE PERSPECTIVES OF FUNCTION PRESERVING MEDIASTINAL LYMPHADENECTOMY

The complications and morbidity associated with radical mediastinal lymph node dissection during esophagectomy are closely linked to the preservation of three critical mediastinal structures: TD, the largest lymphatic channel in the body; the RLN and pulmonary branches of the vagus nerve, which are crucial for sensory and motor functions of the airway; and the tracheobronchial vasculature, essential for maintaining the cellular integrity of the respiratory epithelium. Preserving the TD has been associated with better hemodynamic parameters in the immediate postoperative period and the long-term maintenance of the patient's nutritional status. Also, TD preservation doesn't compromise long-term oncological outcomes. Similarly, preserving the RLN and tracheobronchial vasculature has reduced the incidence of postoperative pulmonary complications and improved long-term quality of life. As documented in various studies, lymphadenectomy with preservation of nerve function doesn't compromise long-term oncological outcomes.[45,46]

Robotic esophagectomy offers several advantages over thoracoscopic esophagectomy, particularly in the context of lymphadenectomy. The enhanced dexterity, precision, and visualization of the robotic systems can potentially improve lymph node yield along RLN with better preservation of nerve function. While some studies have shown an equivalent RLN palsy rate between conventional and robot-assisted minimally invasive esophagectomy, others have shown better lymphadenectomy and preservation of nerve function with the robotic approach, especially in the setting of neoadjuvant therapy.[57,58] The outcomes of each component of function-preserving mediastinal lymphadenectomy have often been analyzed separately. However, as this is a relatively new surgical concept, more comprehensive studies are needed to assess the long-term functional and oncological outcomes that integrate all aspects of function-preserving mediastinal lymphadenectomy.

AUTHOR CONTRIBUTIONS

Raja Kalayarasan: Conceptualization; resources; supervision; writing – original draft; writing – review and editing. **Pothugunta Sai Krishna:** Writing – original draft; writing – review and editing.

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