The Recurrent and Superior Laryngeal Nerves

Gregory W. Randolph
Editor

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This book is dedicated

*to **Robert Sofferman** an artist, friend and champion*

Then I heard the voice of the Lord saying "Whom shall I send and who will go for us?" And I said, "here I am; send me!" Isaiah Chapter 6 Verse 6.

and

*to the life and work of **Michael Brauckhoff***

The early lilacs became part of this child and grass and white and red morning glories and white and red clover and the song of the Phoebe bird.... All became part of him. -Leaves of Grass by Walt Whitman.

Preface

This book represents a comprehensive state-of-the-art review of knowledge of the recurrent laryngeal nerve and superior laryngeal nerve as it relates to the thyroid and parathyroid surgical endeavor embracing surgical anatomy, surgical techniques, and the latest technological advances including neural monitoring relating to preservation of these nerves as well as detection and management of neural injuries occurring during thyroid surgery.

This text underscores the electrophysiologic nature of the thyroid and parathyroid surgery. These nerves play an extremely important role in the family life, profession, and sometimes even spiritual life of our patients. The chapters range from neurolaryngology, basic laryngeal function, laryngoscopy indications, and techniques to anatomy and surgical management of both the recurrent and superior laryngeal nerves. Recent advances in intraoperative neural monitoring are given special emphasis including new horizons in both superior laryngeal nerve and continuous vagal monitoring.

Throughout, we have endeavored to impart the material simply in both tabular and visual representations. The strength of the whole book relates to the quality of each part. Each contributor is drawn from the most elite group of researchers, clinicians, and surgeons around the world. They are carefully selected so that their areas of clinical and research contributions to the medical literature match with their chapter topic areas. These contributors provide an overarching unique orientation to their respective topics that goes beyond the individual disparate facts. In numerous chapters, experts from different regions in the world and sometimes from different specialties have been paired to provide a collaborative blending of various heterogeneous elements.

We believe this is the first book that specifically focuses on the neural innervation of the larynx as it relates to the thyroid surgical endeavor. We hope it represents a resource for practicing and academic thyroid and parathyroid surgeons both in training and those with significant experience.

I would like to recognize all the individuals without whom this project would not have been possible. Firstly, I thank the associate editors, namely, Henning Dralle, Gianlorenzo Dionigi, Marcin Barczynski, and Feng-Yu Chiang. In addition I would like to thank my friend and colleague Dr. Dipti Kamani, for her tireless research assistance. I would also like to thank John and Claire Bertucci as well as Mike and Liz Ruane for their friendship and ongoing support over the years. Finally, I would like to acknowledge some of the physicians who have been influential in the development of this book,

especially Dr. Brad Welling who is my chairman, friend, and mentor, for his continual support in the evolution of my thyroid surgical practice in Boston and my career. I would like to additionally thank Drs. Keith Lillemoe and Ken Tanabe for their belief in a true collaborative environment and commitment to modern endocrine surgery.

Boston, MA, USA Gregory W. Randolph

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Part I

Introduction

Henning Dralle

Rates of RLN and SLN Injury: Data from National Quality Registries and the Literature

1

Neil S. Tolley, Konstantinos Chaidas, and Anders Bergenfelz

'The extirpation of the thyroid gland typifies, perhaps better than any operation, the supreme triumph of the surgeon's art, a feat which today can be accomplished by any competent operator without danger of mishap and which was conceived more than one thousand years ago. There are operations today more delicate and perhaps more difficult, but is there any operative problem propounded so long ago and attacked by so many which has yielded results as bountiful and so adequate?'

Dr. William S. Halsted, 1920.

Abstract

The impact of thyroid surgery on voice is a key performance indicator of surgical quality. This chapter discusses factors that can impact on the incidence of both recurrent and external laryngeal nerve (external branch of superior laryngeal nerve—EBSLN) injury. The literature is reviewed and reported incidence of nerve palsy following thyroid surgery is presented. Particular reference is made to the British and Scandinavian database registries. The present evidence supports that the true injury rate is underreported. Factors that might influence nerve injury are presented in an evidence-based manner.

A centrally important dynamic in this area of study is that there is clear positive correlation between the rate of postoperative vocal cord examination and palsy. Overall, 10 % of patients can sustain a temporary laryngeal palsy following thyroidectomy. Permanent voice problems are common

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and the true incidence of permanent palsy remains unknown. There is little doubt, however, that the literature grossly underestimates its true incidence. Thirty percent of patients with a known vocal palsy may not complain of voice symptoms which again endorses the importance of routine post-operative vocal cord examination. Voice change secondary to EBSLN injury is also common and again the true incidence remains unknown. This situation prevails due to the difficulty of precise diagnosis with extant non-invasive methods of cord examination.

The importance of surgical volume to patient outcomes is emphasized. Surgery for cancer particularly when involving nodal dissection has been identified as a significant and higher risk for nerve palsy as have been revision and more extensive thyroid surgery. Similarly, higher rates of nerve injury are reported with retrosternal goitres. The literature is unclear as to whether the side of thyroidectomy is a risk factor or whether certain benign pathology such as Graves' disease confers a higher risk of injury.

Keywords

Recurrent laryngeal nerve injury • BAETS database • Scandinavian quality register • External laryngeal nerve injury • EBSLN • Superior laryngeal nerve

Introduction

Safe thyroid surgery is well established in clinical practice. Significant advances have taken place since the early pioneering work of the nineteenth century which resulted in thyroidectomy being outlawed in France and regarded with derision by physician colleagues.

Surgical pioneers combined with advances in antisepsis, anaesthesia, technology, understanding of pathophysiology, anatomy, and pharmaceutical therapies have all played a role in achieving a low mortality. William Halsted's statement still holds true nearly a hundred years later. Surprisingly, the true morbidity of thyroid surgery is little studied particularly with regard to the impact on voice.

Humans have adapted laryngeal function to produce voice and speech which is a unique human quality. Our ability to produce voice confers individuality and has immense social and professional importance. We express emotions, thoughts, and personality through our voice. The ancient Greeks considered voice so important that they believed it originated in the heart.

Thyroidectomy is presently performed by surgeons with a wide range of surgical experience. There is evidence showing a lower complication rate in surgeons having a high volume practice [1–3]. Nonetheless, the literature shows that approximately 75 % of all thyroidectomies in the USA and the UK are performed by low volume surgeons (less than 20 cases per year) [4, 5].

The negative impact of laryngeal nerve injury on voice is the most common reason for litigation in thyroid surgery [6]. Ten percent of patients may sustain a temporary laryngeal nerve injury following thyroid surgery with persistent hoarseness occurring in 4 % [7].

'Seek and you shall find…'
Matthew the Apostle 7:7–8:

The true incidence of nerve injury following thyroid surgery is unknown and likely to be considerably underreported. Studies show that the laryngeal palsy rate is proportional to the rate of post-thyroidectomy laryngeal examination [8, 9].

Eighty percent of patients may complain of voice changes following thyroidectomy [10] and these can be broadly classified into neural and non-neural causes as shown in Table 1.1 [11].

Table 1.1 Causes of thyroidectomy-related voice change

Neural	Consequences on voice quality
Recurrent laryngeal nerve (RLN) injury	Hoarse voice, breathy voice, vocal fatigue
External branch of the superior laryngeal nerve (EBSLN) injury	Reduced ability to produce high frequency tones, hoarse voice, breathy voice, vocal fatigue
Non-neural	
Direct cricothyroid muscle injury	Reduced ability to produce high frequency tones, hoarse voice, breathy voice, vocal fatigue
Regional soft tissue injury, strap muscles injury, local haematoma, and/or oedema	Vocal fatigue, decreased vocal range, monotone speech, lower vocal pitch
Intubation-related injury	Hoarse voice
Unrelated inter-current upper respiratory tract infection (URTI)	Hoarse voice, breathy voice

Although injury to the recurrent laryngeal nerve (RLN) may cause significant handicap, up to 30 % of patients with proven palsy do not complain of voice symptoms [12]. In addition, external branch of the superior laryngeal nerve (EBSLN) injury, although more difficult to diagnose, can cause significant morbidity due to impact on pitch and vocal projection [13]. Injury to the EBSLN can produce a significant voice change in the professional voice. The impact of non-neural influences such as cricothyroid and strap muscle injury, intubation trauma, and reduced laryngeal mobility from scarring remain unknown.

Importantly, pre-intubation and post-extubation assessment have revealed that vocal cord injury can occur in approximately 30 % of patients, attributable to intubation injury [6].

The Recurrent Laryngeal Nerve

History

Galen first described and named the RLN during the second century AD [14]. Paulus Aeginetus, in the seventh century AD even proposed that the RLN should be avoided during thyroidectomy. However, it was Vesalius in 1543 that provided the first anatomical drawings. In 1938, Lahey and Hoover demonstrated that routine identification and dissection of the RLN during thyroid surgery resulted in a significantly decreased RLN injury rate [15] which is now standard practice for most thyroid surgeons.

Structure and Function

The RLN is a mixed nerve consisting of motor, sensory, and autonomic fibres. Motor fibres are class A myelinated with approximately 80 % having adductor function.

Nerve diameter varies between 1 and 3 mm with no significant difference between the sides [16–18].

The RLN is approximately 10 cm and 8.5 cm on the left and right, respectively, leading to higher nerve latency on the left [19]. Branching is frequently seen in approximately 30 % of nerves with 90 % occurring above its intersection with the inferior thyroid artery [20, 21].

The RLN tracks close to the posterior aspect of the thyroid gland and enters the larynx posterior to the cricothyroid joint. It courses dorsal to the posterior suspensory ligament of Berry, although it can commonly pass through the ligament of Berry, which can place the nerve at considerable risk during thyroidectomy as a result of assistant retraction.

The mechanisms that determine cord position following nerve injury are unknown.

Mechanism of Injury

Several studies provide evidence of poor surgical sensitivity in detecting nerve injury at the time of thyroidectomy even when RLN integrity was ‘assured’ by visual inspection. Lo et al. [22] reported that only 5 out of 33 nerve injuries were recognized during surgery. Similarly, Patow et al.

[23] reported that only 1 out of 10 cases of RLN injury was noticed intraoperatively. In another study by Chiang et al., 40 nerves developed cord paralysis while recognized nerve injury was diagnosed in only 3 patients [24]. Data from the Scandinavian Quality Register show that only 10 % of nerve injuries are suspected by the surgeon intraoperatively [9].

The greatest site at risk is where the RLN passes close to or through Berry's ligament. Stretching and compression by Berry's fibres is likely responsible. In addition, thermal or mechanical injury during dissection contributes to injury.

There are reports of the RLN diameter increasing significantly after thyroid surgery probably due to edema [17]. This might contribute to voice change in the absence of a diagnosed RLN palsy.

Consequences of Injury

Symptoms arising from RLN paralysis are wide, ranging from little to severe voice change in unilateral lesions to stridor and acute airway obstruction with bilateral damage [25]. Although dysphonia after thyroid surgery is usually related to RLN injury, this nevertheless often occurs in patients with 'normal' vocal cord mobility. Postoperative voice change either temporary or permanent can significantly alter patient life quality especially in professional voice users.

RLN injury can also lead to sensory alteration resulting in swallowing impairment and aspiration [25]. The posterior branches of the RLN often provide innervation to both the cricopharyngeus muscle and esophagus. Injury can result in dysphagia in up to 56 % of patients with unilateral vocal fold injury. Aspiration can also be a significant problem in 44 % of patients [26–28].

Despite these literature reports, many patients with RLN injury may be without symptoms. This might be because of remaining partial neural function, variability in the position of the paralyzed vocal cord, or compensation from the contralateral cord. Up to one-third of patients with a unilateral vocal cord palsy may be symptom free [12].

Diagnosis of RLN Injury

Early recognition of nerve injury is important as it provides an opportunity for early speech therapy and rehabilitation which enhances voice outcomes and life quality. Common methods used for assessing voice include validated voice and thyroidectomy questionnaires, acoustic measurements, and laryngeal examination which is the standard of care [11].

Dionigi et al. reported that the RLN palsy rate 14 days post-surgery was significantly less compared with examination on postoperative day 0 or 1. It has been proposed on the basis of this finding that laryngeal examination should take place prior to hospital discharge [29].

There has been no internationally agreed definition of 'transient' and 'permanent' RLN palsy. It is evident that partial lesions start to recover within the first few days postoperatively with normal nerve function returning within a few weeks [29, 30]. Two-thirds of transient palsies will recover within 4 weeks [31], and 89 % of all temporary palsies will have resolved by 12 months [29]. There is however, a low possibility that RLN function may recover up to 2 years postoperatively [32]. From a pragmatic point of view, several groups support a diagnosis of permanent RLN palsy if there has been a failure of functional return by 12 months [22, 29, 33, 34].

Factors Influencing RLN Injury Rate

Nerve Identification

Lahey and Hoover introduced the principle of routine identification of the RLN during thyroid surgery in 1938 showing that this significantly decreased RLN injury [15]. Several studies have supported this finding [24, 30, 35–37].

The reported risk for nerve injury if the RLN is not identified intraoperatively is 1.41 times higher according to a large multi-centre German study [38] and 3–4 times higher as demonstrated by Mountain et al [39]. The rate of RLN injury following nerve identification has been reported to be as low as 0.5 % at some specialized centres [40–45].

Several authors have suggested that the RLN is extremely vulnerable to surgical dissection and postulated that extensively dissected and exposed RLNs are subject to a higher risk of palsy. It has been recommended that the RLN should undergo as minimal dissection as possible during thyroidectomy [46–48]. In contrast, Chiang et al. showed that extensive dissection of the RLN did not increase the risk of nerve injury and that careful extensive surgical dissection is well tolerated [49].

Revision Surgery

Patients undergoing revision surgery are at increased risk of RLN injury, although wide range of palsy rates are reported [1, 38, 50]. It is estimated that the risk of RLN paralysis is between 2 and 30 % in revision surgery [1, 24, 38, 51–53].

Jatzko et al. report revision benign goitre surgery has an incidence of RLN palsy approaching 8 % compared with almost zero for primary surgery [36]. A large prospective study by Thomusch et al. reported a relative risk of 3.1 for RLN palsy in revision compared with primary benign goitre surgery [38]. Lo et al. report similar results for all the types of histopathological diagnosis [22]; they quote a 4 % incidence of palsy for revision surgery compared with less than 1 % for primary procedures. Hayward et al. showed a significant increase in permanent palsy occurred in revision surgery compared with primary surgery. A higher transient palsy rate of 4.41 % in revision surgery was also found compared to 1.13 % in primary surgery [26]. The British Association of Endocrine and Thyroid Surgeons (BAETS) audit showed that the incidence of a postoperative palsy was six times higher in revision surgery [4, 8, 54].

Surgeon Experience

The literature reveals the relationship between surgical outcomes and surgeon experience. RLN injury rates of less than 1 % have been associated with high-volume surgeons [1–3]. Dralle et al. reported significantly reduced RLN palsy rates for surgeons performing greater than 45 nerves at risk (NAR) procedures per year compared with those with less than 45 (0.72 % versus 1.06 %), with both groups matched for the type of surgery and pathology [1]. Sosa et al. found a significant association between surgeon volume and outcomes following thyroidectomy. Surgeons who performed more than 100 thyroid operations per year had a lower rate of RLN injury [3]. This was evident despite the fact that experienced surgeons were performing a far greater proportion of 'complex' procedures, which might bias complication rates unfavourably. A large study by Kandil et al. established similar findings in that surgeon volume was significantly associated with post-operative complication rates for patients undergoing total thyroidectomy [2]. The group of low-volume surgeons had a significantly higher RLN palsy rate.

Other studies, however, show no difference in RLN palsy incidence when a supervised trainee performs the operation [38, 55–57]. These data demonstrate that surgeons' training as well as caseload has an impact on RLN palsy rate. Surgeons having undergone thyroid-specific specialty training were found to have a similar RLN palsy rate regardless of their surgical volume [58].

Nerve Monitoring

There is not enough evidence in the literature to support that intraoperative nerve monitoring (IONM) reduces significantly the risk of RLN injury during thyroid surgery. A meta-analysis of the combined results of four individual studies including 1513 patients and 2912 NAR did not demonstrate a statistically significant decrease in the risk of temporary or permanent RLN injury with the use of IONM in comparison with common practice of search and identification of the nerve [59].

Similarly, a large meta-analysis by Higgins et al. after evaluating 64,699 NAR did not demonstrate a statistically significant difference in temporary or permanent RLN injury after using IONM versus nerve identification alone during thyroidectomy (2.74 % and 0.75 % versus 2.49 % and 0.58 %, respectively) [33].

A further meta-analysis by Zheng et al., after evaluation of 36.487 NAR, identified statistically significant difference in the incidence of transient RLN injury (2.56 % with IONM versus 2.71 % with nerve identification alone). However, no difference in the incidence of permanent RLN injury was identified (0.78 % versus 0.96 %, respectively) [60].

In a randomized controlled trial in 1000 patients undergoing bilateral thyroidectomy, the rate of temporary RLN palsy was 3.8 % in the group with visualization only of the RLN, and 1.2 % in the IONM group ($p=0.011$). The rate of permanent RLN paresis did not differ, 1.9 % and 0.8 % in the two groups respectively, although this could be due to the fact that the study was under powered. A further analysis showed that the benefit of IONM was conferred to patients with more complex operations [61]. This study suggests that IONM may reduce the rate of nerve injury.

Extent of Surgery

It is generally accepted that extended resections carry a higher risk of RLN palsy [62]. A study by Erbil et al., in 3250 patients, reported a 12.6 times greater risk of RLN palsy in those undergoing extended thyroidectomy compared with conservative surgery (subtotal resection) for thyroid cancer [63]. Similarly, Dralle et al. demonstrated that the risk of permanent RLN palsy was significantly higher in patients undergoing lobectomy versus subtotal lobar resection (1.34 % and 0.68 %, respectively) [1]. Near-total thyroidectomy has a lower risk of RLN palsy as thyroid tissue adjacent to the nerve at Berry's ligament is left on one side [64, 65].

Side of Surgery

Despite differences in anatomy, the literature does not provide clear evidence of a relationship between rate of palsy and the laterality of the nerve. Some reports support a higher incidence of injury on the right side [45]. Serpell et al. reported a higher right-sided palsy rate (65 %) during bilateral procedures [66]. This agrees with the findings of Rosato et al. (75 %—right side) and Zambudio et al. (62 %—right side) [45, 67].

Contrary to these findings however, Serpell later was to report that injury to the left nerve occurred 2.7 times more frequently than the right during unilateral surgery. [66]

Potential reasons for a greater rate of right-sided injury include the more oblique course of the nerve, a greater incidence of branching, and both the size and presence of a contralateral lobe which might influence the degree of retraction and the tension on the nerve. Finally, whether a surgeon has a dominant right or left hand might also influence injury during surgery.

Despite these theoretical risks, there are other studies that demonstrate no difference in the laterality of nerve injuries. Dionigi et al. [29] reported no dominance of side and these findings are supported by other studies [22, 62]. A large series by Hayward et al. showed no significant difference in the side of injury among 51 RLN palsies (1.37 % of 1742 NAR on the left versus 1.35 % of 1990 NAR on the right) [26].

Cancer Surgery

Patients undergoing thyroid surgery for cancer are at increased risk of RLN palsy, often due to tumour invasion of the surrounding soft tissue or even the nerve itself, as it is reported that the nerve is invaded in up to 20 % of patients with thyroid cancer [24].

Dralle et al. reported permanent RLN palsy in 1.52 % of patients undergoing primary thyroid cancer surgery compared to 0.5 % in benign disease [1]. A prospective study by Lo et al. reported significantly increased rates of nerve injury after surgery for cancer (5.26 %) compared to benign disease (0.7 %) [22]. Likewise, Hayward et al. also demonstrated an increased incidence of permanent and temporary RLN injury in cancer (0.28 % and 1.82 %, respectively) compared with benign disease surgery (0.13 % and 1.12 %, respectively) [26]. These findings are supported by several other smaller studies, with RLN palsy rates in thyroid cancer operations ranging from 2 % to 50 % [1, 22, 32, 43, 63, 68]. The risk for nerve injury is even higher when surgery for thyroid cancer includes central neck dissection as demonstrated by several studies [69–71].

Graves' Disease

It has been suggested that surgery for Graves' disease is associated with increased RLN palsy risk. This is refuted in several studies where no significant difference in RLN palsy rates was seen between any specific benign pathology [1, 26, 63, 72].

Retrosternal Goitre

It is not clear whether surgery for retrosternal goiter carries an increased risk of nerve injury. It has been suggested that these patients may have an increased palsy rate [1, 73–75]. Agha et al. reported an 8.5 % temporary RLN palsy rate and a 5.1 % permanent RLN palsy rate in 59 patients with surgical treatment of a retrosternal goitre [73]. However, evidence from a large case series showed that there was no increased risk of RLN palsy [76]. Randolph et al. reported although large cervical and retrosternal goitres might be associated with a displaced RLN, a careful identification and dissection of RLN intraoperatively prevents injury [77].

RLN Injury Rate

A review of 27 articles and 25,000 patients showed that the average incidence of temporary postoperative vocal fold palsy was 9.8 % and the incidence of permanent RLN injury was 2.3 %. A wide range of injury, ranging from 2.3 and 26 % was found which may be partly related to the laryngeal examination use and time after surgery [7].

Thomusch et al. reviewed 7266 patients undergoing thyroid surgery for benign disease. They report a 2.1 % transient and 1.1 % for permanent RLN palsy [38]. Rosato et al. report a 3.4 % temporary and 1.4 % permanent injury after thyroid surgery in 14,934 patients [78]. Several other smaller studies demonstrate that the incidence of RLN palsy ranges between 0.3 and 3 % for permanent palsy and up to 8 % for temporary palsy [22, 24, 38, 55, 71, 79–81].

It could be conjectured that units with unfavourable data are less likely to report their findings which would conceal the true rate of RLN palsy. It is expected that compulsory reporting in nationwide audit databases should provide a more accurate picture of true RLN morbidity.

The 2012 Scandinavian quality register was based on the findings of approximately 2000 thyroidectomies performed within 1 year in 31 endocrine surgical units from Sweden and Denmark [82]. A temporary rate of 3.02 % (≤6 weeks) and permanent rate of 1 % (≥6 months) was reported. However, postoperative routine laryngoscopy was performed in only 52 % of patients.

These findings were similar to those published in 2011 [83], where a temporary rate of 3.2 % and a permanent rate of 0.6 % were reported with postoperative laryngeal exam in only 30.2 % of patients irrespectively of voice symptoms and in 50.4 % of patients in total (pre- and post-surgery).

Previous analysis of the register data had shown that the rate of postoperative RLN palsy doubled when patients were submitted to routine laryngeal examination after surgery compared to laryngoscopy performed only in patients with persistent and severe voice change [9].

In October 2012, the fourth BAETS audit was published based on a database of 18,904 thyroidectomies submitted by 142 surgeons.

In this publication, RLN palsy rates for first time surgery ranged between 2.01 % in 2007 and 1.8 % in 2011 [8]. A 3 % rate for revision surgery was reported. For 2610 patients who had first-time surgery within a period of a year (2010–2011), the reported incidence of RLN palsy was 1.3 % after lobectomy and 2.3 % after total thyroidectomy. These figures increased to 2.5 % and 10.0 %, respectively, with revision surgery.

Furthermore, different RLN palsy rates were demonstrated depending on the rate of performance of postoperative laryngeal exam. A 1.7 % rate of RLN palsy was reported when laryngoscopy was performed in less than 30 % of cases. This increased to 2.5 % with a 30–80 % postoperative laryngoscopy rate and to 4.2 % with a postoperative laryngoscopy rate higher than 80 %.

The overall mean rate of preoperative laryngoscopy in the BAETS audit was only 60.9 % increasing to 86.7 % for revision surgery. Disturbingly, the average postoperative laryngoscopy rate was less than 20 % overall for both primary and revision surgery. The true incidence of temporary and permanent cord palsy in the UK therefore remains unknown.

Superior Laryngeal Nerve

History

In 1543, Vesalius provided anatomic drawings of the superior laryngeal nerve (SLN) and over 3 centuries later, in 1892, Fort first reported that the EBSLN provides motor supply to the cricothyroid muscle (CTM).

Relatively little attention was paid to the role of the SLN in thyroid surgery although its importance was demonstrated in 1935, when the career of the famous opera singer Amelita Galli-Curci was ended by a presumed SLN injury. Amelita underwent surgery under local anaesthesia in order to protect her RLNs. Despite this, her voice became permanently hoarse postoperatively due to SLN injury [84, 85].

Structure and Function

Tschiassny in 1944 and Arnold in 1961 demonstrated the influence of the contraction of the CTM on voice production and therefore the importance of the SLN [86, 87]. During the subsequent decades, several authors have described methods to identify and preserve the SLN during thyroidectomy [88–92]. Lennquist has described the SLN as 'the neglected nerve in thyroid surgery' despite the fact that injury can cause significant disability [93].

The SLN is one of the first branches of the vagus nerve. It originates just below the nodose ganglion approximately 4 cm cranial to the carotid artery bifurcation. The SLN divides into two branches, the internal and the external branch [94, 95]. The internal branch travels medial to the carotid system and penetrates the larynx through the thyrohyoid membrane. The external branch travels downward toward the superior pole, along or underneath the inferior constrictor fascia, before entering the CTM. The EBSLN approaches the larynx within the sternothyroid-laryngeal triangle (Joll's Triangle), which is delineated by the sternothyroid muscle superiorly, the cricothyroid and inferior constrictor muscles medially and the superior thyroid pole inferiorly [88, 92, 95].

In most circumstances, the EBSLN passes well above the superior thyroid pole, but variations in its caudal extent in relation to the superior pole region have been well described. For this reason, many anatomic classifications have been proposed. The most popular classification is the one described by Cernea in 1992, based on the relationship between the nerve, the superior thyroid artery, and the superior thyroid pole [89, 90]. In 1998, Kierner et al. published a similar classification, adding a fourth category [96]. More recently, Friedman, LoSavio, and Ibrahim [91] proposed a different classification based on the relationship between the EBSLN and the inferior constrictor muscle [91].

The internal branch of the SLN supplies the sensory innervation to the mucosa of the larynx above the vocal cord, and it may also be responsible for some motor innervations of laryngeal muscles [94, 95].

The EBSLN innervates the CTM. The cricothyroid has two bellies, the pars recta and the pars obliqua. The combined action of these bellies tilts the thyroid cartilage relative to the cricoid cartilage and increases the length and the tension of the ipsilateral vocal cord. Vocal fold tension and thickness influence the frequency of the vibration, influencing the characteristic timbre of voice. Therefore, the EBSLN has an important influence on voice quality, projection, and the production of high-pitched sounds [13].

There are interconnections between the superior and recurrent laryngeal nerves, particularly in the region of the interarytenoid muscle known as the anastomosis of Galen [97, 98].

Mechanisms of Injury

The EBSLN is at risk during thyroid surgery due to its close anatomical relationship with the superior thyroid vasculature and the superior thyroid pole region. Inadvertent stretching, electrothermal damage, or even ligation of the EBSLN can occur during dissection of the superior pole of the thyroid gland and clamping of the superior thyroid vessels.

Consequences of Injury

Complications of thyroid surgery related to the RLN and parathyroid glands have been widely reported in the literature. In contrast, intraoperative injury to the EBSLN is less clearly defined, although this may lead to temporary or permanent voice change. Injury to the EBSLN can cause dysfunction of the CTM, resulting in changes in voice quality and projection and reduced ability to produce high frequency tones. Inability to create high-pitched sounds is the most common presentation of CTM paralysis. Patients may also present with a hoarse breathy voice with increased throat clearing and vocal fatigue [91, 92]. These symptoms may be subliminal to many patients but are a significant disability to professional voice users. The presence of aspiration is not common as CTM muscle weakness does not directly affect glottic closure. However, this might occur with injury of the internal branch of the SLN.

Diagnosis of EBSLN Injury

The diagnosis of EBSLN injury is difficult to confirm based solely on clinical or endoscopic findings due to the variable associated voice changes and the absence of clear findings during postoperative laryngoscopy.

The effect of CTM dysfunction on the appearance of the larynx is controversial. Variable laryngoscopic findings have been reported. These include posterior glottis rotation toward the affected side [99–102], a lower vocal fold level on the paralyzed side [99, 102, 103], thinning and foreshortening of the cord, decreased vocal fold mobility, asymmetric vibration of the vocal folds, [102–104] and epiglottic petiole deviation toward the affected side [100].

The detection of these laryngeal findings via laryngoscopy is extremely difficult. Given the fact that the clinical manifestations are often subtle and the laryngeal findings often inconclusive and controversial, EMG remains the standard modality for definitive diagnosis of injury [88, 105]. It shows a decreased recruitment and polyphasic action potentials that might attain electrical silence with complete paralysis. EMG is invasive as well, sometimes painful examination and is not widely available or acceptable to patients.

Factors Influencing EBSLN Injury Rate

Nerve Identification

Many surgeons still prefer to try to 'avoid' the EBSLN and do not routinely attempt to identify it intraoperatively. However, the authors view is that routine identification of the EBSLN during surgery should become standard as it reduces nerve damage [25]. Although a few studies have reported no statistically significant decrease in injury rates after EBSLN identification during thyroidectomy [106, 107], there is growing evidence in the published literature that routine identification of the EBSLN during thyroid surgery reduces nerve injury. Cernea et al. documented a 0 % EBSLN injury rate when the nerve was identified compared to a 12–28 % incidence when nerve identification was not performed intraoperatively [89, 90].

Similarly, Hurtado-Lopez et al. report the incidence of injury decreases from 20 % without intraoperative nerve identification to 8 % after nerve visualization [108]. Overall, the documented incidence of permanent EBSLN injury decreased to 0.5 % after routine nerve identification in specialized centres [45, 106].

Nerve Monitoring of EBSLN

Identification of the EBSLN during thyroid surgery can be difficult due to its variable course, thyroid pathology, and the fact that it can lie deep to the inferior constrictor muscle [89–91, 109, 110]. Visualization alone may not identify up to 20 % of the nerves that are sub-fascial [109]. However, identification can be facilitated by using IONM [88, 105]. Increasing use of nerve stimulation or IONM techniques in recent years has resulted in improved identification and the functional preservation rate of the nerve [89, 90, 111, 112].

A meta-analysis to assess nerve injury with and without neuromonitoring compared to identification alone revealed no difference. However, IONM significantly decreased the risk of temporary

EBSLN injury and there was a nonsignificant trend toward a lower risk of permanent EBSLN injury [59].

Surgeon Experience

It is not known if surgical volume correlates with EBSLN injury. Cernea et al. documented a higher EBSLN injury rate in less experienced surgeons [89, 90]. He reported that EBSLN injury occurred in 12 % of NAR when the surgeon performing the operation was of consultant grade compared to an incidence of 28 % in trainees.

Cancer

Although there is a paucity of evidence in the literature, a study by Hurtado-Lopez et al. reported that the presence of cancer, even when extracapsular extension exists has no influence on the frequency of EBSLN injury [108].

EBSLN Injury Rate

Accurate EBSLN injury rate assessment is difficult due to limited data and heterogeneous methods used in different studies. The reported prevalence varies widely from 0 to 58 %; therefore, EBSLN injury is believed to be the most commonly underestimated morbidity following thyroid surgery [113–117].

Several studies have used laryngoscopy and voice assessment in order to evaluate EBSLN function after attempting to identify and preserve the nerve during surgery. Reeve et al. examined 157 NAR and found that injury occurred in 1.9 % [117]. Lennquist et al. and Kark et al. demonstrated an injury incidence of 2 % and 5 %, respectively [109, 115]. A larger study by Lore et al. reported 0.1 % injury rate among 934 NAR based on laryngoscopic findings increasing to 7.6 % for permanent and 13.6 % for temporary injury when voice evaluation was performed [116]. Jonas et al. found a 4.6 % temporary injury rate among 190 NAR using nerve monitoring instead of visual nerve identification intraoperatively [112].

Videostroboscopy and voice evaluation have also been used for EBSLN injury assessment in a few studies. Barczyński et al. evaluated 420 NAR and demonstrated 6 % incidence of temporary injury after visual nerve identification decreasing to 1.5 % when IONM was used [111]. A large randomized study examining 459 NAR by Bellantone et al. reported 0.5 % temporary nerve injury after routine nerve identification increasing to 0.8 % without visual nerve identification [106].

It is evident that EMG is the only accurate diagnostic tool for diagnosing EBSLN injury. Several studies using EMG to assess EBSLN function after thyroid surgery exist in the literature. By using EMG and without attempting to visualize the nerve intraoperatively, Jansson et al. reported a 58 % rate of temporary and a 3.8 % rate of permanent EBSLN injury after examining 26 NAR [114].

Following similar methodology, Teitelbaum and Wenig found a 5 % incidence of injury in 20 patients [102], whereas Aluffi et al. reported a 14 % injury among 35 NAR [113]. Cernea et al. examined 90 NAR and reported a 12–28 % injury rate when the EBSLN was not identified during surgery which dropped to 0 % when IONM was used [89, 90, 106]. Similarly, Selvan et al. found a 0 % incidence among 70 NAR when IONM was used [118]. A study by Hurtado-Lopez et al. examining 100 patients demonstrated a 20 % injury when the nerve was not identified intraoperatively decreasing to 8 % after nerve visualization [108].

A recent meta-analysis showed 1.4 % incidence of temporary EBSLN palsy when IONM was used increasing to 5.7 % when the nerve was identified visually during surgery without IONM. Permanent injury occurred in 0.3 % of nerves in the neuromonitoring group in comparison with 0.9 % in the visualization group [59].

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Laryngeal Exam Indications and Techniques

2

Catherine F. Sinclair, William S. Duke, Anca M. Barbu, and Gregory W. Randolph

Abstract

Postoperative voice changes are one of the most common and feared complications of thyroid surgery. In most cases, postoperative hoarseness is due to recurrent laryngeal nerve (RLN) injury, although injury to the external branch of the superior laryngeal nerve (EBSLN) can also result in significant vocal issues, including diminished vocal projection and inability to attain higher vocal registers. Voice complaints can also occur in the absence of neural dysfunction and may be present prior to any surgery being performed. Thus, timely and accurate evaluation of laryngeal function optimizes ongoing management efforts and provides important prognostic and outcome information.

Only recently has increased awareness of the importance of voice outcomes in thyroid surgery led to the publication of a number of important papers on this topic, with several professional organizations starting to make reference to voice and laryngeal function in their guidelines for best practice. However, recommendations in these guidelines vary, especially with regard to laryngeal examination for patients without voice impairments, with many surgeons using voice symptoms alone to guide the need for laryngeal examination. True laryngeal function may be inaccurately

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predicted by voice symptoms, and thus controversy remains regarding need for routine laryngeal examination, timing of any such examination, and optimal examination technique(s). This chapter will discuss indications for laryngeal examination in thyroid surgery and current techniques available for voice and laryngeal examination.

Keywords

Laryngeal examination • Laryngoscopy • Vocal fold paralysis • Vocal cord paralysis • Recurrent laryngeal nerve • Superior laryngeal nerve • Thyroidectomy • Dysphonia • Larynx

Introduction

Postoperative voice changes are one of the most common and feared complications of thyroid surgery. In most cases, postoperative hoarseness is due to recurrent laryngeal nerve (RLN) injury, although injury to the external branch of the superior laryngeal nerve (EBSLN) can also result in significant vocal issues, including diminished vocal projection and inability to attain higher vocal registers. Voice complaints can also occur in the absence of neural dysfunction and may be present prior to any surgery being performed. Thus, timely and accurate evaluation of laryngeal function optimizes ongoing management efforts and provides important prognostic and outcome information.

Only recently has increased awareness of the importance of voice outcomes in thyroid surgery led to the publication of a number of papers on this topic, with several professional organizations starting to make reference to voice and laryngeal function in their guidelines for best practice. However, recommendations in these guidelines vary widely, especially with regard to laryngeal examination for patients without voice impairments, with many surgeons using voice symptoms alone to guide the need for laryngeal examination. True laryngeal function may be inaccurately predicted by voice symptoms, and thus controversy remains regarding need for routine laryngeal examination, timing of any such examination, and optimal examination technique(s). This chapter will discuss indications for laryngeal examination in thyroid surgery and current techniques available for voice and laryngeal examination.

Indications for Laryngeal Examination in Thyroid Surgery

Preoperative Indications

It has been estimated that up to 33 % of individuals undergoing thyroid surgery may exhibit voice impairment preoperatively [1, 2]. However, preoperative subtle voice changes are not easily volunteered by patients and may be difficult for clinicians to detect. Also, there is a significant divergence between voice symptoms and objective vocal fold function. Indeed, the sensitivity of voice change in predicting vocal fold paralysis ranged from 33 to 68 % in two recent studies [3, 4]. Similarly, another study reported that one-third of 98 patients with postoperative vocal fold paralysis were ultimately judged to be asymptomatic in terms of vocal symptoms [5]. Thus, vocal fold paralysis may be present without significant vocal symptoms. This discrepancy between voice symptoms and vocal fold function on laryngeal examination may be due to a number of factors including residual fold function, variability in the position of the affected vocal fold, and variability in contralateral vocal fold compensation. This discrepancy provides a rationale for the inclusion of a glottic examination in all patients, both preoperatively and postoperatively. However, many surgeons use voice symptoms alone to screen for RLN injury and, at present, only 6.1–54 % of thyroidectomy patients undergo a preoperative laryngeal exam [6].

A number of professional thyroid organizations have begun to make reference to laryngeal examination in their guideline statements. The

German Association of Endocrine Surgeons [7] and a recent consensus statement of the British Association of Endocrine and Thyroid Surgeons (BAETS) [8] recommend that all patients undergoing thyroid surgery should have preoperative and postoperative laryngeal examinations. The International Neural Monitoring Study Group (INMSG) recommends pre- and postoperative laryngoscopy in all patients undergoing thyroid surgery with use of intraoperative neural monitoring (IONM) [9]. The recent clinical practice guidelines published by the American Academy of Otolaryngology Head and Neck Surgery (AAOHNS) recommend that the surgeon should document assessment of the patient's voice once a decision has been made to proceed with thyroid surgery [6]. At a minimum, this should involve subjective assessment of voice by the surgeon, patient, and family, with documentation in the patient chart as to whether these parties consider the patient's voice to be abnormal, impaired, or less than satisfactory. If there is any detectable voice impairment, or when there is a past history of voice disorder, more thorough voice investigation is indicated, which may include a validated quality of life measure, referral to an otolaryngologist, and/or assessment by a speech and language pathologist. In addition, preoperative laryngeal examination should be performed on all patients undergoing thyroid surgery when the voice is abnormal or, in the case of normal voice, if there is preoperative suggestion of thyroid cancer with suspected extrathyroidal extension or a past history of surgery in which the vagus or recurrent laryngeal nerves were at risk. Similarly, the British Thyroid Association recommends the larynx be examined in patients with preoperative voice changes and for those undergoing thyroid cancer surgery, and the National Comprehensive Cancer Network (NCCN) guidelines suggests preoperative laryngeal exam for all patients with thyroid cancers [10]. The American Thyroid Association (ATA) 2009 clinical guidelines on thyroid nodules and differentiated thyroid cancer make no reference to laryngeal examination; however, their guidelines for anaplastic thyroid carcinoma strongly recommend every patient undergo initial evaluation of the vocal folds [11, 12]. However, the most recent ATA 2015 clinical guidelines on thyroid nodules in differentiated thyroid cancer recommend voice evaluation on all patients preoperatively and laryngeal exam to be performed on patients in accordance with the American Academy of Otolaryngology recent guidelines noted above [13].

There are many reasons as to why laryngeal examination prior to thyroid surgery is important. Firstly, vocal fold paralysis, as noted earlier, can be present without significant vocal symptoms, and preoperative voice symptoms or lack of such symptoms are not reliable indicators of RLN function. Secondly, preoperative recognition of vocal fold paralysis is essential in planning a thyroid procedure. Total thyroidectomy, whether for benign or malignant disease, imparts a risk of bilateral vocal fold palsy due to both RLNs being at risk. Preoperative laryngoscopy may identify those individuals, with or without an impaired voice, who have preexisting vocal fold weakness and who would be at increased risk for bilateral vocal fold paralysis with its resultant airway obstruction, respiratory distress, and possibly the need for urgent interventions such as tracheotomy. Thus, the potential for significant postoperative morbidity is minimized and patients can be counseled appropriately about the risks of surgery. With regard to thyroid malignancy, a finding of vocal fold paralysis on preoperative examination strongly suggests the presence of invasive disease and help guide the surgical approach, as RLN invasion identified at surgery is managed based on knowledge of its preoperative function [14]. Third, identification of preoperative neural palsy may facilitate optimization of long-term voice outcomes. One study demonstrated that individuals identified with presurgical RLN impairment due to tumor invasion exhibited improved voice function outcomes after a subsequent voice surgery compared to those who were not so identified [15]. Additionally, from a medicolegal viewpoint, preoperative assessment of vocal fold function is necessary before assuming responsibility for any vocal fold dysfunction found postoperatively. Finally, with surgical outcome measures assuming increasing importance in day-to-day surgical practice, accurate interpretation of postoperative thyroidectomy laryngeal outcomes can only be accomplished if preoperative function is known.

Postoperative Indications

RLN injury with resultant dysphonia (and possibly dysphagia) is one of the main concerns for patients undergoing thyroid surgery. Incidence rates for RLN injury during thyroid surgery vary and are dependent on the pathology, involvement of the nerve with tumor, or need to resect or transect the nerve. Estimates of RLN injury can approach 13 % for thyroid cancer operations and as high as 30 % for revision thyroid surgery [16]. In patients where the nerve is spared, the traditionally low rates of reported vocal fold paralysis (1 %) are likely significantly underestimated. A recent analysis of 27 articles reviewing over 25,000 patients undergoing thyroidectomy found an average temporary vocal fold paralysis rate of 9.8 % [17]. In addition, recent quality registers of European and UK endocrine surgeons focusing on thyroid surgery have quoted rates between 2.5 and 4.3 % and administrators of these databases deemed their rates of temporary and permanent vocal fold paralysis to be severely underestimated [6]. Postoperative voice complaints can also occur in the absence of neural dysfunction, possibly due to direct cricothyroid muscle (CTM) dysfunction, strap muscle injury, peri-laryngeal scarring, or regional soft tissue changes, with a number of recent large series quoting subjective postoperative voice complaints in 30–87 % of patients [18–21]. Nonsurgical causes of postoperative voice change may include laryngeal irritation, edema, or injury from airway management [22]. In a prospective nonrandomized study of 100 patients, subjective voice changes occurred in one-third of patients with preserved vocal fold movement [23]. Another prospective single-arm study of 395 patients reported that 50 % of patients had early subjective voice changes, with voice symptoms improving within 6 months in 85 % of patients and within 1 year in 98 % [24].

As previously mentioned, subjective voice findings are a poor predictor of vocal fold paralysis and, even if the goal of the surgeon is only to identify the presence of vocal fold immobility, relying on a change in voice may not capture all patients. The Scandinavian quality register reported a vocal fold paralysis rate of 4.3 % nerves at risk, based on 3660 thyroid operations performed in 2008 in 26 endocrine surgical units from Sweden and Denmark [25]. Detection of vocal fold paralysis doubled when patients were submitted to routine laryngeal exam after surgery as compared to laryngoscopy performed only in patients with persistent and severe voice changes. In another recent study of 98 patients with vocal fold paralysis, voice was judged to be normal in 20 % and improved to normal in an additional 8 %. Thus, overall, nearly one-third of patients with vocal fold paralysis were or became asymptomatic [26].

Examination of vocal fold motion after thyroid surgery is appropriate in patients with postoperative dysphonia to assess the cause of the dysphonia, establish prognosis, and facilitate the design of treatment options to be instituted as necessary in a timely fashion.

Recent evidence suggests that early identification of vocal fold paralysis with surgical intervention via injection laryngoplasty within 3 months of injury can significantly improve long-term prognosis for functional recovery with minimal morbidity with less likely need for open formal thyroplasty surgery [27, 28]. These studies postulate that early medialization of the vocal fold creates a more favorable vocal fold position for phonation that can be maintained by synkinetic reinnervation. Referral of patients with vocal fold palsy to a speech language therapist for voice therapy can also improve glottal closure and minimize maladaptive compensatory strategies such as supraglottic hyperfunction. However, none of these strategies can be implemented unless the larynx is examined and thus all patients with dysphonia following thyroid surgery should have an examination of vocal fold mobility.

In patients with minimal voice disruption after thyroid surgery, a strong case for laryngeal examination can still be made. Laryngeal examination in this situation may identify asymptomatic vocal fold motion abnormalities and, in doing so, mitigate the risks of injury to the contralateral nerve for patients requiring subsequent surgery, such as other neck procedures, revision thyroid or parathyroid surgery, carotid endarterectomy, anterior

cervical approaches to the spine, or other neck or major chest surgery. Asymptomatic undiagnosed vocal fold paralysis can also have significant impact on swallowing safety and aspiration risk, particularly in elderly patients. In addition, given that postoperative vocal symptoms are not necessarily predictive of objective vocal fold function, postoperative laryngeal examination is an important consideration as part of a surgical quality assessment evaluation.

Timing of postoperative laryngeal examination is controversial. In the first 7–14 days after surgery, symptoms of vocal fold paralysis may be offset by early postoperative vocal fold intubation-related edema and, during later phases of the postoperative period, vocal fold paralysis can become asymptomatic due to a variety of mechanisms including remaining partial neural function, variability in paralytic vocal fold position, and variability in contralateral vocal fold compensation. Thus assessing voice too early postoperatively may result in excessive false positive referrals for speech/voice assessment whereas assessing too late may preclude the utility of early forms of intervention and negatively impact eventual functional recovery. Given this, the surgeon should document whether there has been a change in voice between 2 weeks and 2 months following thyroid surgery as stated in the recent AAOHNS guidelines [6].

Techniques of Laryngeal Examination

Modern laryngoscopy began in the early to mid-1800s, when physicians began employing various devices designed to channel candlelight or sunlight along a series of mirrors to illuminate and visualize the laryngeal structures [29]. Examination of the larynx was initially performed on awake patients in the office setting, but operative laryngoscopy was increasingly common in the early 1900s, as anesthesia became safer and endoscopic equipment improved. However, by the late twentieth century many operative laryngeal procedures had migrated back to office setting [29]. This shift was made possible by improvements in instrumentation and topical anesthesia, high intensity illumination sources, advanced rigid and fiberoptic imaging technology, and flexible laser delivery systems. In addition to being more efficient than operative laryngoscopy, office-based examination allows for better assessment of laryngeal motion and function because patients can respire, phonate, and swallow during their procedure.

The ideal laryngeal examination technique would provide information on the neurologic integrity of both the recurrent and superior laryngeal nerves, and would assess the function of each intrinsic laryngeal muscle and the mobility of the cricoarytenoid joint. It would also evaluate the phonotory function of the larynx by providing detailed imaging of the true vocal fold mucosal wave, and would allow for visualization of any masses or lesions. The test would be noninvasive, easy to perform, cause minimal risk or discomfort to the patient, and be inexpensive and quick. It would permit the patient to perform a full range of laryngeal functions during the exam, allow high definition video recording of the findings, and provide a mechanism for procedural intervention.

Since this ideal examination technique does not exist, the choice of any laryngeal examination technique depends on the goals of testing. For most patients, including those undergoing evaluation for routine thyroid and parathyroid surgery, laryngoscopy to assess for mucosal lesions and an evaluation of gross motor function of the RLNs is sufficient [6, 9]. Other patients, such as those with dysphagia or concerns for aspiration, may require testing of laryngeal sensation and airway protection mechanisms, while patients with dysphonia may require more detailed stroboscopic or electromyographic studies [30].

Laryngeal History and Physical Examination

Evaluation of the larynx and vocal function begins with a thorough history and assessment of the patient's voice. Although there are more objective methods to assess laryngeal function

and voice production as discussed below, the patient's voice before and after thyroid surgery plays a significant role in the threshold physicians have for proceeding to further examination.

The patient's voice complaints are completely investigated, including a history of any concomitant swallowing and/or breathing problems. The time of onset of the voice complaints is important because problems that were present prior to thyroid surgery may indicate preoperative vocal disturbances that may or may not be related to RLN function. It is also important to note whether the patient's voice has ever returned back to its baseline, even temporarily, as this may indicate causes unrelated to neuro-laryngological function.

Patient rating scales are available for assessment of vocal quality. The most common rating scales for patients are the Voice Handicap Index (VHI) [31] and its shorter version, the VHI-10 [32], as well as the Voice-Related Quality of Life (V-RQoL) questionnaire [33]. These instruments serve to quantify a patient's perception of his or her voice, while the GRBAS serves as a measure of the examiner's impression of voice quality. The GRBAS scale of the Japan Society of Logopaedics and Phoniatrics became internationally known after publication of Hirano's *Clinical Examination of Voice* in 1981 [34]. It is an auditory-perceptual scale used by clinicians to categorize the voice using five descriptive perceptual parameters: overall grade (G), roughness (R) of the voice, breathiness (B), asthenia (A), and strain (S). Despite the wide variety of scales available, each is meant to provide unique information and they should be thought of as complementary clinical tools [35].

Once the patient history and rating scales have been reviewed, the next component of the laryngeal physical examination is neck palpation. When examining the neck, it is important to palpate the hyoid bone, thyrohyoid space, thyroid cartilage, cricothyroid space, and cricoid cartilage. Some pathology may cause tightness in the membranous spaces, such as thyrohyoid space tenderness or tightness as seen with muscle tension dysphonia. Lateral movement of the larynx over the anterior cervical bodies may produce some crepitus, which is normal. There should also be normal excursion of the larynx upward and forward with swallowing. Any tracheal deviation or thyroid gland findings on neck palpation should also be noted.

Mirror Indirect Laryngoscopy

Mirror indirect laryngoscopy is one of the oldest methods of laryngeal examination still practiced today. The procedure has persisted because it is fast, straightforward, and most importantly offers adequate views of the larynx with minimal equipment or expense.

The patient sits upright and leans slightly forward. The tongue is grasped with gauze and gently retracted anteriorly. The laryngeal mirror is treated to prevent fogging. This can be accomplished with warming beads, a commercial antifog solution, or by touching the mirror to the patient's tongue or inner cheek to coat it with saliva. Using a head mirror or headlight for illumination, the laryngeal mirror is advanced just below or barely touching the soft palate until it is adjacent to the uvula, then angled into the oropharynx to expose the larynx. The patient is asked to phonate ("eee"), and vocal fold movement is assessed.

The procedure can be performed in seconds by an experienced examiner with a compliant patient, and is generally adequate to assess gross vocal fold mobility before or after thyroid and parathyroid surgery. However, mirror indirect laryngoscopy may be limited by patient tolerance and gag response. Visualization of the anterior larynx may be difficult [36], and dynamic voice evaluation and swallowing is restricted. Additionally, there is no ability to magnify the view or record the examination for serial comparison, consultation, or patient education.

Rigid Laryngoscopy

Rigid laryngoscopy is primarily used to evaluate dysphonia. It produces excellent image quality and offers stroboscopic capabilities for detailed analysis of laryngeal motion. Examinations can

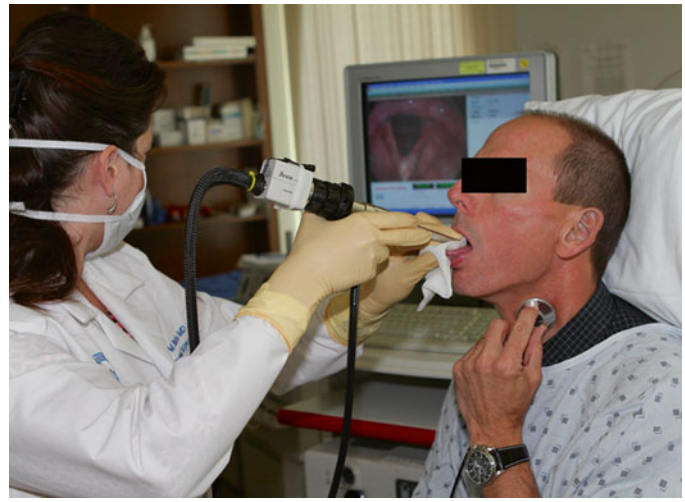

Fig. 2.1 Rigid laryngoscopy. The patient's tongue is gently retracted anteriorly, facilitating visualization of the glottis

be recorded for serial comparison, consultation, and patient education.

The patient sits upright in the examination chair. Though topical anesthesia is not required, it may be beneficial in patients with a strong gag response. The examiner grasps the tongue with gauze and gently retracts it anteriorly. Alternatively, patients may retract their own tongue, allowing the examiner to stabilize the endoscope with one hand while advancing the scope with another (Fig. 2.1). A 70° or 90° rigid endoscope is attached to a light source and video monitor, then treated with a commercial anti-fog solution. The endoscope is advanced past the soft palate adjacent to the uvula and into the oropharynx without touching the tongue, then rotated to view the larynx as the patient phonates.

Rigid endoscopy offers many advantages over mirror laryngoscopy, but may also be subject to patient tolerance. Additionally, only limited dynamic evaluation of the larynx can be performed, and swallowing function cannot be assessed. This technology may also not be available outside of specialized office practices.

Flexible Laryngoscopy

Flexible fiberoptic laryngoscopy, also referred to as nasopharyngoscopy, is the most widely used procedure to evaluate laryngeal function. It is fast, well tolerated by patients, easy to learn [36], and provides excellent visualization of the nasal cavity and all pharyngeal structures. Patients are able to swallow and perform a full range of vocalization during the procedure, and laryngeal sensation can be tested. The image quality is excellent, especially when using distal chip endoscopes, and many systems allow stroboscopic examination of the larynx. The exam findings can be recorded for consultation and serial comparison, and the examination can be displayed in real time on a video monitor, allowing patients to see their disease and enhancing biofeedback techniques. Additional diagnostic and therapeutic procedures such as biopsy of suspicious lesions and laser treatments can be performed in the office through flexible endoscopes with a working channel.

The procedure begins by decongesting the nasal cavity and anesthetizing the nose and pharynx with an aerosolized 50/50 mixture of 4 % lidocaine and oxymetazoline. After an appropriate period of time to allow the medications to work, the patient leans forward slightly with the neck and chin mildly extended anteriorly, and the endoscope is introduced into the nasal cavity. A commercial anti-fog solution may be used or the tip of the scope may be touched to the patient's tongue, but generally these are unnecessary, as the patient's body heat generally clears the scope and prevents further fogging by the time the inferior turbinate is encountered. The examiner's dominant hand operates the scope,

while the nondominant hand is placed gently on the patient's nose or cheek to stabilize the scope.

The endoscope is advanced along the floor of the nose between the nasal septum and inferior turbinate. If severe septal deviation or nasal spurs are present, the scope can be advanced through a more superior pathway above the inferior turbinate or placed in the contralateral side. The patient is instructed to breathe through the nose, which drops the soft palate and exposes the oropharynx. The endoscope is then advanced inferiorly to visualize the larynx and hypopharynx. The patient is asked to swallow or perform a variety of vocalizations, depending on the indications for the procedure. A normal larynx demonstrates brisk and complete volitional abduction and adduction of the true vocal folds, no pooling of secretions or signs of laryngeal penetration or aspiration, and a strong cough or gag response to laryngeal palpation with the tip of the endoscope (when indicated) (Fig. 2.2a).

When assessing laryngeal function before or after thyroid or parathyroid surgery, the examiner looks for signs of recurrent and superior laryngeal nerve dysfunction, such as bilateral true vocal fold paresis or paralysis, vocal fold atrophy (late finding), pooling of secretions, and evidence of reduced laryngeal sensation (Fig. 2.2b). Patients are asked to cough or perform repetitive phonotory exercises (e.g. "eee"-sniff) to demonstrate vocal fold mobility. It should be noted that flexible laryngoscopy does not distinguish between vocal fold immobility due to nerve injury and immobility of the cricoarytenoid joint. If there is a history of traumatic intubation or other conditions that may affect cricoarytenoid joint function, then operative laryngoscopy with palpation of the joint may be necessary.

Flexible fiberoptic laryngoscopy is easily performed in the majority of patients and is generally well tolerated. Epistaxis and mild discomfort during the insertion of the endoscope may occur, but these can be minimized by appropriate decongestion and anesthesia and careful technique. Nasal abnormalities such as severe septal deviation may challenge the exposure, but rarely do they preclude the procedure.

Laryngeal Electromyography

Though flexible laryngoscopy is currently the most commonly used method to clinically evaluate vocal fold mobility, it cannot distinguish between neurologic and mechanical causes of immobility (i.e., RLN injury vs. cricoarytenoid joint pathology), and it cannot offer prognostic information about the potential for neurologic recovery. Electromyography (EMG) measures the electrical activity of a muscle in response to neural stimulation and displays the resulting

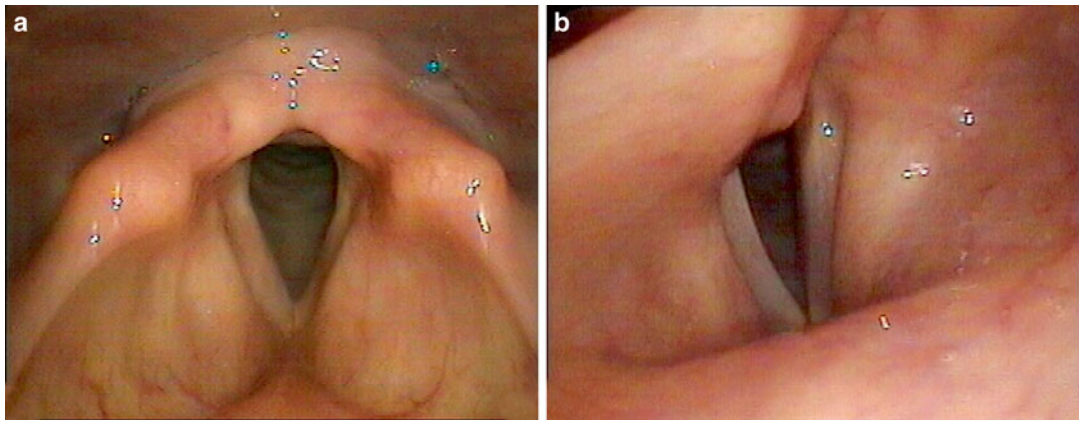

Fig. 2.2 Flexible laryngoscopy. (**a**) Symmetric normal vocal fold abduction. (**b**) Unilateral paralysis of the right true vocal fold. Note that the right vocal fold is bowed and foreshortened, with medial prolapse of the arytenoid

motor unit action potential. Laryngeal electromyography (LEMG) may be used to assess the neurologic integrity of both the recurrent and superior laryngeal nerves, evaluate spontaneous and voluntary laryngeal muscle function, differentiate vocal fold immobility caused by nerve injury from that caused by cricoarytenoid joint disorders, evaluate neurologic disorders affecting the larynx, predict recovery after a nerve injury, help determine the timing of treatment after nerve injury, and guide interventions such as laryngeal injection of botulinum toxin [37–41].

A number of different electrode options are available for LEMG, and they can be placed either transorally or transcutaneously [39–41]. Transoral LEMG requires endoscopic visualization of the larynx, which may also be beneficial in some cases of transcutaneous LEMG [41]. Depending on the technique and type of electrodes used, LEMG is able to test the integrity of individual laryngeal muscles.

Transcutaneous LEMG, which is more common in the outpatient setting, is generally performed by an otolaryngologist or neurologist. The patient sits upright in an examination chair or is placed supine, depending on their comfort and the preferences of the examiner. Topical laryngeal or cutaneous local anesthesia is used at the discretion of the physician, but it is not always necessary [39, 41]. The sequence of the examination depends on the examiner's preference and the specific muscles that require testing, but evaluation of the thyroarytenoid, posterior cricoarytenoid, and cricothyroid muscles provides information on the crucial functions of both the recurrent and superior laryngeal nerves.

Evaluation of the thyroarytenoid muscle begins by inserting the needle in the midline of the cricothyroid membrane, just beneath the inferior border of the thyroid cartilage, then directing it 30° laterally and 15° superiorly. The needle should be advanced approximately 15 mm, into the thyroarytenoid muscle. Care should be taken to avoid entering the airway, which may produce coughing. Appropriate placement is confirmed by increased, sustained EMG activity with phonation or a short burst of activity with swallowing or breath holding [41].

The posterior cricoarytenoid muscle is accessed by rotating the larynx and introducing the needle posterior to the thyroid cartilage or anteriorly, passing through the airway and cricoid cartilage. This latter approach may be difficult if the cartilage is ossified. Placement is confirmed by increased EMG activity with sniffing, and weaker activity with phonation [39, 41].

The CTM is identified by inserting the needle 5 mm lateral from the midline into the region of the CTM. The needle is then advanced laterally at 30–50° for 15–20 mm until the muscle is entered. The patient phonates at a low pitch, then raises the voice to a high pitch. A sharp increase in EMG activity confirms appropriate placement [39, 41].

Normal neuromuscular activity generates biphasic motor unit potentials. An incomplete nerve injury may produce irregular, unstable or decreased signals, and provocative maneuvers may reveal evidence of synkinesis or polyphasic reinnervation potentials of various amplitudes. Acute nerve transection may show no voluntary muscle activity, followed in 2–3 weeks by fibrillation potentials, which indicate denervation [38, 41].

LEMG helps predict which patients will benefit from early intervention after nerve injury, and may change the diagnosis in up to 30 % of cases compared to endoscopy findings. The results should be interpreted with caution in patients who have had prior laryngeal surgery, as scarring and medialization materials may alter the results [40]. The procedure is qualitative, with no normative quantitative data for comparison [42]. It is invasive and requires significant compliance and participation by the patient. Access to the technology is limited outside of specialty practices, and the techniques and equipment are not standardized.

Ultrasound

Though flexible fiberoptic laryngoscopy is currently the most utilized and, arguably, the most clinically useful method for determining vocal fold mobility, the procedures may be perceived as invasive and uncomfortable by some patients.

Additionally, the equipment required to perform laryngeal visualization may not be present outside of otolaryngology-trained surgeons' offices, meaning that some patients may need to be referred to an otolaryngologist for formal evaluation of laryngeal function before undergoing thyroid or parathyroid surgery. For these reasons, alternate imaging modalities such as ultrasound have been investigated as potential methods to evaluate laryngeal function.

Ultrasound is a noninvasive, inexpensive way to visualize vocal fold mobility. It does not subject patients to radiation exposure, and can be performed by the surgeon during their office ultrasound examination of the thyroid or parathyroid glands. The technique does require in-office ultrasound capabilities and specific ultrasound training. Visualization of true vocal fold movement may be limited, and the reported sensitivity, specificity, and positive predictive value (PPV) of this technique varies considerably [43–47].

The evaluation is performed by placing the patient in a supine position with the neck slightly extended. A high frequency linear ultrasound transducer is placed over the thyroid cartilage and used to visualize the laryngeal structures. The image quality may be improved by decreasing the frequency and increasing the gain compared to the settings typically used for cervical ultrasound [47]. The bodies of the true vocal folds are hypoechoic, with a hyperechoic stripe medially, representing the vocal ligament [43] (Fig. 2.3). The false vocal folds are hyperechoic [43], and the arytenoids appear as paired oval structures posterior to the vocal folds [48, 49]. The patient is observed during both passive respiration and volitional phonation, permitting real-time assessment of vocal fold or arytenoid motion. Performing a sustained Valsalva maneuver adducts the vocal folds and may improve visualization of the vocal ligament in the midline [47].

Unequivocal identification of normal bilateral vocal fold movement on laryngeal ultrasound is considered sufficient proof of normal recurrent laryngeal nerve function. The limitation of ultrasound, however, is that the laryngeal anatomy is often inadequately and incompletely viewed with this modality. In Asian populations, the vocal folds could not be adequately visualized in 5–18 % of patients [43–45]. In a multi-institutional trial of Western patients, adequate visualization varied from 41 to 89 % [47]. The false vocal folds and arytenoids are identified most commonly (93 % and 90 %, respectively), while visualization of the true vocal folds is reported as low as 37 % [43]. Though there is no clear consensus as to what constitutes adequate vocal fold visualization [47], some authors propose that identifying normal movement in any one of these structures is sufficient to exclude vocal fold palsy [43].

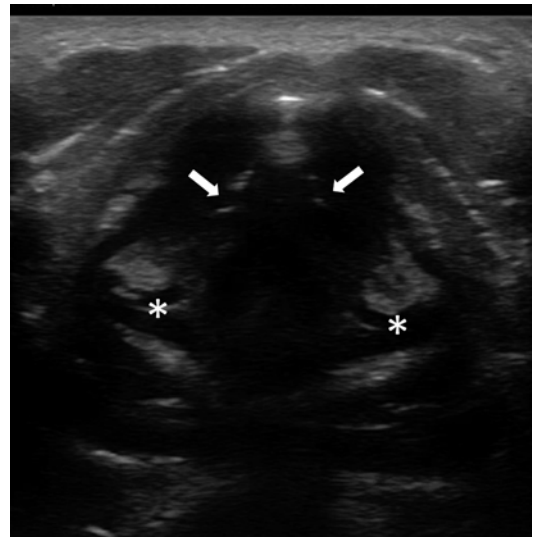

Fig. 2.3 Laryngeal ultrasound. The true vocal folds appear as hypoechoic structures with a hyperechoic medial border, representing the vocal ligament (*arrows*). The arytenoid cartilages are seen posteriorly (*asterisks*)

Laryngeal ultrasound may be limited by several factors. Though most experienced head and neck ultrasonographers should be able to visualize the larynx, keeping the ultrasound beam perfectly aligned to provide constant clear visualization of the relatively narrow true vocal folds can be challenging, especially during phonation. In patients with thin necks, it may be difficult to maintain contact between the full length of the ultrasound probe and the neck. In these cases, the probe may need to be angled slightly, limiting visualization to only one side of the larynx at a time. Alternatively, a saline-filled glove may be placed between the probe and the patient's skin to increase the contact surface area [44].

Laryngeal visualization is significantly better in females and in patients without significant thyroid cartilage calcification. While ultrasound may be useful in distinguishing normal vocal fold movement from paralysis, the technique is less accurate for patients with paresis [47]. If the larynx is incompletely visualized with this technique, or if there is any question about the mobility of a vocal fold on ultrasound, then flexible laryngoscopy should be performed.

Computed Tomography and Magnetic Resonance Imaging

In addition to ultrasound, both computed tomography (CT) and magnetic resonance imaging (MRI) have been used to assess laryngeal function. While neither modality can directly visualize the extracranial portion of the vagus nerve or the laryngeal nerves, characteristic findings may suggest vocal fold paralysis and nerve injury [50, 51]. Additionally, unlike other methods of laryngeal examination, these imaging techniques allow for the entire course of the nerves to be evaluated from brain stem to mediastinum, and can detect potential causes of vocal fold immobility due to inflammatory or neoplastic pathology adjacent to the nerves or lesions affecting the larynx directly. While dynamic MRI has been described in research settings for investigating laryngeal motion during speech and swallowing, it is clinically used primarily to evaluate for lesions that may be causing vocal fold paralysis, rather than diagnosing it [52–54]. CT has been more extensively evaluated for its role in diagnosing vocal fold paralysis, based on a constellation of suggestive findings.

When performing CT to assess for vocal fold paralysis, the axial images should be obtained in a plane parallel to the true vocal folds to avoid distortion caused by oblique sectioning, with a slice thickness between 2 and 3 mm. Patients can be examined during a number of glottic activities, but images obtained during quiet respiration are generally preferred [50]. Axial, coronal, and sagittal views are evaluated to give a more comprehensive assessment of potential signs of nerve injury.

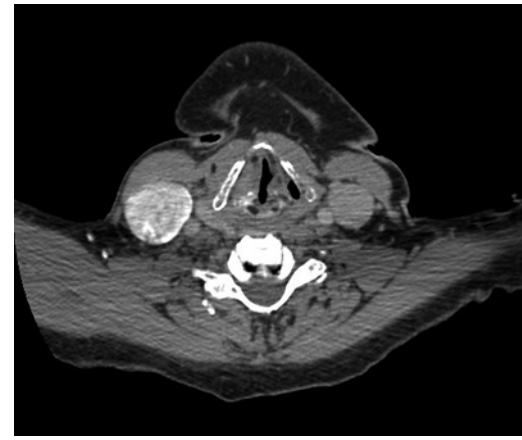

Fig. 2.4 Computed tomography of left vocal fold paralysis. There is atrophy of the vocal fold with asymmetric prominence of the left pyriform sinus and laryngeal ventricle, suggesting chronic denervation

It can be difficult to distinguish between paralyzed and mobile vocal folds on CT [51]. Since vocal fold movement is typically not captured by CT, the images are examined for a number of associated findings that, taken together, suggest a denervation injury of the larynx (Fig. 2.4). The most specific of these findings include enlargement of the laryngeal ventricle (due to thyroarytenoid atrophy), ipsilateral pyriform sinus dilation, posterior cricoarytenoid muscle atrophy and medialization, and thickening of the aryepiglottic fold [50, 51]. Additional supporting findings on axial imaging include ipsilateral atrophy of the constrictor muscles, dilation of the ipsilateral oropharynx, deviation of the uvula away from the affected side, and tilting of the thyroid cartilage due to CTM atrophy (in cases of high vagal or superior laryngeal nerve injury) [50, 51]. In addition to several of the above findings, coronal imaging may also reveal loss or flattening of the subglottic arch [50].

Due to cost and radiation concerns, CT is not used as a primary tool in evaluating laryngeal function. Additionally, CT results can be complicated by a number of factors. Oblique image acquisition or patient rotation or movement can prevent adequate imaging. Cricoarytenoid joint pathology or imaging artifacts from prior laryngeal procedures, especially medialization implant substances, can complicate image interpretation [50].

Finally, neoplastic or inflammatory disorders of the larynx or hypopharynx may produce some of the radiographic changes typically associated with neurologic injury. Findings suggestive of laryngeal nerve injury on CT should be further evaluated with laryngoscopy.

Conclusion

Perioperative voice complaints are common in patients undergoing thyroid surgery. Although neurologic injuries contribute to many cases of postoperative dysphonia, subjective voice findings are a poor predictor of vocal fold paralysis and many patients with vocal fold paralysis may be asymptomatic. Conversely, patients without any evidence of neural injury can have significant postoperative dysphonia. Formal voice assessment is therefore recommended before thyroid or parathyroid surgery, and objective documentation of vocal fold mobility should be strongly considered during the preoperative evaluation and in any patient with postoperative voice changes. Though several methods exist for evaluating laryngeal function, flexible endoscopic laryngoscopy remains the most widely available technique to provide unequivocal examination of vocal fold mobility.

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Part II

RLN Neural Anatomy

Gregory W. Randolph

Neurologic Control of the Larynx

3

Gayle E. Woodson

Abstract

The larynx is a multifunctional organ. It is a valve that plays key roles in breathing, swallowing, and speech, as well as defecation and stabilization of the thorax during heavy lifting. The larynx is also a sensory organ, densely supplied with receptors that are activated by a variety of mechanical and chemical stimuli. Neural control of the larynx is, therefore, complex and varies according to function. Protection of the airway is the most primitive function of the larynx. It closes tightly during a swallow and in response to noxious stimuli. Laryngospasm may result from saturation of the pathways that stimulate laryngeal closure. The larynx opens and closes during breathing to control airflow. This activity is controlled by central pattern generators in response to respiratory demand, but can be overridden by voluntary activity. The laryngeal valve is also very active during a cough: opening widely during the inspiratory phase, closing tightly during the compressive phase, and then suddenly opening in the expulsive phase. As with respiratory motion, cough may be reflexive, or voluntary. Voice production requires appropriate approximation of the vocal folds to achieve oscillation during exhalation. Pitch is controlled by intricate control of the length, tension, and thickness of the vocal folds, in precise coordination with respiratory muscles. Speech also requires precise coordination between the actions of laryngeal muscles, respiratory muscles, and the muscles of articulation: lips, tongue, palate, jaws, and pharyngeal constrictors. Laryngeal motor neurons are located in the nucleus ambiguous. In nonhuman mammals, phonation is controlled at subcortical levels. This system is also present in humans. But humans, and humans alone, have direct cortical control of laryngeal muscles. The complex actions of the small muscles in the larynx are quite vulnerable to distortion by peripheral nerve injury.

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Keywords

Motor control • Reflexes • Voice • Respiration

Laryngeal paralysis is a serious complication of thyroid and parathyroid surgery. Although laryngeal nerves usually regenerate after injury, normal function is rarely restored, because of the failure of regenerating nerve fibers to connect with their original targets [1]. The consequences of such synkinetic reinnervation are variable, because the larynx is a multifunctional organ with multiple small muscles that have intricate actions and complex neural connections. In casual conversation, we call it the voice box. But the larynx also plays a role in breathing, swallowing, and even—via the Valsalva maneuver—roles in defecation and intense physical effort. In addition to motor activity, the larynx is a sensory organ. The surface area of the larynx is miniscule in comparison to that of the lungs; yet there are several times more afferent nerve fibers from the larynx. Laryngeal receptors respond to touch, airflow, and motion of the larynx, as well as chloride concentration and noxious substances in inspired air [2, 3]. Stimulation of laryngeal receptors exerts influences on breathing and cardiovascular function (Fig. 3.1) [3]. Therefore, in addition to muscle weakness, laryngeal nerve lesions can impair or distort the physiologic responses and sensory function of the larynx.

Respiratory Function

At its essence, the larynx is a valve that sits at the top of the lower respiratory tract and directs air traffic. The larynx must close rapidly and tightly during a swallow, to prevent spillage into the lungs. It must also remain open during the negative pressure generated by inspiration. But the larynx is not a simple flap that is either opened or closed. It is a variable resistor that regulates in and out of the lungs. It is better adapted than any other portion of the respiratory tract for the production of sudden airway closure or rapid alterations in airflow resistance. The larynx is also essential for generation of an effective cough. All of these respiratory functions require precise coordination with other muscles throughout the respiratory tract.

During quiet ventilation, the vocal folds abduct slightly just before the onset of inhalation, and adduct during exhalation. This expiratory adduction is not insignificant. Under normal conditions, the rate of breathing is determined by the expiratory narrowing of the vocal folds. That is to say, the inter-breath interval (between the end of exhalation and the beginning of the next inspiration) remains relatively constant while the duration of expiration varies. Control of the interbreath interval is sometimes passive, but often active, sometimes unconscious and sometimes volitional. Expiratory duration is primarily controlled by expiratory resistance, of the larynx, although the diaphragm can also be recruited. Expiratory adduction of the larynx is sometimes a passive phenomenon (abductor muscle relaxation), but the thyroarytenoid muscle (TA) is usually active in expiration during wakefulness. Simultaneous recordings of TA electromyography (EMG), upper airway pressure, and respiratory duration have documented that the TA contracts during exhalation. TA EMG level correlates with expiratory duration and inversely correlates with airflow (Figs. 3.1 and 3.2). Conversely, breathing becomes faster when closure of the vocal folds is delayed or inhibited. The rate of airflow during exhalation tracks TA activity (Fig. 3.3) [4].

With increased respiratory demands, the diaphragm, intercostal muscles, genioglossus, ala nasae, and extrinsic laryngeal muscles are all stimulated [5]. Laryngeal motion is also increased: vocal folds abduct more widely during inspiration, and expiratory closure is inhibited or delayed. EMG recordings during increased respiratory

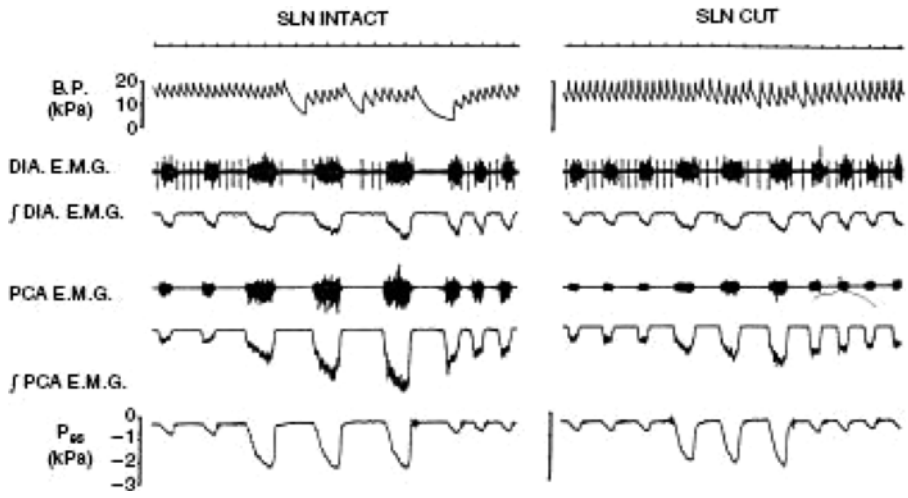

Fig. 3.1 The effects of upper airway occlusion on arterial blood (B.P.) pressure in an anesthetized dog before and after transection of the superior laryngeal nerve (SLN). In each panel, the top trace marks time in seconds. The third and fifth traces are raw and integrated electromyographic activity of the diaphragm (DIA) and posterior cricoarytenoid muscle (PCA). The bottom trace is intraesophageal pressure (Pes) as an indicator of respiratory effort [Reprinted from Sant'Ambrogio FB, Mathew OP, Clark WD, Sant'Ambrogio G. Laryngeal influences on breathing pattern and posterior cricoarytenoid muscle activity. J Appl Physiol. 1985;58:1298. With permission from American Physiological Society]

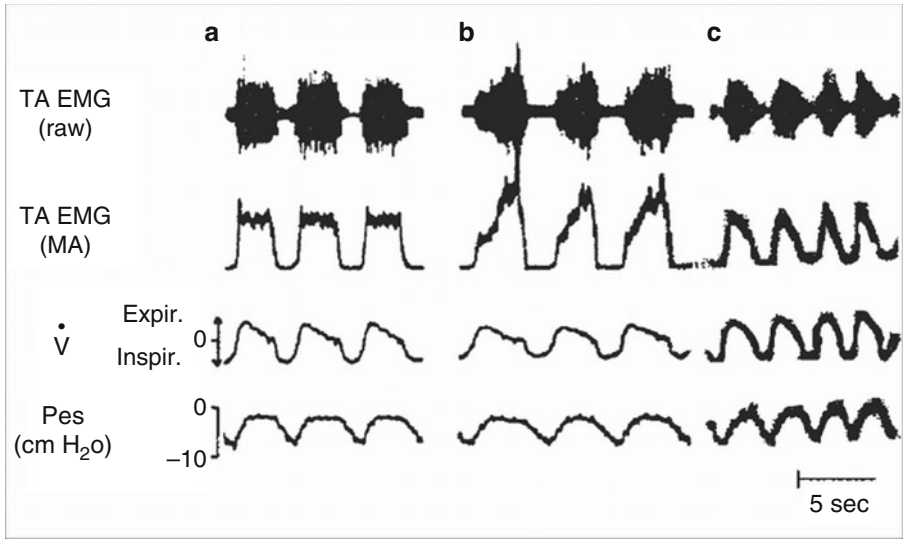

Fig. 3.2 Laryngeal adductor activity during breathing as shown on electromyography. (a) Plateau in thyroarytenoid muscle activity (TA EMG) correlates with decreasing flow. (b) Progressive increase in TA activity correlates with flattened airflow trace and longer exhalation. (c) Decreasing activity during expiration correlates with shorter exhalation. Expir., expiration; Inspir., inspiration; MA, averaged; v with a dot over it is airflow Pes, esophageal (intrathoracic) pressure;, airflow [Reprinted from Kuna ST, Insalaco G, Woodson GE. Thyroarytenoid muscle activity during wakefulness and sleep in normal adults. J Appl Physiol. 1988;65(3):1332–1339. With permission from the American Physiological Society.]

effort show that the major abductor muscle of the larynx, the posterior cricoarytenoid muscle (PCA), contracts more strongly during inspiration, and continues to contract during expiration, after the diaphragm has relaxed. This results in decreased airway resistance and faster outflow of air, which shortens the duration of expiration and increases the rate of breathing. There are significant

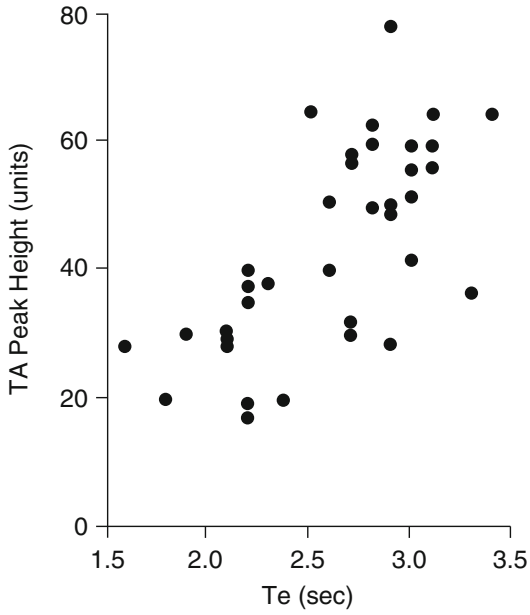

Fig. 3.3 The peak electromyography activity of the thyroarytenoid muscle (TA peak height) as a function of expiratory time in an awake human. Correlation coefficient = 0.680 [Reprinted from Kuna ST, Insalaco G, Woodson GE. Thyroarytenoid muscle activity during wakefulness and sleep in normal adults. J Appl Physiol. 1988;65(3):1332–1339. With permission from the American Physiological Society.]

differences between the responses to respiratory demand by laryngeal muscles and the primary muscles of respiration. EMG studies have documented that the PCA is always activated before the diaphragm [3]. As a result, the glottic lumen is stabilized before the development of negative airway pressure.

Sensory Input to Respiratory Control

Three major types of laryngeal receptors with afferent fibers in the superior laryngeal nerve (SLN) are activated by breathing: airflow receptors, pressure receptors, and "drive" receptors. Airflow receptors also respond to the application of cold or menthol. Therefore they are essentially activated like thermistors, responding to the temperature drop induced by air flowing past. Drive receptors behave like proprioceptors that respond to respiratory motion of the larynx [6]. All three receptors normally influence the central control of breathing. Laryngeal receptors also respond to touch and chemical stimuli, and can decrease ventilation or cause apnea.

With upper airway obstruction, inspiratory EMG activity of the PCA, as well as other upper airway dilating muscles (e.g., genioglossus and ala nasae muscles), increases dramatically. This effect is primarily driven by response to negative pressure receptors in the larynx, and to a lesser extent by the deficit in lung inflation. In contrast, the response of the diaphragm to negative upper airway pressure is to increase the duration of inspiration but not the intensity of diaphragm muscle contraction [5]. Figure 3.4 illustrates the difference between genioglossus and diaphragmatic EMG in response to upper airway obstruction. This pattern of muscle response makes sense. Upper airway muscles activate in order to counteract the negative airway pressure. But stronger contraction of the diaphragm would increase the negative pressure, favoring collapse of the upper airway. Chemoreceptor stimuli by hypoxia or hypercarbia are a potent stimulus of respiratory drive to the diaphragm and intercostal muscles. Laryngeal muscles respond to this increased respiratory drive, but there is no direct influence of arterial chemoreceptors on laryngeal muscles [7].

Phonatory Function

Phonation is a relatively late evolutionary adaptation of the larynx. Sound is generated by passive vibration of the vocal folds: exhaled air induces vibration of the adducted vocal folds. However, human speech involves much more than simple apposition of the vocal folds. The vocal folds must be close enough to be entrained by airflow, but not closed too tightly. The shape of the glottal inlet and the strength of the adducting force are highly variable. The vocal processes of the vocal folds may be touching, or there may be a posterior gap. The vestibular folds may be pulled in over the vocal folds or not. Such variations have profound effects on the quality of the voice produced. For example, in a pressed voice, there is

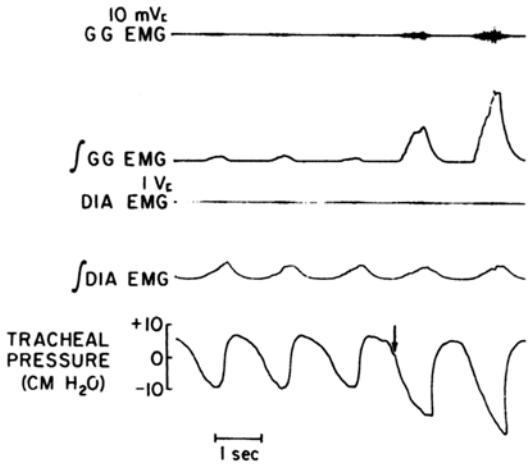

Fig. 3.4 The diaphragm (DIA) and genioglossus (GG) muscle responses to nasal occlusion (beginning at *arrow*) in an anesthetized vagotomized rabbit. The upper trace is raw electromyographic activity (EMG) of the genioglossus muscle (GG) in millivolts, and the second trace is integrated GG activity in volts. The third and fourth traces are raw and integrated EMG of the diaphragm (DIA) [Reprinted from Mathew OP, Abu-Osba YK, Thach BT. Influence of upper airway pressure changes in respiratory frequency. J Appl Physiol. 1982;52:483. With permission from American Physiological Society]

tight pressure on the vocal folds, so that high subglottic pressure is required to push the vocal folds apart and the closed phase of vibration is prolonged. In a breathy voice, the vocal folds do not completely close during the glottal cycle. Constricting the ventricular folds changes the timbre of the voice. Pitch is controlled by changes in the length and tension of the vocal folds. Most speakers unconsciously make these changes in response to their emotional state, or intended differences in the quality of the voice. Trained singers, actors, and ventriloquists can acquire exquisitely precise control of laryngeal muscles, to achieve desired vocal quality, yet they are also unaware of the precise mechanisms involved. In any event, normal expressive speech involves complex control of laryngeal muscles.

Laryngeal Innervation

The nerve supply to the larynx is via two branches of the tenth cranial nerve (vagus nerve): the SLN and the recurrent laryngeal nerve (RLN). The SLN separates from the vagus just below the nodose ganglion. There are two divisions of the SLN. The internal branch is purely sensory, carrying afferent fibers from the supraglottic larynx and the vocal folds. It enters the larynx laterally through the thyrohyoid membrane, a centimeter or so medial to the inferior cornu or the hyoid bone. A simplistic concept of laryngeal motor innervation is that the external branch supplies motor fibers to the cricothyroid muscle (CTM), while the RLN supplies all other intrinsic muscles of the larynx and mediates sensation from the subglottis and trachea. However, there are significant neural connections between the RLN and SLN systems. Galen's anastomosis, a nerve that connects the RLN and SLN, was described many years ago, as an occasional finding. But it is now recognized that connections between the SLN and RLN are always present [8].

The PCA, CTM, and TA all appear to be composed of functionally distinct compartments with separate nerve branches [9–11]. The medial portion of the TA muscle, also known as the vocalis muscle, has a very complex nerve plexus [11].

Motor Function

The vocal folds do not simply move in one plane, like windshield wipers. They move and change shape in three dimensions. The vocal folds are anchored on the anterior commissure of the thyroid cartilage and suspended on the arytenoid cartilage. Motion of the vocal fold is produced by the action of muscles on the cricoarytenoid joint. Each laryngeal muscle has a unique action on this joint; in fact each compartment within a laryngeal muscle has its own unique force vector. The cricoarytenoid joint is multiaxial, sort of a flattened ball and socket joint. No laryngeal muscle ever contracts in isolation. Laryngeal motion is determined by the resultant force of the combined actions of all intrinsic muscles on the cricoarytenoid joint [12].

The strongest adductor of the vocal fold is the lateral cricoarytenoid muscle (LCA) which originates on the anterolateral aspect of the cricoid and inserts on the muscular process of the arytenoid. Contraction of the LCA pulls the muscular process

of the arytenoid cartilage forward, internally rotating that cartilage about a nearly vertical axis [12, 13]. This results in medial displacement of the vocal process, dragging the vocal fold along.

The TA originates on the anterior interior surface of the thyroid cartilage and inserts on the anterior surface of the arytenoid. It has at least two compartments which are histologically distinct and supplied by separate nerve branches. The medial compartment, frequently referred to as the vocalis, has little or no adductor function and is more involved in controlling length and tension of the vocal fold. Recent evidence indicates that this small muscle is further divided into rostral and caudal compartments, for a total of three compartments within the TA [11]. The larger, lateral compartment of the TA comprises most of the bulk of the anterior vocal fold. The lateral portion of the TA, like the LCA, pulls the muscular process of the arytenoid forward to inwardly rotate the cartilage, but its most medial fibers insert near the vocal process itself, and therefore do not contribute to rotation [12]. Laryngeal EMG studies indicate that in phonation, LCA activity peaks at the onset, suggesting it is important in "setting" the phonatory position of the vocal fold. The TA has been documented by many as being active throughout phonation [14]. In a study of 11 normal subjects, Hillel found that the pattern of TA activity was the similar to that of the LCA: active at the onset of phonation and then tapering down [15]. Different observations may be explained by differences in electrode placement as the muscle does have a complex innervation pattern—there is actually evidence for three bellies in this muscle—and so it is likely that activity can vary within these three compartments [11]. The TA has the smallest motor unit size of all the intrinsic laryngeal muscles, with a ratio of less than ten muscle fibers per motor neuron [16]. Different tasks likely recruit the muscle differently. This muscle, along with the CTM, is important in controlling pitch. And there are significant interpersonal differences. A study of single fiber laryngeal EMG found that in males with deep voices, it is not uncommon to see little or no activation of the TA with phonation [17].

The action of the PCA is also complex. The muscle is actually divided into two separate compartments supplied by separate nerve branches [9]. Both "bellies" originate broadly from the posterior surface of the cricoid, but have different vectors of pull on the arytenoid. The "horizontal" belly inserts onto the posteromedial surface of the muscular process of the arytenoid, and rotates the arytenoid around a nearly vertical axis, pulling the vocal process laterally, thereby abducting the vocal fold. The "oblique" belly inserts on the anterolateral aspect of the muscular process. It also abducts the vocal fold, but it rotates about a different axis, pulling the vocal process upwards as well as laterally [18]. The abductor function of the PCA is widely recognized; however, this muscle is also activated in speech [19]. The PCA appears to provide posterior traction in regulating the tension of the vocal fold and maintaining an upright posture of the arytenoid. In flaccid paralysis of the vocal fold, due to complete disruption of the RLN, the vocal fold is not only immobilized in a lateral position—the vocal process is displaced inferiorly, as the arytenoid is tipped forward, due to loss of support from the PCA [20].

The interarytenoid muscle is the only unpaired muscle in the larynx. It connects the medial aspects of the arytenoid cartilage. Its location suggests that it is an adductor muscle. However, biomechanical modeling indicates that its function is mixed, and it actually plays a role in abducting the vocal fold [12]. Recall that the primary motion of the arytenoid is rotation, not gliding. Thus, contraction of the interarytenoid muscles pulls the posterior ends of the arytenoids together, and therefore it contributes to external rotation of the most anterior edge of the arytenoid, which is the vocal process.

There are also some muscle fibers in the vestibular fold, connecting the epiglottis and the arytenoid. They are present in the human but are largely absent in other species [21]. These "false fold" muscles appear to constrict the supraglottis. They are postulated to play a role in vestibular fold shaping for speech and may to be the muscles used in plica dysphonia ventricularis. These fibers are supplied by branches of the SLN, instead of the RLN. Thus, they probably play a role in

phonatory compensation after unilateral RLN injuries.

The CTM pulls the cricoid and thyroid cartilages together anteriorly to increase the length and tension of the vocal folds [22]. It is activated in high pitch phonation and falsetto.

All intrinsic muscles work in concert to control pitch and loudness of the voice, but EMG studies in normal subjects indicate that the patterns of activation vary among individuals. For example, to increase loudness, some subjects increase their TA or LCA muscle activity. But just as many speakers do not increase adductor muscle activity, and instead rely on increasing subglottic air pressure [23]. The CTM and TA muscles work together to control pitch, but there is considerable variability between speakers, and even between sentences in the same person, in how the muscles are activated [24]. In addition to changes in pitch and loudness, laryngeal muscles are recruited differently to produce different vocal registers. Vocal fold vibration is profoundly different in chest and falsetto register. In chest register, vocal folds are thicker, there is a large mucosal wave, and vocal folds come into complete contact during the closed phase of vibration. During falsetto register, the CTM is strongly activated. Vocal folds are thinner, the mucosal wave is reduced or absent, and the vocal folds may never completely close [25].

Laryngeal Reflexes

The laryngeal adductor reflex is a rapid brief protective closure of the true vocal folds in response to stimulation of laryngeal mucosa. Apnea may occur in response to such diverse chemical agents such as ammonia, phenyl diguanide, and cigarette smoke. SLN damage impairs laryngeal sensation and can result in dysphagia and aspiration. Laryngeal sensation can be tested by using air puffs to trigger reflex closure [26].

Mechanical stimulation of the larynx can cause apnea, laryngospasm, bronchoconstriction, or cardiovascular collapse [2]. These responses are not often seen, because the larynx is not in an exposed, external position. Most of us have experienced a mild episode of laryngeal reflux stimulation, when some ingested food or drink "goes down the wrong way," with exposure to noxious fumes, or when we experience gastroesophageal reflux. Laryngospasm, the forceful and prolonged closure of the larynx, is sometimes seen in the operating room. This is most frequently observed immediately after removal of an endotracheal tube, when the patient is well oxygenated and emerging from general anesthesia. It can also occur in the conscious state under certain pathologic conditions such as upper respiratory infection or severe and chronic gastroesophageal reflux. Sometimes a decreased threshold for laryngospasm can persist for many months after an infection, resulting in frequent episodes of frightening total airway obstruction. Episodic laryngospasm is also a rare complication of RLN injury. It develops several months after nerve damage, and likely is the result of misguided regenerating nerve axons. It is debilitating and can be life threatening, requiring a tracheotomy. Recurrent laryngospasm can respond to local injections of botulinum toxin, but is sometimes paradoxically exacerbated by this treatment. A more lasting treatment is laryngeal reinnervation, transecting the aberrantly regenerated RLN, and reinnervating with a branch of the ansa cervicalis.

