

*Case Report*

## Safe Resection of Esophageal Cancer with a Non-Recurrent Inferior Laryngeal Nerve Associated with an Aberrant Right Subclavian Artery Using Intraoperative Nerve Monitoring

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In thoracic esophageal cancer, lymph node dissection around the recurrent laryngeal nerve is crucial but poses a risk of nerve palsy, affecting postoperative quality of life. In cases with an aberrant right subclavian artery (ARSA), the right recurrent laryngeal nerve is absent, and the non-recurrent inferior laryngeal nerve (NRILN) enters the larynx directly from the vagus nerve in the cervical region. Identifying the course of the NRILN is vital to avoid injury. A case of esophageal cancer with an ARSA, in which the course of the NRILN was preserved using the Nerve Integrity Monitoring (NIM) system during surgery, is described.

**Key words:** esophageal cancer, intraoperative nerve monitoring, aberrant right subclavian artery, non-recurrent inferior laryngeal nerve, thoracoscopic esophagectomy

In thoracic esophageal cancer, metastases to lymph nodes surrounding the recurrent laryngeal nerve (RLN) are known to occur early, regardless of tumor location, making their dissection highly important [1]. However, RLN palsy resulting from dissection can lead to complications such as hoarseness, aspiration, and respiratory problems, thereby compromising patients' postoperative quality of life (QOL). Consequently, adequate lymph node dissection and reliable nerve preservation are required.

The RLN branches from the vagus nerve, with the right nerve looping around the subclavian artery and the left nerve looping around the aortic arch before ascending through the tracheoesophageal groove to the larynx. Accurate knowledge of their anatomical courses is essential for their identification and preservation. In

rare cases, anatomical variations, such as the non-recurrent inferior laryngeal nerve (NRILN), may occur. The NRILN is typically associated with a congenital aberrant right subclavian artery (ARSA), which can be diagnosed by computed tomography (CT) [2].

The use of intraoperative nerve monitoring (IONM), introduced to assess nerve function and identify nerve courses during thyroid and parathyroid surgeries, has expanded and was included in Japan's medical insurance coverage for esophageal cancer surgery following the 2020 revision of the medical fee schedule. This has facilitated its implementation in various institutions.

In this report, a case of esophageal cancer with an ARSA, in which the Nerve Integrity Monitoring System (NIM system) was used during surgery, is presented. By using intermittent IONM (IIONM), the course of the NRILN was inferred, and nerve injury was pre-

vented. In addition, continuous IONM (CIONM) enabled safe lymph node dissection around the left RLN in a narrow surgical field.

### Case Presentation

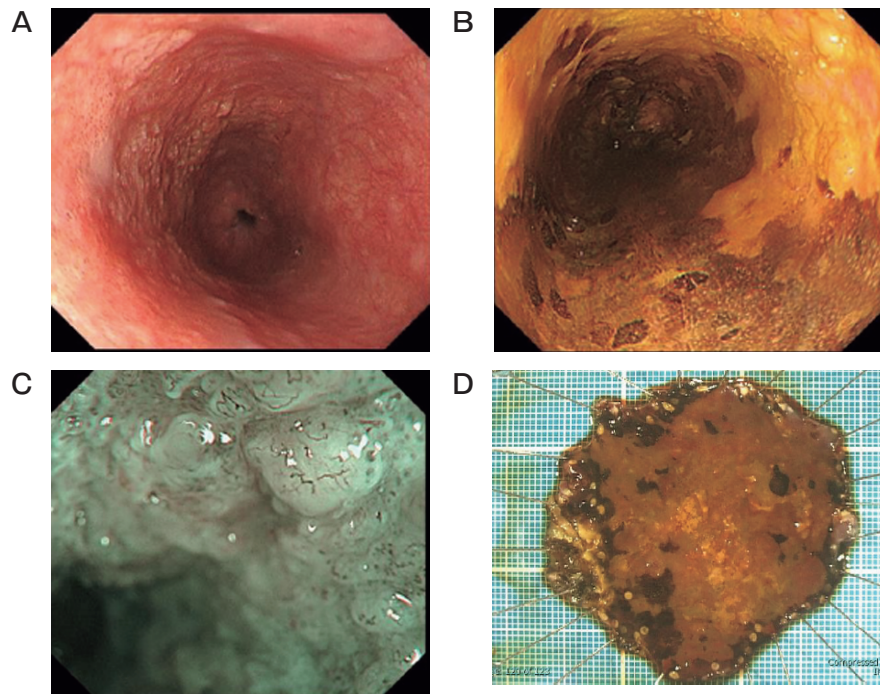
A 72-year-old woman presented to a local clinic with shortness of breath. CT showed an abnormal shadow in the right upper lobe of the lung, raising suspicion of right upper lobe lung cancer. She was referred to our respiratory surgery department. Positron emission tomography (PET)-CT performed for preoperative evaluation showed abnormal uptake in the esophagus. Upper gastrointestinal endoscopy showed superficial cancer in the lower thoracic esophagus. Endoscopic submucosal dissection (ESD) was performed, and esophageal squamous cell carcinoma (SCC), pT1b (SM2), pHM0, pVM0, INFb, ly1 (D2-40), v0 (EvG) was diagnosed on pathological examination. The patient was referred to our department for additional resection.

