The evolution and progress of studies of the anatomy & electrophysiology of the laryngeal nerves in thyroid surgery

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Abstract: Thyroid surgery has always been closely involved with the recurrent laryngeal nerve (RLN) and the external branch of the superior laryngeal nerve (EBSLN). The goal of thyroid surgery is to remove all pathological thyroid tissue while preserving the parathyroid glands and both laryngeal nerves to ensure patients the highest quality of life after the operation. The goal of this paper was to assess the evolution and progress of studies of the anatomy & electrophysiology of the laryngeal nerves in thyroid surgery. Our knowledge of the anatomy and electrophysiology of laryngeal nerves in relation to thyroid operations has evolved over the centuries from visual RLN identification to the functional RLN identification with intraoperative neural monitoring (IONM). The progress in RLN identification has changed the surgical technic, surgical strategy in order to minimize the rate of complications. Now the thyroid surgery is safe procedure with the high quality of voice after this operation.

Keywords: Thyroid surgery; laryngeal nerves; intraoperative nerve monitoring

Introduction

Thyroid surgery has always been closely involved with the recurrent laryngeal nerve (RLN) and the external branch of the superior laryngeal nerve (EBSLN). The goal of thyroid surgery is to remove all pathological thyroid tissue while preserving the parathyroid glands and both laryngeal nerves to ensure patients the highest quality of life after the operation. In cases of unilateral RLN damage, if there is a hoarse or breathy voice or vocal fatigue, then in cases of bilateral injury we could expect acute airway obstruction requiring tracheostomy (1). A reduction in the ability to produce high frequency tones, a breathy voice and hoarseness are also observed in patients who have undergone thyroidectomies with EBSLN injury (2). In one of the biggest review analyses we find that the

prevalence of temporary vocal fold palsy is 9.8%, and that of permanent vocal fold palsy is 2.3%. The rate of EBSLN injury is among the most underestimated complications, but according to the latest study by Barczyński , its prevalence could range as high as 58% (2,3). Injuries to the laryngeal nerves have a major impact on the quality of life after thyroid surgery, because the voice is not only the basic tool of human communication; it is also often a professional tool. Taking into account the fact that, according to Chandrasekhar *et al.* (4), one in ten thyroidectomy patients have temporary injuries, with longer-lasting problems in up to 25%, detailed knowledge of the anatomy and the physiology of the laryngeal nerves is essential to modern thyroid surgery.

Our knowledge of the anatomy and electrophysiology of laryngeal nerves in relation to thyroid operations has

evolved over the centuries, and the aim of this paper is to present an overview of that progress.

The history of the RLN

The Sushruta Samhita, a medical text written in India in the 6th century BC, stated that an injury in the neck in the region of the angle of the jaw caused hoarseness. This was the first described relationship between the voice and the RLN; the author, however, thought that the hoarseness was due to injury to the vessels of the neck (5). In the 1st century AD, Rufus of Ephesus was the first to discover that injuries to a nerve, not to vessels, were responsible for this type of vocal change (6). Galen's work in the 2nd century contributed significantly to our knowledge of the anatomy and physiology of the RLN. He described the nerves in detail, finding that they are in contact with the laryngeal muscles, and called them recurrent nerves (*reversivi*). In his scientific work on animals Galen demonstrated that when the nerves are cut, pigs stopped squealing (7). He discovered vocal problems in patients operated on by surgeons with poor knowledge of the anatomy of the nerve. Undoubtedly, Galen's discoveries initiated further research on the RLN among surgeons and anatomists. Galen's studies led successive generations to recommend caution around the vocal nerves and the carotid arteries, to avoid cutting a blood vessel or nerve (8-10).

The Renaissance saw the next milestone in medical knowledge of the RLN with Leonardo da Vinci's and Vesalius's accurate descriptions and rich illustrations of the nerves' course (11,12). In the 17th and 18th centuries, there were more and more works on the complications and mechanisms of injuries to the RLN and ways to avoid such complications. The 19th century was a great period in the development of surgery, but the results of thyroid treatments were still unsatisfactory. Thanks largely to improvements in antiseptics, the rate of mortality in Billroth's series of thyroidectomies fell from over 40% in 1877 to 8.3% in 1881. Voice-related complications were very high; 25% of the patients had unilateral nerve injuries and 4.5% had bilateral damage; as many as 10.5% required tracheostomies (13). It is worth emphasizing that the incidence of RLN injury was probably higher than these statistics, because laryngeal examinations were not done. At the end of the 19th century, Kocher reported much better results regarding RLN injury (14). Billroth, Kocher and Mikulicz protected the nerve by identifying the inferior thyroid artery as a landmark for the RLN, or by leaving the posterior part of the goiter.