Cardiac arrhythmias and hypotension can occur in response to laryngeal stimulation, as with intubation during general anesthesia, or even in patients with obstructive sleep apnea, due to stimulation of the larynx by extreme negative airway pressure. The physiologic reason for the laryngeal closure reflex is clear, as the most primitive function of the larynx is to prevent anything harmful from entering the lungs. But neither the purpose of cardiovascular reflexes to laryngeal stimulation, nor the central pathways responsible for mediating such reflexes are clearly understood. The afferent limb is clearly the SLN. Transection of the SLN abolishes cardiovascular responses to laryngeal stimulation, and electrical stimulation of this nerve affects heart rate and blood pressure. The vagus nerve mediates the efferent limb of the reflex for bradycardia. The efferent pathway for blood pressure change is not known but may be a sympathetic response, mediated

through central respiratory control mechanisms. Recordings from cervical sympathetic roots in the neck have documented phasic activity with breathing. The teleological significance of this is attributed to a feed forward mechanism of accommodation for increased blood return into the heart during the negative intrathoracic pressure generated by inspiration. This respiratory variation is suppressed by electrical stimulation of the SLN, suggesting that input from laryngeal receptors plays a role. Therefore the pathways that mediate this reflex may account for cardiovascular responses to laryngeal stimulation.

Central Control of the Larynx

The motor neurons of all intrinsic laryngeal muscles are primarily located in the nucleus ambiguus (NA) of the brainstem. Our understanding of the location of the neurons controlling specific laryngeal muscles is based on retrograde tracing studies in animals. While some overlap has been observed in the regions controlling individual muscles, there is a clear rostro-caudal somatotopic organization [27, 28]. Neurons innervating the CTM are most rostral, located just ventral to the compact formation of the NA. PCA neurons are also located ventrally, in the semicompact area of the NA, just caudal to the CTM neurons. PCA and CTM neurons are significantly smaller than TA or LCA neurons. The LCA neuron pool is more caudal than the PCA and CTM areas and in a more dorsomedial location. The TA motor neuron pool overlaps the area occupied by PCA and LCA neurons, and TA neurons are more numerous than PCA or LCA neurons [27]. Additional neurons supplying the CTM and PCA have been identified in the retrofacial nucleus [28]. The somatotopic organization of laryngeal motor neurons is significantly altered after RLN injury, even when the nerve is only crushed, rather than transected [29]. This explains why normal laryngeal motor function is rarely completely recovered after peripheral nerve injury.

All intrinsic laryngeal muscles, with the exception of the interarytenoid muscle, are supplied by ipsilateral neurons. However, laryngeal behaviors always involve bilateral activation of laryngeal muscles. This implies that the brainstem neurons of the larynx receive bilateral input from higher levels of the brain.

Our concepts of the brainstem level input to laryngeal motor neurons are extrapolated from animal studies, primarily in the rat. Tracing studies using cholera B toxin indicate that the dendrites of laryngeal motor neurons receive input from respiratory, phonatory, and swallowing neurons [30]. Pharyngeal and laryngeal motor neurons have been compared by studying the fine structure of the NA. Laryngeal motoneurons are slightly larger than pharyngeal motor neurons (42×30 μm vs. 39×29 μm) and have more connections. An average of 339 synapses were identified for each laryngeal motor neuron, compared to an average of 182 synapses per pharyngeal neuron [31]. Significant differences have been identified between CTM and PCA motor neurons. While motoneurons innervating CTM are located in the semicompact formation of the NA, those innervating the PCA are located in the loose formation. Ultrastructural study of the types of vesicles in the somata indicates that CTM motor neurons receive mostly excitatory input, while the PCA is regulated by inhibitory as well as excitatory neurons [32].

The human brain appears to be unique in having two separate neural pathways to the laryngeal muscles for vocalization [33]. Other animals, and even anencephalic infants with an intact brainstem, can vocalize in response to painful stimuli [34]. However, learned laryngeal behaviors in humans, such as speaking and singing, as well as voluntary acts involving the larynx, are controlled by the motor cortex in the cerebrum. Voluntary laryngeal acts would include the production on demand of laughter, coughing, breathing, and sighing. A tracing study in a human patient documented direct corticobulbar projections to the NA [35]. No such direct corticobulbar projections have been found in monkeys or chimpanzees [36].

Animal vocalization is controlled by a system that includes the anterior cingulate cortex, the periaqueductal gray, nucleus retroambiguus, and NA [37, 38]. The periaqueductal gray is a region

of the brainstem that activates central pattern generators in the pons and brainstem. Electrical stimulation of this area can produce vocalization. Humans also have this pathway, which likely mediates emotional vocalizations, such as laughter, cry, and spontaneous expressions of fear. However, volitional acts, including speech, seem to require direct control of motor neurons via the corticobulbar pathways. An enigmatic disorder, spasmodic dysphonia, disrupts speech, with preservation of other vocal behaviors, such as shouting, singing, and crying [37]. For years, this selective impairment of speech was accepted as proof that spasmodic dysphonia was a psychosomatic disorder. However, there is now clear evidence that spasmodic dysphonia is a neurologic impairment. The existence of two separate pathways for control of vocalization offers a means of accounting for the selective involvement of speech.

Summary

The larynx is a small organ, located in a critical location for "directing traffic" in the aerodigestive tract. It is not essential for life, as we can compensate when it is bypassed by tracheotomy or removed by laryngectomy. However, it is essential for normal human speech, and when it is in situ, its dysfunction can be incapacitating or even life-threatening. Neural control of the larynx is complex, and damage to the peripheral nerve supply can result in severe disruption of laryngeal function.

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Micro-neuroanatomy of the Vagus, Superior Laryngeal, and Recurrent Laryngeal Nerves

4

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Abstract

The micro-neuroanatomy of the vagus nerve (VN), superior laryngeal nerve (SLN), recurrent laryngeal nerve (RLN), and their respective central connections are complex. While there has been some clarity amongst animal and human studies, there is considerable debate regarding central contributions and topography, as well as peripheral fiber types, topographical organization, and function. This chapter will discuss the micro-neuroanatomy of the central connections, neural ganglia, and each nerve separately. Meanwhile, because the micro-neuroanatomy provides information regarding the form underlying the function of the larynx, further consideration of laryngeal dysfunction is addressed through additional sections covering age-related changes, neural injury, and neural regeneration.

Keywords

Micro-neuroanatomy • Topography • Morphometric • Myelin • Nucleus ambiguus • Vagus nerve • Superior laryngeal nerve • Recurrent laryngeal nerve • Neural injury • Neural regeneration • Reinnervation

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Introduction

The micro-neuroanatomy of the vagus nerve (VN), superior laryngeal nerve (SLN), recurrent laryngeal nerve (RLN), and their respective central connections have long been studied. There is a complex interrelationship between multiple brainstem nuclei, peripheral ganglia, and nerve fibers providing motor, sensory, and autonomic function to varied regions of the human body. While there has been some topographical clarity with regard to

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central contributions, the peripheral nerves themselves have long been the subject of debate regarding fiber types, topographical organization, and function. Meanwhile, the nuanced micro-neuroanatomy of these nerves underscores both the challenges and importance to the study of neural aging, injury, and regeneration.

Central Connections and Cell Body Locations

Motor function reliant on the VN, SLN, and RLN primarily originates in the nucleus ambiguus (NA) in the lateral medulla. Cell bodies in the NA project to supradiaphragmatic structures, including the pharynx, larynx, trachea, bronchi, and esophagus, as well as subdiaphragmatic structures, including the heart and viscera of the thorax and abdomen to the left colic flexure [1]. The topographical organization of the NA has been shown by lesion and retrograde labeling studies in various animal models and, while certain pools of fibers are distinguishable, there is considerable overlap. From rostral to caudal, lower motor neurons arise to innervate the cricothyroid, posterior cricoarytenoid, then the adductor muscles (adductor fiber arrangement varies based on report). The lower motor neurons supplying the cricothyroid muscles (CTMs) arise from a more medial and ventral location compared to abductor and adductor lower motor neurons, while abductor lower motor neurons arise ventral to the adductor lower motor neurons. The abductor and, particularly, adductor fibers have a more diffuse arrangement in the NA compared to the more compactly arranged fibers to the CTM [2, 3].

Overlapping motor contributions to the VN, SLN, and RLN also arise in the brainstem outside the NA. The cricothyroid and posterior cricoarytenoid muscles receive contributions from fibers originating in the retrofacial nucleus. The posterior cricoarytenoid muscles receive contributions by the dorsal and ventral respiratory groups of the nucleus of the solitary tract (ST) thought to contribute to abduction during respiration. Finally, swallowing interneurons have been shown in the nucleus of the ST and lateral reticular formation surrounding the NA thought to play a role in laryngeal motor control during swallowing [2, 3].

Autonomic motor contributions to the viscera of the neck, thorax, and abdomen arise from preganglionic parasympathetic neurons located in the dorsal motor nucleus, which then project to intramural ganglia of the visceral organs [4]. The SLN and RLN receive sympathetic nerve fibers from the superior cervical ganglion that are responsible for regulating laryngeal blood flow and glandular secretions. The ganglionic innervation occurs rostro-caudally in the larynx, including rostral innervation by the superior cervical ganglion, mid-laryngeal innervation by the middle cervical ganglion, and caudal laryngeal and tracheal innervation by the stellate ganglion [5].

Sensory functions of the VN, SLN, and RLN project primarily to the nucleus of the ST and the nucleus of the spinal trigeminal tract (TT). Sensation of the mucous membranes of the pharynx, larynx, esophagus, trachea, and thoracic and abdominal viscera to the left colic flexure has cell bodies housed in the nodose (inferior) ganglion projecting to the nucleus of the ST. Neurons mediating taste derived from the epiglottis and portions of the pharynx also have cell bodies housed in the nodose ganglion projecting to the nucleus of the ST. Sensation of the infratentorial dura and portions of the auricle, external auditory canal, and external surface of the tympanic membrane have cell bodies housed in the jugular (superior) ganglion projecting to the nucleus of the TT [4]. Additional cell bodies housed in the nodose ganglion provide pulmonary, cardiovascular, and gastrointestinal vagal afferents [6].

Vagus Nerve

The VN arises from the ventral medulla between the cerebellar peduncle and inferior olive and exits the skull through the jugular foramen. The VN carries motor, sensory, and autonomic fibers. Lower motor neurons supplying the larynx are located anteriorly in the most superior aspect of the VN, but the topography seen in the brainstem is essentially lost in the peripheral nerves, which rotate medially during descent [7]. Early work on

motor nerve fibers in the VN suggested discrete adductor and abductor bundles within the VN. However, later work suggested that adductor and abductor nerve fibers are arranged in a loose pattern without any distinguishable organization [8]. When comparing the fiber distribution of motor to sensory, the VN has been shown to be primarily composed of nonmyelinated afferent fibers, up to 70 % [9]. In fact, in rabbits treated with selective vagotomy at various levels and examined histologically, the cervical vagus nerve was found to be 20–40 % efferent. When examined by fiber size, 40–50 % of large-sized fibers were found to be efferent, and almost all of the medium-sized fibers were afferent [10].

Superior Laryngeal Nerve

The SLN arises from the caudal pole of the nodose ganglion and has been reported to have 15,000 myelinated fibers in humans [11]. The SLN travels with the VN before separating anteriorly and inferiorly toward the larynx several centimeters cephalad to the carotid bifurcation [12]. The internal and external branches typically separate 1.5 cm below the nodose ganglion, but can separate at the ganglion itself. The external branch has been shown to be approximately 8 cm long and 0.2 mm thick [13] and the internal branch has been shown to be about 7 cm long and 1.8–2.0 mm thick before dividing into superior, middle, and inferior divisions near the thyrohyoid membrane [14]. In human cadavers, the SLN intraperineural area and number of myelinated fibers were not different between sides [15].

In a rat model utilizing histology and nerve conduction analysis, four distinct branches from the main trunk of the SLN were identified (see Fig. 4.1): (1) Branch 1 was the equivalent of the internal branch providing primarily sensory function to the level of the vocal folds, (2) Branch 2 was the equivalent of the external branch providing primarily motor control of the CTM, (3) Branch 3 was a sensory branch to the subglottis and esophagus, and (4) Branch 4 was a more inconsistently found branch anastomosing to the RLN. Comparative conduction studies found predominant motor function in Branch 2 (external branch), which had large fibers to the CTM. Other smaller motor fibers were identified in Branch 1 thought to be secretomotor, Branch 3 thought to provide motor contribution to the esophagus, and Branch 4 providing unknown motor contribution. Afferent fibers were largest and most prominent in Branch 1 (internal branch), which was correlated

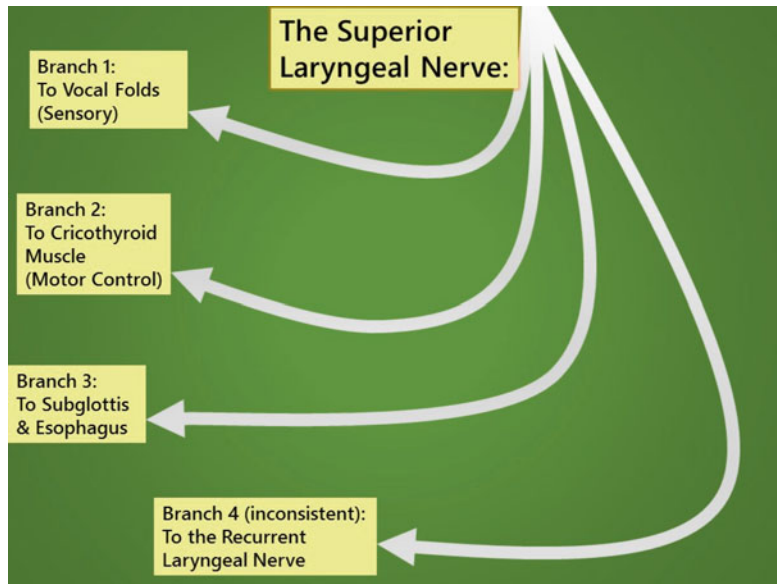

Fig. 4.1 Branches of the superior laryngeal nerve. [Based on data from Ref. 16]

with joint proprioceptive, stretch receptor, fast touch, chemoreceptor, and common chemical sensation. Smaller sensory fibers were found in Branch 2 (external branch) of unclear sensory function, Branch 3 thought to provide esophageal muscle sensation, and Branch 4 thought to provide aortic baroceptors and esophageal muscle sensation [16].

The internal laryngeal nerve innervates superficial and deep sensory receptors. Discharge activity recordings of sensory fibers have shown the greatest sensitivity to mechanical stimulation, displacement of the laryngeal structures, and contraction of the laryngeal muscles [17]. Meanwhile, animal models have shown that a large number of fibers are responsive to mechanical stimulation, airflow, upper airway pressure, and contraction of upper airway respiratory muscles [18]. Substance P, a neuropeptide that acts as a neurotransmitter of primary afferent neurons, has been shown in a canine model to be distributed in various locations in the epithelium and to contribute to the function of sensory endings in the laryngeal mucosa [19]. Transient receptor potential vanilloid type 1 (TRPV1), a transducer expressed by sensory nerve terminals felt to be a molecular gateway to nociceptive sensation in somatic and visceral tissues, has been found in human, rat, and mouse laryngeal tissue [20] and is thought to be involved in vagally-mediated airway hypersensitivity and chronic cough [21]. Stimulation or irritation of the larynx has been demonstrated to cause reflex bronchoconstriction mediated through TRPV1 expressing neurons [22], while sensitized airways have exaggerated expression of TRPV1 [23].

Attempts have been made either to determine the presence of independent adductory function of the external branch of the SLN (EBSLN) or to identify a communicating nerve between the external branch and the RLN contributing to adduction. Arguments in favor of adductory function have suggested the external branch's innervation of the CTM may lead to adduction, while others propose distinct innervation of the vocalis through either the external branch or a communicating branch. A pig model has been reported suggesting innervation through the external branch itself. Through evoked electromyography (EMG) of the cricothyroid, thyroarytenoid, lateral cricoarytenoid, and posterior cricoarytenoid muscles, the SLN was shown to provide motor efferents to the latter three muscles, and most consistently the adductor muscles [24]. Supporting a communicating branch, a human cadaver study utilizing histological staining pattern analysis showed a communicating nerve separate from the external branch in 44 % of specimens with staining within the vocalis suggestive of independent innervation [25]. Such studies may explain the more lateral positioning of the vocal fold in high vagal injuries as compared to RLN injuries.

Recurrent Laryngeal Nerve

The RLN arises on the left at the aortic arch and on the right at the subclavian artery. In humans, the left RLN has been shown to be approximately 11 cm longer than the right [26]. There are conflicting data comparing the morphometric parameters of left versus right, most notably including fiber diameter [15, 27, 28] and number of myelinated fibers [29]. Other reported differences include greater cross-sectional area and number of fibers proximally, near the RLN origin, compared to distally, closer to the larynx [30], as well as larger intraperineural area, total number of fibers, axonal area, axonal diameter, and area occupied by myelinated fibers in men compared to women [31]. While there is conflicting evidence in terms of comparing micro-neural differences between left and right, there likely are differences because of the ability for the left RLN to create a simultaneous motor impulse to the larynx despite its longer anatomical course.

While early animal studies suggested that laryngeal efferent fibers could be differentiated within the RLN, a human study showed that fascicles within the RLN housed fibers contributing to both adductor and abductor function with no predisposition to any position within the nerve. Furthermore, a plexus formation was shown along the course of the RLN that created fiber intermingling and rearrangements and that fiber

size and density varied along the course of the RLN. Even after branching of distal nerve endings near the entrance into the larynx, there continued to be both adductor and abductor nerve fibers [32]. Later tracer studies attempting to differentiate adductor and abductor fibers showed that the two fiber types were scattered throughout the nerve [8]. However, distinct differences between laryngeal and non-laryngeal fibers have been reported. A non-laryngeal fascicle was found to carry smaller myelinated nerves supply the trachea and esophagus, while a laryngeal fascicle contained larger nerve fibers supplying laryngeal sensation and motor function [10, 30, 33–35].

Age-Related Changes to the SLN and RLN

Age-related changes to the SLN have been reported in animal [36] and human [37] models. In a study utilizing electron microscopy in the rat, the internal branch of the SLN showed preservation of quantitative measures, including total fiber counts and fiber size for myelinated and nonmyelinated fibers. However, observed qualitative changes included segmental demyelination and axonal degeneration, increased Schwann cell cytoplasm, decreased density of neurofilaments, and increased intrafascicular extracellular space. The changes were thought to contribute to decreased conduction velocity [36]. In a study evaluating human cadaveric SLNs with electron microscopy, a 31 % reduction in myelinated fiber number was observed in the advanced age group compared to the young group. The overall loss of myelinated fibers was largely attributed to a 67 % loss in small myelinated fibers. Meanwhile, fiber diameter was also reduced by 67 % in small myelinated fibers [37]. In another human cadaver study, no difference in intraperineural area or number of myelinated fibers were found between specimens from subjects less than 60 years old compared to those greater than 60 [15].

Studies have also attempted to identify age-related change in the RLN [38, 39]. In a rat model using ultrastructural techniques, several changes were noted when comparing young, old, and very old age groups. In myelinated fibers, while the total fiber numbers were preserved, there was a reduction in fiber count for fibers between 4 and 7 μm in diameter and an increase in fiber count for those greater than 7 μm with advancing age, while abnormally thin myelin was observed in aging rats as well. In nonmyelinated fibers, there were no significant changes in fiber number or size. Overall structural changes included increased endoneurial extracellular space in the very old age group [38]. A human cadaver study showed a disappearance of large axons and an overall reduction in axonal area and perimeter measures in patients of advanced age utilizing microscopy techniques [39]. A more recent human cadaveric study showed a reduction in the number of total number of fibers and of those of very small diameter with age (1–3 μm compared to 4 μm or greater) [15].

Though data appears to be conflicting for some measures, such animal and human cadaver studies show that there do appear to be quantitative and qualitative changes to the SLN and RLN microenvironment with aging. Such changes may underlay some of the sensory and motor dysfunction seen with advanced age [40, 41], as well as certain age-related outcome differences in clinical studies. For example, in a multi-institutional, randomized trial of laryngeal reinnervation versus medialization laryngoplasty for unilateral vocal fold paralysis, poorer voice results were found in older individuals treated with laryngeal reinnervation compared with younger subjects [42].

Neural Injury

The organization of peripheral nerve injuries was greatly impacted by Seddon's clarifying work in 1943 [43]. Due to what was thought to be an insufficient ability to organize the nature of these injuries, he offered three central types: neuropraxia, axonotmesis, and neurotmesis.

Neuropraxia is defined as a lesion that does not lead to axonal degeneration, but may lead to local

degeneration of the myelin sheath. Neuropraxia leads to spontaneous and complete recovery that is more rapid and occurs following Wallerian degeneration and requisite regeneration. Axonotmesis is defined as an injury leading to complete histological interruption of axons and preservation of structures around the nerve serving a supporting role, including Schwann cells, endoneurium, and perineurium. Wallerian degeneration occurs distally in axonotmesis and recovery is spontaneous. Neurotmesis is defined as an injury in which the nerve and supporting structures are all damaged severely, for example with transection. Wallerian degeneration occurs distally and spontaneous recovery rarely occurs and typically leads to poor function [43].

Continuing the work of Seddon and seeking to further clarify peripheral nerve injuries was Sunderland, who in 1951 advocated for a 5-tiered classification of peripheral nerve injury based on the extent of damage to the normal nerve trunk anatomy (Fig. 4.2) [44].

First degree injury is defined as an injury leading to an electrical conduction block at the site of injury without damaging the anatomical structure of the nerve. There is no Wallerian degeneration and the injury that caused the conduction block is deemed reversible with return to activity being spontaneous after a brief period. Function is not only thought to be restored rapidly, but also fully. Second degree injury is defined as an injury leading to damage to the axon without damaging the axon sheath, endoneurium, perineurium, or epineurium. Central to these injuries is distal Wallerian degeneration. The damaged nerve fibers regenerate and do so along the course of the intact endoneurial tube, which directs fibers back to their original location. Thus, reinnervation may lead to fully restored function. Third degree injury is defined as an injury leading to damage of the axon and endoneurium without damage to the perineurium or epineurium. Wallerian degeneration occurs and the continuity of the endoneurial tube is destroyed, which leads to disorganization and fibrosis during neural regeneration. Reinnervation can be misguided as fibers are either blocked or misdirected toward their final destination. Therefore, function can be altered and synkinesis can result. Fourth degree injury is defined as an injury leading to damage of the axons, endoneurium, and perineurium without damage to the epineurium. While the nerve continuity is preserved, it is composed of disorganized connective tissue, Schwann cells, and regenerating axons. A traumatic neuroma can

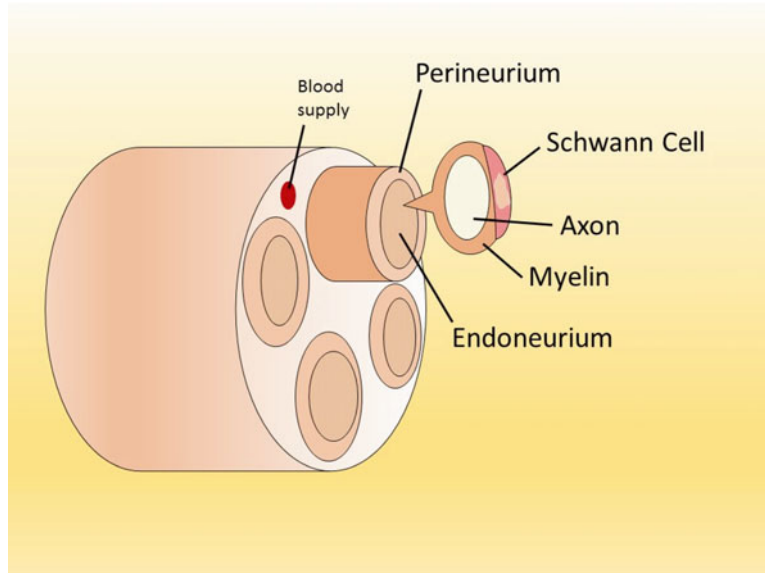

Fig. 4.2 Basic micro-neuroanatomy. The epineurium surrounds the entire nerve, perineurium surrounds a neural fascicle, and endoneurium surrounds individual nerves within a fascicle

result. Because of further loss of supporting structure, organized reinnervation is further challenged and there is a greater chance for aberrant function with reinnervation. Fifth degree injury is defined as an injury leading to damage to all components of the nerve, essentially complete transection. Because the injury involves complete axonotomy, there is little to no opportunity of neural regeneration because of loss of both axons and all structural components [44].

Recent studies have further defined the underlying changes related to peripheral nerve injury, particularly with nerve transection. The structural changes are thought to be related to complex local molecular pathways, which include distal Wallerian degeneration, influx of calcium ions, and activation of calcium-dependent proteases resulting in axonal swelling and cytoskeleton breakdown [45]. Within hours of nerve transection, surrounding Schwann cells initiate an inflammatory cascade through the release of inflammatory cytokines and recruitment of macrophages to remove the myelin and axonal debris. De-innervated Schwann cells also downregulate their expression of structural proteins, resulting in the destruction of their myelin sheaths and further contributing to degenerative debris. Macrophages play a major role in removal of debris as the process transitions to neural regeneration [46, 47].

Neural Regeneration

The cascade underlying neural injury and reinnervation is complex. While macrophages have a critical role in debris removal accumulated from the degenerative process, they also remove proteins that inhibit motor neuron outgrowth such as myelin-associated glycoprotein important in the process of regeneration [46, 47]. After debris removal, Schwann cells proliferate and align using contact guidance and regulatory factors that induce axonal elongation and regeneration to the motor endplate target. Schwann cells also form bridges from de-innervated endplates to innervated endplates to provide a mechanism for uninjured axons to participate in neuron sprouting and reinnervation of adjacent de-innervated endplates [48].

Although axonal regeneration varies based on mechanism of injury and local conditions, axonal growth typically occurs at a rate of 1–2 mm per day [49]. In peripheral nerve injuries, proximity of axotomy lesion is a major determinant of the potential for spontaneous reinnervation, with larger spatial separation resulting in delayed reinnervation. As previously mentioned, the myofiber changes that occur during prolonged de-innervation, such as fiber atrophy and increased connective tissue and fibrosis, impede reinnervation by creating a physical barrier between the regenerating motor neurons on motor endplates.

It could be rationalized that RLN injuries are followed by a higher rate of spontaneous reinnervation than VN injuries simply due to closer proximity of the RLN with the larynx. However, studies have shown that RLN injuries are not universally followed by spontaneous reinnervation via the injured RLN, but surrounding neuronal sources such as the sympathetic chain often contribute to laryngeal reinnervation following RLN transection injury. With neural injury, it is theorized that vacated neuromuscular junctions may become replaced by autonomic nerve fiber ingrowth, which may lead to the regeneration of muscle despite appropriate function. This theory underlies the idea that reinnervation procedures should be performed as early as possible [50, 51].

Reinnervation of laryngeal musculature can also be through the SLN. In a study of rats following chronic RLN injury, posterior cricoarytenoid muscles were found to have neural sprouting and stimulation via the ipsilateral SLN, indicating dual innervation via the RLN and SLN, then neural takeover of adjacent motor endplates by the SLN [52]. The spontaneous reinnervation seen after RLN injury relative to VN injury is likely related to microenvironmental changes that attract motoneuron sprouting, potentially including both Schwann cell and myofiber-mediated events. This concept was demonstrated in a rat model, where RLN axotomy was performed followed by neurotrophic growth factor injection into the ipsilateral thyroarytenoid and inhibiting factor into the posterior cricoarytenoid, which led to selective reinnervation of the adductor muscle

[53]. Future work relying on promoting and inhibiting factors may help to drive more appropriate reinnervation following injury to the RLN.

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Intralaryngeal Anatomy of the Recurrent Laryngeal Nerve

5

Michael I. Orestes and Gerald S. Berke

Abstract

Detailed anatomical knowledge of the intralaryngeal course of the recurrent laryngeal nerve (RLN) is critical for performing complex thyroid surgery, partial laryngeal surgery, and selective reinnervation of the larynx specifically for rehabilitation of bilateral vocal fold paralysis and laryngeal transplant. The RLN enters the larynx at the level of the cricopharyngeus where it can divide into an anterior (motor) branch and posterior (sensory) branch; the anterior branch, typically termed the inferior laryngeal nerve, divides into several branches to the laryngeal muscle. First, the nerve innervates the posterior cricoarytenoid muscle, then the interarytenoid muscle, followed by innervation of the lateral cricoarytenoid and thyroarytenoid muscles distally. The posterior cricoarytenoid, interarytenoid, and lateral cricoarytenoid nerves display the most variability from human to human. This variability makes it difficult to reinnervate the posterior cricoarytenoid muscle completely without inadvertently innervating the interarytenoid. The sensory nerves to the larynx are very variable and it is likely that there is significant overlap in the distribution from the recurrent and superior laryngeal nerves. There is also some compelling evidence that there is a motor connection from the superior laryngeal nerve to the laryngeal adductors known as the human communicating nerve, however, the significance of this is unknown.

Keywords

Recurrent laryngeal nerve • Inferior laryngeal nerve • Extralaryngeal branches • Intralaryngeal nerves • Posterior cricoarytenoid • Lateral

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cricoarytenoid • Interarytenoid • Thyroarytenoid • Human communicating nerve • Galen's anastomosis

Introduction

The course of the recurrent laryngeal nerve (RLN) has been studied throughout the history of modern surgery. This has been primarily due to great interest in anterior neck and thyroid surgery for both benign and malignant tumors of the thyroid. The complex intralaryngeal branching patterns of the RLN are often forgotten. As it enters the larynx, the RLN provides both sensory and motor input. Some of the earliest research on the detailed intralaryngeal course of the RLN was based on the work of Exner in 1884 who examined both rabbit and canine larynges [1]. This was furthered by Dilworth [1], who dissected 33 adult human cadaveric larynges to form the current basis of the intralaryngeal anatomy known today.

The intralaryngeal branching patterns are far from esoteric knowledge. Working knowledge of this area allows for more precise dissection of the larynx for partial laryngeal surgery for cancer, surgical treatment of neurological voice disorders, reinnervation of the larynx for both bilateral vocal fold paralysis and laryngeal transplantation as well as for complex thyroid surgery requiring dissection within the larynx or deep to the cricopharyngeus. Furthermore, the laryngeal muscles themselves are more complex than often credited. Several have more than one belly with separate sources of innervation for each. In addition, the sensory innervation is far from straight forward and likely does not conform to the traditional thought that the RLN only innervates the glottis, subglottic and tracheal mucosa. There is likely a significant overlap in innervation between the superior and recurrent laryngeal nerve systems.

Intralaryngeal Transition and Nerve to the Inferior Constrictor

The transition point from extralaryngeal portion of the RLN to the intralaryngeal portion is typically defined as the point where the nerve passes under the inferior border of the inferior constrictor muscle [2–4]. Occasionally, this is defined as the passage of the nerve past the level of the inferior cornu of the thyroid cartilage and likely represents the same portion of the nerve [5]. Although not commonly referenced by surgeons, this division is often referred to as the inferior laryngeal nerve by anatomists [4]. The inferior laryngeal nerve is defined as the main trunk of the RLN after it has given off branches to the trachea, thyroid, esophagus, and inferior constrictor muscles.

Nguyen et al. [2] found via dissection of 30 cadavers that 87 % of the RLNs branched at least once prior to diving deep to the inferior constrictor. In all cases, the posterior branch represented a communicating branch, which in this region would represent Galen's anastomosis [6]. They also noted several smaller collateral branches including the thyroid branch and the nerve to the inferior constrictor branching just before the nerve dives deep to the inferior border of the inferior constrictor muscle (Fig. 5.1). Yalcin et al. [4] performed extensive work on extralaryngeal divisions of the RLN, better defining the term "inferior laryngeal nerve". After careful dissection of 60 cadavers, they also determined that 85.8 % of cadavers had two laryngeal branches, consisting of an anterior branch which supplied the laryngeal musculature and a posterior branch that supplied the mucosa inferior to the vocal folds. They also noted that there were

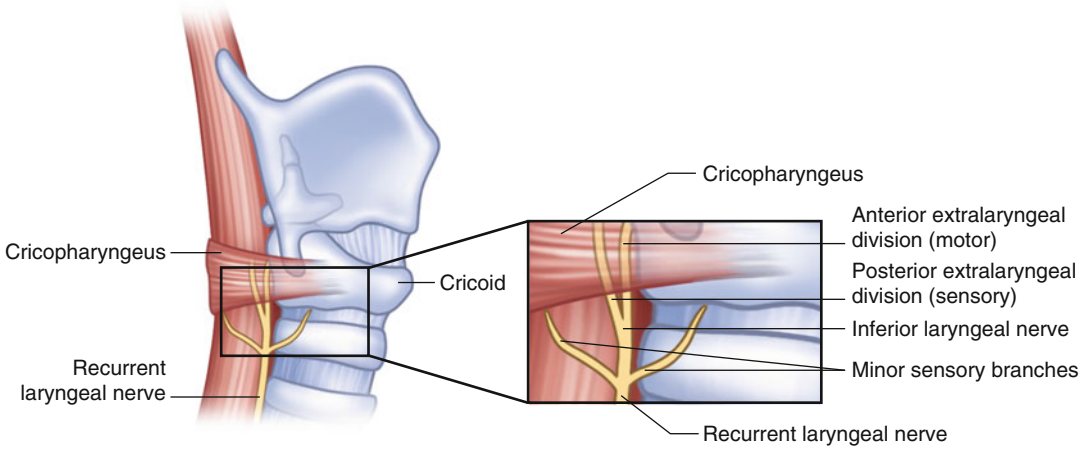

Fig. 5.1 Intralaryngeal transition of the recurrent laryngeal nerve

one to three additional branches just inferior to this division extending toward the esophagus, pharynx, and thyroid gland.

This concept of multiple branches prior to the entrance of the RLN past the cricopharyngeus muscle is widely debated in the surgical literature as a potential risk factor for RLN paralysis following thyroidectomy. Casella et al. [7], evaluated 195 RLNs exposed during thyroidectomy and found there was a relative risk of 13.25 % for permanent RLN paralysis in the setting of a "branched nerve" versus an "unbranched nerve". The authors of this study mention concern about an extralaryngeal branch extending to the posterior muscles of the larynx; however, this has not been demonstrated in a cadaveric model or in our clinical experience with intralaryngeal reinnervation of the RLN [2, 4, 8]. Further evidence is given in the next section of this chapter detailing the exact course of the nerve to the posterior cricoarytenoid muscle which is typically the first motor division of the inferior laryngeal nerve.

While preservation of all branches of the RLN is preferred, preservation of the most anterior branch of substantial size will maintain innervation to the laryngeal muscles. In most cases, preservation of all of the branches will be possible. If sacrifice of individual branches is needed for tumor clearance, the cricopharyngeus can be divided and the nerve can be traced distally into the larynx to confirm which one represents the motor branch.

Motor Branches of the Intralaryngeal Portion of the Recurrent Laryngeal Nerve

Posterior Cricoarytenoid Branch

After travelling distal to the cricopharyngeus muscle's inferior edge, the inferior laryngeal nerve gives off branches to the posterior cricoarytenoid muscle (Figs. 5.2 and 5.3). Unlike in the canine model where the nerve is superficial to the posterior cricoarytenoid muscle, the human nerve runs deep to the muscle before innervating it [9]. A detailed study in human cadavers was performed by Nguyen et al. [2], utilizing careful microdissection of the RLN. Three main variations in innervation of the posterior cricoarytenoid muscles were identified. In a Type I posterior cricoarytenoid nerve, there is a single nerve pedicle that innervates the posterior cricoarytenoid muscle directly off the main trunk of the inferior laryngeal nerve. However, this would sometimes divide into 2–3 further branches distally, likely innervating different bellies of the muscle. Type

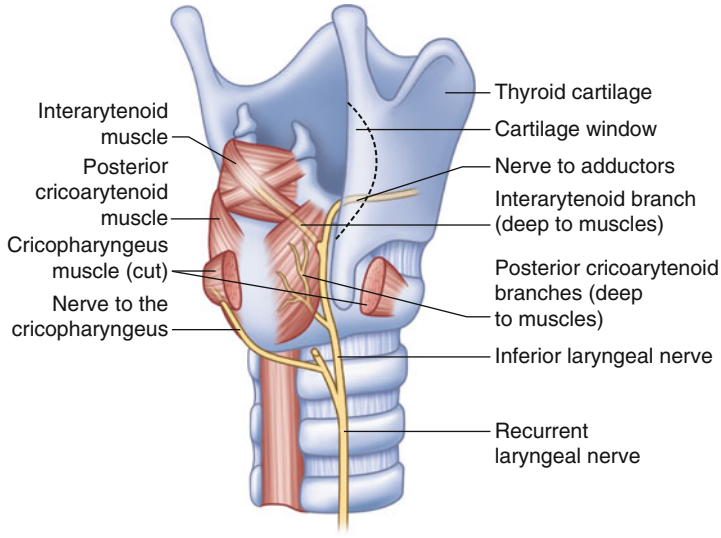

Fig. 5.2 Intralaryngeal anatomy of the abductor branch of the recurrent laryngeal nerve and branch to the interarytenoid muscle

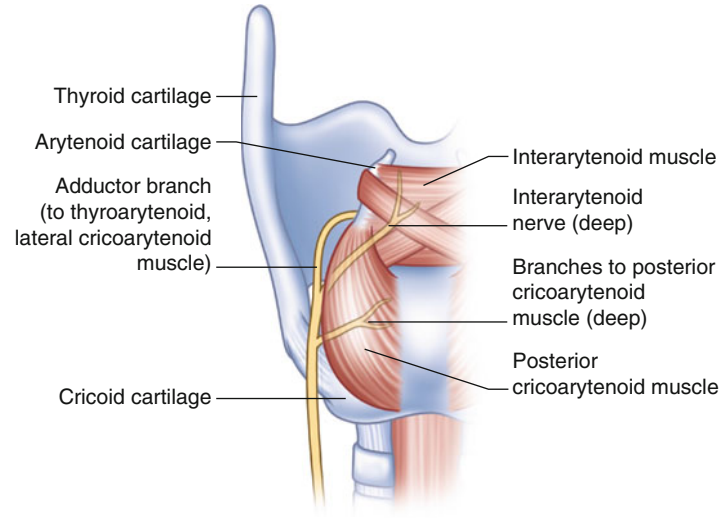

Fig. 5.3 Posterior view, intralaryngeal anatomy of the abductor branch of the recurrent laryngeal nerve and branch to the interarytenoid muscle

1 anatomy was the most common (observed in 66 % of cadavers). A Type II nerve consisted of two separate pedicles, while a Type III nerve consisted of three separate pedicles. Type II and III nerves were less commonly noted (26.7 % and 6.7 %, respectively). There were also several variations within the Type II and III divisions, including those in which a branch to the posterior cricoarytenoid muscle arose from a common trunk with the nerve to the interarytenoid muscle (Type IIc, d and Type IIIb nerves). While infrequent, these variations represented 6.7 % of Type II nerves and 1.7 % of Type III nerves. Further research by Damrose et al. [9], demonstrated similar results. However, no posterior cricoarytenoid branches were noted from the interarytenoid nerve, possibly due to the smaller sample size and relative infrequency of the occurrence. They also demonstrated that the mean distance between the last posterior cricoarytenoid nerve and the occurrence of the interarytenoid branch was an average of 5.7 mm and suggested that the inferior

cricothyroid ligament was a good landmark for identifying the separation between the abductor and adductor components of the inferior laryngeal nerve. However, this study was only performed in ten cadavers and may be overestimating the true incidence of this occurrence when compared with the study by Nguyen et al. [2]. In contrast, Prades et al. [3] found Type II (separate branches to the posterior cricoarytenoid muscle) to be the most common variation, noted within nearly half of the specimens. The authors demonstrated that in as many as 88 % of the specimens, at least one of the pedicles shared a common trunk with the nerve to IA. Furthermore, a detailed study of 75 cadavers by Maranillo et al. [10] noted a high incidence of variability in innervation of the laryngeal muscles, noting that as many as 88 % of the abductor and adductor branches came from a common trunk, particularly with the interarytenoid and lateral cricoarytenoid nerves. In addition, Sanders et al. [11] and Sanders et al. [12] demonstrated using Sihler staining in human cadaveric larynges that the nerves to the posterior cricoarytenoid muscle originated from two distinct branches and innervated two different portions of the muscle (horizontal section and vertical/oblique section). In two-thirds of their specimens, there were two branches from the RLN, while in one-third there was a single branch which subsequently divided to innervate the two bellies separately. Furthermore, the nerve to the horizontal or medial aspect of the muscle often arose in conjunction with the nerve to the interarytenoid muscle.

In terms of function, the posterior cricoarytenoid muscle plays the most important role with regard to selective reinnervation of the laryngeal muscles. While a benefit in phonation can been seen without utilizing selective reinnervation of the RLN [13], improvement in active abduction of the posterior cricoarytenoid (required for improved respiration) likely requires more than just tone alone. Knowledge of posterior cricoarytenoid innervation is critical for restoration of respiratory function with bilateral vocal fold paralysis and successful decannulation for laryngeal transplantation. In our experience with attempts at reinnervation of the posterior cricoarytenoid muscle in the setting of bilateral vocal fold paralysis, direct nerve to nerve anastomosis of the recurrent or inferior laryngeal nerve prior to the takeoff of nerve pedicles directed toward the posterior cricoarytenoid muscle in conjunction with sectioning of the interarytenoid muscle to prevent inadvertent synkinetic motion has yielded the best results (unpublished data). Despite some of the variations in human anatomy, there is consistent evidence that the posterior cricoarytenoid branch(es) come off as the first intralaryngeal motor branches off of the inferior laryngeal nerve, typically arising shortly after the nerve travels posterior to the inferior cornu, but just prior to the inferior cricothyroid ligament. In some cases a second or even third branch may be present and may come off the interarytenoid branch instead of directly off the inferior laryngeal nerve.

Interarytenoid Branch

After giving off branches to the posterior cricoarytenoid muscle, the inferior laryngeal nerve continues along the lateral border of the posterior cricoarytenoid muscle. After the nerve crosses the inferior cricothyroid ligament, it gives off a branch to the interarytenoid muscle which travels deep to the horizontal belly of the posterior cricoarytenoid muscle (Figs. 5.2 and 5.3). As noted in the section above, a branch to the horizontal belly of the posterior cricoarytenoid muscle may arise directly off this branch [2, 9, 12]. Nguyen et al. [2] noted that this nerve terminates on the inferior border of the transverse arytenoid muscle, running deep to the posterior cricoarytenoid muscle. They also noted that there were two additional types of branches extending from this nerve: one innervating a portion of the posterior cricothyroid muscle and a second type of smaller branches which form collaterals with the superior laryngeal nerve (SLN) which they postulated to be proprioceptive fibers. Mu et al. [14] reported similar findings with regard to the course of the nerve, noting that it originated near the cricoarytenoid joint and ran posterior to the posterior cricoarytenoid muscle until it entered the inferior lateral border of the

interarytenoid. However, they noted that in one of the ten larynges they dissected that the nerve came off the inferior laryngeal nerve as two branches before coalescing into one branch and entering the muscle. Once entering the muscle, they noted a diverse network of branches individually innervating portions of the muscle and some branches creating anastomoses with the internal branch of the SLN. This data supports earlier studies regarding the internal branch of the SLN by Vogel [15], which reports that the interarytenoid muscle in humans is innervated in part by the internal branch of the SLN. In fact, the concept that the internal branch of the SLN is purely sensory without any motor component seems to stem from early studies performed in a canine model [15].

Understanding interarytenoid and posterior cricoarytenoid nerve relationship is critical for successful reinnervation of the larynx for the purpose of voluntary abduction, as noted above. The muscle has an extremely complex neural network and contains bilateral RLN innervation and possibly internal branch of the SLN innervation. Both Damrose et al. [9] and Kwak et al. [16] were able to find distinct interarytenoid branches without disarticulating the cricothyroid joint via large thyroidotomy windows. The distance between the last posterior cricoarytenoid branches noted by Damrose et al. [9] was a mean of 5.7 mm. Kwak et al. [16] found that the distance was variable from side to side and between males and females, ranging from 2–11 mm (mean of 5 mm), noting a slightly shorter distance on the left than the right. Neither work noted significant branches from the interarytenoid nerve to the posterior cricoarytenoid muscle. Kwak et al. required reflection of the posterior cricoarytenoid muscle to confirm the course of the nerve to the interarytenoid muscle.

While both articles above suggest it may be possible to separately reinnervate the interarytenoid muscle, in our experience, in the setting of bilateral vocal fold paralysis, sectioning of this muscle provides the most efficient method of preventing its adductor effect as it effectively prevents any undesired adductor effect from either side. Complex and potentially variable innervation to the posterior cricoarytenoid would require careful dissection of the nerve to the interarytenoid in nearly all cases. This would require reflection of the posterior cricoarytenoid muscle which would likely affect its function.

Lateral Cricoarytenoid Branch

The inferior laryngeal nerve, after giving off branches to the interarytenoid, turns and continues anteriorly into the larynx slightly inferior to the muscular process of the arytenoid (Fig. 5.4). Nguyen et al. [2] noted three possible innervation pedicles in their series of 60 dissections. They noted that in 70 % of cases there was a single nerve pedicle, while in 25 % there were two nerves and in 7 % there were three nerves supplying this muscle. There was also some variation in the takeoff point for this nerve, ranging from occurring close to the interarytenoid muscle branch to originating far anteriorly toward the interarytenoid muscle. Contrary to the findings of Nguyen et al. [2], Sanders et al. [11] noted that all of the specimens contained a single nerve branch to the lateral cricoarytenoid muscle which extended into a dense network of nerves within the muscle, this appeared consistent from specimen to specimen. However, since the bi- or tripedicled innervation is relatively uncommon, it is possible that they may have not seen these variants due to the smaller sample size. Maranillo et al. [10] noted one to six nerve branches to the lateral cricoarytenoid muscle in a study of 75 cadavers, reporting the three-branch pattern to be the most common (43.3 %) and even noted a small portion (2.6 %) shared a common branch with posterior cricoarytenoid/interarytenoid muscles.

In our clinical experience with selective adductor denervation and reinnervation surgery, the lateral cricoarytenoid muscle branch is often visualized extending from the deep surface of the anterior branch of the inferior laryngeal nerve into the lateral cricoarytenoid muscle.

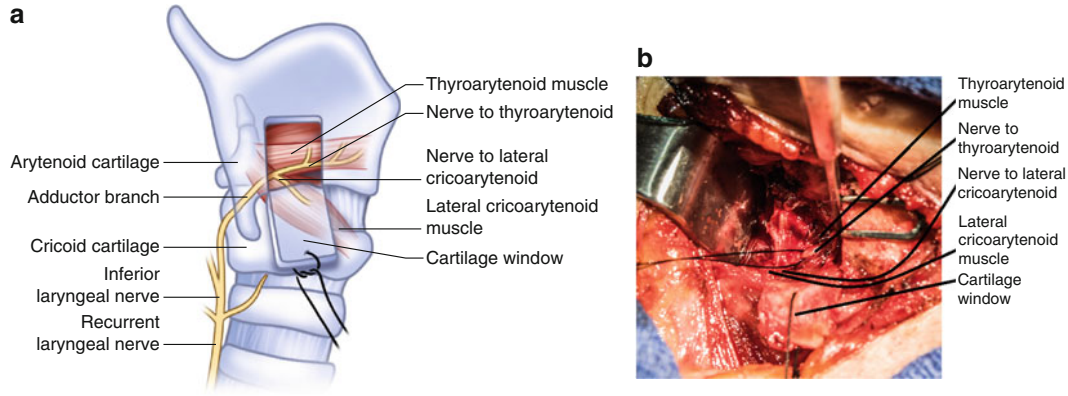

Fig. 5.4 (**a**) Intralaryngeal anatomy of the adductor branch of the recurrent laryngeal nerve (nerve to lateral cricoarytenoid and thyroarytenoid muscles). (**b**) Intralaryngeal anatomy of the adductor branch of the recurrent laryngeal nerve (nerve to lateral cricoarytenoid and thyroarytenoid muscles)

This typically occurs at the anterior portion of our window, just deep to oblique line. This nerve, however, is not always noted, possibility due to variation in the nerve anatomy as noted in several studies. With regards to surgery for spasmodic dysphonia where interruption of the adductor muscles is desired, we find that sectioning of the lateral cricoarytenoid muscle itself is necessary [17]. In addition, we have noted that when the anterior branch of the inferior laryngeal nerve is identified it varies in caliber significantly. This may indicate a posterior pedicle where the nerve to the lateral cricoarytenoid has already innervated the muscle.

Thyroarytenoid Branch

The thyroarytenoid nerve branch represents the terminal branch of the inferior laryngeal nerve. This nerve typically travels along the anterior face of the lateral cricoarytenoid muscle and extends anteriorly through the paraglottic space where it gives off several branches to the thyroarytenoid muscle (Fig. 5.4a, b). There is little variation in the course of the nerve to the muscle, but some variation in the entrance of the nerve into the muscle can occur. This can be a single entrance point into the muscle, versus multiple nerve branches entering the muscle surface [2]. Sanders et al. [14] noted a dense innervation of both the thyroarytenoid and false vocal fold using Sihler staining. They also reported that it had the most dense nerve network of any laryngeal muscle.

We reinnervate the thyroarytenoid nerve branch for selective adductor denervation and reinnervation surgery [17]. In our experience, there is very little variation in the course of the anterior branch of the nerve (Fig. 5.4a). It typically runs from the posterior inferior aspect of the thyroid cartilage (posterior aspect of our window), and runs anteriorly and slightly superiorly through the created window (Fig. 5.4b). After giving its branch to the lateral cricoarytenoid muscle, it innervates the thyroarytenoid muscle. It is cut after stimulating it to confirm thyroarytenoid action. We will occasionally note more than a single branch to the thyroarytenoid muscle, which can be separately reinnervated by multiple small terminal branches of the ansa cervicalis.

Sensory Branches of the Recurrent Laryngeal Nerve

Compared to studies evaluating the course and distribution of motor fibers from the RLN, there is relatively little research on the sensory fibers. This is likely due to the fact the upper pharyngeal and superior laryngeal nerve branches play a large role in swallowing and laryngeal sensation. However, the RLN does contain a significant amount of sensory fibers, both in the form of small sensory fibers to the esophagus and trachea extending from the main trunk of the RLN prior to entering the larynx, as well as the posterior branch of the inferior laryngeal nerve, as described in the first section of this chapter [4]. In addition, there are numerous proprioceptive fibers that likely supply the laryngeal musculature from the RLN [6]. Physiologic experiments by Sant'Ambrogio et al. [18] in a canine model demonstrated relatively few afferents from the RLN when compared with the internal branch of the superior laryngeal nerve. However, they only measured various forms of irritation of the larynx and trachea with regards to cough. Many of these sensory fibers may actually represent proprioceptive elements. Furthermore, the canine and human larynges are very different with regard to the sensory innervation; the canine model likely has more segregation between the superior laryngeal and recurrent laryngeal function than in humans. While overall the larynges are very similar, when it comes to intralaryngeal anatomy of the RLN, they begin to differ substantially [15]. This is particularly true for the sensory components, which require detailed physiologic experiments to be performed in animals. Unlike the similarities in canine and human motor function, sensory function is likely drastically different. Koizumi [19] noted that the canine sensory epithelium resembled that of a 10-month-old human embryo.

The sensory function of the RLN, particularly the intralaryngeal component, is poorly understood. There is significant room for further research into this area.

Galen's Anastomosis

Galen's anastomosis is defined as the communication between the posterior division of the RLN and the most inferior portion of the internal branch of the SLN [20]. Sanudo et al. [6] evaluated 180 hemilarynges that specifically look at the laryngeal communicating branches. They noted in nearly all of the larynges that there was a contribution of the posterior branch of the RLN prior to the entrance into the larynx to Galen's anastomosis. Other studies have not found the anastomosis to be a consistent finding [6, 11, 20]. This communicating branch can be either a single trunk, a double trunk or a plexus of nerves coursing over the posterior surface of the posterior cricoarytenoid and interarytenoid and range in reported incidence in the literature from 15.8–100 % [20]. The role of this nerve and its connection to the SLN is highly controversial. Naidu et al. [20] noted some branches extend to the posterior cricoarytenoid muscle, but it is unclear if this represents motor or sensory function. It is likely this contains pure sensory function, supplying mostly proprioceptive fibers primarily to the posterior cricoarytenoid muscle and later to the remainder of the laryngeal muscles via the arytenoid plexus. However, sensory innervation of the mucosa of the piriform sinus, subglottic larynx and trachea or even motor innervation to the posterior cricoarytenoid has also been suggested [6, 20].

In our experience, Galen's anastomosis is rarely seen within the surgical field. It is likely that posterior dissection to the extent where the nerve would be seen is not required for even the most complex intralaryngeal surgery. However, it may also be that the posterior sensory branches of the RLN and the inferior most branches of the internal branch of the SLN simply come in such close proximity to each other that on fixed cadaveric tissues small pieces of fibrous connective tissue make these nerves appear connected. More research is needed to determine what role Galen's anastomosis plays in the functional role of the larynx.

Arytenoid Plexus

A dense plexus of nerves is present within the interarytenoid muscle, along with numerous interconnected branches between the RLN and SLN systems [11, 14]. Sanders et al. [11] noted that this was a consistent finding on all ten specimens, but its exact course was highly variable. Sanudo et al. [6] went further to note that a deep arytenoid plexus was present in nearly all specimens, but a more superficial plexus was only present in 86 %. Like Galen's anastomosis, the function of this plexus is unclear. It is possible this represents cross innervation of the interarytenoid muscle from the SLN, complex proprioceptive innervation to the laryngeal muscles or multilevel sensory innervation of the posterior commissure [6, 11].

Although this plexus is noted intraoperatively in only a minority of cases we have performed, there is convincing evidence it is present. The posterior commissure is clinically the most sensitive area of the larynx and stimulating that area often rapidly causes a laryngeal adductor response. Furthermore, there is likely some role of this plexus in diseases such as paradoxical vocal fold motion and it would likely play an important role in laryngeal reinnervation.

Human Communicating Nerve

Connections between the external branch of the superior laryngeal nerve (EBSLN) and the RLN have also been described as occurring near the cricothyroid muscle (CTM) and inferior border of the thyroid cartilage [1, 6, 11, 21]. This is often referred to as the "human communicating nerve" or cricothyroid anastomosis [6, 21, 22]. This was first noted in passing by Dilworth [1], who noted this in two of his specimens. Sanders et al. and Wu et al. [11, 21] noted a communicating branch exiting the medial surface of the CTM and then entering the lateral surface of the thyroarytenoid muscle in 44 % of the specimens. They went on to further study the nerves, utilizing AChE staining to identify motor fibers. They determined that approximately 31 % of the fibers within this nerve were myelinated fibers consistent with motor innervation. The remainder was likely sensory fibers running toward the subglottic mucosa. The significance of this branch is not well known. What Wu et al. [21] postulated was that this may represent the fifth branchial arch nerve, which may be important in laryngeal sphincter function. It is well known that the SLN, particularly the internal branch is important in the glottic closure reflex [23, 24]. It is possible that this connecting branch may represent an additional efferent branch in this pathway. Intraoperative nerve monitoring (IONM) literature provides further physiologic evidence supporting a motor branch connection in the region. There is a significant body of evidence that stimulation of the EBSLN leads to a small but physiologic signal likely within a portion of the thyroarytenoid muscle, as detected by surface electrodes on an endotracheal tube with surface EMG electrodes [25–27].

The presence of this potential communicating nerve may have implications in spasmodic dysphonia that is not controlled with denervation of the RLN, issues with reflex glottic closure such as aspiration and laryngospasm symptoms and may help explain the difference in laryngeal position between various individuals with vagal nerve or RLN paralysis.

Conclusion

Mapping the intralaryngeal RLN anatomy is critical for understanding the pathophysiology of various laryngeal conditions such as vocal fold paralysis, spasmodic dysphonia, and other causes of neurological dysfunction of the larynx. Knowledge of specific branches and their potential course is particularly important for proper reinnervation of the larynx. In addition, for the ablative surgeon, knowledge of the intralaryngeal course may allow for more complete thyroid or partial laryngeal surgery while maintaining nerve supply to the intrinsic muscles of the larynx.

Being able to cut involved sensory branches such as the posterior extralaryngeal branch of the RLN may help clear tumor from near the cricoarytenoid joint more effectively without fear of denervation of the larynx.

The variability of the nerve to the posterior cricoarytenoid and interarytenoid branches likely explains the variable outcomes of PCA reinnervation to restore dynamic function to a person with bilateral vocal fold paralysis and in the function of a transplanted larynx. Furthermore, adequate knowledge of the course of the branch to the lateral cricoarytenoid and thyroarytenoid muscles allows for potential selective reinnervation of these muscles for vocal fold paralysis as well as selective lysis for hyperadductive processes such as spasmodic dysphonia.

Finally, the complex intralaryngeal network of sensory fibers and communicating branches represent a poorly explored field of research. Further advances in understanding the function of these communicating branches may lead to improved surgeries and treatments for pathology of the larynx in the future.

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Imaging of the Recurrent Laryngeal Nerve

6

Jayender Jagadeesan, Gregory W. Randolph, and Daniel T. Ruan

Abstract

Recurrent laryngeal nerve (RLN) preservation is critical in both parathyroid and thyroid surgery. RLN imaging can determine both the location and trajectory relative to key cervical structures. In this chapter, we present an overview of nerve imaging methods using Magnetic Resonance Imaging (MRI). We highlight key techniques that enable the resolution required to image small nerves, such as the facial and cranial nerves. Furthermore, we discuss the challenges involved in RLN imaging and present preliminary MRI results using a novel phase-navigated T2-Turbo Spin-Echo and Constructive Interference in Steady-State sequences. Ultimately, preoperative MRI images can guide surgical planning or be used with a navigation system during surgery to localize and preserve the RLN in real-time.

Keywords

MRI • Recurrent laryngeal nerve • Facial nerve • Cranial nerve • Constructive Interference in Steady-State sequence • T2 TSE • Phase navigation

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Introduction

Recurrent laryngeal nerve (RLN) preservation is an essential component of thyroid and parathyroid surgery. Each RLN innervates key intrinsic muscles of the larynx, including the ipsilateral posterior cricoarytenoid muscle. Permanent RLN injury can result in a variety of troublesome symptoms including, but not limited to, dysphonia, aspiration, and dyspnea. Disability from RLN dysfunction can have a significant and sustained impact on patient quality of life [1].

The left and right RLNs originate from the ipsilateral vagus nerves near the aortic arch and right subclavian artery, respectively. The RLNs ascend medially in the central neck near the tracheoesophageal groove. The RLNs typically travel between the ipsilateral parathyroid glands and posterior to the thyroid prior to entering the larynx just under the inferior constrictor muscle. Specifically, the upper and lower parathyroid glands are consistently located posterolateral and anteromedial to the RLN, respectively. The RLNs often branch prior to traversing the thyrohyoid membrane, although the location and degree of branching is variable. Given this anatomic configuration, the RLNs are susceptible to injury during thyroid and parathyroid procedures.

RLN injury can result from direct sharp injury, thermal damage, compression, or traction. Identification of the RLN and prevention of nerve injury are essential elements of central neck surgery, but thyroid and parathyroid procedures in particular. Thyroidectomy is performed for a variety of pathologic conditions including cancer, hyperthyroidism, autoimmune disease, and benign enlargement. Although RLN identification can be a routine task for experienced surgeons, thyroid pathology can obfuscate nerve appearance and location. Thyroid pathology can influence the anatomic location of the RLN (e.g., displacement from multinodular goiter), the surgeon's ability to visualize and discriminate the nerve from the thyroid capsule (e.g., inflammation from Hashimoto's thyroiditis), and malignant lesions can potentially adhere to or invade the RLN (e.g., direct invasion from carcinoma). For difficult cases, surgical adjuncts, such as intraoperative imaging and nerve monitoring, have the potential to improve a surgeon's chance of RLN identification and preservation during central neck surgery. This chapter will describe how MRI techniques are used to image peripheral nerves and how these protocols can be applied to the RLN.

MRI Techniques for Peripheral Nerves

Although some surgeons routinely perform bilateral parathyroid exploration for primary hyperparathyroidism without preoperative image guidance, many attempt to localize abnormal parathyroid tissue prior to surgery. A wide variety of diagnostic imaging techniques are used to localize parathyroid disease, such as ultrasound, computerized tomography (CT), nuclear medicine scintigraphy, and magnetic resonance imaging (MRI). Furthermore, imaging modalities are also commonly used for thyroid carcinoma staging (e.g., ultrasound and CT) and to define the extent of a multinodular goiter and assess for airway compression and deviation. The conventional cross-sectional imaging techniques used for these purposes cannot visualize the RLN.

This is due to technical limitations of CT and MRI, using current protocols, which lack the power and resolution to delineate the RLN, which is both small and subject to physiologic motion. The average diameter of the RLN is 2.0 mm with a 95 % confidence interval of 1.84–2.06 mm [2]. The technical limit for MRI imaging of peripheral nerves approximates 0.4 mm, which is within the range of most RLNs. Furthermore, techniques can be used to enhance nerve detection and to compensate for motion artifacts from breathing, arterial blood flow, and swallowing.

MRI is performed by placing patients within the bore of a strong, homogeneous magnetic field. Patient tissues, including peripheral nerves, contain water molecules that can be manipulated by the magnet to generate information that can be processed to create an image. Specifically, the protons within water are transiently excited by energy from the magnetic field, which eventually return to an equilibrium state. The emission of a radio frequency signal, measured by a receiving coil, is determined and the differences in signal

between neighboring tissues are used to contrast internal structures. A computer linked to the MRI device converts this signal information to create two-dimensional (2D) sectional images of a three-dimensional (3D) patient.

MRI image quality and resolution is dependent upon signal and field strength. The typical field strength for current commercially available MRI machines varies from 0.2 to 7 T. The "T" in this designation stands for "tesla", which is a unit of measure regarding the strength of a magnetic field. Technically speaking, one T is equal to one weber per square meter. Due to the strong magnetic field, the protons in the water molecules of the tissue align parallel (low-energy state) or anti-parallel (high-energy state) to the direction of the magnetic field. The proton also precesses along the long axis of the primary magnetic field at a frequency called the Larmor frequency. The Larmor frequency is dependent on the strength of the magnetic field. For example, the Larmor frequency is 63.9 MHz at 1.5 T. Furthermore, there are additional gradient coils along the three direction axis that modify the primary magnetic field according to the position, thereby changing the precession frequency.

This can then be used for spatial localization of the spins along x, y, and z axis and therefore are called spatial encoding. The radiofrequency (RF) coils are used to excite the protons by emitting a RF pulse and reading the signal when the protons return to their relaxed state. When the protons relax to their original state after removal of the RF pulse, the longitudinal magnetization is recovered through the spin lattice relaxation (T1 relaxation) while the transverse magnetization is reduced through the spin–spin relaxation (T2 relaxation). The T1 and T2 relaxation vary according to tissue composition. While the protons return to their relaxed state, they emit RF signal that is detected by the coils. The signals from all locations are then processed to obtain the MRI image. Furthermore, MRI can also determine the diffusion of water molecules along selective directions that can be further utilized to image fibers or tracts.

MRI of peripheral nerves requires an understanding of anatomic context. As explained above, key to imaging structures is highlighting the difference in signal between the nerve of interest and surrounding structures. Imaging the RLN is challenging partly due to its small size, since it is difficult to achieve adequate signal from the nerve. In addition, physiologic motion in the central neck near the tracheoesophageal groove imparts a separate technical challenge.

The RLNs are located near the carotid arteries, trachea, and esophagus, which complicates cross-sectional imaging from the patient's pulse, breathing, and swallowing. Ultimately, motion-compensated techniques are required to image the RLN and the neighboring structures which will be discussed in the next section. Below, we briefly discuss some of the most important techniques to image small peripheral nerves and how these techniques can be adapted to image the RLN.

Facial Nerve

Anatomy

The facial nerve has a complex set of sensory, motor, and parasympathetic fibers. Among these, the motor fibers constitute a dominant 70 % of the total nerve axon.

The sensory root is composed of both parasympathetic motor and sensory components. The function of the sensory root is to enable taste for two-thirds of the tongue, sensory control of the stapedial reflex, and sensory control of lacrimation. The sensory nuclei of the facial nerve are located in the upper medulla and lower pons. The motor root of the facial nerve arises from the primary facial nucleus, which is located within the pontine tegmentum, in proximity to the spinal nucleus of the trigeminal nerve. Reports of the mean facial nerve diameter range between 0.5 and 1.18 mm, which is significantly smaller than the RLN [3, 4].

MR Imaging

MR imaging of the facial nerve is performed with the patient in a supine position. A circular polarized head coil is typically utilized in a high-field-strength magnet (1.5 or 3 T) to obtain good signal-to-noise ratio. Contrast enhancement is generally preferred

for performing facial nerve imaging using 0.1 mmol/kg Gadolinium-DTPA. Pre-contrast, T1-weighted spin-echo (SE) or gradient echo sequence and a T2-weighted turbo spin-echo sequence with high spatial resolution are performed in the axial direction. The MRI field of view should include the brainstem and facial nuclei.

T1-weighted (T1W) sequence: T1W sequences are performed with intravenous Gadolinium injection for examining the facial nerve in cerebellopontine angle (CPA) and the parotid gland with a 1–1.5 mm slice thickness. Normal enhancement is possible in all parts of the facial nerve canal due to the presence of a perineural plexus. Spin-echo T1W images without fat saturation provides enough resolution to discern the facial nerve, adjacent fat, and the start of the facial nerve in the parotid gland.

T2-weighted (T2W) sequence: High-resolution T2W imaging enables analysis of the facial nerve trajectory and size. It also allows for tracing the course in the CPA and the internal auditory meatus (IAM). T2W sequences using gradient echo or spin-echo sequences are utilized. Several investigators have also reported the use of high-resolution T2W images performed approximately 15 min after contrast injection to depict physiological enhancement in the petrous facial canal. Slice thickness of 0.4 mm are currently used to evaluate normal and pathological enhancement of the nerve both in children and adults (Fig. 6.1) [5].

FIESTA (fast imaging employing steady-state acquisition) sequence: Kazikawa et al. [6] reported the use of the FIESTA sequence on 110 individuals for imaging 220 nerves using a 3 T GE scanner. The pulse parameters were as follows: Axial acquisition, TR (repetition time): 5.5 ms, TE (echo time): 2.5 ms, slice thickness: 0.4 mm with no gap, matrix size: 224×224, field of view: 14 cm, flip angle: 50°, number of excitations: 1, and bandwidth: 62.50. In addition, time-of-flight spoiled gradient recalled acquisition in the steady state; 3D MR angiography was performed in the axial plane by using the following parameters: TR: 25 ms, TE: 3.3 ms, flip angle: 20°, matrix size: 512×224, field of view: 18 cm, slice thickness: 0.5 mm with no gap, number of excitations: 1.0, and bandwidth: 31.25. The time-of-flight images were utilized to determine if the vessels were arteries.

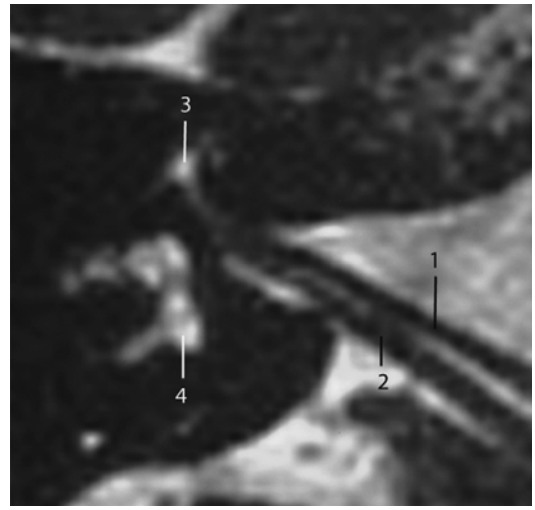

Fig. 6.1 High-resolution T2W imaging showing the normal nerve anatomy (*1*) Facial Nerve (*2*) Vestibular nerve (*3*) Geniculate ganglion (*4*) Vestibule [Reprinted from F. Veillona, L. Ramos-Taboada, M. Abu-Eid, A. Charpiot, and S. Riehm. Imaging of the facial nerve. Eur. J. Radiol. 2010; 74(2): 341–8. With permission from Elsevier.]

Multiplanar reconstruction (MPR) views parallel to the trigeminal nerve and facial nerve and parallel to the long axis of the bilateral nerves were obtained. To evaluate the utility of the nerve, the length of the nerves on the images was measured. The mean length of the facial nerve was 29.78 ± 2.31 mm, the mean distance between the bilateral facial nerves was 28.65 ± 2.22 mm, the angle between the nerve and midline was 69.68 ± 5.84°, and the vertical ratio at the porus acusticus was 0.467 ± 0.169. The sequence proved valuable to determine the course of the facial nerves.

GRASS (gradient recalled acquisition in the steady-state) sequence: Takahashi et al. [7] reported the use of GRASS sequence in 13 patients to identify benign parotid tumors, ducts, and facial nerves. Axial images were obtained using a 1.5 T with a circular receiver coil. The pulse parameters were as follows: TR: 30 ms, TE: 4.2 ms, flip angle: 30°, FOV: 100 mm, imaging matrix: 256×256, slice thickness: 1.5 mm, no intersection gap; single signal acquired; data acquisition time: 5 min 42 s. The main trunks and cervicofacial and temporofacial divisions of the facial nerves were identified in 100, 84.1, and 53.8 % of the images, respectively.

Parotid ducts appeared as structures of low intensity on GRASS images (81.8 %).

FLAIR (fluid-attenuated inversion-recovery) sequence: Hong et al. [8] evaluated the enhancement pattern of normal nerves in a 3 T MRI using FLAIR sequence. The details of the protocol were as follows: axial T_2 FLAIR acquisition, TR: 9500 ms, TE: 120 ms IT: 2250 ms and T1 FLAIR axial TR: 2600 ms, TE: 8.9, IT: 920 ms images, slice thickness: 3 mm and slice gaps: 0.1 mm were obtained. The facial nerve was divided into five anatomical segments for the evaluation of the enhancement patterns: (i) cisternal—internal auditory canalicular, (ii) labyrinthine, (iii) geniculate ganglion, (iv) tympanic and (v) mastoid or vertical. All 40 nerves (100 %) were visibly enhanced along at least one segment of the facial nerve. This is a striking result in nerve imaging, since the facial nerve is at least 2–4 times smaller than the RLN (Fig. 6.2).

PSIF-DWI (reversed fast imaging with steady-state precession with diffusion weighted imaging sequence: Chu et al. [9] utilized the 3D PSIF-DWI sequence at 3 T to image the intraparotid facial nerve. The details of the protocol were as follows: Parameters were as follows: T1WI: TR/TE: 520/15 ms; T2WI: TR/TE: 4000/80 ms, thickness: 3 mm; FOV: 240×240 mm, 3D-PSIF-DWI: TR/TE: 9.3/4.2 ms, thickness: 0.6 mm, FOV: 220×220 mm, flip angle: 35°, matrix size: 256×256, bandwidth: 446 Hz, spatial resolution: 0.6×0.6×0.6 mm, number of 3D partitions: 288, diffusion moment in the readout direction: 40 mT/m (*) ms, number of acquisitions: 1, acquisition time: 6 min 45 s (Fig. 6.3).

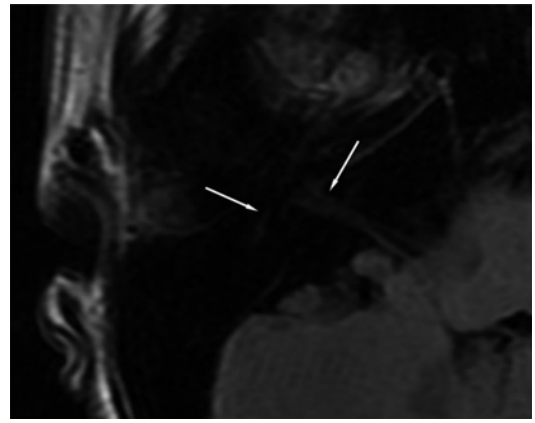

Fig. 6.2 Pre-contrast axial T1 fluid-attenuated inversion-recovery axial image of the facial nerve (*arrows*) at the cerebellopontine angle (CP) angle, left arrow is pointing to the tympanic segment of the facial nerve and the right arrow is pointing to the labyrinthine segment of the facial nerve [Reprinted from H. S. Hong, B.-H. Yi, J.-G. Cha, S.-J. Park, D. H. Kim, H. K. Lee, and J.-D. Lee. Enhancement pattern of the normal facial nerve at 3.0 T temporal MRI. Br. J. Radiol. 2010; 83(986): 118–21. With permission from British Institute of Radiology.]

Cranial Nerve Imaging

Anatomy

The cranial nerves are essential for vision, hearing, smell, and taste functions. There are 12 cranial nerves, of which 10 exit the brainstem from the ponto-mesencephalic junction to the medulla oblongata, travel through the perimesencephalic and basal cisterns, and exit the intracranial compartment through the neurovascular foramina of the skull base from anterior to posterior. Reports of cochlear nerve diameter range between 1.1–1.4 mm, which approximates 50 % the diameter of the RLN [10, 11].

MR Imaging

Several imaging sequences exist for cranial nerve imaging. For the cisternal segments, heavily T2W sequences are most useful to depict the nerves as hypointense structures surrounded by hyperintense CSF. Sequences such as CISS (constructive interference in steady-state), DRIVE (driven equilibrium radio frequency reset pulse), or FIESTA provide good CSF-nerve contrast and very thin image sections. To differentiate nerves from vessels, high-resolution time-of-flight MRA sequences (3D FISP or FLASH, fast low-angle shot) and/or contrast-enhanced MRA are sequences of choice. Some of the sequences that are commonly used are described below.

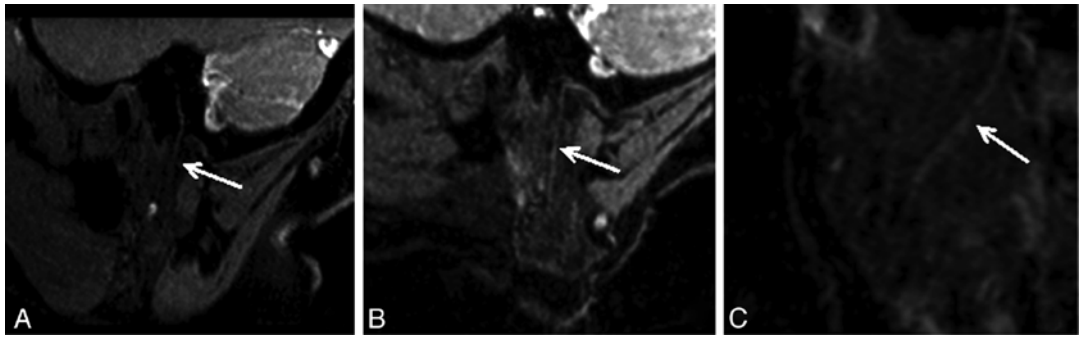

Fig. 6.3 3D-PSIF-DWI (**a**) Oblique sagittal MPR image shows the main trunk of the intraparotid facial nerve as a linear structure of high-signal intensity compared with the parotid gland (*arrow*). (**b**) Oblique sagittal MIP image shows the main trunk of the intraparotid facial nerve and cervicofacial division. (**c**) Oblique coronal MIP view also displays the main trunk of the intra-parotid facial nerve and cervicofacial division [Reprinted from J. Chu, Z. Zhou, G. Hong, J. Guan, S. Li, L. Rao, Q. Meng, and Z. Yang. High-resolution MRI of the intraparotid facial nerve based on a microsurface coil and a 3D reversed fast imaging with steady-state precession DWI sequence at 3 T. AJNR. Am. J. Neuroradiol. 2013; 34(8): 1643–8. With permission from Williams & Wilkins Co.]

T1-weighted MP-RAGE (magnetization prepared rapid gradient echo) sequence: Seitz et al. [12] described the use of a T1-weighted MP-RAGE sequence for imaging suspected lesions of the cranial nerves in 17 consecutive patients using a 1.5 T Siemens Magnetom Symphony MRI. Circular polarized head coil was used. The details of the protocol were as follows: Sagittal acquisition without and with IV contrast medium (0.1 mmol/kg b.w. Gd-DTPA, Magnevist; Schering), TR: 11.08 ms, TE: 4.3 ms, TI: 300 ms, flip angle: 150, band width: 130 Hz/pixel, slice thickness: 1 mm, pixel size: 1.2 × 0.9 mm, acquisition time 7 min 22 s. On a scale of 1–4 (1 = excellently visible, 2 = visible, 3 = barely visible, 4 = not visible), the average score for the MP-RAGE sequence for visualizing the lesions of the cranial nerves surrounded by CSF was 2.64 ± 0.49, while for cranial nerve lesions not surrounded by CSF, the visualization score was 2.57 ± 0.79.

T2 FSE (fast spin-echo) sequence: Yousry et al. [13] investigated the utility of T2 FSE sequence in identifying all the cranial nerves in their cisternal course. The imaging sequence was tested on 20 healthy volunteers using a 1.5 T Siemens Magnetom scanner. The details of the protocol were as follows: Axial and coronal acquisitions, TR: 2600 ms, TE: 17 ms, FOV: 260 × 234 mm, matrix size: 512 × 240, pixel size: 0.51 × 0.98 mm, slice thickness: 3 mm, interslice spacing: 0.3 mm, echo train length: 5, acquisitions: 4, acquisition time: 8.4 min. Using a T2 FSE sequence, nine (olfactory bulb, optic, oculomotor, trigeminal, facial, vestibulocochlear, glossopharyngeal, vagus, and accessories nerves) of the 12 cranial nerves could be identified with a variable degree of certainty. The olfactory bulb, optic, trigeminal, facial, and vestibulocochlear nerves were always (100 %) identified. In contrast, trochlear, abducens, and hypoglossal were usually not identified (Fig. 6.4).

3D FIESTA sequence: The 3D FIESTA sequence has been utilized by several groups to image the cranial nerves [14–16]. Hatipoğlu et al. [17] evaluated the utility of the 3D FIESTA sequence in the imaging of cisternal parts of cranial nerves. MRI imaging of 800 nerves in 50 patients were obtained using the 3D FIESTA sequence in a 1.5 T GE MRI. The details of the protocol were as follows: TR: 4.8 ms, TE: 1.4 ms, slice thickness: 0.5 mm, FOV: 18 × 18 cm; matrix: 352 × 192; NEX: 4. The visualization rates of all these cranial nerves (partially and completely visualized) with the 3D FIESTA sequence were as follows: trigeminal nerve = 100 %, abducens nerve = 98 %, facial nerve = 100 %, vestibulocochlear nerve = 100 %, lower cranial nerve complex glossopharyngeal, vagus, and accessory nerves = 100 %, hypoglossal nerve = 91 % (Fig. 6.5).

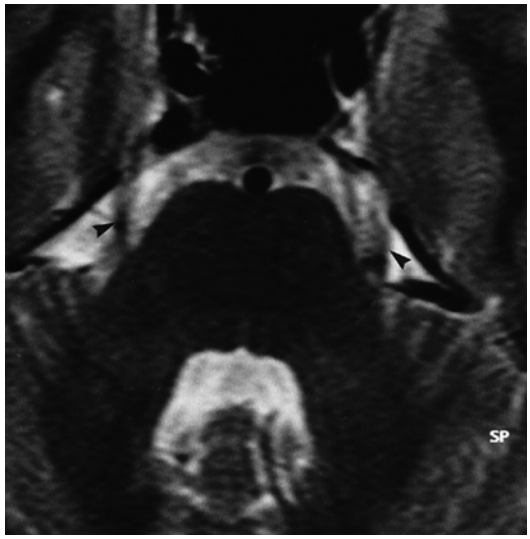

Fig. 6.4 Axial T2 FSE image showing the trigeminal nerve [Reprinted from Yousry, S. Camelio, U. D. Schmid, M. A. Horsfield, M. Wiesmann, H. Brückmann, and T. A. Yousry. Visualization of cranial nerves I-XII: value of 3D CISS and T2-weighted FSE sequences. Eur. Radiol. 2010;10(7): 1061–7. With permission from Springer Verlag]

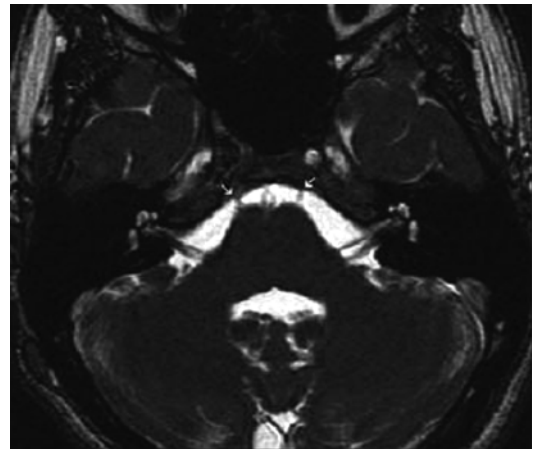

Fig. 6.5 Cranial nerve VI [Reprinted from H. G. Hatipoğlu, T. Durakoğlugil, D. Ciliz, and E. Yüksel. Comparison of FSE T2W and 3D FIESTA sequences in the evaluation of posterior fossa cranial nerves with MR cisternography. Diagn. Interv. Radiol. 2007; 13(2): 56–60. With permission from Turkish Society of Radiology.]

CISS sequence: The CISS sequence is the most effective method of visualizing the cranial nerves [12, 13, 18, 19]. Yagi et al. [18] evaluated the utility of 3D CISS MR imaging for visualizing cranial nerves in the cistern in 76 normal cavernous sinuses using a 1.5 T Siemens Magnetom scanner. For all patients, Gadodiamide hydrate (Omniscan; Daiichi Pharmaceutical Co., Tokyo, Japan) was administered at a dose of 0.1 mmol/kg body weight. The details of the protocol were as follows: TR: 11.84 ms, TE: 5.92 ms, NEX: 1, flip angle: 700, FOV: 180×180 mm, matrix: 256×224, 56 3D partitions, pixel size: 0.7×0.8 mm, slice thickness: 0.7 mm, acquisition time: 4 min 28 s. The authors report that the intracavernous segments of the oculomotor, trochlear, ophthalmic, maxillary, and abducens nerves were identified on contrast-enhanced 3D CISS MR imaging in 76 (100 %), 46 (61 %), 70 (92 %), 67 (88 %), and 73 (96 %) of the 76 cavernous sinuses, respectively (Fig. 6.6).

FISP (fast imaging with steady-state precession) sequence: Zhang et al. [20] have also reported the use of 3D PSIF-DWI MR sequence to delineate the normal anatomy of the cranial nerves and the adjacent structures. The sequence was tested on 22 healthy volunteers using a Siemens Magnetom Trio using a standard head-and-neck coil. The details of the protocol were as follows: TR: 9.26 ms, TE: 4.91 ms, flip angle: 350, matrix size: 448×448, field of view: 250×250 mm, bandwidth: 446 Hz, fat suppression, effective spatial resolution: 0.5×0.5×0.5 mm, diffusion moment: 20 mT/mxm-sec, number of acquisitions: 1, acquisition time: 9 min 59 s. The 3D-PSIF sequence appears to delineate the cranial nerves with high signal-to-noise ratios (SNR) and excellent contrast compared to the surrounding structures. It is claimed that in all subjects, the intracranial portions of all cranial nerves except the olfactory nerve and the extracranial portions of the cranial nerves were identified with high certainty (Fig. 6.7).

MR Imaging Techniques for the RLN

Imaging the RLN is fraught with several technical challenges, including physiological motion in the neck, which can obscure results and create radiologic artifacts. We have tried VIBE (volumetric interpolated brain examination), T1 and T2 TSE, MPRAGE, CISS and PSIF techniques in our effort to reliably image the RLN. After optimization,

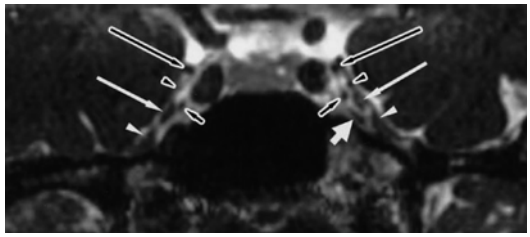

Fig. 6.6 Coronal view shows bilateral oculomotor (*long black arrow*), trochlear nerve (*black arrow head*), ophthalmic nerve (*long white arrow*), maxillary nerve (*white arrow head*), and abducens nerve (*short black arrow*) [Reprinted from Yagi, N. Sato, A. Taketomi, T. Nakajima, H. Morita, Y. Koyama, J. Aoki, and K. Endo. Normal cranial nerves in the cavernous sinuses: contrast-enhanced three-dimensional constructive interference in the steady state MR imaging. AJNR. Am. J. Neuroradiol. 2005;26(4): 946–50. With permission from Williams & Wilkins Co.]

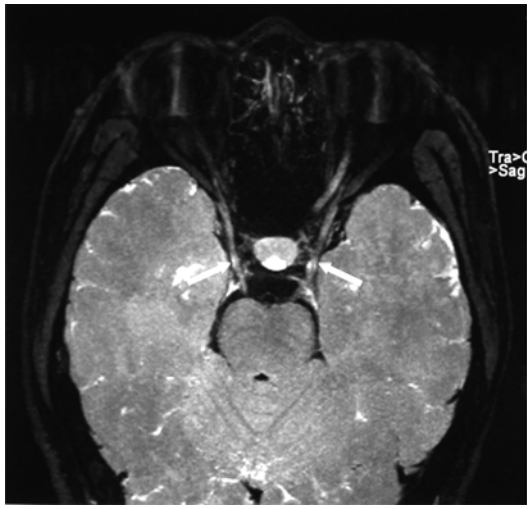

Fig. 6.7 Reconstructed MIP image showing the oculomotor nerve [Reprinted from Z. Zhang, Q. Meng, Y. Chen, Z. Li, B. Luo, Z. Yang, L. Mao, and E. Lin. 3-T imaging of the cranial nerves using three-dimensional reversed FISP with diffusion-weighted MR sequence. J. Magn. Reson. Imaging. 2008; 27(3): 454–8. With permission from John Wiley & Sons, Inc.]

CISS and T2 TSE appear to have the most promise. The imaging protocol helped highlight the fat surrounding the nerve, thereby allowing the clear distinction between the surrounding tissue and the nerve. In addition, a novel phase-navigated sequence can overcome the motion artifacts caused by physiological motions such as respiration and pulsatile motion. The following protocol details enable the best imaging results.

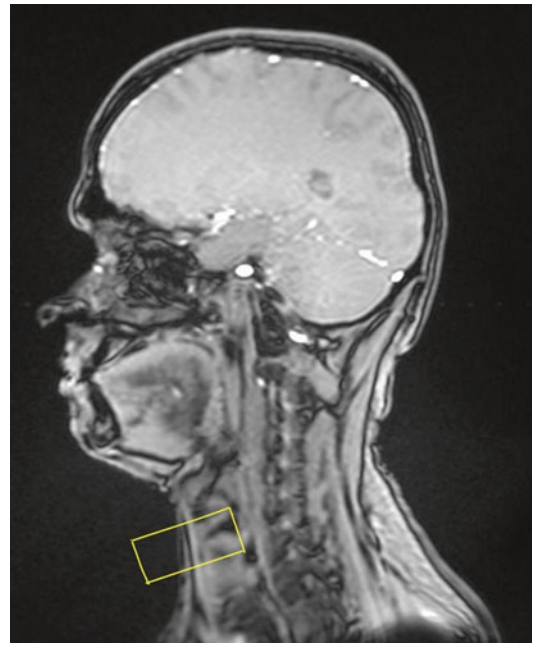

Fig. 6.8 Placement of the navigator

Patients should be placed in the supine position with the neck gently extended in a wide bore 3 T scanner. A 20-channel head–neck coil should be used along with body and spine matrix coils. The details of the CISS protocol were as follows: 3D acquisition, pixel size: 0.8 mm isotropic, FOV of 240 mm, TE: 2.2 ms, TR = 5 ms, pixel bandwidth = 505, flip angle = 42° without breath hold. A novel phase-navigated T2 TSE sequence was also used without fat saturation to accentuate the RLN. The details of the T2 TSE sequence: 2D acquisition, slice thickness = 2 mm, TR = 3991 ms, TE = 95 ms, number of averages = 3, number of phase encoding steps = 361, echo train length = 20, pixel bandwidth = 195, matrix size = 384 × 384, flip angle = 160°, pixel spacing = 0.52 × 0.52 mm. The novelty of the phase navigator lies in the ability to navigate on the larynx.

Figures 6.8 and 6.9 shows the placement of the navigator and the corresponding laryngeal motion. Figure 6.10 shows the RLN (indicated by a green arrow) and the vagus nerve (indicated by a red arrow) on the T2 TSE. The RLN was identified by tracing the vagus around the aortic arch. Figures. 6.11 and 6.12 are the sagittal views of T2 TSE and CISS and Figs. 6.13 and 6.14 are their corresponding axial views. As seen from

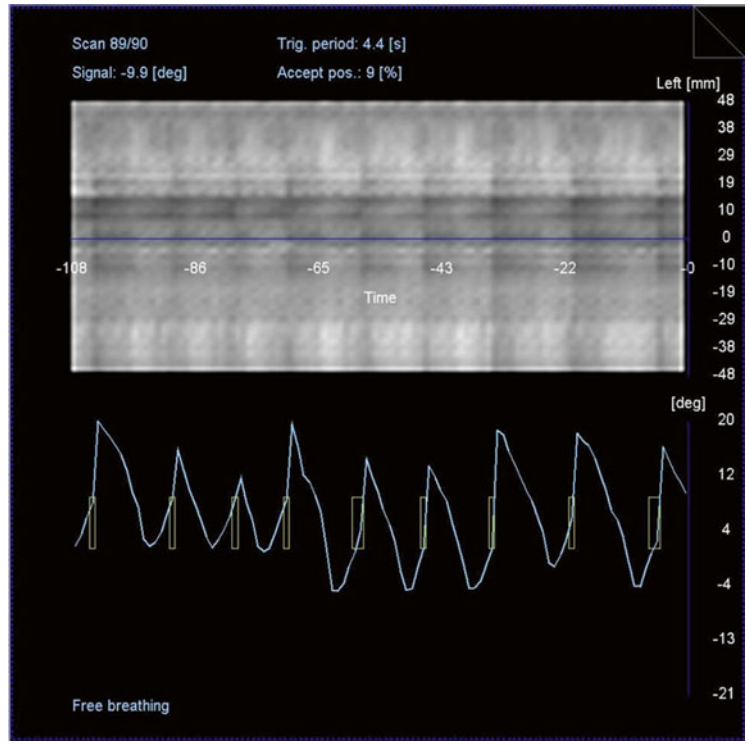

Fig. 6.9 Laryngeal motion as detected by the navigator

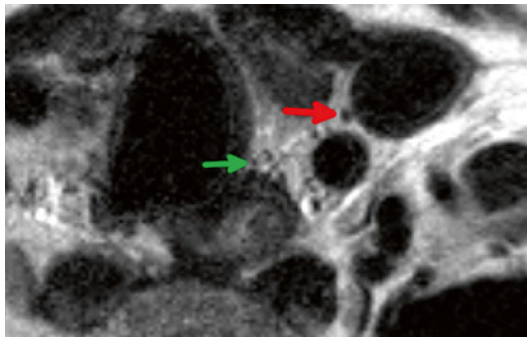

Fig. 6.10 *Green arrow* shows the recurrent laryngeal nerve. *Red arrow* shows the vagus nerve on T2 TSE

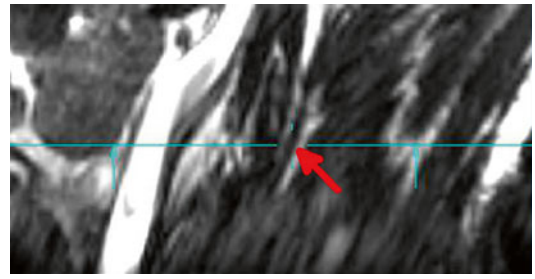

Fig. 6.12 Sagittal views of CISS sequence with the *red arrow* showing the Vagus nerve

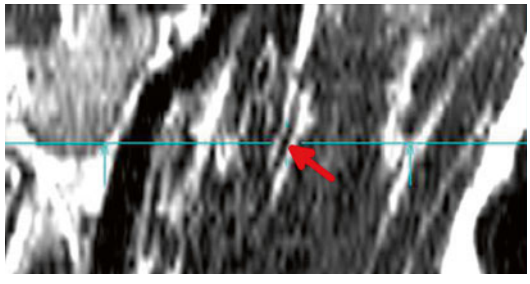

Fig. 6.11 Sagittal views of T2 TSE with the *red arrow* showing the Vagus nerve

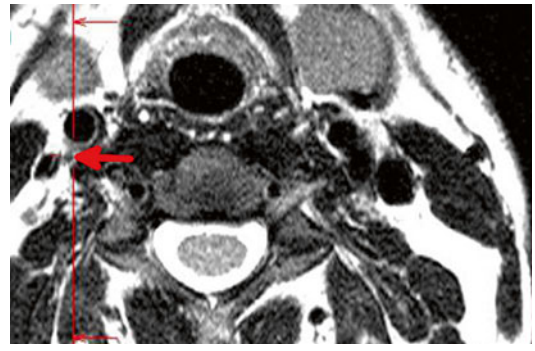

Fig. 6.13 Axial view of the T2 TSE sequence

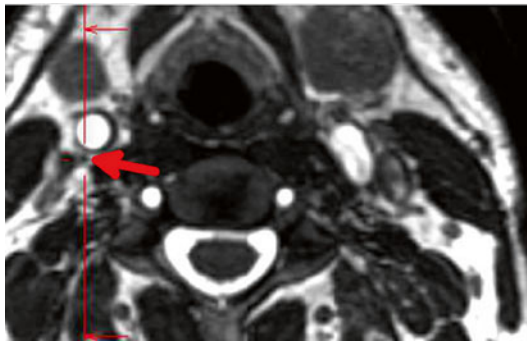

Fig. 6.14 Axial view of the CISS sequence

these images the vagus can be visualized on both T2 TSE and CISS (indicated by an arrow), however it is better delineated on the T2 TSE. The RLN and vagus can be visualized on the CISS and T2 TSE. However, due to the phase navigator, the nerves are better delineated on the motion-compensated T2 TSE.