The patient had a past medical history significant for appendectomy, gastric ulcer, hypertension, angina

pectoris, and hyperuricemia. In terms of lifestyle history, the patient smoked 20 cigarettes per day from the age of 20 until 71 years. Alcohol consumption included two servings of shochu per day until the diagnosis of esophageal cancer. Family history revealed no notable findings.

Laboratory tests indicated normal blood biochemistry, and tumor markers (CEA, CA19-9, and SCC) were within normal limits. Upper gastrointestinal endoscopy showed a 2/3 circumferential lesion at 36-42 cm from the incisors, with mixed Type B1 and B2 vessels on narrow-band imaging (NBI). Biopsy confirmed SCC. The lesion was classified as esophageal cancer, Lt (36-42 cm), anterior wall, 2/3 circumferential, Type 0-IIa, SCC, cT1a (MM), cN0, cM0, cStage0 according to the 12th edition of the Japanese classification of esophageal cancer [3, 4]. The pathological diagnosis post-ESD was esophageal cancer, pT1b (SM2), pHM0, pVM0, INFb, ly1 (D2-40), v0 (EvG), warranting additional resection (Fig. 1).

Contrast-enhanced computed tomography (CT) revealed an aberrant right subclavian artery (ARSA)



**Fig. 1** **A-C**, Esophagoscopy shows a Type 0-IIa tumor with unstained iodine occupying approximately two-thirds of the circumference of the esophageal wall. NBI (narrow-band imaging) shows a mixture of Type B1 and B2 blood vessels within the lesion; **D**, Endoscopic submucosal dissection (ESD) is performed, and the pathological diagnosis is pT1b (SM2), pHM0, pVM0, INFb, ly1 (D2-40), v0 (EVG). Based on this, additional resection was considered appropriate.