Summary

The identification and preservation of the RLN is an essential goal of thyroid and parathyroid surgery. Imaging the RLN represents a promising adjunctive technique to assist surgeons in this respect with the potential to decrease RLN injury rates. The small diameter of the RLN and physiologic motion near the tracheoesophageal groove are substantial technical challenges to mapping the course of this nerve in a reliable and accurate manner. However, protocols to map the facial nerve, which is approximately 2–4 times smaller in diameter, are now published. Using the techniques that were optimized to visualize the facial and cranial nerves, MRI of the RLN is possible using the novel phase-navigated T2 TSE and CISS sequences. Ultimately, fine peripheral nerve MRI resolution should continue to improve over time with advances in MRI technology. Future studies will determine if surgical adjuncts, such as MRI, can reduce RLN injury rates in patients who require thyroid or parathyroid resection.

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Part III

RLN Surgical Anatomy

Gregory W. Randolph

RLN Nerve and Inferior Thyroid Crossing

7

Celestino Pio Lombardi, Marco Raffaelli, Carmela De Crea, Giulia Carnassale, and Rocco Bellantone

Abstract

One of the most important post thyroidectomy complications is recurrent laryngeal nerve (RLN) injury; the routine exposure and preservation of this important structure should be a standard procedure during thyroidectomy. Therefore, an accurate knowledge of the anatomy of the RLN and its anatomical abnormalities, variations, and relationship is fundamental for the thyroid surgeon. In particular, the relationship between the RLN and the inferior thyroid artery (ITA) is an important and helpful landmark for isolating the RLN and its branches during surgery.

Keywords

Recurrent laryngeal nerve • Inferior thyroid artery • Thyroid gland • Anatomic relationship • Thyroid surgery

RLN Anatomy

The course of the recurrent laryngeal nerve (RLN) is determined by the pattern of development of the arteries with which it becomes related, and the variations of this pattern will determine variations in the anatomical disposition of this nerve [1]. The usual course of the RLN differs in the two sides of the neck. The two nerves arise from the vagus nerve in the superior part of the thorax. The right nerve crosses the undersurface of the right subclavian artery and ascends in the neck to extend to the right tracheoesophageal groove. It may cross superficially or deeply to the inferior thyroid artery (ITA) or between its branches (Fig. 7.1). The left RLN hooks around the arch of the aorta and ascends more vertically in the left tracheoesophageal groove (Fig. 7.2). It may have a similar relationship to the left ITA, as the right nerve.

Furthermore, on rare occasions (0.3–0.8 %), the right inferior laryngeal nerve does not recur [2]. In these cases it originates from the cervical portion of the vagus nerve. Nonrecurrence of the right inferior laryngeal nerve results from a vascular

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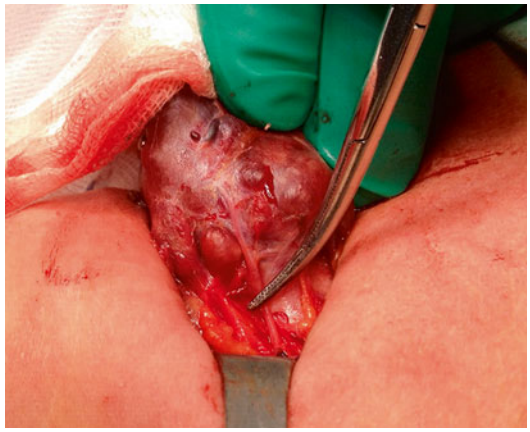

Fig. 7.1 Right recurrent nerve crossing deeply to the inferior thyroid artery

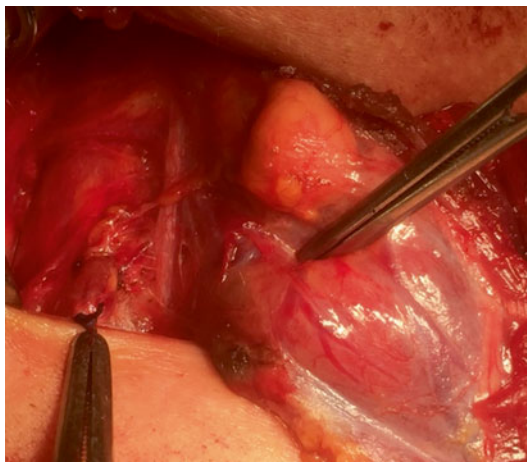

Fig. 7.2 The left recurrent nerve ascends vertically in the left tracheoesophageal groove

anomaly during the embryonic development of the aortic arches, determined by the absence of the innominate artery and the formation of an aberrant right subclavian artery that arises directly from the aorta left of the midline and crossing the esophagus [3]. This anatomic variant is exceptional on the left side [3]. Finally, the surgeon should also be aware that enlarged anastomic branches between the normal RLN and the cervical sympathetic chain may mimic a nonrecurrent laryngeal nerve (NRLN) in up to 7.5 % of the cases [4]. Another confounding condition is represented by small branches connecting an NRLN and the stellate sympathetic ganglion with a course that is similar to that of a normally recurring inferior laryngeal nerve [4].

Both right and left nerves enter the larynx at the cricothyroid articulation beneath the fibers of the inferior constrictor muscles of the pharynx. When approaching the inferior pole of the gland, the RLN may be deep or superficial to the ITA or may pass between the arterial ramifications. Indeed, one of the routine patterns for identifying the RLN is to find the ITA used as an anatomic landmark. However, because of the numerous variations of this neurovascular relationship altered also by pathologic conditions of the gland, identification of the artery does not assure consequent identification and preservation of the RLN in all circumstances. The incidence of injury to the RLN in thyroidectomies ranges from 0 to 11 % [5]. Damage to this nerve can cause important vocal, breathing, and swallowing difficulties. Moreover, the RLN palsy can be responsible for major psychological and social difficulties for patients [5]. According to Titche [6], thyroidectomy accounts for 35.71 % of surgical causes of injury to the RLN, and accounts for 3.73 % of all causes.

The ITA is tremendously important as it relates to RLN management during surgery. Transection injury may occur when a mistaken branch of the ITA is inadvertently sectioned. In an attempt to achieve hemostasis, the nerve is clipped and/or separated with the arterial branch [5]. A correct knowledge of its passage, of its anatomical relationships, and of the variations in regional neurovascular anatomy is essential in order to avoid an injury. The most important piece in preventing nerve injury is to know the course of the RLN and the relationship with the ITA.

Relationship of RLN and Inferior Thyroid Artery

The ITA comes off the thyrocervical trunk, the first branch of the subclavian artery. Then, the ITA ascends deep to all of the structures of the neck (including the carotid sheath) and descends toward the inferior pole of the thyroid gland behind the common carotid artery, and then branches within this central compartment. There typically are two

significant branches of the ITA: the anterior and posterior branches. The trunks and the branches of the ITA cross the RLN as it ascends toward the larynx [7]. However, the relationship of the RLN to the ITA is highly variable. The basic relationship, however, is that the artery and nerve intersect. The RLN may be deep or superficial, or may ramify branches of the artery. Unilateral or bilateral absence of the ITA is not a rare variation, and is described in 3–6 % of cases [8]. In the literature, there are several classification systems relating to the relationship between the RLN and the ITA and most of these studies were carried out in cadavers. Campos and Henriques [9] reviewed 17 studies performed between 1929 and 2000. They reported that most of the authors described three types of relationships between the RLN and the ITA, as follows: (1) the RLN anterior to the ITA; (2) the RLN posterior to the ITA; and (3) the RLN between the branches of the ITA. This review reported an overall higher incidence of the RLN being posterior relative to the ITA [9]. However Flament et al. [10] had observed a higher percentage of the relationship between the branches. Reed [11] described 28 different types of relationships; but, they were grouped within three main types described above. Freschi et al. [12] reported eight types of relationships. Campos et al. [9] found statistically significant difference in the distribution of these three types of relationships between right and left sides. On the right side in most cases, the RLN was found between the branches of the ITA, followed by, in decreasing order of frequency, positions anterior and posterior to the artery. On the left, the RLN was also placed more frequently between the branches of the ITA, followed by, in decreasing order of frequency, positions posterior and anterior to the ITA. In 62.68 % of the cases, the relationship found on one side did not occur again on the opposing side. There are authors who evaluate the distribution for each category according to sex. Lee et al. [13], found the distribution of RLN posterior to the ITA greater in females than in males (51.7 % vs. 38.8 %).

There are several noteworthy recent studies that investigated the relationship between the branches of RLN and the ITA. In particular, Sun et al. [14] described five types of relationships: Type A: the branches of the RLN are superficial to the arterial trunk or its branches; Type B: the branches of the RLN are between the arterial branches; Type C: the branches of the RLN are deep to the artery; Type D: the artery passing among the RLN branches; Type E: branches of RLN and ITA are interlaced.

Kulekci et al. [15] developed a classification based on RLN and ITA trunk anatomy and branching rather than the specific passage of the ITA anterior or posterior to the RLN. The six types are as follows: Type A, a relationship between the main trunk of the ITA and the main trunk of the RLN; Type B, a relationship between the branches of the ITA and the main trunk of the RLN; Type C, a relationship between the main trunk of the ITA and the branches of the RLN; Type D, a relationship between the branches of the ITA and the main trunk and branches of the RLN; Type E, a relationship between the branches of the ITA and the branches of the RLN; and Type F, no ITA. Yalçxin [16] also explored the RLN trunk and branch anatomic pattern, as well as the relationship between the extralaryngeal branching of the RLN and ITA and developed a detailed classification system of 20 subtypes. It is perhaps difficult for a surgeon to keep in mind a classification consisting of 20 subtypes in detail. Nonetheless, all of these 20 subtypes have been photographed and the relationship between the ITA and the branches of the RLN has been clearly demonstrated; this publication is a valuable reference for understanding the detailed relationship between the ITA and the RLN.

Some investigators [16] do not recommend the use of the ITA as the only landmark when searching for the nerve. This statement is based on the observation of variable pattern of branching between the RLN and the ITA and the potential of absence of the ITA. In this context, it is always recommended that, before ligating any vessels and resecting any thyroid tissue, the RLN should be exposed and identified, keeping the nerve in sight [17].

Surgeons and anatomists have explored various procedures and used many different techniques to protect the RLN from injury during thyroid surgery. Unfortunately, injury to the RLN still occurs and is the cause of disability and reduced quality of life with an impact on daily

and occupational functions, as well as being the most important reason of malpractice litigation [18]. The risk is greater with inexperience of the surgeon and insufficient knowledge of the anatomy of the RLN [19]. A particularly high-risk situation occurs when the RLN has distal ramifications occurring below or at the point at the ITA crossing point. In such cases, the risk is additionally higher if the artery is also divided into many ramifications close to its origin and branches of both the structures intertwine.

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Recurrent Laryngeal Nerve Branching

8

Manuel Durán, Jose Sañudo, Juan J. Sancho, Beata Wojtczak, Eva Maranillo, and Antonio Sitges-Serra

Abstract

Recurrent laryngeal nerve (RLN) dysfunction is among the most common and feared complications of thyroidectomy and is an increasingly common cause for malpractice suits against endocrine surgeons. Temporary or permanent vocal cord palsy may carry a significant burden of disease. Thorough knowledge of the normal anatomy and its variants, a meticulous surgical technique, and a gentle handling of tissues with routine identification of the RLN represent the standard of care for a safe thyroidectomy. Temporary palsy of the RLN occurs in up to 10 % of cases and permanent paralysis in <2 % of patients. Inadvertent injury to the nerve is directly influenced by the common anatomic variations of the RLN along its expected and unexpected cervical course. These variations include the extralaryngeal bifurcation of the RLN that constitutes a frequent event present in up to 30–40 % of cases. Branching of the nerve typically occurs at the level of the ligament of Berry along the distal 1 or 2 cm of the RLN cervical course before its entry into the larynx. Branching of the RLN represents a major risk factor for both transient and permanent nerve palsy. Thus, intraoperative recognition and verification of functional and anatomic integrity of premature division of the nerve is crucial during thyroid operations. Initial studies using intraoperative nerve monitoring suggest

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that the anterior branch of the bifid RLNs is the one supplying motor fibers to the posterior cricoarytenoid muscle and vocalis muscle. Identification, exposure, and preservation of extralaryngeal branches of the RLN are mandatory and represent basic surgical principles in thyroid surgery to prevent nerve injury and its associated morbidity.

Keywords
Recurrent laryngeal nerve • Anatomy • Extralaryngeal branching • Intraoperative nerve monitoring • Vocal cord paralysis • Thyroidectomy

Introduction

The successful surgical treatment of thyroid disease is based on a thorough knowledge of the surgical anatomy and pathology of the thyroid gland, a meticulous surgical technique with anatomic and functional preservation of the recurrent laryngeal nerve (RLN), and an adequate hemostasis during the entire procedure. The fulfillment of these three premises is critical to ensure the success and safety of thyroidectomy.

Although uncommon in expert hands, iatrogenic injury to the RLN is one of the major complications of thyroidectomy leading to temporary or permanent vocal cord dysfunction often associated with aspiration and dysphagia. Several factors influence the likelihood of injury to the RLN including the underlying disease with special mention to large goiters, revision surgery, the extent of thyroid resection, and surgeon's experience. Patients with injury to one nerve may be asymptomatic but often complain of hoarseness and, to a lesser extent, swallowing difficulties. Both of these symptoms are due to incompetent glottic function. Bilateral nerve injury is an uncommon (0.1–0.5 %) but serious complication associated with voice impairment and different degrees of respiratory distress due to glottic narrowing. It may lead to a dramatic scenario with severe acute upper airway obstruction requiring reintubation and/or emergency tracheostomy.

RLN dysfunction is among the most frequent causes of medicolegal litigation after thyroid and parathyroid surgery; transient paralysis occurs in up to 10 % of cases and permanent vocal cord dysfunction up to 2 % [1–3]. The severity of symptoms after RLN injury is influenced by the degree of nerve injury (neurapraxia, axonotmesis, or neurotmesis), ability of regeneration of the nerve, and compensatory functional laryngeal reserve.

Detailed and comprehensive knowledge of the RLNs' anatomic relationships and variations is of paramount importance in order to avoid nerve injury during thyroidectomy. Anatomical variations of RLN through its cervical course, particularly if unexpected [4], are a well-known risk factor for nerve injury. These include the variable course of the RLN at the level of the inferior thyroid artery hilum, the ligament of Berry, its course along the tracheoesophageal groove, the Zuckerkandl's tubercle, the nonrecurrent laryngeal nerve (NRLN) and extralaryngeal bifurcation [5, 6]. In addition, disease-related factors such as large multinodular goiter or massive nodal metastasis in compartment VI from papillary or medullary cancer do influence the anatomy of the RLN. In order to avoid injury to the RLN, the surgeon should be familiar with these variations and very cautious when looking for the RLN, particularly if he or she suspects that the nerve branches below or at the level of its crossing with the inferior thyroid artery.

Since the work of Lahey [7], the identification, careful dissection, and preservation of the RLN are thought to be mandatory to prevent vocal cord paralysis (VCP). This may be particularly true for the vulnerable branched RLNs.

The prevalence and clinical significance of extralaryngeal RLN branching have been described in the literature but few references to this subject are made in textbooks of general and

endocrine surgery [8]. The aim of this chapter is to define and discuss the anatomical relevance of extralaryngeal RLN branching and its surgical and clinical implications.

RLN Anatomy

The RLN arises from the vagus nerve at the level of the arch of the aorta on the left and the right subclavian artery on the right. The nerve becomes recurrent by turning back on itself in the chest emerging superiorly back into the central neck to provide motor innervation to all laryngeal intrinsic muscles except the cricothyroid muscle (CTM). Both RLNs emerge from the superior thoracic outlet behind the common carotid artery and ascend along the tracheoesophageal groove in a triangle bounded medially by the trachea and esophagus and laterally by the internal jugular vein and common carotid artery to enter the larynx [9, 10] (Fig. 8.1). The right and left RLNs have different anatomical courses. The mean diameter of the RLN ranges from 1 to 3 mm. The left nerve is longer, usually 12 cm between its origin in the vagus nerve and its entrance into the larynx, whereas on the right side is approximately 7 cm long from where it winds around the subclavian artery to the larynx [11].

Three anatomical landmarks are useful to identify the RLN: the inferior thyroid artery, the tracheoesophageal groove, and the laryngeal entry point (cricothyroid joint). Surgeons should be experienced in using these three landmarks to approach the nerve through different routes as required according to the specific anatomy of each case. Whenever possible we recommend the inferior approach below the main trunk of the inferior thyroid artery where RLN branching can be easily detected.

The anatomical relationship between the RLN, the trachea and the esophagus varies between left and right sides and patient to patient. The right RLN runs more laterally in the aforementioned triangle with a more oblique course in the neck in comparison with the left RLN that has a vertical course and ascends medially along the tracheoesophageal groove.

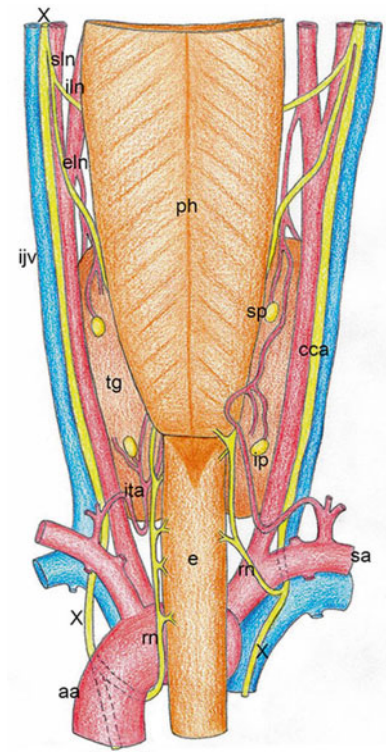

Fig. 8.1 Posterior view of the pharynx (ph), esophagus (e) and the thyroid gland (tg) flanked by the common carotid arteries (cca), internal jugular veins (ijv) and the vagus nerve (X). Note the relationships of both recurrent laryngeal nerves (rn) with different anatomical landmarks, especially with the inferior thyroid arteries (ita). Note the location of the superior (sp) and inferior (ip) parathyroid glands. The internal (iln) and external (eln) laryngeal branches of the superior laryngeal nerve (sln) emerging from the vagus nerve are also shown. (*aa* aortic arch, *sa* subclavian artery) [Courtesy of Jose Sañudo, PhD]

On their way to the larynx, both nerves cross the branches of the inferior thyroid artery exhibiting much anatomical variation that makes them vulnerable, particularly on the right side where the nerve is anterior to the artery in over 40 % of cases. Even so, the relationship of the RLN to the inferior thyroid artery is a commonly used landmark to identify the nerve [12].

The RLN ascends and becomes paratracheal in its last segment and then runs underneath the inferior constrictor muscle to reach the entry point into the larynx at the inferior edge of the thyroid cartilage (inferior cornu). The entry point into the larynx is considered the most constant

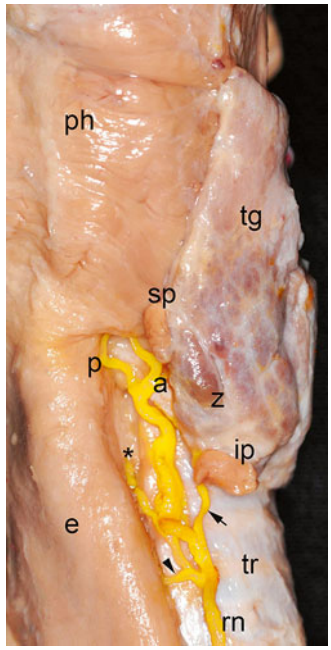

Fig. 8.2 Lateral view of a right side of the neck in a human adult cadaver showing the right thyroid lobe (tg: thyroid gland) and its relations to the pharynx (ph), esophagus (e), and trachea (tr). The distal course of the right recurrent laryngeal nerve (rn) is observed ascending in the tracheoesophageal groove. The rn along its cervical course gives off esophageal (*arrow head*), glandular (arrow), and tracheal (*asterisk*) branches previous to its terminal division in two branches, anterior (a) and posterior (p) branch, before entering the larynx. Superior (sp) and inferior (ip) parathyroid glands and the Zuckerkandl's tubercle (z) are also shown

landmark for nerve identification in thyroid surgery since the course of the RLN at this level is not subject to distortion regardless of the thyroid pathology [13, 14]. All along its cervical course, the RLN gives off multiple branches, the majority of which are of sensory nature to the trachea, esophagus, hypopharynx, and larynx (Fig. 8.2). Their clinical significance is far from being understood but may be involved in aerodigestive symptoms after thyroidectomy [15].

The RLN is most prone to injury in the last 2 cm before it enters the larynx in the vicinity of the ligament of Berry.

A dangerous anatomic variation of the RLN is the presence of a NRLN [16]. A NRLN nearly always occurs on the right side and has been reported in 0.5–1 % of cases. It originates as a direct medial branch from the cervical portion of the vagus nerve in association with an absence of development of the fourth right aortic arch during the embryonic development, and a retroesophageal right subclavian artery [9, 17, 18]. The presence of a left-sided NRLN is extremely rare and is associated with a situs inversus totalis [19–21]. Intraoperative identification and preservation of a NRLN can be a challenging task. The rarity of this entity makes it extremely vulnerable especially if it is mistaken for a branch of the inferior thyroid artery or it is included in the ligature or clamping of the superior pole vessels. Visual misidentification, therefore, plays an important role in the occurrence of nerve injury.

Extralaryngeal RLN Branching

The existence of thin sensory extralaryngeal branches originating from the RLN has been reported in up to 90 % of cases and underlines the importance of a comprehensive knowledge of neural anatomy and its variations [22]. The most relevant branching, however, is the bifurcation of the main RLN trunk into two (occasionally three) laryngeal branches. Its prevalence in cadaver and surgical dissection series varies between 30 and 76 % of cases [8, 23–28]. This vast range may probably be due to the fact that eventually all RLNs bifurcate just after entering the larynx. From a clinical and surgical standpoint, the relevant branching is the one occurring before the laryngeal entry point. Branches that contain motor fibers to the laryngeal intrinsic musculature enter the larynx in close relation with the lowest fibers of the inferior constrictor muscle and are responsible for laryngeal motor function as opposed to the sensory or extralaryngeal motor branches. The terminal division of the RLN should always be identified and preserved during surgery. Knowledge of this terminal division of the RLN is crucial and of major importance for the safety of thyroidectomy.

Branching of the nerve typically occurs along its cervical course in the last 2 cm (distal RLN segment) prior to laryngeal entry at the level of the ligament of Berry and above the intersection of

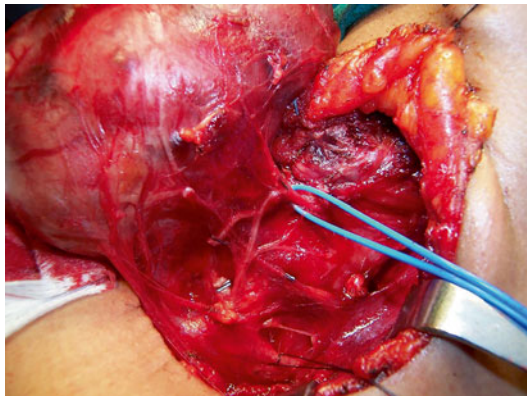

Fig. 8.3 Branching of the left recurrent laryngeal nerve (*blue loop*) above its intersection with the inferior thyroid artery (*also in loop*). Note the close relationship of the anterior branch of the nerve with an ascending retroneural branch of the inferior thyroid artery

the RLN and the inferior thyroid artery in 90 % of cases [8, 11, 13, 29] (Fig. 8.3). Serpell et al. measured the branching point distance defined as the distance from the anatomical point of RLN bifurcation to its entrance into the larynx under the inferior constrictor muscle. The median branching distance was 18 mm on the right and 13 mm on the left with a range of 5–34 mm [8, 30]. Asgharpour et al. studying the neck of 143 human adult cadavers reported an extralaryngeal division of the RLN at a mean distance from the inferior horn of the thyroid cartilage of 13 mm on the right side and 12.6 mm on the left side with a similar caliber in both sides [11]. Kandil et al. recorded a median branching distance of 6.33 mm on the right and of 6.37 mm on the left [31]. Therefore, division of the RLN, when present, usually occurs close to the ligament of Berry where it becomes particularly vulnerable [8, 16, 32]. Routine inspection at this point to identify branching of the RLN is essential to avoid injury to the nerve. RLN branching is uncommon below the inferior thyroid artery but should always be suspected when a thin "main trunk" is identified. At this stage, it is worth dissecting the nerve retrograde to make sure that the identified RLN is not the posterior branch of a very proximally bifurcated RLN.

Gurleyik has proposed a classification of extralaryngeal terminal division of the RLN based on surgical exposition steps of the entire nerve through its cervical course and on the different anatomic landmarks of the division point. The location of the bifurcation point divides the RLN along its cervical course in four segments: arterial, post-arterial, pre-laryngeal and pre-arterial [33, 34]. In type 1 (arterial; 46.3 %), division occurs near inferior thyroid artery. In type 2 (post-arterial; 31.5 %), division is found on post-arterial segment. In type 3 (prelaryngeal; 11 %), division is located very close to laryngeal entry point. In type 4 (prearterial; 11 %), bifurcation takes place before the nerve crossing the inferior thyroid artery. Increasing the surgeon's awareness of these variations may lead to exposing bifurcated nerves safely, preventing injury to extralaryngeal terminal branches of the RLN.

RLN branching may occur unilaterally or bilaterally [27, 31, 33–35]. RLN division rates and patterns may vary from side to side in the same patient. In a recent study of 292 bifid nerves [34], unilateral bifurcation was observed in 71.4 % and bilateral bifurcation in 28.6 % of patients undergoing thyroidectomy [8, 30, 31, 35].

Benegarama et al. [8] identified a higher rate of bifurcation and trifurcation of the right RLN compared with the left RLN, which is in agreement with previous studies [4, 8, 11, 30, 31, 35]. Explanations of these variations from side to side in branching pattern can be attributed to embryological differences regarding the different recurrent course of each nerve in the chest and its position in the neck. Due to the higher incidence of bifurcation and the presence of more complex surgical field on the right side as compared to the left side the right RLN is at higher risk of injury during surgery. Other authors have reported a more commonly bifurcated nerve on the left side [33, 36]. Anatomical differences between both nerves may justify the higher rate at the left side. The left RLN is longer, usually 12 cm from where it turns around the aortic arch, than the right one which winds around the right subclavian artery.

A great disparity of branching pattern has been reported in literature. Although most bifid RLNs have two branches [8, 27, 33], up to eight terminal branches have been described [8, 11, 26, 28, 37–40] (Fig. 8.4). Fontenot et al. [13] in a retrospective study of 719 RLNs in 491 patients described racial and gender variations in the prevalence of RLN branching. African-American

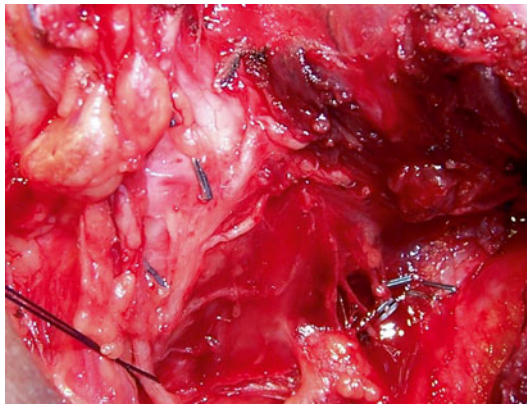

Fig. 8.4 Multibranched left recurrent laryngeal nerve crossing the main trunk of the inferior thyroid artery (looped) in a posterior course along the tracheoesophageal groove

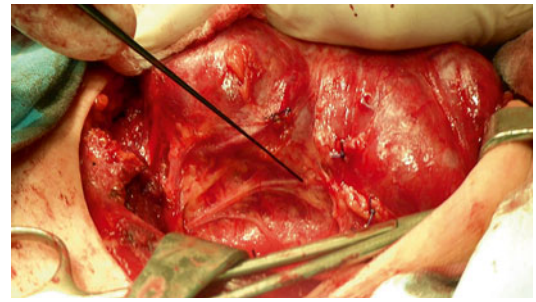

Fig. 8.5 The left recurrent laryngeal nerve before entering the larynx divides into numerous branches. The nerve stimulation probe is stimulating the anterior branch

patients had a higher rate of bifurcation (42.1 %) compared with Caucasians (33.2 %) which leads to a collective greater risk of nerve injury within this population. Distance from the bifurcation point to the nerve entry into the larynx was measured in both populations with an average of 10.07 ± 0.55 mm in African-American patients compared to 11.15 ± 0.91 mm in Caucasians, a nonsignificant difference. Female patients presented RLNs that bifurcated at longer distances from the laryngeal entry point resulting in greater lengths of bifid nerves. In conclusion, gender and race characteristics of branched RLNs could be considered risk factors for nerve injury as female patients with longer courses of bifid nerves and African-American patients with a higher frequency of branched nerves could justify this particular propensity for nerve damage.

Extralaryngeal RLN Branching and Intraoperative Nerve Monitoring

Routine dissection and visual identification of the RLN have reduced the rates of permanent RLN palsy during thyroid operations. Unexpected RLN palsy, however, still occurs even at high-volume units. Inadvertent injury to the RLN may happen despite the surgeon believing that the nerve was preserved with full anatomic integrity after surgery. In addition, most nerve injuries are not fully recognized intraoperatively and visualization of the nerve alone is insufficient to assess for nerve damage. This is especially important if the surgeon is not aware that the RLN has bifurcated before entering the larynx.

Intraoperative neuromonitoring (IONM) of the RLN represents an adjunct to direct visualization of the nerve during surgery and provides a broader vision of surgical anatomy incorporating functional information into surgical practice, based on the analysis of electromyography (EMG) data [2]. Nerve monitoring during surgery allows the transformation of laryngeal muscle activity into audible and visual EMG signals whenever the RLN or vagus nerve is stimulated intraoperatively [41]. The rationale for routine use of IONM in thyroid surgery is based on three main aims: identification of the nerve during dissection (including neural mapping), aid in dissection especially in difficult areas (e.g., reoperative surgery), and the intraoperative prognostication of postoperative nerve function [41–44].

IONM is of particular interest, especially when extralaryngeal branching is present, serving as an aid to identification and to the assessment of the functional status of the RLN. Nerve stimulation may be used to avoid visual misidentification of extralaryngeal branches and to assess their function since visual identification is insufficient to predict RLN integrity [29]. Neural monitoring allows the surgeon to differentiate between sensory or extralaryngeal branches and the main motor branch; the use of IONM allows anatomical identification and location of the

motor fibers in the branched RLN (Fig. 8.5). Very proximal division of laryngeal motor fibers may be detected with the use of IONM. Such premature extralaryngeal motor fiber branching may occur in up to 10 % of patients and is a well-known cause of RLN injury.

Functional Variability of RLN Branches

When extralaryngeal RLN branching is present, functional activity of individual branches has been reported very unevenly in the medical literature. It was previously thought that when extralaryngeal branching of the RLN was present, the anterior branch contained adductor fibers and the abductor fibers were located in the posterior branch [45–48]. Some reports even described that the anterior branch contains the motor fibers for both the adduction and abduction of the vocal folds and the posterior branch contains the sensory fibers [4, 8, 11, 30, 31, 40, 49]. In 1951, Sunderland and Swaney postulated that both branches contain a mixture of sensory and motor fibers suggesting that both abductor and adductor muscles might be innervated by either branch or both [50]. These results are in agreement with the study of 90 cadaveric and 13 intraoperative (laryngectomy) studies by Sañudo's group. This group investigated the anatomy and functional relevance of the connecting fibers between laryngeal nerves and the implication of these anastomoses in the motor and sensory supply of the larynx with special emphasis in the functional activity of intralaryngeal RLN branching and Galen's anastomosis [51, 52] (Fig. 8.6).

Maranillo et al. [53] studied the posterior cricoarytenoid muscle (PCA) nerve supply in 75 cadaveric human larynxes. In all cases, a nerve supply to the PCA from the anterior branch of the RLN was identified; in six cases (4 %), a small branch also arose from the ramus anastomoticus (posterior division of the RLN) highlighting the variability of functional activity of terminal branches of the RLN.

Nerve monitoring has made a definitive contribution to the study of the motor activity of RLN branches. In a prospective in vivo study of 838 RLNs, Serpell et al. [30] concluded that in all

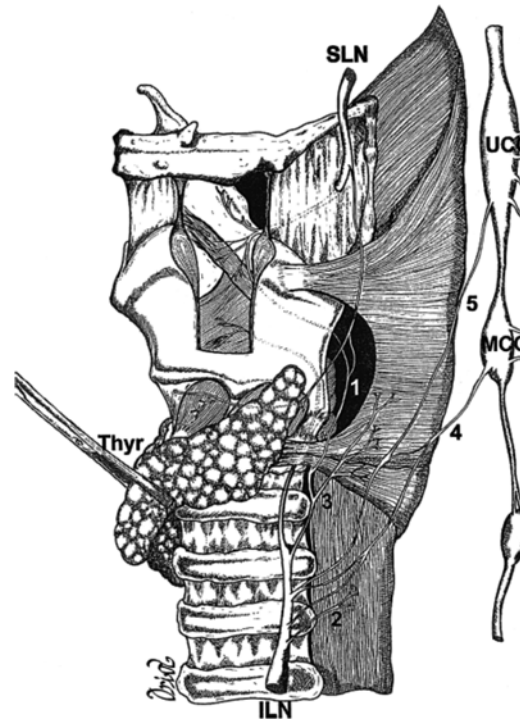

Fig. 8.6 Lateral view of a left hemineck showing the complex anatomic arrangement of perivisceral cervical neural plexus involving the autonomic innervation and the two major laryngeal nerves. UCG, Upper cervical ganglion; MCG, middle cervical ganglion; SLN, superior laryngeal nerve; ILN, inferior laryngeal nerve; Thyr, thyroid gland; *1* Galen's anastomosis; *2* esophageal branch; *3* pharyngeal branch; *4–5*, anastomotic branches between ILN, UCG, and MCG [Reprinted from Pereira JA, Girvent M, Sancho JJ, Parada C, Sitges-Serra A. Prevalence of long-term upper aerodigestive symptoms after uncomplicated bilateral thyroidectomy. Surgery 2003; 133(3): 318–22. With permission from Elsevier.]

the branched RLNs assessed by IONM and finger palpation for detection of laryngeal twitch, motor fibers for adduction and abduction were located exclusively in the anterior branch. This is in agreement with the study of Kandil et al. in which the functional motor branches for the larynx muscles, excluding the cricothyroid, were located in the anterior extralaryngeal branch of the RLN [4, 31]. Although more studies are probably needed to confirm these findings in a larger number of cases, these pioneering findings are of paramount importance for the practicing surgeon.

The human RLN is composed of 2000–3000 myelinated fibers. Its anterior division contains between 500 and 1000 myelinated axons, 25 % of

which innervate the PCA and the other 75 %, which innervate the adductors of the vocal folds [48, 54]. The RLN in its proximal course is composed of nearly half motor fibers and half sensory fibers. The percentage of motor fibers rises to 80 % distally at the entry into the larynx with sensory fibers having branched to neighbor locations [48].

Fontenot et al. in their study identified three patients whose posterior RLN branch produced an evoked motor response on IONM stimulation similar to the corresponding responses of anterior branches suggesting a shared functional motor activity between both branches of the RLN [13].

In order to understand the functional significance and variability of extralaryngeal RLN branching and to correctly interpret the information provided by IONM, the thyroid surgeon must have a thorough knowledge of the surgical anatomy and variations of RLN and the superior laryngeal nerve (SLN) and the interconnections between both. A recent study by Martín-Oviedo et al. [52] has shown that laryngeal functional neuroanatomy is more complex than that of classical anatomic cadaveric descriptions providing a new vision of the functional role of human laryngeal nerve connections and their implications in the mobility of the vocal folds. The variability of connections between the SLN and RLN [51, 55] may explain the different clinical scenarios and the variable position of the vocal folds observed after laryngeal nerve injuries at laryngoscopy in the postoperative period.

RLN Branching and Vocal Cord Paralysis

Routine identification and dissection of the RLN are considered as the gold standard for intraoperative care for reducing the chance of injury [7, 57–60]. Numerous mechanisms for nerve injury have been proposed including distension-stretching, compression, devascularization, heat, crushing, transection, electrical injury, edema or more rarely, infective causes or toxic neuritis [32, 61]. Neurapraxia appears to be the main pathophysiological mechanism of injury to the RLN during surgery. Serpell's group has reported that RLN diameter significantly increases during thyroidectomy with a mean diameter difference between RLN at initial identification and RLN at the completion of lobectomy of 0.71 mm, due to edema; this was accompanied by a paradoxical increase of EMG amplitude on RLN stimulation [62]. Neurapraxia due to stretching and excessive tension of the nerve (as happens during medial retraction of the thyroid lobe by the assistant) may result from ischemia and myelin sheath damage with interruption of nerve conduction despite intact axons.

In the study by Serpell et al. [63], nerve diameter increased most in the last 2 cm of its extralaryngeal course which corresponds with the most vulnerable area for nerve injury. This, however, could not be correlated with a higher incidence of transient RLN palsy (3 %), but might explain voice changes in the absence of RLN palsy [62]. In a further study by the same group, right and left sided differential rates of post-thyroidectomy RLN palsies were shown to be partly due to different RLN diameters; the thinner the nerve, the more prone it was to injury. Thus, RLN diameter changes appear to play an important role in the etiological mechanism of RLN neurapraxia.

This may explain why branched nerves are more easily injured during dissection [35]. Bifurcated branches are thinner than the main trunk of the RLN, more fragile and have less neural coverage (epineuria) along its distal course [13]. A thin RLN should alert the surgeon of the possibility of a branched RLN. Extralaryngeal RLN is often observed bilaterally, with different location points of bifurcation in the left and right sides. Therefore, nerve damage can affect both sides of the neck leading to possible bilateral RLN palsy. RLNs that divide early and follow a bifid course before their entrance into the larynx have a higher risk of injury during dissection compared to unbranched nerves.

Sancho et al. [64] assessed the impact of surgical injury to the branches of the RLN on vocal cord dysfunction in an observational study of 188

patients with 302 RLNs at risk. They reported extralaryngeal bifurcation in 37.4 % of 302 nerves at risk. The branches of dysfunctional nerves were significantly longer than those of functioning nerves (29.4 ± 10 vs. 19.1 ± 9.8 mm; $P = 0.003$). Thinner anterior branches suffered a similar or greater amount of manipulation-mobilization stress than non-branched RLNs but showed a higher proportion of VCP. Cord dysfunction (paralysis or paresis) was almost two times as common in patients with branched nerves than those with unbranched nerves (15.8 % vs. 8.1 %; $P = 0.022$). They concluded that branched nerves suffered more injuries during surgical interventions and were more likely to be associated with vocal cord dysfunction (two-fold higher risk) than unbranched RLNs. This work further emphasizes the need to intraoperatively recognize RLN bifurcation and to proceed with much care when dissecting the thin anterior branch that, which is now known to contain motor fibers. In this setting, IONM could eventually play a role in the reduction of VCP by assisting the surgeon in identifying a proximal branching and in assessing the nerve function during RLN dissection. Casella and his colleagues confirmed Sancho et al.'s findings by similarly showing that branched nerves are at increased risk of injury during surgery: the presence of a branched RLN was associated with a 7–13 times increased rate of transient and permanent nerve paralysis compared to non-branched RLNs [35].

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The Recurrent Laryngeal Nerve and the Tubercle of Zuckerkandl

9

Steven R. Bomeli, Beata Wojtczak, Hisham Abdullah, Romain E. Kania, and David J. Terris

Abstract

The tubercle of Zuckerkandl is the posterior and lateral projection of the thyroid gland. It was originally described by anatomists, and later became of interest to thyroid and parathyroid surgeons because of its close proximity to the recurrent laryngeal nerve and the superior parathyroid gland. It is more frequently found on the right side of the body, and when found bilaterally it is often larger on the right. It has been postulated that an enlarged tubercle of Zuckerkandl can cause symptoms of compression even in the absence of a large goiter, but it is clinically significant because of its use as a landmark for finding the recurrent laryngeal nerve and the superior parathyroid gland during surgery.

Keywords

Zuckerkandl • Tubercle • Recurrent laryngeal nerve • Superior parathyroid gland

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Fig. 9.1 Emil Zuckerkandl (1849–1910) [Reprinted from Shoja MM, Tubbs RS, Loukas M, Shokouhi G, Jerry Oakes W. Emil Zuckerkandl (1849–1910): anatomist and pathologist. *Annals of Anatomy—Anatomischer Anzeiger: Official Organ of the Anatomische Gesellschaft* 2008; 190(1): 33–6, with permission from Elsevier.]

Introduction

The structure now known as the tubercle of Zuckerkandl was originally recognized in 1867 by a German surgeon named Otto Wilhelm Madelung [1]. At that time, it was described as the "posterior horn of the thyroid," but it was later redefined by Emil Zuckerkandl, whose name the eponym reflects, as the "tuberculum" or the "processus posterior glandulae thyroideae" [2]. Though interesting to anatomists at that time, it was largely unknown to surgeons until more recent times because of its close proximity to the superior parathyroid gland and especially because of its relationship to the recurrent laryngeal nerve.

History

Emil Zuckerkandl (1849–1910) was an Austrian anatomist and pathologist at the Vienna School of anatomy (Fig. 9.1). He began studying medicine at the University of Vienna in 1867, and obtained his degree in 1874. He studied under anatomist Joseph Hyrtl (1810–1894), worked closely with Carl Freiherr von Rokitansky (1804–1878) and Carl von Langer (1819–1887), and ultimately became chair of anatomy at the University of Vienna. Though his study encompassed the entire body, he is well known for his contributions to head and neck anatomy, particularly normal and pathological sinonasal anatomy [3].

In addition to the tubercle of Zuckerkandl which is part of the thyroid gland, his name is honored through several eponyms throughout the medical literature: the organ of Zuckerkandl (para-aortic chromaffin body), Zuckerkandl's fascia (posterior layer of the renal fascia), Zuckerkandl's gyrus (subcallosal area), Zuckerkandl's operation (perineal prostatectomy), Zuckerkandl's dehiscence (fissures in the ethmoid bone), and concha of Zuckerkandl (a rare nasal concha). Though his name is well known to endocrine surgeons for his study of the thyroid gland, he is best remembered for his descriptions of chromaffin tissue found in the para-aortic location, which represent the largest concentrations of extra-adrenal paraganglia of sympathetic origin. He was a prolific writer, publishing 164 manuscripts before the time of his death.

The portion of the thyroid which projects laterally and posteriorly near the location of the juncture of the thyroid and cricoid cartilages is now known as the tubercle of Zuckerkandl. The first description of the structure dates back to 1867, when a German surgeon Otto Wilhelm Madelung described it as a "posterior horn of the thyroid" [1]. The eponym was chosen based on the published description of the structure by Emil Zuckerkandl in 1902 as a posterior projection of thyroid tissue described as the "tuberculum" or the "processus posterior glandulae thyroideae" [2].

Embryology

The thyroid gland develops during the fifth week of gestation with the fusion of the paired lateral thyroid anlages and the larger medial thyroid anlage [4]. There is some controversy over the fusion process, as well as the exact origin of the involved tissues [5]. The remnant of the lateral portion comprises the tubercle, which arises

embryologically from the ultimobranchial body of the fourth branchial cleft [6]. There is a high concentration of parafollicular C-cells in this location, as they originate from the lateral thyroid anlage [7]. The superior parathyroid glands originate as a proliferation of the dorsal wing of the fourth pharyngeal pouch. The ultimobranchial bodies and the superior parathyroid glands fuse with the thyroid gland, which explains the relatively constant anatomic relationship between the tubercle of Zuckerkandl and the superior parathyroid glands [5, 8].

Anatomy

The location of the tubercle of Zuckerkandl and its relationship to the recurrent laryngeal nerve and superior parathyroid gland was first described by Gilmour in 1938 [9]. Its presence was largely ignored by surgeons and anatomists for the next 50 years. It reemerged in the literature in the 1980s and 1990s as a landmark for the recurrent laryngeal nerve and the superior parathyroid gland, and as a structure at risk for being left behind during a total thyroidectomy [10–12]. In 1998, Pellizzo et al. described the tubercle as "an arrow pointing to the recurrent laryngeal nerve," since the nerve is found between the tubercle of Zuckerkandl and the surface of the trachea [13]. The nerve then passes lateral to, or through Berry's ligament before entering the larynx, at which point it may have a rather acute angle of entry [14]. Other authors disagree that the relationship is so simple, primarily because of the variable existence and size of the tubercle, as well as the possibility of the tubercle being located superior to the nerve in 3.8 % of instances [15]. For any surgeon, it is helpful to understand the proximity and relationship of the recurrent laryngeal nerve to the tubercle (when present) in order to perform thyroid surgery safely without nerve injury. In patients with an identifiable tubercle of Zuckerkandl, the recurrent laryngeal nerve is located medial to the tubercle in the vast majority of instances (Fig. 9.2). The incidence of the nerve running lateral to the tubercle has been reported to be low, ranging from 0.8 to 7 %, but was 45.3 % in one study of cadaveric dissections performed in Kenya [6, 16, 17]. It is thought that it is merely nodular growth within a tubercle of Zuckerkandl that causes the rare instance of the recurrent laryngeal nerve being found superficial to the tubercle [16]. In rare instances (4-5 %), the tubercle has been noted to be bilobed, but this too may just be a consequence of nodular growth within the tubercle [6]. The tubercle is composed of thyroid tissue, and is therefore susceptible to hyperplastic or neoplastic thyroid disorders and the numerous anatomic distortions which may occur.

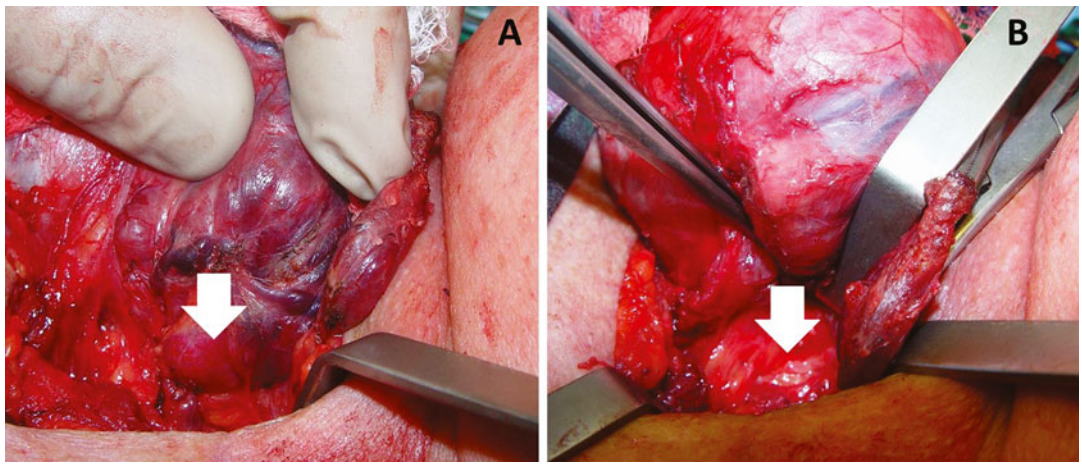

Fig. 9.2 The tubercle of Zuckerkandl (*arrow* in **A**) is dissected and retracted medially to reveal the recurrent laryngeal nerve (*arrow* in **B**) [Courtesy of David J. Terris, MD]

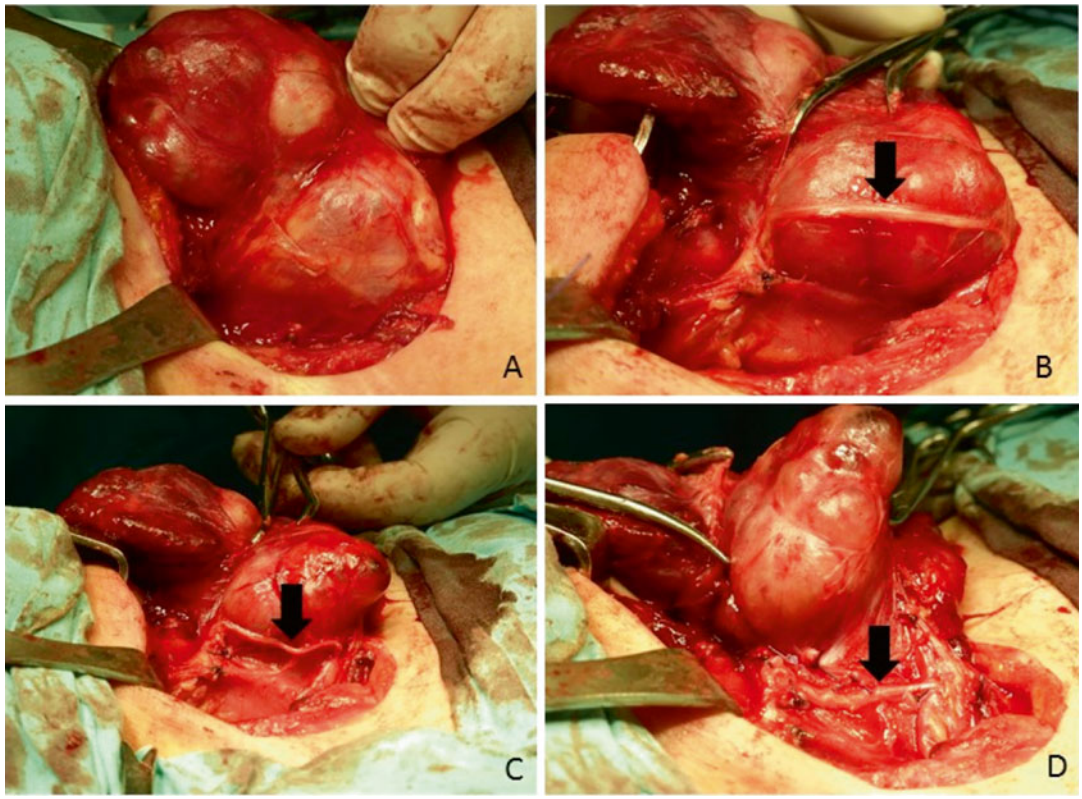

Fig. 9.3 Nodular growth within the tubercle of Zuckerkandl (**A**) has stretched the recurrent laryngeal nerve. The stretched nerve (*arrow*) is not clearly visible in the early stages of dissection, but becomes apparent with careful dissection (**B**–**D**)

In instances where the nerve branches proximal to its entry point into the larynx, it is possible that one branch may be found in the normal position, whereas others may be displaced by nodular growth into abnormal locations [14]. Regardless of the cause or true incidence, recognition of these exceptions is important since the recurrent laryngeal nerve is at greater risk of injury during dissection when they occur (Fig. 9.3).

The superior parathyroid gland is nearly always posterior and superior to the tubercle of Zuckerkandl, and it is found in close proximity to the inferior thyroid artery (which is deep to the tubercle) [4, 12, 16]. While most consider the tubercle to be a reliable landmark for the superior parathyroid gland, some do not feel that the anatomic relationship is reliable enough to be utilized as a surgical landmark [18].

Pelizzo et al. have defined a grading system for the tubercle of Zuckerkandl [13]. Their classification is a numerical scale from 0 to 3, with 0 being unrecognizable, 1 being only a thickening of the lateral edge of the thyroid lobe, 2 measuring smaller than 1 cm, and 3 measuring larger than 1 cm in size (Fig. 9.4). In their series in which 104 thyroid lobes were assessed, grade 0 was present in 23 % of lobes, grade 1 in 9 %, grade 2 in 54 %, and grade 3 in 14 %. Gauger et al. more recently explored the presence of a tubercle in 100 patients undergoing thyroidectomy and found a distinct tubercle in 63 % of patients, which was >1 cm in size in 45 % [12]. Gil-Carcedo et al. found that a tubercle was present in 79.5 % of patients [19]. They also proposed a modification of Pelizzo's grading system, where grade 0 is unrecognizable, grade 1 is

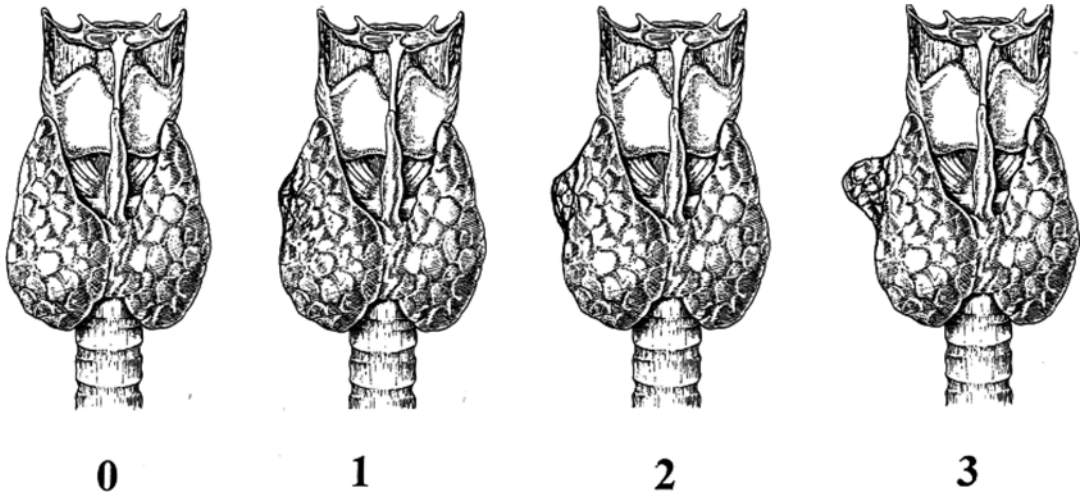

Fig. 9.4 Classification of Zuckerkandl's tuberculum size. (0) Unrecognizable. (1) Only a thickening of the lateral edge of the thyroid lobe. (2) Smaller than 1 cm. (3) Larger than 1 cm [Reprinted from Pelizzo MR, Toniato A, Gemo G. Zuckerkandl's tuberculum: an *arrow* pointing to the recurrent laryngeal nerve (constant anatomical landmark). *Journal of the American College of Surgeons* 1998; 187(3): 333–6, with permission from Elsevier]

doubtful in existence, grade 2 is <10 mm, grade 3 is between 10 and 20 mm, and grade 4 is >20 mm [19]. Studies from around the world therefore suggest that the incidence and size of the tubercle varies based on an unknown combination of environmental or genetic causes [17].

Numerous authors have found that the tubercle is more frequently present on the right when compared to the left. Although there is overlap within the range of these figures (69.6–84.8 % on the right, 53.2–73.9 % on the left [6, 16, 19]), all studies independently found a higher frequency on the right. Furthermore, the tubercle was consistently larger on the right ($p<0.001$) [6]. There is considerable variation of these numbers, and it has been speculated that the surgical technique of thyroidectomy may play a role in the classification and measurement of the tubercle of Zuckerkandl [18].

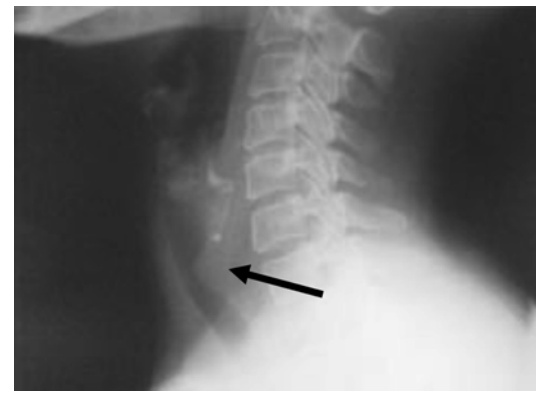

Fig. 9.5 This lateral neck radiograph shows an enlarged prevertebral space and a posterior indentation of the trachea by a grade three tubercle of Zuckerkandl [Reprinted from Hisham AN, Sarojah A, Mastura T, Lim TO. Prevertebral soft tissue measurements in thyroid enlargement: the value of lateral neck radiographs. *Asian Journal of Surgery* 2004; 27(3): 172–5, with permission from Elsevier]

Imaging

Although a common anatomic landmark in the operating room, the tubercle has also been studied radiographically. On lateral neck radiography, a measurement of prevertebral soft tissue at the C4 level of greater than 16.5 mm has been correlated with a grade 3 (>1 cm) tubercle of Zuckerkandl (Fig. 9.5) [20]. The imaging characteristics on axial CT scan vary considerably, as would be expected from the known variations in the anatomy. In a study of 96 patients, the tubercle of Zuckerkandl was defined as the portion of the thyroid which extends posterior to the tracheo-esophageal groove on axial imaging [21]. The authors point out that the appearance

varies from complete absence, to a large nodule, to a mass extending posteriorly through a narrow stalk, to even a mass appearing discontinuous with the thyroid gland. An untrained eye may mistake these rare configurations of the tubercle for a suspicious mass or metastatic lymph node on CT scan, particularly when streak artifact from the shoulders lowers the attenuation [21]. Knowledge of the configuration of the tubercle may assist with surgical planning, and in other instances it may obviate the need for additional sonographic imaging, biopsy, or surgery altogether.

Clinical Significance

An enlarged tubercle of Zuckerkandl can cause the symptom of pressure in the neck. Hisham and Aina evaluated the size of the tubercle in 66 patients undergoing thyroidectomy and reported that 87 % of patients with pressure symptoms were found to have a grade 3 (>1 cm) tubercle [22]. Interestingly, the size of the tubercle, not the size of the thyroid gland itself, correlated more with the symptom of pressure. None of the patients who described neck pressure preoperatively experienced persistent symptoms at the endpoint of three months after surgery. Other authors have not been able to confirm this association, as the size and position of the tubercle of Zuckerkandl did not correlate with preoperative compressive symptoms in two other studies with sample sizes of 100 or more patients [6, 12, 19].

Recognition of the tubercle of Zuckerkandl is clinically important during thyroid surgery. The tubercle of Zuckerkandl is a useful landmark for identification and dissection of the recurrent laryngeal nerve. Since the recurrent laryngeal nerve is medial to the tubercle of Zuckerkandl in the vast majority of cases, elevation of the tubercle of Zuckerkandl allows for safe identification of the recurrent laryngeal nerve. The recurrent laryngeal nerve appears once the tubercle of Zuckerkandl is elevated. This maneuver is optimally performed through a lateral approach at the extralaryngeal termination of the recurrent laryngeal nerve (see Video 9.1). In the past, the identification of the recurrent laryngeal nerve low in the trachea-esophageal groove obliged the surgeon to perform a more extensive dissection of the recurrent laryngeal nerve along its cervical course, and potentially compromise the blood supply to the parathyroid glands in the process. Although the tubercle is generally a welcome landmark that can increase the efficiency with which the recurrent laryngeal nerve is identified, a large nodule in this structure can be vexing since it may be challenging to release it and deliver it ventrally in order to expose the nerve.

Inadvertent transection of the tubercle from the main thyroidectomy specimen may leave a variable amount of thyroid tissue present after surgery [10] (although some surgeons deliberately transect the tubercle to protect the nerve, a practice that should generally be discouraged). With benign disease this is rarely of consequence, but in instances of thyroid carcinoma, remnant thyroid tissue may be a source of persistent radioactive iodine uptake when postoperative scanning is performed. For this reason, complete dissection and removal of the tubercle of Zuckerkandl is advocated [16].

Conclusion

The tubercle of Zuckerkandl is a lateral and posterior projection of the thyroid gland. It is variably present, and it is more often found on the right side in humans. The tubercle of Zuckerkandl is important to endocrine surgeons because of its close proximity to the recurrent laryngeal nerve and the superior parathyroid gland. The tubercle is located inferior to the superior parathyroid gland, and superficial to the recurrent laryngeal nerve. It is susceptible to hyperplastic and neoplastic diseases of the thyroid gland, and the anatomic relationships can be altered in these circumstances. An understanding of the normal anatomy and its variants can benefit surgeons who perform thyroid or parathyroid surgery so that the risks of injury to the recurrent laryngeal nerve or the superior parathyroid gland are minimized, and so that diseased tissue is not left behind when a total thyroidectomy is performed.

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The Ligament of Berry

10

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Abstract

The last 2 cm of the extralaryngeal course of the recurrent laryngeal nerve is an area of critical anatomical importance. It is the site of greatest risk for neuropraxia, the site of development of the artificial genu and point of maximal tension within the recurrent laryngeal nerve at thyroidectomy and the site of bifurcation of the recurrent laryngeal nerve. In this last 2 cm segment, the Ligament of Berry which attaches the thyroid to the trachea is located. Two fascial layers are described in the region of the Ligament of Berry, covering the last 2 cm of the extralaryngeal course of the recurrent nerve. The more superficial layer, the superficial vascular fascial layer, contains branches of the inferior thyroid artery, the superior parathyroid gland, and the Tubercle of Zuckerkandl. Following dissection and division of this layer, the recurrent laryngeal nerve will be seen to lie on the deeper layer, the more fibrous and denser true Ligament of Berry. At thyroidectomy, once the fibrous Ligament of Berry layer is divided, the recurrent laryngeal nerve relaxes and adopts a serpiginous course in the tracheoesophageal groove. The Ligament of Berry maybe in two layers with thyroid tissue between the two layers. Because of anteromedial rotation of the thyroid and larynx and trachea, the recurrent laryngeal nerve lies lateral to the Ligament of Berry and deep to the superficial vascular fascial layer. The recurrent laryngeal nerve thus lies between the two layers but does not pass through the Ligament of Berry.

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Keywords
Recurrent laryngeal nerve • Ligament of Berry • Superficial vascular fascial layer • Tubercle of Zuckerkandl • Bifid recurrent laryngeal nerve • Artificial genu and tensile stress within recurrent laryngeal nerve • Extralaryngeal branching of recurrent laryngeal nerve

Introduction

One of the key aims of thyroid and parathyroid surgery is the preservation of the recurrent laryngeal nerve, (RLN) [1]. Routine visual identification and complete dissection of the RLN have been shown to result in a lower incidence of RLN injury in multiple studies. Despite this, permanent injury to the RLN during thyroid surgery is reported in 0.25–0.7 % of thyroidectomies in large series from world centers of excellence [2–4], with a median permanent RLN palsy rate of 2.3 % [5]. The most common site of injury to the RLN when performing thyroidectomy is in the final 2 cm before the nerve enters the larynx. Here, the RLN is intimately related to the Ligament of Berry, the Tubercle of Zuckerkandl, the inferior thyroid artery, and the superior parathyroid gland [6, 7].

The precise pathophysiological mechanism of RLN palsy in most cases is unknown, but it is presumed to be associated with stretching and compression at fixed point sites, which in turn causes neuropraxia, which resolves in most cases. Rare causes of injury include division, entrapment within a ligature, thermal injury, electrical injury, ischemia, crushing with a hemostat, and even pharmacological and viral causes. It is axiomatic then, that a thorough understanding of the normal anatomy of this region, anatomical variations, and distortion by disease is vital in minimizing the risk to the nerve when performing thyroid surgery.

On its approach to the Ligament of Berry, the anatomy of the RLN in its distal 2 cm extralaryngeal course can further be defined by its relationship with several key anatomic structures that may aid in surgical identification of the nerve: the Inferior Thyroid artery, the Tubercle of Zuckerkandl, the superior parathyroid gland, and the fascial layers of the ligament and neurovascular bundle itself (Fig. 10.1). Several surgical techniques have been described for identification of the RLN. This distal 2 cm of the nerve also requires particular attention as extralaryngeal bifurcation of the nerve, which occurs in up to 36 % of cases, is most likely to occur here [7], further complicating the dissection of the nerve in this region.

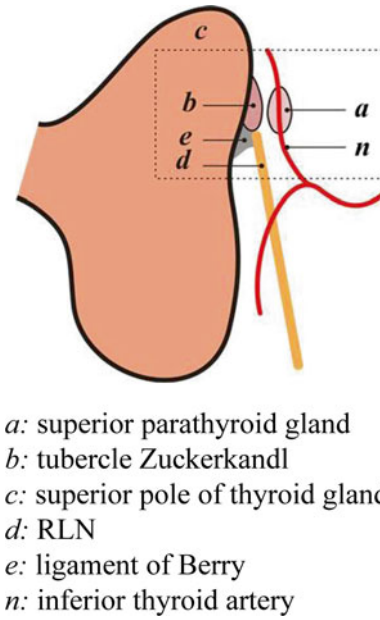
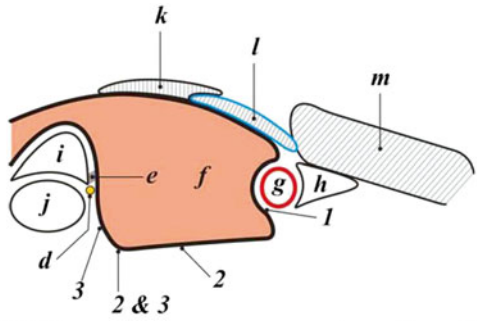


Fig. 10.1 The region of the final 2 cm extralaryngeal course of the Recurrent Laryngeal Nerve (RLN). Left thyroid lobe anterior view [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

In Situ vs. Operative Anatomy

Another distinction to highlight is the difference between in situ and intraoperative anatomy of the region. The in situ normal anatomy will differ to that seen at operation because it is disturbed by the pathology of the gland, and because surgery rotates and delivers the thyroid lobe anteromedially through almost 120°. The posterior and lateral aspects of the thyroid lobe mold itself to adjacent structures in the normal in situ position [9] (Fig. 10.2).

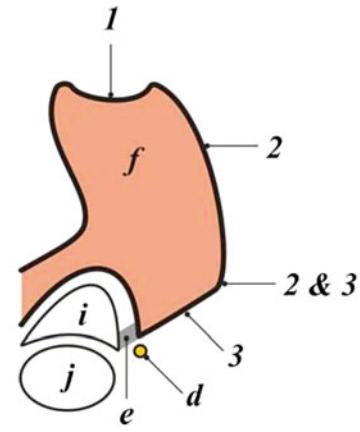
When performing a hemi-thyroidectomy, the first step after dividing the middle thyroid vein is to enter the loose areolar tissue plane between the common carotid artery and the lateral surface of the thyroid, designated *surface 1* in Fig. 10.2. This then allows access to mobilize the thyroid lobe forward through a further 90°, exposing the posterior *surface 2*. At the junction between *surfaces 2* and *3*, the tertiary branches of the inferior thyroid artery and tributaries of the vein enter and leave the thyroid lobe. Progressive mobilization and forward rotation of the thyroid lobe expose this. The result is rotation of the thyroid lobe through approximately 120°, which in turn pulls the RLN forward, applying a tensile force to it and straightening it. It also tends to pull the RLN forward out of the tracheoesophageal groove, forming an artificial *genu* above the level of the inferior thyroid artery. *Surface 3* in Figs. 10.2 and 10.3 is exposed only when the tertiary branches of the inferior thyroid vein and artery are divided, thereby exposing the RLN.



d: RLN
e: ligament of Berry
f: thyroid gland
g: common carotid artery
h: internal jugular vein
i: trachea
j: esophagus
k: sternohyoid muscle
l: sternothyroid muscle
m: sternocleidomastoid muscle

1: surface 1
2: surface 2
3: surface 3

Fig. 10.2 Transverse section of thyroid lobe in situ [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]



d: RLN
e: ligament of Berry
f: thyroid gland
i: trachea
j: esophagus

1: surface 1
2: surface 2
3: surface 3

Fig. 10.3 Anatomy of thyroid lobe after 120° Anteromedial rotation [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

Distal RLN Anatomy (Distal 2 cm Above ITA)

The inferior thyroid artery represents the commencement of the distal 2 cm region of the extralaryngeal RLN pathway. The inferior

thyroid artery arises from the fourth aortic arch. The inferior thyroid artery originates from the thyro-cervical trunk, which itself arises from the superior surface of the second part of the subclavian artery. It arches medially, in a bold curve in front of the apex of the pyramidal space, at the level of C6. It then descends behind the vagus nerve and common carotid artery to reach the posterior border of the thyroid gland where it is closely related to the recurrent laryngeal nerve [10]. The artery itself divides into four or five branches outside the pre-tracheal fascia that pierce the fascia separately to reach the lower pole of the thyroid gland.

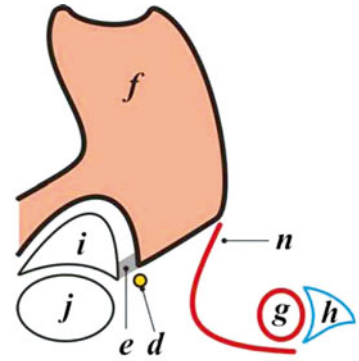
Relations of the ITA and the RLN

Upon reaching the ITA, the RLN passes either behind, in front of, or between the branches of the ITA at the level of the trunk (Figs. 10.4 and 10.5). Simon et al. described the recurrent laryngeal nerve as passing medial (75.6 %), lateral (17.4 %), or between (7 %) these ITA branches [11].

In more recent literature, Ardito et al. in a study of >2500 RLNs, found the RLN anterior to the right ITA in 12 %, and the left in 1.9 %, posterior to the right ITA in 61 %, and the left in 77.4 %, and between the branches on the right in 27 % and the left in 20.5 % [6].

Despite the above described three anatomical "options" for nerve and artery relations, Steinberg et al. found that in as many as 75 % of cases, there was no constant anatomical relationship between the recurrent laryngeal nerve and the branches of the ITA. Instead, the branches of the recurrent laryngeal nerve were seen to form an intertwining delta of branches with the branches of the ITA [12]. One study reported 28 such variations in nerve-artery relations [13].

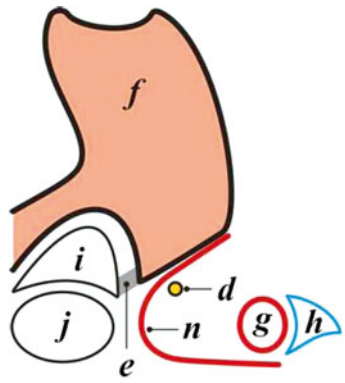
Given the above described variability, it is not surprising that the RLN junction with the ITA is considered by many authors to be a vulnerable location for RLN injury in thyroidectomy.



d: RLN
e: ligament of Berry
f: thyroid gland
g: common carotid artery
h: internal jugular vein
i: trachea
j: esophagus
n: inferior thyroid artery

Fig. 10.4 Relation of RLN to trunk of the inferior thyroid artery; posterior to ITA [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

However, once above the ITA, the course of the RLN is fairly constant and similar on both sides. This has important implications for a right nonrecurrent nerve which occurs in 0.5 % of cases. Arising from the vagus and traversing the neck, they tend to pass anteromedially either at or just below the level of the ITA. They then ascend in the normal position within the tracheoesophageal groove. The nonrecurrent laryngeal nerve less commonly can parallel the course of superior thyroid blood vessels and in this location be at increased risk of injury when mistaken for a blood vessel branch.



d: RLN
e: ligament of Berry
f: thyroid gland
g: common carotid artery
h: internal jugular vein
i: trachea
j: esophagus
n: inferior thyroid artery

Fig. 10.5 Relation of RLN to trunk of the inferior thyroid artery; anterior to ITA [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

The Tubercle of Zuckerkandl

First described in the medical literature in 1867 by Madelung [14] as the "posterior horn of the thyroid," and then in 1902 as the "processus posterior glandulae thyroideae" by Emil Zuckerkandl [15]; the Tubercle of Zuckerkandl (TZ) is a distinct, well-described anatomical feature of the thyroid gland with a plausible embryological basis of genesis.

In the adult, the Tuberculum of Zuckerkandl is the most posterior extension of the lateral lobes of the thyroid gland at the area of the Ligament of Berry and is closely related to the superior parathyroid gland.

Embryology

The Tuberculum of Zuckerkandl has a common origin from the fusion of the fifth and the ventral portion of the fourth pharyngeal pouches (the lateral thyroid anlage). Evidence for this origin include the tuberculum's close relation with the superior parathyroid glands and the high frequency of parafollicular C cells in this part of the thyroid (ultimo-branchial body).

The RLN branches off the vagus nerve in the mesenchyme between the fourth and fifth pharyngeal pouches. It extends around the fourth aortic arch and is immediately covered by the thyroid tissue arising from the lateral anlages of the fourth branchial pouch.

As a consequence of these embryological origins, the relationship of the Tuberculum, (when present) and the termination of the recurrent laryngeal nerve before it enters the larynx is fairly constant [16], and is often described as an "arrow pointing to the Recurrent Laryngeal Nerve."

Dimensions and Frequency

The Tuberculum is highly variable in size. This is due to a variability in parafollicular C cell content and the involvement of Zuckerkandl's tuberculum by hyperplastic or neoplastic thyroid disorders. It ranges from a mere thickening of the lateral edge of the thyroid lobe to a mediastinal enlargement [16]. A size grading classification from 0 (unrecognizable) to 3 (>1 cm) was proposed by Pellizo et al. [16]. In their small dissection study, Grade 3 Tubercula were identified in only 14.4 % of cases, while Grades 1 and 2 Tubercula were found in a further 62.3 % of patients.

The literature describes a highly variable Tuberculum frequency, ranging from 14 to 55 % of thyroidectomies [16, 17]. While differences in disease process, duration and percentage of the thyroid gland affected might explain the discrepancy in tubercle frequency, this perceived variability may be an artifact of the Tuberculum's

marked variability in size, and the perseverance of the surgeon's search during thyroidectomy and the surgical approach employed.

Relationship to the RLN

A resurgent interest in the Tuberculum of Zuckerkandl has occurred in the last 30 years as an important anatomical landmark for the location of the recurrent laryngeal nerve.

In 1998, Pelizzo et al. "rediscovered" this Tubercle as a reliable, almost constant anatomical surgical landmark for identifying the RLN [16].

As a result of its embryogenesis, it has a constant relationship with the recurrent laryngeal nerve, the inferior thyroid artery and its branches, and the parathyroid glands, at least in the disease-free thyroid gland.

Gauger et al. [17] reported that in 93 % of cases the recurrent laryngeal nerve lies medial to Zuckerkandl's tubercle, while in 7 % of cases the nerve is found laterally, in a location vulnerable to injury.

When lying in a medial position, the recurrent laryngeal nerve runs in a tunnel close to the Tuberculum of Zuckerkandl which, when it is more developed, passes over the nerve like a bridge [16].

It must be noted that in the diseased thyroid this constant relationship may be distorted [18]. Thompson et al. [13] argued that when a nodule arises within the Tubercle of Zuckerkandl itself, the RLN may be found on the surface of the lobe or posterior to it. A developing nodule within the Tubercle of Zuckerkandl may rarely work itself posterior to the RLN as it enlarges and elevates the RLN onto the anterior surface of the nodule, thereby placing the RLN at increased risk of injury when mistaken for a blood vessel to the thyroid.

Chevalier et al. [19] also noted that when a goiter arises from the Tubercle, the RLN can be incarcerated between the thyroid and trachea, adherent to the anterior surface of the Tubercle, or found between the tubercle and the anterior portion of the lobe.

Yalcin et al. found that the tubercle pointed to (when small) or passed over (when large) the RLN and its laryngeal branches, and thus supported the notion that it be used as a landmark to expose the RLN or the laryngeal branches [20].

Ligament of Berry and the Recurrent Laryngeal Nerve

Embryology

The Ligament of Berry is a dense condensation of pre-tracheal vascular fascia that attaches the thyroid to the crico-tracheal structures posteriorly. It was first described by Berry in 1888 who coined the suspensory ligament of the thyroid gland [21].

While the distal 2 cm of the extralaryngeal RLN has long been recognized as an area of intricate surgical anatomy and the region of highest iatrogenic risk to the extralaryngeal RLN, most anatomic endocrine surgical texts have offered a surprisingly brief commentary on this complex area.

Operative vs. In Situ Anatomy

A key distinction in discussing the distal RLN and Ligament of Berry involves an understanding of the differences in the operative and in situ anatomy. As outlined above, there are three discrete surfaces of the thyroid lobe, brought into play by anteromedial traction during lobectomy [9].

- Surface 1—This is the lateral surface of the thyroid lobe, and abuts the common carotid artery
- Surface 2—Posterior surface of the thyroid lobe
- Surface 3—Medial surface of the thyroid lobe, exposed on division of the tertiary branches of the inferior thyroid artery and vein

Tensile anteromedial force on the thyroid lobe, after division of the middle thyroid vein, allows a near 120° arc of rotation, which results in a straightening of the RLN and its displacement out of the trachea-esophageal groove.

Above the inferior thyroid artery, this creates an artificial distal *genu*, which is recognized as the site of greatest RLN injury [22].

This tractional force on the thyroid lobe is an important concept, generated by the intimate relationship between the RLN and the fibrous, fixed Ligament of Berry. Anteromedial traction creates a tensile force within the nerve, and a compressive force at its two fixed points: around the arch of aorta at the ligamentum arteriosum on the left; or the first part of the subclavian artery on the right, and just posterior to the inferior crico-thyroid joint, where the nerve enters the larynx under the cricopharyngeus [9]. When the RLN has extralaryngeal branching proximal to the Ligament of Berry the anteromedial traction is more evident to the anterior branch, typically motor, than the posterior branch, typically sensory. In this case, the maximal proximal tensile force within the thinner anterior motor branch is located at its take-off from the thicker main RLN trunk [23].

This distal RLN *genu* at the laryngeal entry point is vulnerable to injury from a multitude of factors. Bleeding can occur from the Ligament of Berry; there is a close association with often densely adherent thyroid tissue; and multiple extralaryngeal branching may be present [24]. Meticulous and delicate dissection is advised in this portion of the lobectomy (see Fig. 10.6).

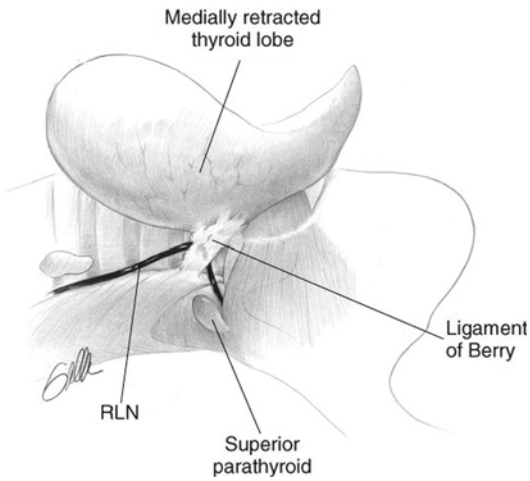


Fig. 10.6 Operative view of the retracted thyroid lobe and RLN [Reprinted with permission from Randolph GW. Surgery of the Thyroid and Parathyroid, 2nd edition. Published by Elsevier © 2012.]

Extralaryngeal RLN Branching/Role of Intraoperative Nerve Monitoring

Extralaryngeal RLN branching bears close relation to the Ligament of Berry. Various surgical and cadaveric studies have reported extralaryngeal branching from 30 to 78 % of patients [25–29]. Of note however, it is estimated that 20–30 % of patients exhibit extralaryngeal branching containing intrinsic motor supply, displaying EMG activity [7, 30].

When present, extralaryngeal branching occurs from the distal RLN segment, above the intersection of the RLN and inferior thyroid artery [25], but not always.

The most common branch point occurred in the distal 2 cm course of the RLN measured from the bottom of the inferior constrictor and averaged approximately 18 mm with a range of 5–34 mm [7, 30].

Thus, extralaryngeal nerve branches, when present, usually exist at the level of the Ligament of Berry and are usually not present below the inferior thyroid artery. However, when extralaryngeal branching does occur at or below the inferior thyroid artery, the anterior motor branch of the RLN can be mistaken for a blood vessel visually.

The most important message regarding patients with extralaryngeal branching, because of this increased anatomic complexity and narrow diameter of the branched RLN, and because the motor fibers are in the anterior branch, is that they are at increased risk for both transient vocal cord paralysis from traction and permanent vocal cord paralysis from misidentification of the branched RLN.

Ligament of Berry Vascularity

The Ligament of Berry contains terminal branches of the inferior thyroid artery, which are encountered in the final stages of lobe delivery. Most significant is the inferior laryngeal artery, which is a posterior branch of the inferior thyroid artery. This and adjacent small peri-tracheal vessels are in close proximity to the terminal extralaryngeal RLN, and must be dealt with delicately and precisely. Unnoticed vessel retraction can predispose to a postoperative hemorrhage with severe consequences.

Surgical maneuvers can include gentle pressure with a neurosurgical pledget soaked in epinephrine. Bipolar cautery is useful, but caution is mandatory. A fine-tipped jeweler's bipolar cautery is advisable, and transient, brief use is recommended to minimize thermal trauma to the adjacent the RLN [24]. The RLN should be under full view during these maneuvers. Suturing of vessels after clamping with fine mosquito forceps or using small ligaclips for hemostasis are options for avoiding the risk of thermal damage. The danger however, is that of RLN (or RLN branch) entrapment in an indiscriminate suture or ligating clip and the potential for damage to intrinsic laryngeal motor supply. Laryngeal EMG monitoring has utility here, as repeated stimulation of the RLN confirms intact stimulability (and allows assessment of waveform integrity and amplitude) to ensure there has been no damage to nerve conduction by any of these surgical maneuvers. Well known with the advent of widespread intraoperative nerve monitoring is that a visually intact RLN does not equate to functionality.

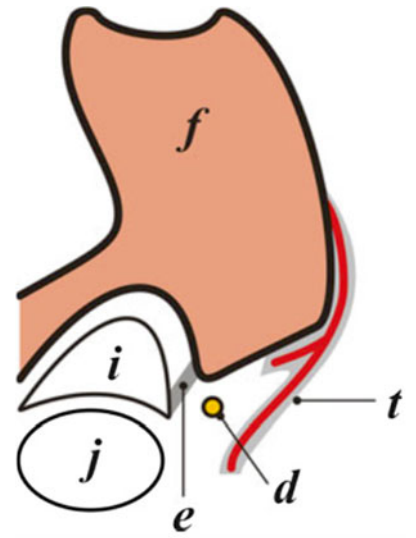


Fig. 10.7 The two fascial layers surrounding the RLN. [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

The Fascial Layers of the Ligament of Berry and Recurrent Laryngeal Nerve

Once above the inferior thyroid artery, both left and right RLNs proceed in a similar course essentially in the tracheoesophageal groove, with minimal difference between the two sides.

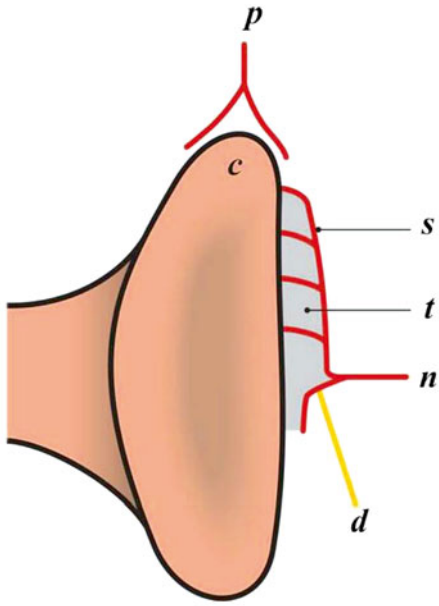
In this final 2 cm extralaryngeal course of the RLN, two fascial layers are described—the superficial vascular and deep fibrous fascial layer which envelops the distal RLN on its path to the larynx. They are key additional landmarks in the safe identification, dissection, and preservation of the RLN [9] (Fig. 10.7).

The Superficial Vascular Fascial Layer

This condensed layer of the thyroid/pre-tracheal fascia extends from the posterior lip of the thyroid gland laterally. It contains the tertiary branches and tributaries of the inferior thyroid artery and vein as they travel to and from the gland, respectively.

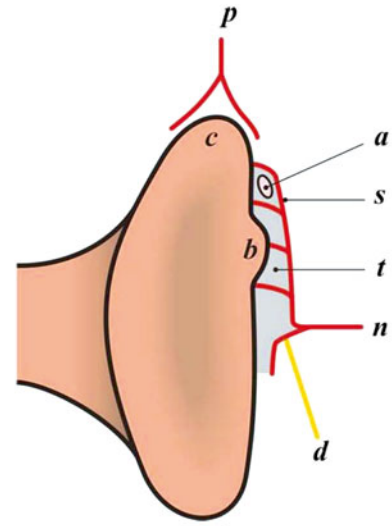
It extends inferiorly, along the posterior aspect of the thyroid gland, lying slightly lateral to the RLN, between the aforementioned *surfaces 2* and *3*.

When the thyroid lobe is rotated 120° antero-medially, this fascial layer becomes antero-lateral to the RLN at a level above the ITA trunk. This is regardless of whether the RLN travels lateral or medial to the ITA trunk more inferiorly. Once this superficial vascular layer is dissected and divided, the underlying RLN will be exposed, in turn lying upon the underlying deep fibrous layer, condensing into the Ligament of Berry (Figs. 10.8 and 10.9).



c: superior pole of thyroid gland
d: RLN
n: inferior thyroid artery
p: superior thyroid vessels
s: approximate level of entry RLN beneath cricopharyngeus
t: superficial vascular fascial layer containing branches inferior thyroid artery overlying the RLN

Fig. 10.8 Superficial vascular layer: left thyroid lobe, rotated medially, viewed from anterior, surface 2 shaded, showing the superficially vascular layer covering the recurrent laryngeal nerve above the level of the inferior thyroid artery [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]



a: superior parathyroid gland
b: tubercle Zuckerkandl
c: superior pole of thyroid gland
d: RLN
n: inferior thyroid artery
p: superior thyroid vessels
s: approximate level of entry RLN beneath cricopharyngeus
t: superficial vascular fascial layer containing branches inferior thyroid artery overlying the RLN

Fig. 10.9 Tubercle of Zuckerkandl and superior parathyroid gland in the superficial vascular fascial layer [Adapted from Serpell JW. New operative surgical concept of two fascial layers enveloping the recurrent laryngeal nerve. Annals of Surgical Oncology. 2010;17(6):1628–1636. With permission from Springer Science]

The True Ligament of Berry

Medially and deeper, lies a fibrous, relatively avascular layer—the true Ligament of Berry. After dissection of the vascular, superficial fascial layer, the RLN is seen lying on the underlying, fibrous Ligament of Berry [9].

Cadaveric studies by Sasou et al. describe the dimensions of the Ligament of Berry. It extends as a dense fibrous band from the cricoid onto the first to third tracheal rings. This length is 8–11 mm, with a thickness of 2–7 mm (mean 4.4 mm) [22].

The true Ligament of Berry often consists of two layers, between which may contain thyroid tissue [9]. Gently pushing the RLN in a posterio-lateral direction allows dissection of the underlying fibrous ligament, and allows a total thyroid lobectomy. While this plane is relative avascular, again, caution is mandatory in dealing with terminal inferior thyroid branches—particularly the inferior laryngeal artery—as described above.

Division of the fibrous Ligament of Berry results in an immediate relaxation of the tensed RLN, which then adopts a serpiginous course, relaxing into the trachea-esophageal groove. Frequently, the RLN assumes a linear course to the laryngeal entry point, but sometimes maintains a buckled or prominent serpiginous course. Final, ipsilateral stimulation of the RLN and vagus nerve is advisable at this point to ensure intact neural conduction. Herein lies a key advantage of intraoperative nerve monitoring. A true loss of signal would allow the surgeon to consider a delay of contralateral lobectomy and eliminate the risk of bilateral RLN cord palsy and the risk of tracheostomy [31].

Does the RLN Penetrate the Ligament of Berry?

This anatomical association is strongly debated in the surgical literature. Numerous authors have described a penetration of the Ligament of Berry by the RLN. Various authors have described the RLN as invested by, passing through, or embedded in a portion of the Ligament of Berry in some patients [32]. In other cadaveric studies, authors have argued that the RLN remains lateral to the true Ligament of Berry in 100 % of cases [22, 33].

The series of Serpell et al. discusses that a discordance in nomenclature underlies this contradiction in the literature [9]. If the Ligament of Berry is taken as the deeper, fibrous fascial layer, the RLN passes lateral to it in all cases. In their study, 977 RLNs were all identified remaining lateral to the true Ligament of Berry, including the 241 nerves (24.7 %) that exhibited extralaryngeal bifurcation [7, 9, 30].

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The Nonrecurrent Inferior Laryngeal Nerve

11

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Gregory W. Randolph, and Richard J. Wong

Abstract

Nonrecurrent inferior laryngeal nerve is a rare (NRLN), asymptomatic anomaly. Given the consequences of iatrogenic injury, intimate knowledge of all possible anatomic variations and correlated vascular aberrancies is critical to thyroid surgeons. With awareness and meticulous dissection, injury can be avoided.

The routine use of intraoperative nerve monitoring with an algorithm for identifying the nonrecurrent inferior laryngeal nerve may be associated with reduced nerve injury rates. A technique of stimulating both the proximal vagus nerve at the upper border of the thyroid cartilage and the distal vagus nerve at the fourth tracheal ring allows for the reliable intraoperative identification of an NRLN.

The surgical approach is predicated on the preoperative absence or knowledge of the vascular anomaly associated with an NRLN and the surgical practice of the operating surgeon in terms of distal or proximal identification of the RLN as it relates to its insertion in the larynx. Each of these factors will impact upon the successful management of this rare anatomic variant.

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Nonrecurrent laryngeal nerve • Inferior laryngeal nerve • Thyroid embryology

Historical Perspective

Aortic arch vascular aberrancies are described as early as the early eighteenth century with Hunauld depicting the first case of the right aberrant subclavian artery [1]. Descriptions of an associated nonrecurrent inferior laryngeal nerve (NRLN) are not noted in the literature until early nineteenth century. In Stedman's report in 1823 of a cadaveric dissection, he describes the right laryngeal nerve coursing directly from the vagus nerve into the larynx within the neck. In this report he also describes a concurrent aortic arch abnormality—an aberrant right subclavian artery arising distal to the left subclavian artery and coursing from left, the right behind the esophagus. Additional case reports of right NRLN by Hart and Hilton followed shortly thereafter [2, 3]. Pemberton and Beaver were the first to acknowledge the surgical risk of this aberrant anatomy [4]. It was not until over a century later, in 1935, that the first left-sided NRLN was reported in conjunction with *situs inversus* during a cadaveric dissection by Berlin [5].

Embryology

An expert surgeon is meticulous and consistent in the surgical approach to a patient and can anticipate the unexpected by maintaining a thorough understanding of normal and aberrant anatomy that may be encountered. It is this latter skill that is most critical in minimizing harm to patients. Moreover, a complete understanding of surgical anatomy requires an awareness of developmental embryology. Knowledge of the complex embryological relationships during both normal and anomalous development can allow for earlier detection of an abnormality and, ultimately, avoid injury.

Iatrogenic injury to the recurrent laryngeal nerve (RLN) is of paramount concern to every endocrine, head and neck, and thoracic surgeon as damage anywhere along its course can cause permanent hoarseness, dysphonia, dysphagia, and risk of aspiration. Anatomic variability of the RLN in relationship to the inferior thyroid artery, tubercle of Zuckerkandl, and pre-laryngeal arborization is common. Much less commonly found, is the presence of an NRLN. In order to anticipate this rare anatomic aberrancy, one must understand the normal embryological thyroid and great vessel development.

In early embryologic development the inferior laryngeal nerve arises from the vagus nerve from the sixth visceral arches and both RLNs recur under the sixth branchial arch. Of the six pairs of branchial arches, only the fourth arch remains at the end of normal embryogenesis. The right fifth and six branchial arches resorb allowing the right RLN to ascend upwards below the fourth branchial arch (which forms the right subclavian artery). Ultimately, the right RLN arises from the right vagus nerve and wraps posteriorly around the right subclavian artery and ascends into the neck behind the common carotid and into the tracheoesophageal groove. On the left side, the sixth branchial arch forms the ductus arteriosus, holding the left RLN within the thorax. The left RLN arises from the vagus in the thorax wrapping posteriorly around the aortic arch lateral to the ligamentum arteriosus before ascending into the left tracheoesophageal groove (Fig. 11.1).

NRLNs occur in conjunction with abnormal embryologic formation of the aortic arch (Fig. 11.2). Prevalence of a right-sided NRLN is reported in 0.6–1.0 % in the largest case series (Table 11.1) and is thought to be a consequence of abnormal absorption of the fourth right branchial arch, resulting in a left-sided aortic arch and aberrant right subclavian artery anatomy [6, 7].

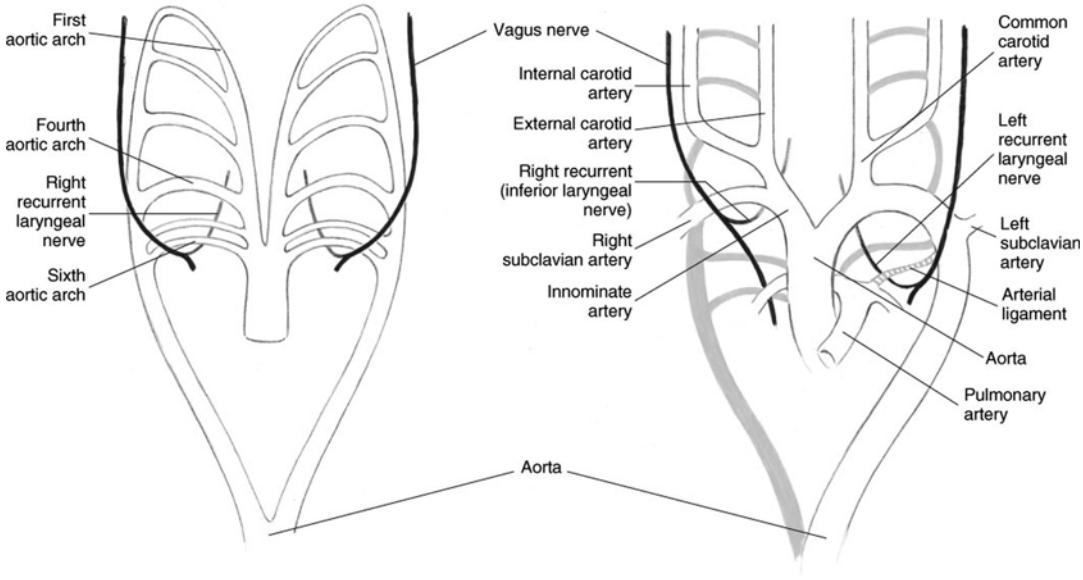

Fig. 11.1 Normal embryonic development of the aortic arches. The inferior laryngeal nerves are dragged down by the lowest persisting aortic arches. On the *right* side the inferior laryngeal nerve recurs around the fourth arch, which is the subclavian artery. On the *left* side the inferior laryngeal nerve recurs around the sixth arch, which is the arterial ligament [Reprinted with permission from Randolph GW. Surgery of the Thyroid and Parathyroid, 2nd edition. Published by Elsevier © 2012.]

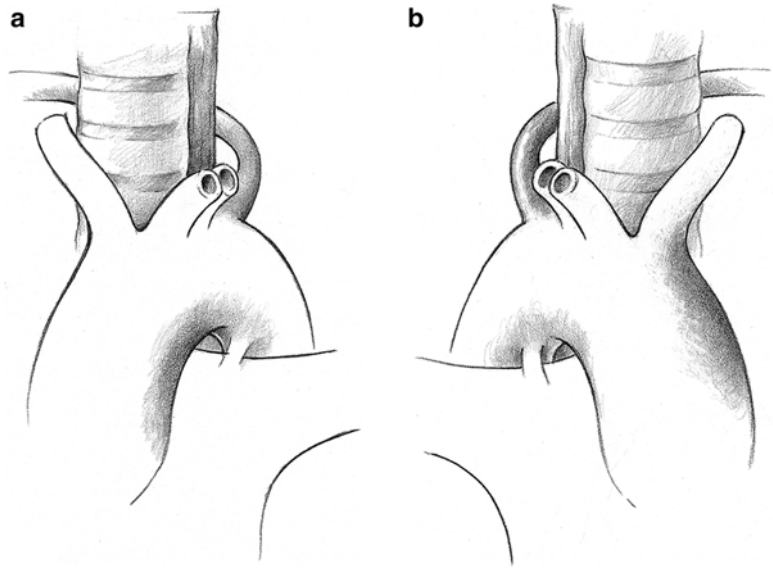

Fig. 11.2 Vascular anomalies required to observe a nonrecurrent inferior laryngeal nerve. (**a**) On the *right* side, the right retroesophageal subclavian artery arises as the fourth branch of the aortic arch, after the right and left common carotid arteries and the left subclavian artery. No innominate artery is present. (**b**) On the *left* side, (1) right aortic arch, (2) the left retroesophageal subclavian artery arises as the fourth branch of the aortic arch after the left and right common carotid arteries and the right subclavian artery, and (3) the arterial ligament is on the *right* [Reprinted with permission from Randolph GW. Surgery of the Thyroid and Parathyroid, 2nd edition. Published by Elsevier © 2012.]

Table 11.1 Reported incidence of nonrecurrent inferior laryngeal nerves

Author (Year)	Location	Right side		Left side		References
		No. of nerves at risk	NRLN, *n* (%)	No. of nerves at risk	NRLN, *n* (%)	
Ardito et al. (1998)	Italy	773	2 (0.3)	724	0	[31]
Avisse et al. (1998)	France	1700[a]	17 (1.0)	1700[a]	0	[1]
Chiang et al. (2012)	Taiwan	310	4 (1.3)	293	0	[27]
Defechereux et al. (2000)	Belgium	2517	20 (0.8)	–	–	[32]
Dolezel et al. (2014)	Czech Republic	725	4 (0.6)	714	0	[33]
Donatini et al. (2013)	Italy	402	11 (2.7)	404	0	[28]
Geraci et al. (2011)	Italy	804[a]	3 (0.4)	804[a]	0	[34]
Henry et al. (1988)	France	4921	31 (0.6)	4673	2 (0.04)	[10]
Hisham and Lukman (2002)	Malaysia	502[a]	1 (0.2)	502[a]	0	[16]
Hong et al. (2014)	Korea	2187	15 (0.7)	2145	0	[13]
Katz and Nemiroff (1993)	USA	719[a]	11 (1.0)	719[a]	0	[14]
Page et al. (2008)	France	787	3 (0.4)	770	0	[35]
Proye et al. (1991)	France	6961	56 (0.8)	6961	0	[20]
Reeve et al. (1969)	Australia	1200[a]	7 (0.6)	1200[a]	0	[15]
Sanders et al. (1983)	USA	2000	7 (0.7)	2000	0	[21]
Stewart et al. (1972)	USA	1817	6 (0.3)	1750	0	[36]
Tartaglia et al. (2011)	Italy	2713[a]	17 (0.6)	2713[a]	0	[37]
Toniato et al. (2004)	Italy	6000[a]	31 (0.5)	6000[a]	0	[12]
Vallicioni et al. (2003)	France	2128[a]	13 (0.4)	2128[a]	0	[38]
Vuillard et al. (1978)	France	1889	15 (0.8)	–	–	[39]
Watanabe et al. (2014)	Japan	486	4 (0.8)	469	0	[30]
Wijetilaka et al. (1978)	Sri Lanka	203[a]	2 (1.0)	203[a]	0	[40]
Yetisir et al. (2012)	Turkey	309	6 (2.0)	299	0	[41]

NRLN nonrecurrent inferior laryngeal nerve
[a]Number of patients

The "arteria lusoria"—coined by Arkin in 1936, meaning quirky artery—vascular abnormality has a reported incidence of 0.5–2.0 % [8]. Instead of arising from the innominate artery, the right subclavian and right common carotid arteries arise directly from the aortic arch, with the subclavian being the fourth branch arising from the dorsal aorta. The aberrant right subclavian artery then travels posterior to the esophagus or in rare cases between the trachea and esophagus. Dysphagia lusoria, or the symptom of "obstructive deglutition" described first in 1794 by Bayford, is attributed to this vascular anomaly [9]. In practice, however, dysphagia symptoms are not consistent in cases of NRLN and are frequently not distinguishable from those caused by other thyroid pathology [1, 10]. Additional arterial anomalies associated with an aberrant right subclavian artery and NRLN have been reported including aplasia of the circle of Willis [11].

In normal development the RLN is pulled down by the development of the right subclavian artery from the fourth branchial pouch. When this does not occur, the right-sided NRLN arises directly from the vagus nerve within the neck behind the common carotid artery and courses medially to the laryngeal entry behind the inferior cornu of the thyroid cartilage. The right-sided NRLN can arise anywhere along the cervical vagus as cranial at the superior thyroid pole or as caudal as the inferior thyroid artery. A number of classification systems have been proposed. Avisse et al. classified their 17 cases of right-sided NRLN: seven "type I" nerves (a short superior course behind the superior pole of the thyroid) and ten "type II" (arising more caudal and traveling alongside the inferior thyroid artery) [1]. Toniato et al. classify the more cranial course as Type I (i.e., association with the superior pole vessels) and Type II deriving from the

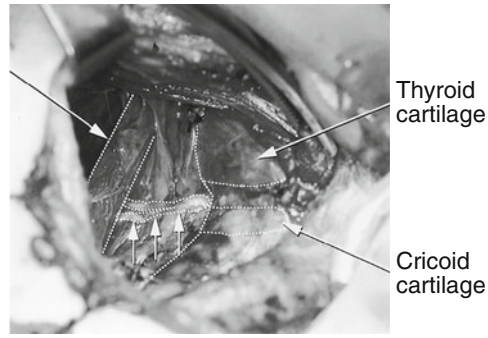

Fig. 11.3 Right lateral thyroid bed region showing the nonrecurrent right recurrent laryngeal nerve (RLN). Three *small white arrows* point to bifid nonrecurrent right RLN emerging from behind the carotid artery (laterally, outlined in *white dots*) and extending to the larynx. The thyroid and cricoid cartilages and trachea (medially) are outlined in white dots [Reprinted with permission from Randolph GW. Surgery of the Thyroid and Parathyroid, 2nd edition. Published by Elsevier © 2012.]

vagus more inferiorly at the level of the laryngotracheal junction traveling either along the path of the inferior thyroid artery (IIA) or dropping below the level of the inferior thyroid artery before traveling cranially to the laryngeal entry (IIB) [12]. Hong and colleagues found 15 of 2187 (0.68 %) of right inferior laryngeal nerves to be nonrecurrent [13]. They describe four traveling patterns of right NRLNs: descending (5/15), vertical (4/15), ascending (3/15), and V-shaped (3/15).

Similar to the RLN, bifid nerves and arborization of the terminal nerve is present in up to 40 % of NRLN cases (Fig. 11.3) [10, 14–16]. Toniato and others have also reported a case in which the right-sided NRLN arose from a medially (to the carotid artery) positioned vagus [17, 18]. An additional case report highlights a right-sided NRLN coursing anterior to the carotid artery from the vagus nerve directly into the larynx [19].

Making identification even more challenging are reported cases of nonrecurrent nerves in conjunction with a RLN [20]. In their report of 1177 nerves at risk, Katz report that 5 of 11 nonrecurrent nerves also had a recurrent branch [14]. Sanders reported this variant in two of seven right-sided NRLN cases [21]. Some experts argue that this abnormality is not possible embryologically and postulate that a branch from the cervical sympathetic chain to the RLN is mistaken for an NRLN if not dissected to the origin in the sympathetic chain [22]. Large sympathetic inferior laryngeal branches occur more frequently (1.5 %) than NRLNs (<1 %). In a cadaveric study of over 277 neck dissections, a communication branch between the sympathetic trunk and the RLN in 17 % of cadavers. Importantly, the diameter of the sympathetic branch was similar to the RLN making it visually indistinguishable from an NRLN. Caution and meticulous dissection are critical in differentiating and preserving the two (see surgical approach below). The finding of a small narrow right RLN should alert the surgeon to search for a larger nonrecurrent laryngeal nerve trunk. Neural monitoring can arguably assist with identifying the motor branches (see intraoperative nerve monitoring below).

A left-sided NRLN is extremely rare with only a few reported cases [6, 10, 23]. Henry only identified two left-sided NRLN in over 4600 dissections (less than 0.04 % of cases) [10]. The left-sided NRLN was thought to only occur with *situs inversus*, a right-sided aortic arch, and displacement of the ligamentum arteriosum. With these arch anomalies, the left subclavian artery or "arteria lusoria sinistra" courses posterior to the esophagus from the right. While it is a commonly held belief that nonrecurrent nerves must be accompanied by aortic arch anomalies, Coady et al. reported one case of NRLN noted during carotid endarterectomy without associated arch anomalies [6]. It is postulated that in the cases of left-sided NRLN and absence of arteria lusoria sinistra that the ductus arteriosus must still remain on the left [1, 24]. Fellmer and colleagues reported one case of a left-sided NRLN in association with a right-sided aorta, truncus arteriosus, and aberrant left innominate artery [23].

Intraoperative Nerve Monitoring (IONM) for the Nonrecurrent Laryngeal Nerve

Intraoperative nerve monitoring (IONM) during thyroid and parathyroid surgery allows for a dynamic assessment of laryngeal nerve function, which may subsequently facilitate nerve identification and management. The use of IONM is rising, with the majority of otolaryngologists and general surgeons in the United States now using this technique. The American Academy of Otolaryngology—Head and Neck Surgery recently published guidelines and recommendations to support the optimal application of IONM [25]. Since the nonrecurrent laryngeal nerve is at higher risk for injury during surgery, the appropriate use of IONM may potentially decrease the risk of nerve injury.

Prior studies have suggested that IONM may be helpful in identifying the nonrecurrent laryngeal nerve [26–29]. In four previous retrospective studies, a collective total of 34 patients with nonrecurrent laryngeal nerves underwent thyroidectomy with IONM; all 34 patients had nerve preservation and intact nerve function postoperatively [26–29]. In comparison, one retrospective study of 31 patients with nonrecurrent laryngeal nerves who underwent thyroidectomy without IONM was reported to have a 12.9 % rate of a postoperative vocal cord deficit [12].

IONM Technique for the Identification of the Nonrecurrent Laryngeal Nerve

Braukhoff and Kamani have outlined similar algorithms for using IONM to identify a nonrecurrent laryngeal nerve that both involve correlating distal nerve stimulation with proximal vagal stimulation [26, 29]. Braukhoff et al. proposed using IONM to stimulate the distal vagus, opposite the thyroid lower pole [26]. The absence of a response at this location may suggest a potential NRLN, as the stimulus does not propagate in a retrograde direction. A positive proximal vagal stimulation in this setting would confirm the presence of an intact NRLN.

The approach taken by Kamani et al. was similar, and advocated using anatomic landmarks to guide the location of the vagal stimulation [29]. They noted that proximal stimulation of the vagus nerve at the level of the superior border of the thyroid cartilage resulted in a reliable EMG response, whereas distal stimulation of the vagus nerve at the level of the fourth trachea ring resulted in no response in all ten of the NRLN cases reported in this study. Furthermore, this group noted that landmarks account for variations of the course of NRLN with respect to sites of vagus nerve takeoff, as well as its course of to the larynx. Interestingly, Kamani et al. also performed an assessment of electrophysiological IONM parameters of the NRLN [29]. They found that the NRLN is equivalent to the normal RLN with respect to amplitude of waveform, latency of waveform, and neural threshold stimulation levels. Such electrophysiological parameters, therefore, cannot substitute for an anatomic localization of the NRLN through the vagal stimulation techniques describe above.

Surgical Strategies to the Nonrecurrent Laryngeal Nerve

Based on the described anatomical variations of the NRLN and the potential use of nerve monitoring, there are two dominant factors which impact upon the surgical strategy for this patient population. The factors are (1) the knowledge of the vascular anatomic abnormality, the “arteria lusoria”, prior to the surgical intervention and (2) the practice of the surgeon in terms of identification of the nerve in relationship to the entry of the nerve to the larynx. A multitude of issues can impact whether the surgeon is aware of the associated “arteria lusoria” vascular anomaly which is most commonly associated with an NRLN. In some instances, prior imaging or medical history may lead to the knowledge of a suspected arteria lusoria. Cross-sectional imaging obtained for the evaluation of a patient being considered for surgical

management may result in this new diagnosis. CT or MRI obtained for patients with substernal goiter or patients being evaluated for metastatic nodal disease can lead to this previously unknown diagnosis.

Watanabe et al. studying preoperative CT scans in 594 patients, was able to preoperatively predict a right-sided NRLN if the right subclavian artery on axial CT scanning was detected on the dorsal side of the membranous wall of the trachea [30]. The awareness of the vascular abnormality preoperatively is the most significant factor in terms of ease of performing surgical management in this rare patient population. The other critical factor in the surgical management of this population is the site at which the surgeon typically identifies the recurrent laryngeal nerve. There are two typical sites at which surgeons identify the recurrent laryngeal nerve: (1) proximally where the nerve is in close proximity to the superior nerve as it enters the cricoarytenoid joint (superior approach), and (2) distally in the tracheoesophageal groove at the level of the lower pole of the thyroid (inferior approach). The authors will describe the impact of the constellation of these two approaches as it impacts on identification and preservation of the NRLN.

As noted above, preoperative knowledge of a suspected NRLN will dramatically impact the ease and safety of surgery in this patient population. All four of the authors routinely utilize nerve monitoring for thyroid surgery and this patient population is no exception. For patients with a known arteria lusoria, a wide surgical exposure is employed. This allows for exposure of the carotid sheath with proximal identification of the vagus nerve and the ability to identify the origin of the NRLN and trace into its insertion in the larynx. As noted previously one must be aware of both the proximal and distal configurations (i.e., the type I or II variant described above), the potential for extra-laryngeal branching, or combinations of recurrent and nonrecurrent laryngeal nerves. For those surgeons who identify the nerve in close proximity to the superior parathyroid gland, the angulation of the nerve may be quite unusual, particularly in the instance of a type I, descending nerve. The authors can identify little advantage in beginning the exploration in the tracheoesophageal groove, as the likelihood of successful identification is low and incurs unnecessary operative time and potential frustration on the part of the surgeon.

Based on the literature, the authors infer that a majority of patients with an NRLN are not known prior to the time of surgery. It is in this instance that the practice of the surgeon impacts the duration of surgery and the safety of the procedure. For those surgeons who identify the nerve at the lower pole of the thyroid, this can be a source of frustration and concern. The knowledge and awareness of the potential for this anomaly will play a key role in the decision to abandon the inferior approach and proceed with the superior approach. One could argue for all surgeons utilizing the inferior approach, asking the question at the beginning of each right-sided dissection, "Could this be an NRLN?" will have significant value on the rare case in which it is present. No structure passing medially from the carotid sheath except the middle thyroid vein should be divided until after the RLN (or NRLN) is identified. For the surgeon who employs the superior exposure to the RLN as part of the identification and preservation of the superior parathyroid gland, identification and preservation of the NRLN will be a much easier task. For patients with the type II configuration, there will be a nearly traditional relationship between the nerve and the superior parathyroid gland. It is possible that the surgeon might mistake it for the traditional recurrent laryngeal nerve anatomy. For the patient with the type II configuration, identification of the nerve may be challenging due to the superior lateral to inferior medial path of the nerve. It is this instance in which the routine use of nerve monitoring that assists in confirmation of the nerve. One must take extreme care in preserving the superior parathyroid gland and its vasculature to assure anatomic and physiologic preservation of the type II NRLN. In the instance in which the surgeon is unable to identify the nerve, one may consider expansion of the surgical field as described in the preceding paragraph for the purpose of identification of the vagus nerve and repeating the steps as outlined above.

For all intents and purposes, situs inversus is an anatomic "unicorn" the existence of which is extraordinarily rare. As witnessed by the aforementioned terminology, none of the four authors have performed thyroidectomy in this rare population. The majority of these patients have this condition identified in their routine medical care. For the unusual patient in whom this was not previously identified, preoperative chest X-ray and EKG will lead to the identification and evaluation of this condition. The authors presume surgical management would mirror that of a known NRLN on the right-sided laterality.

In conclusion, it is the combination of awareness of the embryology, deployment of nerve monitoring, and appropriate surgical strategy that benefits the approximate 1 % of patients with an NRLN. It is this thought process that should be in the armamentarium of every thyroid surgeon.

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The International RLN Anatomic Classification System

12

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"People see what they are prepared to see"—Ralph Waldo Emerson journals 1863
"I am convinced that the best management of RLN injuries is of the preventative character"

—Frank Lahey 1938

Abstract

With this chapter we offer an anatomy-based classification system of recurrent laryngeal nerve (RLN); a classification that embraces normal anatomy as well as embryological and acquired sources of variation in the trajectory of the right and left RLN in human neck. We endeavor to put forth a classification system that encompasses all of the above sources of variations and is simple and surgically relevant so that it is maximally valuable to the surgeon during thyroidectomy.

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This classification system relates to the path/trajectory of the main trunk of the RLN. We appreciate that specific interactions between the nerve and the thyroid gland occur at the tubercle of Zuckerkandl (described in Chap. 9), ligament of Berry (described in Chap. 10) and with the inferior thyroid artery (described in Chap. 7). The surgical approach to the nerve can be conceptualized in a number of different ways and this is detailed in Chap. 13. In this chapter both the basic classification of RLN surgical anatomic path in the neck base as it relates to the thyroid surgery as well as vagal carotid sheath anatomy are described.

Keywords
Surgical anatomy • Recurrent laryngeal nerve • Classification • Acquired changes in RLN • Nonrecurrent laryngeal nerve • RLN branching

Section 1: Vagus Carotid Sheath Anatomy

A better understanding of the anatomy and variability in the topographical position of the vagal nerve (VN) with in carotid sheath may be useful not only to minimize complications but also to insure accurate and safe intraoperative nerve monitoring (IONM). The carotid sheath is an anatomical term for the fibrous connective tissue that surrounds the vascular compartment of the neck and is part of the deep cervical fascia of the neck [1, 2] The medial location of the common carotid artery (CCA) and anterolateral or lateral location of the internal jugular vein (IJV) are the most common configurations in the carotid sheath [1, 2]. Rare cases of medial IJV position are observed [1, 2]. In the largest series to date, Dionigi et al. have suggested an anatomical classification of vagal nerve based on its position relative to the great vessels and have demonstrated a reproducible scheme for the identification of the VN and its course in the carotid sheath [2]. The relative location of the VN has been classified into various configurations where *A* denotes anterior to the CCA and IJV, *P* denotes VN posterior to the CCA and the IJV, *Pj* denotes posterior to internal jugular vein and *Pc* denotes posterior to the common carotid artery [2]. The *P* (*73 %*) location of the VN is the most common configuration observed on either side followed by the *Pc* (15 %), *Pj* (8 %) locations. About 4 % of cases of *A* location are observed overall (Fig. 12.1) [2]. Such classification is useful in the intraoperative setting to localize the VN for IONM. VN identification may also be expedited without direct visual identification of VN by using the stimulation probe at 2 mA with blind stimulation of the carotid sheath between the carotid and jugular.

Section 2: The Basic Classification of RLN Surgical Anatomic Path in the Neck Base

In this section the basic classification of RLN surgical anatomic path in the neck base as it relates to the thyroid surgical procedure is described, this classification broadly categorizes RLN as:

1. Normal trajectory
2. Abnormal-acquired
3. Abnormal-embryological

Each of these classes is described in detail and subclassified based on further anatomic

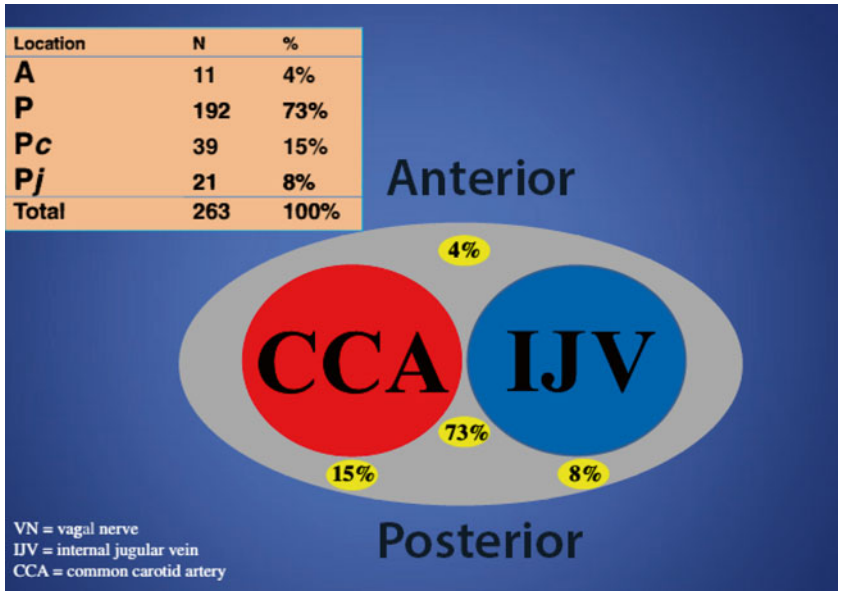

Fig. 12.1 Location/classification of VN within carotid sheath, *VN* vagus nerve

deviations. The classification specifics and the estimated prevalence of the classes are depicted in Table 12.1.

Normal Trajectory: L1 and R1

As the heart and great vessels descend during embryologic life, RLN is drawn down by the lowest persistent aortic arch. Vagus nerves on the right and left sides track differently. The right vagus nerve courses from the posterior aspect of the carotid sheath in the neck base and tracks anterior to the first segment of the subclavian artery. The RLN branches from vagus nerve at this point, first travels inferoposteriorly to loop around this segment of the subclavian artery (the fourth branchial arch remnant) to progress superomedially along the neck floor behind the common carotid artery into the right thoracic inlet in the base of the neck and then extends superiorly more obliquely from lateral to medial direction as it ascends the neck. The left vagus nerve courses from the posterior aspect of the left carotid sheath in the neck base anterior to the aortic arch and the left RLN branches underneath the aortic arch just lateral to the obliterated ductus arteriosus and courses posterosuperiorly. The left RLN is medial and ascends into the paratracheal region in a straight course within the tracheoesophageal groove as compared to the oblique profile of the right RLN in the right paratracheal region (Figs. 12.2A–C and 12.3a,b). Multiple studies show that the left RLN travels in a path that is parallel to the tracheoesophageal groove or at an angle less than 30° in at least 80 % of cases whereas the right RLN travels in a path between 15 and 45° relative to the tracheoesophageal groove in nearly 80 % of cases. In their distal most course, before entering the larynx at the edge of the cricoid cartilage, both right and left RLNs travel along the trajectory that more closely parallels the tracheoesophageal groove [3–6]. The relationship

Table 12.1 The RLN anatomical classification and the estimated prevalence of each class

Class	Description[a]	Estimated prevalence
I. Left recurrent laryngeal nerve class		
L1	Normal trajectory	95 %
L2a	Abnormal acquired-lateral	5 %
L2b	Abnormal acquired-ventral	<1 %
L3	Abnormal embryologic - left nonrecurrent (NRLN)	0.04 %
II. Right recurrent laryngeal nerve class		
R1	Normal trajectory	90 %
R2a	Abnormal acquired-medial	5–10 %
R2b	Abnormal acquired-ventral	<1 %
R3	Abnormal embryologic-right nonrecurrent (NRLN)	0.5–1 %
III. Clinically important neural feature		
Anatomical		
F-Fixed/splayed/entrapped	Capsular Association through fascial bands, vessels, or goiterous change	With substernal goiter 15 % [7]
I-Invaded	Neural invasion	With cancer <5 % [7]
L-posterior Ligament of Berry entrapment	Posterior ligament of Berry or associated vessel neural entrapment	10 % [7]
B-branched	Extralaryngeal RLN branching	24.3–72 % [15–19]
T-Thin caliber nerve	Neural caliber <1 mm	<2.5 % [20, 21]
Dynamic		
LOS-loss of signal	Loss of electrophysiologic monitoring signal	
D-extensive neural dissection	Extensive nerve dissection or 360° neural bridging off	

[a] *1* normal trajectory, *2* abnormal-acquired, *3* abnormal-embryological

of both right and left RLNs with the ligament of Berry and the details of their laryngeal entry point have been well described previously [7].

Abnormal Left Recurrent Laryngeal Nerve Classes

Acquired Variation of Left RLN: L2a

When goiter on the left side is significantly infiltrating tracheoesophageal groove, a more lateral displacement of the left RLN may occur. Figures 12.2D and 12.3a, c demonstrate the lateral displacement of the left RLN in a patient in whom the goiter infiltrated the tracheoesophageal groove. This acquired variation of the left RLN is labeled as L2a.

Acquired Variation of the Left RLN: L2b

If a left-sided goiter excavates the region deep to the trachea, the left RLN maybe brought ventral to the main thyroid lobar element where it may be draped over the ventral surface of the lobe as seen after strap muscle retraction. In our system this nerve is defined as L2b (Figs. 12.2E and 12.3a).

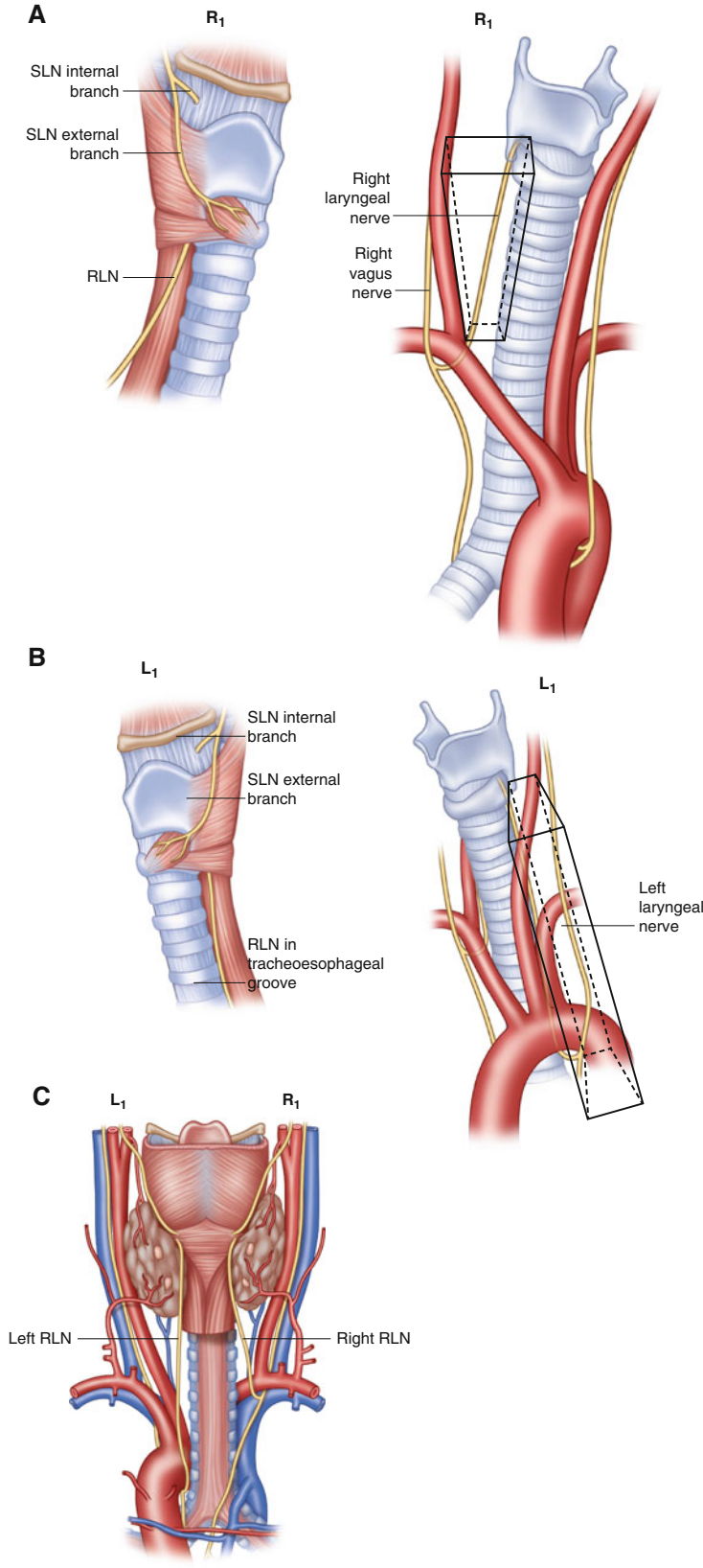

Fig. 12.2 (**A**) R1—Normal pathway of the right RLN through the right paratracheal region. (**B**) L1—Normal pathway of the left RLN through the left paratracheal region (**C**) (*left side*) L1—Normal pathway of the left RLN through the left paratracheal region. (*Right side*) R1—Normal pathway of the right RLN through the right paratracheal region.

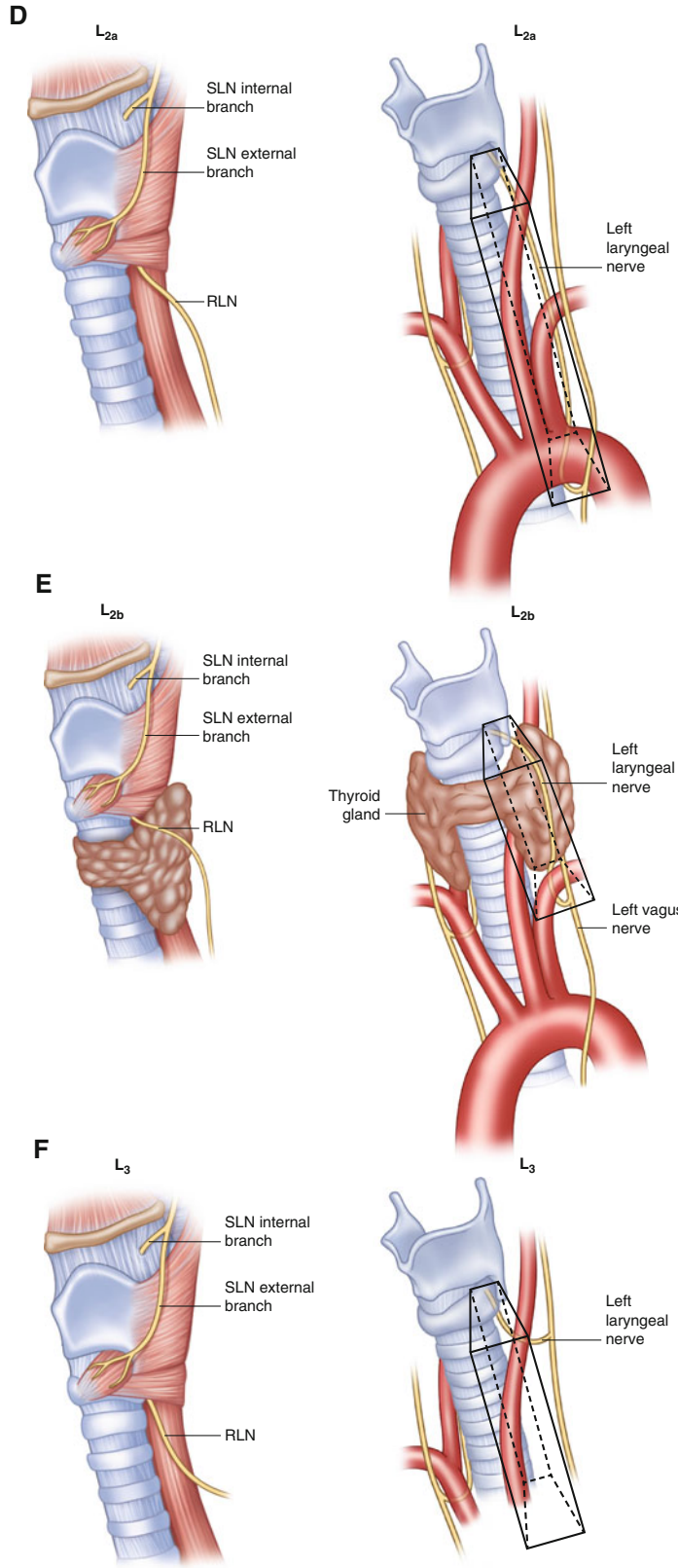

Fig. 12.2 (continued) (**D**) L2a—Abnormal acquired-lateral displacement of the left RLN (**E**) L2b—Abnormal acquired-ventral displacement of the left RLN on the thyroid gland (thyroid gland is shown). (**F**) L3: Abnormal embryological left RLN–L NRLN

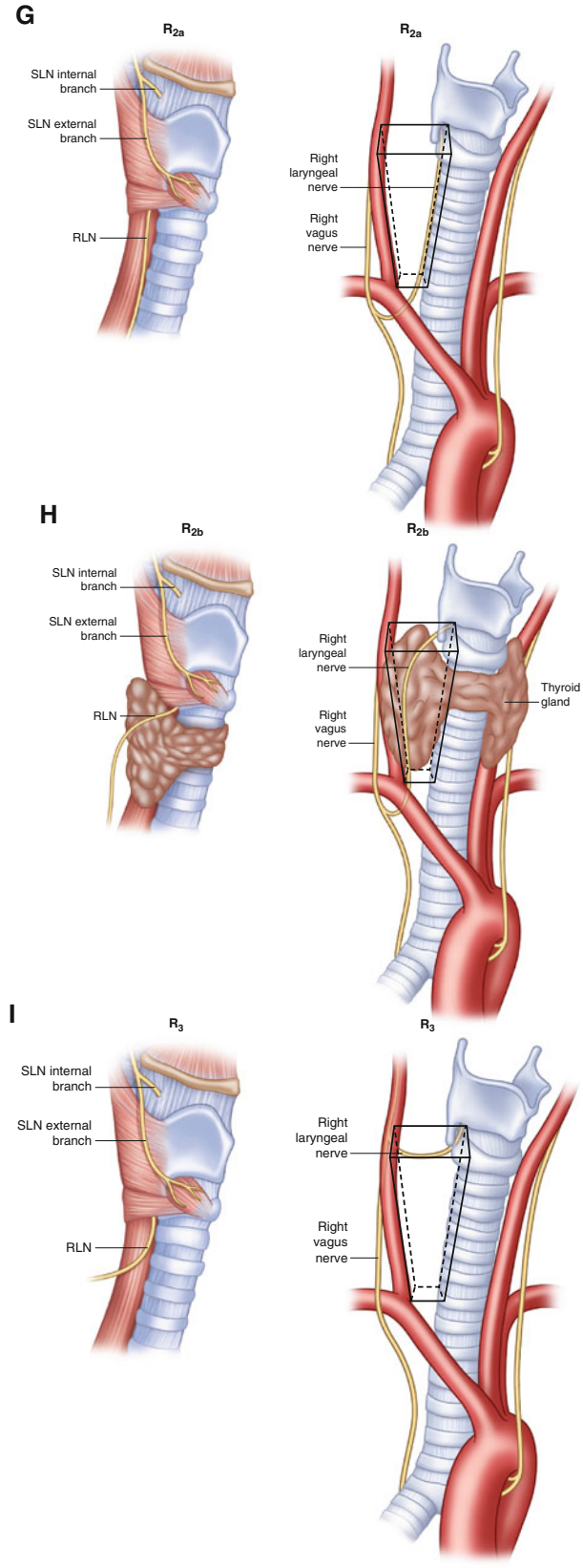

Fig. 12.2 (continued) (**G**) R2a—Abnormal acquired medial displacement of the right RLN. (**H**) R2b—Abnormal acquired-ventral displacement of the right RLN on the thyroid gland (thyroid gland is shown) (**I**) R3: Abnormal embryological right RLN–R NRLN

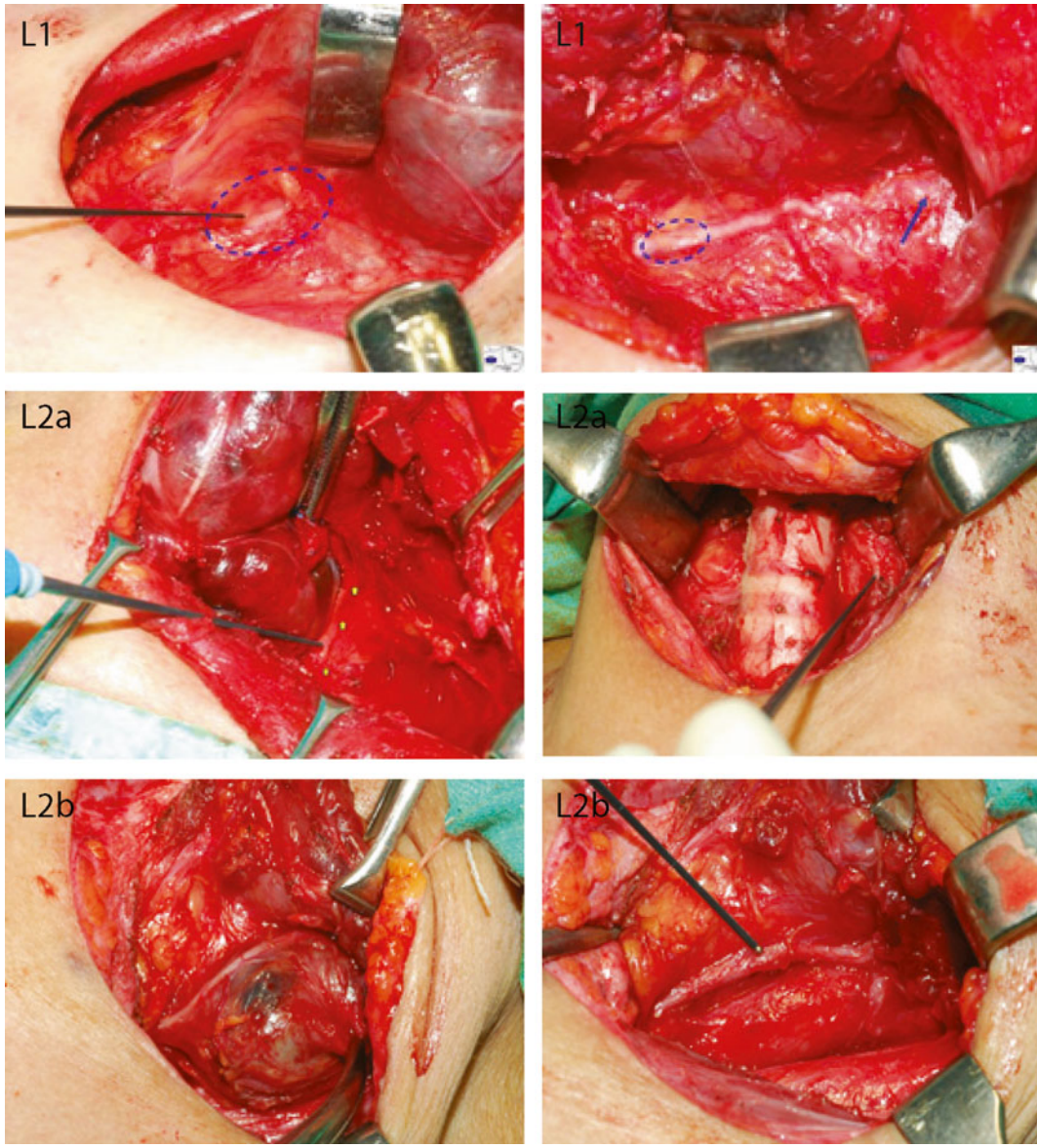

Fig. 12.3 (**a**) Left recurrent laryngeal nerve types, *L1*: Normal trajectory, *L2a*: Abnormal acquired-lateral, *L2b*: Abnormal acquired-ventral

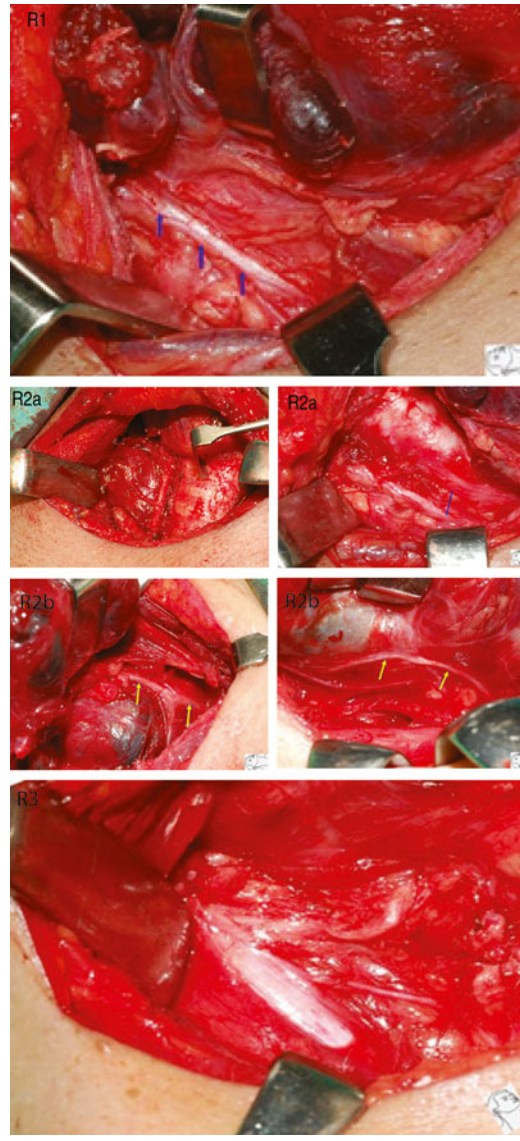

Fig. 12.3 (continued) (**b**) right recurrent laryngeal nerve types, *R1*: normal trajectory, *R2a*: Abnormal acquired-medial, *R2b*: Abnormal acquired-ventral, *R3*: Abnormal embryologic-right NRLN

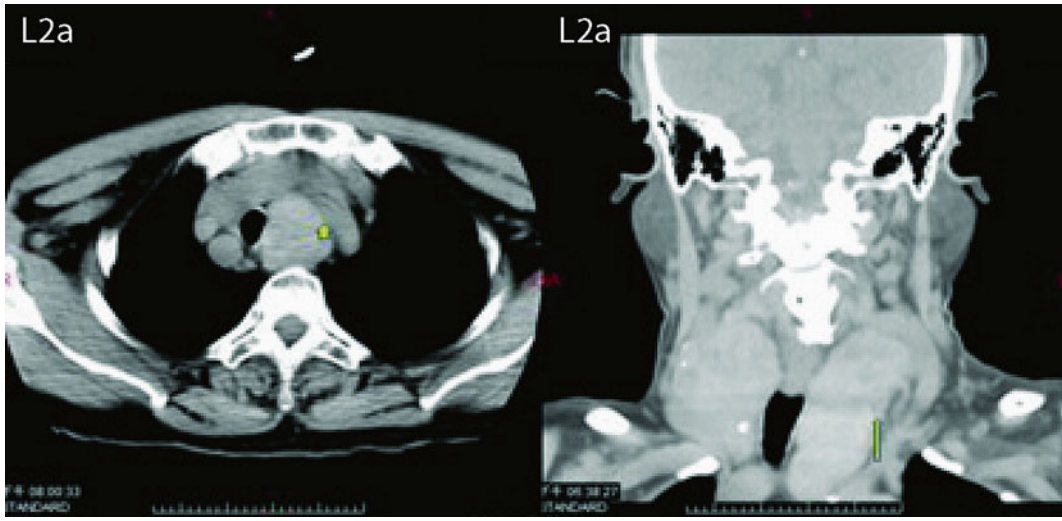

Fig. 12.3 (continued) (**c**) CT Scan images showing *L2a* Abnormal acquired-lateral

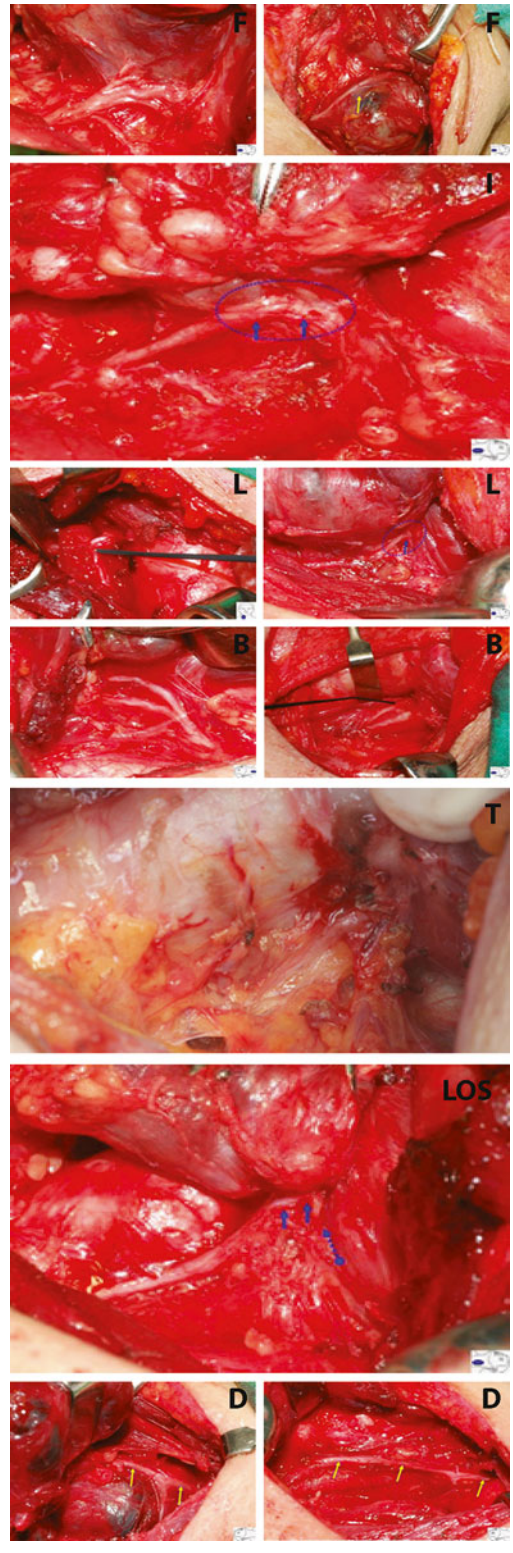

Fig. 12.3 (continued) (**d**) Recurrent laryngeal types based on clinically important neural feature; *Anatomical features*: *F* Fixed/splayed/entrapped, *I* Invaded, *L* posterior ligament of Berry entrapment, *B* branched, *T* Thin caliber nerve; *Dynamic features*: *LOS* loss of signal (RLN traction with LOS at two *small blue arrows*), *D* Extensive neural dissection

Embryologic Variation of the Left RLN: The Left NRLN or L3

This is extremely rare and non recurrent laryngeal nerve (NRLN) on the left side has been described with estimated incidence of only 0.04 % [8]. Henry in 1988 described two NRLNs on the left [8]. The left NRLN is termed as L3 (Fig. 12.2F). The embryologic anatomical requirements for a left NRLN are that it should be accompanied by simultaneous occurrence of other anomalies, namely situs invertus, aberrant subclavian artery, and absent left ductus arteriosus [9] (NRLN is described in detail in Chap. 11).

Abnormal Right Recurrent Laryngeal Nerve Classes

Acquired Variation of Right RLN: R2a

Goiterous change of certain aspects of the normal thyroid lobe especially the more dorsal aspects of the mid-inferior pole may serve to displace the normally oblique right RLN medially into a straighter tracheoesophageal groove position, thus pushing the right RLN from the original lateral to the newly acquired medial position. This is termed as the R2a (Figs. 12.2G and 12.3b).

Acquired Variation of Right RLN: R2b

When thyroid tissue extends from a dorsally oriented tubercle of Zuckerkandl and forms a retrotracheal cervical goiter or posterior mediastinal goiter, substernal goiters type IIA and B, the RLN may be excavated posteriorly by this segment of tissue and potentially result in significant displacement of the RLN ventrally [7]. This produces a segment of thyroid tissue dorsal to the nerve. The RLN is then brought ventral to this segment of tissue (Figs. 12.2H and 12.3b). This we term right RLN class R2b.

Embryologic Variation of the Right RLN: The Right NRLN or R3

The embryologic considerations imply that when the right subclavian artery arises from the distal aortic arch and extends to the right in a retroesophageal course the right RLN runs a more direct and medial course from the vagus to its laryngeal entry point. Several different sloping patterns have been described (NRLN) [10]. This is right NRLN which is denoted in our system as R3 (Figs. 12.2I and 12.3b). It should be noted that a relatively common anastomotic branch from the sympathetic chain to the RLN occurring in up to 1.5 % of patients may be misinterpreted as a right NRLN [11] (NRLN is described in detail in Chap. 11).

Clinically Important Neural Features

In addition to the above L1–L3 and R1–R3 classes, other factors are also important in surgical anatomic classification system of both the right and left RLN classes. These can be denoted by additional lettering added to the L or R and can be classified as Anatomical or Dynamic.

Anatomical:

F: fixed/splayed/entrapped,

I: invaded,

L: posterior ligament of Berry -entrapped, B: branched,

T: thin caliber

Dynamic:

LOS: loss of electrophysiologic signal,

D: extensive nerve dissection.

Anatomical

Goitrous enlargement of the thyroid gland will often result in the mass being closely associated with the RLN, which may splay the nerve or trap

the nerve with bridging vessels depending on the size of the goiter. It is estimated that up to 15 % of substernal goiters may be associated with this neural finding [7]. These types of RLN are denoted by letter F (Fig 12.3d). Blunt delivery of the goiter in these circumstances risks neural stretch.

Similarly, the RLNs may be invaded by a malignant tumor; while this does not relate to the underlying neural anatomy, it substantially changes the surgical anatomy and so should be designated in a nerve classification system (denoted by letter I) (Fig. 12.3d).

Neural monitoring studies of Chiang and Snyder [12, 13] beautifully demonstrate that the ligament of Berry, especially when associated with a posterior ligament or vascular elements relevant to the nerve, is the site of traction injury in up to 75 % of neuropraxic nerve injuries. Therefore the entrapment of the nerve in the ligament of Berry should be noted in a nerve classification system (in this classification, it is denoted by letter L) (Fig. 12.3d).

RLN branching patterns have been extensively evaluated (detailed in Chap. 8 in this book). The work of Sancho and Sitges-Serra [14] has shown that more extensive branching patterns are associated with higher risk of surgical injury and so branching patterns recognized at surgery should be incorporated in the neural classification system, denoted by letter B (Fig. 12.3d).

Our work has suggested that the caliber of the nerve especially of the nerve segment interacting with the ligament of Berry relates to the potential risk of nerve injury. The thinner caliber RLNs are more likely to be subject to traction injury at the ligament of Berry. For this reason we include nerve caliber as a qualifying parameter in our nerve classification system (denoted by letter T).

Dynamic

Many surgeons use IONM, loss of signal during IONM has been shown to be a reliable predictor of postoperative glottic function and so this new electrophysiologic element is included in our RLN classification system, as it has great functional significance [3]. This is denoted as LOS in our classification system (Fig. 12.3d).

Finally the extent of neural dissection may relate to postoperative function. We found that especially in cases of thin caliber nerves that are dissected all around (360° dissection), separating the nerve off its bed places the nerve at greater risk for traction injury. Hence the extent of neural dissection is included as an added qualifying parameter in our nerve classification system, denoted in the classification by letter D (Fig. 12.3d).

Examples of Applying the Classification System

Using our classification system a right RLN which is displaced medially and is branched and has lost neural signal during surgery is categorized as R2a/B, LOS. A right RLN travelling in a normal right trajectory and requires extensive neural dissection is categorized as R1/D.

Similarly a left RLN that is laterally displaced, is of thin caliber and is invaded by cancer is recorded as L2a/T, I. A left RLN that followed a normal or typical left-sided trajectory and was branched would be categorized as L1/B.

Conclusion

We hope that this classification would help us develop a better understanding of the surgical anatomy as well as functioning of the RLN when encountered during surgery by allowing more effective communication amongst surgeons and also by assisting in a more rational and uniform data collection in future research work.

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Surgical Approaches to the Recurrent Laryngeal Nerve

13

Emad Kandil, Michael Singer, Ahmed Deniwar, and Gregory W. Randolph

Abstract

During thyroid and parathyroid surgery, avoiding injury to the recurrent laryngeal nerve (RLN) is critical. Several general principles should be adhered to when performing these surgeries in order to protect the nerve. Visual identification and dissection of the RLN is now the standard technique for its preservation during thyroid surgery. Based on the pathology and indication for surgery, the optimal approach to the RLN, lateral, superior or inferior, should be utilized.

Keywords

Recurrent laryngeal nerve • Surgery • Dissection • Thyroidectomy • Remote access • Robotic thyroidectomy

Overall Approach

While several techniques for identifying the recurrent laryngeal nerve (RLN) are available to surgeons, the most fundamental question is whether risk of injury is minimized by nerve identification or avoidance. Historically, many surgeons adopted surgical approaches that were designed to avoid identification and dissection of the RLN [1]. These were premised on the belief that manipulation of the nerve was likely to lead to injury [2]. Additionally, it was thought that by

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performing strict capsular dissection the nerve would simply not be encountered during surgery. However, as discussed in other chapters, the anatomy of the nerve does not guarantee that avoidance will maintain its integrity.

Many studies have now confirmed that identification and visualization of RLN is the safest method for nerve management [3, 4].

Identification of the RLN is based on an expert knowledge of both normal and aberrant anatomy of the nerve and surrounding structures. Rather than a single structure dictating the location of the nerve, an understanding of a host of anatomical relationships (discussed in detail in other chapters) should be employed when seeking it. Until recently, dissection and identification were based on visual clues only. Many surgeons now promote the use of a nerve monitoring system to aid in initial localization of the RLN by "neural mapping."

General Principles

When dissecting the RLN, proper exposure during surgery is critical. To facilitate that, in cases of goiter, the strap muscles can be divided if retraction does not provide adequate exposure. To optimally reveal the region of the RLN, while retracting the strap muscles laterally, the laryngotracheal complex with the thyroid should be retracted ventromedially.

Blood may obscure visualization of the nerve, so a bloodless field is important for nerve identification. Despite meticulous attempts at hemostasis, bleeding, particularly from the area of the ligament of Berry, can occur during dissection or after extraction of the thyroid gland. This is best managed with careful, pinpoint bipolar cautery or clamping of specific sources of bleeding while fully visualizing the RLN. Blind clamping or cautery in the region of the RLN without direct nerve visualization exposes the nerve to injury.

Critically, when dissecting the nerve, no structure should be cut unless the position of the RLN is clearly understood. Strict adherence to this rule will reduce transection injuries to very low rates. While the nerve is traced, close attention should be paid to the degree of tension that is applied to the nerve. Excessive retraction of the thyroid gland can lead to a RLN traction injury [5]. As the gland is moved medially, the larynx can be displaced upwards, stretching the distal RLN and increasing the risk of neuronal dysfunction. One proposed technique for RLN identification, the palpation technique, exploits the tension that can be placed on the nerve [6]. In theory, this tension makes palpating the nerve easier. While plausible, use of this technique should be avoided because of the injury that might result from this tension.

Specific Techniques

While each patient demands a slightly different technique for management of the RLN, the methods for identifying and dissecting the nerve can be broadly divided into three approaches: lateral, superior, and inferior. Surgeons performing thyroid surgery should be familiar with all three techniques, as it cannot always be predicted when a specific approach may be required [7].

Lateral Approach

The lateral approach is the most commonly utilized RLN technique during routine open thyroidectomy. In this approach, the RLN is sought at the level of the middle of the thyroid lobe [8].

In the lateral approach, mobilizing the sternohyoid and sternothyroid muscles exposes the thyroid and central compartment. The strap muscles are retracted laterally exposing the carotid artery and jugular vein. The carotid artery is then carefully retracted laterally and the thyroid medially to access the paratracheal soft tissue. This is the general area where the RLN lies.

The inferior and superior thyroid poles are dissected and the vessels in those areas are managed appropriately. Dividing the middle thyroid vein facilitates retraction of the thyroid medially and improves exposure of the paratracheal region. To preserve the vascular supply to the inferior parathyroid gland, it is best to dissect the parathyroid from the inferior pole before retracting the lobe medially [9].

As noted earlier, a number of structures can act as approximate landmarks for seeking the

nerve, including the parathyroid glands, the tubercle of Zuckerkandl, the inferior thyroid artery, and the inferior edge of the inferior cornu of the thyroid cartilage. Using all of these structures as clues often leads to prompt identification of the RLN.

One significant benefit of the lateral approach is that the nerve is identified and dissected only in its last few distal centimeters prior to it passing deep to the inferior constrictor muscle. It avoids uncovering the nerve at the thoracic inlet and lower cervical region, thus allows for more limited RLN dissection. Additionally, avoiding dissection of the nerve in the lower cervical region aids in preserving the vascular supply to the inferior parathyroid gland.

This approach may not be suitable in some circumstances that limit exposure of the lateral thyroid region, such as with a large goiter or a well-developed tubercle of Zuckerkandl. The application of this approach in revision thyroid surgery is challenging because of dense scar tissue that often obscures the lateral thyroid region. In revision thyroidectomy, it is often easier to identify the RLN in an area which contains minimal scar tissue from the previous surgery. By working inferior to the plane of previous dissection, scar tissue can often be avoided.

Several other factors should be considered when utilizing the lateral approach. As the RLN is found rather distally in its course with this approach, extralaryngeal branching may have already occurred. One cannot simply assume that a nervous structure represents the entirety of the RLN and care must be taken that all branches of the nerve are identified and preserved. The unusual situation of a nonrecurrent laryngeal nerve also presents significant risk when using the lateral approach. Due to its aberrant course, often running almost perpendicular to its expected orientation, such a nerve can be easily overlooked and transected [10].

Superior Approach

The superior approach to the RLN can be challenging but invaluable in cases with large cervical or substernal goiters. Large glands prevent adequate retraction to expose the nerve in the regions seen with the lateral or inferior approaches. This technique can also be used if the RLN is not successfully found using one of the other approaches or in cases where there is a suspicion of a nonrecurrent laryngeal nerve. If performing remote access surgery using a retroauricular incision, the vector of approach to the thyroid is from superior to inferior. The superior approach for finding the RLN is consequently the evident technique in these cases.

In the superior approach, the superior pole of the gland is exposed and the pedicle is ligated. Particularly, in large goiters the external branch of the superior laryngeal nerve can extend inferiorly along the superior pole and as a result can be easily injured if care is not taken to protect it. After division, the superior pole is reflected in the ventral–lateral direction. This maneuver will expose the inferior constrictor muscle. At the inferior margin of this muscle, the ligament of Berry will be encountered. The RLN will be found in this area running under the inferior constrictor muscle. This is an advantage of the superior approach as the laryngeal entry point is the most constant anatomical site of the RLN. In addition to visual recognition, use of neuromonitoring can greatly aid in this approach.

While ideal in certain situations, the superior approach does present some challenges. Dissection at the fibrous ligament of Berry can be arduous as it bleeds easily and small amounts of blood can easily visually obstruct the field. As the RLN extends distally its caliber can decrease, causing it to be difficult to distinguish from adjacent small vessels. Also, surgeons must remember that this distal segment of the nerve is relatively fixed and consequently is particularly susceptible to stretch and neuropraxic injury. Care should be taken to avoid exerting excessive tension on the nerve either while dissecting or simply by overly retracting on the superior pole.

Inferior Approach

The inferior approach was popularized by Sedgwick and Lore in the 1970s [11, 12]. This technique was taught to many surgeons as the

standard approach for finding the RLN and can be used in most routine thyroidectomies. However in patients with large goiters, particularly if substernal, the inferior approach cannot be used due to an inability to expose the RLN triangle.

The RLN triangle is the key concept in the inferior approach. The RLN is sought in this inverted triangle, whose apex extends inferiorly toward the thoracic inlet [13]. The retracted inferior thyroid pole represents the base of the triangle, and the medial and lateral walls are formed by the trachea and the retracted strap muscles.

The bed of tissue in this area is soft and the RLN is not fixed in position (such as it is at the ligament of Berry). Both of these factors facilitate dissection of the nerve without injury. Further, the nerve in this area consists of a single trunk without branches and tends to have a larger diameter.

The inferior approach can be used routinely, however many surgeons now avoid it for several reasons. As the RLN is identified quite proximally along its course, a long segment of the nerve must be dissected to trace it to its entry into the larynx. This increased length of dissection may increase the risk of injury. Another potential disadvantage of this approach is the possibility of devascularization of the parathyroids, especially the inferior glands, due to the extensive dissection.

Revision thyroid surgery is an optimal situation for utilization of the inferior approach. As noted earlier, in patients who previously have undergone thyroidectomy the lateral approach is often not feasible due to extensive scarring and fibrosis. By seeking the nerve in an area inferior to the plane of the previous surgery, it can often be found without great difficulty.

Minimally Invasive and Remote Access Surgery

Over the last two decades a number of minimally invasive approaches to thyroid surgery have been described, the most popular of which is the video-assisted approach (MIVAT) described by Miccoli et al. [14]. More recently, remote access techniques, in which the incision is not placed on the anterior neck, have garnered significant attention [15, 16]. These procedures require surgeons to be familiar with approaches to the RLN that have slightly different vectors than those used in more conventional surgery.

During MIVAT, while viewed through an endoscope, the thyroid compartment is visualized in the same orientation as in conventional thyroidectomy. Consequently, the approach to the RLN is similar to the lateral approach. During these cases, in order to adequately expose the paratracheal area it is crucial to retract the thyroid not only in a medial but also in a ventral direction. By rotating the thyroid from its paratracheal location, the RLN can be identified just proximal and deep to the tubercle of Zuckerkandl. Dissection of the thyrotracheal groove is carried out using small atraumatic instruments under endoscopic magnification. This magnification provides excellent visualization of the nerve. After delivery of the gland through the incision, surgeons should pay particular attention to avoid excessive retraction, which potentially increases the risk of RLN stretch injury.

The approach to the RLN during remote access thyroid surgery is determined by where the incision is made. Using a retroauricular (or facelift) incision, the gland is encountered from above. As a result, the RLN is most successfully found using the superior approach. The superior pedicle is encountered and ligated. The superior pole is then retracted inferiorly and ventrally, exposing the area of the inferior constrictor muscle. Due to the orientation of this technique, after the nerve is found the area of the ligament of Berry is easily managed.

Another popular remote access technique, the transaxillary procedure, approaches the gland from an inferolateral direction. The gland is first mobilized by releasing the superior and inferior poles and the anterior surface of the trachea is exposed. The gland is then retracted medially. The RLN is sought and dissected in the tracheo-esophageal groove. The orientation when seeking the RLN in transaxillary thyroidectomy is quite different from traditional thyroid surgery. Rather

than visualizing and approaching the surgical bed in a ventral to dorsal trajectory, the RLN is sought in along a lateral to medial axis.

RLN Dissection Tips and Pitfalls

There is no replacement for clinical experience and expert knowledge of the surgical anatomy. However, the following tips can help facilitate safe identification and dissection of the RLN [9]:

- As noted above, applying the simple rule of not cutting any structure when dissecting the nerve until its course is fully identified will reduce permanent nerve injury rates to a minimum. If tracing the nerve visually, the nerve must be in full view when dividing overlying tissue. If neuromonitoring is being used to guide dissection, tissue must be stimulated and provide a negative response before transection.
- After the RLN is identified, only the minimal amount of dissection of the nerve necessary to complete the surgery should be performed. Any dissection around the nerve needed to expose and reveal its course is appropriate. However once this is achieved, any extraneous dissection should be avoided.
- Great care should be taken when retracting the gland medially as the RLN is traced distally. Tension placed on the thyroid can be transferred to the RLN, particularly by the fibrous attachments of the ligament of Berry. As tissue attachments to the thyroid are released the same amount of force is distributed over a narrower area, increasing the tension placed on these tissues. It is critical to avoid excessive tension to prevent a neuropraxic injury of the nerve. With retraction, pressure can also be applied to the nerve by a blood vessel bowstringing across it.
- The RLN always divides ultimately into at least a single anterior and single posterior branch [17]. However the branching pattern can be markedly more complex, including multiple anterior or sensory branches [18]. Consequently, surgeons must be certain that they are tracing the anterior branch of the nerve and that additional motor branches are not being overlooked. Mistakenly following the posterior branch of the nerve can result in inadvertent transection of the crucial anterior branch. If an anterior branch has a small caliber, one must be suspicious that it represents just one of the elements of motor division of the RLN. In this situation, retrograde dissection can be performed to exclude proximal branching.
- Small caliber nerves or those enmeshed in the ligament of Berry have a higher risk of injury. If the RLN is at high risk of injury, a small part of normal thyroid tissue (away from cancer margins if present) may be left at the point of nerve entry to avoid damage [9].
- Any form of cautery should be applied cautiously when working within a close proximity to the nerve. It is common after gland removal to have small sources of bleeding, particularly in the area of the ligament of Berry. Hemostasis must be achieved without exposing the RLN to risk of excessive thermal trauma. Bipolar cautery, which can be delivered precisely with a fine jeweler's forceps and should be activated only transiently, is the optimal device for hemostasis in the region of the nerve.
- While dissecting the nerve, if a parathyroid gland that is closely adherent to the thyroid capsule is encountered, then preservation of the gland with an adequate blood supply should be attempted. However, if this is prohibitively difficult and puts the nerve at risk, the gland should be removed and then autotransplanted. It should be remembered that preservation of the RLN is paramount.
- Large goiters, especially if substernal, can stretch the RLN, which may be redundant after extraction of the enlarged gland. Lack of attention to the nerve at its distal segment after thyroid gland extraction can lead to injury. Therefore in these cases, the nerve should be identified up to the point where it enters the larynx.
- Aggressive suctioning or vigorous use of peanuts or gauze during nerve dissection can injure the nerve, so this should be minimized.
- The anterior arch of the cricoid cartilage serves as an important landmark in thyroidectomy. The RLN enters the larynx just deep to

the inferior constrictor muscle, which rests on the cricoid cartilage. After this point, the nerve is within the larynx and no longer in the surgical field.

- The cricothyroid muscle should be dissected cautiously, as cautery of the ventral surface of the muscle can lead to injury and laryngeal dysfunction postoperatively.

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Part IV

IONM of the RLN

Gianlorenzo Dionigi

IONM of the Recurrent Laryngeal Nerve

14

Gianlorenzo Dionigi, Henning Dralle, Whitney Liddy, Dipti Kamani, Natalia Kyriazidis, and Gregory W. Randolph

Abstract

Thyroid surgery can pose risk to both the right and the left recurrent laryngeal nerves (RLN) in a single surgical procedure. Unilateral vocal cord palsy (VCP) can lead to morbidity related to changes in voice, especially in professional voice users, as well as potential dysphagia and aspiration, while bilateral VCP may require tracheostomy. Visualization of the RLN during surgery has been considered the gold standard for preventing injury to the RLN; however, an intraoperatively visualized and structurally intact nerve does not necessarily represent a postoperatively functioning nerve. Neural monitoring has increasingly gained the attention of surgeons performing thyroid and parathyroid surgeries around the world. Current studies suggest that a majority of general and head and neck surgeons use neural monitoring in at least some of their thyroid surgical cases. This chapter presents a historical overview and usage patterns of intraoperative

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neural monitoring (IONM) of the RLN and discusses its impact on surgical practice, including intraoperative applications of IONM, medicolegal aspects and standards of IONM, normative data, as well as current advances in IONM such as continuous IONM.

Keywords
IONM • RLN • Vocal cord paralysis • Standards of IONM • Thyroid surgery • Injury to RLN • Medicolegal issues in thyroid surgery

Introduction

By conveying both information and emotion in a unique way, the voice represents an essential part of human communication. Although modern thyroid surgery origins can be traced to more than 100 years ago, recurrent laryngeal nerve (RLN) injury is still the most dreaded complication. In 1938, Lahey from Boston first proposed routine identification of the RLN during thyroid surgery, effectively reducing RLN palsy rates. Lahey, in his report of over 3000 thyroidectomies performed with routine visualization of the RLN, stated that "careful dissection would definitely decrease the number of injuries to the RLN" and was able to show a decrease in the RLN injury rate from 1.6 % to 0.3 % [1]. Karlan (1984), Jatzko (1994), and Hermann (2002) demonstrated that extensive dissection of the RLN facilitates visual control of nerve integrity during resection, with reported RLN palsy rates of 1–2 %, and is therefore superior to more limited nerve exposure or lack of nerve identification [2–4]. Presently, an overall RLN palsy rate of about 10 % is reported in routine thyroid surgery; 0.5–2 % in goiters and up to 20 % in cancer, Graves' disease or revision thyroidectomies [5, 6]. Since approximately 5–7 % of the world population suffers from thyroid disease, and approximately 10–15 % of this group will undergo surgery, clearly optimal RLN management is needed. RLN injuries are avoided with meticulous anatomic localization during surgical dissection [7, 8]. The standards for RLN management during thyroid surgery include comprehensive knowledge of RLN anatomy, cervical exposure and routine visual identification of the RLN, gained experience and training, and pre- and postoperative laryngoscopy (Table 14.1) [5, 9, 10]. Standards of care do change over time, with new technologies proposed and applied in thyroid surgery, including intraoperative neural monitoring (IONM) [11–13]. This chapter reviews relevant literature with a focus on the prevalence of IONM use and its technique, as well as how IONM may improve standards of the modern technique of thyroidectomy [12, 13]. The authors make their recommendations based on the literature, guidelines, and experience [14–16]. This report does not endorse any specific company or set of monitoring equipment.

Table 14.1 Standards for RLN management during thyroid surgery

- Extensive knowledge of RLN anatomy
- Routine visual identification of RLN
- Cervical exposure of RLN
- Experience
- Training
- Pre- and postoperative laryngoscopy

Historical Overview

In 1848, Du Bois-Reymond first demonstrated the action potential of nerves and described the electrical activity of muscle with performance of the first electromyography (EMG) [14]. The first use of intraoperative electroencephalography (EEG) was by Foerster and Alternberger in 1935 [14]. IONM has been utilized in attempts to minimize neurological morbidity from operative

manipulations [14]. The goal of monitoring is to identify changes in nerve function prior to irreversible damage. IONM is used to localize neural structures (such as cranial nerves during skull base surgery), to test function of these structures, and to provide early detection of intraoperative injury, allowing for immediate corrective measures [14]. Neuromonitoring has been most commonly used by spine surgeons, but neurosurgeons, vascular surgeons, orthopedic surgeons, otolaryngologists, and urologists also utilize neuromonitoring to some extent. The actual procedures where neuromonitoring is most commonly applied include spine surgery, selected brain surgeries, carotid endarterectomy, and ENT procedures including acoustic neuroma (vestibular schwannoma) resection, parotidectomy, and neck dissection surgery. Motor-evoked potentials have also been used in surgery for thoraco-abdominal aortic aneurysms [14]. In 1966, Shedd and Durhan from Yale University first published the electrical stimulation, identification, and response evaluation of the RLN and superior laryngeal nerve (SLN) in a canine model using endolaryngeal balloon spirography [17]. The experiments indicated that a pressure recording from a balloon in the larynx consistently showed recognizable changes upon electrical stimulation of the RLN. This provided a method for electrical identification of the RLN. For the SLN, pressure changes on stimulation were more variable but still definite enough to permit identification. The same authors performed a clinical evaluation of the procedure in human thyroid operations and reported that the endolaryngeal balloon pressure recording clearly signaled when the RLN and SLN were stimulated in the first two patients [17]. Riddell in 1970 published the results of RLN identification during thyroid surgery over 23 consecutive years (1946–69), with a description of an additional safety measure, i.e., laryngeal palpation with stimulation of the RLN [18]. Galivan and Galivan in 1986 presented a safe and simple technique for RLN identification during thyroid and parathyroid surgery that did not require additional surgical instruments and could be performed routinely by palpation of the posterior cricoarytenoid muscle with stimulation of 0.5–2.0 mA [19]. Nonetheless, the authors emphasized that thorough knowledge of cervical anatomy still remained the most important skill in this surgery.

Since 1980, different IONM techniques have been proposed including invasive and noninvasive devices, laryngeal palpation, glottic pressure monitoring, glottic observation, endoscopically placed intramuscular vocal cord electrodes, endotracheal tube-based surface electrodes, and postcricoid surface electrodes [15, 20]. The system of endotracheal tube-based surface electrodes has become popular for IONM of the RLN in thyroid surgery because of several advantages, including ease of setup and use, its noninvasive nature, and the capacity of a surface electrode to contact larger areas of target muscles with summation of responses reflected in the EMG [15, 20–22]. Among the various methods of RLN monitoring reported in the literature, the use of surface electrodes fixed directly to the endotracheal tube is considered to be similar (from a practical surgical point of view) to the use of monopolar electrodes placed endoscopically in laryngeal muscles, bipolar electrodes placed during surgery through the cricothyroid membrane, and surface electrodes placed in contact with postcricoid muscles [15, 20–22]. Although the muscle potentials recorded with surface electrodes may have lower amplitudes, they demonstrate similar stimulation thresholds [23]. Systems equipped with surface electrodes directly fixed to the endotracheal tube are easier to use than intramuscular electrodes, which are more complicated to insert, may be implanted in the wrong location, may migrate during the operation, or may even break.

The standardization of IONM technique offers a uniform application of IONM [24–26]. The evolution of technology has led to the use of new systems capable of performing continuous monitoring (C-IONM) with documentation of any impending stress to the RLN [27]. In 2006, the International Neural Monitoring Study Group (INMSG) was founded to serve the emerging field of neurophysiologic monitoring of the laryngeal nerves in thyroid and parathyroid surgery [33]. The INMSG is a multidisciplinary

international group of surgeons and researchers selected based on clinical experience and expertise in thyroid and parathyroid surgery, neural monitoring, and related fields. The INMSG includes surgeons (otolaryngologists, general surgeons, and endocrine surgeons), laryngologists, voice and laryngeal EMG specialists, anesthesiologists, neurophysiologists, and technologists. The INMSG has published guidelines on RLN and external branch of the superior laryngeal nerve (EBSLN) IONM standards for monitored thyroid and parathyroid surgery [15, 34]. Goals of the INMSG are to improve the quality of IONM, reduce inappropriate variations in IONM technique, adhere to strict standardization, foster the growth and stature of neurophysiological monitoring, encourage research, clarify limits, improve and update guidelines, implement IONM courses, develop quality standards for practice and training, define unequivocal references of RLN neurophysiology and pathology, refine EBSLN monitoring and evaluate new developing technology such as C-IONM. The First World Congress of Neural Monitoring in Thyroid and Parathyroid Surgery was held in 2015 in Krakow [35].

Prevalence of Monitoring Use

There is an increasing interest in IONM with numerous institutions around the world beginning to perform more monitored thyroidectomies in the last several years [22, 36–46]. Attitudes have changed with the introduction of noninvasive monitoring devices, the publication of randomized prospective trials, guidelines defining standards for RLN and EBSLN monitoring, structured training courses, and descriptions of clinical, legal, and research implications (Table 14.2) [15, 16, 21, 26, 28–32, 47–49]. In 2007, Horn first reported a prevalence survey on RLN monitoring among otolaryngologists in the United States using a mailed questionnaire, with 685/1685 (40 %) questionnaires returned [36]. Of the 81 % of respondents reporting performance of thyroidectomies, 28 % used intraoperative monitoring for all cases. Respondents were 3.14 times more likely to currently use intraoperative monitoring if they used it during their training. Surgeons using intraoperative RLN monitoring during thyroidectomy were 41 % less likely to report permanent RLN injury.

Table 14.2 Reasons for increasing use of IONM in thyroid surgery

- Introduction of noninvasive monitoring devices (endotracheal tube-based systems)
- User-friendly software
- Publication of randomized prospective trials
- Guidelines and standardization (defining standards for RLN and EBSLN IONM)
- Structured training courses
- Medicolegal issues
- Research implications
- Society recommendations
- Commercial effort

Attitudes about neuromonitoring, usage patterns, and predictors of use were formally evaluated by the American Association of Endocrine Surgeons (AAES) in 2006 [37]. Members of the AAES were surveyed by e-mail, with 117 surveys (41 %) completed. Respondents were categorized into two groups based on use (37 %) or nonuse (62 %) of IONM. The use category was composed of routine (13 %) and selective (23 %) users. The nonuse category was composed of those who have never used neuromonitoring (49 %) and those who have abandoned its use (13 %). Nonusers were older ($p=0.023$) and reported a lower case volume ($p=0.003$), less familiarity with the technology ($p<0.001$), and less access to the equipment ($p<0.001$). Nonusers also reported a lower frequency of patient-initiated discussions about neuromonitoring ($p<0.001$) and were less likely to initiate a discussion with patients ($p<0.001$). In total, 56 % of users and 90 % of nonusers believed neuromonitoring did not improve the safety of thyroidectomy ($p<0.01$). Despite this, the percentage of surgeons who always use neural monitoring has increased, from 7 % in 2001 to 37 % in 2007, with young surgeons, academic surgeons, and those in high volume centers being most likely to always use IONM [37].

A survey from Pennsylvania State University compared usage patterns and motivations behind

IONM among otolaryngology–head-and-neck surgeons (OTO-HNS) and general surgeons (GS) performing thyroid and parathyroid surgery [38]. The study was a multi-institutional survey of 103 otolaryngology and 103 affiliated GS programs in the United States. Two hundred and six surveys were sent to OTO-HNS and GS academic program directors with a response rate of 44.7 %. Of those performing thyroid surgery, 80.6 % of OTO-HNS and 48.0 % of GS surgeons used IONM, with 44.3 % of OTO-HNS and 30.8 % of GS using IONM in all thyroid cases. For thyroid surgery, as surgical volume increased, surgeons were more likely to use IONM with greater frequency. Fourteen percent of OTO-HNS and 42 % of GS respondents used IONM primarily to locate the RLN, while 40 % of OTO-HNS and 8 % of GS respondents used IONM for medicolegal reasons.

IONM is now the standard of care in Germany [39]. According to a national survey in 2010, 90 % of surgical departments in Germany are equipped with nerve monitors. RLN monitoring was used in 93 % of thyroidectomies, with the addition of routine vagal nerve stimulation in 49 % before (V1) and 73 % after resection (V2). Ninety-three percent of surgeons changed the resection plan for the contralateral side in bilateral thyroid surgery after loss of signal (LOS) had occurred on the first side.

In the United Kingdom, IONM is used by a small but slowly increasing minority of members of the British Association of Endocrine and Thyroid Surgeons (BAETS) [40]. Data was collected from January 2000 to November 2012 in the prospective national BAETS audit, showing 26,365 registered thyroid surgeries. Of these thyroid surgeries, IONM was used in 1,902 cases and not used in 13,655 cases, and data was not available in 10,808 cases. Of BAETS members, the majority were nonusers (60 %), many (20 %) used it seldomly (<5 % cases), and only 10 % used it for >50 % of cases. There was a small number of "converters," i.e., previously nonusers who have become routine users. Patient age did not impact the use of IONM: 13 % use in patients <16 years old (22/174) vs. 13 % use in patients >16 years old (1857/14718). A significant increase in the use of IONM was noted for malignant vs. benign surgery (15 % vs. 12 %, $p<0.0001$) and for revision vs. first-time surgery (16 % vs. 12 %, $p<0.00001$). The audit further presented an apparent difference in vocal cord palsy (VCP) rates between IONM (3.1 %) vs. non-IONM groups (1.3 %). The authors concluded that lack of level 1 evidence on the incidence of postoperative VCP and financial concerns are likely to be sufficient to explain the contrasting attitude of surgeons in the United Kingdom regarding IONM use. Finally, a recent postal survey of otolaryngologists in the United Kingdom revealed that only 24 % routinely use RLN monitoring in all cases. The percentage increased to 35 % in revision surgery [41].

In Denmark, Godballe reported an IONM usage rate of 77 % from a registry of surgical results in 2007 [42]. In France, the number of IONM procedures increased from 6200 in 2008 to 10,000 in 2010 [43]. In Spain, 613 monitored procedures were performed in 2009 and 1956 in 2011 [44]. In Poland, about 8 % of thyroid surgeries are monitored yearly [45]. In China, Chiang revealed that about 12,000 IONM procedures were performed in 2013 [46]. Finally, a survey formally describing the patterns of use, management, and documentation of IONM during thyroid surgery in Italy states that IONM is currently utilized in 48 surgery programs (including 24 general surgery, 22 ENT, and 2 thoracic surgery programs). Overall, 12,853 IONM procedures were performed from 2006 to 2013, with an increase from 253 in 2007 to 5100 in 2013. In 2013, the distribution of IONM by specialty included: general surgery (50 %), ENT (46 %), and thoracic surgery (4 %). The distribution according to hospital type was: public 48 %, academic 37 %, and private 15 %. High volume thyroid hospitals represented 33 % of IONM usage. In 2013, IONM included audio and graphic monitoring in 98 % of cases, EMG surface electrode endotracheal tube-based monitoring systems in 98 % of cases, and monopolar stimulating probes in 82 % of cases. Also in 2013, C-IONM was introduced in 5 academic centers (3 General Surgery and 2 ENT) [22]. Overall, motivations for IONM use primarily included medicolegal

reasons (30 %), RLN confirmation (20 %), RLN identification (20 %), prognosis (10 %), difficult cases (10 %), decreased surgical time (5 %), and education (5 %). Most of the responders (62 %) reported selective use of IONM (high-risk procedures). Response rate for correct application of sequential EMG data points intraoperatively (including V1, R1, R2, and V2) was 28 %. High volume and academic centers reported use more consistent with published guidelines of IONM (78 % and 64 %, respectively). With regards to information provided for patients, general IONM information and/or specific IONM informed consent on possible consequences of IONM usage (e.g., staged thyroidectomy after LOS on the first side) was reported in 8 % of centers, and EMG documentation was included in the medical chart in 20 % [22].

The prevalence of RLN monitoring has been assessed in several countries via surveys conducted to critically record current practice and trends in usage among hospitals (Table 14.3) [36–46]. Even though IONM of the RLN was introduced almost 30 years ago, at present, IONM is not the standard of care in most countries, with the exception of Germany. Current proposed standards for RLN management include extensive knowledge of anatomy, routine visual identification, cervical exposure, experience, training and preoperative and postoperative laryngoscopy [5, 9, 10].

While factors affecting IONM use in most countries are not yet clear, the increasing use of IONM appears to be multifactorial and includes availability of noninvasive IONM devices, increased safety, user-friendly systems, recognition of clinical benefit by randomized trials, guidelines for standardization, training courses, medicolegal concerns, educational and research issues [15, 16, 21, 26, 28–32, 47–49]. Trends in IONM among subspecialties have shown increased utilization among otolaryngology–head-and-neck surgeons. IONM of the facial nerve during otologic and parotid surgery is becoming more common, with 60 % of US ENT surgeons using intraoperative neuromonitoring in parotidectomies [15, 16, 21, 26, 28–32, 47–49]. Academic centers are more likely to use IONM, in part due to the higher number of difficult cases performed, but also for resident training and education [15, 20, 21, 26, 28–32, 47–49]. It is important to actively implement systematic IONM courses focused on standardized problem-solving algorithms.

Medicolegal issues are one of the most cited reasons in surveys for use of IONM [22, 36–46]. These issues likely relate to (a) reduction in major injury such as bilateral RLN palsy and (b) recorded and documented RLN EMG signals.

Impact of IONM on Surgical Practice

The authors of this chapter believe that IONM as an adjunct to the gold standard of visual nerve identification affects the quality of thyroid procedures by adding a new functional dynamic during thyroid surgery (Table 14.4) [49]. An argument can be made that neural monitoring, if used at all, should be performed routinely given that difficult cases cannot always be predicted preoperatively and routine IONM application has shown to steepen learning curves through greater experience in interpretation of the signal and troubleshooting system malfunction [48].

Evidence-Based Analysis

In order to perform a critical analysis of the scientific literature on IONM, two important preliminary considerations must be assessed. First, the incidence of permanent and transient RLN injury is an end-point with a relatively low incidence [48, 58–61] and therefore in order to reach an adequate statistical power, studies with a sufficiently wide sample size are needed [48]. Second, most of the studies published so far present significant heterogeneity [48]. In fact, there are several conditions that can influence the incidence of neural injury, and in order to avoid bias, they must be considered in the inclusion and exclusion criteria inherent in these various studies. In particular, the neural injury rate can be related to the surgeon's expertise, to the histologic nature of the pathology (benign or malignant neoplasm,

Table 14.3 Summary of regional surveys on IONM utilization and management in thyroid surgery

Reference	Year	Country	Prevalence	Specialty
Horne SK et al. Otolaryngol Head Neck Surg. 2007; 136(6):952–6	2007	USA	28 %	Otolaryngologists
Sturgeon C et al. World J Surg. 2009; 33(3):417–25	2009	USA	37 %	American Association of Endocrine Surgeons
Ho Y, et al. Eur Arch Otorhinolaryngol. 2013 Sep;270(9):2525–30	2013	USA	80.6 % of OTO-HNS and 48.0 % of GS surgeons reported using IONM	Otolaryngologist–head-and-neck surgeons (OTO-HNS) and general surgeons (GS)
Dralle H, et al. Br J Surg. 2012 Aug;99(8):1089–95	2012	Germany	90 %	General surgeons
Mihai R, Chadwick D on behalf of BAETS, 2013 Annual Meeting, Rome	2013	UK	20 % used it seldomly (<5 % cases) and only 10 % used it for >50 % of cases	British Association of Endocrine and Thyroid Surgeons (BAETS) members
Hopkins C, et al. Clin Otolaryngol. 2005 Apr;30(2):195–8	2005	UK	24 %	ENT
Godballe C. Registry of Surgical results: organization and outcomes. In 34th Annual meeting of the European Thyroid Association. ETA Lisbon 2009	2009	Denmark	77 %	ENT
Carnaille B.—General and Endocrine Surgery, Centre Hospitalier Universitaire Lille, France during the 6th Meeting of the International Neural Monitoring Study Group—INMSG, 2013	2013	France	IONM procedures: 6200 in 2008 to 10,000 in 2010	General surgeons
Duran Poveda MC—Department of Endocrine Surgery, University Hospital of Fuenlabrada Health Sciences School, King Juan carlos University, Madrid, Spain during the 6th Meeting of the International Neural Monitoring Study Group—INMSG, 2013	2013	Spain	IONM procedures: 613 (2009) to 1,956 (2011)	General surgeons
Barczyński M—Third Department of General Surgery, Jagiellonian University Medical College, Kraków, Poland, during the Polish Club of Endocrine Surgery in 2014	2014	Poland	8 %	General surgeons
Chiang FY—the Department of Otolaryngology—Head and Neck Surgery, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, during the 7th Meeting of the INMSG, 2014	2014	China	12,000 IONM procedures in 2013	General surgeons
Dionigi G, et al. Updates Surg. 2014 Dec;66(4):269–76	2014	Italy	13 %	General surgeons and ENT

Table 14.4 Summary of the impact of IONM in surgical practice

- Reduction in transient RLN palsy rate in high-risk procedures
- Intraoperative (not postoperative) diagnosis of RLN injury
- RLN prognosis
- Early RLN identification and confirmation
- Aids in RLN dissection
- RLN branching detection
- Management of distorted RLN
- Management of intertwining between branches of the RLN and ITA
- Non-RLN assessment
- Assist in completeness of a total thyroidectomy
- Tumor involvement of RLN
- Staged thyroidectomy
- Serves in endoscopic thyroidectomy
- Research
- Educational asset
- Medicolegal issues

Graves' disease, multinodular goiter), and finally to the type and extent of the surgical procedure (revision vs. first procedure, total vs. subtotal thyroidectomy) [4, 47, 62–69]. Additionally, another point that should be considered is that some of these studies do not consider preoperative and postoperative laryngoscopy as a mandatory tool for vocal mobility assessment [47, 48]. Moreover, different formats of IONM have been evaluated (invasive and noninvasive devices, audio only, audio and EMG documentation), and data on the correct standardized application is often not available [48]. For example, one study showed novice monitoring surgeons underuse vagal stimulation during IONM [48].

Barczynski et al. studied more than 850 patients undergoing revision thyroidectomy to test the hypothesis that IONM can reduce the prevalence of neural injury [70]. In their study, transient and permanent RLN injuries were found in 2.6 % and 1.4 % nerves with IONM vs. 6.3 % and 2.4 % nerves without IONM, respectively. They concluded that IONM statistically significantly reduces the percentage of transient paralysis in redo surgery. The lack of statistically significant differences in permanent paralysis rates may be due to insufficient sample size (952 patients per arm would have been required). Similarly, Snyder et al. performed a retrospective analysis on more than 3400 nerves at risk with consideration for the impact of IONM on surgical outcome [71]. They reported a statistically significant reduction in the rate of neural injury after 20 months from the onset of IONM use. In particular, they endorsed the importance of IONM in technically difficult cases and in detection of anatomical variations. Alesina et al. reported the postoperative outcome of more than 1100 thyroidectomies performed by trainees in order to test the potential advantages of IONM during surgical training [72]. The authors concluded that IONM offers the young surgeon an intraoperative advantage similar to that provided by the assistance of a senior, more experienced surgeon.

Notwithstanding the difficulties related to the design of scientific studies to test the utility of IONM in the prevention of RLN damage, some important prospective randomized studies on the topic have been published [47, 48]. Barczynski et al. investigated the role of IONM by comparing two groups of surgical patients (with 1000 nerves at risk per arm), those with and without IONM [47]. Globally, the prevalence of transient nerve damage was lower in the IONM group (difference of 2.9 % between groups) among high-risk patients [47]. Additionally, there was a difference between low-risk and high-risk patients as well (difference of 0.9 % between groups), but this did not reach statistical significance. The authors concluded that IONM, compared to visualization alone, reduces the incidence of transient damage (in particular in high-risk patients) but there is no statistically supported reduction in permanent nerve injury [47]. Sari et al. prospectively analyzed the economic impact of IONM, comparing more than 200 patients with IONM and almost 200 patients without IONM [73]. They showed that, while the RLN injury rate was similar between groups, the global operative time and the time taken to identify the RLN were lower in the IONM group. Notably, this demonstrates the economic advantage of IONM, which can reduce the operative time and related costs. Thomusch et al. recommend IONM of the RLN in thyroid surgery as it

significantly ($p<0.05$) lowered rates of transient and permanent RLN palsy as compared to visual RLN identification in a study of over 5000 procedures. The rates of transient and permanent RLN palsy based on nerves at risk were 1.4 % and 0.4 % with IONM and 2.1 % and 0.8 % with RLN visual identification alone [69]. A multivariate logistic regression analysis confirmed that the use of IONM decreases the rate of postoperative transient ($p<0.008$) and permanent ($p<0.004$) RLN palsies as an independent factor by 0.58 and 0.30, respectively [69]. Dionigi et al. evaluated the role of IONM in video-assisted thyroidectomy with a particular focus on RLN and EBSLN identification [74]. He compared video-assisted RLN visualization alone with localization of RLN via IONM and reported that the rate of transient nerve injury was 8.3 % in the visualization-alone group vs. 2.7 % in the IONM group. He further stated that EBSLN visualization is made easier using IONM with a related identification rate of >83 % vs. 42 % in the visualization-alone group [74]. Barczynski et al. reported that voice quality after thyroidectomy was better in the IONM group, there was a lower rate of transient RLN injury in the IONM group (1 % vs. 2 %), and the EBSLN identification rate was >80 % vs. 34 % without IONM [75]. Lifante and Khaled Hjaled et al. also showed a better postoperative voice quality and EBSLN identification rate in the IONM group [76, 77].