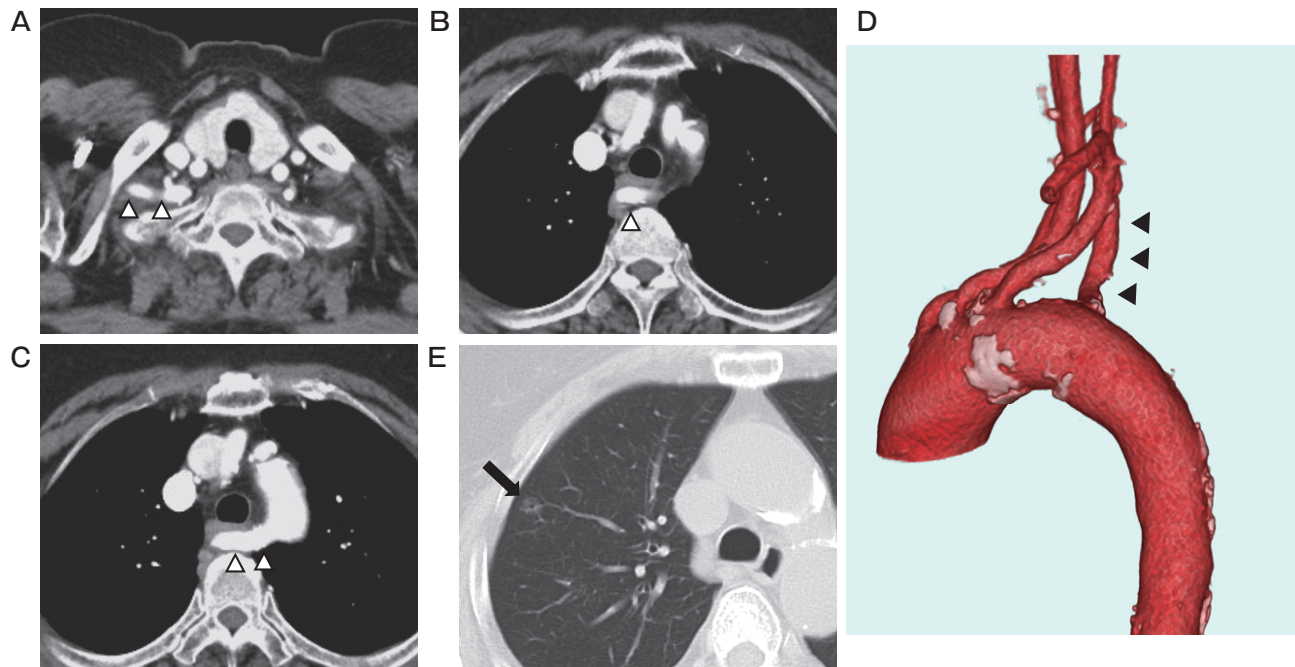
arising directly from the distal aortic arch, running retroesophageal before curving into the right subclavian region. No lymph node or distant metastases were detected. A 1-cm, ground-glass nodule was observed in the right upper lobe of the lung (Fig. 2). Based on these findings, the preoperative diagnosis was esophageal cancer (post-ESD, pT1b-SM2, Stage I), and the planned procedure included prone thoracoscopic subtotal esophagectomy with two-field lymph node dissection, laparoscopic gastric tube construction, and retrosternal reconstruction with cervical anastomosis. Right upper lobe resection for suspected lung cancer was also scheduled.

Intraoperatively, given the presence of ARSA and a potential NRILN, the NIM system was used. An endotracheal tube with integrated electrodes (NIM TriVantage EMG Tube, Medtronic, Minneapolis, MN, USA) was used. Thoracic esophagectomy typically uses IIONM with a monopolar electrode contacting the RLN. However, due to the limited operative space in the upper left mediastinum caused by ARSA, CIONM was also used by attaching APS electrodes to the vagus nerve proximally.