There have been several meta-analyses with discordant conclusions published on the topic of IONM. In particular, there are two interesting and important meta-analyses that collected data from not only prospective trials but also from cohort studies, allowing for a wider sample analysis but with reduced methodological quality [62, 63]. Zheng et al. analyzed 5 prospective randomized studies and 12 comparative non-randomized studies with a global sample of more than 36,000 nerves at risk [62]. Results for transient neural damage were statistically significant (2.56 % in the IONM group vs. 2.71 % without IONM), but permanent events showed no statistical significance (0.78 % with IONM and 0.96 % without IONM). Pisanu et al. analyzed 3 prospective studies and 17 comparative nonrandomized trials for a total of over 35,500 nerves at risk and reported a similar RLN paralysis rate between groups (with and without IONM) [63]. Additionally, Sanabria et al. analyzed six prospective randomized-controlled studies, with a global sample of more than 3000 nerves at risk (1523 with IONM and 1541 without IONM) [78]. There was a cumulative transient paralysis rate of 4.2 % with IONM and 7.7 % without IONM. The permanent paralysis rate was 1.0 % with IONM and 1.6 % without IONM. However, none of these results were statistically significant.

Summarizing the available data, a few statistically supported conclusions can be drawn despite the great heterogeneity of claims and opinions on the role of IONM in thyroid surgery [48, 79–83]. We believe increasing trends in IONM usage and the current development of new IONM modalities (e.g., C-IONM) are strongly driven by the clinical evidence of the positive surgical impact that this technology presently has and will have in the future [79–87]. IONM is the only way to perform a reliable, real-time, repeatable, and accurate intraoperative functional assessment of RLN integrity. The reliability of the data provided by IONM has been extensively demonstrated [48, 79–87].

One of the main goals during thyroid and parathyroid surgery is the preservation of RLN function, allowing for better clinical outcomes for the patient and avoiding potential medicolegal concerns for the surgeon. Patients are beginning to be aware of the advantages of IONM, and some request its use during their operation. For this reason, it is not easy to enroll patients in trials where IONM is not used. Further, in light of the available literature supporting the use of IONM, some authors no longer think it is ethical to design a prospective randomized study including an arm without the use of IONM. This has led to significant challenges in proposing studies without the use of IONM. Considering all of the aforementioned data, expert opinions, and important clinical outcomes produced, we believe that in the future, IONM will be progressively and increasingly utilized.

Intraoperative Diagnosis of RLN Injury

Causes of intraoperative RLN injuries are manifold and most are due to surgical technique errors: sectioning of the nerve, ligature entrapment, traction during the medialization of the lobe, clamping injury, suction near the nerve, compression, contusion, pressure, ischemia by excessive dissection, electrical and thermal injury [88, 89]. Anatomical nerve variations may also contribute to some cases of postoperative VCP. [88, 89]. Snyder, Chiang, and Dionigi revealed with IONM that the major cause of RLN injury during thyroid and parathyroid surgery is traction (67–93 % of all cases) [71, 90, 91]. Complete transection of the RLN was very uncommon in their extensive surgical experience [71, 90, 91]. Several studies have shown that surgeons (even experienced) underestimate actual RLN injury [8, 71, 74, 90–94]. RLN insults (including thermal, traction, compression, or contusion) may be undetected by the surgeon's eyes, and only a functional assessment of the RLN with IONM can exclude such an insult (Fig. 14.1). New energy-based devices (now widely used in operating rooms) have the potential for undesirable heat-related iatrogenic injury to adjacent structures such as the laryngeal nerves [95, 96]. IONM aids in demonstration of the loss of RLN function intraoperatively even when the nerve is still visually intact to the surgeon [48, 95]. The intraoperative (not postoperative) assessment of RLN function with IONM during thyroid surgery is important for several reasons [48]: (a) intraoperative prediction of postoperative function (prognosis); (b) prevention of bilateral RLN injury through a "staged thyroidectomy" (when LOS occurs on the first side of a planned bilateral procedure); (c) IONM localization of disrupted nerve conduction with identification of how and when the RLN was injured [48]. Elucidating the mechanism of RLN injury helps the thyroid surgeon to better refine surgical technique. If the RLN injury site is identified by IONM and is caused by ligature entrapment or clip, they can be immediately removed with potential reversal of RLN damage.

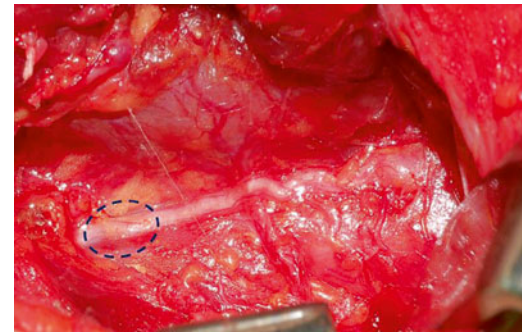

Fig. 14.1 Intraoperative diagnosis of RLN injury. RLN insults due to thermal injury caused by energy-based devices may not be visually apparent to the surgeon's eye and may go unrecognized intraoperatively. Functional assessment of the RLN with IONM can aid in localization and identification of RLN injury

Early RLN Identification, Confirmation, and Mapping

Early and definite identification of the RLN is an important step to avoid inadvertent nerve injury during complicated thyroid operations. IONM can locate the RLN before visual confirmation [97]. Multiple studies suggest that IONM improves nerve identification rates [98–100]. The rate of RLN identification without IONM is 90 % vs. 99.3 % with IONM [98–100]. With IONM, the RLN is mapped out in the paratracheal region through probe stimulation and then visually identified through directed dissection provided by this previous neural mapping [97]. IONM distinguishes between blood vessels and the nerve. Once the nerve is identified, additional intermittent stimulation of adjacent non-neural tissue vs. nerve can help in tracing the nerve and all of its branches through the dissected field [15, 20, 97]. In particular, we use the stimulator continually both prior to (for identification) and during (for monitoring) the neural dissection of the tracheoesophageal groove (Fig. 14.2 a, b) [15, 20,

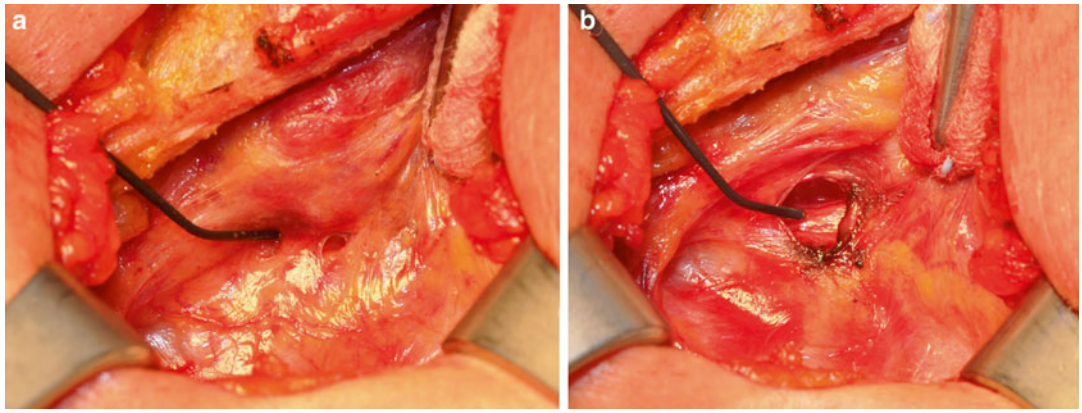

Fig. 14.2 Early identification and confirmation of the RLN. IONM can locate the RLN before visual confirmation. For identification of the RLN we suggest delivering an electric current of 2 mA to map and search for the nerve (**a**). Once the nerve is visually identified, intermittent stimulation at a current of 1 mA to the nerve vs. adjacent non-nerve tissue can help to trace the nerve and its branches (**b**)

97]. A stimulation current of 2 mA is recommended for identification of the RLN. For confirmation of RLN identification and further intraoperative monitoring, we recommend a stimulation current of 1 mA [23, 97].

Aid in RLN Dissection

The stimulator itself is useful to indicate the correct plane of dissection, giving constant information about laryngeal nerve function intraoperatively [20, 101]. With IONM, the entire cervical course of the RLN can be traced safely. IONM is also useful to control and manage bleeding. For example, hemostasis at the ligament of Berry is best controlled with IONM by first accurately mapping out the course of the RLN prior to using indiscriminate clamping and cautery [97, 101].

RLN Branching Detection

Anatomical variations of the RLN, such as extralaryngeal branches, intertwining of branches of the RLN and inferior thyroid artery (ITA), and a nonrecurrent laryngeal nerve (NRLN), can be optimally managed with the added information from IONM [102]. Anatomical variations of the RLN usually cannot be predicted preoperatively and can be associated with higher rates of RLN injury [20, 102]. The use of IONM enhances the surgeon's ability to identify a branched RLN: extralaryngeal RLN bifurcation was identified in 42 (28 %) vs. 25 (17 %) patients operated on with vs. without IONM, respectively ($p = 0.001$) [103]. EMG signal and twitch of the larynx can be induced through anterior branch stimulation with IONM. Serpell et al. reported that the motor fibers of the RLN are located in the anterior extralaryngeal branch [104]. In some circumstances, the anterior branch of the RLN can be stretched by traction forces at Berry's ligament. The diameter of the posterior branch of the RLN can sometimes be larger than that of the anterior branch, and the bifurcation can occur at or rarely even below the level of the ITA. In this situation, partial exposure of the nerve at the region of Berry's ligament alone can place the RLN at a high risk of injury. However, these variations and pitfalls can be easily recognized if the RLN is identified at the level of the ITA and confirmed with IONM. It should be noted that when a posterior branch of the nerve or an adjacent small artery runs close to the true motor branch, the stimulus current can shunt to the nerve resulting in EMG activity (Fig. 14.3) [102].

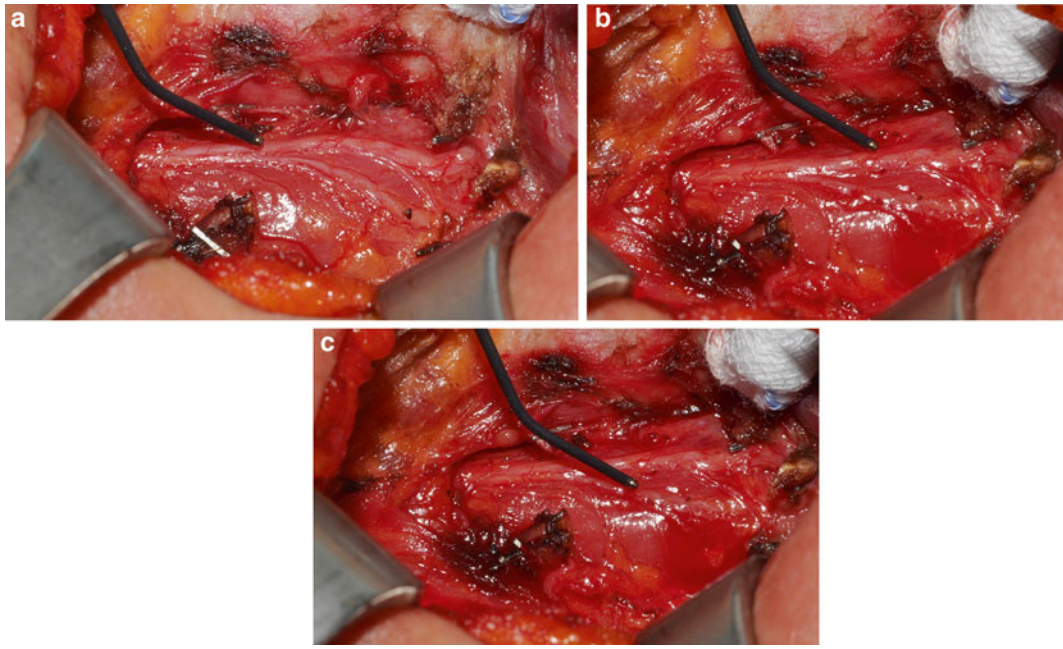

Fig. 14.3 RLN ramification identification. When two structures run close together, a false EMG signal can be induced by a shunt stimulus, thus we suggest lowering the stimulation level to 0.5 mA. EMG signal and twitch of the larynx can be induced with IONM only on the most anterior branch of the RLN (motor branch). (**a**, **b**) Main trunk of the RLN is indicated by the probe-stimulator with EMG signal. (**c**) Stimulation of the posterior branch evoked no laryngeal EMG signal but did produce cervical esophageal contraction

Distorted RLN

RLN position can be significantly abnormal in patients with large goiter with substernal extension or recurrent large goiter (Fig. 14.4). The RLN can be displaced in any direction and might even come to lie ventral to the inferior pole [20]. This leads to disorientation and places the nerve at extreme risk, even in experienced hands. Sometimes, the RLN can be found adherent to the capsule of a large recurrent goiter [4, 20, 26, 49, 102]. In these situations, the distorted nerve can be mistaken for a blood vessel and be transected inadvertently. With the application of IONM, these variations and pitfalls can be more easily recognized, and the distorted RLN can be preserved [4, 20, 26, 49, 102]. We therefore recommend that

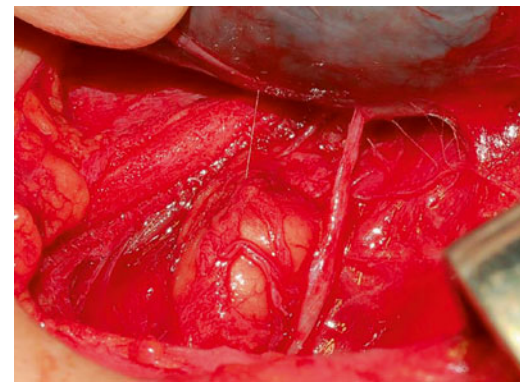

Fig. 14.4 Distorted RLN. RLN position can be significantly abnormal in patients with goiter with substernal extension or recurrent large goiter. We recommend not clamping or transecting any structure during lateral dissection of the thyroid before definite identification of the RLN with IONM

clamping or transecting any structure during lateral dissection of the thyroid should be avoided before definite identification of the RLN with IONM [4, 20, 26, 49, 102].

Branches of the RLN and ITA

The relationship between the RLN and ITA is highly variable [105]. A particularly high-risk situation occurs when the ITA is divided into many ramifications close to the RLN and the branches of both structures intertwine [105]. Some nerve injuries can be caused by clamping or electrocauterization in an attempt to stop bleeding. Sometimes, the RLN can run parallel to a branch of the ITA, and visual misidentification can occur if the RLN is partially exposed (Fig. 14.5) [105].

Completeness of a Total Thyroidectomy

Recent consensus guidelines have recommended more extended surgery for differentiated thyroid cancers (DTC) and benign thyroid disease, i.e., total thyroidectomy [106–109]. During total thyroidectomy, most difficulty occurs during dissection of thyroid tissue in the region of Berry's ligament [5, 110–114]. This is a very frequent source of accidental injury to the RLN. The RLN is most commonly injured in the last 2 cm of its cervical course [71, 90, 91]. The bifurcated RLN is particularly prone to injury near Berry's ligament [71, 90, 91, 103]. At this level, the RLN may have an intracapsular course and actually penetrates thyroid parenchyma in 10 % of cases according to Berlin, 15 % for Armstrong, and 38 % for Wafae [112–114]. Therefore, the surgeon requires vigilance, optimal exposure, and neurophysiologic confirmation of a visually intact nerve during dissection of the RLN at Berry's ligament in order to perform a complete and secure resection of all thyroid tissues in that specific area as required in a total thyroidectomy [20]. Moreover, hemostasis in this area is best controlled with careful mapping of the RLN via IONM—indiscriminate clamping and cautery will likely result in nerve injury [20, 103]. The use of IONM may improve the oncological and surgical outcomes among thyroid cancer patients by increasing the completeness of total thyroidectomy [103].

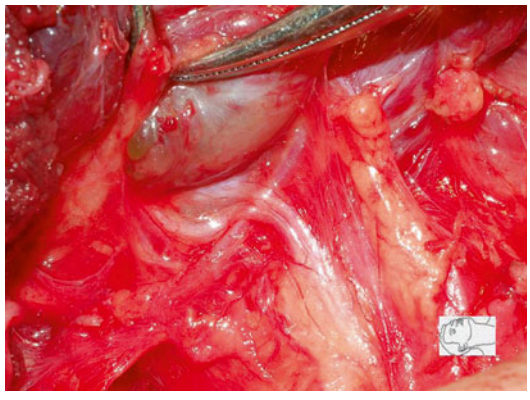

Fig. 14.5 Intertwining between branches of the RLN and ITA. A particularly high-risk situation is when the ITA is also divided into many ramifications close to the RLN, and the branches of both structures intertwine. We recommend that the RLN should be identified and followed through Berry's ligament until the nerve enters the larynx

Tumor Invasion of the RLN

Recently, preservation of the RLN using IONM despite local invasion of the nerve by extrathyroidal extension or regional lymph node metastases has been justified [115–119]. Chi and associates demonstrated that even in cases of RLN palsy, a positive EMG response may still be yielded with monitoring [119]. Their standard technique is to preserve even the palsied nerve whenever possible if a positive EMG response is present, in order to prevent complete atrophy of a paralyzed vocal cord. Moreover, in patients with a previously sectioned RLN, IONM is of great help in finding the distal part of the cut laryngeal nerve for re-anastomosis [115–119].

Prognostication of Postoperative Neural Function and Lesion Site Identification

The application of IONM has great significance in the prevention of bilateral VCP given the bilateral nature of the typical thyroid procedure [48].

Prognostication is varied due to a number of factors discussed in this chapter, but electrical testing represents a significant improvement in the accuracy of neural function prognostic testing when compared to visual inspection of the nerve alone. Further, prior to neural monitoring, no mechanism to identify the injured segment of nerve was available [48]. Based on existing prognostic studies, uniform and robust LOS evaluation algorithms would be expected to increase and provide more uniform positive predictive values (PPV). It is particularly important to apply the standards of IONM for equipment setup, system assessment, and troubleshooting, to facilitate uniform comparable and accurate neural monitoring.

Intraoperative Surgical Strategy

With alteration of IONM signal, modification of the surgical strategy becomes possible [4, 8, 20, 48, 71, 74, 90–94]. By means of IONM the surgeon can intraoperatively map and identify the site of neural injury. If the lesion is due to a clip, ligature, or binding, the surgeon can release the cause of injury and potentially permit early recovery prior to irreversible damage [4, 8, 20, 48, 71, 74, 90–94]. IONM also has the potential to prevent bilateral RLN palsy associated with total thyroidectomy by alerting the surgeon to consider staging the procedure when LOS occurs [120, 121]. Staged thyroidectomy is defined as thyroid/neck resection performed at two different times: the operation is at first limited to excision of the dominant lobe, and the second side is operated on later. In 1929, Pemberton first described modifications of the operative procedure to reduce risk [122]. Other reports of the staged procedure are described by Porta (1811) and Blizzard, Billroth, Wolfler, Kocher, and Mayo (early 1900s) for the treatment of both benign and malignant thyroid disease [122]. With LOS of the RLN on the initially operated side, the surgeon can now carefully consider the optimal timing of surgery on the contralateral side. With LOS, the surgeon must consider that the ipsilateral nerve is injured at least temporarily. This permits considering whether it is important and in the patient's best interest to perform surgery on the contralateral side on the same day given the intraoperative information of potential ipsilateral paralysis [39, 123, 124]. According to Goretzki, a failed IONM stimulation of the RLN after resection of the first thyroid lobe is specific enough to reconsider the surgical strategy in patients with bilateral thyroid disease to ensure prevention of bilateral RLN palsy [123]. In fact, in 85 % of patients with known nerve injury, and in 56 % with negative IONM stimulation on the side of the initial dissection, the surgical strategy was changed with successful avoidance of potential postoperative bilateral RLN palsy. This contrasts with the 17 % rate of bilateral RLN palsy ($p<0.05$) when surgeons were not aware of a preexisting nerve injury or intraoperative LOS on the first side of thyroid dissection [123]. Moreover, after LOS on the first side of resection in bilateral goiter, more than 93 % of German surgeons declared their willingness to change the resection plan for the contralateral side to avoid the risk of bilateral RLN palsy. This resulted in discontinuation of surgery (84 %) or undertaking a less extensive resection for completion of the other side than originally planned (9 %) [39]. Departments with the heaviest institutional caseload reportedly changed their surgical plans more often than those with a lower institutional volume [39]. The results of Sadowski's study raise several considerations for debate [124]. The first observation is relative to IONM troubleshooting algorithms. Given the potential impact of LOS on the surgical plan (i.e., aborting the second side surgery), it is critical that the surgeon using IONM is perfectly experienced in LOS troubleshooting algorithms [4]. With correct application of a detailed LOS troubleshooting algorithm, the rate of a negative signal at the end of surgery becomes reduced, and the incidence of postoperative VCP associated with a negative signal becomes substantially higher [4]. The INMSG recommends adding laryngeal twitch and contralateral vagal nerve stimulation assessments to the intraoperative available EMG data [4].

It is optimal to start the thyroidectomy on the dominant side. This approach allows at least con-

trol and monitoring of the disease that led to the indication for surgery by the endocrinologist. Analysis of the morbidity of those patients who undergo completion thyroidectomy through a staged procedure revealed no additional surgical or anesthesia-related complications [4, 120, 125]. Unfortunately, not all surgeons start the surgical procedure with the dominant lobe [4, 120, 125].

Does the surgeon have to stop the operation in case of LOS following completion of the first side for malignant disease? Thyroid cancer varies regarding tumor biology, metastatic behavior, and prognosis [106, 120]. DTCs have an acceptable prognosis despite local invasion and distant metastases. Further guidelines are needed to define the indications of staged procedures in cancer patients [106, 120, 125].

The decision to stage the surgical procedure should be discussed with the anesthesiologist, patient and endocrinologist [39, 123, 124]. The surgeon must communicate with the anesthesiologist to determine potential risks of undergoing general anesthesia a second time in order to decide if the patient with LOS on the first side should undergo a second procedure [39, 123, 124]. As for the endocrinologist, a medical option for treatment of the remnant contralateral lobe can be considered. For example, in the case of Graves' disease, the remnant contralateral lobe may be amenable to radioiodine ablation if it is relatively small.

One may move forward with contralateral surgery when postoperative laryngoscopy confirms resolution of neuropraxia, which typically occurs 6–8 weeks after surgery [126].

IONM should be mentioned in the preoperative informed consent for primary and secondary interventions [120]. If the patient is informed about the use of IONM, he/she should also be informed about the consequences of intraoperative LOS [120]. The additional expense of a two-stage procedure is of concern [50, 120]. A staged thyroidectomy can lead to an increase in healthcare costs as two hospitalizations are required to complete the intervention [50, 120]. These costs, however, must be balanced against possible post-discharge costs of uni- and bilateral RLN injuries including speech and/or medical therapy, repeat laryngeal exams, and even vocal cord surgery and legal claims [51–57].

Educational Asset

Monitoring is not a substitute for perfect and extensive knowledge of the anatomy of the thyroid gland and surrounding tissues [5, 9, 10]. IONM of the RLN is an important teaching tool to help surgical residents incorporate new technology, a standardized technique of thyroidectomy with vagal stimulation, RLN identification, anatomy, neurophysiology, and neuropathology into their surgical skills [4, 71, 90, 91]. Understanding the mechanism of nerve injury is important for residents for their future operations [4, 71, 90, 91]. Elucidating the intraoperative mechanism of RLN injury helps the thyroid surgeon to refine his technique, reducing mechanical trauma and the rate of nerve injury. IONM improves professional standards and reduces complication rates [4, 71, 90, 91]. Moreover, Dralle reported on the risk of VCP with RLN monitoring vs. visual or no RLN identification in nearly 30,000 RLNs at risk of injury. For less-experienced (low-volume) surgeons, RLN monitoring significantly decreased the observed frequency of permanent RLN paralysis [48].

Medicolegal Issues

RLN injury following thyroidectomy can lead to malpractice litigation regardless of the use of RLN monitoring. Surgeons should not overstate the benefits of neuromonitoring to patients during the preoperative informed consent [4, 49, 51–57]. Few specific legal data exist on the use of IONM in thyroid surgery [51–57]. The introduction of IONM in standard thyroidectomy needs both legal and ethical considerations [47, 51–57]:

(a) *Reduction of major complications such as bilateral RLN palsy*. This is a great advantage in the modern era of thyroid surgery. IONM allows the surgeon to stage contralateral surgery if RLN damage is diagnosed, thereby

avoiding the potential for bilateral VCP [4, 47, 51–57].

(b) *RLN recorded and documented EMG signal*. IONM data can often be printed in the medical record. Documentation of the final normal neurophysiologic signals of the RLNs at the end of the surgical procedure may allow for early differentiation between RLN-related and unrelated voice changes. EMG serves as proof of intact nerve function [51–57]. Authors have suggested that nerve monitoring during surgical procedures may reduce the medicolegal liability for surgeons with a reduction of economic loss to the patient, healthcare system, and insurance [51–57].

Table 14.5 Standardized IONM procedure

- Structured informed consent (staged procedure in cases of LOS on the first side)
- Preoperative laryngeal examination (L1)
- Vagal stimulation before thyroid dissection (V1)
- RLN stimulation at initial identification (R1)
- RLN stimulation at the end of thyroid dissection and complete hemostasis (R2)
- Stimulation of EBSLN at identification (S1)
- Stimulation of EBSLN at final dissection (S2)
- Vagal stimulation after complete thyroidectomy and hemostasis (V2)
- EMG documentation included in patient medical charts (V1, R1, R2, V2 for each side)
- Postoperative laryngeal examination (L2)

Standards for IONM

Multidisciplinary collaboration and standardization of technique are prerequisites for successful nerve monitoring [15, 20, 26, 48, 79]. Both the surgeon and the anesthesiologist must be familiar with the appropriate use of laryngeal electrodes, optimal endotracheal tube positioning, and sources of false negative errors [26, 79, 127–130].

Pre- and Postoperative Management

IONM procedures should be performed by thyroid surgeons with perfect knowledge of both basic IONM [i.e., standards of anesthesia equipment, setup, and monitoring with routine vagal stimulation before dissection (V1) and at the end of thyroidectomy (V2)] and advanced IONM (i.e., perfect knowledge of problem-solving algorithms, LOS evaluation, interpretation of EMG signal) [15, 20, 26, 39, 48, 65, 79, 127–130]. The learning curve for IONM is between 50 and 350 procedures [72, 131–133]. The different learning curve patterns among surgeons may reflect the variable degree to which surgeons will modify their own dissection technique. Moreover, if IONM technology is compromised before or during surgery, the surgeon must rely on alternate methods, surgical skills, experience, and good anatomical knowledge to prevent damage to the RLN [79]. Pre- (L1) and postoperative laryngeal examination (L2) are essential with IONM to improve the prognostic correlation between continuous vagal stimulation and pre- and postoperative glottis function [20]. L1 is a reference for V1 (pre-dissection vagal stimulation) and L2 is a reference for V2 (post-dissection vagal stimulation) [20, 126]. IONM documentation is required and includes time-traceable measurements of amplitude, latency, waveform morphology, and magnitude of stimulation current of V1, R1, R2, and V2 for each thyroid lobe/side (Table 14.5) [39].

Equipment and Setup

IONM is performed according to standards of equipment setup, induction, and maintenance of anesthesia, correct endotracheal tube positioning verification tests, and EMG definitions described by the INMSG [15]. Monitor assessment should include checking impedance values. At this time, the monitor should be checked for an appropriate event threshold at 100 μV and a stimulator probe should be set to deliver 1–2 mA of current.

Endotracheal tubes used for IONM may be pre-fashioned with integrated paired left and right stainless steel electrodes embedded within the endotracheal tube surface, which are exposed at the level of the glottis [15, 20, 48]. Alternately,

standard endotracheal tubes may be used as monitoring tubes by placement of a thin adhesive pad containing the paired electrodes [15, 20, 48]. Proper tube position is verified by direct visualization after neck extension prior to the operation and then intraoperatively by obtaining a first vagal nerve (V1) stimulation value >500 μV [15, 20]. The position of the surface tube electrodes can be displaced after the patient is fully positioned with head extension [127, 129]. The surgeon must work closely with the anesthesiologist for repeat visualization of the glottis with direct or fiberoptic laryngoscopy after final patient positioning [15]. During IONM, paralyzing anesthetic agents cannot be used as they can significantly reduce, if not completely eliminate, EMG responses to direct or passive nerve stimulation [127].

Normative Vagal Nerve and RLN EMG Quantitative Parameters: Optimizing EMG Signal

INMSG members have proposed a proper definition/level for V1 amplitude of >500 μV [15, 20, 23, 26, 48]. The V1 signal is a prerequisite for the correct interpretation, diagnosis, and verification of a functionally intact RLN and for the definitions of a "significant" reduction of signal as well as true LOS (Table 14.6). According to a published series, mean amplitudes of EMG signals obtained from vagal nerve stimulation were 750 ± 279 μV, lower than those obtained with direct RLN stimulation (1086 ± 349 μV) [134]. Normative latency analysis showed mean right and left vagal latencies of 5.47 ms (±0.73) and 8.14 ms (±0.86), respectively ($P < .0001$). Pooled RLN latency was 3.96 ms (±0.69), and pooled EBSLN latency was 3.56 ms (±0.49), both significantly shorter than vagal latencies ($P < .0001$) [135]. There was no association of amplitude and latency parameters with tumor size (> or <5 cm), body mass index (> or <25), age (> or <50 years), gender, or degree of neural dissection [135]. The unique right vagus, left vagus, and RLN latencies are characteristic of the individual nerves and allow identification (through the characteristic waveform latency) of an intact left or right vagus/RLN system.

Table 14.6 Interpretation of EMG signal

Unequivocal definition of normative V1 is fundamental to make any surgical deliberations and for safety and reduction of false positive results. INMSG proposed V1 mean value amplitude is >500 μV. V1 signal is a prerequisite for the correct interpretation, diagnosis, and verification of:
• Functionally intact RLN
• Definition of a "significant" reduction of signal
• Identification of "re-entry" signal
• LOS evaluation
• Preoperative VCP (nerve conduction\EMG signal preserved)

Safety of IONM

IONM is a safe procedure [15], but certain key points must be addressed to ensure its safe introduction into clinical practice. International guidelines have been published with the intention to improve the quality and safety of monitoring and to discourage inappropriate variations on IONM technique both for the RLN and for the SLN [15, 34]. The surgeon must adhere to and comply with a strict standardized IONM technique to preserve results, quality, and safety [13, 26]. IONM should be a team effort between the surgeon and the anesthesiologist [24, 83].

Current Limitations of Intermittent IONM

Considering the upward increasing trend in the use of IONM, it is important to evaluate the current limits of IONM technology [22, 36–46]. IONM still has relevant limitations in that it provides intermittent evaluation of the functional integrity of the RLN, allowing the nerve to be at risk of injury in between stimulations (Table 14.7) [79]. This has led to the current evaluation of C-IONM as a possible method to decrease and predict impending stress to the RLN.

Table 14.7 Current limitations of intermittent IONM

- RLN palsy can still occur with IONM
- Functional assessment of the integrity of the RLN is limited to the short-time interval of stimulations and the site of direct nerve stimulation by the surgeon, i.e., the RLN is still at risk for damage during the surgical procedure proximal to the site of stimulation and during the interval between nerve stimulations
- No uniformity in application of the standardized IONM technique
- Knowledge of most common pitfalls and troubleshooting algorithms
- IONM does not replace clinical judgment—it is a helpful adjunct
- Relatively low positive predictive value
- Cost-effectiveness is still not evaluated
- Operative time
- Need for further research focused on neurophysiology of the RLN
- Assessment of the posterior branch of the RLN
- Thyroidectomy under local anesthesia

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Continuous Intraoperative Neuromonitoring (CIONM) of the Recurrent Laryngeal Nerve

15

Rick Schneider, Kerstin Lorenz, Andreas Machens, Phuong Nguyen Thanh, Gregory W. Randolph, and Henning Dralle

Abstract

Continuous intraoperative nerve monitoring (CIONM) is an advanced tool to improve risk management of the recurrent laryngeal nerve (RLN) by ongoing determination of vagus amplitude and latency during thyroid surgery. The advantage of CIONM compared to intermittent nerve stimulation (IIONM) becomes apparent in technically demanding operations because CIONM provides instant alerts as soon as a surgical procedure impinges on the RLN. This is why CIONM is set to overcome the principal methodological limitation of IIONM, which is identification of RLN malfunction only *after* the damage has taken place.

Animal and human studies have consistently confirmed the feasibility, safety, and reliability of CIONM. By implication, accurate prediction of impending RLN injury hinges on the evaluation of wave changes which indicate nerve dysfunction that ultimately may result in complete loss of electromyographical (EMG) signal (LOS). "Combined events," defined as concordant EMG changes in both amplitude (decreases to less than 50 % of initial baseline) and latency (increase to more than 110 % of initial baseline), typically precede postoperative vocal fold palsy and are reversible in 80 % of cases upon release of the nerve. CIONM also helps identifying functional nerve recovery with restitution of the amplitude to ≥50 % of its baseline so that surgical plans can be adjusted accordingly.

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CIONM can prompt corrective actions before LOS occurs. Recent evidence suggests that CIONM may afford better nerve protection than IIONM, which resulted in permanent RLN palsy rates of 0 % with CIONM vs. 0.4 % with IIONM ($P=0.019$).

Keywords

Vagus nerve stimulation • Continuous intraoperative nerve monitoring • CIONM • Combined EMG event • Loss of signal • Recurrent laryngeal nerve injury • Thyroid surgery • Vocal fold palsy

Introduction

The inability to monitor recurrent laryngeal nerve (RLN) function between two stimulation cycles puts the nerve at risk during unmonitored dissection intervals, and remains to be the most significant disadvantage of intermittent intraoperative neuromonitoring (IIONM). For the purpose of risk minimization, a monitoring system is required that continuously monitors the integrity of RLN function during the operation [1–3].

It was only in the mid-1990s that IIONM was introduced into thyroid surgery [4]. To this end, a double-balloon tube was employed, subsequently replaced by endotracheal tube electrodes, for transtracheal stimulation of the RLN [4, 5]. In 2007, continuous intraoperative neuromonitoring (CIONM) was facilitated by an electrode placed on the vagus nerve, which basic principle has stood the test of time [6, 7]. To minimize the potential for stray current and to protect the nerve, the biocompatible hybrid cuff electrode was optimized regarding resilience and geometric design to ensure intimate electrode contact with the vagus nerve and to prevent nerve injury from incidental electrode dislocation or extraction. For analysis of real-time electromyographic (EMG) signals, a commercially available multichannel EMG system was used that provided acoustical and visual feedback.

A variety of electrodes have been forthcoming that are categorized according to the extent of dissection around the vagus nerve required to put them in place (Fig. 15.1). Once the electrodes have been rested on the vagus nerve, there is no need to interrupt the surgery for stimulation of the vagus nerve. This continuity is exactly what the "C" ("*continuous*") in the acronym CIONM refers to: continuity in nerve monitoring by continuous vagus nerve stimulation. In the proper sense of the term, continuity in stimulation would necessitate uninterrupted, and hence unphysiological stimulation of a motor nerve, resulting in a durable single contraction of the dependent vocal muscle. "*Continuous*" stimulation therefore is better described as "repetitive pulsed" stimulation that is contemporaneous with surgical maneuvers during the operation [8]. CIONM affords close monitoring in real time of the functional integrity of the entire vagus nerve/RLN axis so that impending nerve injury can be detected on time, enabling quick corrective action (Table 15.1) [6, 9, 10].

Standards for CIONM

Mode of Action

Although CIONM also uses IIONM equipment such as multichannel EMG system, EMG display, endotracheal tube sensing surface electrodes, and handheld stimulation electrodes, CIONM, unlike IIONM, necessitates placement of a stimulating electrode on the vagus nerve for the duration of the operation. These commercial devices, differing in EMG display, alarm limits, and configuration of the vagus electrodes, are supplied by several manufactures (Fig. 15.1).

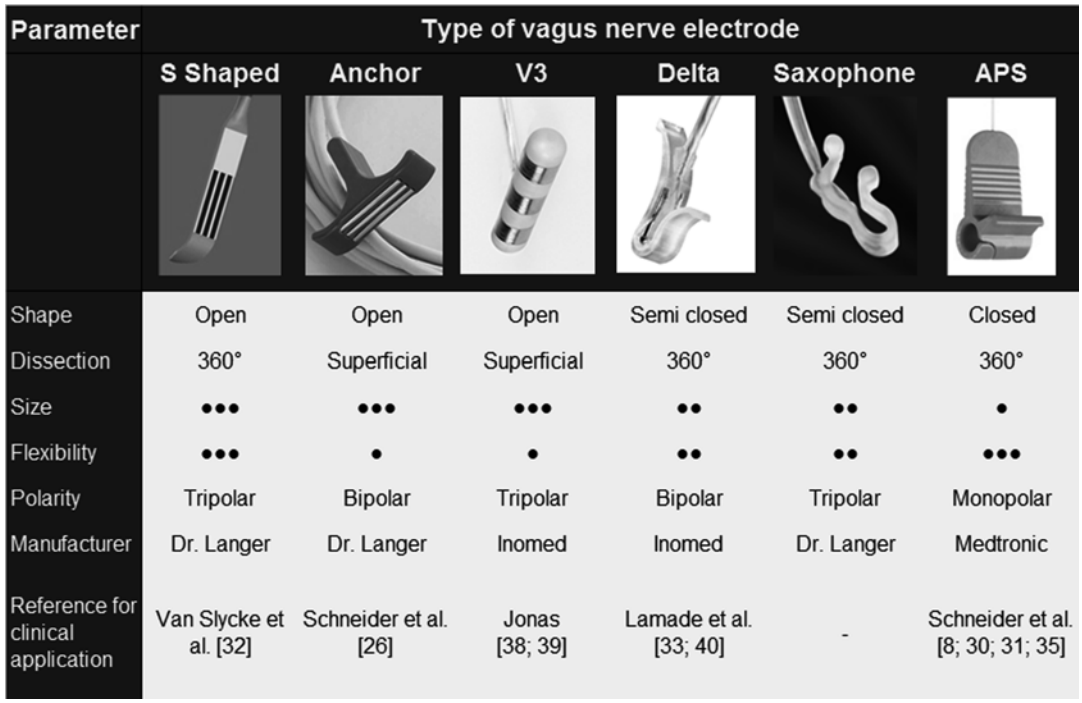

Fig. 15.1 Analysis of the characteristics of commercial vagal electrodes (Based on data from [41])

Table 15.1 Strengths and weaknesses of intermittent and continuous intraoperative neuromonitoring

	Intermittent intraoperative neuromonitoring	Continuous intraoperative neuromonitoring
Impending loss of the EMG signal	Limited	Excellent
Loss of the EMG signal	Excellent	Excellent
Recovery after loss of the EMG signal	Very limited	Excellent

Direct identification and tracking of the RLN during dissection, using the same handheld stimulation probe and technique, is recommended for both CIONM and IIONM [11]. Unlike CIONM, IIONM requires a halt of all surgical activities and the repeated search for the vagus nerve inside the carotid sheath for stimulation.

For CIONM, a stimulating electrode is positioned at the level of the cricoid cartilage onto the vagus nerve proximal to the branching of the RLN. Stimulation of the vagus nerve is performed via this electrode at a predetermined rate and intensity, causing contraction of the dependent vocal muscle. The endotracheal tube electrodes can pick up that contraction, transforming it into acoustic and graphical signals.

For vagus nerve stimulation, the use of a current of 1 mA is ideal to depolarize all vagal type A and B nerve fibers without recruitment of vagal type C fibers. This stimulation ensures elicitation of maximum nerve amplitudes without incurring vasovagal side effects mediated by vagal type C fibers [9, 12–15]. The most common stimulation frequency is 1 Hz (on a manufacturer-dependent scale up to a maximum of 3 Hz). The pulse is rectangular, negative, and lasts for 100 or 200 μs. In the authors' experience, stimulation with 1 Hz provides for intervals between two stimulation cycles that, on balance, are small enough to enable close, almost "continuous" monitoring of RLN function with no need to wait for the next stimulation cycle. Studies have clearly shown that such repetitive low-current, short duration pulsatile vagal nerve stimulation is safe to the vagus nerve, RLN, and larynx and without cardiac or pulmonary effects.

The EMG tracing typically consists of a biphasic or triphasic curve. The monitoring system converts these curves into acoustic tones identified by monitor unit speaker. Nerve amplitude and latency are determined as unique baseline for the given patient at the beginning of the surgery, being ultimately determined by a combination of factors such as contact of the endotracheal tube electrodes with the tracheal wall, reflecting tube size and position, as well as RLN and neck anatomy.

For detection of clinically relevant EMG changes, it is crucial to maximize the nerve amplitude on which the IONM system is calibrated such that it reaches at least 500 μV [8]. This minimum requirement is achieved by repositioning the endotracheal tube for optimum contact with the vocal fold. This degree of amplitude in turn optimizes our ability to determine any potential decrements suggestive of impending injury during the surgery. Oral cavity packing with gauze can be useful to bring the endotracheal tube closer to the vocal fold and fix it in that position. Once the signal baseline for both amplitude and latency has been calibrated, the IONM system is operational, displaying separate lines centered on patient-specific baselines for nerve amplitude and nerve latency (Video 15.1). The IONM systems also provide options to customize alarm lines, the crossing of which sets off audible and visual alerts.

Electrode Placement

Unlike IIONM [16], CIONM requires the opening of the carotid sheath and dissection of the vagus nerve to rest the stimulation electrode on the nerve. Before any nerve dissection is attempted, the probe utilized for intermittent stimulation should be used to confirm that the vagus nerve is working [17]. In the event of an absent EMG signal, it is recommended to adhere to the International Neural Monitoring Study Group's (INMSG) troubleshooting algorithm [11].

The carotid sheath can be accessed through different surgical routes (Figs. 15.2 and 15.3). For thyroid and parathyroid surgery, the ***anterior*** ("***midline***") ***approach*** is generally preferred (Video 15.1, Fig. 15.2). This approach consists of an incision of the superficial and middle layers of the cervical fascia in the midline and longitudinal division and separation of the left strap muscles from the right. Mobilization and lateral retraction of the sternohyoid and sternothyroid muscles together with medial retraction of the thyroid lobe reveals the carotid sheath. On the downside, the electrode cables run through the operative field, increasing the risk of dislocations of the electrode due to inadvertent traction on the cables. The anterior approach may cause difficulties in the presence of extensive central scarring or large goiters extending into the lateral neck. In this setting, the ***lateral approach*** may be more useful (Video 15.1, Fig. 15.3). It entails incision of the superficial cervical fascia alongside a virtual line formed by the lateral border of the sternohyoid muscle and the medial border of the sternocleidomastoid muscle. Exposure to the carotid sheath is gained after blunt separation of the muscles with the use of retractors. The lateral approach offers better exposure of the lateral lymph node compartment than the anterior approach and is optimal for lateral compartment-oriented lymph node dissection [18].

The carotid sheath is entered at the level of the thyroid cartilage through a short incision, the length of which depends on the dimensions of the stimulation electrode. The vagus nerve most often courses medial and posterior (73 %), and infrequently medial (15 %), lateral (8 %) or anterior (4 %), to the internal jugular vein and the common carotid artery [19]. To accommodate the stimulation electrode, a short segment of the vagus nerve is laid bare for open-design electrodes using a nerve retractor, or dissected free all around its circumference for closed or semi-closed stimulation electrodes. Semi-closed stimulation electrodes better guard against incidental dislocation than open-design electrodes and ensures stable EMG signals that are easier to interpret. Whatever surgical technique is used, utmost care is to be exercised not to devascularize the vagus nerve. The vagus nerve is tremendously robust in the face of standard, careful, meticulous neck surgical technique. There are several lines of evidence to suggest that CIONM practiced in

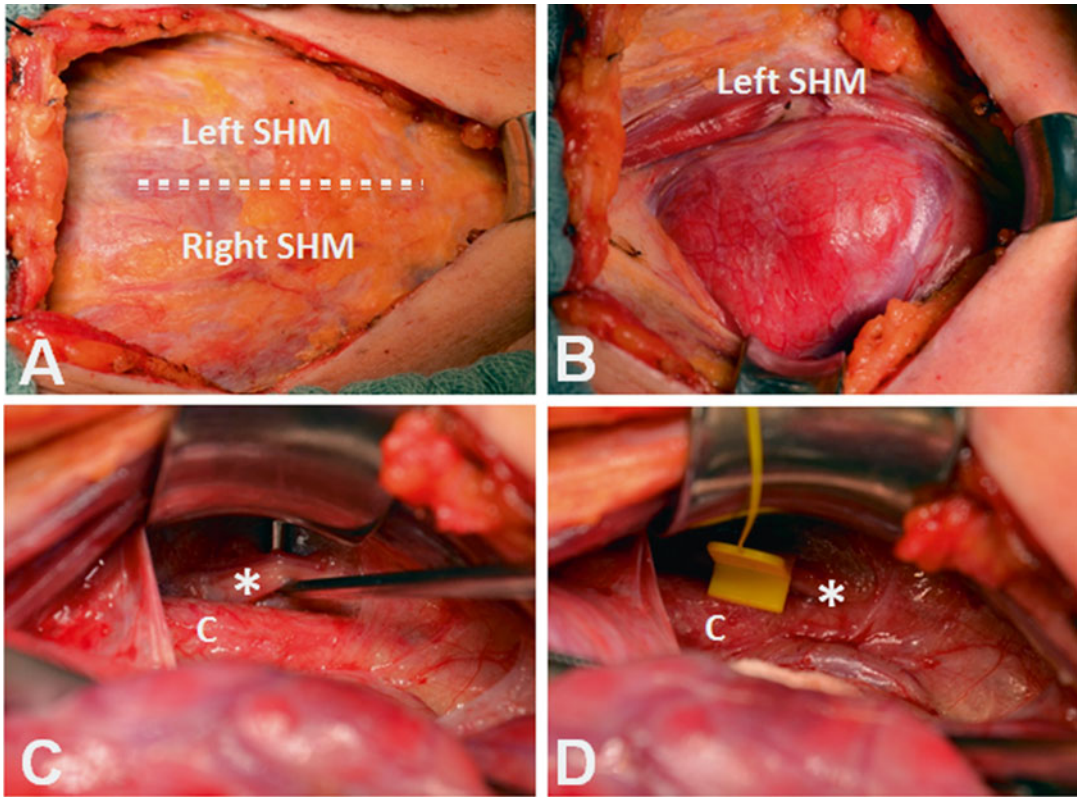

Fig. 15.2 The anterior ("*midline*") surgical approach to the vagus nerve. (**A**) Midline incision (*dashed line*) through the superficial and middle layers of the cervical fascia alongside a virtual line formed by the medial borders of the left and right sternohyoid muscle (SHM). (**B**) Thyroid gland exposed after lateral retraction of the right strap muscle. (**C**) Retraction of the left vagus nerve dissected free over a short distance all around its circumference (*asterisk*). Exposure to the left common carotid artery ("c") is achieved with medial retraction of the left thyroid lobe, lateral retraction of the left internal jugular vein and left strap muscle. (**D**) Automatic Periodic Stimulation (APS)® electrode resting on the left vagus nerve (*asterisk*)

experienced hands, including gentle dissection of the vagus nerve to accommodate the stimulation electrode, is safe [7, 8, 14, 20–25].

On the right side, the proximal vagus nerve should be checked for a nonrecurrent laryngeal nerve, which is found in <1.0 % of patients [26].

Safety of Vagus Nerve Stimulation

For many years, implantable electrodes have been used for stimulation of the vagus nerve to treat chronic conditions such as epilepsy, depression, anxiety, Alzheimer's disease, migraine, and fibromyalgia. No clinically relevant side effects were seen with such permanent vagus nerve stimulation [13, 27–30]. By implication, this reassuring long-term safety experience should also extend to short-term use of CIONM during thyroid surgery.

To clarify the neurophysiological basis of vagus nerve stimulation, basic research has been carried out in animals [9, 12, 15, 32]. A current of 1 mA, as typically used in CIONM, recruits efferent type A motor fibers and myelinated type B autonomic fibers without activating the thin, demyelinated vagal C fibers. These vagal type C fibers are thought to mediate vasovagal symptoms causing central (headache, numbness), cardiac (arrhythmias, bradycardia), pulmonary (bronchospasm), or gastrointestinal (nausea, vomiting) adverse effects [8, 9, 27].

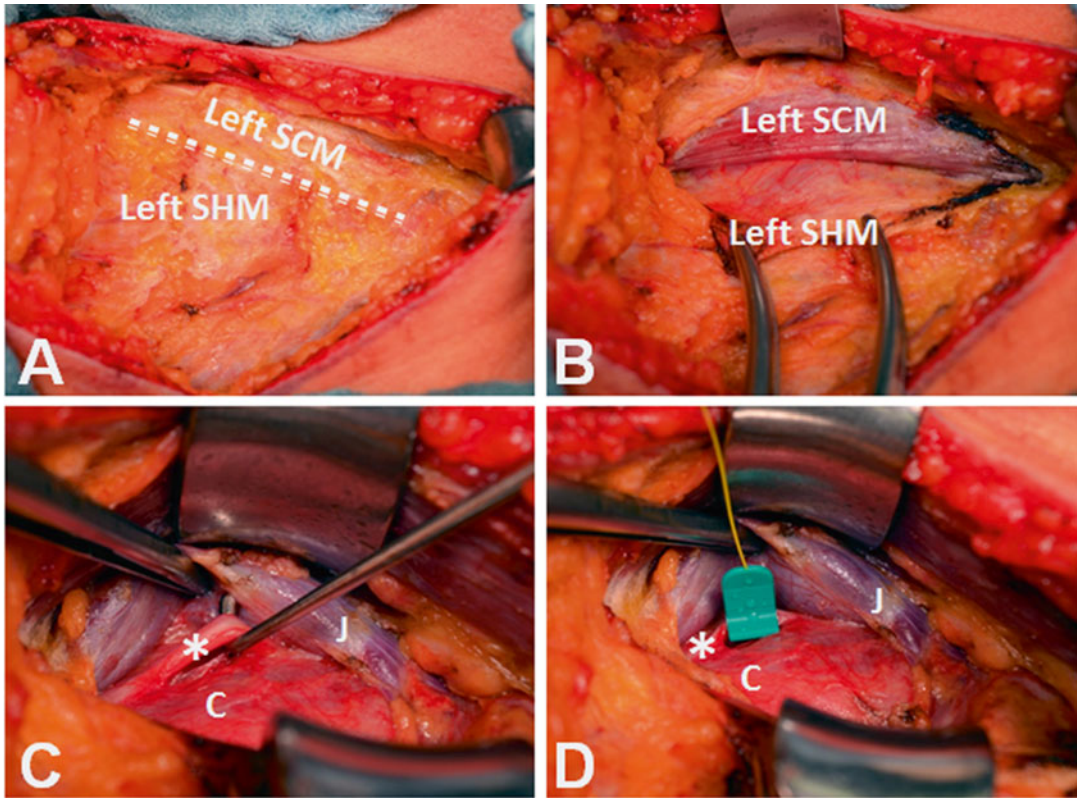

Fig. 15.3 The lateral surgical approach to the vagus nerve. (**A**) Lateral incision (*dashed line*) of the superficial cervical fascia alongside a virtual line formed by the lateral border of the left sternohyoid muscle (SHM) and the medial border of the left sternocleidomastoid muscle (SCM). (**B**) Blunt separation of the muscles with the use of retractors. (**C**) Retraction of the left vagus nerve dissected free over a short distance all around its circumference (*asterisk*). Exposure to the left common carotid artery ("c") and left internal jugular vein ("J") is achieved with medial retraction of thyroid gland and strap muscles and lateral retraction of the left sternocleidomastoid muscle. (**D**) Automatic Periodic Stimulation (APS)® electrode resting on the left vagus nerve (*asterisk*)

Other neurophysiological studies showed that increasing the current beyond a threshold of 0.7–0.8 mA cannot augment the amplitude of the EMG signal further [9, 32]. Groves and Brown found that a minimum current of 2.0 mA is necessary to recruit vagal type C fibers and elicit a cardiopulmonary response [13]. With currents of up to 5.0 mA, greater variability in heart rate was noted during CIONM [14, 21], although that increased variability was asymptomatic and did not trigger a compensatory sympathetic response. Likewise, vagus nerve stimulation with frequencies <30 Hz, the usual frequency for CIONM being ≤3 Hz, has not been associated with vasovagal effects.

Reliability of CIONM

It is important to optimize the nerve amplitude on which the IONM system is calibrated to identify clinically relevant EMG signals [8, 33]. Because latency measurements are influenced by the quality and characteristics of the EMG amplitude, device issues can diminish the performance of the CIONM system.

Electrode Types

There is an array of electrodes that differ in how they connect with the nerve, and in electrode

polarity, shape, size, and resilience (Fig. 15.1). All electrodes represent a compromise between enhanced stability, ensuring more stable EMG signals with fewer electrode dislocations, and greater resilience for better protection of the vagus nerve.

The design of the electrode, open, semi-closed or closed, has an immediate impact on the extent of nerve dissection to bring the electrode into position. The ***open-design electrode*** needs no more than a small incision of the carotid sheath with little, if any, nerve dissection to connect with the vagus nerve. Because they rely on the carotid sheath for support, open-design electrodes are unsuitable if the carotid sheath cannot be preserved, e.g., during resection of great neck vessels invaded by tumor or extensive dissection of the lateral neck nodes. The ***semi-closed or closed electrode design*** requires that a short segment of the vagus nerve is dissected free all around the nerve's circumference so that semi-closed and closed design electrodes can embrace the nerve partially or completely (Video 15.1, Fig. 15.4). Electrodes hooked up onto the vagus nerve are more likely to stay in place and produce higher-quality EMG signals.

To deliver the current pulse for vagal stimulation, a monopolar, bipolar, or tripolar electrode and a closed circuit are required.

Stimulation with a ***monopolar electrode*** is fairly stable, whatever the dryness of the operative field, but less precise so that stray current can recruit adjacent nerves and muscles. For monopolar stimulation, the anode is placed underneath the skin using a subcutaneous needle. Stimulation with ***bipolar or tripolar electrodes*** is more precise, although serum or blood collections around the electrode tips may cause shunting, resulting in understimulation of the vagus nerve. Because the two poles are in direct contact with the nerve or the negative pole is positioned between two positive poles, there is no need for a separate anode, as opposed to monopolar stimulation. The need to keep the poles apart explains why tripolar electrodes are bulkier than bipolar electrodes, which in turn are larger than monopolar electrodes.

EMG Artifacts

Implicit with the application of CIONM is the correct position of the endotracheal tube, which is accomplished by close collaboration between the surgeon and the anesthesiologist. Tube dislocation, tube rotation, and selection of too large or too small tubes should be avoided. For a stable and reliable EMG signal, the nerve amplitude on which the IONM system is calibrated ("baseline amplitude") must attain at least 500 μV (Fig. 15.5A) [8]. This will help circumvent

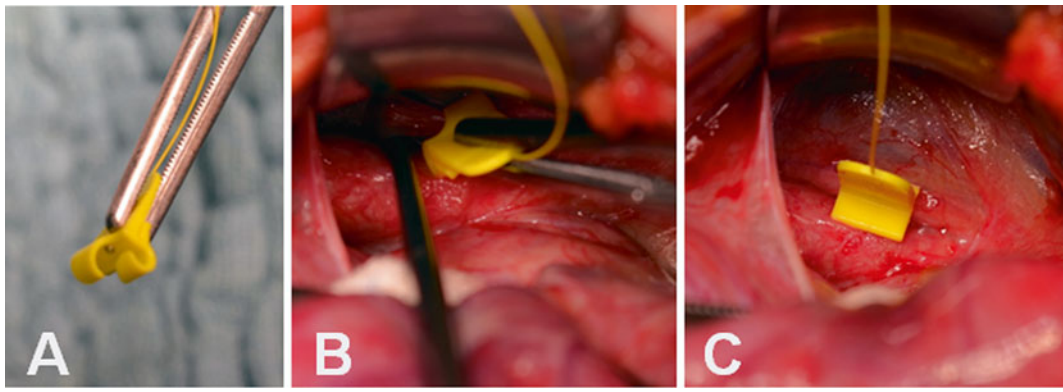

Fig. 15.4 Positioning of the Automatic Periodic Stimulation (APS)® electrode on the vagus nerve. (**A**) View of the monopolar Advanced Periodic Stimulation (APS®) electrode before placement on the vagal nerve. (**B**) Positioning of the APS® electrode with a forceps on the dissected segment of the vagal nerve from a 45°angle. (**C**) View of the APS® electrode resting on the vagal nerve

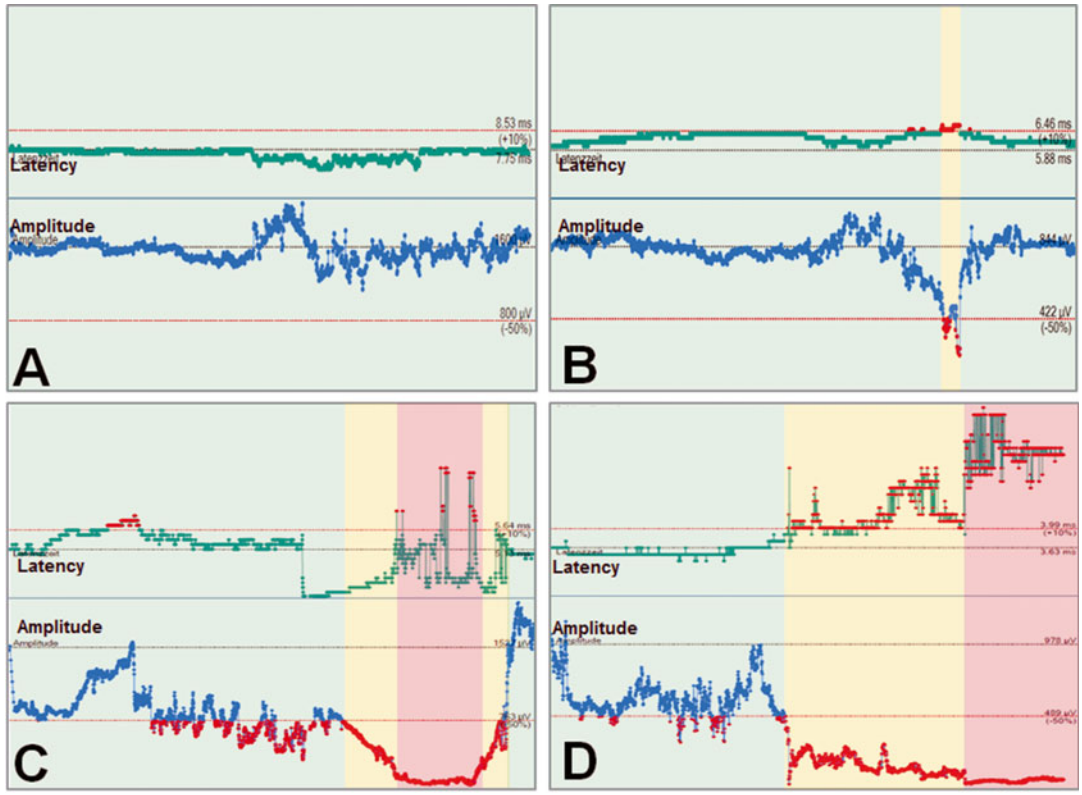

Fig. 15.5 Clinical relevance of distinct EMG changes during continuous intraoperative neuromonitoring. (**A**) Unimportant event (decrease in amplitude <50 %) with increase in latency <10 % relative to baseline, indicating normal vocal fold function. (**B**) Combined event (decrease in amplitude >50 %) with increase in latency >10 % relative to baseline without LOS, indicating normal vocal fold function. (**C**) Temporary LOS (amplitude decrease to <100 μV), with recovery of the amplitude to >50 % of baseline, indicating normal vocal fold function. (**D**) Persistent LOS (amplitude decrease to <100 μV), indicating a >85 % risk of postoperative vocal fold palsy

"latency jumping," a systematic measurement error of latency that occurs when the amplitude is lower than 350 μV [8]. Calibration of high-signal amplitudes standing out of the background noise facilitates detection of impending nerve injury.

Isolated events, such as periods of minor decreases or increases of amplitude or latency alone that are unrelated to surgical manipulation, can be interpreted as EMG changes of minor importance concerning nerve function. Such events are often related to endotracheal tube positional changes or other equipment issues rather than true RLN dysfunction (Fig. 15.6A–F) [8]. Repositioning the endotracheal tube augments the recorded EMG signal by bringing the tube electrode closer to the vocal muscle. Bipolar forceps, coagulation, and detachment of the vagus electrode lead to silencing, deterioration, or temporary loss of the EMG signal, respectively. Irrigation of the surgical field with a cold sodium chloride solution may cause rapid decreases in amplitude followed by gradual increases in latency. Because the clinical relevance of these temperature-induced EMG changes is unclear, cold solutions should not be used to rinse the operative field [8, 23].

Prevention of Ipsilateral Vocal Fold Palsy

Direct traction, pressure, and heat applied to the RLN change the EMG signal in a reproducible characteristic manner. Typically, changes in amp-

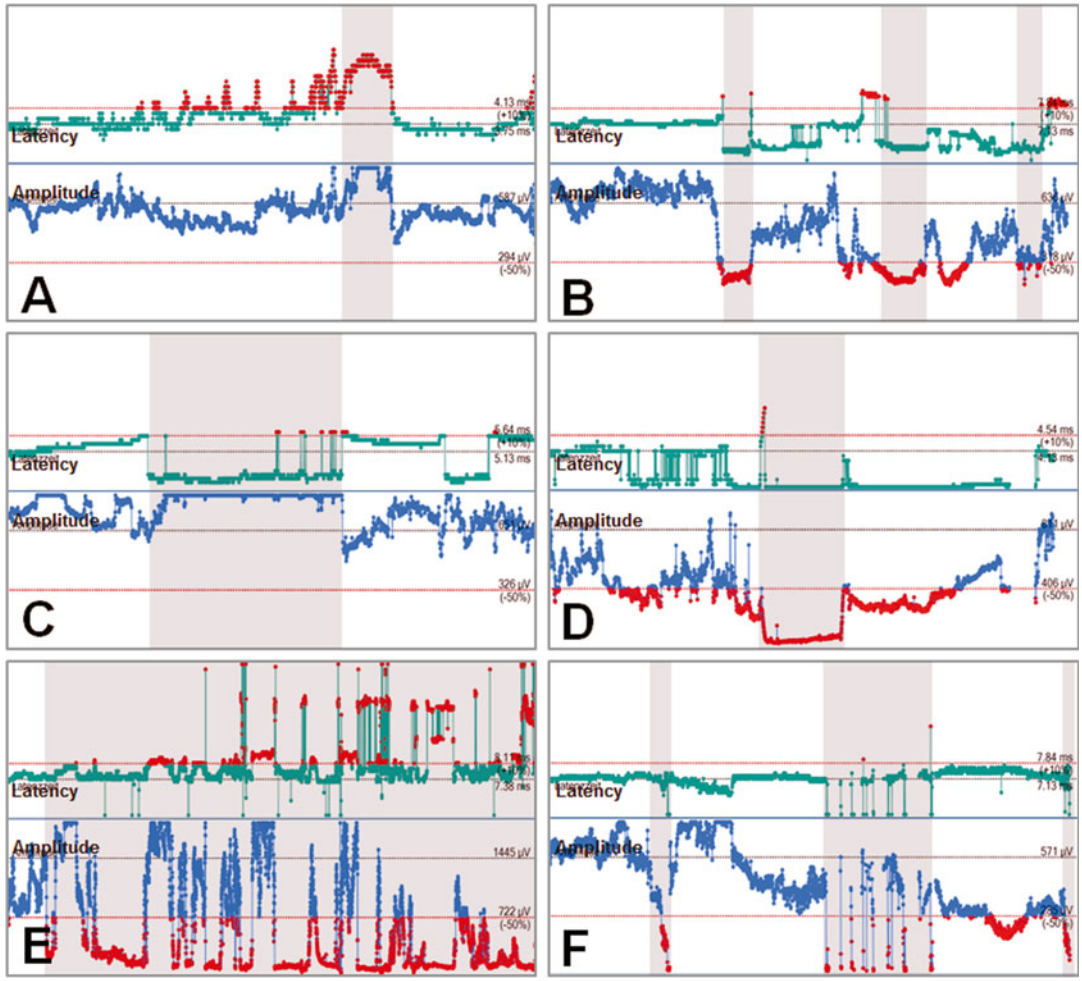

Fig. 15.6 Artificial EMG changes during continuous intraoperative neuromonitoring. (**A**) Increases in both amplitude and latency caused by rotation of the endotracheal tube after tracheal displacement, reversible with release of the trachea. (**B**) Repetitive decreases in both amplitude and latency caused by downward shifts of the endotracheal tube when pulling the trachea upward, reversible with release of the trachea. (**C**) Decrease in amplitude with increase of latency caused by rotation of the endotracheal tube after tracheal displacement, reversible with release of the trachea. (**D**) LOS (amplitude <100 μV) caused by intraoperative injection of 10 mg of the muscle-relaxant rocuronium, with complete recovery (>50 % of baseline) after antagonization with 300 mg of sugammadex IV. (**E**) "*EMG storm*" produced by poor vagus contact of a too large vagal electrode. (**F**) Rarefaction of EMG signals due to repeated dislocation of a too small vagal electrode

litude (decreases by 40–60 %) are more marked than changes in latency (increases by 15 %) [9]. Subacute RLN injury sets out with a decrease of the nerve amplitude, due to the loss of functional nerve fibers, before latency increase begins to take effect, signifying deterioration of signal transmission in the remaining nerve fibers (Fig. 15.7).

Reversibility of Nerve Injury Before Loss of Signal

A recent proof-of-concept study (52 patients with CIONM; 52 nerves at risk) defined concordant changes in both signal amplitude (decreases >50 %) and latency (increases >10 %) as "combined events" indicative of impending nerve injury

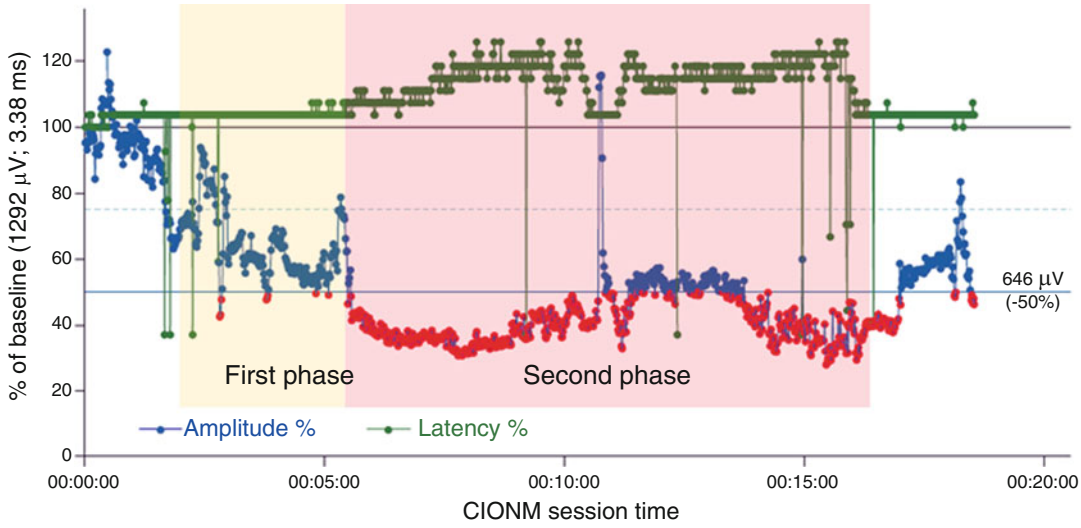

Fig. 15.7 Sequential decrease in amplitude followed by an increase in latency, signifying impending nerve injury (diffuse LOS type 2)

(Fig. 15.5B) [8]. Inappropriate traction on the thyroid produced stretch injury where the RLN coursed through the ligament of Berry or intersected with the inferior thyroid artery. The anterior motor branch of the RLN at the ligament of Berry was at a particular risk of traction injury when motor fibers branched outside the larynx. Medial retraction of the thyroid lobe reduced the amplitude by more than 60 %, with full restoration after reversal of the surgical maneuver. Traction on the laryngotracheal angle, with compromise of the RLN at its laryngeal entry site, triggered combined events, as did lobar retraction distant from the RLN. Among all 13 combined events, traction accounted for 10 (77 %) and cautery for 3 (23 %) combined events. Vocal fold palsy (VCP) developed when multiple combined events degraded into LOS during the operation, but was averted in 70 % of patients with multiple combined events after stopping the causative surgical maneuver.

Another series of 102 patients defined severe combined events as amplitude decrease to <70 % with increase in latency to >10 % of baseline [23]. Both intraoperative severe combined events and LOS heralded postoperative VCP. Combined events had a positive predictive value (PPV) of 33 % and a negative predictive value (NPV) of 97 % for vocal fold palsy and were reversible in 73 %, whereas LOS had a PPV of 83 % and NPV of 98 % for VCP and was reversible in 17 % only. Isolated amplitude or latency changes were unassociated with postoperative VCP.

These findings were confirmed in a large study of 788 patients (1314 nerves at risk) with CIONM, in which 63 (82 %) of 77 combined events were reversible by discontinuing the causative surgical maneuvers (Fig. 15.5C) [25].

These data demonstrated that CIONM can prompt corrective actions before nerve injury becomes permanent (Table 15.1).

Recovery of the EMG Amplitude After Loss of Signal

The INMSG defines complete LOS as a decrease in nerve amplitude to below <100 µV (Fig. 15.5D) [11]. The Group further subdivides LOS into segmental LOS "type 1" and diffuse LOS "type 2."

Segmental LOS type 1 is caused most of the time by direct trauma to the nerve after nerve transection, clamping, ligation, pinching, or

coagulation, leaving little, if any, time for corrective action. Anatomic peculiarities, such as a thin nerve, extralaryngeal branching, or a nerve coursing anterior to the inferior thyroid artery are thought to predispose to segmental LOS type 1 [34–36].

Diffuse LOS type 2 is incompletely understood but may originate from within the larynx. It is produced by more indirect forces, including traction on the airway or on tissues around the nerve. Because it is typically preceded by combined events, there is frequently an opportunity for corrective action and prevention of VCP [35].

In a study of 785 patients (1291 nerves at risk), 18 patients developed segmental LOS type 1 (1.4 %) and 23 patients global LOS type 2 (1.8 %) after CIONM [35]. In LOS type 1, the EMG signal disappeared abruptly (median time to LOS was 2 s), but declined more slowly in LOS type 2 (median time to LOS was 156 s). In LOS type 1, nerve latency remained essentially unchanged, pointing to acute nerve injury. All 29 vocal fold palsies were unilateral and resolved completely within 2 months of the operation. Recovery of vocal fold function required a longer period of time in cases where the nerve monitoring signal was abruptly lost. LOS type 1 vocal fold palsies, consistent with severe damage, took longer to resolve (median time to recovery was 62 days) than LOS type 2 vocal fold palsies (median time to recovery was 27 days), indicating less severe damage.

In that investigation, signal recovery ≥50 % of the baseline nerve amplitude during surgery always signified normal postoperative vocal fold function (Table 15.1). Conversely, signal recovery <50 % of the baseline nerve amplitude indicated postoperative VCP in all patients with segmental LOS type 1 and in two-thirds of patients with global LOS type 2 (Fig. 15.8). LOS without intraoperative recovery predicted VCP in all patients with segmental LOS type 1 and three-quarters of patients with global LOS type 2 [35].

These findings suggest that an injured nerve should be given a minimum wait time of 20 minutes upon LOS to recover ≥50 % of its baseline amplitude before moving on with completion thyroidectomy on the unaffected side (Fig. 15.9) [35, 37].

Performance of CIONM vs. IIONM in Preventing Postoperative Vocal Fold Palsies

A recent study compared CIONM (788 patients with 1314 nerves at risk) to IIONM (738 patients with 965 nerves at risk) regarding prediction of postoperative VCP [24]. Herein, the early postoperative VCP rate was comparable between CIONM and IIONM (2.5 % vs. 2.4 %; $P=0.84$), whereas the permanent VCP rate was lower after CIONM than IIONM (0 % vs. 0.4 %; $P=0.019$; Table 15.2).

For early postoperative VCP, the sensitivity of CIONM tended to be higher (90.9 % vs. 73.9 %; $P=0.09$) in that study so that CIONM predicted 9 of 10 RLN palsies correctly. A test with a higher sensitivity (CIONM) is more useful for ruling out a condition (VCP) if a person tests negative (normal EMG signals). The failure to detect a VCP using nerve monitors, i.e., the problem of imperfect sensitivity, is a potential liability issue that is taken very seriously in the medical profession.

Based on this study and considering a hypothetical planned bilateral procedure with loss of the EMG signal on the first side of resection, an unnecessary two-staged procedure would have been performed in 12 % of patients after CIONM, but in 23 % of patients after IIONM.

Normal monitoring signals after thyroid surgery almost always indicate a functionally intact nerve, carrying a risk of early postoperative VCP of 0.2 % for CIONM, but 0.6 % for IIONM (Table 15.2).

Conclusion

CIONM is an advanced tool to improve risk management of the RLN by online registration of vagus nerve amplitude and latency during thyroid

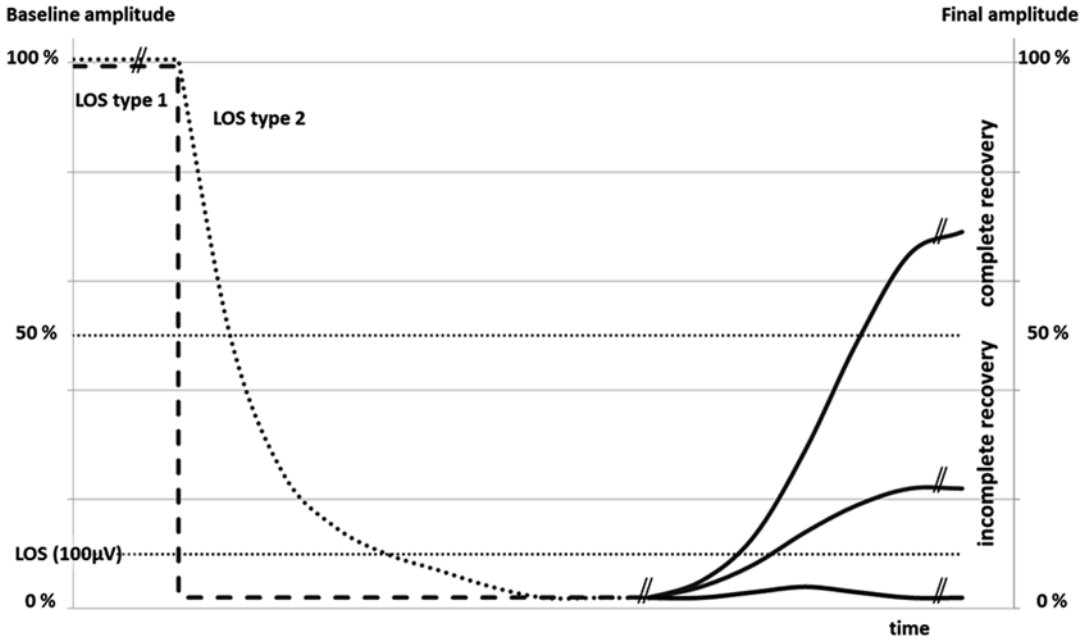

Fig. 15.8 Dynamics of loss and recovery of the EMG amplitude and clinical outcome after LOS type 1 (*dashed line*) and LOS type 2 (*dotted line*). No or incomplete intraoperative recovery of amplitude after LOS (<50 % of initial baseline amplitude) denote a 100 % (LOS type 1) and 75 % vs. 67 % (LOS type 2) risk of postoperative vocal fold palsy, whereas complete intraoperative recovery of amplitude after LOS (>50 % of initial baseline amplitude) indicates normal postoperative vocal fold palsy (LOS type 1 and 2) (Based on data from [35])

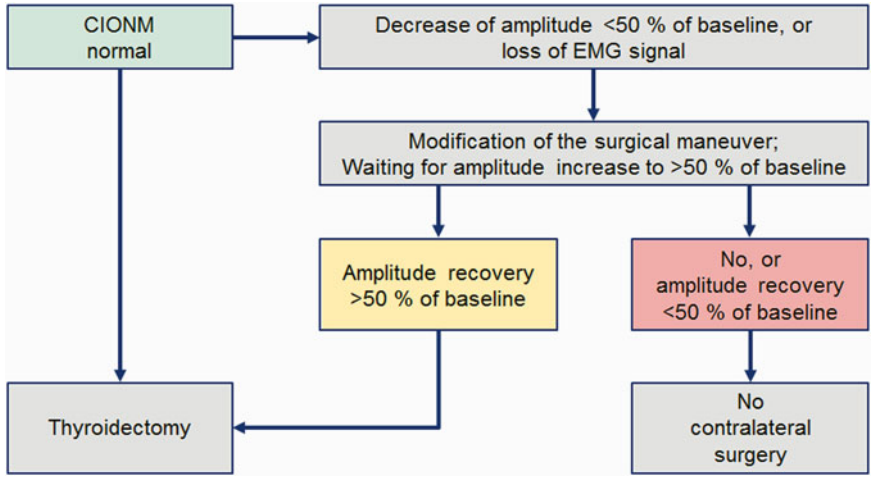

Fig. 15.9 Surgical algorithm for amplitude decreases <50 % or complete loss of the EMG signal on the first side of resection in planned thyroidectomy (Based on data from [35, 37])

surgery. Both types of neuromonitoring, IIONM and CIONM, have strengths and weaknesses in common:

- Differentiation between intact RLN function and malfunction, and between segmental LOS 1 and diffuse LOS 2;
- Prediction of postoperative vocal fold function; and
- Inability to prevent immediate nerve injuries characterized by sudden complete LOS

The competitive advantage of CIONM over IIONM becomes apparent in technically demanding

Table 15.2 Validity of intermittent and continuous intraoperative neuromonitoring

	Intermittent intraoperative neuromonitoring (965 nerves at risk); *n* (%)	Continuous intraoperative neuromonitoring (1314 nerves at risk); n (%)	*P*
True-positive result	17 (77.3)	30 (88.2)	0.745
True-negative result	937 (99.4)	1277 (99.8)	0.238
False-positive result	5 (0.5)	4 (0.3)	0.358
False-negative result	6 (0.6)	3 (0.2)	0.142
Early postoperative vocal fold palsy	23 (2.4)	33 (2.5)	0.844
Permanent vocal fold palsy	**4 (0.4)**	**0**	**0.019**

Based on data from [24]

operations in which CIONM alerts the surgeon as soon as a surgical procedure impinges on the RLN.

One major advantage is prompt recognition of nerve dysfunction developing with mild to moderate traction on the nerve and having the potential for progression to LOS. Unlike IIONM, CIONM provides constant feedback regarding RLN function to the surgeon so that corrective action can be initiated immediately to release a distressed nerve. "Combined events," concordant signal changes in both amplitude (decreases to less than 50 % of initial baseline) and latency (increases to more than 110 % of initial baseline), typically precede postoperative VCP and are reversible in 80 % of cases upon release of the nerve. The surgeon's response to these EMG changes marks the difference of IIONM, by stopping harmful surgical activity, giving the nerve a chance to recover before the damage has become complete. CIONM, therefore, is set to overcome the principal methodological limitation of IIONM which identifies RLN dysfunction and LOS only *after* the damage has taken place.

Another major advantage of CIONM is its ability to help identify functional nerve recovery, which occurs with restitution of the amplitude to ≥50 % of its baseline, and predicts normal postoperative vocal fold function.

Recent evidence suggests that CIONM affords better nerve protection than IIONM, which resulted in permanent RLN palsy rates of 0 % with CIONM vs. 0.4 % with IIONM ($P=0.019$) [24].

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Part V

SLN Surgical Anatomy and Monitoring

Marcin Barczyński

External Branch of Superior Laryngeal Nerve (EBSLN) Anatomic Classification

16

Marcin Barczyński, Jeremy L. Freeman, and Claudio R. Cernea

Abstract

The external branch of the superior laryngeal nerve (EBSLN) has a close anatomical relationship with the superior thyroid pedicle and is at risk of injury during dissection of these vessels. Thorough knowledge of the surgical anatomy of the EBSLN and its variations is mandatory to avoid damage to the nerve during thyroidectomy. In recent years, several EBSLN anatomical classification systems have been proposed including the Cernea classification, Kierner classification, Friedman classification, and Selvan classification. In this chapter, these classifications are presented and discussed on the background of the published research in the field. The most widely recognized surgical classification of the EBSLN was proposed in 1992 by Cernea. This classification is based on the potential risk of injury to the nerve during thyroid surgery. It categorizes the nerve in relation to superior thyroid vessels and the upper edge of the superior thyroid pole into three types. A type-1 nerve crosses the superior thyroid vessels more than 1 cm above the upper edge of the thyroid superior pole and occurs in 68 % of patients with small goiter and in 23 % of patients with large goiter. A type-2A nerve crosses the vessels less than 1 cm above the upper edge of the superior pole and occurs in 18 % of patients with small goiter and 15 % of patients with large goiter. A type-2B nerve crosses the superior thyroid pedicle below the upper border of the superior thyroid

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pole and occurs in 14 % of patients with small goiters and 54 % of patients with large goiters. Obviously, a type-2B nerve is most vulnerable to inadvertent injury. The remaining classification systems should be considered as complementary to Cernea's classification system, providing useful information for intraoperative identification of the nerve.

Keywords

Superior laryngeal nerve • External branch of the superior laryngeal nerve • Cernea classification • Kierner classification • Friedman classification • Selvan classification

Introduction

The surgical technique of thyroidectomy has changed little since the original development pioneered by Kocher [1]. The most common complications of thyroid surgery include injury to the recurrent laryngeal nerve (RLN) and hypoparathyroidism. However, injury to the external branch of the superior laryngeal nerve (EBSLN) can occur during the dissection and clamping of the superior thyroid vessels. This injury causes paralysis of the cricothyroid muscle (CTM), impairing the production of high tones and altering the voice's fundamental frequency, which may be especially problematic for women and professional singers. The effects of EBSLN paralysis are difficult to detect during routine postoperative laryngoscopy, yet functional consequences can be disastrous for those people who depend professionally on their voices. With thorough knowledge of the anatomic variations of the superior thyroid pole area, and through meticulous dissection of the superior thyroid pedicle, one may avoid such injury.

Historical Perspective

In 1892, Fort reported the anatomic features of the CTM, including its motor supply by the EBSLN [2]. Several publications have studied the anatomy of the EBSLN, generally in cadaver series [3–9]. The largest report, by Moosman and DeWeese, included 200 fresh cadavers [6].

Little attention was initially paid to the surgical anatomy of the EBSLN during the beginning of the twentieth century. In fact, even Kocher did not specifically mention this nerve in his book, which was considered the cornerstone of thyroid surgery at the time, and documented his personal experience in more than 3000 thyroidectomies [1]. The importance of the preservation of the EBSLN was highlighted by the unfortunate result of a thyroidectomy performed in 1935. At that time, Amelita Galli-Curci was the most famous soprano in the world. She underwent a thyroidectomy under local anesthesia (her surgeon asked her to actually speak during the surgery, to be sure that the recurrent nerves suffered no damage) for a 170-g goiter, with careful identification and preservation of the RLNs. However, her vocal registry dramatically lowered postoperatively, and her voice became permanently hoarse. She had to give up singing, and the press at the time wrote, "the surprising voice is gone forever; the sad specter of a ghost replaced the velvet softness" [10]. Since that time, the EBSLN has been known as "the nerve of Amelita Galli-Curci." Interestingly enough, some authors have recently questioned the veracity of this event [10]. In 1957, Gregg stated that despite the large experience of his service (8000 thyroidectomies), he was unsure how to prevent or detect damage to the EBSLN [11]. Subsequently, several authors proposed that the dissection of the superior thyroid pole should be performed with great care to avoid including the nerve in the ligature of the superior thyroid vessels [12–16].

There are few reports in the literature describing methods to identify the EBSLN during thyroidectomy. Some authors have based their identification only upon the anatomic appearance of the nerve [8, 10]. Others have tried some form of electrical stimulation to aid in identification [17–21], mainly when dealing with a markedly enlarged thyroid gland [22]. However, in 2013 the International Neural Monitoring Study Group (INMSG) published a guideline statement on EBSLN monitoring during thyroid and parathyroid surgery. The hypothesis explored in that review was that the use of a standardized approach to the functional preservation of the EBSLN could be facilitated by application of intraoperative neural monitoring (IONM) resulting in improved preservation of voice following thyroidectomy or parathyroidectomy. Those guidelines were intended to improve the practice of neural monitoring of the EBSLN during thyroidectomy and parathyroidectomy and to optimize clinical utility of this technique based on available evidence and consensus of experts [18].

Anatomy

The superior laryngeal nerve (SLN) is one of the first branches of the vagus after it exits the skull base. It typically originates from the vagus at the nodose ganglion at the level of C2, about 4 cm cranially to the carotid artery bifurcation [12]. About 1.5 cm caudally, the SLN divides into an internal and external branch (EBSLN) [6]. The EBSLN descends dorsal to the carotid sheath, and then crosses medially, extending to the larynx. In its course, the EBSLN is usually located dorsal to the superior thyroid artery and superficial to the inferior pharyngeal constrictor muscle as it descends and travels medially to innervate the CTM on the anterolateral aspect of the lower portion of the cricoid cartilage of the larynx.

Moosman and DeWeese found the EBSLN in a study of 200 human cadaver dissections to be approaching the larynx within the so-called

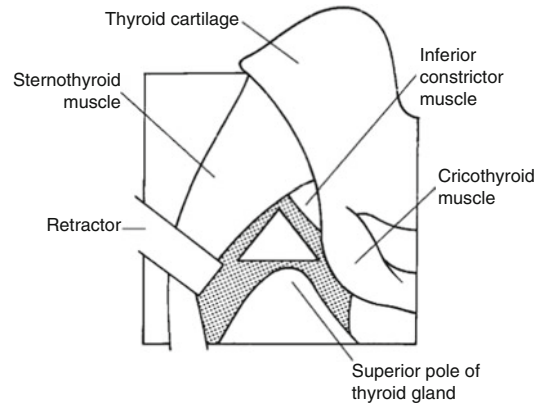

Fig. 16.1 The sternothyroid-laryngeal triangle [Reprinted with permission from Randolph GW. Surgery of the Thyroid and Parathyroid, 2nd edition. Published by Elsevier © 2012.]

sternothyroid-laryngeal triangle (Jolls space) formed as the progressively dissected superior pole is retracted laterally and inferiorly (Fig. 16.1). This sternothyroid-laryngeal triangle is defined medially by the inferior pharyngeal constrictor and CTMs, anteriorly by the sternothyroid muscle, and laterally by the laterally retracted superior thyroid pole [6]. After the EBSLN travels down the lateral surface of the larynx on the inferior pharyngeal constrictor muscle, the EBSLN typically bifurcates into two branches at the level of the cricoid, entering separately into the *pars recta* and *pars oblique* of the CTM bellies (Fig. 16.2). The EBSLN is usually about 0.8 mm wide and its total length varies between 8 and 8.9 cm [19, 20].

Wu et al. processed 27 human hemilarynges with Sihler's stain, a technique that clears soft tissue and counterstains nerve. In this study, a neural connection was found in 44 % of the 27 specimens that exited the medial surface of the CTM (on the outside of the larynx) and then entered into the larynx extending through the cricothyroid membrane and ramifying in the anterior third of the ipsilateral thyroarytenoid muscle [21]. Similar observations were made in the canine by Nasri et al. who identified cross-innervation of the thyroarytenoid muscle by the EBSLN in 42.9 % of subjects. This was con-

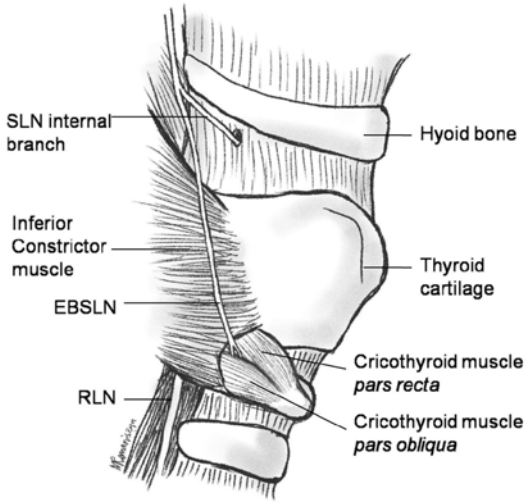

Fig. 16.2 The EBSLN descends routing to the larynx and innervates two bellies of the cricothyroid muscle [Courtesy of Marcin Barczyński]. SLN - superior laryngeal nerve; EBSLN - external branch of the SLN; RLN - recurrent laryngeal nerve

firmed by EMG recordings from thyroarytenoid muscle following electrical stimulation applied to the EBSLN [22]. Sanudo et al. found that in 68 % of 90 human microdissected specimens, the EBSLN after innervating the CTM continues on, extending through the cricothyroid membrane to innervate the anterior thyroarytenoid muscle region [23]. Maranillo et al. studied the existence of a neural connection between the external laryngeal nerve and the RLN using microdissection technique in 103 human larynges obtained from necropsies. The human communicating nerve was identified in 85 % of cases in this study (bilaterally in 44 % and unilaterally in 41 %) [24]. Thus, the human communicating nerve provides documented connection to the vocal fold in 41–85 % of patients [21–26]. The variability of this neural connection, variability in recording the small and early glottic waveform associated with EBSLN stimulation, and variability in endotracheal tube position are all likely responsible for the defined waveforms being recordable in less than 100 % of patients during EBSLN stimulation with currently available standard monitoring technology [26–28]. However, utilization of a novel endotracheal tube with additional anterior surface electrodes allows for quantifiable EBSLN electromyographic activity in 100 % of cases. Monopolar and bipolar stimulator probes produced similar EMG data [29].

The surgical importance of the EBSLN is due to the close anatomical relationship between the nerve and the superior thyroid vessels. In most circumstances the EBSLN extends medially to the larynx well above the superior thyroid pole and would therefore be at minimal risk of surgical injury during capsular dissection and individual ligation of branches of the superior thyroid vessels. However, there is variability in the caudal extent of the nerve relative to the superior pole region (see classification systems discussed below). In those with a large goiter, a thyroid tumor localized within the upper thyroid pole, or in patients with a short neck, the anatomical relationship between the nerve and the superior thyroid pole vessel can be much more intimate, exposing the EBSLN to a higher risk of inadvertent injury [9, 30].

Contrary to routine dissection of the RLN, most surgeons tend to avoid rather than routinely expose the EBSLN during thyroidectomy. Nevertheless, visual localization of the EBSLN was reported to be highly successful in expert hands of thyroid surgeons with an identification rate exceeding 98 % [31]. In the hands of Freeman, only 3 of 178 EBSLNs (1.7 %) could not be identified using routine thyroidectomy technique in a group of 112 consecutive patients [31]. Unfortunately, visual identification of the EBSLN can be challenging for less-experienced surgeons, particularly in difficult cases [26]. In addition, in approximately 20 % of patients in whom the nerve is located deep to the fascia of the inferior constrictor muscle, visual identification can be impossible unless there is intramuscular dissection [8]. In the remaining 80 % of patients, the nerve is located superficial to the inferior constrictor fascia and is therefore able to be visualized. With IONM, all EBSLNs should be able to be stimulated and identified, even those that are subfascial in location and not able to be directly visualized.

There are few surgical classifications of the EBSLN anatomical variations. However, the most widely recognized surgical classification of the EBSLN was proposed in 1992 by Cernea et al. [9]. This classification is based on the potential risk of injury to the nerve during thyroid surgery. It categorizes the nerve in relation to the superior thyroid vessels and upper edge of the superior thyroid pole (Fig. 16.3).

Cernea EBSLN Classification Scheme

- *Type-1*: Nerve crosses the superior thyroid vessels more than 1 cm above the upper edge of the thyroid superior pole and occurs in 68 % of patients with small goiter and in 23 % of patients with large goiter.
- *Type-2A*: Nerve crosses the vessels less than 1 cm above the upper edge of the superior pole and occurs in 18 % of patients with small goiter and 15 % of patients with large goiter.
- *Type-2B*: Nerve crosses the superior thyroid pedicle below the upper border of the superior thyroid pole and occurs in 14 % of patients with small goiters and 54 % of patients with large goiters.

Types 2A and 2B are particularly prone to injury during dissection and ligation of the superior thyroid vessels due to their low-lying course [9, 32]. It is of interest to note that most studies on the anatomy of the EBSLN have been performed in Western countries. Hence, they may have some limitations in their application to other nations, particularly to Asian patients. Hwang et al. investigated 92 EBSLNs during 50 thyroid operations performed on adult Korean patients in Seoul and found that type-1 EBSLN was observed in 15 of the 92 nerves (16.3 %), type-2A EBSLN was noted in 52 (56.5 %) and type-2B EBSLN was noted in 25 (27.2 %). Patients with types 2A and 2B were at higher risk of injuries, and these types were more frequently observed (83.7 %) compared with previous Western studies. It was also found that 35.9 % of distal insertion sites of EBSLNs were located within 1 cm of the center of the cricoid cartilage [33].

In 1998, Kierner et al. published a similar classification to the Cernea system, adding a fourth category of the EBSLN running dorsally to the superior thyroid pedicle, which was observed in 13 % of their dissection studies and was considered more difficult to visually identify [34] (Fig. 16.4).

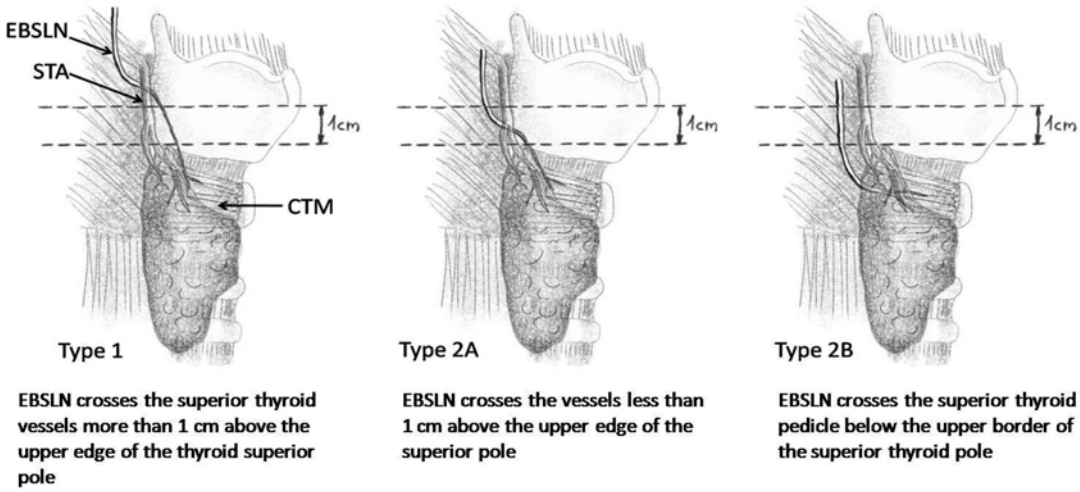

Fig. 16.3 Cernea EBSLN classification scheme [Courtesy of Marcin Barczyński]. EBSLN - external branch of the superior laryngeal nerve; CTM - cricothyroid muscle; STA - superior thyroid artery

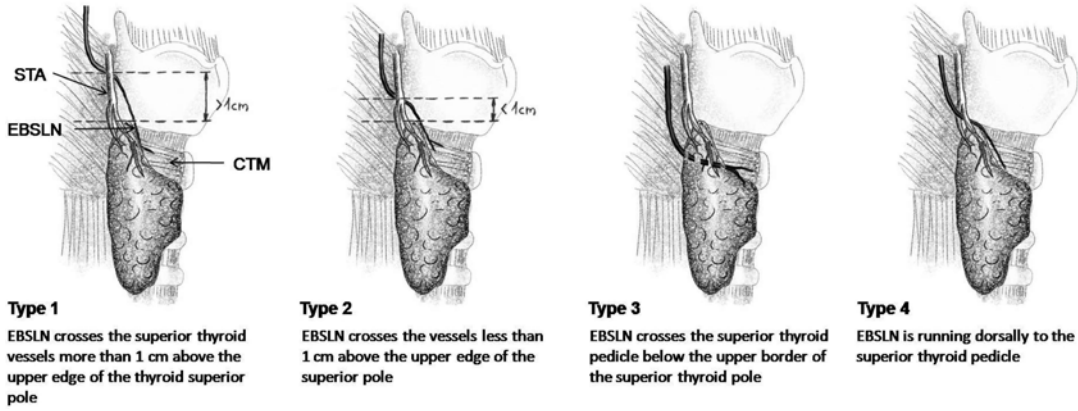

Fig. 16.4 Kierner EBSLN classification scheme [Courtesy of Marcin Barczyński]. STA - superior thyroid artery; CTM - cricothyroid muscle; EBSLN - external branch of the superior laryngeal nerve

Kierner EBSLN Classification Scheme

- *Type-1*: Nerve crosses the superior thyroid vessels more than 1 cm above the upper edge of the thyroid superior pole.
- *Type-2*: Nerve crosses the vessels less than 1 cm above the upper edge of the superior pole.
- *Type-3*: Nerve crosses the superior thyroid pedicle below the upper border of the superior thyroid pole.
- *Type-4*: Nerve is running dorsally to the superior thyroid pedicle.

Another classification system of the EBSLN was proposed by Friedman et al. [35]. This classification system is focused on the anatomy of the EBSLN prior to its insertion into the CTM. Friedman's classification system was not intended to replace the classification system proposed by Cernea et al. In contrast, it should be considered as a complementary classification system, useful for intraoperative identification of the nerve. Three variations have been described by Friedman et al. for the main trunk of the EBSLN prior to terminal branching (Fig. 16.5).

Friedman EBSLN classification scheme

- In the type-1 variation, the nerve runs its whole course superficially or laterally to the inferior constrictor, descending with the superior thyroid vessels until it terminates in the CTM.
- In the type-2 variation, the EBSLN penetrates the inferior constrictor in the lower portion of the muscle. In this case, it is only partially protected by the inferior constrictor.
- In the type-3 variation, the nerve dives under the superior fibers of the inferior constrictor, remaining covered by this muscle throughout its course to the CTM.

In 2009, Selvan et al. proposed a new clinical typing of the EBSLN based on a prospective, descriptive dissection study of 70 nerves in 35 patients. In this report, the cricothyroid compound muscle action potential (CMAP) was recorded using EMG to identify the EBSLN, which was then classified according to clinical variation during routine thyroid operations [36]. This classification categorizes the nerve in relation to superior thyroid vessels and the cricoid cartilage. (Fig. 16.6)

Selvan EBSLN Classification Scheme

- *Type 1a*: Nerve that was located within 1 cm of the entry of the vessels into the gland, either anterior or between the branches of the superior thyroid vessels and within 3 cm from the cricoid cartilage (9 % of patients).
- *Type 1b*: Nerve that was located posterior to the vessels but within 1 cm of the entry of the

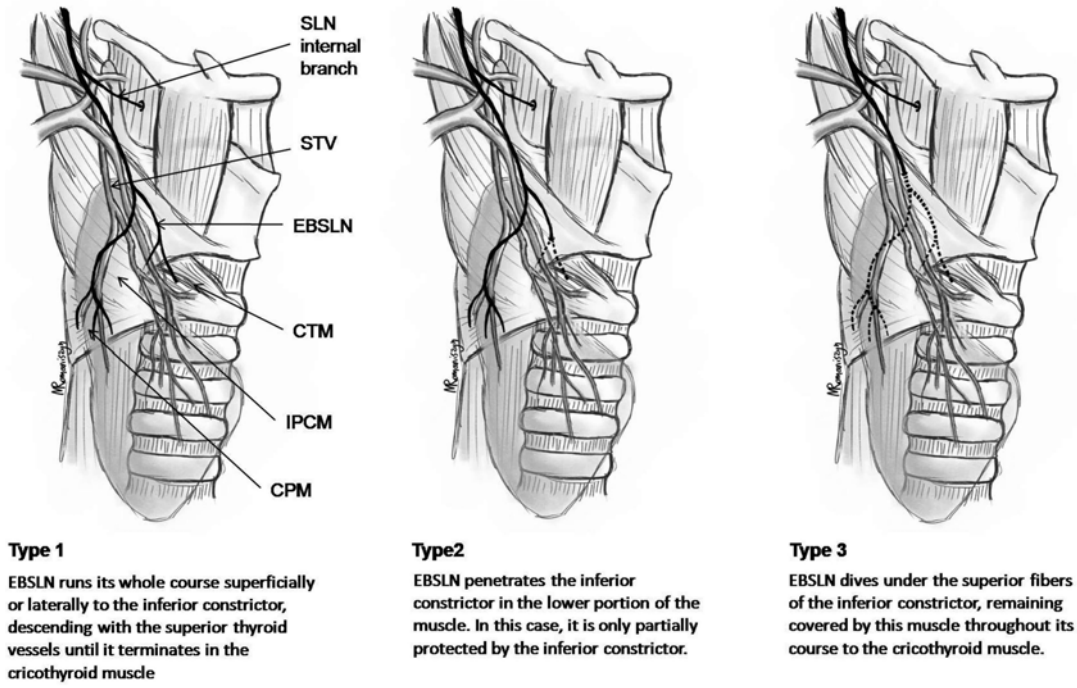

Fig. 16.5 Friedman EBSLN classification scheme [Courtesy of Marcin Barczyński]. SLN - superior laryngeal nerve; STV - superior thyroid vessels; EBSLN - external branch of the SLN; CTM - cricothyroid muscle; IPCM - inferior pharyngeal constrictor muscle; CPM - cricopharyngeal muscle

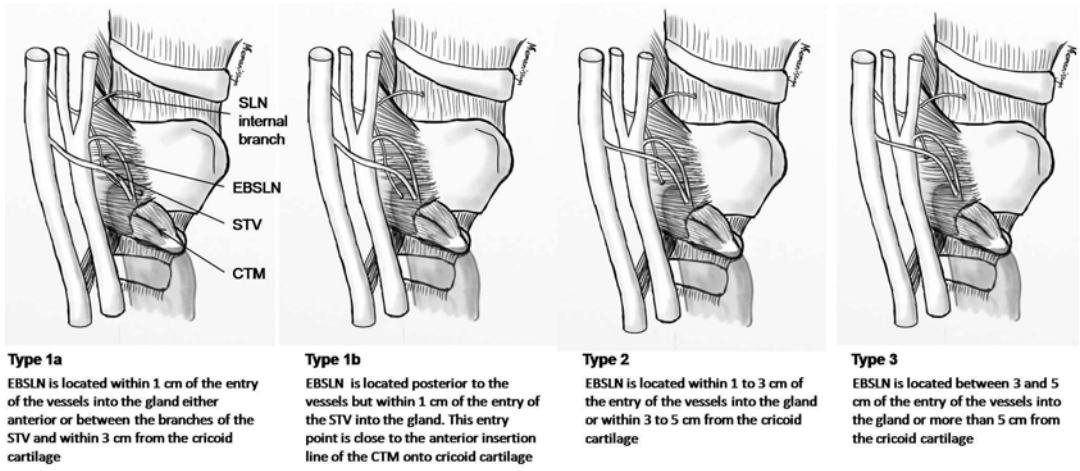

Fig. 16.6 Selvan EBSLN classification scheme [Courtesy of Marcin Barczyński]. SLN - superior laryngeal nerve; EBSLN - external branch of the SLN; STV - superior thyroid vessels; CTM - cricothyroid muscle

superior thyroid vessel into the gland. This entry point is close to the anterior insertion line of the CTM onto the cricoid cartilage (present in 3 % of patients).

- *Type 2*: Nerve that was located within 1–3 cm of the entry of the vessels into the gland or within 3–5 cm from the cricoid cartilage (present in 68 % of patients).
- *Type 3*: Nerve that was located between 3 and 5 cm of the entry of the vessels into the gland or more than 5 cm from the cricoid cartilage (present in 20 % of patients).

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Surgical Approach and Monitoring of the External Branch of the Superior Laryngeal Nerve (EBSLN)

17

Marcin Barczyński and Gregory W. Randolph

Abstract

In this chapter, methods of intraoperative preservation and monitoring of the external branch of the superior laryngeal nerve (EBSLN) are described in detail. Contrary to routine dissection of the recurrent laryngeal nerve (RLN), most surgeons tend to avoid rather than routinely expose and identify the EBSLN during thyroidectomy. The EBSLN is believed to be the most commonly underestimated morbidity following thyroid surgery and is at a high risk of injury during dissection of the superior thyroid pole in the course of thyroidectomy in approximately one-third of patients (Cernea type 2A and 2B nerves). The laryngeal head of the sternothyroid muscle is a robust landmark for the course of the EBSLN as it descends along the inferior constrictor to the cricothyroid muscle (CTM). In up to 20 % of cases the nerve may not be able to be visualized due to a subfascial course along the inferior constrictor muscle, and hence use of intraoperative neural monitoring (IONM) can significantly improve the identification rate of the EBSLN during thyroidectomy. CTM twitch and glottic EMG recordings are both methods of IONM which are recommended in all cases of thyroid surgery, especially those which might jeopardize the EBSLN. A technique of togging the stimulator probe between the tissue of the superior thyroid pole vessels (with negative stimulation) and the region of the laryngeal head of the sternothyroid muscle (with positive stimulation) is recommended to assure preservation of the EBSLN. Transverse division

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of the superior edge of sternothyroid muscle and gentle traction of the superior thyroid pole into lateral and caudal direction followed by blunt dissection within the avascular plane of sternothyroid-laryngeal triangle allow for improving exposure of the EBSLN which is usually descending parallel to superior thyroid artery and is lying on the fascia or between the fibers of the inferior constrictor muscle before its termination within CTM. Nerve stimulation can objectively identify the EBSLN, leading to a visible CTM twitch in all cases. EMG activity can currently be quantified in nearly 80 % of cases using standard EMG tubes, but in all patients using novel EMG tubes with anterior surface electrodes. The role of measuring the waveform amplitude in prognostication of EBSLN function is yet to be determined.

Keywords

Superior laryngeal nerve • External branch of the superior laryngeal nerve • Nerve identification • Nerve stimulation • Nerve monitoring • Thyroid surgery

Introduction

The most common morbidity following thyroid surgery is recurrent laryngeal nerve (RLN) paralysis and hypoparathyroidism. However, injury of the external branch of the superior laryngeal nerve (EBSLN) can occur during the dissection and ligation of the superior thyroid vessels in up to 58 % of patients and its detection postoperatively is hampered by the varying and subtle symptoms and changes on postoperative laryngoscopy [1–3]. EBSLN injury results in dysfunction of the cricothyroid muscle (CTM), which results in altered fundamental frequency of the voice, a deterioration in voice performance in producing high-frequency sounds, and reduced vocal projection. This can be particularly significant for those using their voice professionally. EBSLN injury can be difficult to identify intraoperatively, and is difficult to detect during routine postoperative laryngoscopy [4].

In recent years, intraoperative neural monitoring (IONM) has gained widespread acceptance as an adjunct to the gold standard of visual nerve identification and this technique can be used to identify both the RLN and the EBSLN [5, 6]. In contrast to RLN monitoring, EBSLN monitoring is based on two distinct outcome measures following stimulation of the EBSLN:

1. Evaluation of cricothyroid twitch (present in all patients).
2. Electromyographic (EMG) glottic response of vocal cord depolarization identified on surface endotracheal tube electrode arrays in approximately 70–80 % of patients when using standard EMG tubes. Glottic response after stimulation of the EBSLN is felt to be mediated through the EBSLN's distal/terminal fibers which extend through the two heads of the CTM to the anterior glottis, and are termed the human communicating nerve. Current data available suggests such glottis response with current standard endotracheal tube electrode arrays may be identified in 70–80 % of patients during EBSLN stimulation. Newer electrode arrays and methods of monitoring may allow for improvement in the percent of patients in whom this glottis response with EBSLN stimulation can be identified. A novel EMG tube with additional and more proximally located anterior surface electrodes allowed for identification of EMG response after stimulation of the EBSLN in all (100 %) patients [7]. Armed

with thorough knowledge of the surgical anatomy of the EBSLN within the superior thyroid pole area and IONM technique, one may expect improved anatomic and functional identification and optimal preservation of the EBSLN.

Surgical Dissection Technique of the EBSLN

Several techniques have been described to minimize the potential risk of injury to the EBSLN during superior thyroid vessels dissection and ligation:

1. Ligation of the individual branches of the superior thyroid vessels under direct vision on the thyroid capsule without attempts to visually identify the nerve [8],
2. Visual identification of the nerve before ligation of the superior thyroid pole vessels [9],
3. The use of either a nerve stimulator or IONM for mapping and confirmation of the EBSLN identification [4, 6, 10–17].

The thyroid surgeon should use careful and meticulous surgical dissection technique within the area of the superior thyroid pole in order to preserve both the EBSLN and the CTM. At the very least, the surgeon should ensure that the EBSLN is not injured at the time of dividing tissue at the superior pole by identification of its course or excluding its presence in the divided tissue visually or by nerve monitoring. To that end, the surgeon should be aware of the variations of EBSLN location by thorough knowledge of the anatomy in proximity to the superior pole of the thyroid (see above). Initial blunt dissection of the superior pole of the thyroid lobe should be undertaken in the avascular space located between the medial aspect of the superior pole and CTM to obtain good exposure of the sternothyroid-laryngeal triangle harboring the EBSLN (Fig. 17.1). In most cases of a normal size or only slightly enlarged gland, there is no need for transverse division of the strap muscles. However, in cases of large masses within the superior portion of the thyroid lobe or in a patient with a short neck, a partial division of the sternothyroid muscle with cautery may improve access to the superior thyroid pedicle (Fig. 17.2). Gentle traction of the thyroid lobe in a latero-caudal direction may

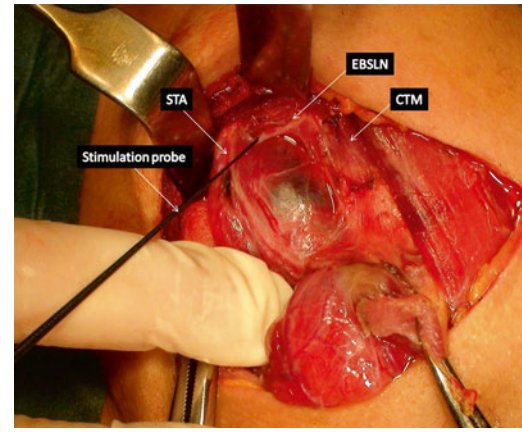

Fig. 17.1 The right-sided intraoperative view—visual identification of the EBSLN can be confirmed by applying the stimulation probe directly to the nerve. *EBSLN* external branch of the superior laryngeal nerve, *CTM* cricothyroid muscle, *STA* superior thyroid artery

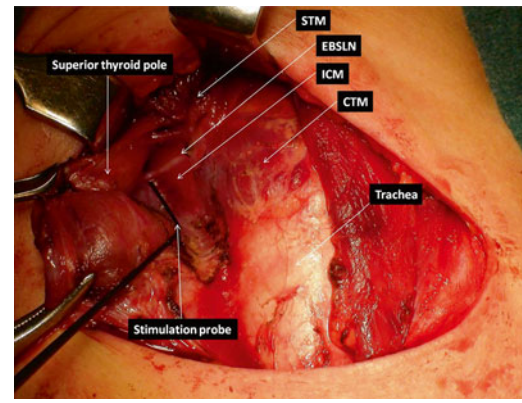

Fig. 17.2 The right-sided intraoperative view—transverse division of the superior edge of sternothyroid muscle and gentle traction of the superior thyroid pole into lateral and caudal direction followed by blunt dissection within the avascular plane of sternothyroid-laryngeal triangle allow for improving exposure of the EBSLN which is usually descending parallel to superior thyroid artery and is lying on the inferior constrictor muscle before its termination within cricothyroid muscle. *EBSLN* external branch of the superior laryngeal nerve, *CTM* cricothyroid muscle, *ICM* inferior constrictor muscle, *STM* sternothyroid muscle, *STA* superior thyroid artery

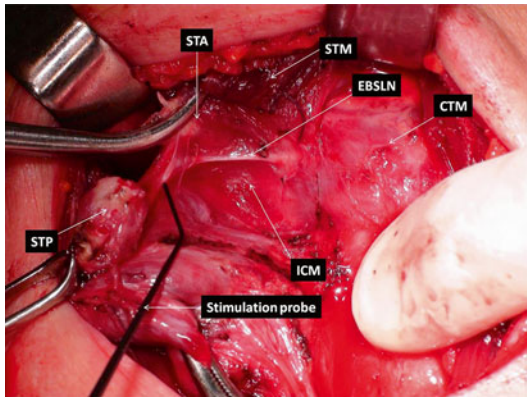

Fig. 17.3 The right-sided intraoperative view—step by step ligation of individual branches of the superior thyroid artery can be undertaken under both visual control and stimulation of the EBSLN to assure not only anatomical but also functional preservation of the nerve which can be documented as a positive "cricothyroid twitch." *EBSLN* external branch of the superior laryngeal nerve, *CTM* cricothyroid muscle, *ICM* inferior constrictor muscle, *STM* sternothyroid muscle, *STA* superior thyroid artery, *STP* superior thyroid pole

be helpful in obtaining good exposure of the sternothyroid-laryngeal triangle. The superior thyroid vessels should be isolated by meticulous blunt dissection and individual branches of the superior thyroid artery should be exposed at their penetration point of the thyroid capsule (Fig. 17.3). It is worth emphasizing that transverse division of the superior edge of sternothyroid muscle and gentle traction of the superior thyroid pole into a lateral and caudal direction followed by blunt dissection within the avascular plane of sternothyroid-laryngeal triangle enable improved exposure of the EBSLN which is usually descending parallel to superior thyroid artery and is lying on the inferior constrictor muscle before its termination within the CTM (Fig. 17.2).

Contrary to routine dissection of the RLN, most surgeons tend to avoid rather than routinely expose the EBSLN during thyroidectomy. In the most recent guideline statement, the International Neural Monitoring Study Group (INMSG) underlined importance to visually search for the nerve in all cases [6]. Visual localization of the EBSLN was reported to be highly successful in expert hands of thyroid surgeons with identification rate exceeding 98 % [18]. However, Lennquist and Freidman reported that nearly 20 % of EBSLNs couldn't be visually identified due to their subfascial/intramuscular course [19, 20]. Thus, visual identification of the EBSLN is usually not possible in approximately 20 % of patients in whom the nerve is located deep to the fascia of the inferior constrictor muscle unless there is intramuscular microdissection. In addition, Selvan has shown that in many cases, non-neural fibers or tendinous fibers of regional musculature can be mistaken for the EBSLN [21]. Hence, the INMSG has recommended recently that in all patients, attempts should be made to visually identify the EBSLN, but in addition neural stimulation technique should be used with assessment of both CTM twitch and glottic endotracheal EMG monitoring (see below) to ensure preservation of the EBSLN during thyroidectomy [6].

Dissection of the superior thyroid pole is much more difficult and potentially dangerous for the EBSLN in operations on large goiter or in patients with a short neck. In such cases, the upper border of the superior pole is markedly elevated resulting in adherence of the nerve to the thyroid. Cernea et al. have documented that the incidence of type 2B nerve, which is particularly prone to injury, in patients with goiters above 100 g may rise to 54 % [4, 11]. The increased number of type 2B nerves may be due to the upward enlargement of the superior pole of the thyroid rather than the low descending course of the EBSLN. Similar conclusions were drawn by Furlan et al. who evaluated some "intrinsic risk factors" for a surgical injury of the EBSLN based on its anatomic relationship with the thyroid gland. Based on 72 neck dissections of fresh human adult cadavers, they found that individual stature (a short neck) and a large volume of the hemi-thyroid gland were risk factors for EBSLN injury. In this study among "large goiters," where the thyroid gland weight was at least 240 g, the incidence of Type 1 nerve was 41 %, Type 2a nerve 25 %, and Type 2b 24 % [22]. Thus, the technique of mass ligation should be avoided at all costs because it is unsafe and inevitably may jeopardize the EBSLN in the process.

It is crucial to keep in mind that in operations employing energy-based devices (EBD) for sealing of vessels of the superior thyroid pole, there is a high risk of collateral iatrogenic heat injury to the adjacent structures including the EBSLN, the RLN, and parathyroid glands [13]. Thus, any use of the EBD should be preceded by either visual identification or nerve mapping of the EBSLN to ensure its presence away from the danger zone of possible heat injury. For this reason, traditional suture ligation for securing the upper thyroid pole vessels remains a valuable alternative to EBD. Moreover, if a suture ligation or a vascular clip is identified near the EBSLN and IONM suggests dysfunction of the nerve, both sutures and clips can be removed limiting the risk of permanent nerve injury at this level.

IONM of the EBSLN Technique I: Stimulation—CTM Twitch Technique

The principles of electrophysiologic RLN monitoring during thyroid surgery described in detail in a recently published International Standards Guideline Statement can be applied to EBSLN stimulation and monitoring with few important differences outlined below [5].

Attempts to directly visualize the EBSLN as outlined above should be made. In addition, the INMSG proposed based on its experience and the existing literature ideal management of the superior pole and EBSLN preservation involving two maneuvers available only with neural monitoring/stimulation and that with these maneuvers EBSLN preservation is maximally assured:

1. The EBSLN needs to be stimulated as clearly present (through CTM visual twitch assessment or endotracheal glottic waveform if observable) cranially and medial to the evolving superior pole pedicle. This response serves as a true positive stimulation.
2. Stimulation of the pedicle that is to be divided is stimulated as negative for EBSLN (i.e., no CTM visual twitch or endotracheal glottic waveform). This serves as a true negative for absence of neural tissue in the pedicle (as long as there has been true positive stimulation as noted in #1) [6].

The INMSG strongly recognized that this sequence of neural monitoring data optimizes preservation of the EBSLN [6]. The rationale for this algorithm is supported by several recently published studies confirming that the use of IONM can improve the identification rate of the EBSLN, limiting the risk of inadvertent nerve injury [10–17]. Through this sequence of stimulation maneuvers, the presence of the EBSLN is effectively excluded in the tissues being surgically treated at the superior pole.

In a prospective study on video-assisted thyroidectomies, Dionigi et al. randomized 72 patients to two groups and found that the identification rate of the EBSLN in the group in which IONM was used was 84 % compared to 42 % in the non-IONM group [13]. In a study of 47 patients with 69 nerves at risk, Lifante et al. also found a greater rate of EBSLN identification during thyroidectomies under regional anesthesia, with 65 % using neuromonitoring vs. 33 % without it [14].

In a randomized controlled prospective study of 210 patients, Barczynski et al. demonstrated that identification of the EBSLN was improved when IONM was used versus visualization alone. They documented an identification rate of 34 % without IONM vs. 84 % ($p < 0.001$) when IONM was used. IONM also reduced the prevalence of transient but not permanent EBSLN injury in the monitored vs. the non-monitored group (1.0 % vs. 5.0 %, respectively; $p = 0.02$), and reduced the risk of early but not permanent phonation changes following thyroidectomy [10].

Similar encouraging data were recently published by Masuoka et al. based on a prospective randomized study on injury of the EBSLN during thyroidectomy comparing IONM and a conventional technique. This study comprised of 252 patients undergoing thyroidectomy who were randomly assigned to group N (in which the

NIM-Response 3.0 system was used) or group C (in which the conventional technique using the Vari-Stim 3 was used) to identify the EBSLNs. The primary endpoint of this study was the identification rate of the EBSLN. The secondary endpoint was the incidence of postoperative voice impairment. The visual and the electrophysiologic identification rates of the EBSLN in group N and group C were 48.8 % vs. 17.8 % ($p<0.001$) and 89.2 % vs. 17.8 % ($p<0.001$), respectively. The proportion of female patients who had subjective voice impairment was significantly lower in group N than in group C. Thus, authors concluded that the use of the NIM-Response 3.0 significantly improved the identification rate of the EBSLN during thyroidectomy, reducing voice impairment [23].

Aina et al. used a nerve stimulator for identification of the EBSLN in 151 consecutive patients and 218 nerves at risk. The identification rate of the EBSLN was very high in this study and equal to 92.7 %. In primary thyroid surgery, the successful identification of the nerve was possible in 95.5 %; however, in secondary thyroid surgery, only 65.0 % of the nerves were identified [15].

In Selvan's study, 100 % of EBSLNs were found using nerve stimulation and EMG of the CTM in 35 patients and 70 nerves at risk. In this study, a considerable number of false-positives were seen when visual identification alone was used prior to electrical stimulation [21]. In many cases, nonneural fibers or tendinous fibers of the cricothyroid or inferior constrictor muscles were wrongly assumed to be the EBSLN but were unmasked by the lack of an action potential upon stimulation. This finding suggests that visual identification of the EBSLN without EMG confirmation may likely be flawed. It is our belief that adding quantitative data to this technique could make the process of nerve identification and preservation more definitive and precise.

Nerve stimulation technique has a substantial advantage in identifying all nerve types, including Cernea type 1 which is found at a higher position and sometimes is crowded under the laryngeal head of the sternothyroid muscle, as well as descending types 2A and 2B, which are most vulnerable to surgical manipulation injury [10].

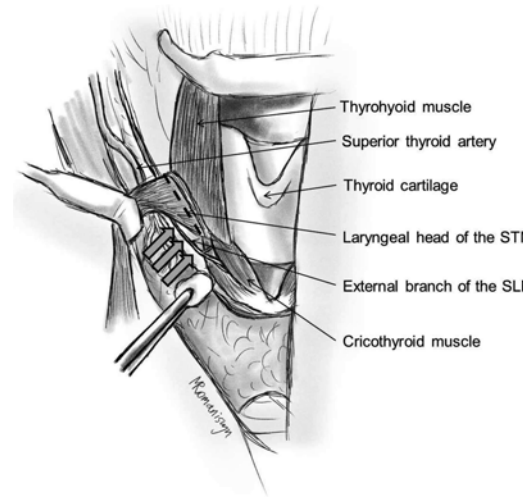

Fig. 17.4 To facilitate localization of the EBSLN it is recommended to stimulate tissues parallel and underneath the laryngeal head of the STM (marked with the *dashed line*) which can be regarded as a highly reliable landmark for the identification of the EBSLN in its distal course before termination within the cricothyroid muscle [24]. *STM* sternothyroid muscle, *SLN* superior laryngeal nerve [Courtesy of Marcin Barczyński]

It is recommended by the INMSG to use IONM (with the current of stimulation set at 1 mA) at this stage of the dissection to rule out entrapment of the EBSLN during each portion of superior pole dissection by togging the stimulator probe between the tissue and the CTM [6]. Visual identification of the EBSLN can be confirmed by applying the stimulation probe directly to the nerve (if seen) above the entry point into the CTM (Figs. 17.1, 17.2, and 17.3). To facilitate localization of the EBSLN, it is recommended to stimulate tissues parallel and underneath the laryngeal head of the sternothyroid muscle which can be regarded as a highly reliable landmark for the identification of the EBSLN in its distal course before termination within the CTM (Fig. 17.4) [24].

One of the significant advantages of EBSLN monitoring is that even in those cases where the EBSLN is not able to be identified visually due to

its course deep to the inferior pharyngeal constrictor muscle fascia, it can be revealed through the technique of nerve mapping (the current of stimulation can be increased from 1 to 2 mA) [5]. As already mentioned, the laryngeal head of the sternothyroid muscle is an excellent landmark for the linear oblique path of the EBSLN as it traverses down along the inferior constrictor towards the CTM. Within 1–2 mm of this obliquely oriented laryngeal line (the laryngeal head of the sternothyroid muscle which inserts onto the thyroid cartilage lamina), the EBSLN can be found with a high degree of certainty where the nerve's course parallels the course of the sternothyroid muscles insertion on the larynx (Fig. 17.4). Blind stimulation in this area with the neural stimulator uniformly results in the identification of a linear path which when stimulated results in discrete CTM contraction. In this way, neural stimulation of the EBSLN should be able to identify this nerve in 100 % of cases. A positive identification of the nerve should be confirmed by observing contractions of the CTM ("CTM twitch") which in some cases can be also accompanied by hearing an auditory signal and an EMG response on the monitor (see discussion below). After completion of the superior thyroid pole dissection, the functional integrity of the nerve may be documented through electrical stimulation and a positive CTM twitch response (Fig. 17.3). This is the most reliable outcome measure following the EBSLN stimulation (present in 100 % of cases). This technique is recommended not only for open thyroidectomy but also for Minimally Invasive Video-Assisted Thyroidectomy (MIVAT) [13].

The CTM must be clearly localized visually as a triangular muscle profile on the anterolateral aspect of the cricoid cartilage. Its twitch is unmistakable and is quite easy to recognize as long as one is appropriately oriented to the basic laryngeal anatomy available during all thyroid and parathyroid surgery (Video 17.1, Fig. 17.2).

With neural monitoring and assessment of the CTM twitch during EBSLN stimulation, we are able to identify 100 % of EBSLNs, even those not able to be visually assessed. At the end of superior pole management, positive stimulation of the EBSLN proximal (i.e., superior, cranially) to the region of superior pole vessel dissection indicates a functioning nerve postoperatively.

IONM of the EBSLN Technique II: Stimulation—Glottic EMG Technique

In contrast to RLN monitoring, EBSLN monitoring is based on two distinct outcome measures following stimulation of the EBSLN: evaluation of cricothyroid twitch (present in all patients) and EMG response recorded by the monitor via surface tube electrode within the vocal folds (present in 70–80 % of patients using standard EMG tubes) (Fig. 17.5).

Potenza et al. carried out a prospective study of EBSLN and RLN IONM data in 72 consecutive thyroid surgeries. Normative EMG data and CTM twitch response during EBSLN stimulation were recorded and analyzed. Authors found that stimulation of the EBSLN resulted in a positive CTM twitch response in 100 % of cases, whereas EMG response was recordable in 80 % of cases. Electromyographic amplitude was approximately one-third of ipsilateral RLN amplitude and did not change through the case with multiple stimulations. Stimulation of the EBSLN was similar for men and women at 1 and 2 mA stimulation levels. Authors concluded that IONM of the EBSLN aids in EBSLN identification and provides EMG information in 80 % of cases [25]. Thus, during EBSLN stimulation, the EMG waveform can be detected on the monitor by standard endotracheal tube electrodes in approximately 70-80 % of cases (Fig. 17.3). However, this is a much more variable outcome measure following stimulation of the EBSLN and occurs due to the external human communicating nerve - a nerve which represents an extension of the EBSLN, ramifying the two heads of the CTM and extending into the larynx to innervate the anterior half of the ipsilateral vocal cord. This depolarization

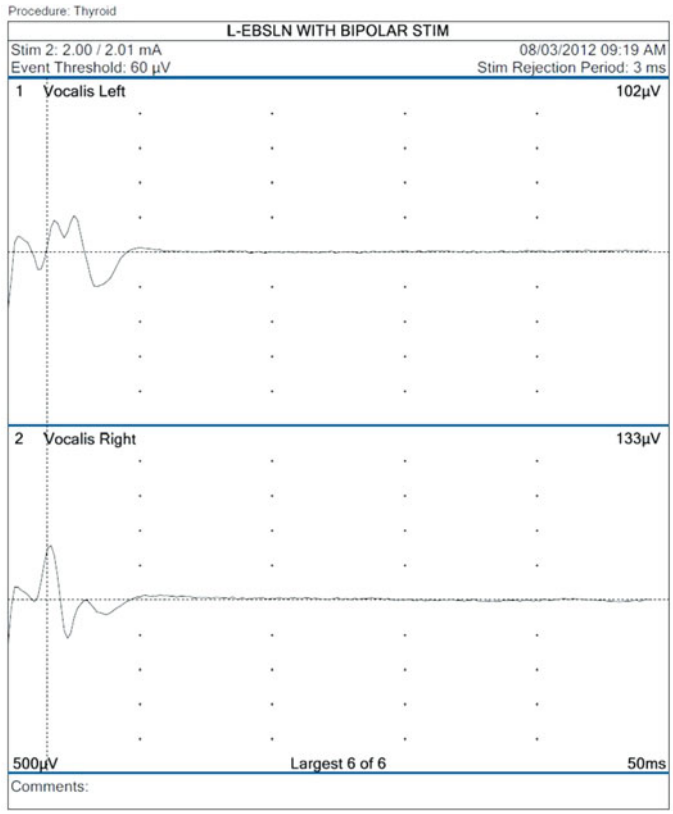

Fig. 17.5 EMG waveform detected by endotracheal tube electrodes after bipolar stimulation of the left EBSLN. This recording is not thought to be an artifact of field effect because there is a clear waveform with defined but short latency from the stimulation artifact that is biphasic following probe-stimulation and is identified at the time of cricothyroid muscle twitch activation with a small but clear-cut recognizable amplitude. Adjacent stimulation of inferior constrictor musculature without direct EBSLN stimulation results in regional inferior constrictor twitch but no cricothyroid muscle twitch and no glottic waveform. The latency of response also is inconsistent with a central affect SLN to vagus reflex response. *EBSLN* external branch of the superior laryngeal nerve

is then measured on glottic surface endotracheal tube electrodes. The human communicating nerve has been described in up to 85 % of anatomical dissection studies [26–28]. Masuoka et al. performed EMG studies in 50 patients during thyroidectomy (20 total, 30 hemithyroidectomies), stimulating the EBSLN, the RLN, and the vagus nerve. Responses were evaluated by visual observation of the CTM and by EMG responses using needle electrodes inserted into the CTM. Seventy CTMs were evaluated in this study. RLN stimulation yielded both visible contractions and clear EMG responses (>300 µV) in 27 (39 %), either response in 24 (34 %), and neither response in 19 (27 %) of the CTMs. Vagus stimulation gave similar results. The authors concluded that the RLN innervated the CTM at least in 39 % of cases [29].

The reason why EBSLN results in glottis identifiable waveform in only 70–80 % when using standard EMG tubes is unclear and this phenomen is likely due to equipment-related measurement issues. It is of note that sampling epoch timeframes available during EBSLN stimulation and glottis waveform recording are too fast for the EBSLN EMG activity to be a result of afferent SLN stimulation—central mediated—reflex vagal glottic activity. Such activity would have a much greater latency than observed with EBSLN-evoked glottis EMG activity. The waveform generated is of small amplitude and so may not be noted by monitoring software as a

significant and recognizable waveform. This may be controlled to some degree by lowering the monitor amplitude threshold setting to lower than the typical threshold of 100–150 mV used for RLN monitoring. Also, the waveform is of very short latency given the short distance to the larynx, and may be silenced by monitoring software that intentionally suppresses very early responses which could be tail of EMG activity related to the stimulation artifact of the current delivered. This may be controlled to some extent by shortening the preset "stimulation suppression artifact period" on the monitor. The variability in obtaining glottic EMG with EBSLN stimulation is also likely due to the fact that the EBSLN innervates primarily the anterior 1/3 of the cord and so its measurement may be especially sensitive to endotracheal tube positioning. Also this variability may conceivably relate to variability in anatomic presence of the human communicating nerve, though such anatomic variability seems unintuitive. Preliminary studies with improved glottic measuring electrodes suggest that in time newer monitoring systems will evolve to be able to record EMG in all patients during EBSLN stimulation.

Darr et al. performed a prospective study of EBSLN, RLN, and vagus nerve EMG data in 22 thyroid surgeries. Normative EMG data were acquired using both a standard monopolar and a novel bipolar stimulator probe, as well as a novel endotracheal tube. CTM twitch response during EBSLN stimulation was analyzed. In 100 % of cases, EBSLN was identified and a quantifiable EMG response was observed. EMG amplitude did not change despite extensive nerve dissection and multiple nerve stimulations. EBSLN amplitude was similar for left and right sides in patients under the age 50 and patients 50 or older, for both genders, and with monopolar and bipolar stimulators. In conclusion, authors stressed that IONM may be used to safely assist in EBSLN identification during thyroid surgery in 100 % of patients. A novel endotracheal tube allowed for quantifiable EBSLN EMG activity in 100 % of cases. Monopolar and bipolar stimulator probes produced similar EMG data [7].

Equipment for the EBSLN Monitoring

Many different nerve-monitoring formats have been studied, including laryngeal palpation, glottic observation, glottic pressure monitoring, endoscopically placed intramuscular vocal cord electrodes, intramuscular electrodes placed through the cricothyroid membrane, endotracheal tube-based surface electrodes, and postcricoid surface electrodes. For a variety of reasons including safety, utility, and simplicity, systems that rely on endotracheal tube-based surface electrodes have proliferated and represent the most common monitoring equipment format to date [5].

As outlined in the INMSG guideline statement, the endotracheal tube-based systems that include graphic monitor documentation of waveforms should be preferred for neural monitoring of both the RLN and the EBSLN. Audio-only systems are problematic in that the EMG response to both RLN and EBSLN stimulation cannot be quantified (waveform morphology, amplitude, threshold, and latency) [5]. Stimulating electrodes may be monopolar or bipolar. Bipolar stimulating electrodes may offer the potential advantage of greater sensitivity through focal nerve stimulation and perhaps less stimulation artifact.

Technique of the EBSLN Monitoring

Certain standards of anesthesia, equipment setup, endotracheal tube placement, and verification tests of correct tube positioning are the same for IONM of the EBSLN as for the RLN [5, 6]. The monitor should be set for an appropriate event threshold at 100 μV (or lower as noted above), and a stimulator probe should be set on a value of 1–2 mA. Once the EBSLN has been visually confirmed, the stimulator probe should be set to deliver 1 mA of current. However, for EBSLN mapping a higher value of up to 2 mA should be used. Pulsatile stimulus with 100 μs duration at 4 Hz can be applied through a flexible stimulator probe (which can be monopolar or bipolar). One must be aware that if a bipolar array is used for

nerve stimulation, the exact orientation of the positive (anode) and negative (cathode) stimulating electrodes as they are placed on the nerve is of extreme importance in efficient nerve stimulation. In addition, the bipolar probe may not be optimal for mapping of the nerve because stimulation is more focal at the point of contact as compared with the monopolar probe, which provides more diffuse current spread, facilitating mapping of a larger area.

Normative Data of the EBSLN Monitoring

Barczynski et al. recently found in a group of 210 EBSLNs at risk that following 1 mA stimulation of the EBSLN the mean amplitude of evoked potential recorded by standard surface electromyography electrodes on the endotracheal tube was present in 73.9 % of patients and was equal to 249.5 ± 144.3 μV. It is important to note that the mean amplitude after EBSLN stimulation was significantly lower than the mean amplitude of evoked potential observed during stimulation of the RLN, which was equal to 638.5 ± 568.4 μV ($p < 0.001$) [10].

Similar observations were made recently by Randolph et al. who reviewed data of 72 consecutive patients undergoing thyroid surgery. Ninety-three RLNs were stimulated and 73 EBSLNs were found and stimulated with either 1 or 2 mA. A clear EMG waveform following EBSLN stimulation was obtained in 57 (78.1 %) of the cases. The mean amplitude response for EBSLN was 269.9 ± 178.6 μV. The mean RLN amplitude was 782.2 ± 178.6 μV. For the EBSLN, the mean amplitude response obtained initially was 270.7 ± 190.7 μV and the mean post-dissection response was 260.3 ± 177.9 μV. There was no significant difference between initial and final amplitudes of response ($p = 0.469$). There was no significant difference between EBSLN stimulated with 1 mA (280.8 ± 216.9 μV) and those stimulated with 2 mA (261.8 ± 142.4 μV), $p = 0.704$. The mean amplitude of the EBSLN action potential was significantly lower than the mean RLN amplitude—about one third of the RLN amplitude in comparison [25]. However, Darr et al. tested a novel commercially available endotracheal tube which was designed for acquisition of EMG activity from the CTMs and found that quantifiable EBSLN EMG activity could have been recorded in 100 % of cases [7].

Because there is great variability in amplitude values and because there may be an influence of tube position in the size of the action potentials, looking at the EBSLN amplitude values as a percentage of those values obtained for RLN and vagal nerve in each individual case may be a useful tool to determine which are the normal parameters of EBSLN neuromonitoring other than using only an absolute value or a range as reference. Response amplitudes were similar among both genders. No difference was found in RLN amplitudes on the left and right side. However, EBSLN amplitudes were higher on the right than left side. The explanation for this finding is still unclear.

Definitions of the EBSLN Monitoring

True positive result, which implies the correct identification of the EBSLN, is confirmed when a CTM twitch is present following stimulation of the ipsilateral nerve with a current of 1 mA (with or without corresponding EMG response). A true negative result is defined as no CTM twitch following stimulation of the non-EBSLN tissue. False positive stimulation implying incorrect identification of the EBSLN is defined as a positive CTM twitch (with or without corresponding EMG response) in the case of nonneural shunt stimulation. Such a scenario is sometimes seen during nerve mapping with a current of 2 mA. To rule out the nonneural shunt stimulations, it is best to turn down the stimulation current to a level where false positive stimulation is silenced (usually between 0.8 and 1 mA). A false negative result, which implies misidentification of the EBSLN for a nonneural structure is defined as no CTM twitch (and no corresponding EMG response) following the stimulation of the EBSLN. The most common reasons for this scenario

include various equipment problems on the stimulation side, blood or fascia covering the stimulated nerve segment, insufficient stimulation current, neuromuscular blockage, and transient neurapraxia of the EBSLN.

Prevalence of the EBSLN Injury

The actual prevalence of EBSLN injury is difficult to assess due to limited data and heterogeneous methods used in different studies. Given the variability of vocal symptoms and subtle and variable findings at laryngeal exam postoperatively, the only definitive way to diagnose EBSLN injury is with CTM EMG. The reported prevalence of this event varies widely from 0 to 58 %. Hence, EBSLN injury is believed to be the most commonly underestimated morbidity following thyroid surgery [2, 30–34]. Nonetheless, there is growing evidence in the published literature that as higher surgical attention is paid to the EBSLN during the dissection of the superior thyroid vessels, the lower prevalence of the nerve dysfunction may be expected. In addition, increasing use of nerve stimulation or IONM techniques in recent years has resulted in improved identification and functional preservation rate of the nerve [4, 10, 16, 35]. Jansson et al. examined EMG activity of the cricothyroid muscles in 26 patients after thyroidectomy with no EBSLN identification intraoperatively and found temporary EBSLN injury in 58 %, and permanent in 3.8 % of them [2]. Cernea et al. found between 12 and 28 % incidence of injury when the EBSLN was not identified intraoperatively, and some of these injuries were permanent, as confirmed by long-term EMG evaluation [4, 11]. On the other hand, Bellantone et al. demonstrated in a randomized study that accurate distal ligation of the branches of the superior thyroid vessels without attempts to visually identify the nerve is a safe technique in expert hands with similar prevalence of EBSLN injury as routine nerve identification (0.5 vs. 0.8 % for temporary lesions) but the study did not include EMG definition of CTM function [8].

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Part VI

Neural Injury

Feng-Yu Chiang

Loss of Signal in IONM and Staged Thyroid Surgery

18

Kerstin Lorenz, Rick Schneider, Andreas Machens, Carsten Sekulla, Gregory W. Randolph, and Henning Dralle

Abstract

Intraoperative neuromonitoring (IONM) through vagus nerve (VN) stimulation in thyroid surgery provides indisputable recurrent laryngeal nerve (RLN) identification and comprehensive functional assessment of neural integrity during the process of thyroid resection. Neurostimulation of the RLN and VN generates an electromyogram with audio-tone. Relevant information regarding neural integrity using IONM is gained by observing the EMG parameters of amplitude, latency, and signal configuration. Relevant changes and corresponding surgical maneuvers must be considered to react timely and thereby possibly prevent neural injury. The hallmark of neural injury that corresponds with postoperative vocal cord dysfunction is the loss of signal (LOS) without recovery during IONM-guided thyroid surgery. Therefore, after LOS on the first side operated, staging of the planned bilateral surgery by postponing the second side until RLN function is restored is recommended. In this chapter, detailed definitions of the relevant IONM parameters and LOS are provided, and a description of IONM application with procedural recommendations is presented.

Keywords

Intraoperative neuromonitoring • Loss of signal • EMG • Signal recovery • Bilateral vocal cord palsy • Staged thyroidectomy

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Introduction

Intraoperative neuromonitoring (IONM), when used in a standardized fashion as provided by the International Neural Monitoring Study Group (INMSG), gives a competitive edge over mere visual identification of the inferior recurrent laryngeal nerve (RLN) by faster identification of the nerve along with any co-existing extralaryngeal branches and by continual confirmation of the nerve's functional integrity as the dissection moves forward [1–5]. Comprehensive functional assessment of the complete RLN, from its separation off the vagus nerve (VN) to its laryngeal entry point, is dependent on stimulation of the ipsilateral VN.

Although gross anatomic injury to the RLN typically results in RLN dysfunction and vocal cord palsy (VCP), the converse does not necessarily hold true: gross morphological nerve integrity is not definitively correlated with functional nerve integrity. Only IONM, affording almost real-time monitoring of RLN function, can give reasonable assurance of intact postoperative vocal cord function [1–7]. Prevention of bilateral VCP with the potential of permanent tracheostomy remains a key priority of surgical strategy in the neck. The success of that strategy hinges on the reliability of intraoperative information about the functional status of the RLN on the first side of resection before embarking on completion of the other side.

Reliability of IONM

The reliability of IONM signals is only assured when the L1, V1, R1, R2, V2, L2 approach published by INMSG is strictly adhered to [1–12]:

1. Determination of baseline vocal cord function on preoperative laryngoscopy (L1).
2. Stimulation of the VN and RLN before (V1, R1) and during/after (R2, V2) resection to confirm the functional integrity of the VN–RLN axis, using the troubleshooting algorithm in the event of loss of signal (LOS).
3. Confirmation of vocal cord function on postoperative laryngoscopy (L2).

Strict observation of these conditions is set to improve the reliability of IONM, the positive predictive value (PPV) of which ranges from 62.5 % to 77.8 % (intermittent IONM) and 88.2 % (continuous IONM) in the most current literature [5] (Table 18.1).

Definition of LOS

Based on current literature and the international standards guideline statement published by the INMSG [1], LOS is defined as loss of the audiotone and/or decrease of the nerve amplitude to below 100 μV on stimulation with 1–2 mA in the corresponding electromyogram. To make that determination, vocal cord function must be normal on preoperative laryngoscopy, and the baseline amplitude of the RLN should not be lower than 500 μV (and in no event lower than 300 μV) with normal nerve latency [8, 10, 13–18].

The severity of nerve damage is reflected by the rapidity of onset of LOS and fall of nerve amplitude. Unfolding damage can be picked up faster with continuous IONM, rather than intermittent IONM. Structural injury is caused by transection, clamping, or thermal injury to the nerve, whereas traction and stretch of the RLN tends to produce a more slowly evolving and perhaps more subtle nerve injury.

Solitary or serial increases in nerve latency or decreases in nerve amplitude, even when they surpass thresholds of 10 % and 50 % relative to baseline, respectively, are considered mild events. Combined events (the joint occurrence of increases in latency and decreases in nerve amplitude) qualify as severe events because they may develop into LOS after exceeding the above thresholds of 10 % increase in latency and 50 % decrease in amplitude [7]. Decreases in nerve amplitude, in isolation, are clinically less relevant

Table 18.1 Prediction of transient and permanent postoperative vocal cord palsy by intermittent and continuous intraoperative neuromonitoring

Author	Year	NAR	Sensitivity	Specificity	PPV (%)	NPV (%)	Transient VCP (%)	Permanent VCP (%)
IIONM								
Hamelmann et al. [34]	2002	428	23.5	98.5	40.0	96.8	19 (4.4)	1 (0.2)
Thomusch et al. [35]	2004	12,486	33.0	98.3	36.7	97.9	413 (2.7)[a]	104 (0.7)[b]
Beldi et al. [36]	2004	429	40	98	67	91	37 (8.7)	6 (1.4)
Hermann et al. [37]	2004	475	57.1	99.3	87.0	96.6	43 (8.9)[c]	15 (3.1)[c]
Chan et al. [38]	2006	271	53	94	35	97	15 (5.5)	2 (0.7)
Tomoda et al. [39]	2006	2197	69.3	99.7	92.1	98.5	80 (3.6)	21 (1.0)
Barczynski et al. [40]	2009	1000	63.0	97.1	37.8	98.9	27 (2.7)	8 (0.8)
Melin et al. [41]	2014	3426	85.4	99.0	68.0	99.6	82 (2.4)	N/A
Calò et al. [42]	2014	2068	91.3	99.4	77.8	99.8	23 (1.1)	6 (0.3)
De Falco et al. [43]	2014	600	83.3	99.5	62.5	99.8	5 (0.8)	4 (0.7)
Schneider et al. [5]	2015	965	73.9	99.5	77.3	99.4	23 (2.4)	4 (0.4)
CIONM								
Schneider et al. [5]	2015	1314	90.9	99.7	88.2	99.8	33 (2.5)	0 (0)

CIONM continuous intraoperative neuromonitoring, *IIONM* intermittent intraoperative neuromonitoring, *N/A* not available, *NAR* nerves at risk, *NPV* negative predictive value, *PPV* positive predictive value, *VCP* vocal cord palsy
[a]Based on 15,403 nerves at risk with follow-up information
[b]Based on 15,340 nerves at risk with follow-up information
[c]Based on 481 nerves at risk with follow-up information
Based on data from [5]

than decreases in amplitude with concordant increases in latency and often may be caused by dislocation of the endotracheal tube during the operation [19].

LOS comes in two varieties: segmental LOS type 1 and global LOS type 2.

Segmental LOS Type 1

Segmental LOS type 1 is defined by loss of nerve function downstream of, distal to, or towards the larynx from a point of damage, regardless of the level of upstream (proximal) nerve stimulation (Fig. 18.1). A handheld stimulation probe can help pinpoint the location of injury, below which regular electromyographical (EMG) signals can be elicited [19]. In this setting, stimulation of the VN failing to produce a response signal below the level of nerve injury quickly clarifies the situation.

This point of damage can be located anywhere along the course of the RLN. The nerve segments at risk of injury are listed below in descending frequency:

1. Between the intersection of the RLN with the inferior thyroid artery (ITA) and the entry of the RLN into the larynx (P1; encompassing the ligament of Berry).
2. Around the intersection of the RLN with the ITA (P2).
3. Below the intersection of the RLN with the ITA (P3).

The most common mechanism of injury underlying segmental LOS type 1 is direct trauma, as a result of pinching, clamping, clipping, or thermal injury to the nerve. Such trauma may strike instantly, in which case LOS type 1 is not heralded by premonitory EMG signals. LOS type 1 typically happens all of a sudden, with a plunge of the nerve amplitude that leaves little, if any, room for corrective action (even if continuous IONM was employed). When segmental LOS type 1 has manifested on the first side of

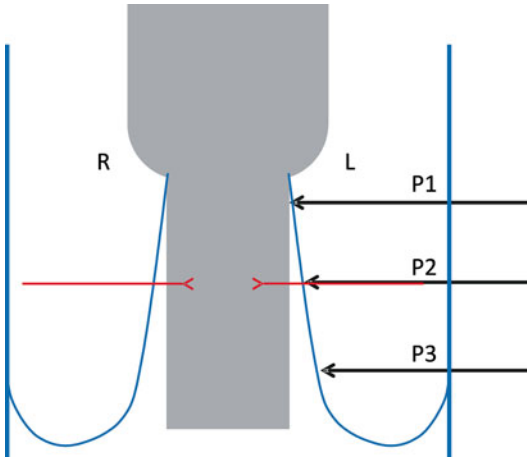

Fig. 18.1 Location of type 1 (segmental) loss of signal anatomical localization. P1: neural lesion superior to the intersection of the RLN with the inferior thyroid artery (ITA). P2: neural lesion at the level of RLN/ITA intersection. P3: neural lesion inferior to the intersection of the RLN with the ITA

resection and fails to resolve during the operation, a staged thyroidectomy needs to be considered.

Global LOS Type 2

Global LOS type 2 denotes a complete loss of the audio-tone, often with a progressive decline in nerve amplitude, in the absence of an identifiable point of damage and is associated with LOS along the VN–RLN axis. Global LOS type 2 may reflect more indirect mechanisms of injury, typically secondary to traction on the nerve through more distant maneuvers. This type of LOS tends to unfold more gradually and most of the time is preceded by the mild or severe events as previously defined. Although intermittent IONM is usually spaced out too much to allow for immediate corrective action in the event of imminent LOS type 2, continuous IONM frequently gives sufficient lead time to release a distressed nerve before the damage has become permanent. This is why global LOS type 2, by and large, has a better clinical outcome than segmental LOS type 1.

Troubleshooting Algorithm for LOS

Dislocation of the endotracheal tube, technical failures (e.g., defective hardware, disconnection of cables, impedance issues as a result of salivary pooling), and the use of muscle relaxants can mimic LOS even though nerve function is perfectly normal. Because they may trigger unnecessary actions, false-positive findings must be uncovered. A troubleshooting algorithm has been published by the INMSG (Fig. 18.2) to aid in this endeavor.

If stimulation of the contralateral VN fails to return normal EMG signals, it is crucial to exclude the intraoperative use of muscle relaxants, double-check the position of the endotracheal tube, and check the connections of the stimulation device. If contralateral VN stimulation elicits normal electrophysiological responses, injury to the ipsilateral VN–RLN axis is a reasonable possibility necessitating further work-up. Absence of a laryngeal twitch on palpation supports a diagnosis of LOS.

Intraoperative Recovery of Nerve Function after LOS

Once LOS has occurred, intraoperative recovery of nerve amplitude to >50 % of its baseline, also referred to as "complete recovery" [20], is hard to predict but should be given a mandatory waiting time after initial LOS. During the intraoperative wait (usually for a minimum of 20 min), all surgical activity must cease, and traction on the RLN, ligament of Berry, and trachea (in addition to any lifting of the thyroid lobe on the side of LOS) is to be avoided [20, 21].

Corrective action depends on the type of LOS. In segmental LOS type 1, care must be taken to quickly identify and remove any clips or ligatures that impinge on the RLN near the point of damage. In the event of thermal injury, no effective remedy may be available because the damage has already been done. In global LOS type 2, the gradual decrease of the nerve amplitude calls for interruption of the underlying surgical maneuver.

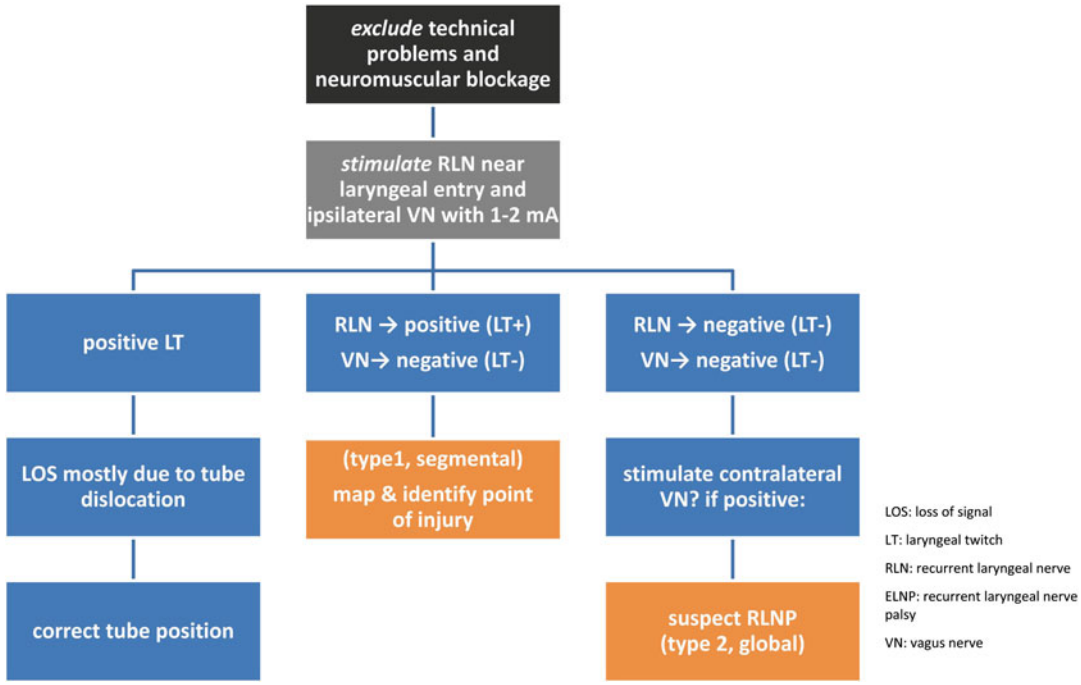

Fig. 18.2 LOS troubleshooting algorithm. [Based on data from 3, 45]

Using continuous IONM (C-IONM), recovery of nerve amplitude can be monitored almost in real time. After expectant observation for 20 min, during which all surgical activity is stopped, complete recovery of the nerve becomes increasingly unlikely. Incomplete recovery (failure of the nerve amplitude to recoup more than 50 % of its baseline), unlike complete recovery, carries a high risk of postoperative VCP. To date, there is little evidence to suggest that intravenous steroids or calcium channel blockers are effective in restoring RLN function once LOS has taken place [22–24]. In a double-blind, placebo-controlled, randomized study, however, preoperative administration of 8 mg of dexamethasone was reported to reduce transient RLN palsies from 8.4 to 4.9 % ($P=0.04$) [25].

Modification of the Surgical Plan after LOS

For safety reasons, surgery should start on the most severely affected side, leaving the surgeon and patient with more options after LOS on the first side of resection [26]. Modifications of the surgical plan, in the event of LOS or invasion of the RLN by tumor, should be anticipated and discussed with the patient during the informed consent process.

When LOS has been confirmed after checking the troubleshooting algorithm, and the nerve amplitude fails to recover at least 50 % of its preoperative baseline during the operation, there is a 62.5 %–77.8 % (intermittent IONM) to 88.2 % (C-IONM) risk of postoperative VCP [2, 19, 22, 26–28] (Table 18.2; Fig. 18.3).

These data mandate a reconsideration of the surgical plan especially when LOS has happened on the first side of resection or involves the only intact RLN. Depending on clinical circumstances (type of thyroid disease, related urgency of surgical intervention, and surgeon skill and experience), options include:

1. Postponement of completion surgery (staged thyroidectomy) until the RLN has made a full recovery [8, 14, 26, 29].
2. Contralateral subtotal (rather than total) completion lobectomy during the same surgical

session, staying as far away from the contralateral RLN as possible [26, 30–33].
3. In exceptional circumstances (high-risk approach; not generally recommended), continuation of completion surgery exercising utmost diligence to protect the contralateral RLN. This should be engaged only in the most experienced settings.

Postoperative Airway Management After LOS

Prediction of postoperative vocal fold function is also beneficial in unilateral thyroid surgery. Because this information has immediate bearing on the patient's postoperative airway management, close collaboration between surgeons and anesthesiologists is pivotal. In addition to enforcing modifications to the surgical plan, evidence of LOS warrants careful monitoring of the patient, with the anesthesiologist being present during extubation [8, 29].

Postoperative Recovery of Nerve Function

Because voice changes also reflect laryngeal inflammation and swelling after tracheal intubation, postoperative laryngoscopy (L2) is mandatory to determine postoperative vocal cord function. Determination of postoperative vocal cord function on the day of surgery may be disadvantageous because the patient may not be fully awake and cooperative and laryngeal swelling may compromise the examination [11, 15, 29]. This examination is frequently performed on the second postoperative day because the VCP rate on that day is not higher than that on the day of surgery [31]. In the event of early postoperative VCP, serial laryngoscopies are scheduled to monitor restitution of RLN function. Occasionally, vocal cord function is normal in the face of intraoperative LOS confirmed after troubleshooting. This unusual finding may represent a defect of intraoperative troubleshooting or recovery of an injured nerve in the early postoperative phase.

Because the repair mechanisms of a nerve are typically activated within a few days of injury, nerve function is usually restored within a few weeks' time. Randolph and Dralle [1] found that "mild cases" of vocal cord dysfunction revert to the previous functional state 6–8 weeks after LOS. Although VCPs lasting for more than 6 months are generally considered permanent, 91 % of injured nerves make a full recovery within 6 months after LOS [31]. Infrequently, injured nerves can make a full recovery 12 months or later [32].

Staged Thyroid Surgery

As a matter of principle, completion thyroidectomy on the non-injured side is contingent on prior restitution of RLN function on the injured side, as documented by normal vocal cord function on laryngoscopy. Because scar formation sets in one week after surgery, completion thyroid surgery is best carried out within the first week of surgery or 3 months later.

Rarely, the thyroid disease may dictate completion thyroid surgery on the uninjured side in the presence of VCP on the other side of the neck. The decision to complete the non-injured side, jeopardizing the only fully functional nerve, should be based on broad interdisciplinary consensus and should include the patient's explicit acceptance of the risk of bilateral VCP and its ramifications (e.g., permanent tracheostomy).

These high-risk patients should be referred to expert surgical centers well experienced in advanced neck surgery. Risk minimization measures, including the use of C-IONM, should also be implemented.

Medicolegal Considerations

In order to have several options to choose from when LOS occurs on the first side of resection, the thyroid operation must tackle the most severely affected side first [26]. For determination of that side, criteria such as volume of the

Table 18.2 Synopsis of published data on intraoperative change of surgical strategy in LOS at first side in intended bilateral thyroid resection and outcome

Author	Intended bilateral thyroidectomy	LOS on first side	Type of LOS 1 = segmental 2 = global	Intraoperative strategy after LOS on first side, *n*			Staged procedures	Unilateral VCP	Bilateral VCP	FN	FP	Time to completion thyroidectomy
	n/NAR	n/%		No contralateral resection	Limited contralateral resection	Contralateral hemithyroidectomy	n	Trans/perm, *n* (%)	Trans/ perm, *n* (%)	*n*	*n*	
Goretzki et al. [30]	1321/2642	36/2.7	n.a.	15	5	16	9	32 (2.4)/4 (0.3)	3 (0.2)/0 (0)	2	n.a.	po day 1–po 4 months
Melin et al. [41]	2546/4012	98/3.8	n.a.	40	–	24	18	119 (2.9)/ 15 (0.37)	4 (0.1)/6 (0.2)	22	47	po day 1– po > 24 months
Périé et al. [13]	100/200	4/4.0	n.a.	4	0	0	3	9 (9.6)/2 (2.0)	2 (2.0)/0 (0)	2	n.a.	2–6 po months
Sadowski et al. [25]	220/440	9/4.1	n.a.	9	0	0	8	7 (3.2)/	0 (0)/0 (0)	0	2	po day 3–po 6 months
Sitges-Serra et al. [20]	290/580	16/5.5	1:11	0	4	14	0	10 (3.4)/n.a.	0 (0)/0 (0)	3	0	–
			2:5									
Schneider et al. [44]	1049/2086	27/2.6	1:11	12	4	11	9	26 (2.5)/4 (0.4)	0 (0)/0 (0)	5	6	n.a.
			2:16									
Fontenot et al. [9]	206/412		n.a.	10	–	–	10	8 (1.9)/1 (0.5)	0 (0)/0 (0)	0	2	14.1 ± 11.7 mean po weeks

[a]Partial overlap with duplicate data compilation in Goretzki et al.
FN false negative (intact intraoperative IONM with postoperative vocal cord palsy), *FP* false positive (loss of signal in intraoperative IONM with intact postoperative vocal cord mobility), *n.a.* not assessed

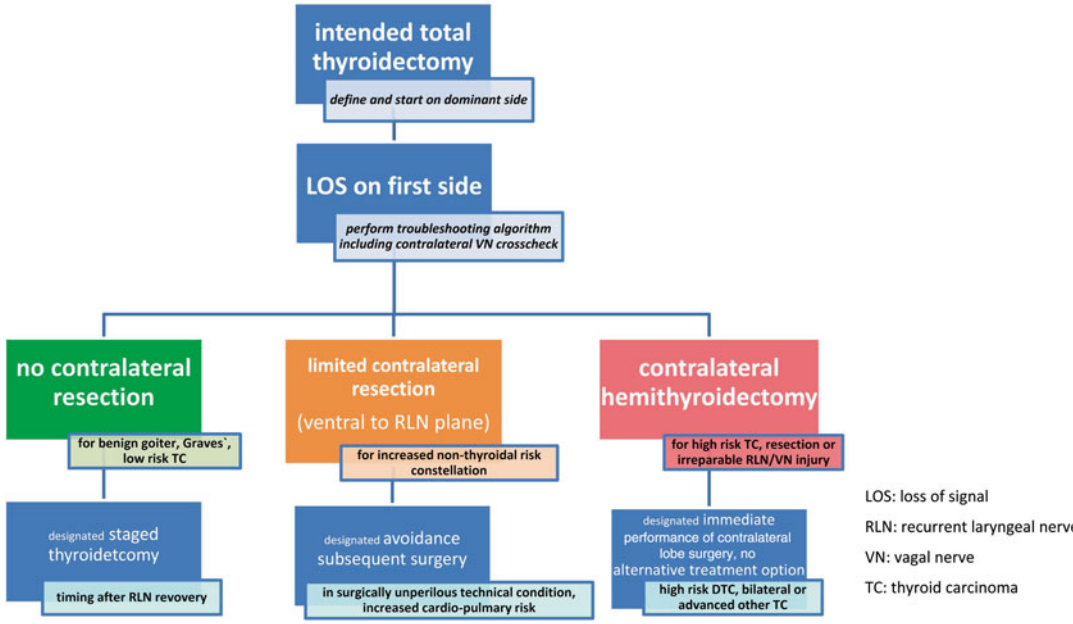

Fig. 18.3 Change of strategy and surgical options in intraoperative LOS at first side of resection for intended bilateral thyroidectomy. [Based on data from 44]

thyroid mass, risk of malignancy, and difficulty of resection need to be considered [30].

Changes of strategy that may become necessary during the operation, such as staged thyroid surgery after LOS on the first side of resection, should be anticipated and fully covered by the patient's informed consent. It is also important to detail to the patient the residual risk

1. that staged thyroid surgery, requiring an additional operation, may turn out unnecessary in hindsight because of a false-positive IONM result.
2. that RLN palsies can get missed owing to a false-negative IONM result [4, 20].

There is overwhelming evidence to suggest that IONM and staged thyroid surgery after LOS on the first side of resection prevent bilateral VCP [3, 5, 9, 25, 27, 30]. Accordingly, the surgeon's adaptation of the intended type and extent of thyroid resection due to IONM events increases. In a recent survey among thyroid surgeons in Germany, overall more than 90 % of IONM users expressed compliance to IONM events and either stopped surgery after resection of the first side or limited the intended resection of the contralateral side in occurrence of LOS [29] (Table 18.3). It is of note that particularly high-volume thyroid surgeons with >200 thyroid procedures per year with routine IONM utilization expressed a willingness to stop surgery in the event of LOS on the first side of resection. Whenever IONM is widely available as a risk minimization tool, the failure to use it becomes hard to defend, even more so in the event of bilateral VCP. There is increasing awareness regarding the medicolegal implications of the widespread utilization of IONM in Germany, as it may be perceived as standard of care just by the high prevalence of application. Moreover, the indication, correct use, and documentation of IONM can become the subject matter of heightened medicolegal scrutiny as is evidenced in recent legal decisions in court or conciliation committees.

Conclusion

Since its advent as a fledgling new technology, IONM has come a long way in maturing into a valuable risk minimization tool. Intermittent IONM, characterized by unsupervised dissection

Table 18.3 Surgeons' choice of preferred procedure after LOS in intended bilateral goiter surgery in German IONM users

		Surgical strategy after LOS at first side operated		
Hospital volume TT/year	IONM with IONM RLN[a]	Termination after LOS (%)	Limited contralateral resection (%)	Unlimited contralateral resection (%)
<50	3400	70.7	20.4	8.9
50–99	12,800	73.6	18.3	8.1
100–199	1600	75.7	14.9	9.4
≥200	44,200	92.3	3.0	4.7
Total	76,400	84.7	8.8	6.4

[a]Total numbers rounded to nearest 100 as numbers of thyroidectomies multiplied by IONM of RLN (owing to rounding not all numbers add up)
[Based on data from 29]
IONM intraoperative neuromonitoring, *LOS* loss of signal, *TT* bilateral thyroid lobectomy

periods between two stimulation cycles, displays LOS typically only after RLN injury has happened. In contrast, C-IONM can monitor RLN injury almost in real time, providing the surgeon with the opportunity to immediately release a distressed nerve. As a step in innovation, C-IONM enables earlier corrective action than intermittent IONM before the palsy becomes irreversible.

Recent achievements include the distinction between segmental LOS type 1 and global LOS type 2, reflecting different modes of RLN injury (acute and direct vs. gradual and indirect) and clinical outcome (worse vs. better). To make best use of that information, it is critical to heed the INMSG's troubleshooting algorithm.

Once LOS has been confirmed, a 20-minute wait period will allow the surgeon to know whether the affected nerve will recover fully or not and whether a staged thyroid surgery needs to be considered after the first side of resection is completed. This surgical strategy is widely accepted and has become part of the informed consent process in Germany [30], but this strategy is not yet implemented all around the globe [33].

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Mechanism of Injury

19

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Abstract

Causes of recurrent laryngeal nerve (RLN) injury during thyroidectomy are varied, with most injuries resulting from the following surgical errors: sectioning of the nerve, ligation, traction, clamping injury, suction, compression, contusion, electrical and thermal injury. Surgeons underestimate the actual rate of RLN injury. Intraoperative nerve monitoring (IONM) during thyroidectomy, parathyroidectomy, or related central neck procedures can elucidate actual or potential mechanisms of RLN injury that were previously unknown to the thyroid surgeon, especially in visually intact nerves. IONM is useful in open conventional thyroid surgery for localizing the point of disrupted nerve conduction in addition to identifying how and when the RLN was injured. Studying the mechanisms of RLN injury during thyroidectomy is instructive for future operations and may allow for identification of potentially reversible causes of RLN injury. During thyroidectomy and parathyroidectomy, intraoperative RLN injury is typically associated with a visually intact RLN rather than a transected

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nerve. The anterior motor branch of a RLN bifurcating near the ligament of Berry is particularly at risk of traction injury. Traction injury is the most frequent cause of postoperative vocal cord palsy.

Keywords
Thyroidectomy • Minimally invasive video-assisted thyroidectomy • Recurrent laryngeal nerve • Mechanism of injury • Morbidity • Neuromonitoring • Traction injury

Introduction

Recurrent laryngeal nerve (RLN) paralysis refers to any dysfunction of the RLN or its dependent branches that result in dysesthesias or paresthesias in the appropriate dermatomes or in decreased motor control to innervated muscles. The use of intraoperative nerve monitoring (IONM) during thyroidectomy and parathyroidectomy procedures has given surgeons a tool for better understanding the mechanisms of RLN injury and injury to the external branch of the superior laryngeal nerve (EBSLN) [1, 2]. Before IONM, the surgeon would only be aware of an injury to the laryngeal nerves if there were visible trauma to the identified nerve. Earlier studies on the frequency of RLN injury clearly demonstrated that the practice of visually identifying and preserving the RLN intraoperatively led to a lower incidence of injury [3]. However, when postoperative alteration of voice quality was present with confirmed laryngoscopic evidence of deficient function of one of the vocal folds, the surgeon was left to only conjecture as to what occurred during surgery to produce injury of an apparently visually identified and intact RLN [1].

With IONM, the surgeon can confirm visual identification of the RLN or superior laryngeal nerve (SLN) with functional identification by stimulating the nerve with resultant recorded contraction of the vocal fold muscle (thyroarytenoid or vocalis), the posterior cricoarytenoid muscle or the cricothyroid muscle (CTM). When performing IONM with an electrode-imbedded endotracheal tube connected to an electromyographic (EMG) recorder, nerve stimulation leads to vocal fold muscle activation/contraction with associated surface depolarization that can be measured in microvolts. The latency of nerve conduction (in microseconds) between nerve stimulation and vocal fold contraction can also be measured. By repeatedly testing the RLN with nerve stimulation during thyroidectomy, the surgeon can identify a decrease in amplitude of vocal fold contraction and an increase in latency of nerve conduction that both warn of impending RLN injury. At times there may be a total loss of nerve conduction with attempted nerve stimulation, indicating RLN injury has occurred. The surgeon can then evaluate the technical surgical maneuver that produced the impending or actual RLN injury. Experience with IONM has revealed that RLN injury occurs more often with a visually intact nerve than a visually damaged nerve.

Anatomy and Risk Factors

Some variations of RLN anatomy will place the nerve at increased risk of injury. The details of RLN anatomy have been covered earlier in this textbook, but it is important to understand some of the variations of RLN anatomy that increase the risk of injury. The RLN is a complex nerve containing both sensory fibers to the larynx as well as motor fibers that produce opposing functions of both abduction and adduction of the vocal fold muscles. After its recurrent course around the major vascular structures of the mediastinum and neck base, the RLN can give off sensory branches to the trachea and muscular branches to the esophagus and pharynx while coursing upward to the laryngeal entry point.

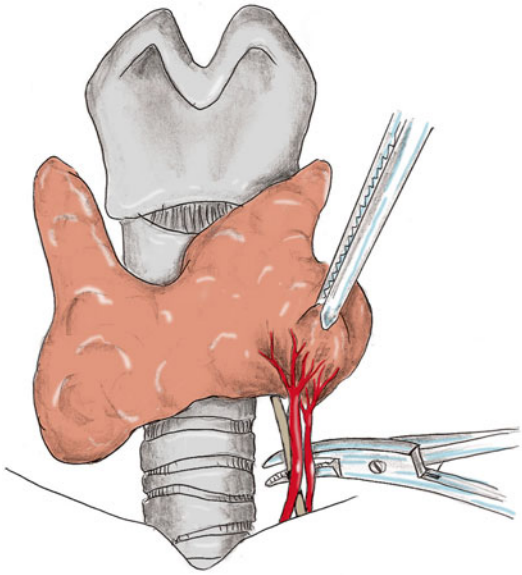

Fig. 19.1 RLN at risk due to proximity to adjacent vessels. [Courtesy of John C. Hendricks, MD, FACS]

Anomalies in the course of the RLN can place it at increased risk of injury. Usually the course of the RLN is more oblique on the right as it courses from the neck base through the paratracheal region on its way to the laryngeal entry point. If the RLN is displaced medially closer to the trachea below the inferior pole of the thyroid lobe, then the RLN can parallel vessel branches to the inferior pole. If the RLN is immediately posterior to one of these blood vessels, it is at risk of being injured during efforts for hemostasis (Fig. 19.1). Nodular thyroid disease, particularly involving the tubercle of Zuckerkandl, can result in growth under the RLN that pushes the RLN anteriorly, giving it the appearance of a blood vessel entering the thyroid, which could result in injury during hemostatic efforts (Fig. 19.2). Substernal extension of a large goiter from the posterior aspect of the thyroid, especially on the right side, can elevate the RLN considerably so that it courses over the substernal goiter on its anterior surface to end in a medially displaced position near the trachea, placing it at high risk of injury. Inflammatory conditions of the thyroid can also be responsible for adherence of the RLN to the surface of the thyroid. An embryological anomaly in the RLN course, especially on the right, can also lead to a nonrecurrent laryngeal nerve (NRLN).

Typically, the RLN bifurcates into an anterior and posterior branch within the larynx. However, in some cases this branching occurs before reaching the laryngeal entry point, frequently in the last 1 cm of its extralaryngeal course [4]. Sometimes the RLN will even trifurcate. When the branching occurs even more proximally, particularly before crossing the inferior thyroid artery or reaching the ligament of Berry, the RLN is at increased risk of injury (Fig. 19.3). IONM has revealed that the anterior branch is typically the motor branch with the posterior branch containing the sensory fibers. It should be noted that in a small percentage of patients, motor fibers particularly to the posterior cricoarytenoid muscle and/or the inferior constrictor muscle of the pharynx can be present in the posterior branch. The nerve branches are thinner after bifurcation

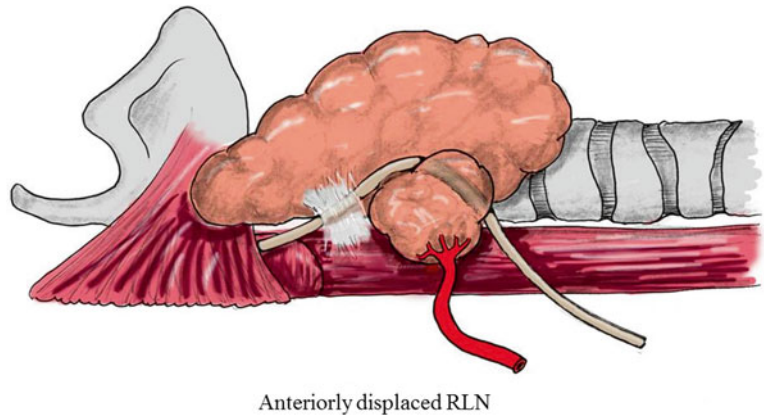

Fig. 19.2 Anteriorly displaced RLN by a nodule in the tubercle of Zuckerkandl [Courtesy of John C. Hendricks, MD, FACS]

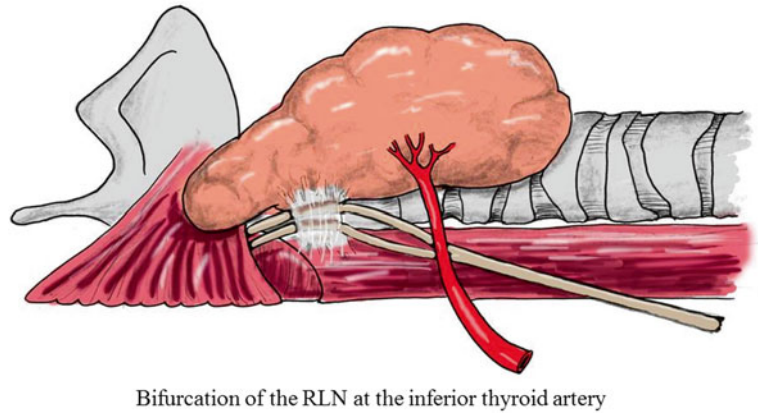

Fig. 19.3 Bifurcation of the RLN at the inferior thyroid artery [Courtesy of John C. Hendricks, MD, FACS]

making them more mobile with traction and therefore subject to stretch injury. The anterior motor branch is particularly at risk as it receives more of the traction force with the final phases of elevation and retraction of the mobilized thyroid lobe. Typically, the posterior sensory branch will be visually identified first during mobilization of the thyroid lobe. If this branch is mistaken for the entire RLN, the anterior motor branch is at risk of being mistaken for a blood vessel coursing to the thyroid. IONM aids in identifying extralaryngeal branching of the RLN, but even with IONM, branch identification can be misleading if there are motor fibers in the posterior sensory branch as well. Identifying a nerve branch that only produces a pharyngeal muscle contraction with nerve stimulation alerts the surgeon to the presence of a bifurcated nerve and should prompt a search for the anterior motor branch. The last 2 cm of the extralaryngeal course of the RLN before its laryngeal entry point has the highest risk for nerve injury because of the proximity of the RLN to the thyroid, the multiplicity of small blood vessels present and the fibrous ligament of Berry. The majority of RLN injuries occur in this location [1].

Certain pathologic conditions increase the risk of RLN injury by causing increased difficulty in identifying the RLN, altering the course of the RLN, or by being adherent to the RLN [5]. Dense scar tissue from prior surgery in the central neck compartment will make identification of the RLN more difficult and increase the risk of nerve injury. A goiter associated with Graves' disease or a large vascular multinodular goiter will increase the risk of injury secondary to hypervascularity resulting in increased bleeding that hampers identification and separation of the RLN from blood vessels adjacent to the thyroid capsule. A large substernal goiter increases the risk of RLN injury through difficulty visualizing the RLN during mobilization of the substernal component or adherence of the RLN to the substernal component. Hashimoto's goiter can place the RLN at increased risk of traction injury during elevation of the thyroid lobe secondary to increased adherence of the RLN to the inflammatory surface of the thyroid. The rubbery firm nature of the thyroid in Hashimoto's thyroiditis often makes it more difficult to visualize the course of the RLN without applying more traction force on the thyroid lobe. The greatest risk of RLN injury, however, is present in thyroid cancer cases where the nerve is involved by perithyroidal tissue invasion or metastatic lymphadenopathy.

Mechanisms of RLN Injury

There are basically three main mechanisms of RLN injury: visible structural trauma that occurs with transection or thermal injury, compression as can occur with a ligature, or stretch/traction injury (neuropraxia). There do remain some unexplained (idiopathic) injuries thought possibly secondary to ischemia or an intralaryngeal focus of traction. IONM can aid in determining

the mechanism of injury given the fact that the majority of injuries occur to a visibly intact and anatomically normal-appearing nerve [1]. Understanding the mechanisms of injury is essential to pursuing the goal of reducing rates of RLN injury during thyroidectomy and parathyroidectomy.

Transection

Preservation of the RLN is best achieved with visual identification and clear exposure of the nerve through careful dissection along its course. A transection injury, therefore, indicates an error in accurately locating the RLN or following the nerve to its laryngeal entry point. As stated earlier, there are variations in the course of the RLN that place it at higher risk of traumatic injury secondary to misidentification or lack of identification of the nerve. These variations include medial displacement, anterior displacement, nonrecurrence, and extralaryngeal bifurcation. The presence of scar tissue or cancer adherence along the course of the RLN can make it difficult to track the nerve accurately and lead to traumatic injury. In elderly patients, significant arteriosclerosis of arteries makes them whitish in color, thus mimicking a neural structure visually. The actual RLN can then be transected if mistaken for an arteriosclerotic artery.

Thermal

The more widespread use of energy devices (Harmonic Scalpel, Ligasure, etc.) and electrocautery (monopolar or bipolar) has likely led to an increased risk of thermal injury through improper application of heat to accomplish dissection around the RLN. It is possible to accomplish thyroidectomy safely with thermal devices, but there exists the added risk of extreme heat close to the course of the RLN [6]. While all energy devices generate some lateral spread of heat, the amount produced varies between the devices. If the applied heat is too close to the RLN, then permanent structural damage to the nerve can occur (Fig. 19.4). During a thyroidectomy, the highest risk of thermal injury to the nerve exists around the ligament of Berry, where the RLN is closest to the thyroid. Generally more than 2 mm of separation between the energy device and the RLN is needed to avoid thermal injury [6]. Even when the energy device is used simply as a dissecting instrument, there is a risk of accidental application of heat too close to the RLN during isolation of blood vessels just anterior to the nerve. During dissection, it is important to know precisely what tissues the heat-generating portion of the device is touching and also what other tissue is within the expected lateral spread of heat.

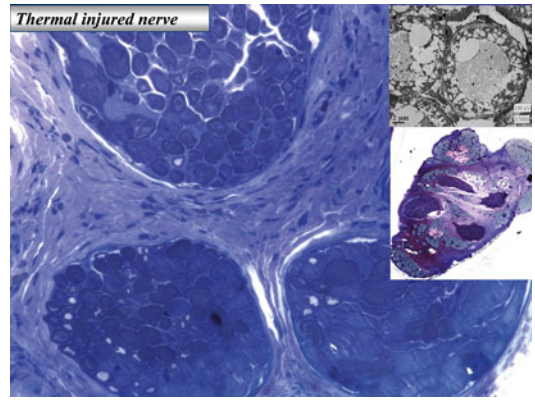

Fig. 19.4 Animal model of thermal injury. The outer nerve structures remain intact, but the inner structures show severe injury. This is the reason why thermal injury of the RLN is less reversible than traction injury [15]

Ligature

Nerve injury occurs when a vessel suture ligature or clip inadvertently incorporates the RLN (Fig. 19.5). This can occur particularly when the course of the RLN is tortuous or knuckled, placing a portion of the nerve more anterior in location and at risk of being caught in a suture ligature. The anterior motor branch of a bifurcated RLN is thin, potentially tortuous, and tends to be more mobile with traction. When tying a suture ligature, adjacent tissue can sometimes be inadvertently wrapped up in the suture

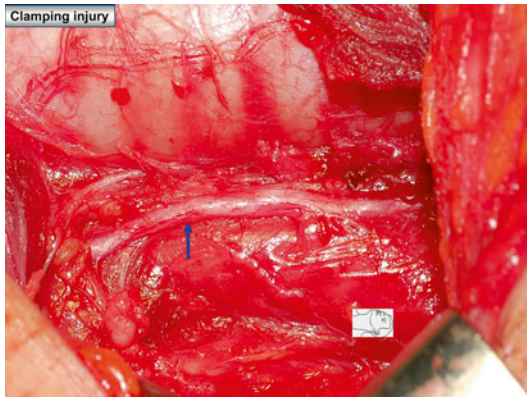

Fig. 19.5 A clamping injury is difficult to find through visualization alone, but IONM detected the nerve injury (↑). EMG signal was normal distal to the injured point but lost proximal to the injured point

Fig. 19.6 After dividing this artery, the injured point (↓) was detected and the EMG signal was normal distal to this point. The nerve injury was caused by compression of the crossing artery during medial thyroid traction

material, posing a risk to the RLN if it is within this tissue. It is important to visually follow each suture ligature carefully to the ligated blood vessel to ensure that tissue wrapping does not occur. Brisk or excessive bleeding obscures the visual field and places additional risk to the RLN during attempts at hemostasis. Carefully applied suction to clear blood from the operative field and patience while trying to determine the source of bleeding is required to avoid grasping the RLN in a ligature. At the end of the procedure, IONM allows confirmation of intact RLN function through stimulation of the vagus nerve or the most proximally exposed portion of the RLN. If there is a loss of signal (LOS) to stimulation, the RLN must be followed to the laryngeal entry point to determine the source or site of injury. If an intact RLN is trapped in a ligature, then the ligature is carefully released without damaging the nerve. No matter how long the ligature has been around the RLN, once release is confirmed visually and the nerve is found to be anatomically intact, return of RLN function can be confidently anticipated, usually within 2–3 months [1]. If a ligature incorporating the RLN is not released, then a permanent RLN injury can occur.

Compression

IONM allows repeated testing of the RLN during a central neck procedure and thus can reveal a loss of function of the RLN due to inadvertent compression. Use of a retracting instrument on the trachea to improve surgical exposure risks pressing the RLN against the trachea, particularly if the RLN is medially displaced, and can produce a compression injury. Tracheal retraction must be precisely performed to avoid this form of RLN injury. Compression injury of the RLN can also occur when a small artery crosses the distal RLN close to the laryngeal entry point and becomes taut across the nerve as a result of thyroid lobe traction, thereby indenting and compressing the nerve.

Stretch/Traction (Neuropraxia)

This is the most common mechanism of RLN injury and is optimally appreciated with IONM (Fig. 19.6) [1]. Stretch injury principally occurs with anterior and medial traction to the thyroid lobe for exposure of the base of the thyroid when completing a lobectomy. The RLN gets elevated

with traction on the thyroid, especially if there is fibrous entrapment of the RLN at the ligament of Berry. Traction applies a stretch force on the RLN that is affected by the following parameters: degree of traction (how forcefully the surgeon pulls on the thyroid), duration of traction (how long the pull lasts), and direction of traction. Being aware of these force vector parameters is critical to prevention of traction injury by keeping the traction force minimal, periodically releasing the traction, and altering the direction of traction. With IONM, loss of RLN stimulation proximal to the point of traction injury and retention of stimulation distal to the point of traction injury is seen (Video 19.1).

It is important to understand that traction injury is not a sudden onset, all or nothing, injury like compression with a ligature or direct trauma to the RLN. Traction injury is a gradual stretch injury that occurs over time as traction is applied. There are numerous motor fibers within the RLN. When traction is applied, the fibers closest to the point of maximal traction should break first. With continued traction, additional fibers break in an anterior to posterior direction within the nerve until there is sufficient disruption of motor fibers (or their sheaths) to result in a motor deficit. IONM signals to the surgeon when a traction injury is evolving through both a gradual decrease in amplitude (as fewer motor fibers are functional) and a gradual increase in latency of the stimulated contraction on the EMG monitor (Fig. 19.7) [7]. The potential temporary nature of traction injury, as seen with IONM, is somewhat unique [1]. There can be loss of motor function to nerve stimulation that later returns when the traction force has been released for a period of time. This suggests that there is a point in time when the RLN is only "stunned" and can recover normal function if the insulting force is stopped. Repeated nerve stimulation will let the surgeon recognize early loss of motor function or decreased amplitude of evoked vocal fold contraction on EMG in time to change dissection techniques to recover normal motor function.

The extralaryngeal bifurcated RLN is uniquely susceptible to traction injury, particularly if the bifurcation occurs prior to crossing the inferior thyroid artery. The motor fibers are typically in

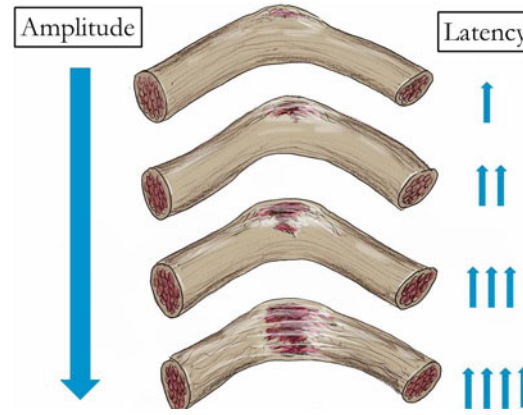

Fig. 19.7 Point traction injury of the RLN with reduction in amplitude and increase in latency of the stimulated vocal fold contraction [Courtesy of John C. Hendricks, MD, FACS]

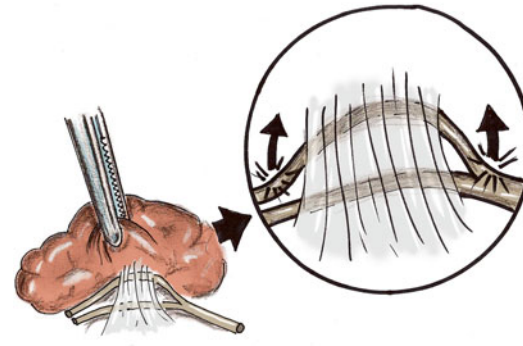

Fig. 19.8 Traction injury to the anterior motor branch of an RLN with extralaryngeal bifurcation [Courtesy of John C. Hendricks, MD, FACS]

the anterior branch, which is thinner and more mobile than the posterior branch, allowing for increased risk of traction during elevation. Maximal stretch of the anterior branch does not occur at the point of applied traction but rather at the point of greatest fixation. This point is usually at the initial takeoff of the anterior branch from the thicker proximal nerve, but it can also occur at the laryngeal entry point where the nerve is relatively more fixed (Fig. 19.8) [1]. When traction injury occurs at the RLN bifurcation, IONM will indicate loss of nerve stimulation proximally and preserved stimulation distally along the anterior motor branch. Identification of extralaryngeal branching of the RLN should prompt the

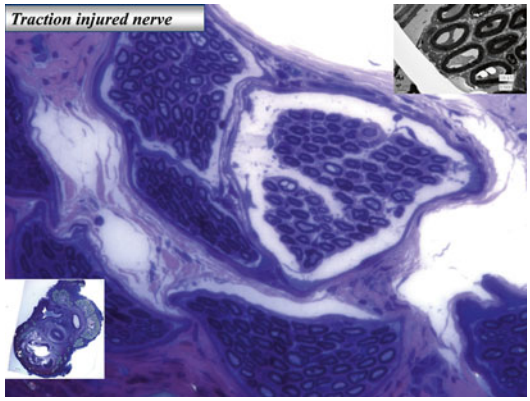

Fig. 19.9 Animal model of traction injury. The outer nerve structure was distorted, but the inner myelin sheath and axons remained intact

surgeon to be cautious about the degree of traction applied to the nerve. An anatomically intact and normal-appearing RLN can be expected to eventually recover normal function within 2–3 months after a traction injury (Fig. 19.9) [1].

Idiopathic (Possible Ischemia)

There are times when the etiology of a LOS is unclear, such as when the entire RLN has loss of function all the way through to the laryngeal entry point (LOS Type 2). Possible explanations include intralaryngeal traction injury or nerve ischemia. The RLN blood supply is through the vasa nervorum that can be visible on the ventral surface of the neural sheath. The blood supply is augmented through side branches and appears very resistant to ischemic injury. It would seem that a paratracheal lymph node dissection has the greatest likelihood of compromising the blood supply to the RLN, but in practice this rarely occurs. Furthermore, it is essentially impossible to document ischemia as the mechanism of RLN injury and to distinguish it from other potential idiopathic causes.