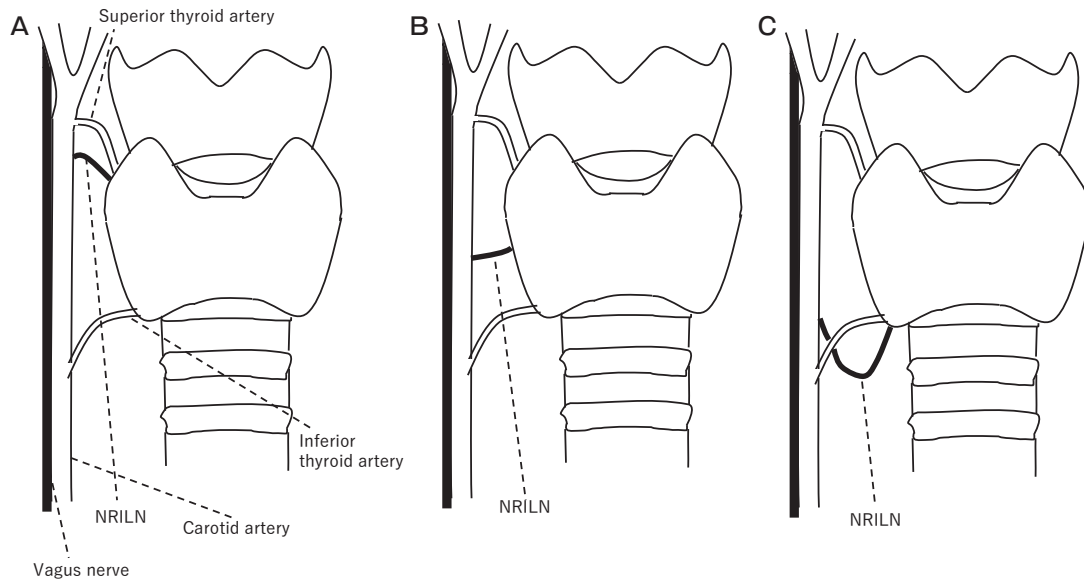
For the planned thoracoabdominal two-field lymph node dissection, the NRILN was identified preoperatively by cervical exploration. Following a midline neck incision, the left vagus nerve was identified and equipped with APS electrodes for continuous monitoring. The right NRILN was identified using a monopolar stimulator near the upper pole of the thyroid gland, consistent with Type 1 of Toniato's NRILN classification (Fig. 3A). With the nerve's course clarified, thoracic procedures proceeded without incident.

During thoracoscopy, the ARSA was confirmed to arise directly from the aortic arch following a retroesophageal course. Despite narrowed fields in the upper left mediastinum, IONM facilitated precise lymph node dissection without nerve injury. Right upper lobe resection, gastric tube construction, and reconstruction were completed uneventfully. Surgery lasted 11 h and 57 min, with 340 mL of blood loss and no intraoperative complications (Fig. 4).

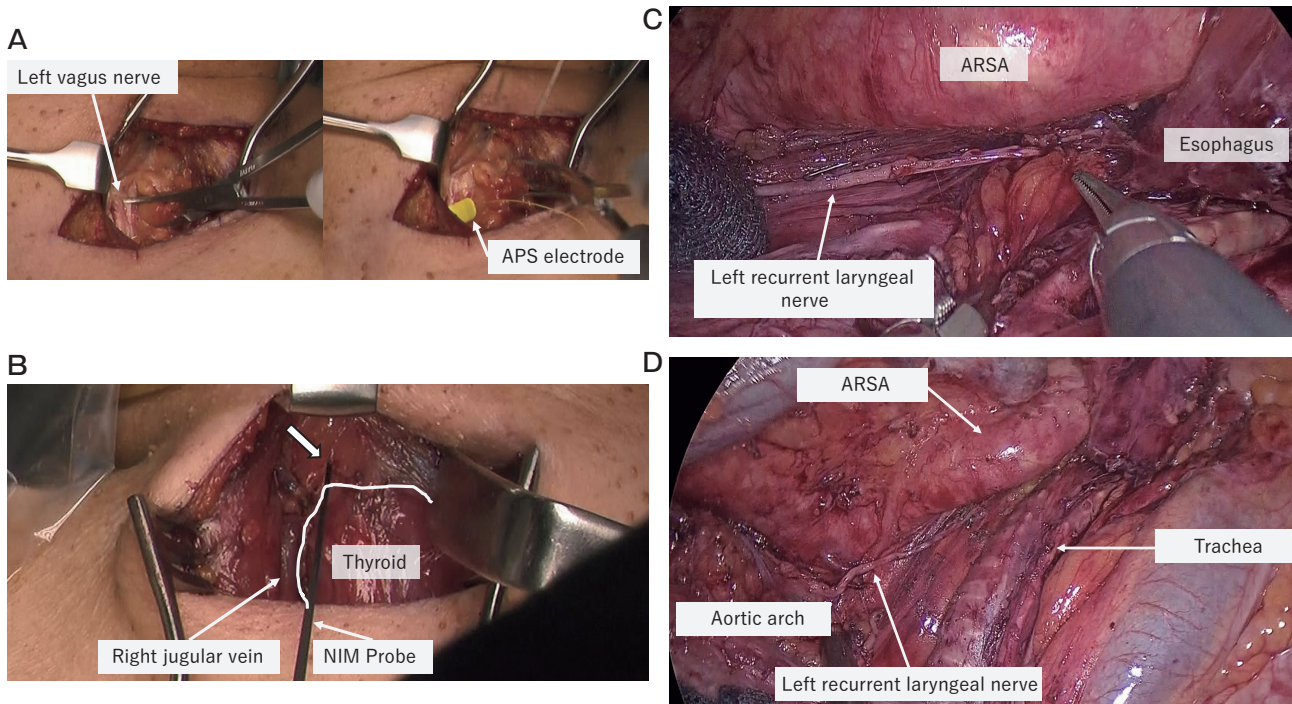
Postoperatively, the patient was extubated on postoperative day 1 without evidence of RLN palsy. Recovery was uneventful, and the patient was transferred for rehabilitation on day 19.