Prevalence

The introductory chapter of this textbook deliberates the incidence of RLN injury in detail. It should be noted that early postoperative laryngoscopy or ultrasound assessment of normal vocal fold function is essential to document the presence or absence of RLN injury. Voice function alone can be misleading as an assessment tool. Laryngoscopy is necessary to separate instances of vocal fold paresis from paralysis. Follow-up laryngoscopy is then necessary for up to a year to separate instances of temporary from permanent vocal fold paresis or paralysis. The reported prevalence of RLN injury in the literature varies from 1–2 % to 8–10 % or greater and is dependent on whether referencing prevalence per procedure or per nerve-at-risk [8]. Studies have confirmed that experience improves results, especially if surgeons perform at least 50–100 procedures per year [9]. A longitudinal study over 7.5 years showed an overall prevalence of RLN injury per nerve-at-risk of 2.0–3.8 % per year with permanent RLN injury of only 0.32 % for experienced surgeons [10]. The prevalence of RLN injury varies with the type of central neck procedure, increasing from partial thyroid lobectomy (1.28 %) to parathyroidectomy/parathyroid exploration (2.46 %), thyroid lobectomy (2.80 %), paratracheal lymph node dissection (3.37 %), and finally paratracheal lymph node dissection with thyroid lobectomy (4.21 %) [10].

Increased Susceptibility of RLN to Injury

In the perioperative period, the RLN can be injured in a variety of ways with descriptions in the literature including direct trauma, traction, excessive pressure (compression), stretch, friction, angulation, percussion, laceration of the nerve, and transection [1, 2, 11]. Multiple etiologies can further be present at the same time, such as combined traction and compression (entrapment) injuries. RLN compression may occur preoperatively (goiter compression, nodule compression) or intraoperatively. Damage may occur by either direct mechanical compression or by compression of the intrinsic blood supply to the nerve causing local ischemia. Ischemia may be a crucial element in many of these injuries [12]. Mechanical compressive forces of ≥30 mmHg retard blood flow [12]. Similarly, compression has

Table 19.1 Diseases and conditions that cause a predisposition to neuropathies

• Acromegaly
• Amyloidosis
• Carcinoma
• Cryoglobulinemia
• Chronic obstructive lung disease
• Diabetes mellitus
• Hereditary predisposition to pressure palsy
• Hypoglycemia
• Hypothyroidism
• Liver disease
• Lymphoma
• Macroglobulinemia
• Malabsorption syndromes and vitamin deficiencies
• Monoclonal gammopathy
• Multiple myeloma
• Polycythemia vera
• Porphyrias
• Uremia

Table 19.2 Drugs and chemicals that cause predisposition to neuropathies

• Acrylamide
• Amiodarone
• Arsenic
• Aurothioglucose
• Buckthorn (toxic berry)
• Carbon disulfide
• Cisplatin
• Dapsone
• Diketone hexacarbons
• Dimethylamino propionitrile
• Diphtheria
• Disulfiram
• Hydralazine
• Isoniazid
• Lead
• Metronidazole
• Misonidazole
• Organophosphates
• Perhexiline
• Phenytoin
• Pyridoxin
• Thalidomide
• Thallium
• Vincristine

been shown to interfere with axonal transport pathways [12]. Larger fibers containing more myelin are more susceptible to compression than smaller non-myelinated fibers [13]. Nerves can stretch 10–20 % before becoming structurally damaged [14]. Tables 19.1 and 19.2 summarize drugs, chemicals, diseases, and conditions that may predispose patients to neuropathy and increased susceptibility to RLN injury.

Grades of Nerve Injury

Classification of nerve injury depends upon the neural components affected, loss of functionality, and the ability to recover spontaneously [16, 17]. Two grading systems are used to stage the extent of nerve injury: Seddon's system and Sunderland's system [16, 17]. Seddon proposed a three-tiered model for nerve injury based on increasing severity: neuropraxia, axonotmesis, and neurotmesis. According to this system, the *neuropraxic* stage involves a reversible conduction block characterized by local ischemia and selective demyelination of the axon sheath. The axon's continuity is retained, and although conduction across the nerve injury is inhibited, conduction within the nerve both proximal and distal to the lesion remains intact [18]. The prognosis for an injured nerve at this stage is good, and recovery occurs within weeks to months [18]. *Axonotmesis* is a more severe stage of injury with disruption of not only the myelin sheath but the axon as well. The epineurium and perineurium remain intact, meaning there is still some continuity within the nerve [16]. Axonotmesis leads to *Wallerian degeneration*, a process whereby the part of the axon that is separated from the neuronal cell body disintegrates distal to the injury [16]. The prognosis for nerves at this stage is fair, and recovery may require months. *Neurotmesis*, the most severe form of nerve injury, is associated with complete nerve division and disruption of the endoneurium. In neurotmesis, the axon, myelin sheath, and connective tissue components of the nerve are damaged, disrupted, or transected. As with axonotmesis, neurotmesis initiates Wallerian degeneration but the prognosis for

nerve recovery is poor. Neurotmesis is commonly seen after lacerations or ischemic injury. Sunderland's classification divides nerve injuries into grades 1–5 [17]. A grade 1 injury is equivalent to neuropraxia according to the Seddon classification. A grade 2 injury is equivalent to axonotmesis and involves injury to the axon without loss of supporting structures. In addition to axonal loss, grade 3 injuries are associated with a loss of endoneurium and grade 4 injuries with a loss of perineurium, leaving only some connective tissues and epineurium remaining. Finally, grade 5 injuries represent a complete transection of the nerve. Grade 4 and 5 injuries involve extensive loss of supporting structures, resulting in scar tissue formation. They are associated with lack of spontaneous regeneration and require surgical exploration, reconstruction, possible neurolysis, and possible nerve grafting [17].

Cellular Processes in Nerve Injury

Multiple pathophysiological, neurochemical, and anatomical changes are triggered by nerve injury. Specific mechanisms triggered by injury to nerve cells vary depending on the site and type of trauma [19–21]. Axonal laceration induces an immediate influx of calcium, which disrupts the ionic balance of the nerve cell and initiates transport of a number of intracellular and extracellular chemicals to the nerve cell body in the dorsal root ganglion [19–21]. Abrupt non-transection trauma can also cause injury to axons, which then begin to degenerate over the next several days leading to cell death in a delayed, progressive fashion [19–21]. Degeneration of the central and peripheral terminal projections of the damaged and dying nerve cells leads to sprouting of terminal projections of neighboring undamaged nerve cells, constituting a morphologic central reorganization of neuronal circuitry and peripheral innervation of tissues [19–21].

Axonal trauma alters normal orthograde flow of proteins toward the cell body in the dorsal root ganglion as well as retrograde flow toward the peripheral terminal along intracellular filaments [19–21]. This alters the information arriving to protein assembly mechanisms in the cell body and leads to changes in gene expression. Changes in gene expression follow a temporally specific pattern indicating that different cellular contents are produced at varying times following trauma to a peripheral nerve. In addition to changes in the expression of proteins, there are also changes in the cellular distribution of these proteins, particularly of sodium and calcium channels, which are critically involved in neuronal excitability and conduction. Changes in the expression of specific proteins are particularly relevant to secondary injury with changes in the expression of neurotransmitters such as substance P, trophic factors such as brain-derived neurotrophic factor, as well as kinases and other degradative enzymes [19–21]. Changes also occur in supporting Schwann cells and are important to understand because of their pivotal role in sustaining the physiologic properties of peripheral nerve cells and their involvement in a degenerative process termed "Wallerian degeneration" [19–21]. Schwann cells are the glial cells of the peripheral nervous system and include myelinating cells and non-myelinating satellite cells. As the Schwann cells decompose so do the myelin sheaths. The products of this decomposition trigger proliferation of new undifferentiated Schwann cells that align along the Bungner's bands that constitute the tubes within which nerve bundles are contained along with their support cells.

Intraoperative Evidence of RLN Injury

Several studies have shown that surgeons underestimate the rate of RLN injury (Table 19.3) [1, 2, 11, 22–24]. Causes of RLN injury are manifold, but most are due to errors in surgical technique including transection of the nerve, ligature entrapment, traction, clamping, suctioning too close to the nerve, compression, contusion, pressure, and thermal injuries. Several studies have shown that surgeons, even if experienced, underestimate actual RLN injuries in conventional thyroidectomy [1, 2, 11, 22–24]. The rate of intraoperative evidence of RLN injury as assessed by surgeons

Table 19.3 Intraoperative evidence of RLN injury

Author	Reference	*N*, %
Bergenfelz A	Langenbecks Arch Surg 2008	1/10, 10 %
Chiang FY	Surgery 2005	3/40, 7.5 %
Dionigi G	Surg Endoscopy 2012	1/10, 10 %
Lo CY	Arch Surg 2000	5/33, 15 %
Patlow CA	Arch Surg 1986	1/10, 10 %
Caldarelli D	Otolaryngol Clin North Am 1980	1/10, 10 %

is between 7.5 and 15 % [1, 2, 11, 22–24]. Certain RLN injuries including thermal, traction, compression, contusion, or pressure injuries may not be detected visually by the surgeon; only a functional assessment of the RLN with IONM can detect such insults (Fig. 19.10).

Role of Intraoperative Neuromonitoring Studies in Diagnosis, Management, and Prognosis of RLN Injury

Much of what is known regarding the pathophysiology of RLN injury has been learned through animal studies. Although limited in number, such studies support the idea that the pathophysiologic mechanisms discovered in animal models are valuable and relevant to our understanding of human neuropathic injury [25–28]. There are several animal models of RLN neuropathic injury focused on the type of primary injury or nerve trauma [25–28]. Evaluation of nerve injury through these models includes the assessment of EMG parameters such as amplitude and latency by means of IONM.

In the clinical setting, routine visual identification of the RLN during thyroidectomy has been recommended by many studies as the gold standard of care to minimize risk of nerve injury because of its association with a lower postoperative palsy rate [29, 30]. However, despite routine visualization of the nerve, RLN palsy still occurs, and the mechanism of most injuries remains unrecognized intraoperatively [30]. The RLN can be injured secondary to difficult identification or misidentification, such as with anatomic variation or in cases of large goiter or recurrent goiter; these cases may play an important role in the occurrence of permanent nerve palsy [2, 31]. In recent decades, IONM has been recommended as an adjunct to help facilitate the identification and dissection of the RLN as well as detection of nerve injury and its mechanism to improve surgical technique [1, 2, 11, 32]. In addition, IONM also helps predict the outcome of vocal cord function after resection of a thyroid lobe.

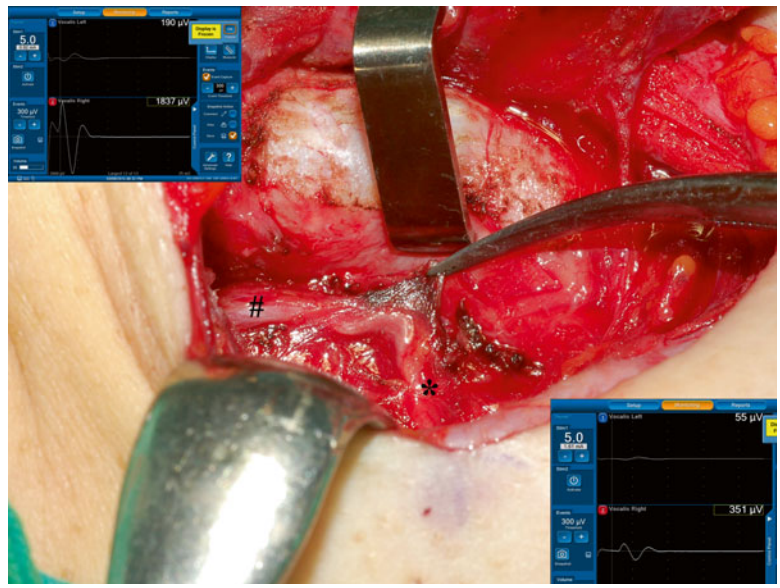

Fig. 19.10 The RLN looks normal but EMG signal was severely decreased due to thermal injury. The EMG signal was 1837 µV at the distal portion (#) and 351 µV at the proximal portion (*) of the injured segment. The patient had postoperative vocal cord palsy

Nevertheless, several studies have reported that the additional use of IONM does not result in lower postoperative RLN palsy rates compared with visualization alone [33–36]. Chiang et al. found that permanent and temporary palsy rates during the learning curve of IONM had no statistical difference compared with visual identification alone but that palsy rates were significantly reduced after following standardized IONM procedures [2, 32]. Dralle et al. have also emphasized that the lack of standardization of IONM leads to highly variable results [35]. Therefore, learning and following standardized IONM procedures are essential for the optimal prevention of nerve injury [32, 37, 38].

Loss of Signal

Loss of R_2 (the response obtained by stimulating the most proximally exposed portion of the RLN after complete dissection) and V_2 (the response obtained by final stimulation of the vagus nerve after complete hemostasis of the surgical field) signals indicate that the RLN might have been injured during manipulation. An effort should be made to identify the disrupted point of nerve conduction and elucidate the mechanism of injury. The disrupted point of nerve conduction can be located by testing the RLN starting from its most distal portion near the laryngeal entry point. If a signal is obtained, testing should continue proximally along the nerve until a response cannot be elicited. If the point of disruption in nerve conduction is not detected, the contralateral vagus nerve should be stimulated to exclude the possibility of a false LOS, such as EMG tube displacement, monitor dysfunction, misuse of neuromuscular blocking agents, etc.

Weak Signal

Partial injury of the RLN can occur through surgical maneuvers including traction, compression, clamping, mechanical trauma, or electrocauterization. Partial injury features a weak point of nerve conduction that is detected in an exposed RLN with visual anatomical integrity [1, 2, 11]. The correlation between vocal cord function and percentage of EMG amplitude reduction is still unknown. Chiang's unpublished data suggests that when final EMG amplitude is reduced by >60 %, the possibility of vocal cord paralysis (VCP) should be considered. Other research is ongoing regarding the specific percent decrease or absolute number below which amplitude depression and latency elevation are associated with VCP postoperatively. The positioning of the endotracheal tube and alteration of contact between the vocal cord and the tube electrodes (secondary to surgical manipulation of the thyroid or trachea) can result in substantial changes in EMG amplitude. Rechecking and adjusting the endotracheal tube and electrode position is necessary [39].

Strategies for Preventing Nerve Injury

Most RLN injuries occur during lateral thyroid and RLN dissection due to inadvertent clamping, transection, electrothermal, or traction injury. Several strategies are recommended for the prevention of RLN injury: (1) definite identification of the RLN before certain surgical maneuvers including clamping, transection or electrocauterization; (2) strict prohibition of the use of any energy-based device adjacent to the nerve; and (3) employing gentle traction of the thyroid throughout the surgery. In our experience, inadvertent clamping, transection, and thermal injury will occur less frequently if the above principles are strictly followed [32]. However, traction injury is still challenging to avoid and is presently the most common mechanism of RLN injury. Several studies have reported that about 70–80 % of nerve injuries are caused by traction injury [1, 2, 11], with IONM showing a characteristic LOS after thyroid resection despite visual anatomic integrity of the RLN.

Real-Time IONM

The present standard IONM technique provides an intermittent stimulation with a handheld stimulating probe. The functional integrity of the RLN is limited to the short time interval of the direct nerve stimulation. The RLN is still at risk for damage in the time gap between two nerve stimulations. To overcome the limitations of intermittent IONM (I-IONM), real-time IONM has been designed for seamless monitoring of nerve function during the whole course of surgery [40, 41]. Recent studies also reveal its potential for detecting adverse signal change earlier with prevention of imminent traction injury [27, 42, 43]. There are two types of real-time IONM: continuous vagal nerve stimulation and stimulation with a dissecting instrument. During continuous vagal nerve stimulation, Schneider et al. observed that durable reduction in EMG amplitude paralleled by an increase in latency occurred before the EMG signal degraded to definitive LOS with postoperative RLN palsy [42]. In an animal experiment by Wu et al., EMG signal showed a progressive change of combined amplitude decrease and latency increase during acute traction distress [27]. The EMG signal showed a nearly full recovery (92–100 %) if traction stress was relieved before LOS, but the recovery became worse if prolonged or repeated traction was applied to the nerve. The combined events (amplitude decrease and latency increase) alert surgeons to correct certain surgical maneuvers immediately to prevent irreversible nerve injury.

The stimulating dissecting instrument (SDI) functions as a stimulating probe as well as a dissecting instrument, allowing for a simple and convenient way to dissect structures while confirming intact RLN function (and exclusion of the RLN from dissected tissues). SDI also provides real-time monitoring of nerve function during lateral thyroid and RLN dissection. When EMG amplitude decreases by >50 %, surgical maneuvers should be paused and thyroid traction should be released immediately. The EMG amplitude showed gradual recovery within a few minutes and reached a maximal recovery within 10 minutes in a clinical observation by Wu et al. [27].

Topics such as NRLN injury, EBSLN injury, injury occurring due to variation in RLN branching patterns and details of standard IONM technique are discussed in depth in the relevant chapters in this book.

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Intraoperative Neural Injury Management: Neuropraxic Non-transection Injury

20

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Abstract

During thyroid surgery, the macroscopically intact recurrent laryngeal nerve (RLN) may cease to function, even though it is not transected. Traction, cautery, pressure, crush, or being tied in surrounding tissue are some causes of impaired function during surgery. Invisible RLN injuries (such as thermal, traction, compression, contusion, or pressure) are not detected by the surgeon's eye; only a functional assessment of the RLN with intraoperative nerve monitoring (IONM) can detect such insults. With the application of IONM, we appreciate that traction is the major cause of RLN injury during thyroid surgery.

Keywords

Recurrent laryngeal nerve • Superior laryngeal nerve • Mechanism of injury • Neurobiology • Neurophysiology • Management • Intraoperative corticosteroids • Neuromonitoring

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Introduction

The larynx is innervated by two peripheral nerves, the recurrent (RLN) and superior (SLN) laryngeal nerve. Both nerves originate from the vagus nerve and carry motor, sensory, and autonomic (parasympathetic) fibers to the larynx [1]. The lower motor neurons of the special efferent system that controls the intrinsic laryngeal muscles are located in the nucleus ambiguus in the lower brainstem in a fairly well-studied somatotopical arrangement [2–10]. The sensory neurons are located in the vagal ganglion and the parasympathetic cell bodies are located in the dorsal motor nucleus of the vagus in the brainstem. The mechanically complex functioning of the larynx (including airway protection reflexes, phonation, swallowing) requires a rich and detailed neural control, which is projected through the RLN and SLN.

The RLN can be regarded as the most important motor nerve supply to the larynx, as it innervates 4 out of 5 intrinsic laryngeal muscles. There are also projections from the RLN to the esophagus and trachea [3]. The RLN divides into an anterior and posterior branch either inside the larynx, or, in roughly one-third of cases, in an extralaryngeal manner just before the nerve entry point [11]. The posterior branch projects superiorly to form the anastomosis of Galen with the internal branch of the SLN—this branch is probably sensory in nature [12]. The anterior branch carries motor fibers [13, 14] to the posterior thyroarytenoid muscle, lateral cricoarytenoid muscle, and finally to the thyroarytenoid muscle [15–17]. Within the larynx, the RLN and SLN break up into a plexus-like branching system [18] with several connections between the RLN and SLN [17]. The exact functions of these small nerve branches are not fully known, but animal models have demonstrated that the intrinsic laryngeal muscles receive dual innervation from both the RLN and SLN [19, 20].

The SLN originates from the inferior vagal ganglion at the level of C2 in the neck [21]. It divides into a larger internal branch that enters the larynx through the thyrohyoid membrane (carrying sensory fibers down to the level of the glottis) and a smaller external branch that passes deep to the superior thyroid artery to innervate the cricothyroid muscle (CTM), which is responsible for vocal fold lengthening and tension (important for high vocal pitch) [22]. The external branch of the SLN (EBSLN) continues through the CTM to reach the anterior glottis and the thyroarytenoid muscle. This branch, called the "human communicating nerve" [23] or "cricothyroid connection branch" [24], thus represents an additional motor supply to the intrinsic laryngeal muscles other than the RLN, which may be important following RLN injury and reinnervation. This anatomy enables intraoperative monitoring of the EBSLN through routine surface electrodes in the intubation tube [25], although the exact laryngological function of this nerve branch is not known [26].

Neurobiology Underlying Loss of Function of the RLN During Surgery

During surgery, the macroscopically intact RLN may cease to function even though it is not transected. Cautery, pressure/crush, traction, and ligature entrapment are examples of injuries that lead to various interruptions within the neural circuitry causing impaired function during surgery. It is important from a clinical perspective to make the distinction between nerve conduction block ("neuropraxia") and the more severe "axonotmesis," which means presence of axonal injury. Neuropraxia is the mildest form of injury as it affects surrounding Schwann cells but respects the integrity of the axon. The result is a conduction block lasting typically about 6–8 weeks followed by a complete return of function [27]. This seems to be the most common RLN injury seen at surgery [28]. More severe trauma can cause axonotmesis (varying degrees of axonal injury), leading to neuronal death or dysfunction followed by some degree of reinnervation of the target cells. Axonotmesis, therefore, is associated

with a poorer and more unpredictable outcome for functional restitution.

The RLN is made up of secondary motor neurons that terminate at the neuromuscular junction, the motor end plate. Secondary neurons are part of the peripheral nervous system (PNS), as opposed to primary motor neurons within the central nervous system (CNS) that run from the cortex to terminate on secondary neurons. The myelin around axons in the CNS comes from oligodendrocytes and contains several factors that are inhibitory to axonal growth and regeneration. This inhibition is one of the main problems after CNS injuries, such as stroke or spinal cord injury [29]. In the PNS, on the other hand, the myelin around the axons is derived from the Schwann cell. This milieu is attractive for axonal growth, which is why peripheral nerve injury is usually associated with regeneration after axonal disruption [30–34]. Following a peripheral nerve injury with axonal disruption, the distal end, which is disconnected from the neuron, will be neurophysiologically active until it degenerates [35] (Wallerian degeneration [36]). Under normal conditions, this will take approximately 1 week. Thus, for several days after complete transection of the RLN (with complete separation of the nerve), intraoperative nerve monitoring (IONM) will show a negative signal at the proximal end connected to the motor neuron and a positive signal at the distal end connected to the vocal muscle. Re-exploring the distal end of the RLN for nerve reconstruction confirms the positive signal for up to 5 days after complete injury from thyroid surgery (personal communication). After axonal injury within the macroscopically intact RLN, the distal axon also degenerates and must then regenerate to achieve any functional recovery. In the literature, there has been considerable speculation regarding the reasons for poor (or absent) functional recovery after injury to the RLN despite a macroscopically intact-appearing nerve during surgery. One factor associated with insufficient recovery is a potential misguidance of RLN axons during regeneration, leading to nonfunctional reinnervation of laryngeal muscles. There are, however, studies that show the degree of accurate innervation is very high after crush injury to the peripheral nerve (90 %) [37]. The axon is guided by intact endoneural tubes [38]. Other factors negatively affecting functional recovery after peripheral nerve injury are death of the secondary motor neurons, insufficient regeneration and dysfunctional reinnervation (i.e., collateral reinnervation). Collateral reinnervation occurs when an adjacent ("wrong") peripheral nerve begins to sprout within a target muscle that has been denervated. The result of this dysfunctional reinnervation is an innervated muscle by different motor neurons than before, resulting in trophic support but not functional innervation. This phenomenon has been seen in the rat and pig, where cases of complete injury to the RLN have led to collateral reinnervation by the SLN [19, 20].

The axotomy induces a retrograde injury signal to the neuron in the brainstem, which is attacked by microglia and also surrounded by a profound astroglial reaction [39–41]. The neuron downregulates its production of transmitter substances and turns gene transcription to regeneration and reinnervation. The neuron is exposed to stress and is dependent on a continuous inflow of growth factors from the periphery [33]. Motor neurons are more likely to die in response to peripheral axotomy the closer the axotomy is to the neuronal soma in the brainstem or spinal cord. Local addition of growth factors radically improves the prognosis of the axotomized neuron [42–45]. In addition, there are many experiments supporting that distal peripheral nerve injury, including injury to the RLN, is associated with no or limited nerve cell death [46]. Thus, any functional deficit after RLN injury is most likely to depend on a reinnervation problem rather than neuronal loss.

The distal axotomy in the intact RLN causes a synaptic displacement from the secondary motor neuron in the nucleus ambiguus, which then loses contact with higher cortical centers [47]. These synapses from cortical neurons reappear on the secondary motor neurons as they regenerate and reestablish contact with the target organ (muscle). The proceeding adaptation to the new neural circuits is referred to as plasticity of the nervous

system. Thus, the macroscopically intact but injured RLN will recover spontaneously if there is only a conduction block caused by an impairment of electrical propagation due to Schwann cell dysfunction. If there is a component of axonal injury within the nerve, the axon will not only have to reinnervate the laryngeal muscles, but the neuron in the brainstem will need to reconnect with cortical neurons by reestablishment of their synapses.

Prevalence of Incomplete Non-Transection RLN Injury

The causes of RLN injury are manifold and largely result from errors in surgical technique, including transection of the nerve, ligature entrapment, traction, clamping, aspiration too close to the nerve, compression, contusion, pressure, or thermal injury. IONM studies have revealed that the major cause of RLN injury during thyroid surgery is traction, which results in an invisible, incomplete non-transection lesion to the RLN [48–50]. In a series by Snyder, Chiang, and Dionigi, traction injury accounted for 70–80 % of all injuries [48–50]. Several studies have shown that surgeons, even if experienced, underestimate actual RLN injuries in thyroidectomy [48–52]. The rate of intraoperative evidence of RLN injury as assessed by surgeons is between 7.5 % and 15 % [48–53]. Damage to the RLN by thermal, traction, compression, contusion, or pressure injury is often not detected by the surgeon's eye; only a functional assessment of the RLN with IONM can detect such insults. According to a study by Dionigi, intraoperative evidence of RLN injury is seen only 10 % of the time, even in minimally invasive thyroidectomy under magnification from the endoscope [50]. The following are the most common causes of incomplete non-transection RLN injuries:

Thermal

The more widespread use of energy devices and electrocautery has led to an increased risk of thermal injury from improper application of heat while dissecting around the RLN. All energy devices generate some lateral spread of heat, but some produce more than others. If the applied heat is too close to the RLN, then permanent structural damage to the nerve can occur. The use of energy devices to complete thyroid lobectomy at the ligament of Berry creates heat where the RLN is closest to the thyroid and is at highest risk of thermal injury. Generally, >2 mm of separation between the energy device and the RLN is needed to avoid thermal injury [54]. Energy devices can also be used as dissecting instruments but are not as fine as hemostats. This can lead to accidentally applying heat too close to the RLN, such as when dividing a blood vessel lying just anterior to the nerve. It is important to know precisely what the heat-generating portion of the device is touching and to be aware of what tissues are regionally within the expected lateral spread of heat.

Ligature

Nerve injury occurs when a vessel suture ligature or clip inadvertently incorporates the RLN. This can particularly occur when the course of the RLN is tortuous or knuckled, placing a portion of the nerve more anteriorly and at risk of being caught in a suture ligature. The anterior motor branch of a bifurcated RLN is often thin and potentially tortuous, placing it at greater risk of traction injury. When tying a ligature down, adjacent tissue can sometimes be inadvertently wrapped up in the suture material. If the tissue contains the RLN, then nerve injury occurs. It is important to visually follow each suture all the way down to the ligated blood vessel to ensure that tissue wrapping does not occur. Brisk or excessive bleeding can place the RLN at further risk by obscuring the visual field during attempts to tie off the blood vessel. Carefully applied suction to clear blood from the operative field and patience while trying to determine the precise source of bleeding are required to avoid catching the RLN in a ligature. At the end of the operative procedure, IONM allows confirmation of intact function of the RLN with stimulation of the vagus nerve or the most proximally exposed portion of

the RLN. If there is a loss of signal (LOS) with stimulation, then the RLN must be followed to the laryngeal entry point to determine the site of injury. If an intact RLN is found caught in a ligature, then the ligature is carefully released without damaging the nerve. No matter how long the ligature has been around the RLN, once release is confirmed visually and if the RLN appears anatomically intact, return of function can be confidently anticipated usually within 2–3 months [48]. If a ligature incorporating the RLN is not released, then a permanent RLN injury will occur.

Compression

The RLN is an extremely sensitive nerve and is unlike other musculoskeletal motor nerves that can be pinched to demonstrate the anticipated muscular contraction. Pinching the RLN with pickups or by light clamping will likely result in a loss of function due to nerve compression. IONM allows repeated testing of the RLN during a central neck procedure and thus can reveal loss of function resulting from inadvertent compression of the RLN. Use of a retracting instrument on the trachea for improved wound exposure runs the risk of catching the RLN against the trachea (particularly if it is medially displaced), producing a compression injury. Retraction of the trachea must be precisely performed to avoid this mechanism of RLN injury. Another instance of compression injury occurs when a small artery crossing the distal RLN close to the laryngeal entry point becomes taut across the nerve with thyroid lobe traction, producing a "banding" injury and visible indentation on the nerve with resultant compression injury.

Stretch/Traction (Neuropraxia)

Stretch or traction injury is the most common mechanism of RLN nerve injury and is better appreciated with IONM [48]. The injury largely occurs from application of anterior and medial traction to the thyroid lobe for exposure of the base of the thyroid to complete a lobectomy. The RLN becomes elevated with traction on the thyroid, especially if there is fibrous entrapment of the RLN in the ligament of Berry area. A common concern for the surgeon is how much traction is too much. Traction applies a stretch force on the RLN. The important parameters of this force include the degree of traction (which depends on how hard the surgeon pulls on the thyroid), the duration of traction (which depends on how long the surgeon pulls), and the direction that traction is applied. Being aware of these 3 parameters is critical to preventing traction injury by minimizing the amount of force applied, periodically easing up on traction, and altering the direction of traction. With IONM, the RLN loses stimulation proximal to the point of traction injury and retains nerve stimulation distal to the point of traction injury (Video 20.1).

It is important to understand that traction injury is not a sudden "all or nothing" injury like compression with a ligature or direct trauma to the RLN. Traction injury is a gradual stretch injury that occurs over time as traction is applied. There are numerous motor fibers within the RLN. When traction is applied, the fibers closest to the point of maximal traction should break first. With continued traction, additional fibers break in an anterior to posterior direction within the nerve until there is sufficient disruption of motor fibers to result in a motor deficit. IONM signals to the surgeon when a traction injury is evolving through both a gradual decrease in amplitude (as fewer motor fibers are functional) and a gradual increase in latency of the stimulated contraction on the EMG monitor [55]. Since the motor fibers are usually located in the anterior portion of the RLN (closest to the point of applied traction), it is understandable how a motor deficit can readily occur with only a partial traction injury to the anterior portion of the RLN. Traction injury is also unique in that IONM has revealed that this type of injury can be temporary [48]. There can be loss of motor function to nerve stimulation that later returns when the traction force has been released for a period of time. This suggests that there is a point in time when the RLN is only "stunned" and can recover normal function if the insulting force is stopped. Repeated nerve stimulation will let the surgeon recognize early loss of motor function through

decreased amplitude of the evoked vocal fold contraction on the EMG monitor in time to change dissection techniques to recover normal motor function.

The extralaryngeal bifurcation of RLN is uniquely susceptible to traction injury, particularly if the bifurcation occurs prior to crossing the inferior thyroid artery before the ligament of Berry area. The motor fibers are typically in the anterior branch, which is thinner and more mobile than the posterior branch, allowing for increased risk of traction during elevation. Maximal stretch of the anterior branch does not occur at the point of applied traction, but rather at the point of greatest fixation. This point is usually at the initial takeoff of the anterior branch from the thicker conjoined anterior and posterior branches, but it can also occur at the laryngeal entry point where the nerve is relatively more fixed [48]. When traction injury occurs at the RLN bifurcation, IONM will indicate loss of nerve stimulation proximally and preserved stimulation distally along the anterior motor branch. Identification of extralaryngeal branching of the RLN should prompt the surgeon to be cautious about the degree of traction applied to the nerve. An anatomically intact and normal appearing RLN can be expected to eventually recover normal function within 2–3 months after a traction injury [48].

Idiopathic (Ischemia)

There are times when the etiology of LOS is unclear, such as when the entire RLN has loss of function all the way through the laryngeal entry point. Possible explanations include intralaryngeal traction injury or nerve ischemia. The RLN blood supply is through the vasa nervorum that can be visible on the ventral surface of the neural sheath. The blood supply is augmented through side branches and appears very resistant to ischemic injury. It would seem that a paratracheal lymph node dissection has the greatest likelihood of compromising the blood supply to the RLN, but in practice this rarely occurs. Furthermore, it is essentially impossible to document ischemia as the mechanism of RLN injury and to distinguish it from other potential idiopathic causes.

Intraoperative Management of Impaired Laryngeal Nerve Function

The goal of management is to return function to the damaged\stress nerve and\or improve the quality of life of patients. IONM is useful for ensuring a complete conduction circuit from the vagus nerve to the vocal muscle or for detecting impaired function in the RLN. Since the SLN innervates the anterior third of the vocal muscle, the SLN may also be detected by the same EMG system used for RLN monitoring. However, normal function of the SLN (equivalent to an intact neural circuit) can only be evaluated if the stimulus is applied to the SLN proximal to the site of dissection. This is sometimes difficult to access within the upper thyroid pole dissection field during surgery.

If the RLN is injured and function is lost, the distal part towards the vocal muscle will respond with a positive signal for several days, whereas the proximal part (towards the motor neurons in the brainstem) will remain silent. Therefore, it is possible to locate the nerve conduction block using nerve monitoring. However, it is not possible to distinguish between neuropraxia and axonotmesis just by looking at the nerve conduction block of an intact RLN during surgery. However, *if* there is a degree of axonotmesis within the silent nerve, it is important to optimize care to facilitate regeneration. The intact nerve enveloping well-aligned endoneural tubes constitutes an optimal regeneration environment. A hostile environment includes an intact nerve that is shrunken and pale or discolored over a significant distance due to heat injury. This more severe appearance could result in scarring/fibrosis within the conduction-blocked nerve segment, impairing the regeneration process across this segment. Further, a bipolar injury of the nerve or a “kink” in the nerve from a ligature has poor potential for regeneration. Thus, it is impor-

tant to ensure a macroscopically intact nerve and to inspect the nerve and lesion area to determine potential regeneration issues if the signal is lost.

There are ways to classify intraoperative injuries to the RLN, which is important for future attempts to diagnose and prognosticate RLN injury. One classification system divides injuries into segmental (type 1) or global (type 2). Segmental injury refers to a localized LOS and global injury occurs when the entire nerve is silent. In the case of type 2 injuries, the structural change is located distal to where the nerve can be detected (i.e., beyond the laryngeal nerve entry point behind the inferior constrictor muscle). This could occur in the situation of branching of the RLN between the nerve entry point and the vocal muscle, where undue stretch during mobilization of a thyroid lobe causes structural change and LOS.

Neurophysiology

Postoperative electrodiagnostic methods can be used to determine the presence and type of nerve injury, as well as to characterize ongoing or completed reinnervation processes. Laryngeal electromyography (LEMG) was first introduced more than 60 years ago, and has evolved [56] into a valuable tool for laryngologists to diagnose neurolaryngological disorders. LEMG is primarily a qualitative method of testing [57] that assesses the presence of denervation potentials and degree of motor unit recruitment, making it a subjective test dependent on the examiner and the technical settings. However, LEMG has nevertheless been shown to have high positive predictive value in predicting long-term outcomes of patients with a poor prognosis [58–61] and is used widely to predict recovery regardless of etiology of vocal fold paresis. Patients with pathological EMG findings at least two months after paresis are most likely to need laryngeal framework surgery [60]. In the case of vocal fold paresis after thyroid/parathyroid surgery, the prognostic information obtained from LEMG can be helpful to identify those cases necessitating future interventions, such as surgical or pharmacological reinnervation therapies or vocal fold medialization procedures (Figs. 20.1, 20.2, and 20.3). For patients with only a conduction block (neuropraxia) of the RLN, vocal fold movement is most likely to return. When using LEMG to obtain this information after thyroid surgery, it is important to take into consideration the timing of the examination. Denervation activity (indicating axonotmesis and poor prognosis) typically appears three weeks after RLN injury [27], and lasts until reinnervation is complete. Reinnervation of the intrinsic laryngeal muscles can be expected to take place rather promptly,

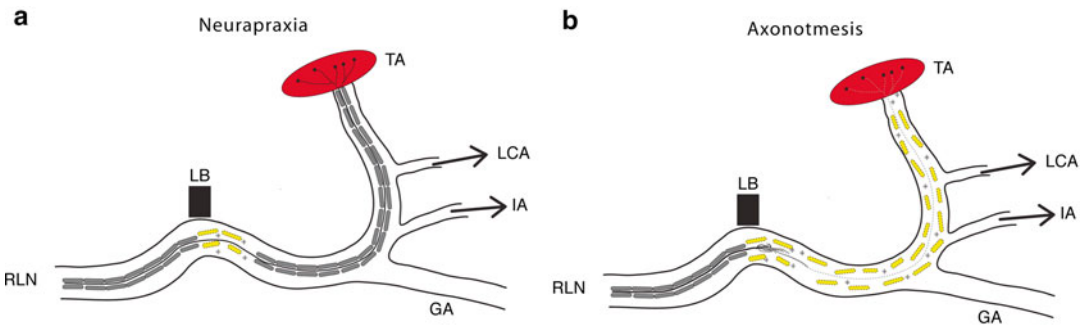

Fig. 20.1 Schematic drawing of the recurrent laryngeal nerve (RLN) with intralaryngeal branches to interarytenoid muscle (IA), lateral cricoarytenoid muscle (LCA) and thyroarytenoid muscle (TA). The axon is surrounded by Schwann cells responsible for electrical propagation. *LB* Ligament of Berry, *GA* Anastomosis of Galen. Neuropraxia (**a**) with intact axonal integrity, facing spontaneous recovery. Axonotmesis (**b**) with disruption of axon and ongoing regeneration [Reprinted from Mattsson P, Hydman J, Svensson M. Recovery of laryngeal after intraoperative injury to the recurrent laryngeal nerve. Gland Surg 2015; 4(1):27–35. With permission from AME Publishing Company]

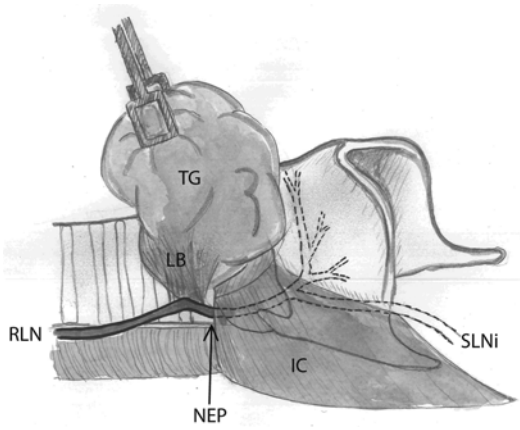

Fig. 20.2 The recurrent laryngeal nerve (RLN) and the nerve entry point (NEP) under the inferior constrictor muscle (IC). *TG* thyroid gland, *SLNi* Superior laryngeal nerve, internal branch, *GA* anastomosis of Galen, *LB* ligament of Berry. NEP may serve as an anatomical landmark in the classification of loss of vagal signal during thyroid surgery, e.g., lesion proximal to NEP (when there is a defined injury segment) or lesion distal to NEP (entire nerve silent to the NEP) [Reprinted from Mattsson P, Hydman J, Svensson M. Recovery of laryngeal after intraoperative injury to the recurrent laryngeal nerve. Gland Surg 2015; 4(1):27–35. With permission from AME Publishing Company]

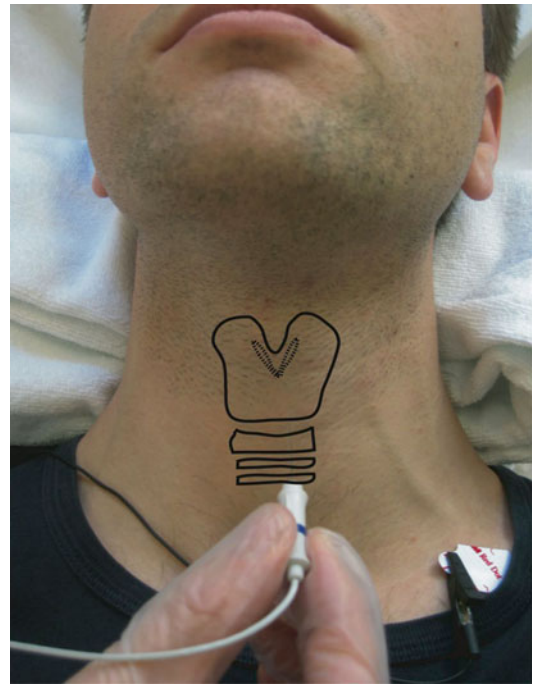

Fig. 20.3 Laryngeal electromyography in the awake patient. By directing a standard EMG needle electrode superior and lateral to the site of insertion through the cricothyroid membrane, it is possible to record motor unit activity from the thyroarytenoid and lateral cricoarytenoid muscles (innervated by the recurrent laryngeal nerve). To investigate superior laryngeal nerve innervation, the electrode is inserted into the cricothyroid muscle on the outer surface of the thyroid cartilage

given the high regenerative capacity of the RLN [62], together with collateral reinnervation by adjacent, intact nerve fibers [20]. The optimal time window for postoperative LEMG seems to be 2–4 weeks after nerve injury [28]. Interpretation and analysis of electrophysiological data requires the expertise of a trained neurologist or clinical neurophysiologist, while insertion of the needle electrodes into the appropriate intrinsic laryngeal muscles is best performed by an ENT specialist. LEMG thus requires the cooperation and coordination of different clinical resources. A consensus paper for LEMG guidelines addressing indications, technical considerations, implementation, and data interpretation was published by Volk et al. [63] in 2012.

Strategies for Preventing Nerve Injury

Several strategies are recommended for the prevention of RLN injury: (1) definite identification of the RLN before certain surgical maneuvers including clamping, transection or electrocauterization; (2) strict prohibition of the use of any energy-based device close to the nerve; and (3) *gentle* traction of the thyroid throughout surgery. Inadvertent clamping, transection, or thermal injury will occur less frequently if the above principles are strictly followed [56]. However, traction injury is still difficult to avoid and has become the most common mechanism of RLN injury. Several studies [48–50] have reported that about 70–80 % of nerve injuries are caused by traction injury. During a monitored thyroidectomy, traction injury will show a LOS after thyroid resection despite visual anatomical integrity of the RLN.

By means of IONM, the surgeon can identify and map the neural injury point, inspect the injury, and often define the likely cause (such as a clip or ligature on the nerve). The surgeon can sometimes remove the cause of injury and free

the nerve, potentially modifying the course of the lesion to permit early recovery prior to irreversible damage [48–50, 52, 64–70]. This makes the role of the surgeon crucial in preventing permanent nerve injury.

Intraoperative Corticosteroids

In 2006, Wang evaluated the role of intraoperative corticosteroids in preventing or treating postoperative RLN palsy [71]. He conducted a prospective study of 295 patients who underwent either total lobectomy or total thyroidectomy with or without the use of intraoperative corticosteroids. Data was analyzed for differences in postoperative temporary or permanent RLN palsy rates and recovery days [71]. If the surgeon identified an injured RLN through IONM, intraoperative corticosteroids were administered in one group and held in the other group. The rates of temporary and permanent RLN palsy were 5.7 % (11 out of 194) and 0.52 % (1 out of 194) for the group with corticosteroids and 6.9 % (12 out of 173) and 0.58 % (1 out of 173) for the group without corticosteroids. This difference did not reach statistical significance. Among those 23 patients who recovered from RLN palsy, the mean time to recovery was significantly shorter for patients receiving intraoperative steroids (28.6 vs. 40.5 days, $P=0.045$). To summarize, a single dose of intraoperative corticosteroids did not produce any benefit in terms of reducing the postoperative temporary/permanent RLN palsy rate, but it did shorten the recovery time for patients suffering from temporary RLN palsy [71].

Continuous Intraoperative Neuromonitoring

Real-time continuous IONM has been designed for seamless monitoring of nerve function during the entire course of surgery [68, 69]. Recent studies also reveal its potential to help detect adverse signal change earlier to prevent imminent traction injury [60, 70, 72–74]. During continuous vagal nerve stimulation, Schneider et al. [70] observed that durable decreases in EMG amplitude paralleled by increases in latency were found before EMG signal degraded to definitive LOS with postoperative RLN palsy. In animal experiments [60], authors found that the EMG signal showed a progressive change with combined amplitude decrease and latency increase during acute traction distress. The EMG signal showed a near full recovery (92–100 %) if traction stress was relieved before LOS, with worsened recovery if prolonged or repeated traction was applied on the nerve. The combined events (amplitude decrease and latency increase) alert surgeons to detect the mechanism of injury and correct certain surgical maneuvers immediately to prevent irreversible nerve injury.

Pharmacological Therapy After RLN Injury

A mixed injury of demyelination (neuropraxia) and axonotmesis within the macroscopically intact RLN has a worse prognosis than demyelination alone, because of the need for regeneration and reinnervation of the target. Reinnervation of the intrinsic laryngeal muscles following axonotmesis is considered problematic [75], due to misguided, unorderly regeneration and, perhaps also, collateral reinnervation originating from adjacent, intact nerve fibers [20]. Pathologic reinnervation leads to changes in the somatotopic map that are not in line with normal vocal fold function.

In vitro, it has been shown that the pace of the regenerating axon is regulated at the tip (growth cone), where movement is highly dependent on regulation of calcium ions [76, 77]. Altering the intracellular concentration of calcium ions has been shown to strictly correlate with the ability of the growth cone to sprout [77]. The regulation of intracellular calcium is also closely linked to the actions of the voltage-gated calcium channels present in the cellular membrane [77]. In vivo, it has been confirmed that transient quick calcium currents across the membrane of the growth cone occur with a certain frequency. If the transient calcium currents are inhibited to some extent, the pace of axonal elongation increases [78–80]. Nimodipine, an antagonist to the flow of L-type voltage-gated calcium channels, has been

evaluated in rodent models, and is a good pharmacologic treatment option because it penetrates the blood–brain barrier better than most other calcium flow antagonists [81]. Experimentally, after systemic administration of nimodipine, an improved regeneration and functional recovery has been achieved after injury to the sciatic [63], facial [73, 74, 82], hypoglossal [83], and RLNs [84]. In patients, nimodipine has been evaluated after recurrent laryngeal [28, 85–87] and facial nerve injury [88–92], with promising functional outcomes. Taken together, there is substantial evidence that the administration of nimodipine after axonal injury to a peripheral nerve probably improves functional outcomes. The level of evidence for the use of nimodipine for intraoperative RLN injury is still modest. Only a fraction of patients with postoperative RLN paresis would benefit from a regeneration-promoting treatment (i.e., cases with axonotmesis).

Axonotmesis within a peripheral nerve requires regeneration. Both the distal part of the peripheral nerve (beyond the axon break) and the denervated target muscle provides a significant increase in growth factors to promote regeneration. A gradient of growth factors develops towards the intended regeneration target muscle, guiding axonal elongation during peripheral nerve regeneration. Exogenous addition of growth factors is highly protective of motor neurons in the brainstem and also improves peripheral regeneration. There have been some successful experimental attempts to add growth factor to the crushed or transected RLN with improved regeneration and outcome. Overall, support for the use of exogenously administered growth factor following peripheral nerve injury is extensive [42–45, 93–97]. However, no clinical drug is on the market for growth factor treatment after peripheral nerve injury. This may be due to accompanying fear of the unexpected long-term effects of growth factor treatment such as tumor development.

Both calcium flow antagonists and growth factors are potentially beneficial when there is a degree of axonotmesis within the electrophysiologically silent RLN during surgery. The majority of patients, however, will have only a demyelination injury, which recovers spontaneously. Some demyelination injuries are caused by local swelling of the RLN, e.g., at the descent below the inferior constrictor muscle or at the ligament of Berry. Therefore, there has been speculation that steroids may be of benefit to reduce demyelination. Although steroids have been shown to be of low benefit (or even hazardous) after axonal damage to the facial nerve [98, 99], in general the potential to improve outcomes is thought to occur through reducing edema of the nerve or surrounding tissue. In clinical prospective studies there is conflicting data about the benefit of steroids in RLN injury, with descriptions of the absence of effect as well as a potential improvement in outcome using preoperative injections of dexamethasone [71, 100]. In conclusion, it is reasonable to speculate that steroid therapy may be advantageous to reduce edema (when needed) but is less likely to affect axonal regeneration, where other more specific drugs are needed.

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Intraoperative Neural Injury Management: Transection and Segmental Defects

21

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Abstract

Patients who have undergone a transection or segmental resection of the recurrent laryngeal nerve (RLN) suffer from hoarseness, reduced phonation time, and aspiration. These injuries can be repaired with a direct anastomosis of the transected nerve ends, free nerve grafting to fill the defect, or an ansa cervicalis-to-RLN anastomosis. Reports have indicated that following nerve reconstruction, patients' voices typically improve, although the vocal cords remain immobile through misdirected regeneration. Despite this, reinnervated vocal cords demonstrate less muscular atrophy. Voice recovery can be obtained regardless of preoperative vocal cord status, age, or gender when nerve reconstruction is performed with a variety of reconstruction modality techniques.

The RLN may be transected accidentally during thyroid or neck surgery, or unintentionally during dissection of the nerve in dense scar. A segment of the nerve may be resected during thyroid cancer surgery. Thyroid cancer often invades the RLN, causing vocal cord paralysis. In most of these cases, the segment of the nerve involving the tumor must be resected. Since reconstruction of the RLN during the thyroid surgery is optimal, all thyroid surgeons should be familiar with different reconstruction techniques.

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Recurrent laryngeal nerve • Vocal cord paralysis • Direct anastomosis • Free nerve grafting • Ansa cervicalis • Ansa cervicalis-RLN anastomosis • Phonatory function • Maximum phonation time • Phonation efficiency index

Introduction

Patients who have undergone a transection or segmental resection of the recurrent laryngeal nerve (RLN) suffer from hoarseness, reduced phonation time, and aspiration. These injuries can be repaired with a direct anastomosis of the transected nerve ends, free nerve grafting to fill the defect, or an ansa cervicalis-to-RLN anastomosis. Reports have indicated that following nerve reconstruction, patients' voices typically improve, although the vocal cords remain immobile through misdirected regeneration. Despite this, reinnervated vocal cords demonstrate less muscular atrophy. Voice recovery can be obtained regardless of preoperative vocal cord status, age, or gender when nerve reconstruction is performed with a variety of reconstruction modality techniques.

The RLN may be transected accidentally during thyroid or neck surgery, or unintentionally during dissection of the nerve in dense scar. A segment of the nerve may be resected during thyroid cancer surgery. Thyroid cancer often invades the RLN, causing vocal cord paralysis (VCP). In most of these cases, the segment of the nerve involving the tumor must be resected. Since reconstruction of the RLN during the thyroid surgery is optimal, all thyroid surgeons should be familiar with different reconstruction techniques.

Direct Anastomosis of the Transected Nerve

Following RLN transection, direct anastomosis of the nerve ends is the most straightforward reparative technique. Although this is most easily achieved after simple transection injuries, some short segment RLN resections may also be amenable to direct anastamosis provided the nerve ends can be brought together without undue tension. In 1909, Horsley first reported on RLN neurorrhaphy after a gunshot transection injury, noting normal postoperative function [1]. Since that time, there have been conflicting reports regarding functional outcomes after RLN neurorrhaphy, with some studies reporting successful results [2, 3] and others noting minimal [4–6] or no [7, 8] return of function. However, most recent studies suggest that vocal outcomes of neurorrhaphy are equivalent to those of other RLN reconstructive methods and are superior to vocal outcomes following nerve resection without reconstruction [9, 10].

There are many reported techniques for repair of a transected RLN, and outcomes are optimized if the repair is done at the time of injury [11]. A report of RLN transection in rats showed that 10 weeks after RLN transection, total thyroarytenoid muscle area decreased by almost 50 % and nerve terminals in the muscle disappeared completely 24 h after denervation, although 70 % of acetylcholine receptors were still preserved [12]. However, the exact length of time between initial nerve injury and nerve reconstruction procedures in humans that will still allow recovery of useful laryngeal muscle function remains uncertain. Following RLN transection and re-anastomosis in rats, electromyography (EMG) shows that polyphasic motor unit action potentials (MUAPs) appear around 4 weeks due to early reinnervation and reach maturity by 16 weeks [13]. EMG activity precedes any observable vocal cord motion by approximately 4–6 weeks.

The RLN is composed of both motor and sensory fibers. Motor fibers supply both adductor and abductor muscles of the laryngeal apparatus. In the brainstem, topographic localization of

these fibers is possible. In the peripheral nervous system, however, such topography is lost. Thus, abductor and adductor fibers have no spatial segregation but instead run scattered within the RLN fascicle. Technically, direct anastomosis is performed in an end-to-end fashion using two to three sutures of 7/0, 8/0, or 9/0 monofilament thread, generally under microscopic control. A recent study suggests that final voice outcome is unaffected by the nerve reconstructive method used, thickness of suture thread, or use of magnification during the operation [9]. Nerve ends should not be under any tension when performing the repair and, if significant tension is noted despite maximal mobilization of proximal and distal limbs, a cable graft should be considered.

Although RLN neurorrhaphy is technically straightforward, the lack of abductor/adductor topography within the RLN nerve sheath means that correct alignment of abductor and adductor nerve fascicles is not possible with current microsurgical techniques. Thus, misdirected (aberrant) regeneration readily occurs whereby abductor and adductor fibers mix during the phase of regrowth [14, 15]. Nerve fibers to laryngeal adductor muscles outnumber abductor fibers by approximately 4:1, and EMG after end-to-end RLN anastomosis have shown that adductor function is preferentially restored with limited abductor function [14, 16, 17]. Vocal folds tend to be fixed in the midline due to the stronger adductor muscle function, and voluntary vocal fold activation, particularly for tasks requiring vocal fold abduction, causes simultaneous activation of antagonistic adducting and abducting muscle forces (i.e., synkinesis) with resultant vocal fold immobility [18]. However, the presence of functional motor units prevents vocal fold muscular atrophy and improves tension during phonation, resulting in an improvement in hoarseness as compared to people with nerve transection who do not undergo re-anastomosis. Research on the utility of neurotrophic factors in re-innervation and vocal fold function is ongoing, with the hope that eventually re-innervation will be induced to occur in an orderly fashion, allowing re-establishment of pre-injury innervation patterns [13, 19].

Repair of the Segmental Defect

Not all cases of segmental nerve involvement by tumor necessarily require full segmental resection of the RLN. Sometimes in patients with a functional vocal cord preoperatively, intraoperatively the RLN may still be found to be involved by thyroid tumor over a segment of the nerve. In such cases, we try to preserve the nerve with sharp dissection off the tumor rather than full segmental resection. The preserved nerves may become thinner than their original thickness as the result of extensive dissection, which we call *partial layer resection* of the RLN [20]. A 2014 study revealed that when the nerves could be preserved with the partial layer resection procedure, vocal cord function recovered in 83 % of 18 patients [20].

In cases of true segmental resection of the RLN, the following procedures have been applied for repair: free nerve grafting to fill the defect, ansa cervicalis-to-RLN anastomosis, and vagus-to-RLN anastomosis, yielding results similar to that of direct anastomosis [9, 10].

Free Nerve Grafting

The graft for free nerve grafting can be harvested from sensory or motor nerves of a thickness similar to that of the RLN. The supraclavicular nerves, transverse cervical nerve, auricular nerves, and ansa cervicalis can be the donor site of the graft in thyroid and neck surgery. The outcomes of free nerve grafting have been similar to those of direct anastomosis of the RLN [9, 10].

The amount of time necessary for the recovery of phonation depends on the distance from the central anastomosis to the laryngeal muscles. Also, free nerve grafting requires two anastomoses. Thus, free nerve grafting might require a slightly longer time for recovery compared to direct anastomosis or ansa cervicalis-to-RLN anastomosis. In addition, free nerve grafting may be very difficult or practically impossible in certain cases, such as those defects extending into the mediastinum.

Ansa Cervicalis-to-RLN Anastomosis

The ansa cervicalis nerve forms a loop in front of the internal jugular vein and gives branches to the sternohyoid, sternothyroid, and omohyoid muscles. It is a motor nerve located in the vicinity of the RLN and is active during respiration and phonation [21]. Its thickness is similar to that of the RLN. Sacrificing the ansa cervicalis has resulted in no obvious functional or cosmetic sequelae. Miyauchi independently reported the ansa cervicalis-to-RLN anastomosis in 1990 [22]. Crumley and Izdebski described two cases using this reconstruction technique in 1986 [23]. The outcomes of ansa cervicalis-to-RLN anastomoses are quite similar to those of direct anastomosis of the severed RLN, showing immobile vocal cords fixed at the midline but with less atrophy compared to vocal cords without neural repair [9, 10, 23, 24]. We have not seen paradoxical movement of the cords following this procedure. Other investigators have confirmed voice recovery following ansa cervicalis-to-RLN anastomosis with perceptual and acoustic evaluations [25–27].

Ansa cervicalis-to-RLN anastomosis requires only one anastomosis, which can be performed in an easily accessible location near the larynx. Thus, the time needed for the recovery of phonation after surgery should be shorter in patients with an ansa cervicalis-to-RLN anastomosis compared to patients with a long free nerve grafting.

In patients with massive lymph node metastases, the ipsilateral ansa cervicalis may not be available. In such cases, the contralateral ansa cervicalis can be used for the anastomosis [28]. In elderly male patients, the length of the ansa cervicalis may be insufficient to reach the peripheral stump of the RLN because of the lower position of the larynx and the larger trachea in this group compared to young female patients. In such cases, interposing a free nerve graft between the ansa cervicalis and the RLN may be a solution to this problem.

The technique of the ansa cervicalis-to-RLN anastomosis can be applied to VCP caused by other etiologies such as thymic cancer, tracheal cancer, lung cancer, esophageal cancer, aortic aneurysm, cervical vagal tumors, or surgeries for these lesions [10, 22]. The ansa cervicalis-to-RLN anastomosis can be a technically straightforward procedure performed in the neck, often in a relatively undissected area. However, the risks and benefits should be cautiously evaluated before applying this procedure in these cases.

Vagus-to-RLN Anastomosis

We performed vagus-to-RLN anastomoses in two patients who had segmental resection of the RLN and the ipsilateral cervical vagus because of thyroid cancer invasion [9]. The patients' voices both recovered following surgery. The vagus nerve in the neck is composed of parasympathetic, sensory and motor nerve fibers. Since the motor component travelling to the RLN is reported to reside medially within the vagus in the lower neck, a surgeon at Kuma Hospital has performed a procedure on several patients in which the cervical vagus is split and the medial half of the nerve is anastomosed to the peripheral stump of the RLN [29]. The voices of some of these patients who underwent this procedure recovered. These vagus-to-RLN anastomoses are not recommended except for rare occasions, since the data regarding these procedures is insufficient to make a definitive recommendation.

Laryngeal Approach

Thyroid cancer often invades the RLN near ligament of Berry. In such cases, the RLN is resected at its laryngeal entry together with the cancer. One might think that nerve reconstruction in such cases is impossible, since the distal stump of the nerve is not seen. However, if the inferior pharyngeal muscle is divided by the surgeon along the lateral edge of the thyroid cartilage, the distal branches can be found behind the thyroid cartilage [10]. The typical innervation of the branches is as follows: the anterior branch innervates the adductor muscles, the middle branch innervates the abductor muscles, and the posterior branch is a sensory nerve forming Galen's anastomosis with a branch of the superior laryngeal nerve (SLN). The anterior branch should be selected for reconstruction to improve phonation.

The procedure described above is possible, but finding the distal stump of the nerve is often difficult. We modified the procedure with a laryngeal approach that involves dividing the inferior pharyngeal muscle before resecting the tumor [30]. With this technique, it may be possible to preserve the RLN with sharp dissection. An approach from both the distal and proximal sides of the RLN involved by tumor makes the dissection easier than approaching the nerve from only one side. If the nerve segment does end up requiring resection with the tumor, reconstruction then becomes easier since the distal branch of the RLN is already secured.

Evaluation After Reinnervation

Laryngoscopic examination does not adequately assess phonatory recovery following nerve repair. The most practical and easiest method of assessment is the periodic measurement of the patient's maximum phonation time (MPT) [9, 10]. Periodic measurements clearly show an increase in MPT with improvement in the voice. The phonation efficiency index (PEI) is the ratio of the MPT to lung vital capacity (s/L), which indicates the effectiveness of the larynx in converting exhaled air into sound energy [9]. A significant gender difference in MPT was observed in both normal subjects and in patients with VCP, but the gender difference disappeared when the PEI was calculated, indicating that the PEI is suitable for evaluating laryngeal phonatory function regardless of gender [9].

The MPT at 1 year after surgery in patients who underwent RLN reconstruction was significantly longer than the MPT in patients with VCP without nerve repair and was comparable to that in normal subjects [9]. Voice recovery following nerve repair as assessed using the PEI at 1 year after surgery was not affected by the presence or absence of preoperative VCP, gender, age at surgery, method of reconstruction, thickness of the suture material, or use of magnification [9].

Summary

In patients who undergo transection or segmental resection of the RLN, nerve reconstruction has resulted in voice recovery even though the vocal cord remains immobile. Voice recovery is obtained regardless of preoperative vocal cord status, age, or gender and is seen with any of the nerve reconstruction modalities described. Since immediate reconstruction of the nerve at the time of injury is optimal, and considering that RLN injury is a potential complication of thyroid surgery, all thyroid surgeons should be familiar with these techniques.

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Nerve Management: Invasive Disease

22

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Abstract

Thyroid cancer which invades the recurrent laryngeal nerve (RLN) and/or visceral axis (esophagus, trachea, larynx) is rare, and the patient with invasion of the recurrent nerve may be completely asymptomatic. Several risk factors and clinical presentations should lead the clinician to perform a thorough and systematic preoperative clinical and radiologic workup, in order to diagnose invasive disease, plan surgery, and inform the patient as to possible consequences of surgery. The recommended preoperative workup of patients with suspected invasive disease will be discussed in this chapter, as well as the pathophysiology of nerve invasion and currently recognized risk factors. There are a number of key factors to consider when deciding intraoperatively to resect, sculpt, or preserve the RLN which are outlined in several algorithms suggested in this chapter.

Keywords

Thyroid cancer • Recurrent laryngeal nerve • Larynx • Trachea • Neuromonitoring

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Introduction

Thyroid cancer which invades the recurrent laryngeal nerve (RLN) and/or visceral axis (esophagus, trachea, and larynx) may be completely asymptomatic. Several risk factors and clinical presentations should lead the clinician to perform a thorough and systematic preoperative clinical and radiologic workup, in order to preoperatively diagnose invasive disease, plan surgery, and inform the patient as to the possible consequences of surgery. Intraoperatively several scenarios are possible, based on the type of nerve invasion which can vary from superficial invasion of the epineurium, amenable to shaving, to through-and-through tumor involvement of all of the nerve layers, in which preservation of the nerve is not possible with complete tumor resection. The algorithm for preoperative and intraoperative decision-making and operative strategies will be discussed in this chapter, taking into account the functionality of the nerve, the type of tumor invasion, and other oncologic prognostic factors involved for differentiated and medullary thyroid carcinomas.

Preoperative Workup

Preoperative workup of patients with the diagnosis, or suspicion of thyroid cancer must include assessment of vocal fold function (Fig. 22.1). This allows for risk stratification of patients with suspected invasive thyroid disease and provides the basis for preoperative counselling.

Preoperative history must elicit symptoms of voice abnormalities and the risk factors for prior injury to the RLN (e.g., history of cervical, laryngeal, or mediastinal surgery). However, voice complaints alone may not identify all patients who are at risk for vocal fold paralysis. When nerve injury is due to a slowly evolving process, compensation of the contralateral vocal fold alleviates voice symptoms. In a retrospective analysis, sensitivity of voice complaints for identifying patients with vocal fold paralysis was 0.68, with specificity of 0.9. This yielded a positive predictive value of 0.38 and a negative predictive value of 0.98 for history alone [1]. Voice and airway assessment should focus on the presence of stridor, breathiness, roughness, strain, low volume, and inability to elevate pitch. Other symptoms that should alert the physician for possible invasive disease include dyspnea, dysphagia, and hemoptysis. Neck exam findings such as a fixed thyroid mass and/or extensive lateral compartment adenopathy increase the risk of invasion.

Indirect visual examination of the larynx with a flexible fiberoptic endoscope is currently the recommended method of evaluating vocal fold movement preoperatively and postoperatively in patients with invasive thyroid cancer according to the recently published American Head and Neck Society (AHNS) guidelines [2]. Endoscopic evaluation has the advantage over mirror laryngoscopy, as it provides improved visualization and allows for digital recording of the exam. This documentation facilitates review of laryngeal function before and after surgery, and is a powerful tool for patient education. Many professional societies recommend preoperative laryngeal examination in *all* patients with thyroid cancer, although the most recent guidelines from the American Thyroid Association (ATA) only recommend laryngeal examination in patients with voice or swallowing symptoms, suspicion of invasive disease, or history of neck surgery, due to the low incidence of preoperative laryngeal paralysis in asymptomatic patients [3].

Preoperative finding of vocal fold paresis or paralysis significantly increases the risk of encountering invasive thyroid malignancy intraoperatively. Among patients with invasive thyroid cancer, as many as 70 % have abnormal vocal fold movement recorded on preoperative laryngoscopy [4]. This finding can influence surgical planning, patient counselling, and the risk of airway complications associated with bilateral vocal fold paralysis. Paralysis may not be limited to the side of the lesion. Diagnosis of prior iatrogenic or idiopathic paralysis of the vocal fold contralateral to the thyroid tumor may be extremely important in guiding intraoperative decision-making on RLN management. In one study retrospectively evaluating patients with

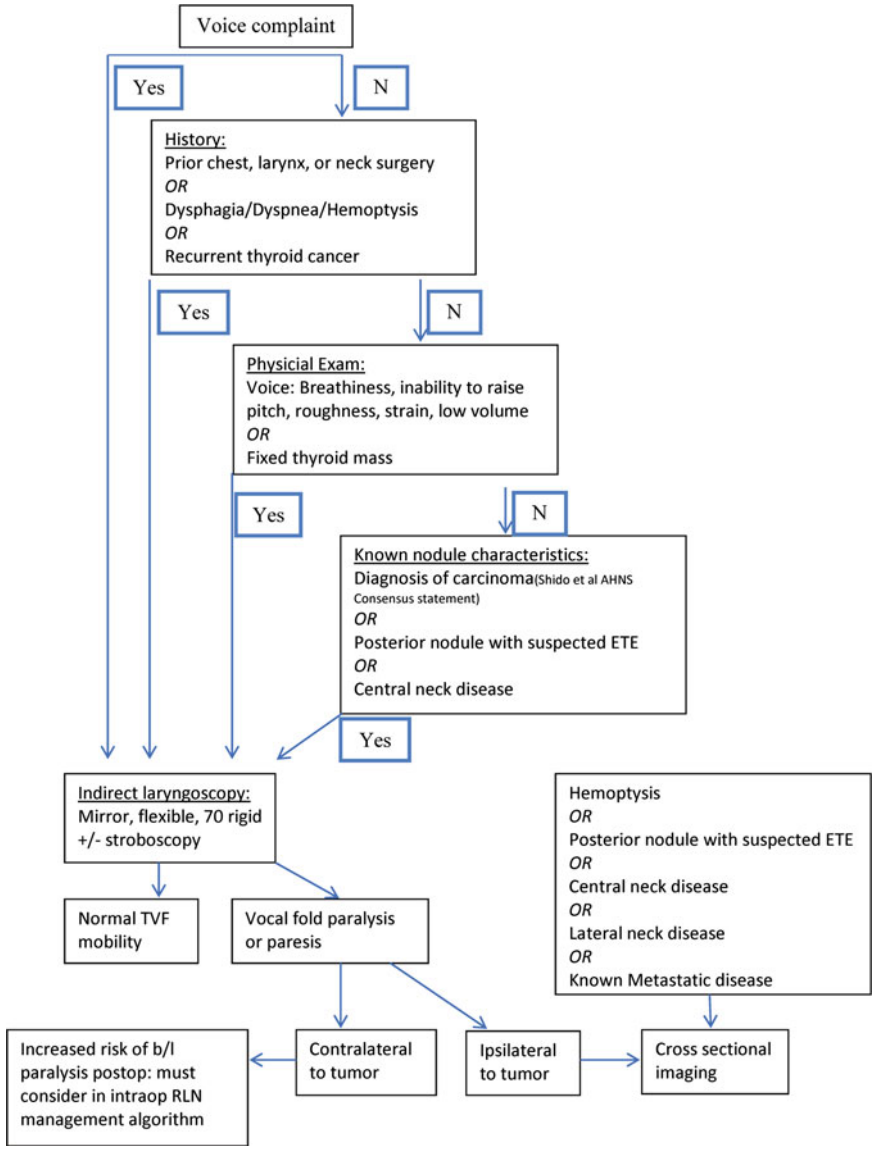

Fig. 22.1 Algorithm for preoperative workup

preoperative vocal fold paralysis, 23 % (5/22) had vocal fold palsy/paresis contralateral to the thyroid lesion. In addition, intraluminal invasion of the airway can be diagnosed preoperatively if an infraglottic or subglottic asymmetry is appreciated on indirect laryngoscopy.

Preoperative identification of RLN paralysis or paresis suggests invasive thyroid malignancy, and should prompt further workup with cross-sectional imaging. While ultrasound is excellent for workup and surveillance of thyroid disease, its sensitivity for identifying tracheal invasion varies from 42.9 to 91 % [5, 6]. Gross extrathyroidal extension posteriorly toward the tracheoesophageal groove and extensive involvement of central compartment lymph nodes raise concern for RLN invasion and should prompt additional imaging. CT or MRI with contrast is recommended for assessment of local invasion. The relationship of the tumor to the tracheal wall and the interface between the gland and

the esophagus are well defined on cross-sectional imaging. MRI finding of effacement of the fatty tissue in the tracheoesophageal groove suggests RLN involvement [5]. Extensive involvement of the lymph nodes of the central neck heightens the concern for RLN invasion [7].

In addition, cross-sectional imaging is helpful in defining the extent of metastatic disease in the lateral neck, workup of locally recurrent disease, thyroid carcinoma presenting with distant metastases, and malignancy with known aggressive biologic behavior as suggested by cytology or surgical pathology.

Invasion of the trachea, larynx, or esophagus can be diagnosed preoperatively, aiding in surgical planning and patient counselling. Office tracheoscopy or operative endoscopy may be indicated for further workup of intraluminal involvement when airway resection and reconstruction is anticipated. Appropriate preoperative risk assessment based on history and workup with indirect laryngoscopy and imaging minimizes unexpected surgical findings. An algorithm for preoperative risk assessment and workup of invasive thyroid disease is presented in Fig. 22.1.

Pathophysiology and Natural History of Invasive Disease

Invasion of the enveloping layers of the nerve (epineurium, perineurium, and endoneurium) by cancer cells, otherwise known as neurotropism, is common in some types of solid tumors including the squamous cell and adenoid cystic carcinomas of the head and neck as well as prostate, pancreatic, and colon adenocarcinomas. It is currently suggested that the tumor cells secrete neural cell adhesion molecules that facilitate specific spread of tumor cells in association with nerve tissue and that the tumor cells acquire the means of responding to molecular signals from nerve tissue, leading to reciprocal signals and neurotropism. Lymphatics do not penetrate the epineurium and thus do not contribute to perineural spread, which can be found in the absence of lymphatic or vascular emboli or metastases. The exact definition of perineural invasion (PNI) is a subject of debate. Many pathologists consider that invasion of any of the three nerve sheaths by tumor cells constitutes PNI, whereas others quantify PNI as involving at least 33 % of the circumference of the nerve [8]. The exact prognostic signification of PNI in various types of cancer is currently not well understood. Perineural invasion and perineural spread of thyroid cancer cells is rare and thyroid cancer is generally not considered as a particularly neurotropic tumor, although systematic recording of perineural invasion in thyroid cancer is often not performed and data is sparse [9]. In two studies, perineural involvement was found in no more than 6 % of the papillary thyroid cancers [10, 11]. In some instances, differentiated thyroid cancer and medullary cancer invade adjacent structures such as muscles, the trachea, and the esophagus, as well as the RLN. The exact mechanism for thyroid cancer involvement of neural tissue is not known. The phenomenon of RLN invasion may just be due to the generally aggressive and locally invasive nature of the disease and the proximity of the nerve to the thyroid cancer with extrathyroidal extension and/or to metastatic lymph nodes with extracapsular spread.

Types of Nerve Invasion

(a) Perineural invasion involving only the epineurium: In such cases, shaving the tumor off the external fibrous layer of the nerve may be technically possible, achieving a macroscopically complete resection. Kihara et al. also have reported a series of patients in whom a partial tangential nerve sheath resection was performed [12]. In these cases, recovery of a functional nerve was observed in 83 % of cases.

(b) Wide or circumferential but superficial invasion: In such cases, a wide surface of epineurium is involved. Shaving may still be possible, with preservation of the perineural layer, but sometimes with incomplete resection (small or microscopic remnant). This requires more extensive shaving and greater manipulation of the nerve, placing it at risk of traction injury. There is little data on the rate of recovery of

nerve function in these cases of nerve invasion. However, in a study of 18 patients by Kihara et al., 83% of patients were reported to have functioning vocal cords at 1 year after surgery [12].

(c) Invasion beyond the fibrous epineural layer with tumor extending into the perineurium or the endoneurium/around the axons themselves: In these cases, the tumor "dissects" into individual fibers of the nerve. A complete resection is technically impossible using a shaving technique due to the wide surface of contact between the nerve fibers and the tumor. Thus, dissection and preservation of the nerve is rarely possible without leaving a macroscopic remnant. However, there is little evidence suggesting a survival difference between complete resection of the tumor with nerve resection versus leaving a small remnant and administering adjuvant therapy [2].

Despite macroscopic and/or microscopic nerve invasion by tumor, the RLN may still be functional with normal laryngoscopy found in 45 % of cases of invaded nerves in the study by Kamani et al. [13]. In this study, even in the presence of abnormal preoperative laryngoscopy, some elicited electrical activity was observed on intraoperative nerve monitoring (IONM) in 33 % of cases. This data demonstrates a certain resistance of the axons themselves to functional disruption by tumor and shows the impact that intraoperative neuromonitoring (IONM) can have on intraoperative decision-making in cases with RLN invasion.

Risk Factors for Recurrent Laryngeal Nerve Invasion

Differentiated thyroid cancer (DTC) invading the visceral axis is estimated to occur in less than 5 % of cases of DTC [14]. McCaffrey et al. reported invasion of the RLN in 47% of patients with papillary thyroid carcinoma (PTC) [15].

Classic risk factors for invasive disease are a large tumor size and extrathyroidal tumor extension; invasive disease is also more prevalent in patients >65 or <18 years of age [16]. A correlation between a positive nodal status (N1) and esophageal invasion has been shown, but this correlation has not been studied for RLN invasion [16]. Aggressive histopathologic variants of DTC are more often invasive, but invasion by these tumors is also correlated to clinical risk factors (age, tumor size, and extrathyroidal extension), so that aggressive histology does not seem to be an independent risk factor for invasive disease [17]. Uptake on 18-fluorodeoxyglucose-positron emission tomography (18-FDG-PET) has also been correlated with more invasive disease, but, as with aggressive variants, it is also correlated with patient age, tumor size, and extrathyroidal extension [18]. The BRAF-V600E mutation has also been correlated with locally invasive disease, as have other gene expression abnormalities such as increased activation of the SRC tyrosine kinase [19]. Despite these known risk factors, invasion of the RLN remains rare and is often discovered intraoperatively.

Prognosis of Recurrent Laryngeal Nerve Invasion

Invasion of the RLN may not be a factor for decreased survival in cases of well-differentiated PTC, in which radioactive iodine can eradicate residual disease. In other instances, nerve invasion is associated with aggressive histopathological subtypes—tall cell, columnar cell, oncocytic, trabecular, insular, and poorly differentiated cancers—which have a more aggressive natural history with a higher rate of recurrence, distant metastases, and disease-related mortality. In one of the largest series of patients with locally invasive disease, McCaffrey et al. found that tracheal and esophageal invasion were the only significant factors related to overall survival [15]. RLN invasion, muscle invasion, or laryngeal invasion did not significantly affect survival. Deep tumor invasion, with preoperative RLN paralysis or invasion of the tracheal or esophageal mucosa, in which a shaving procedure is not possible, has been shown by Hotomi et al. to be a factor for lower disease-free and disease-specific survival [20]. However, invasion of the

trachea and the esophagus portended a worse prognosis than invasion of the RLN alone. Similarly, Ito et al. found that massive extrathyroidal extension with posterior extension invading structures other than the RLN, was the most important independent factor for recurrence-free survival [21]. Invasion of the RLN was only associated with a worse *disease-free* survival as compared to isolated muscle invasion or no invasion at all, but to a lesser degree than tracheal or esophageal invasion. Finally, Chan et al. found no survival difference between nerve resection and shaving tumor from the nerve in invasive disease, but patients with only debulking procedures showed decreased survival [22]. However, high level High-level evidence is lacking, due to the small size of the cohorts studied (due to the relatively rare nature of this disease), the retrospective nature of the studies, and the heterogeneity of the cohorts. Overall, RLN invasion alone seems to be a factor for decreased recurrence-free survival as compared to less invasive disease, however, it is not a factor in *disease-specific* survival [2]. In disease involving the visceral axis, the presence of distant metastases is the main factor impacting the disease-specific survival [20, 23, 24]. In a study of medullary thyroid carcinoma by Pilaete et al., preoperative RLN paralysis was shown to be related to lower disease-specific survival in univariate analysis, but the main prognostic factor remains preoperative calcitonin levels [25, 26].

Intraoperative Decision-Making: Nerve Sparing or Sacrifice

When confronted with a macroscopically invaded RLN, the following questions should be considered to evaluate the risks and benefits of nerve sparing versus nerve resection.

1. What is laryngeal function preoperatively? (normal, paresis, paralysis, preexisting contralateral paralysis)
2. What does the intraoperative EMG signal reveal? (normal, reduced amplitude, absent)
3. Is a macroscopically complete resection (R0/R1) possible?
4. Does complete resection require nerve resection or not?
5. Does leaving residual tumor on the nerve (R1 or R2 resection) put the patient at risk for local complications and/or death from disease?

The oncologic risk of leaving tumor (even a small residue, R1—microscopic residue—or R2—macroscopic residual tumor) should be weighed against disease extent and prognosis. If complete resection (R0) is a prognostic factor for disease-free survival or overall survival, complete nerve resection may be considered. The consequences of nerve resection such as a decrease in quality of life, assessment of contralateral nerve function need for tracheotomy and the risk of aspiration pneumonia in elderly.

Proposed algorithms for management according to presentation are shown in Figs. 22.2, 22.3, 22.4, 22.5, and 22.6. An example of a nerve encased by tumor is shown in Figs. 22.7 and 22.8, and an example of a nerve that may be preserved with a shaving procedure is shown in Fig. 22.9. (Table 22.1)

Preoperative Patient Information

Patients should always be warned of the risk of unilateral or bilateral RLN paralysis in bilateral thyroid surgery. When using IONM, the potential for staging planned bilateral surgery should also be thoroughly discussed should there be ipsilateral loss of signal (LOS) as recommended by the International Neural Monitoring Study Group [27]. Regardless of the presence or absence of preoperative laryngeal dysfunction, the possibility of nerve resection and surgical staging should be discussed in all patients with known risk factors, suspicion on preoperative imaging, and proven locally invasive disease. The benefits and risks of nerve resection versus preservation of the nerve with R1 or R2 tumor resection should be explained along with alternative therapies if a remnant tumor is left on the nerve.

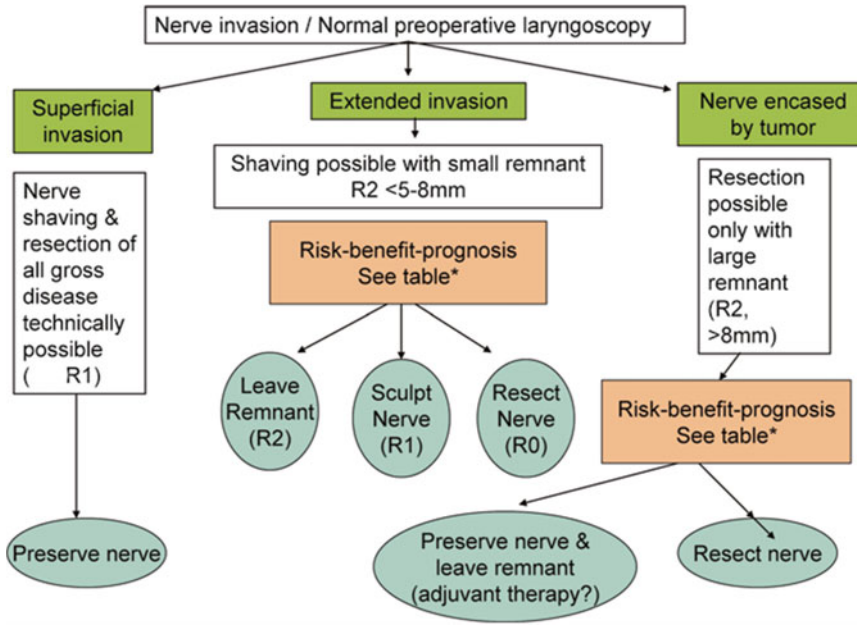

Fig. 22.2 Algorithm to aid in intraoperative decision-making when there is normal laryngeal function preoperatively

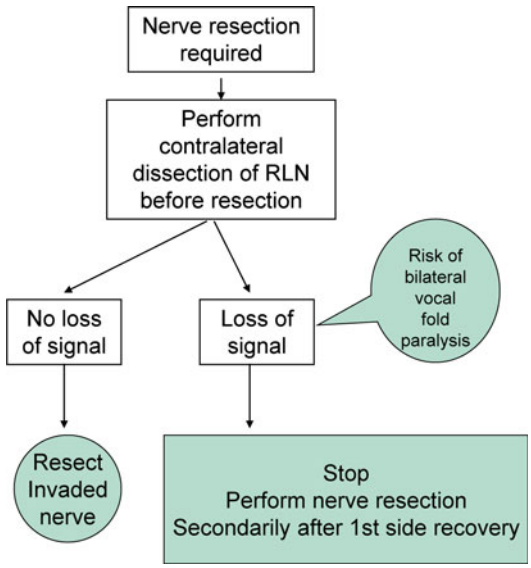

Fig. 22.3 Using intraoperative neuromonitoring to decrease the risk of bilateral recurrent nerve paralysis in invasive disease

Some patients will opt for aggressive and complete tumor resection, if possible, to optimize disease-free survival, prioritizing cure over voice outcomes. Quality of life is related to voice, but also to cancer issues such as need for close follow-up, fear of persistent/recurrent cancer, and fear of death. The prognosis of disease needs to be ascertained preoperatively as clearly as possible in order to determine the risk–benefit ratio as accurately as possible.

Patients should be informed about the expected outcomes. When nerve shaving or sculpting (nerve macroscopically intact +/– EMG normal or subnormal) is performed, vocal fold paralysis or paresis is still possible (neuropraxia or traction injury) but is most likely temporary with some degree of functional recovery expected. With nerve resection, voice may be normal or subnormal for approximately the first 3 weeks, until a certain degree of vocal fold atrophy (if any occurs) sets in. Aspiration may be a problem in the first weeks following surgery, but generally improves over the course of a few months. Some spontaneous improvement of voice may occur over time with synkinesis or other forms of compensation. Tolerance of the dysphonia is variable and depends on patient factors such as age, profession, general voice use, and voice expectations.

Finally, patients should be informed about the various rehabilitative procedures available for treating unilateral or bilateral vocal fold paralysis. Details of the techniques, risks, and functional outcomes, are beyond the scope of this chapter.

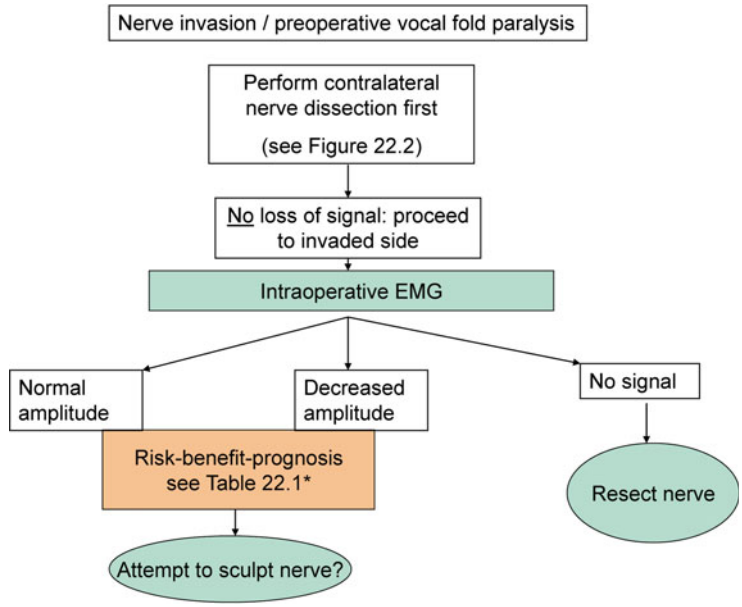

Fig. 22.4 Using intraoperative neuromonitoring to preserve an electromyographically functional or partially functional nerve (which may recover clinical function postoperatively)

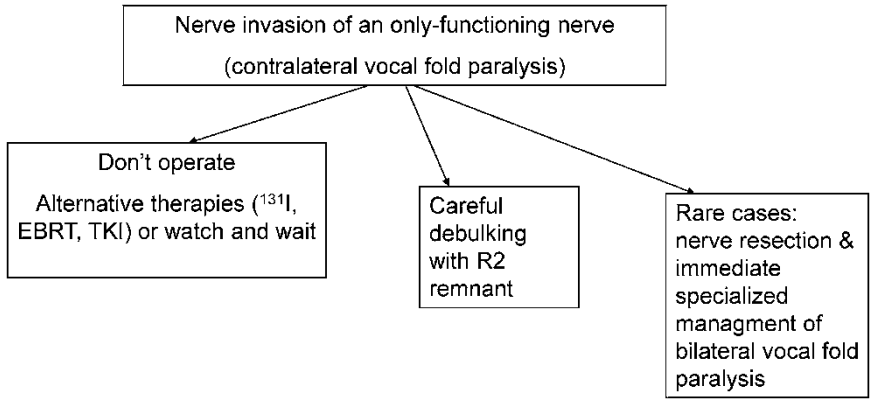

Fig. 22.5 Options for cases with preoperative unilateral vocal fold paralysis on the side contralateral to the invasive tumor: the choice between avoiding or accepting and managing bilateral vocal fold paralysis

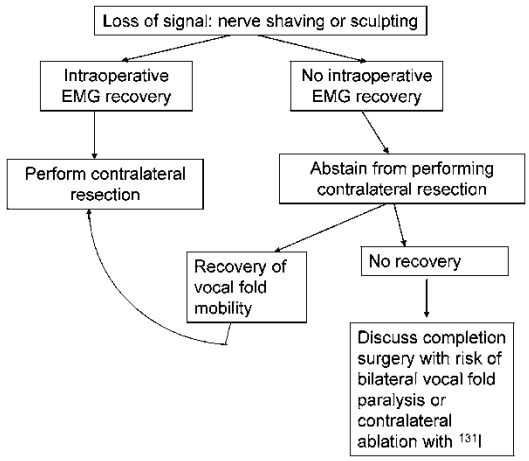

Fig. 22.6 Nerve invasion discovered intraoperatively and loss of electromyographic signal during dissection (risk of bilateral recurrent nerve paralysis)

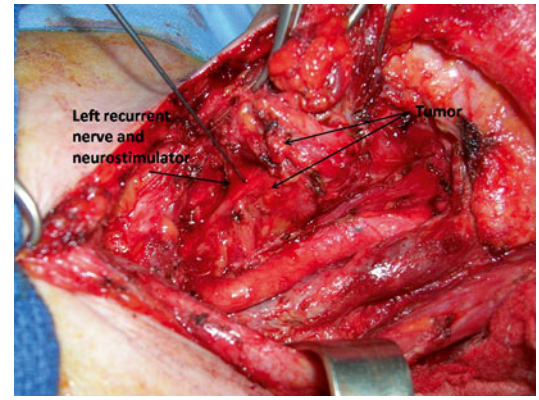

Fig. 22.7 Intraoperative view of a functional left recurrent laryngeal nerve completely encased by tumor

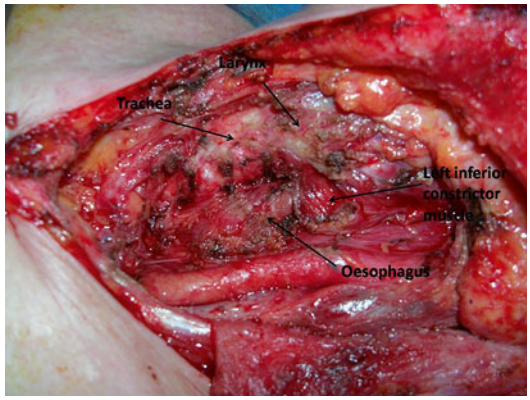

Fig. 22.8 View post-resection. Nerve resection was decided based on prognostic factors (see Table 22.1 and the text). Note the superficial resection of the esophageal muscle, as well as resection of the recurrent laryngeal nerve

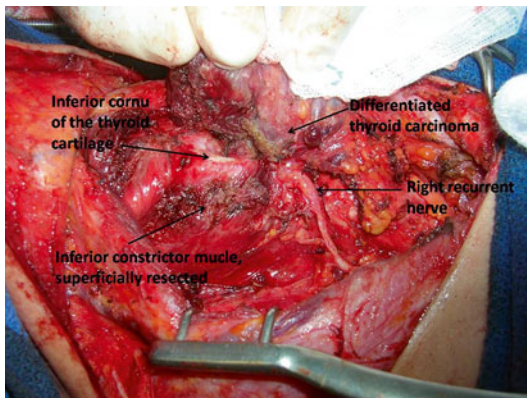

Fig. 22.9 Intraoperative view of a tumor superficially involving the nerve sheath of the right recurrent laryngeal nerve. A nerve-sparing procedure (shaving) was performed and nerve function was normal postoperatively

Table 22.1 Factors to consider when deciding to spare or to sacrifice the recurrent laryngeal nerve

Factors in favor of nerve sparing (even if incomplete tumor resection)	Factors in favor of nerve sacrifice (with complete tumor resection) to improve disease-free or overall survival
Young patients, papillary carcinoma	Aggressive histopathological variants
Generally iodine-avid	Iodine-refractory disease (recurrences)
Several therapeutic administrations of iodine may be necessary (with risk of secondary tumor/leukemia for high cumulative doses)	Previous external beam radiation therapy
	Normal contralateral vocal fold function
	No distant metastases
Efficiency of adjuvant therapy (iodine or external beam radiation therapy)	
Elderly patients (increased risk of aspiration pneumonia)	
Reduced pulmonary capacity, chronic bronchitis (lower tolerance of microaspiration)	
Contralateral vocal fold paralysis	
Voice professionals or patients expressed wishes	
Patients with known distant metastases	

Medullary Thyroid Carcinoma

The same basic algorithms generally apply to medullary thyroid carcinoma (MTC), with the question of resection arising in more cases due to the absence of effective adjuvant treatment such as radioiodine. Prognosis for MTC takes preoperative calcitonin levels into account. For example, a 50 % rate of biological cure has been shown for patients with a preoperative calcitonin level over 300 pg/mL, and a low rate of biological cure with preoperative calcitonin levels >500 pg/mL [26]. In patients with high preoperative calcitonin levels, and a low chance of biological cure, nerve sparing procedures (+/- EBRT) are probably the best option. Complete resection in the neck optimizing postoperative calcitonin levels, however, may allow restaging of the patient into a more favorable prognostic category [28]. Finally, locally invasive disease may contraindicate the use of small-molecule tyrosine kinase inhibitors (particularly in the context of clinical trials), and if such treatment is needed, complete resection in the neck may be warranted.

Overview

- Invasive disease is rare and may be completely asymptomatic.
- Suspicion of invasive disease requires a meticulous preoperative workup and a careful and thoughtful preoperative consultation with the patient including the important preoperative laryngeal exam.
- Resection of a nonfunctional recurrent laryngeal nerve involved with tumor with no intraoperative EMG signal is recommended to optimize complete tumor resection.
- Preservation of a functional recurrent laryngeal nerve—on preoperative laryngoscopy or intraoperative EMG—should be attempted in all cases; however in rare instances it is preferable to resect a functional nerve to optimize tumor resection and oncologic results.

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Postoperative Management of Unilateral RLN Paralysis

23

Phillip C. Song, Inna Hussain, Jean Bruch, and Ramon A. Franco Jr.

Abstract

The most common cause of recurrent laryngeal nerve (RLN) dysfunction is iatrogenic injury, and recognition and management of RLN injury after surgery should be a part of the head and neck surgeon's armamentarium. This chapter discusses the examination and workup of RLN injury, management of vocal fold paresis/paralysis, and interventions that can be offered to the patient in the postoperative setting.