**Fig. 2** A-C, Computed tomography shows the aberrant right subclavian artery (ARSA) that arises from the descending aorta and runs between the esophagus and vertebral column to reach the right cervical region (white arrowheads); D, 3D-CT shows the ARSA (black arrowheads); E, Ground-glass opacity is observed in the right upper lobe (black arrow).



**Fig. 3** **A**, The Type 1 nonrecurrent nerve arises directly from the cervical vagus nerve and runs together with the vessels of the superior thyroid pedicle (present case); **B**, The Type 2A nonrecurrent nerve follows a transverse path parallel to and over the trunk of the inferior thyroid artery; **C**, The Type 2B nonrecurrent nerve follows a transverse path parallel to and under the trunk or between the branches of the inferior thyroid artery.



**Fig. 4** **A**, The left vagus nerve is identified in the left cervical region, and an APS electrode is attached; **B**, After identification of the right vagus nerve in the right cervical region, a monopolar electrode is used to search for the NRILN. A response on the NIM monitor is observed near the upper pole of the thyroid gland (white arrow); **C**, On thoracoscopy, in the dissection around the left recurrent laryngeal nerve, the space is constricted due to the ARSA; **D**, On thoracoscopy, the ARSA branching from the aortic arch is confirmed to run posterior to the esophagus and head toward the right cervical region.

Pathological findings revealed no residual tumor at the ESD scar, and no lymph node metastasis was observed. The final diagnosis was esophageal cancer (pT1b-SM2, Stage I). The resected lung specimen was confirmed to be carcinoma in situ (pTisN0M0, Stage 0).

## Discussion

In radical surgery for thoracic esophageal cancer, thorough dissection of the lymph nodes around the RLN is necessary due to their propensity for early metastasis. However, postoperative RLN paralysis can lead to complications such as respiratory issues, making precise nerve preservation highly desirable. To achieve adequate lymph node dissection while preserving the nerve, esophageal surgeons must be familiar with rare anatomical variations of nerve pathways.

The ARSA arises from the descending aorta as the fourth branch of the left aortic arch and traverses obliquely from the left lower side to the right upper side, typically taking a retroesophageal course behind the esophagus and anterior to the vertebral body in 80% of cases. In 15% of cases, it takes an inter-esophageotracheal route (between the esophagus and trachea), and in 5%, it follows a pretracheal route (in front of the trachea). The cervical branches from the aortic arch follow the order of the right common carotid artery, left common carotid artery, left subclavian artery, and right subclavian artery [2]. The reported incidence of ARSA is 0.5-2% [5,6]. Though an ARSA is often asymptomatic, a retroesophageal ARSA can sometimes cause dysphagia [7]. In the present case, the ARSA followed a retroesophageal course, but remained asymptomatic.

The NRILN is an anomaly in the RLN's course associated with an ARSA. The ARSA results from underdevelopment during embryogenesis due to early closure of the fourth pharyngeal arch. Normally, the inferior laryngeal nerve, derived from the sixth pharyngeal arch, crosses the fourth pharyngeal arch-derived right subclavian artery and descends into the thoracic cavity. In ARSA cases, early closure of the fourth arch prevents such crossing, causing the nerve to branch directly from the vagus nerve and ascend to the larynx. Devezze *et al.* reported that all 104 patients with NRILN had an ARSA [8], emphasizing the importance of anticipating NRILN in surgeries in which the ARSA is identified on preoperative CT. In the present case, the ARSA detected on preoperative imaging allowed the presence of an

NRILN to be anticipated.

The classification of NRILN pathways by Toniato *et al.* is widely recognized. They categorized NRILN into three types: Type 1, in which the nerve runs alongside the superior thyroid artery and vein before entering the larynx; Type 2A, in which it runs alongside the inferior thyroid artery, above the artery; and Type 2B, in which it runs alongside the inferior thyroid artery, below the artery (Fig. 4) [5]. The present case involved a planned thoracoabdominal two-field dissection following ESD for lower thoracic esophageal cancer, with no initial cervical dissection. However, if the NRILN had a Type 2B course, it could be at risk during right upper mediastinal dissection. Thus, identifying the NRILN pathway was necessary, and IONM was used.

IONM, traditionally used in thyroid and parathyroid surgeries for nerve identification and function assessment, was extended to esophageal cancer surgery in 2020 under Japan's revised medical reimbursement system, facilitating its adoption in various institutions. Commonly used materials include EMG endotracheal tubes, stimulating electrodes, and the NIM Response 3.0 system (Medtronic Japan). The tube's electrodes, positioned to contact the vocal cords, detect muscle activity during nerve stimulation. IONM methods include IIONM using monopolar stimulation and CIONM using APS electrodes on the central vagus nerve [9].

In the present case, both IIONM and CIONM were used. Cervical procedures preceded thoracic procedures, with the left vagus nerve identified and fitted with an APS electrode for CIONM, and the NRILN identified on the right using IIONM. On the right side, as previously mentioned, the course of the NRILN corresponds to one of Toniato *et al.*'s classifications. IIONM was used to roughly identify the area in the right cervical region where electrical stimulation induces vocal cord muscle movement and to confirm whether the nerve appearing in the surgical field was the NRILN. On the left side, due to the ARSA, the upper left mediastinum was expected to be narrower than in a typical surgical field. Therefore, CIONM was utilized to continuously monitor the stress exerted on the left recurrent laryngeal nerve during upper left mediastinal dissection. Right superior thyroid stimulation elicited vocal cord responses, indicating a Type 1 pathway according to Toniato's classification. By identifying the nerve's course, right upper mediastinal dissection was

performed safely. This demonstrated IONM's value in ensuring safe surgery in cases with anatomical variations.

Since Hemmerling *et al.*'s 2001 report on IONM use in esophageal cancer surgeries [10], its application has gradually increased. At our institution, both thoracoscopic and robot-assisted esophagectomies are typically performed in the prone position. Ikeda *et al.* first reported IONM use in prone thoracoscopic surgeries in 2014, concluding that it enhances safety in RLN dissection [11]. Kobayashi *et al.* reported in 2018 that IONM significantly reduced postoperative RLN paralysis, aspiration, and hospital stays in esophageal cancer surgeries [12]. Recent reports by Ninomiya *et al.* and Mushiake *et al.* highlight IONM's utility in cases with right aortic arch or double aortic arch anomalies [13,14]. Whereas IONM is highly beneficial for safe resection in cases with anatomical variations, its effectiveness depends on precise surgical technique, underscoring the importance of surgical proficiency.

A notable consideration with IONM is the approximately 30 to 60-minute extension of surgery time due to APS electrode placement, which should be evaluated based on each institution's circumstances.

## Conclusion

A case of thoracic esophageal cancer with an ARSA and associated NRILN that was safely resected using IONM was described. Anatomical variations such as an ARSA and NRILN should be well understood by esophageal surgeons, and IONM is invaluable for safe surgery in cases with such anomalies.