Keywords

Vocal cord paralysis • Vocal cord paresis • Injection laryngoplasty • Medialization • Thyroplasty • Laryngeal EMG • Stroboscopy

Introduction

A recent study suggests that iatrogenic injury after surgery now represents the most common etiology [1, 2] of unilateral vocal fold paralysis (VFP), surpassing neurological disease, iatrogenic paralysis, and neoplasms. Although thyroidectomy continues to be a major cause of iatrogenic vocal fold immobility (VFI) and is still the most common etiology for bilateral VFI, recent studies have shown that other surgeries, such as anterior cervical spine fusions and carotid endarterectomies, have a greater contributing role towards unilateral vocal fold injury. Rosenthal et al. in their 20-year longitudinal study found that that iatrogenic injury was the most common (37 %) etiology for VFI and that non-thyroidal surgeries, primarily cervical spine fusions, were the etiology of the unilateral VFI twice as often as thyroidectomies [1]. Merati et al. found similar findings with a 27.5 % rate following cervical spine procedures compared to 15 % after thyroidectomy. A stretch injury of the recurrent laryngeal nerve (RLN), more so on the right due to its more oblique course, is the likely mechanism of injury during cervical spine surgery [2]. Other procedures associated with VFI

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include cardiac surgeries, esophagectomy, neck dissections, pulmonary resection, and mediastinoscopy. Even endotracheal intubation has been associated with VFI due to nerve compression between an inflated cuff and thyroid cartilage [3] and has been also implicated in arytenoid dislocation [4]. Along with the expected clinical outcomes such as dysphonia and dysphagia, VFI has been associated with an increased length of hospitalization, higher hospital mortality, and it has become an independent predictor of pulmonary complications especially in the cardiothoracic postoperative patients [5, 6].

Evaluation

Clinical presentation following unilateral RLN injury can vary widely with the most common symptom being hoarseness, followed by dysphagia and aspiration. The degree of symptom depends on the resting position of the vocal fold. The RLN supplies motor innervation to the intrinsic muscles of the larynx with the exception of the cricothyroid muscle (CTM), as well as sensory innervation to the larynx below the level of the vocal folds. There is believed to be an anastomosis between the RLN and superior laryngeal nerve (SLN) branches via the nerve of Galen as well as bilateral RLN innervation through the interarytenoid muscle. Severity of functional impairment postoperatively will be influenced by these factors as well as the nature of the injury (i.e., neurapraxia vs. axonal injury), regenerative capacity of the nerve, resting position of the affected vocal fold, degree of sensory loss, and compensatory capabilities. Initial evaluation should focus on assessment of dysphonia, dysphagia, aspiration, and airway concerns [7, 8]. If possible, a detailed account of the surgery should be obtained to estimate the type and severity of nerve injury, as this may help guide diagnostic testing and timing of potential interventions and provide prognostic information regarding likelihood of dysfunctional reinnervation.

Most patients exhibit some degree of dysphonia, which is related to muscular tone and position of the affected vocal fold. Vocal fold position is not considered to be indicative of the site of injury. Glottal incompetence will cause the voice to sound weak and breathy unless compensatory strategies, such as supraglottic compression, are employed. Phonation is often effortful, with vocal fatigue, odynophonia, and decreased projection. Additional symptoms of dysphagia and subjective dyspnea may be present. Patients with dysphagia should be assessed for aspiration risk. With unilateral VFP, airway compromise is unlikely to be of significant concern, although cough may be weak and ineffective. This can interfere with adequate clearing of secretions or compound underlying pulmonary conditions. It is important to note that some patients will be completely asymptomatic [8, 9].

Laryngoscopy

Visualization of the vocal folds can be achieved by several methods. The simplest involves indirect laryngoscopy using a mirror; however, this provides a narrow field of vision with limited view and is recommended only if other means are unavailable. Flexible nasolaryngoscopy is preferred as it offers a more detailed and wider field of view as well as ability to examine the larynx in a physiologic position. Additional advantages include superior illumination, magnification, recording capabilities, and ease of use at the bedside. Videostroboscopy uses a high frequency strobe light to evaluate the vibration and mucosal wave of the vocal folds. This involves use of specialized equipment that may not be readily available in general practice and requires specialty referral [10]. In general, laryngoscopy is recommended for symptoms persisting beyond 2 weeks following surgery [11].

Findings on nasolaryngoscopy commonly include weakness or immobility of the affected vocal fold, incomplete glottic closure on phonation due to lateralized position of the vocal fold, vocal fold bowing/foreshortening and dilation of the laryngeal ventricle, anterior displacement or hooding of the ipsilateral arytenoid, vocal process vertical level mismatch, and dilation of the

ipsilateral pyriform sinus. Passive arytenoid movement on the affected side during respiration and phonation may be seen as the "Jostle sign." Stroboscopy may reveal mucosal wave phase asymmetry and altered vocal fold vibratory characteristics. Compensatory overclosure of the false vocal folds ("plica ventricularis") may obscure visualization of the true vocal folds, which can be unloaded by asking the patient to hum. Repetitive phonatory tasks that produce alternating abduction and adduction, such as having the patient say /I/ followed by a sniff, can unmask more subtle mobility impairment [12, 13]. Testing the sensory function of the larynx via the internal branch of the SLN can be performed by brushing the arytenoids to elicit a cough or spasm.

Swallowing Evaluation

Swallowing evaluation should be performed in patients with dysphagia when there is concern for sensory deficit and aspiration. Modified barium swallow, performed under fluoroscopy in the radiology suite in conjunction with the swallowing therapist and radiologist, is useful to evaluate all phases of the swallowing mechanism. Laryngeal penetration, adequacy of cough to clear material from the airway, pharyngeal pooling of contrast, and frank aspiration of varying consistencies of contrast can be determined. Flexible endoscopic evaluation of swallowing (FEES), sometimes combined with sensory testing (FEESST), can be performed in the office and enables direct visualization of laryngeal penetration and aspiration [14, 15].

Laryngeal EMG

Laryngeal electromyography (L-EMG) evaluates the electrical signal of the neuromuscular discharges from the intrinsic laryngeal muscle and can be a useful examination to determine the integrity of the recurrent and superior laryngeal nerves. Most commonly, a concentric or monopolar needle electrode is inserted into the thyroarytenoid muscle to evaluate the RLN or the CTM to test the external branch of the superior laryngeal nerve (EBSLN). The posterior cricoarytenoid and the lateral cricoarytenoid muscles can also be evaluated, but access is more difficult. Testing is usually performed bilaterally using the intact normal side as the control. Normative values for the laryngeal muscles are lacking which limits the reliability of single-sided testing. Quantitative analysis, nerve conduction studies, and single muscle unit potential analysis are generally unreliable in the larynx and are not usually performed. L-EMG in the postoperative setting can help differentiate nerve damage from cricoarytenoid joint injury, provide prognostic information in the setting of VFI, and gauge the severity of nerve injury.

L-EMG immediately post-op is unreliable because denervated muscle fibers will not exhibit classic EMG findings of denervation such as positive waves and fibrillations for several weeks after injury. These spontaneous findings of denervation typically occur after the neuromuscular junctions begin to reorganize and Wallerian degeneration takes place. Polyphasic activity typically occurs once denervated axons begin to recruit and conglomerate multiple empty neuromuscular junctions, producing large, dyscoordinated motor unit potentials. In general, L-EMG is more accurate at least several weeks after injury, although the exact timing is under question. After 3–4 weeks, the presence of spontaneous activity in the form of fibrillation potentials, positive sharp waves, complex repetitive discharges, polyphasics, and fasciculations denotes severe denervation injury and generally poor prognosis. A difference in recruitment and interference pattern between the weak side and control side can be interpreted as partial weakness or paresis, but given the difficulties associated with accurate needle placement, these differences are often difficult to interpret and quantify.

The utility of laryngeal EMG in the clinical care of postoperative VFI is controversial, and routine usage in RLN assessments is variable from center to center. Laryngeal EMG is fundamentally a subjective analysis of neuromuscular

activity and there are several inherent difficulties with studying the larynx which limit its reliability. Unlike EMG performed in the extremities, the larynx is never truly at rest and is subject to many reflexive behaviors by the patient. The muscles are small and difficult to localize, and the electrode has to penetrate through several compartments within the neck including the cartilage, airway, and mucosa before arriving at the muscle. In 2009, the Neurolaryngology study group from the American Academy of Otolaryngology (AAO) made several recommendations on the utility of laryngeal EMG and found compelling evidence supporting the use of L-EMG in several isolated clinical scenarios. The group recognized multiple barriers facing L-EMG use for the workup and treatment for VFI. They noted that there were significant differences in methodology for L-EMG, as well as differences in interpretation of findings and validations, and cited the lack of normative values as obstacles [16].

Differentiating between vocal fold paralysis and cricoarytenoid joint fixation immediately post-op can be difficult. L-EMG immediately post-op will rely primarily on the recruitment pattern because other indicators of denervation such as spontaneous discharges may take several weeks to develop. Clinical findings such as swelling around the joint, the presence of a lateralized, immobile cord despite significant muscle activity in the false vocal fold, and the absence of any jostle around the joint suggest a possible fixation issue. Direct palpation of the joint with transoral palpation can be performed under local or general anesthesia and can be helpful, especially if suspicion for joint dislocation or subluxation is high and joint reduction is attempted. Although cited frequently, the utility of L-EMG in differentiating cricoarytenoid joint subluxation from neuropathy is not well studied. Subluxation and dislocation as a consequence of intubation injury are rare [17]. Large retrospective studies suggest rates of cricoarytenoid joint injury during intubation of about 0.1 %. Sataloff et al. reported arytenoid dislocation or cricoarytenoid joint fixation in about 2.8 % of patients with vocal fold motion abnormalities, based on routine performance of laryngeal EMG in all patients with vocal fold asymmetries. This is based on the presence of an immobile vocal fold with normal EMG findings [18]. The authors prefer direct operative palpation of the arytenoid over L-EMG if there is a high clinical suspicion for subluxation or dislocation of the cricoarytenoid joint.

Studies evaluating the predictive ability of L-EMG data for RLN recovery show that overall, L-EMG is more accurate in determining poor prognosis rather than recovery. Findings of denervation as evidenced by spontaneous activity are accurate in predicting lack of recovery or permanent vocal fold paralysis (85–93 %) whereas normal findings in the setting of an immobile vocal fold do a relatively poor job of predicting recovery (40–60 % check). Rickert et al. performed a meta-analysis in 2012, reviewing studies that evaluated the prognostic potential of L-EMG for vocal fold paralysis. They found ten articles with information containing sufficient data to evaluate 503 L-EMG examinations. Their review found that positive findings of denervation on L-EMG were highly reliable in predicting persistent immobility, with a positive predictive value of 90.9 %. However when the L-EMG was normal, or negative, and there was no differences between sides, the accuracy was diminished, with a negative predictive value of 55.6 %. In short, the L-EMG is better at predicting persistent paralysis than recovery [19]. It is unclear whether the lack of motion recovery in the setting of good recruitment and neuroelectrical discharges reflects possible post-paralysis joint fixation, misdiagnosis of paralysis for joint injury, or lack of motion despite an intact nerve.

There are several compelling reasons for L-EMG's role in the therapeutic decision-making in postoperative RLN dysfunction [19–21]. The ability of L-EMG to predict poor recovery can be used to support early surgical intervention such as vocal fold medialization. The recognition of axonal injury can also be used to initiate potentially neuroregenerative drugs such as nimodipine. Smith et al. evaluated the impact of L-EMG on the therapeutic treatment of newly diagnosed VFI. They noted diagnosis changes of about 10 % in the cohort of 50 patients and a therapy change in

about 37 %. Most of the therapy changes were a reduction in the rates of observation towards permanent augmentation or medialization. Most of the diagnosis changes were the recognition of SLN injury or cricoarytenoid joint fixation [22].

L-EMG is often helpful to help guide therapy in cases of bilateral VFP. L-EMG can be useful to determine which nerve is more injured and less likely to return to function. This can help determine laterality of surgery in cases of airway surgery such as partial arytenoidectomy or transverse cordotomy. It can also be used to determine the severity of injury, and could help guide botox injections to achieve temporary airway lateralization by paralyzing the adductor laryngeal muscles (cricothyroid, thyroarytenoid, and lateral cricoarytenoid).

At our institution, we routinely offer laryngeal EMG if there is doubt as to the causation of vocal fold paralysis, if there is a need to determine cricoarytenoid joint dislocation and operative palpation is not desired, and in cases of bilateral VFI. L-EMG is also recommended if the patient desires open thyroplasty and/or arytenoid adduction before an observational time of 6 months. Although L-EMG is not routinely used in every case of postoperative VFP, there are indications where it may be useful in therapeutic decision-making.

Treatment

Management strategies for VFI include an observation period, voice and swallow therapy, and both temporary and permanent surgical intervention. A treatment plan should be individualized for each patient as clinical symptoms, expectations, and vocal needs can vary. Classically, the treatment of VFI included a 6–12 month observation period before surgical intervention was considered. This strategy was developed in the 1970s, a time in which injection augmentation with Teflon, a permanent filling agent, was the most common treatment. Since Teflon injection was sometimes associated with adverse effects, an observational period to allow natural recovery was recommended. As the safety and availability of injectable materials increased, the watchful waiting time period prior to surgical intervention decreased.

Timing and mode of intervention should be based on the patient's clinical symptoms and the individual's chance for recovery of function. Early intervention should be considered for symptomatic patients with aspiration, high occupational vocal demands, known resection of RLN, or severe denervation injury on L-EMG. Patients undergoing temporary injection medialization have been shown to less likely undergo permanent medialization laryngoplasty as compared to those who were treated with conservative treatment [23, 24]. It has been suggested that early medialization creates a more favorable vocal fold position that can be maintained once synkinetic reinnervation sets in [25]. In addition, Bhattacharyya et al. found that early vocal cord medialization (≤4 days postoperatively), with both injection laryngoplasty and type I thyroplasty, decreased the postoperative pneumonia rate and the length of stay for patients suffering from VFI after thoracic surgery [26].

Voice Therapy

Voice therapy for VFI can be used as an adjunct to surgery or as a conservative management approach for patients who are unable or unwilling to undergo a procedure. Since the degree of voice complaint depends on the amount of glottal incompetence and on the type of compensatory behaviors present, the amount of benefit may vary. Often dysphonia is the chief complaint amongst patients and their voice is often breathy and hoarse with limited pitch and loudness variation. Phonation time can be short and diplophonia can occur as they try to attain glottic closure. A rough, strained, or low-pitched voice may occur with compensatory hyperfunctional behaviors such as lateral or anterior-posterior compression of the false vocal folds while a falsetto register may be seen with hyperfunction of the CTMs. The goals of voice therapy are to strengthen the intrinsic musculature and improve glottal closure without causing supraglottic hyperfunction and

to help develop abdominal support for breathing. Improvements in endoscopic, aerodynamic, acoustic, perceptual, and self-assessed measurements can be seen after voice therapy suggesting that voice quality and quality of life for patients with VFI may benefit from therapy [27, 28]. In patients undergoing surgical intervention, voice therapy can play an adjuvant role by helping the patient adapt vocal production to a new system. As suggested by Isshiki, phonosurgery may work as "pump-priming" to help facilitate the voice therapy that can follow [29].

Injection Augmentation

Vocal fold augmentation is an established method which addresses the glottal gap resulting from an immobile vocal fold and is an important component in the management of postoperative RLN impairment. In 1911, W Brunings presented a unilateral vocal fold injection to the German Laryngology Congress using hard paraffin wax. He demonstrated increasing the volume of the paralyzed vocal fold enabled compensation by the working vocal fold, resulting in improved glottal closure, stronger cough, and better voice. Contemporary vocal fold augmentation can be performed by peroral and percutaneous injection techniques, in the office with transnasal or transoral endoscopy, or in the operating room with rigid endoscopes. Office-based procedures using peroral or transcutaneous approaches utilize recent advances in endoscopic visualization and injection materials. The percutaneous approaches utilize potential laryngeal spaces such as the thyrohyoid and cricothyroid membranes.

There have been several technical gains in recent years that have advanced our ability to carry out injection laryngoplasty. The development of digital camera technology enables accurate placement of injectable materials with transnasal flexible visualization. Another advance is the improved biocompatibility and variety of materials available for injection. Since the original description of vocal fold injection using paraffin wax, a variety of different techniques and materials have been tried including bone and cartilage paste, fat, Teflon®, glycerine, and silicone with variable success. However, with the popularity of cosmetic collagen implantation, the economic incentives to develop different filler materials available for vocal cord augmentation have increased. These newer materials have better biocompatibility, producing less inflammation and scar than previous injectable agents. Collagen, calcium hydroxylapatite (Prolaryn-Plus®), micronized cadaveric skin (Cymetra®), and crosslinked hyaluronic acid gels (Juvederm®, Restylane®) have become available that are easy to use, off the shelf, with reproducible results and resorption characteristics. In addition, the biocompatibility of these materials results in safer and more superficial injection sites with reduced risk of granulation formation and fibrosis.

The chance of spontaneous neural recovery is felt to be greatest within the first year of onset of the VFP. Traditionally, injection laryngoplasty is used as a temporary means of addressing glottal insufficiency during that first year of injury, whereas afterwards, permanent medialization in the form of open medialization laryngoplasty is discussed. The observational period before open formal medialization laryngoplasty is usually 6 months to 1 year. Recently, several studies suggest that early intervention and treatment for VFP may improve outcomes such as long-term voice improvement as well as fewer aspiration events and shorter hospital stays. As noted above, Bharttacharyya et al., in 2003, retrospectively analyzed 86 patients after thoracic operations who underwent early (defined as within 4 days after surgery) medialization for postoperative unilateral vocal fold paralysis. These patients who underwent early injections had fewer pneumonias, fewer postoperative bronchoscopies, and decreased length of hospital stay after esophagectomies, pneumonectomies, and lobectomies [26].

Vocal fold injections may also reduce the need for subsequent interventions. Arviso et al. looked at the natural history of patents with vocal fold paralysis who underwent vocal fold injections and noted that 71 % of their cohort did not require

further intervention [30]. Yung et al. retrospectively analyzed 54 cases of permanent unilateral VFP and noted that patients who initially underwent "temporary" injection medialization had fewer rates of transitioning to permanent medialization laryngoplasty [23]. Alghonaim et al. performed a retrospective chart review of 66 patients with permanent VFP who underwent injection augmentation. They noted that the majority of patients who underwent injection within 6 months did not undergo transcervical medialization laryngoplasty. They also noted that patients who underwent injection augmentation earlier in the time course of vocal fold paralysis had lower rates of undergoing permanent surgery, suggesting that earlier intervention may be beneficial [24]. This trend was also observed in a study by Friedman [25]. With this in mind, earlier identification of VFI through laryngeal exam post-op is critical to implement this important early evaluation and treatment.

There are many methods for vocal fold injection and there has been no studies suggesting that one methodology is superior in outcomes or complications. Numerous studies have shown an economic advantage in performing vocal fold injections in the office instead of the operating room, citing savings in hospital and operating room resources, manpower, and material costs. The methodology of vocal fold injection is often determined by site of service (hospital vs. office based practices), access to supplies and equipment, surgeon training and preferences, and local practice patterns.

Currently, the authors' preferred method for vocal fold augmentation is an awake transcutaneous injection via the thyrohyoid space (Fig. 23.1). Office injections are performed with the patient seated upright. The nasal cavities are sprayed with 2 % lidocaine and 0.025 % oxymetazoline. Topical anesthesia is administered by transtracheal injection of 2–4 mL of 4 % lidocaine with a 23-gauge needle and having the patient cough to spread the anesthetic agent throughout the larynx. Some patients also receive an injection of 2 mL of 2 % lidocaine with 1:100,000 epinephrine in the pre-epiglottic space. The nasolaryngoscope is used to visualize the larynx. A 25-gauge needle bent at 45°

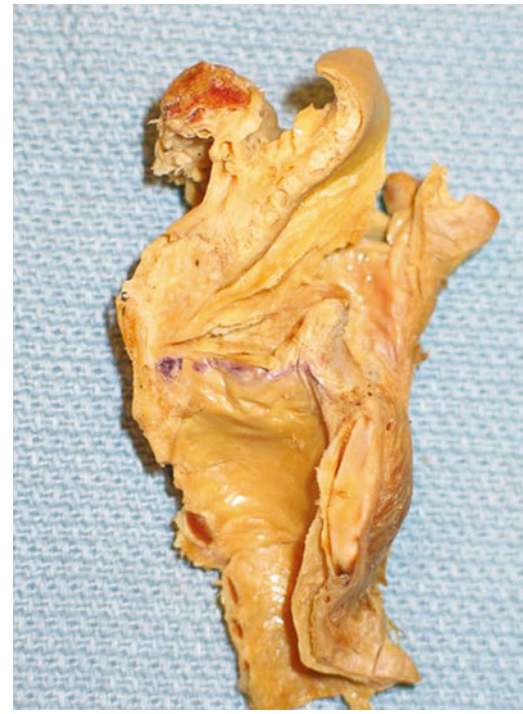

Fig. 23.1 Cross section of the larynx and needle trajectory through the thyrohyoid space towards the vocal folds

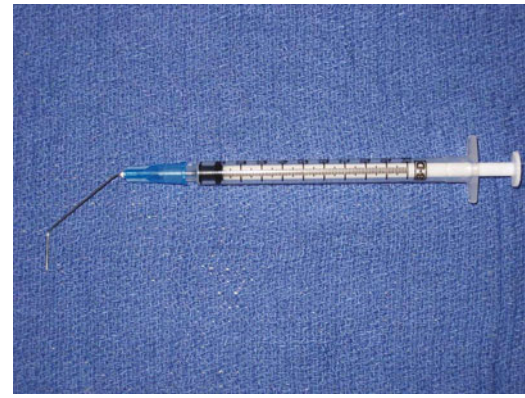

Fig. 23.2 The double needle bend allows the 25-gauge needle-tip to point downwards while the barrel of the syringe is horizontal after the needle (25-gauge, 38 mm) is introduced through the thyrohyoid space to inject the vocal fold

angles at the hub and approximately 1 cm from the tip is attached to the injection syringe and passed through the thyrohyoid membrane just superior to the thyroid notch (Fig. 23.2). The needle enters the larynx inferior to the petiole of the epiglottis and is

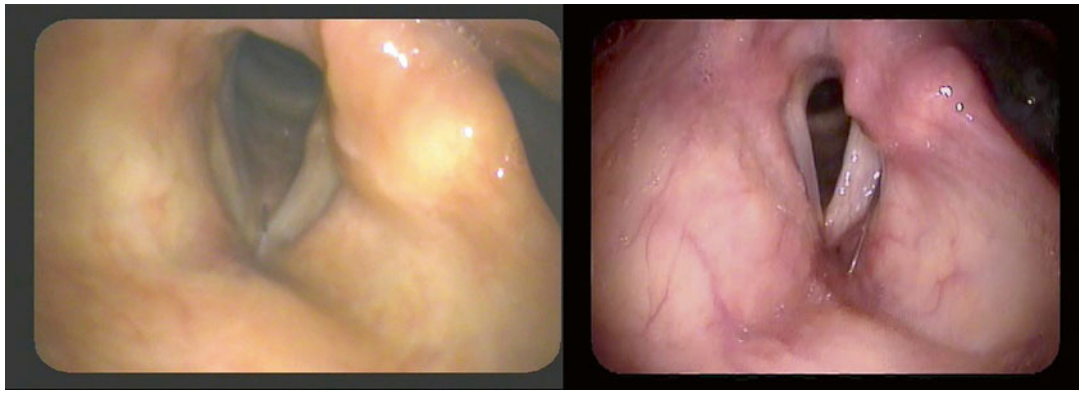

Fig. 23.3 Endoscopic view of the needle entering the larynx (two photos placed side by side)

directed into the vocal fold (Fig. 23.3). The injection is performed into the paraglottic space and can be made just lateral to the arcuate line. The injection is added until the vocal fold is slightly over-corrected [31].

Open Medialization Laryngoplasty with Adduction Arytenopexy

Still in today's environment of minimally invasive approaches to voice disorders, open laryngoplastic phonosurgery occupies a prominent position in the laryngologists' surgical armamentarium for treating patients with VFI. The most common procedure is an open medialization laryngoplasty, or a Type I Thyroplasty where the vocal fold is moved medially to decrease the glottic gap in the membranous region. The arytenoid position can be altered using an arytenoid adduction or adduction arytenopexy if there is a large cartilaginous-region gap or a vertical height discrepancy between the mobile fold and the immobile fold. Tension can be fine-tuned within the immobile vocal fold using the cricothyroid subluxation and the ipsilateral capacious pyriform sinus can be reduced in volume through a hypopharyngoplasty.

There are distinct advantages open medialization has over injection laryngoplasty with a long-lasting injectate. Supporting a flaccid vocal fold with a solid implant via open medialization laryngoplasty can help to restore a strong voice without the need for repeated outpatient interventions since the implant does not degrade over time. The results from medialization laryngoplasty tend to last longer and give the patient a more stable voice over the time the procedure is effective compared to injection laryngoplasty. The ability to manipulate and reposition the arytenoid at the time of medialization is a distinct advantage over injection laryngoplasty. Revision of the implant after open medialization is possible, with total removal of the implant in case of infection or when it is no longer needed. Of course, open medialization requires patients to undergo an awake procedure in the operating room under IV sedation resulting in a neck incision and an overnight stay to monitor the airway and the potential for incision-related sequelae (bleeding, fistulas, infections). In our institution, patients are routinely informed of both the injection and open laryngoplasty options and the risks and benefits of each are weighed to arrive at a decision about which approach best suits the clinical needs in each case.

Surgical Preparation/Identification of Relevant Anatomy

Since the open medialization with adduction arytenopexy surgical procedure has been described in depth in the medical literature [32], this will serve as an overview of the procedure highlighting the most important segments of the procedure. Open

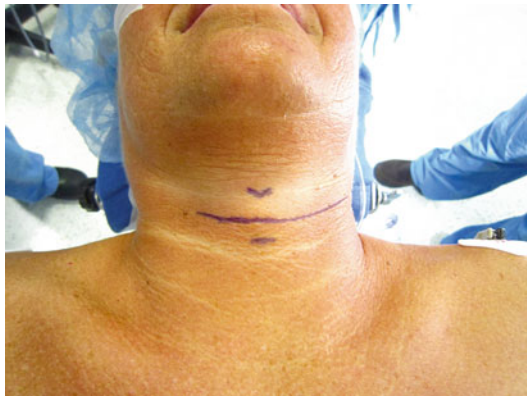

Fig. 23.4 This patient has a left vocal fold that is paralyzed leading to dysphonia. The relevant laryngeal anatomy is outlined with a surgical marking pen (from cephalad to caudal—thyroid notch, horizontal incision-line at the level of the cricothyroid membrane in a natural skin-crease, and the superior rim of the anterior cricoid cartilage) [Courtesy of Ramon A. Franco Jr., MD]

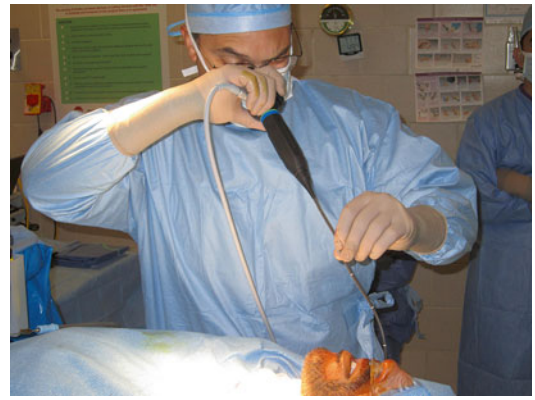

Fig.23.5 A sterile Flexible-Fiberoptic-Nasolaryngoscope is inserted through the nose to visualize the position of the vocal folds. The surgeon takes note of the position of the paralyzed vocal fold, and makes sure there is normal "good vocal fold" function (abduction) to ensure an adequate airway after the arytenoid has been placed back into the midline [Courtesy of Ramon A. Franco Jr., MD]

medialization (Type 1 Thyroplasty) is performed in the operating room as a sterile neck procedure with the use of IV sedation. Patients are positioned with the neck extended, with or without a shoulder roll, allowing access to the anterior neck from the chin to the sternal notch. Preoperative antibiotics and 12 mg of Decadron (dexamethasone 4 mg/cm [3]) are delivered 30–60 min prior to incision. 4 % cocaine, or a combination of 0.25 % oxymetazoline and 2 % lidocaine, is placed on neuropaddies and placed into the nasal cavity that will be used for nasolaryngoscopy during the case. The prominent anatomical landmarks such as the hyoid bone, thyroid cartilage, and cricoid cartilage are outlined thus defining the thyrohyoid and cricothyroid spaces (Fig. 23.4). The proposed incision ideally lies in a natural skin crease that falls in the region of the inferior border of the thyroid cartilage/cricothyroid membrane. The incision is outlined on the side of the immobile vocal fold, just crossing the midline, and will vary in length (3–6 cm) depending on whether an adduction arytenopexy is to be performed at the time of the medialization laryngoplasty. Prior to injecting local anesthesia, the neuropaddies are removed and the flexible nasolaryngoscope is used to evaluate the laryngeal anatomy and function (Fig. 23.5). Special attention is given to the mobility of the vocal folds, the patency of the airway, and the position of the vocal folds—both the medial to lateral, as well as the vertical height on each side (Fig. 23.6). Local anesthesia infiltration can lead to a temporary vocal fold paresis of the "good" vocal fold, placing the patient at risk for acute airway obstruction if an adduction arytenopexy is performed. Good abduction of the normally working vocal fold is a prerequisite for performing the arytenopexy. The scope is removed and the neuropaddies are replaced.

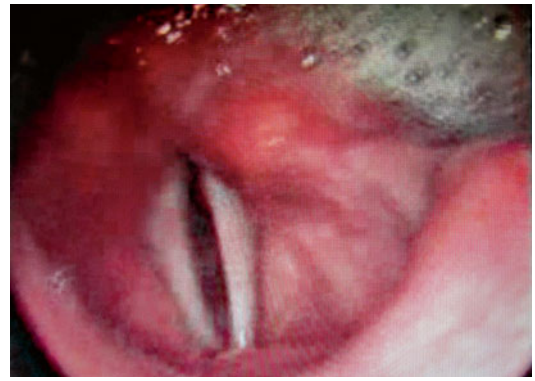

Fig. 23.6 A view of the larynx through a Flexible-Fiberoptic-Nasolaryngoscope. The left vocal fold is immobile, and there are retained secretions within the left pyriform sinus, indicating a sensory and motor deficit to the mucosa and pharyngeal constrictors (RLN injury). The right side of the image corresponds to the patient's left side [Courtesy of Ramon A. Franco Jr., MD]

Adduction Arytenopexy

A small amount of IV sedation is given to make the patient more comfortable while 10–20 cc of a mixture of 1 % lidocaine/0.375 % bupivacaine/1:150,000 epinephrine is injected under the proposed incision line, into the strap muscles and along the posterior border of the thyroid cartilage (into the inferior constrictor muscles). After prepping and draping the patient, a neck incision is created and limited dissection is done to expose the laryngeal framework from the thyroid notch to the cricoid. Self-retaining retractors are used to improve visualization. The thyrohyoid and sternothyroid muscles are elevated away from the thyroid cartilage and transected to allow access to the posterior border of the thyroid cartilage where the inferior constrictor muscle is separated away from the thyroid cartilage. The electrocautery must not be used beyond the posterior thyroid cartilage border since the pyriform sinus resides there and there is risk of creating a delayed pharyngocutaneous fistula. The cricothyroid joint is cut using curved Mayo scissors allowing the thyroid cartilage to be pulled anteriorly, exposing the pyriform sinus whose attachments to the inner posterior thyroid cartilage are bluntly dissected from caudal to cephalad revealing the underlying posterior cricoarytenoid muscle. The RLN can be identified coursing cephalad and posterior to the cut cricothyroid joint. The RLN should be preserved since there can be fibers that are still providing innervation to the laryngeal musculature, and therefore, helping to maintain some muscle bulk. The posterior cricoarytenoid muscle is transected leaving a small "tail" that is used to manipulate the attached arytenoid cartilage. The posterior cricoarytenoid "tail" is lifted up and the cricoarytenoid joint is bluntly entered (Fig. 23.7). The lateral, anterior, and posterior joint capsule attachments are sharply removed allowing the arytenoid to be repositioned more medial and posterior with a 4-0 Prolene suture. The suture is placed in the posterior-lateral aspect of the cricoid cartilage at the level of the cricoarytenoid joint and exits the cricoarytenoid joint in the posterior-medial quadrant. Next, the suture is passed through the anterior-lateral aspect of the arytenoid cartilage from the articulating surface to the superior surface, and finally from the inner cortex to the outer cortex of the cricoid cartilage, anterior to the cricoarytenoid joint. The suture is pulled taut and

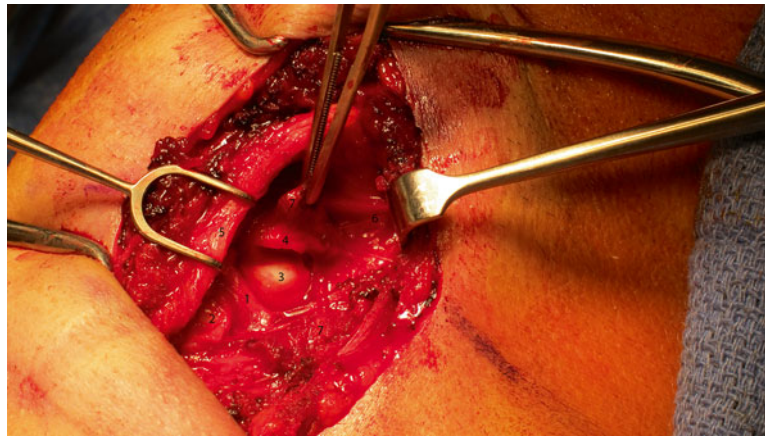

Fig. 23.7 A view of the open cricoarytenoid joint. It highlights the access that is necessary to perform an adduction arytenopexy, as well as the relevant anatomy one encounters in the posterior aspect of the larynx. In this image, the left thyroid cartilage (#5) is being pulled anteriorly and towards the right side, opening a view into the posterior aspect of the larynx. The Recurrent Laryngeal Nerve (#1) can be seen coursing posterior and cephalad to the cut Cricothyroid Joint (#2), and caudal to the cricoid portion of the Cricoarytenoid joint (#3). The pyriform sinus (#6) normally blankets these structures and needs to be retracted away in order to see the Cricoarytenoid joint. The Arytenoid cartilage (#4) is manipulated via a small tail of Posterior Cricoarytenoid muscle (#7) that is preserved attached to the arytenoid. The other cut-end of the PCA muscle is seen at the lower edge of the image (#7). The adduction arytenopexy can now be performed [Courtesy of Ramon A. Franco Jr., MD]

the voice should have more power but still not sound normal since the vocal fold needs lateral support. A quick look using the nasolaryngoscope should reveal good closure at the level of the arytenoids with a persistent musculomembranous gap. If there was a height discrepancy with the immobile vocal fold inferior and lateral compared to the "normal" fold, the arytenoid repositioning should have corrected this. If the surgeon is satisfied with the new position, the suture is tied. Otherwise, the suture can be pulled out and attempted anew.

Hypopharyngoplasty

In the regular course of performing the adduction arytenopexy, the pyriform sinus is dissected free from the surrounding tissue. When there is dysphagia related to the loss of RLN function (paralytic dysphagia) with a dilated and capacious ipsilateral pyriform sinus (with retained secretions), a hypopharyngoplasty can be performed. An articulating 45-GIA stapler is used to cut across the base of the stretched pyriform sinus [32, 33]. This reduces the volume of the paralyzed pyriform sinus, similar to what happens when the patient turns the head to the affected side and performs a chin-tuck. The stapler lays down a double-line of staples, creating a watertight seal, making it possible to feed patients soft foods after surgery (Fig. 23.8).

Medialization Laryngoplasty

After the larynx has been returned to a neutral position, an inferiorly based perichondrial flap is created exposing the inferior thyroid cartilage (Fig. 23.9). The inferior border of the thyroid cartilage is not flat, but rather has several undulations. The thyroplasty window should be placed as low as possible, making it critical that the true inferior border is exposed and found. Depending on the material to be implanted (Gore-tex vs. solid implant), the size and exact location of the window are more or less important. Gore-tex windows tend to be much smaller and, as long as they are placed low, will work well for medialization purposes. Solid implant systems, such as the Montgomery Thyroplasty system, require the use of dedicated measuring calipers and tools to size and position the window for proper implant function (Fig. 23.10). Once the vocal fold is well supported with the proper amount/size of the implant, the voice should sound more normal, and should have much more dynamic range, allowing the patient to speak louder than before the medialization.

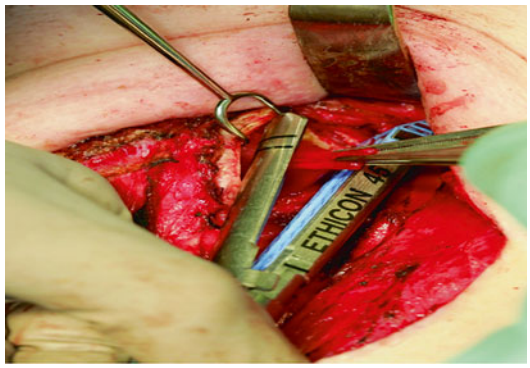

Fig. 23.8 A 45-GIA stapler is used to staple/cut across the pyriform sinus that had been dissected away from the PCA muscle and retracted out of the surgical field in Fig. 23.7. When the patient has a capacious pyriform sinus from flaccidity of the constrictor muscles, reducing the volume of the pyriform sinus can aid in swallowing and decreasing the amount of aspiration [Courtesy of Ramon A. Franco Jr., MD]

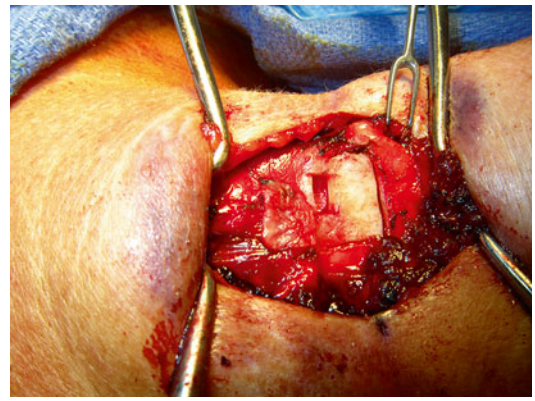

Fig. 23.9 The left thyroid cartilage is seen with an inferiorly based perichondrial flap that exposes the cartilage. A 3 mm × 6 mm window is created using a sagittal saw leaving a 2–4 mm inferior strut that acts as a buttress for the material that is used to fill in the window and bulk the vocal fold [Courtesy of Ramon A. Franco Jr., MD]

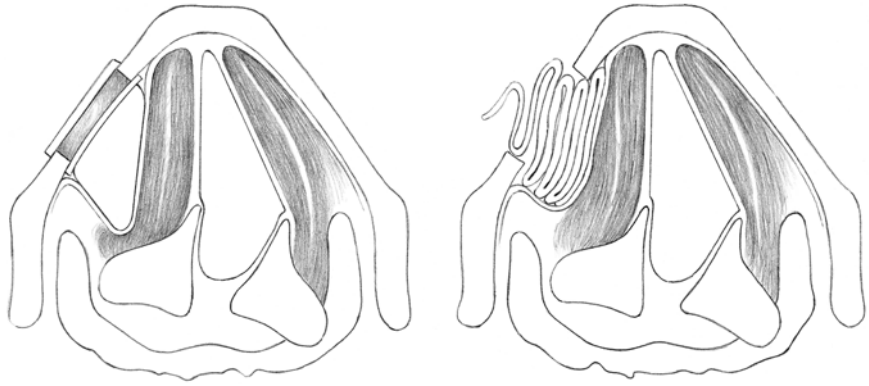

Fig. 23.10 Various materials can be used to bulk the paralyzed vocal fold, including solid implants such as the Montgomery Vocal Cord Implants® (*left side* of the image) and soft material such as Gore-tex® (*right side* of the image) [Courtesy of Ramon A. Franco Jr., MD]

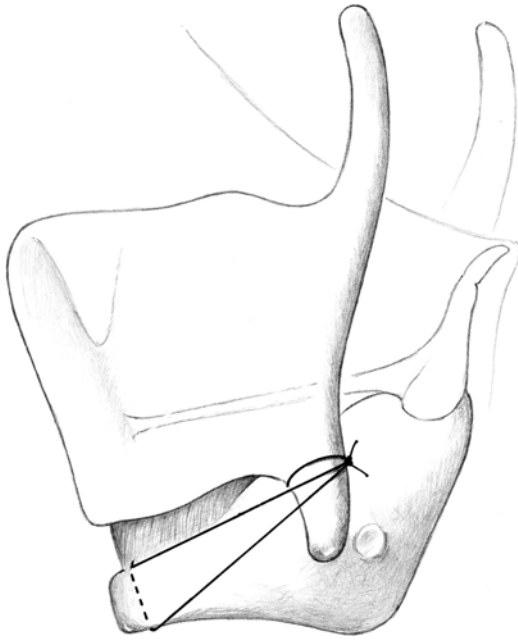

Fig. 23.11 The Cricothyroid Subluxation increases the tension of the paralyzed vocal fold by "pulling" the thyroid cartilage forward, increasing the length of the vocal fold that is suspended between the newly "anchored" arytenoid (s/p adduction arytenopexy) and the inner perichondrium of the thyroid cartilage anteriorly. The amount of tension can be varied and the final amount is determined by the voice quality. The pitch of the voice tends to rise as the tension is increased [Courtesy of Ramon A. Franco Jr., MD]

Cricothyroid Subluxation

At this time a 2-0 Prolene suture is tied around the inferior thyroid cartilage and then is looped around the anterior arch of the cricoid to add tension to the immobile vocal fold via a cricothyroid subluxation (Fig. 23.11). Varying amounts of tension can be applied until the voice sounds smooth or the pitch has been elevated to achieve a normal sounding voice for that patient. Cricothyroid subluxation is not always necessary, but an attempt to try it for each case is made since it can "fine-tune" the voice and add further to the closure and the quality of the voice. This combination of procedures can help to reduce the size of the glottic gap, position the arytenoid in its proper phonatory position, fine-tune the vocal fold tension to adjust the voice quality and facilitate swallowing in those patients suffering from unilateral VFI (Fig. 23.12).

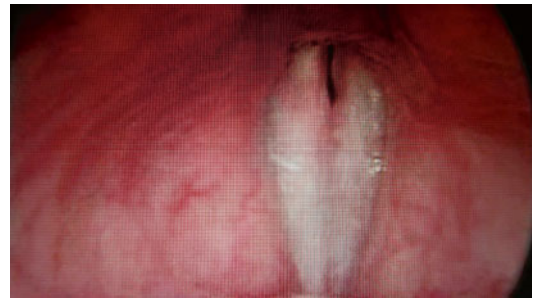

Fig. 23.12 A view of the post-reconstruction larynx. The left vocal fold (on the *right side* of the image) is now midline, with the arytenoid cartilage also in the midline, directly apposed to the opposite arytenoid posteriorly. As can be appreciated in this image, there is no longer a height discrepancy between the vocal folds. This patient now has a loud, normal-sounding voice that does not require large amounts of energy to produce [Courtesy of Ramon A. Franco Jr., MD]

Conclusion

Postoperative management of RLN injury starts with a thorough evaluation to assess the extent of weakness. A host of options exists for the patient

ranging from noninvasive voice therapy techniques to temporary and permanent procedures with a strong emphasis placed on early detection, evaluation, and treatment. The course of treatment is dictated by the patient's clinical presentation and symptoms and often there is great variability between patients depending on factors such as extent of injury, prognosis, and vocal demands.

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Postoperative Management of Bilateral Vocal Cord Paralysis

24

Alexander Gelbardl and James L. Netterville

Abstract

Bilateral vocal cord paralysis is one of the most severe complications of anterior neck surgery. Although a rare complication, it imparts a massive impact on affected patients. While stabilization of the airway to provide adequate ventilation is the initial primary concern, the management of bilateral vocal fold mobility impairment remains an unsatisfactory compromise between voice, breathing, and swallowing. The lack of an ideal solution is aptly illustrated by the abundance of technical reports in the literature over the last 100 years. Current techniques restore airway patency at the cost of worse glottic closure and vocal quality. Therapy tends to be grouped into immediate interventions in the acute setting of respiratory compromise, and long-term interventions aimed restoring glottic patency after the airway has been acutely stabilized. The majority of procedures currently performed are aimed at physically enlarging the laryngeal lumen. Although an area of rapid progress and active development, laryngeal reinnervation has yielded rare mobility gains. Another promising line of research is of implantable stimulators, which maintain mobility and voice patterns, but these have not yet become a mainstream option available to patients outside of experimental protocols.

Keywords

Bilateral vocal cord paralysis • BVFP • Vocal fold paralysis • Tracheostomy • Lateralization • Cordotomy • Laryngeal pacer • Laryngeal reinnervation

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Bilateral vocal cord mobility impairment (BVFMI) is one of the most severe complications of anterior neck surgery. With an incidence ranging from 0.2 to 0.4 % after total thyroidectomy [1, 2], although a rare complication it imparts a massive impact on affected patients. Life-threatening

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airway obstruction, as well as alterations in voice, swallowing, and a deterioration in global quality of life all can be precipitated by bilateral vocal cord paralysis (VCP) [3]. Additionally, bilateral paralysis is associated with significantly increased overall cost, length of hospitalization, and duration of ICU stay [4].

Although nearly 50 % of patients with BVFMI following thyroidectomy present with respiratory compromise, only 25 % need tracheostomy [4]. Admittedly difficult to define precisely owing to its infrequent occurrence, the recovery rates in BVFMI after thyroidectomy have been reported 50 % for one vocal fold, and 23 % for bilateral recovery [4]. While stabilization of the airway to provide adequate ventilation is the initial primary concern when patients present with BVFMI, experience with a large number of these cases each year in our institutions' dedicated multidisciplinary center for complex adult airway problems (AeroVU) has generated a comprehensive diagnostic algorithm we utilize when evaluating and treating these patients.

Initial Diagnostic Work-Up

A thorough initial history helps delineate the etiology of injury in the majority of cases. Patient reports of coughing or choking after eating or drinking (specifically thin liquids) should prompt an assessment by a speech language pathologist to ascertain the severity of swallowing dysfunction, and evaluation of compensatory strategies. Dysphagia in this population is not trivial, 57 % patients presenting to a large tertiary care center with BVFMI (of undescribed etiology) demonstrated evidence of aspiration [5]. The history also helps delineate the overall patient performance status, and contributing comorbid illness (coronary artery disease, diabetes mellitus, neurocognitive impairment) that may impact treatment efficacy.

Physical Examination

Examination begins with an assessment of the patient's ability to maintain adequate ventilation to support their physiologic demands and gauge the severity of airway compromise. Subjective impressions of a patient's general well-being are crucial and can be derived from the overall level of alertness, response to the surrounding environment, and interaction with the examiner. The ability to speak in complete sentences, ambulate up a flight of stairs, or a walk through the clinic speak powerfully about the degree of clinical ventilation impairment.

In patients presenting with ventilation impairment exceeding their physiologic demands, speaking in one-word sentences, substernal retractions, tachypnea, and air hunger (the feeling of not enough oxygen) are suggestive of the need for emergent airway stabilization. Stridor is the most common presenting sign of extrathoracic airway obstruction in adults and warrants prompt investigation. Stridor occurs when the laminar flow through the extrathoracic airway is disrupted by a narrowing or partial obstruction, creating a Venturi effect (the acceleration of flow observed through a narrowed segment of a tube). This flow acceleration results in the development of a more negative intraluminal airway pressure (Bernoulli's principle), exacerbating collapse of the deformable extrathoracic airway. The resulting turbulence and vibration of the airway during inspiration are perceived as stridor on physical examination.

While seemingly simple, occasionally even precise assessment of impaired glottic mobility can prove illusive. Focus on movement of the arytenoid mucosal can be misleading; the best gauge of glottic mobility in the office setting is movement of the vocal process of the arytenoid [6]. In addition to assessment of RLN function via an assessment of glottic mobility, assessment of the sensory and motor components of the superior laryngeal nerve (SLN) adds important diagnostic information to the initial BVFMI evaluation. This nerve is at risk during ligation of the superior thyroid artery and injury during thyroidectomy is thought to occur with greater frequency than RLN injury [2]. Intact sensory function is a critical component to swallowing rehabilitation efforts. The SLN branches from the vagus nerve just inferior to the nodose ganglion, which contains the sensory cell bodies of the SLN. The nerve travels inferiorly along the side of the pharynx, medial to the carotid, and bifurcates near the level

of the hyoid bone. The internal division of the SLN accompanies the laryngeal artery as it pierces the thyrohyoid membrane and supplies sensory innervation to the larynx. The external division of the SLN (EBSLN) lies close to the thyroid artery innervates the cricothyroid muscle (CTM). The CTM contributes to vocal fold lengthening and plays a large role in the control of vocal fundamental frequency (F0) and its psychophysical correlate "vocal pitch" [7]. Injuries to the internal branch of the SLN can be detected by a loss of glottic and supraglottic sensation, while deviation of the *petiole* of the epiglottis during pitch elevation can be a sign of injury to the EBSLN [8].

Diagnostic Studies

Pulmonary function testing (PFT). We obtain baseline PFT measurements on all patients with BVFMI. It offers a rapid, minimally invasive, and inexpensive objective measurement from which subsequent interventions or clinical changes can be compared. When the flow volume loops are compared, neurogenic BVFMI shows the "standard" pattern of extrathoracic airway obstruction (blunting of both the inspiratory and expiratory loops); however, expiration is affected to a lesser degree than inspiration. In contrast, laryngeal fixation due to a mature interarytenoid scar shows a "fixed" pattern of upper airway obstruction with severe blunting of both inspiratory and expiratory loops [9].

Computed tomography. Imaging studies are reserved for patients without a history of anterior neck surgery of intubation. In cases without a clear etiology, imaging helps to rule out compressive lesions in the neck or mediastinum.

Swallowing evaluation. We obtain baseline videofluoroscopic swallow studies (VFSS, i.e., MBS) on all BVFMI patients. While the optimal modality to assess swallowing function in this population is undefined (and an active area of research), we believe it is critical to establish an objective pretreatment baseline. A significant number these patients will have dysphagia on presentation [5], and the presence and magnitude of dysphagia is incorporated into our surgical planning, and need for integration of swallowing rehabilitation directed by a speech pathologist.

Electromyography (EMG). Although some authors advocate the use of laryngeal EMG in delineating the etiology and prognosis for BVFMI, we do not routinely employ this technique. Although it can effectively delineate etiology [10], and reports have described a high predictive value for outcomes following acute peripheral vocal cord injury [11], its utility in the emerging therapeutic paradigm for unilateral vocal fold paralysis (UVFP) has been challenged. Typically, in UVFP outcomes (defined as avoidance of a permanent laryngoplasty procedure) appear better if the patient undergoes injection medialization early (within 3 months) [12, 13]. Thus, a decision for intervention by many groups is no longer based on timing of the injury or likelihood of recovery predicated on EMG results. Rather the immobile true vocal fold is medialized expediently, and the patient followed for the clinical stability of their voice, swallowing, and breathing. Similarly, in our center, the etiology of BVFMI is delineated by history and palpation of cricoarytenoid joints in the OR. The decision for acute intervention (i.e., tracheostomy) is made based on the clinical degree of ventilatory impairment. Additionally, while denervation does produce characteristic EMG findings (decreased voluntary motor units, fibrillation potentials, and positive sharps waves), BVFMI even when of neurogenic origin is not viewed as an isolated issue of denervation. Rather it is thought to be primarily born out of faulty reinnervation dominated by synkinetic adductor function [14]. Our center has not widely embraced laryngeal EMG in its diagnostic algorithm except in unique cases.

Treatment

The management of BVFMI remains an unsatisfactory compromise between voice, breathing, and swallowing. The lack of an ideal solution is aptly illustrated by the abundance of technical reports in the literature over the last 100 years. Current techniques restore airway patency at the cost of worse glottic closure and vocal quality.

Therapy tends to be grouped into immediate interventions in the acute setting of respiratory compromise, and long-term interventions aimed restoring glottic patency after the airway has been acutely stabilized.

The majority of procedures currently performed are aimed at surgically enlarging the laryngeal lumen. Although an area of rapid progress and active development, to date clinically, laryngeal reinnervation has yielded improved muscle tone, less atrophy, and vocal fold bowing, but rare mobility gains [15]. Another promising line of research is of implantable stimulators, which maintain mobility and voice patterns, but these have not yet become a mainstream option available to patients outside of experimental protocols [16].

Acute Treatment

When patients present in the immediate postoperative setting, the intervention is guided by the patient's clinical condition. Acute post-extubation stridor, with persistent tachypnea, and progressive ventilatory decompensation requires reintubation. A decision on tracheostomy can be briefly deferred, as some author advocates a 24–36 h period of intubation with intervenous corticosteroids followed by a repeat trial of extubation. Should the patient again decompensate after the second attempt, the patient requires a tracheostomy.

In patients who require an emergent tracheostomy, all procedures aimed at decannulation represent a compromise between voice and breathing. However, the unique physiology of neurogenic BVFMI allows for a unique solution leaving the larynx intact, while maintaining ventilation, albeit at the expense of an indwelling airway prosthesis.

In neurogenic BVFMI, during inspiration the acceleration of airflow observed after luminal compromise (Venturi effect) results a more negative intraluminal airway pressure (Bernoulli's principle), exacerbating the restriction to inspiration. However, expiration is much less severely affected (contrasted with laryngeal scar or cricoarytenoid joint fixation, where both inspiration and expiration are restricted). A Hood™ stent with a one-way speaking valve allows hands free speech on expiration and excellent inspiratory flow. In appropriately selected patients, this unobtrusive prosthesis provides excellent voice quality, without airway compromise restricting activity.

Neurogenic BVFMI patients that do tolerate extubation, or those that present subacutely, can be closely observed clinically. In patients with BVFMI due to RLN injury, preferential reinnervation of the adductor muscles may account for the medial position of the paralyzed vocal folds [14]. This process occurs over several months and leads to medial placement of the immobile vocal fold. It is often clinically observed that adult patients who suffer from bilateral RLN injuries initially have a flaccid larynx with a breathy voice. As reinnervation occurs, the patients develop a stronger voice; however, they experience more difficulty with respiration [17]. In clinically stable patients presenting with worsening airway obstruction and progressive activity limitation, treatment with Botulinum toxin enables some patients to avoid an ablative surgical intervention or a tracheotomy while awaiting sufficient functional recovery [17].

Botulinum toxin therapy is no panacea and is associated with nearly universal breathy dysphonia and rare dysphagia. Additionally, patients commonly need repeated dosing every 3–6 months to maintain the effect [17].

Long-Term Therapy

Mechanical Aperture Augmentation

As described in 1939, "The desire to get away from the tracheotomy tube has been the father of all operations devised for the relief of bilateral abductor cord paralysis" [18]. Numerous surgical procedures have been proposed to rehabilitate the patient with BVFMI and allow for decannulation. However, the mainstay of surgical therapy for BVFMI over the last 70 years has been augmentation of the glottic lumen. This has been accomplished (with minor variations over time), with three basic procedures. (1) Physical lateralization

of one (or both) vocal fold(s), (2) Ablative augmentation of the posterior glottis, and (3) Lumen augmentation through expansion of the posterior glottic plate. Due to the rarity of BVFMI, the three basic surgical approaches have been employed despite an absence of randomized controlled trials (RCTs) or other rigorous comparative studies to assess their differential effectiveness at avoiding tracheostomy, or their implications for voice or swallowing outcomes. Additionally, it remains unclear which type of procedure is best suited to each of the individual BVFMI grades.

1. Physical lateralization of the true vocal fold: Initially reported as an external, extralaryngeal approach to the arytenoid with utilization of transected omohyoid for unilateral vocal fold lateralization by King in 1939 [18]. Several subsequent authors championed modified external approaches to achieve this common purpose [19, 20]. Ultimately, the rise of transoral endoscopic techniques has relegated open lateralization procedures to largely historical descriptions. Endoscopic suture lateralization was described in 1979 by Kirchner [21] and has been popularized with dedicated instrumentation for endoscopic exposure in the last decade by Lichtenberger [22]. Two polypropylene sutures are looped over one of the paralyzed vocal cords and brought out through the neck skin. A small incision is made, and the sutures are secured in the sternohyoid muscle. The procedure is advocated by its proponents based on its nondestructive nature, reversibility, and minimal invasiveness. The disadvantage to these procedures is that the glottis is widened along the entire length of the vocal fold margin increasing the patient's susceptibility to aspiration while simultaneously decreasing the quality of the voice.
2. Ablative augmentation of the posterior glottis: Resection of the vocal cord and ventricle was first described by Jackson in 1922 [23]. Later, Woodman [24] described external arytenoidectomy and Thornell [25] described transoral arytenoidectomy. All of these techniques required prophylactic tracheostomy and while moderately successful were notable for their poor voice outcomes. In 1984, Ossoff et al. [26] described endoscopic carbon dioxide (CO_2) laser arytenoidectomy. The application of CO_2 laser allowed for increased operative precision through the narrow field of the microscope without the need for tissue manipulation. It improved hemostasis, and decreased intraoperative and postoperative edema.

   Numerous variations of endoscopic arytenoidectomy are described [27–30]. Other investigators have described laser resection of the posterior portion of the membranous true vocal fold [28]. Although direct comparisons are limited due to the conditions' rarity, there do not appear to be identifiable differences in breathing, swallowing, vocal quality, or vocal power outcomes between arytenoidectomy and transverse cordotomy [31]. Ablative laser technique (either arytenoidectomy or cordotomy or a combination of both techniques) remain essentially the standard of care in neurogenic BVFMI. Initially performed posteriorly on one side, it can be repeated in the opposite side if necessary. This procedure can be performed cold; however, most laryngeal surgeons currently employ the CO_2 laser for this purpose [32]. All patients need to be preassessed for baseline swallowing function. This technique has been successful in decannulating patients with bilateral RLN palsies, although some degree of ventilation impairment is still present with exertion and patients typically experience significant trade-offs in voice.
3. Lumen augmentation through expansion of the posterior glottic plate: Posterior cricoid split. Division of the posterior cricoid plate was originally described in 1927 as part of a procedure to address adult laryngeal stenosis [33]; however, it remained an obscure technique in an isolated report, until modification and popularization by Rethi in 1955 [34]. Rethi's original description included laryngofissure, midline vertical posterior cricoid division, interarytenoid muscle resection, wide lateral retraction of the posterior cricoid halves,

and long-term stenting. The raw surface created by separation of the posterior cricoid halves healed by secondary intention with fibrous tissue bridging the gap between the two edges stabilizing the expanded cricoid. The efficacy of core approach Rethi described has subsequently been born out by several other authors' experience [35–38]. Posterior cricoid split has largely been applied to the treatment of BVFMI due to posterior glottic scar or cricoarytenoid joint fixation. Its role in neurogenic BVFMI is undefined.

Reinnervation Procedures

All neural-based rehabilitation attempts seek to restore the function of the posterior cricoarytenoid muscle by reinnervation with nerves presumed to carry neural activity synchronous with inspiration. Nerve anastomosis is an attractive concept, as it would restore the functions of both phonation and respiration. Unfortunately, this technique has been pursued like a holy grail in laryngeal surgery for the last century [39]. Early surgical pioneers, Charles H. Frazier [40], Sir Charles Ballance [41], Frank H. Lahey [42], initially investigated the approach of neural-based therapies for BVFMI after neurogenic injuries. Time and repeated failure have not tempered interest in these approaches [43]. Repair of peripheral nerve injury has undergone a quantum leap in the past hundred years. This has been driven primarily by the introduction of microsurgical optics, instrumentation, and technique. However, equally critical have been fundamental insights into the basic biology of neural repair and regeneration [44] uncovered in the last 20 years. Yet, despite both the technical and biologic advances, clinical outcomes following reinnervation for neurogenic BVFMI have remained underwhelming.

Recently, exploration of the utility of the phrenic nerve in restoring laryngeal abductor function has proceeded under the direction of Professor Jean Paul Marie in Rouen France.

Early animal experiments [45] demonstrated the most superior nerve root of the phrenic provided sufficient stimulation to the abductor muscles of the larynx without denervating the diaphragm. Human studies followed demonstrating the origin of the phrenic nerve arising mainly from the C4 nerve root (with variable C3 and C5 contributions) [46]; the C3 nerve root was felt the best suited for reinnervation of the abductor mechanism of the larynx without compromising diaphragmatic function. Dr. Marie has begun human trials, although results have yet to be published, more than 20 patients have the C3—bilateral abductor (using an ansa cable graft) implantations. The scientific community is anxiously awaiting results.

In 2002, Zheng et al. reported a clinical series of six patients in which one posterior cricoarytenoid muscle was reinnervated using a phrenic nerve and the other using an ansa-NMP transfer. In five of six patients, the phrenic side recovered normal abductor motion but no motion was seen in any of the ansa-reinnervated sides [47]. Building on that success, Li et al. have recently reported on 44 patients treated with selective laryngeal reinnervation utilizing the left phrenic nerve [48]. They report dissection and exposure of the intralaryngeal segment of the left RLN (requiring a posteroinferior thyroid lamina window). All adductor branches of the left RLN, (thyroarytenoid branch, lateral cricoarytenoid branch, and interarytenoid branch) were sectioned. The proximal end of the left phrenic nerve was transposed superiorly and anastomosed to the distal end of the left RLN. They report return of near-normal pulmonary function, sustained voicing, and excellent swallowing outcomes along with EMG evidence of reinnervation. Sixty-five percent of their patients demonstrated moderate to good abduction on clinical exam. By 12 months, they saw a 40–80 % recovery in diaphragmatic movement. The maximum inspiratory pressure (PI_{max}) was decreased significantly compared with normal reference values one year postoperatively, but remained higher than the preoperative values. Their results are exciting and await confirmation with other groups' replication.

Laryngeal Pacing

Building on the successful interface of electrical stimulation technology and human disease within the field of otolaryngology in cochlear implantation, investigators have sought application of external electrode arrays to stimulate the posterior cricoarytenoid muscle to generate abduction. This idea was initially discussed in the 1970s [49], and iteratively advanced over the last 50 years. During the 1980s and 1990s, a variety of animal models offered proof of principle of functional electric stimulation to induce abduction of the vocal folds after transection of the RLN [50].

Small pilot human trials [51] were followed in 1995 by a multi-institutional US Food and Drug Administration study [52]. Funded by Medtronic, Inc., seven patients were implanted with an Itrel II device (whose primary purpose was chronic pain relief). All patients had a tracheotomy prior to this study. There were real gains made by several patients, with three able to achieve decannulation. However, there were technologic issues raised by the human trial, with the study authors noting both long-term susceptibility of the electrode to electrochemical corrosion, as well as the lack of a sensor to pace stimulation with inspiratory effort. Ultimately, due to the technical issues, utilization of the Medtronic devices was stopped. Newer devices including an implantable pulse generator (Genesis XP, St. Jude Medical-Neuro Division, Inc., Plano, Texas, USA), primarily designed for spinal cord stimulation in chronic pain in combination with a deep brain stimulation electrode, have been successfully applied in animal models [53]. Human trials with this device have recently opened enrollment. Continued technologic refinement offers potential for significant application of laryngeal pacing over the ensuing decade.

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The Recurrent Laryngeal Nerve and Medical Malpractice During Thyroid Surgery

25

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Abstract

Medical malpractice litigation for recurrent laryngeal nerve (RLN) injury is relatively rare. The key issues revolve around the use of nerve monitoring, adequacy of postoperative monitoring, and adequacy of consent. It is apparent that the surgeon and surgical facility do an adequate number of procedures to keep complications low and successful surgery high. Consent should be obtained in a thoughtful manner and be adequately recorded in the medical record, preferably in writing. Postoperative monitoring must be adequate to determine the safe time for discharging the patient, and the patient and caregivers must have good postoperative teaching and clear instructions as to where to bring the patient if postoperative complications or questions arise.

Keywords

Thyroid • Malpractice • Recurrent laryngeal nerve • Same-day surgery • Consent

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Introduction

Medical malpractice litigation is seen in nearly every part of the world. The degree to which it affects patient care varies widely. For surgical diseases of the thyroid, injury to the recurrent laryngeal nerve (RLN) is a common allegation [1]. In the USA, a medical malpractice crisis has existed since the 1970s, with increasing costs continuing to the present [2–4]. How much malpractice litigation drives the cost of healthcare through defensive medicine is unknown. Conservative estimates of malpractice costs are now estimated to be $55 billion annually or 2.4 % of total healthcare spending [2].

The tort system in the USA owes its origin to both English common law and the Roman civil law. The founding fathers believed the legal process followed a course of natural selection, through acceptance of law based on customs, the so-called "common law" used by England. This was a process that led to a state of "natural law" that was both innate and unalienable [5, 6].

This evolution of the law in a real sense means that the law is not stagnant. This immutability would be reflected in tort law in the USA and elsewhere, and potentially seen in the trends in medical malpractice. Kern has documented trends in breast cancer litigation, and we have done so with various trends seen in medical malpractice in the head and neck [7–11].

Evaluation of trends, it is hoped, will ultimately lead to risk management strategies and education for physicians and the public. We, and others, have used a computer database to analyze head and neck sub-sites, including the thyroid [9]. In 2003, we published trends in litigation and outcomes from suits settled between 1987 and 2000 [9]. In that study we identified five trends in litigation: delay in diagnosis of cancer, RLN injury, young plaintiff age with a high incidence of female plaintiffs, and plaintiffs exhibiting a "poor outcome," defined as having a persistent active cancer, a permanent neurologic deficit, or being dead.

Management of surgical thyroid disease in the USA, including outpatient management strategies, intraoperative RLN monitoring, and clinical pathway guidelines have changed in recent years. We studied the years 2000–2014 to evaluate changes as reflected in medical malpractice surrounding thyroid surgery [12]. We recorded similar trends in plaintiff demographics and delays in cancer diagnosis and outcomes, and specifically we have evaluated the allegations of RLN injury [12].

The computerized legal database (WESTLAW, West Publishing Co., St. Paul, MN) was used for this study. We searched the database with a variety of terms including thyroid surgery, thyroid disease, thyroid, thyroid carcinoma, and thyroid cancer all in association with medical malpractice. The search includes all state and federal civil trials that involve medical malpractice and surgery of the thyroid gland. Verdict summaries are published from which we abstracted data including plaintiff name, sex, and age; suit's state of origin and date of verdict; verdict outcome and award quantity if plaintiff verdict or settlement; allegations of RLN injury, unilateral or bilateral; if a nerve monitor's presence or absence was alleged, and consent issues. Misdiagnosis or delayed diagnosis of cancer was abstracted, as was outcome. We also recorded allegations of hypoparathyroidism, other surgical complications, and allegations of inadequate postoperative care or monitoring. Negligent credentialing by hospitals or other entities was also recorded.

These databases are voluntarily submitted, and do not contain all the suits occurring, or suits that are dropped prior to settlement or trail. They are, however, the suits that attorneys consider to be highly persuasive, and used to evaluate precedents.

We found 94 suits involving surgery of the thyroid from 1987 to 2014. Twenty-eight (30 %) of suits alleged RLN injury, 9 (32 %) of these were bilateral. Female plaintiffs were seen in 24 (86 %), with a mean age of 49.

Plaintiff awards or settlements were seen in 15 (50.4 %) with a mean award of $1,125,000. Those with a bilateral injury had a plaintiff award or settlement in 5 (55 %), with a mean award or settlement of $1,713,000.

Informed consent would certainly include knowledge of the possibility of RLN injury. Eleven of 28 plaintiffs or 39 % alleged they were not properly informed.

Nerve injury and its sequelae and implications are critical to the head and neck surgeon. Like the thyroid and RLN, the facial nerve is an implicit and paramount risk in parotid surgery. Examining the results of litigation in this area can help illuminate the discussion on the thyroid. In a previous study we analyzed litigation arising from intraoperative facial nerve injury [13]. In these suits, it was apparent that despite the obvious importance and concern for the facial nerve, patients allege in many cases that they were unaware of this complication. Certainly facial nerve paralysis is a primary concern to the surgeon operating in this area, as the RLN is for anterior neck operations. It would seem axiomatic that this discussion occurred and in both cases, it is unlikely that the surgeon did not explicitly bring this to the patient's attention. Nonetheless, in both our thyroid study and the facial nerve study, 30 % of patients believe they were not adequately informed [9–13].

The issue of memory of events is germane to this discussion. Hutson and others demonstrated that patient's recall document a range of 35–57 % retention of information given 7 days before testing [14–16]. Hekkenberg et al., in a study of informed consent for patients undergoing head and neck surgery, found an overall rate of recall of 48 % in patients undergoing thyroidectomy, parathyroidectomy, or parotidectomy [17]. Studies indicate that better recall is seen in better-educated and younger patients, and may be related to anxiety [15–17]. Developing patient rapport is an important risk management consideration. Although much discussion has centered around the reasons patients do not remember warnings about surgical complications, it seems likely that most do understand the gravity and possibility of facial and RLN paralysis. Risk management goals are best met by listing the complication on a written consent form and requiring the patients to sign the form. Providing a copy of the form to the patient not only documents the complication but also may increase the patient's understanding of the procedure and complications [18]. Placing the information regarding complications in the discharge instructions that are produced as part of the EMR is an alternate approach. It has been suggested, and seems likely, that these patients would also be less inclined to seek legal redress for a perceived bad outcome [19].

A second finding in our facial nerve study was that, even with admitted informed consent, plaintiffs sue, and frequently win, when left with this devastating complication like facial nerve paralysis, alleging a surgical misadventure. In our facial nerve study, 31 (84 %) of 37 thought malpractice had been committed even with no allegation of informed consent discrepancies. This supports the claim that there is intrinsic confusion on the part of the lay public regarding complications, outcomes, and actual malpractice. Nonetheless, these plaintiffs persevered in 20 (65 %) of the 31 suits through either plaintiff awards or settlement. Facial and RLN paralysis rates vary, but are low. Procedures have been refined over the years to identify, avoid, or otherwise protect and preserve these nerves [20–22]. Proper training and careful surgical technique are indispensable, but nerve injuries happen to even the best surgeons. Dawes et al. state that patients have a high expectation of a successful outcome and are more inclined to sue for an unsatisfactory outcome [18]. A nerve paralysis is not evidence of malpractice, and negligence can never be imputed from unsatisfactory results. Medical malpractice can only be upheld when all four elements of negligence are proved: the physician has a duty to the patient, there was a breach of that duty, the patient was damaged, and the breach of duty reasonably led to that damage [23]. Certainly the surgeon has a duty to the patient that includes making the correct assessment and plan, discussing the risks benefits and alternatives to proceeding and making sure the patient has a sense of the options. The damage is obvious to all in particular a facial paralysis but also particularly graphic is a patient unable to eat and with a tracheostomy tube as a consequence of bilateral RLN paralysis.

When damage is discovered in the immediate postoperative period it would seem reasonable most often to assume this damage was the result of the operation. The breach of duty is the most nebulous area to prove. The plaintiff has the burden of proof to show that the injury was negligently caused by the defendant and not just that there was injury caused by the defendant. This should be an onerous task. What negligent acts caused the nerve paralysis in these cases? Perhaps a case can be constructed for inadequate scope or training, errors in judgment made intraoperatively, and delays in diagnosis, but in our facial nerve study, 19 of the suits hinged on the paralysis alone and testimony that negligence must have caused that outcome. Facial and RLN paralyses are devastating injuries and doubtless make a compelling sight in court. Awards and settlements can be large, and in our study occurred frequently (12 [63 %] of 19 cases). Careful and thoughtful surgical approaches should, of course, be used. When these are performed, good patient rapport and an honest bedside manner may be all surgeons have to protect themselves if nerve complications occur.

Aside from a careful surgical technique, nerve monitoring has been suggested or studied as a means to prevent or defend against litigation for RLN injury [1, 24–26]. In our study of 94 medical malpractice suits alleging RLN injury, we found only one suit were an allegation of not using a nerve monitor was made [9]. The suit ultimately resulted in a plaintiff verdict of $5,000,000, but had allegations in addition to the omission of a nerve monitor. Abidin et al. in a review using similar methods, but a different computer database, found no allegations of nerve monitors constituting an error of omission [1].

The fact that nerve monitor use does not seem to play any significant role in medical malpractice litigation would be anticipated based on the literature [1, 24–26].

Reasons to use a nerve monitor other than prevention of RLN injury include facilitation of initial localization and confirming an intact nerve at the completion of surgery [27]. Disadvantages include cost and the potential to develop false sense of security. Although some recommend using the monitor during difficult cases, others point out that difficult cases are not always predictable preoperatively [25].

In summary, it seems that medical malpractice litigation for RLN injury is fairly rare. Certainly we must ensure surgeon and surgical facility do an adequate number to keep complications low and successful surgery high. Consent should be obtained in a thoughtful manner and be adequately recorded in the medical record, preferably in writing. Postoperative monitoring must be adequate to determine the safe time for discharging the patient, and the patient and caregivers must have good postoperative teaching and clear instructions as to where to bring the patient if postoperative complications or questions arise.

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Postoperative Management of Superior Laryngeal Nerve Paralysis

26

Craig E. Berzofsky, Amy L. Cooper, and Michael Jay Pitman

Abstract

Superior laryngeal nerve (SLN) injury can cause many symptoms, the most common complaints being the inability to access the upper vocal range, difficulty projecting the voice, and vocal fatigue. Treatment with voice therapy has some limited utility in these patients. Its greatest benefit may be in preventing or treating muscle tension dysphonia, developed in compensation of the SLN injury. Numerous static and one theoretical dynamic procedure have been proposed. These procedures can help augment the cricothyroid distance. These procedures may elevate the modal pitch of the voice with varying success, with only a few patients appreciating improvement in their pitch modulation. The most promising technique described is a muscle-nerve-muscle anastomosis with a neural conduit. This allows the nerve of the healthy cricothyroid muscle to innervate the paralyzed cricothyroid and ultimately leads to simultaneous bilateral muscle contraction. Although patients undergoing this procedure have shown some benefit, it has been reported only in patients who had additional procedures for voice restoration. This results in multiple confounding variables and the true utility of the procedure is unknown. Further research is needed to help identify an optimal treatment for SLN paralysis. Due to the dearth of successful treatment options, prevention of SLN injury should be emphasized.

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Introduction

Superior laryngeal nerve (SLN) injury can cause many symptoms, the most common complaints being the inability to access the upper range of the voice, difficulty projecting the voice, and vocal fatigue. Treatment with voice therapy has some limited utility in these patients. The biomechanical action lost in SLN paralysis is a dynamic one, making surgical restoration difficult. Numerous static and one theoretical dynamic procedure have been proposed with variable success. The most promising technique described is a muscle-nerve-muscle anastomosis with a neural conduit, though evaluation of its success has been difficult. Further research is needed to help identify an optimal treatment for SLN paralysis. Due to the dearth of successful treatment options, prevention of SLN injury should be emphasized.

Anatomy

The external branch of the SLN (EBSLN) controls the ipsilateral cricothyroid muscle (CTM). This branch is more commonly injured than the internal branch, which provides sensation to the supraglottis. Arnold wrote an extensive review of the CTM in 1961 describing its mechanisms of action. The cricothyroid is composed of three bellies: the pars recta, the pars obliqua, and the pars interna. The more midline ventral pars recta extends from the inferio-medial aspect of the thyroid cartilage to the anterior midline portion of the cricoid. The pars obliqua, which is dorsally located, originates more posteriorly on the thyroid cartilage and inserts on the outer surface of the cricoid cartilage. A third muscle belly, the pars interna, extends from the upper cricoid edge to the inner plate of the thyroid cartilage [1]. The pars interna is not described in all descriptions of the CTM. Mu and Sanders further investigated the presence of the pars interna using Sihler's stain, which counterstains nerves and clears muscle tissue. After dissection of the pars oblique and pars recta a horizontal belly of the cricothyroid was identified with similar attachments described by Arnold [2].

Due to its muscular and ligamentous attachments to other cervical structures, the thyroid cartilage is fairly stable and the cricoid cartilage is the more mobile portion of this unit. This movement is articulated on the lateral aspect of the cricoid cartilage and the rounded tips of the inferior thyroid horns [1]. SLN activation leads to contraction of the CTM, which causes approximation of the inferior portion of the thyroid cartilage with the superior aspect of the cricoid cartilage. This elevation of the anterior aspect of the cricoid cartilage causes posterior–inferior displacement of its posterior plate as the cartilage rotates around the focal point of the cricothyroid joint. This in turn pulls the arytenoids and vocal process dorsally, stretching the vocal folds, increasing their tension and the vocal pitch [1].

The pars recta and pars obliqua have imbalanced, but synergistic effects on the cricothyroid joint movement and their effects on voicing. The pars recta is vertically oriented and its contraction causes rotation of the cricothyroid joint. The pars obliqua's more horizontal orientation parallel to the cartilages aids in anterior translation of the cricothyroid joint. Pars recta contraction has a larger effect in the magnitude of change in the fundamental frequency, decreasing the cricothyroid distance and lengthening the vocal folds, than direct stimulation of the pars obliqua. Stimulation of the main trunk of the SLN had the largest effect on the above outcomes, indicating a synergistic effect of the two muscle bellies [3].

Ventrodorsal sliding has also been described with extreme cricothyroid contraction and relaxation. This is minimized by the lateral and posterior ceratocricoid ligaments as well as the cricothyroid articular facets. Despite this, ventrodorsal movement may be responsible for up to 30–40 % of the average change in total length of the vocal fold during voicing [4]. It is clear that the cricoid, though often thought to only move on a hinge, is actually a relatively mobile cartilage. The character of the articular facets and ceratocricoid ligaments influence cricoid motion. Possibly inter-patient differences in these structures are partially responsible for the myriad and disparate movements seen with a unilateral SLN injury. Such inconsistencies in motion have made it difficult to diagnose SLN injury based solely on fiberoptic examination of the larynx.

Presentation

The true rate of SLN injury is unknown. The often-subtle symptoms with a grossly normal voice at modal pitch and inconsistent physical exam findings have likely led to it being grossly underdiagnosed. Arnold described the main symptoms of cricothyroid paralysis as vocal weakness, shortened phonation time, lowering of speaking pitch, reduced vocal range, and loss of singing voice. All of these symptoms are related to the lack of vocal fold tension, which is due to the inability of the cricoid to approximate anteriorly with the thyroid cartilage, thus preventing the posterior movement of the vocal processes and vocal fold stretch [1]. In a study by Dursen et al., similar findings were noted with vocal fatigue being the most common complaint followed by hoarseness, volume disturbance, and loss of range [5]. Nasseri et al. also found vocal fatigue to be the most common complaint, followed by breathiness, dysphagia, poor pitch control, and loss of singing voice [6].

Roy et al. performed a chemical lidocaine block of the EBSLN in ten normal subjects, to mimic SLN injury. They noted a reduction of phonatory frequency, compression of pitch range, and increased speaking fundamental frequency as measured by acoustic analysis. Again, these objective measures indicate the inability to accurately modulate vocal fold length and tension. These patients also complained of weakness, increased effort, and tightness while undergoing the block [7]. Noted in these patients was an elevation of their lower range during speaking and singing. This finding was ascribed to compensatory measures of other vocal fold tensors (vocalis or contralateral cricothyroid muscle) employed to overcome deficits created by SLN injury. Such compensatory measures can often lead to muscle tension dysphonia (MTD) and may be detrimental to the patient's long-term prognosis [5].

Unfortunately, these symptoms and acoustic findings are not specific for SLN injury and can be seen in recurrent laryngeal nerve (RLN) injury as well. As a result, when a patient presents with such complaints, the physician may only be looking for evidence of RLN paralysis on laryngoscopy. Given this need for a higher degree of suspicion, more patients may be affected by SLN injury than previously noted. If patients are not singers, such a specific deficit may go unrealized by patients and may need to be elicited by the physician on questioning or examination.

Glottal Dysfunction

Several studies have tried to identify specific findings on flexible laryngoscopy that would allow for the accurate diagnosis of SLN injury. Unfortunately, the results are often inconsistent and even contradictory.

In his compilation of multiple observational studies Arnold noted different, "typical alterations of glottal appearance" on laryngoscopy. One was the lack of tension of the affected vocal fold. This was thought to be due to intact and unchallenged thyroarytenoid contraction as well as optical comparison to the lengthening of the contralateral vocal fold. There was also loss of vertical symmetry of the vocal folds due to forces of contraction of the cricothyroid. Hypothetically, as the posterior plate rotates posteriorly and inferiorly, the vocal process on the intact side rises

compared to the injured side. Another included lack of tension resulting in a decrease in the blanching of the vocal fold mucosa usually noted with excitation of the SLN. Finally, several studies note anterior arytenoid prolapse [1].

Durson et al. also described multiple findings due to cricothyroid weakness. They noted an absence of "brisk" vocal fold adduction, vocal fold lag on affected side and height disparity. The lack of vocal fold tension due to loss of cricothyroid activity was hypothesized to cause multiple stroboscopic abnormalities in patients with SLN paresis and paralysis. Patients had vocal fold amplitude asymmetry (84.9 %), decreased amplitude (68.2 %), phase asymmetry (92 %), incomplete glottic closure and posterior chink (72.2 %), and decreased mucosal wave (69.1 %). 71.4 % of these patients were noted to have a decreased glissando, which most closely correlates to the clinical manifestation of decreased range [5].

In Arnold's investigation he also described the oblique glottis, which had been observed by others as well. This was suggested to be due to torsion of the cricoid in relation to the thyroid cartilage in the presence of a unilateral SLN injury and cricothyroid dysfunction [1]. Abelson and Tucker studied this glottal configuration after a lidocaine blockade of the SLN. They noted the posterior commissure rotating towards the paralytic side, as well as elongation of the contralateral aryepiglottic fold. As the axis of the larynx rotates, the glottal chink appears oblique with the posterior part of the axis pointing towards the paralyzed side [8].

This "axial rotation/oblique glottis" has, possibly erroneously, become the most consistently cited and most dogmatic laryngeal finding for SLN injury. Despite it prevalence and general acceptance, the sensitivity and specificity of even this finding is controversial. After SLN block, Roy et al. found axial rotation to be inconsistent across multiple tasks. When it was seen, they noted the movement to be opposite of the classical description. In consideration of both of these findings, they suggest that axial rotation is unreliable and is not pathognomonic for SLN paralysis. Comparatively, they noted that petiole deviation towards the paralyzed side during high-pitched tasks was a consistent finding in 60 % of subjects [9].

These conflicting studies, along with the multitude of other unconfirmed findings attributed to SLN injury, highlight the difficulty in accurately diagnosing SLN paralysis on laryngoscopy alone. This reinforces the need to consider a comprehensive history as well as examination of vocal production in addition to laryngoscopic findings when evaluating a patient with vocal complaints and possible SLN paralysis.

Electromyography

Electromyography (EMG) may also be used in the postoperative setting to aid in the diagnosis of SLN injury. Using standard EMG techniques, decreased muscle recruitment, polyphasic action potentials or fibrillation potentials indicate neural injury. Depending on the finding, one could predict the degree of injury and the stage of recovery. These findings can be compared to the contralateral side to increase accuracy [10].

Interestingly, Jansenn performed preoperative and postoperative cricothyroid EMG to identify SLN injury during thyroidectomy. Fifty-two percent (9/17) of patients with a preoperative normal EMG developed a pathologic EMG after surgery. One of the patient's EMG returned to normal, one did not have a follow-up EMG, and the remaining seven patients had persistent EMG abnormalities. Seven of the nine patients with EMG evidence of neuropathy had voice complaints after surgery. In four patients this persisted at last follow-up. A separate group of three patients in this study had preoperative EMG evidence of SLN injury without voice complaints. Each patient's EMG worsened postsurgery with concomitant voice complaints. These symptoms resolved in one. This study, albeit small in size, demonstrates the adjunctive nature of EMG in the diagnosis of SLN injury as well as the high prevalence of SLN neuropathy and persistent dysphonia after thyroidectomy [11].

Dursen et al. also recommend EMG as an adjunctive diagnostic procedure in patients with suspected SLN injury. They had two of their 126 suspected patients who had normal EMGs. They felt the EMG was specific enough that it ruled out SLN paresis as the etiology of their complaints.

It is important to note the specificity of their EMG for SLN neuropathy was not studied with a negative control group, so the accuracy of their EMG is unclear [5]. Despite this, it is likely that EMG is a helpful tool in the diagnosis of SLN neuropathy. Unfortunately, EMG is not a commonly utilized tool in otolaryngology except for some subspecialists and the results are somewhat subjective. Finally, considering the available treatments for SLN neuropathy and the discomfort of EMG, it should be reserved for patients where the information will impact the treatment or if the patient or physician covets a more definitive diagnosis.

Treatments

Unfortunately, treatment of SLN injury is not extremely effective. Voice therapy may help to improve the efficiency of voice use. Several surgical procedures have been described utilizing either static adjustments or reinnervation techniques with varying success.

Voice Therapy

Voice therapy plays an important role in the treatment of SLN injury. Behavioral management generally consists of several key targets including patient education, improvement of vocal function, elimination or prevention of vocally abusive compensatory behaviors, and exercises to increase the fundamental frequency range [12]. Likewise, voice therapy is a key component in managing patient expectations as well as in assisting patients coping with a particularly challenging voice issue.

Decreased ability to modulate the tension of the affected vocal fold often yields compensatory hyperfunction. Early intervention with speech therapy has been postulated to decrease the development of MTD. Dursen et al. noted 23.8 % of patients had concomitant MTD and thought this caused some of the long-term vocal acoustic perturbations in these patients [5]. As such, therapy should commence soon after injury and care must be taken that voice therapy exercises are performed without undo strain. Pitch glides are undertaken with gentle glissandos. In cases of excessively deep-pitched speech or frequent glottal fry, a behavioral goal will often include optimizing the coordination of breath and phonation. More specifically, this includes the elimination of glottal fry, introduction of appropriate phasing and pacing, as well as increased pitch variation for conversational speech, as possible given the underlying pathology. While patients may experience a general lowering of their pitch post-SLN injury, they can still take advantage of improved coordination for more natural-sounding speech. Laryngeal massage, reduction of perilaryngeal tension, relaxed phonation, and increased frontal focus, are all therapy targets to reduce vocal fatigue, ease strain, as well as increase the beauty of the voice.

Most difficult is the case of the singer with SLN injury. Behavioral techniques can do much to normalize the speaking voice, but restoration of premorbid range and vocal dexterity remains a significant challenge. It is helpful, where possible, to engage the singing teacher in the rehabilitation plan, as treatment is likely to be long-term, and gains variable and modest at best.

Framework Procedures

Static procedures were initially employed to help raise a patient's pitch to a more desirable level. Multiple iterations of these procedures have been reported, as well as the justification for their conception. The aim of these procedures was to approximate the anterior cricoid and thyroid ala to replicate their position after contraction of the CTM, resulting in elongation and tensing of the vocal fold.

The first procedures conceptualized were by Arnold, one of which was dynamic and the other static [1]. Although these procedures were never performed, they help to demonstrate the concepts employed to repair the deficit created by SLN injury.

The Thyrohyoido-cricoido-raphy is a dynamic procedure utilizing the distal end of the thyrohyoid muscle and attaching it to the cricoid. The thyrohyoid is released from the oblique line and attached to the CTM or cricoid periosteum depending on

the health of the CTM. Contraction of the thyrohyoid would theoretically elevate the cricoid ring and reduce the cricothyroid distance [1].

The Crico-thyroido-pexy is a static procedure, which fixes the cricoid ring to the thyroid cartilage. This involves static elevation of the cricoid ring. This is performed with the patient awake and phonating so that optimal position of the cricoid can be determined based on the observed vocal change. At this position, the thyroid and cricoid cartilages are fixed using sutures or wires. This procedure statically reproduces the cartilage and vocal fold position after CTM contraction, with the hope of maintaining vocal fold tension and optimizing pitch [1].

Ishikki initially described four phonosurgical procedures. He performed combinations of these procedures on canines immediately after RLN and/or injury [13]. In patients with RLN and EBSLN injury, a persistent glottal chink, height differential of the vocal folds, and laxity of the injured vocal fold were noted after medialization or Type I thyroplasty. To address these persistent deficiencies, Isshiki described a Type IV thyroplasty, which involved approximating the cricoid and thyroid cartilage to simulate contraction of the CTM. This achieved excellent results in the two canines reported. Although Ishikki did not report on these procedures for isolated SLN injury, many of the following procedures are based on this initial description.

Thompson et al. attempted to augment this procedure with fusion of the thyroid and cricoid [14]. They first performed the procedure on canines after SLN transection. The experimental group underwent immediate fusion of the cricoid and thyroid cartilage while no treatment was rendered in the control group. The surgery was performed by exposing the perichondrium of the inferior and superior edge of the thyroid and cricoid cartilage, respectively. They were then fixed together with wire. In addition, a laterally based perichondrial flap was elevated from the thyroid ala, draped over the cricothyroid membrane, and sutured to the cricoid cartilage. Histologic analysis of the surgical site proved that cartilage fusion was possible using this technique. Postoperative analysis comparing the control and experimental vocal folds showed a more favorable position in the experimental group than in the control group.

Shaw et al. utilized a modified Isshiki Type IV thyroplasty, another static procedure, which is similar to the Crico-thyroido-pexy previously mentioned. This procedure involves elevation of the superior-anterior perichondrium of the cricoid and posterior inferior perichondrium of the thyroid cartilage. This modification should allow for direct cartilage interaction and enhance cartilagenous fusion, which was described as the flaw in the original description of Isshiki Type IV thyroplasty. A prolene suture is passed between the exposed cricoid and thyroid cartilage and tension is applied to the suture until optimal voicing is achieved. During several of these procedures a tension meter was used to measure the appropriate vocal pitch in comparison to the appropriate achieved pitch.

Postoperatively all of the patients except one had resolution of their videolaryngoscopic abnormalities including bowing, inferior displaced vocal fold, and posterior glottic rotation. Patients also had statistically significant improvement of fundamental frequency and elevation of falsetto frequency compared to preoperative assessment. Basal fundamental frequency and frequency range showed no significant changes compared to preoperative values. Both self and independent rater perceptual ratings showed significant improvement in all postoperative settings. These improvements were reported up to 1 year after surgery [15].

Though Shaw et al. had success in their series; others found improvement to be less than expected and often temporary. In addition, the voice tended to be weaker with less acoustic power than desired [6]. Due to the suboptimal results obtained after Type IV thyroplasty alone, Nasseri and Maragos combined this with a Type I thyroplasty. By supporting and medializing the affected vocal fold with a medial implant and adding an arytenoid adduction suture as needed, they surmised that vocal power would be restored. A total of nine patients underwent this procedure for isolated SLN injury. The modality of reporting did not elucidate the symptomatic improvement by patient, making it difficult to determine

the overall success of the operation for each patient. Outcome was reported by symptom, as present or not. In most cases symptoms resolved after surgery. In one case a patient developed odynophonia. Of the two patients complaining of an impaired singing voice preoperatively, only one improved. Many of the stroboscopic parameters noted on preoperative assessment resolved, though this was variable, and the noise-to-harmonic ratio was significantly improved.

Reinnervation Procedures

In contrast to framework procedures, reinnervation procedures attempt to reinnervate the denervated CTM, so as to reestablish dynamic function. As the cricothyroid effect on voice is dynamic, this would be the only way to regain full vocal function. Reinnervation has been utilized in the treatment of RLN injury. This is either with RLN reanastomosis or with ansa cervicalis reinnervation of the RLN. After reinnervation, the vocal fold remains immobile but has improved tone and position. This results in better glottal closure and vocal improvement. The lack of movement after RLN reanastomosis is due to synkinesis with random reinnervation by axons from antagonistic muscles. This is unlikely to be an issue in cricothyroid reinnervation as the SLN is not a mixed nerve [16]. As a result, theoretically, reinnervation of the CTM with the SLN may result in dynamic vocal fold movement and tension with restoration of vocal range and function. Unfortunately, there are few reported attempts of such reinnervation.

Reinnervation procedures of the internal branch of the SLN have been performed for sensory function in adults with severe dysphagia. Two adults with lateral medullary brainstem stroke developed severe dysphagia due to sensory disturbance, cricopharyngeal spasm, and poor laryngeal elevation. They were treated with a cricopharyngeal myotomy, laryngeal suspension, and neurorrhaphy from greater auricular nerve to internal branch of SLN. The distal branch of the greater auricular nerve was transposed and anastomosed to the internal branch of the SLN. By 12 months after surgery, both patients had return of laryngeal sensation and were tolerating an oral diet without developing aspiration pneumonia. This report suggests that the sensory function of the SLN can be restored with reinnervation [17].

In the only description of cricothyroid reinnervation, El-Kashlan et al. utilized a muscle nerve muscle neurotization technique to reinnervate the cricothyroid in patients with RLN and SLN injury undergoing concomitant ansa hypoglossi to RLN reinnervation. A free graft of a few centimeters of ansa hypoglossi was used. One end was buried in the innervated cricothyroid belly and the other in the belly of the denervated cricothyroid. This technique allows nerve sprouting from the intact CTM through the neural conduit to the denervated cricothyroid. In theory this would lead to simultaneous contraction of bilateral CTMs, allowing a return to preoperative function. In their study, three patients underwent this procedure with subjective improvement in voice quality. Two of the patients underwent postoperative EMG and both had evidence of cricothyroid reinnervation. Although promising, the conclusions of this study are limited because of the concomitant RLN injury and treatment. As such, identifying improvement due solely to the cricothyroid reinnervation is impossible [18]. This technique needs be performed in patients with only SLN injury to understand its effectiveness. If successful, this could reestablish cricothyroid activity in concordance with the contralateral muscles to allow for bilateral dynamic control over vocal fold tension and pitch range. The procedure would likely need to be refined, possibly with separate grafts from each belly of the cricothyroid to the respective bellies on the denervated side.

Conclusion

The major symptom of isolated SLN injury is lack of vocal range and difficulties with control over pitch change, due to the paralysis of the CTM. Many patients also complain of vocal fatigue and difficulty with projection. SLN injury is a difficult injury to treat due to the lack of surgical procedures that can restore the dynamic

function of the CTM. Reinnervation of the CTM and restoration function may be a possible in the future. Voice therapy may be helpful in patients to improve vocal efficiency and prevent or treat maladaptive compensatory behaviors. The difficulty in treating SLN paralysis highlights the importance of preventing injury of the SLN in the first place.

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Index

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