## References

1. Tachimori Y, Ozawa S, Numasaki H, Matsubara H, Shinoda M, Toh Y, Udagawa H, Fujishiro M, Oyama T, Uno T and Registration Committee for Esophageal Cancer of the Japan Esophageal Society: Efficacy of lymph node dissection by node zones according to tumor location for esophageal squamous cell carcinoma. *Esophagus* (2016) 13: 1–7.
2. Teshima J, Miyata G, Kamei T, Nakano T, Abe S, Katsura K, Taniyama Y, Sato C, Nakagawa T, Ito S and Ouchi N: Three cases of esophageal cancer with aberrant right subclavian artery treated by thoracoscopic esophagectomy. *Esophagus* (2013) 10: 165–169.
3. Mine S, Tanaka K, Kawachi H, Shirakawa Y, Kitagawa Y, Toh Y, Yasuda T, Watanabe M, Kamei T, Oyama T, Seto Y, Murakami K, Arai T, Muto M and Doki Y: Japanese Classification of Esophageal Cancer, 12th Edition: Part I. *Esophagus* (2024) 21: 179–215.
4. Doki Y, Tanaka K, Kawachi H, Shirakawa Y, Kitagawa Y, Toh Y, Yasuda T, Watanabe M, Kamei T, Oyama T, Seto Y, Murakami K, Arai T, Muto M and Mine S: Japanese Classification of Esophageal Cancer, 12th Edition: Part II. *Esophagus* (2024) 21: 216–269.
5. Toniato A, Mazzarotto R, Piotto A, Bernante P, Pagetta C and Pelizzo MR: Identification of the nonrecurrent laryngeal nerve during thyroid surgery: 20-year experience. *World J Surg* (2004) 28: 659–661.
6. Natsis K, Didagelos M, Gkiouliava A, Lazaridis N, Vyzas V and Piagkou M: The aberrant right subclavian artery: cadaveric study and literature review. *Surg Radiol Anat* (2017) 39: 559–565.
7. Kau T, Sinzig M, Gasser J, Lesnik G, Rabitsch E, Celedin S, Eicher W, Illiasch H and Hausegger KA: Aortic development and anomalies. *Semin Intervent Radiol* (2007) 24: 141–152.
8. Devèze A, Sebag F, Hubbard J, Jaunay M, Maweja S and Henry JF: Identification of patients with a non-recurrent inferior laryngeal nerve by duplex ultrasound of the brachiocephalic artery. *Surg Radiol Anat* (2003) 25: 263–269.
9. Aygun N, Kostek M, Isgor A and Uludag M: Recent Developments of Intraoperative Neuromonitoring in Thyroidectomy. *Sisli Etfal Hastan Tip Bul* (2021) 55: 273–285.
10. Hemmerling TM, Schmidt J, Jacobi KE and Klein P: Intraoperative monitoring of the recurrent laryngeal nerve during single-lung ventilation in esophagectomy. *Anesth Analg* (2001) 92: 662–664.
11. Ikeda Y, Inoue T, Ogawa E, Horikawa M, Inaba T and Fukushima R: Recurrent laryngeal nerve monitoring during thoracoscopic esophagectomy. *World J Surg* (2014) 38: 897–901.
12. Kobayashi H, Kondo M, Mizumoto M, Hashida H, Kaihara S and Hosotani R: Technique and surgical outcomes of mesenterization and intra-operative neural monitoring to reduce recurrent laryngeal nerve paralysis after thoracoscopic esophagectomy: A cohort study. *Int J Surg* (2018) 56: 301–306.
13. Ninomiya Y, Oguma J, Ozawa S, Koyanagi K, Kazuno A, Yamamoto M and Yatabe K: Thoracoscopic esophagectomy with left recurrent laryngeal nerve monitoring for thoracic esophageal cancer in a patient with a right aortic arch: a case report. *Surg Case Rep* (2020) 30: 62.
14. Mushiake S, Taniguchi K, Lee SW, Shimizu T, Imai Y, Tanaka R, Honda K, Tashiro K, Kawai M and Uchiyama K: The usefulness of intraoperative neurological monitoring for esophageal cancer with double aortic arch; a case report. *BMC Surg* (2020) 20: 86.