In the early 20th century, Alexander Bobrov, a famous Russian surgeon, was the first to propose visual identification of the RLN; similarly, August Bier from Berlin recommended routinely exposing the RLN (15). These views, however, were in contrast to other surgeons in this period. One of the best-known surgeons of this era, George Crile, believed that the region of the RLN is a "no man's land", which meant that the posterior capsule of the nerve should be left untouched (16). The saying "a nerve if seen is injured" originated with William H. Prioleau in 1933, and functioned for many years to come (15). An undoubtedly major breakthrough in thyroid surgery was the appearance of Frank Lahey's study in 1938. On the basis of more than 3,000 thyroid operations, Lahey reported that routine visual identification of the RLN does not increase, but definitely reduces the number of RLN injuries, showing a decrease in RLN palsy from 1.6% to 0.3% (17). Lahey's work was a step into modern thyroid surgery. Further progress was made in 1970, when V. H. Riddell pointed out that visual identification of the RLN resulted most often in transient injury, as opposed to permanent injury in cases where the nerve was not identified (15).

Interestingly, despite the developments described above, no attention was paid to the EBSLN until 1935, when the world-famous operatic soprano Amelita Galli-Curci underwent a catastrophic thyroid operation, which led to interest in the EBSLN (15).

Visual identification of the RLNs

Throughout the rest of the 20th century and into the 21st, visual RLN identification was the basis of modern and safe thyroid surgery. In 1994, a big multicenter study by Jatzko *et al.* enrolled 12,211 patients undergoing thyroidectomies, and compered thyroid operations with and without RLN identification. This study showed that the rates of transient and permanent RLN injury were 7.9% and 5.2% respectively without nerve identification, and 2.7% and 1.2% respectively with RLN identification; the differences were statistically significant (18). Similar conclusions were drawn by Hermann in 2002, who pointed out that extensive dissection of the RLN allows surgeons to monitor the nerve, with a palsy rate about 1–2%, which was lower than without any exposure of the nerve (19).

Nowadays, RLN identification is the gold standard in thyroid surgery, and there is no doubt that it protects the nerve against inadvertent injury (15,18,19). Because of

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Table 1 Advantages of IONM in surgical practice

The impact of IONM on surgical practice
RLN identification
Aid in RLN Dissection
Diagnosis of RLN injury
Identification of the mechanisms of RLN injury
Prognostication of RLN postoperative function
Staged thyroidectomy
Prevention of bilateral paresis
Minimization of the rate of vocal palsy
Identification of anatomical variants
Identification of non-recurrent laryngeal nerves
Greater completeness of thyroid operations
Educational value for residents in training
Reduced medicolegal issues
Research

IONM, intraoperative neural monitoring; RLN, recurrent laryngeal nerve.

the many anatomical variants of the RLN and different pathologies of the thyroid, visual RLN identification can be challenging, even for skilled surgeons. It requires extensive knowledge of RLN anatomy, experience and training (20). Many surgical techniques have been described for removing pathological thyroid tissue and avoiding injury to the RLN with visual RLN identification. Usually three main approaches to the nerve are used during thyroid operations: lateral, inferior or superior. In routine cases the lateral approach is popular, finding the nerve laterally at the mid-polar level with medial thyroid lobe retraction. This technique, however, is insufficient in cases of large thyroid goiters or in reoperations in a scarred field. The inferior approach identifies the RLN at the thoracic inlet: in the lateral thoracic inlet on the right side and in the paratracheal thoracic inlet on the left. The main use of this approach is in reoperations and in cases of huge cervical goiter. The superior approach helps surgeons find the RLN at the laryngeal entry point, which is useful in substernal goiters, or if other approaches have failed (15). In visual RLN identification, surgeons often use landmarks, such as the inferior thyroid artery or Zuckerkandl's tubercle, to find the nerve. Knowledge of the relationships between these structures is crucial when exposing the nerve (21,22).

There are many different techniques in RLN visualization: palpation of the nerve, retraction of a partially mobilized thyroid lobe, and snapping palpation or "plucking" of the nerve, allowing identification (15). Some surgeons use magnifying glasses during thyroid operations to improve nerve identification. For many years, surgeons believed that visual RLN identification is enough to protect the nerve from damage, but now we know that visual identification only confirms that the RLN is anatomically intact, and RLN palsy after thyroid surgery can also happen when the nerve is preserved anatomically intact. This is because of different causes of RLN injury, including ligation, traction, clamping injury, suction, compression, contusion, electrical or thermal injury to anatomical intact nerves (15,18,23,24). Increased awareness of the mechanisms of RLN injury led to a search for new and better methods of monitoring the RLN during thyroidectomy.

Functional identification of the laryngeal nerve

Visualization of the RLN is still is the gold standard in thyroid surgery for preventing nerve injury, but an intraoperatively visualized and structurally intact nerve does not represent its functional status. Introducing neural monitoring of the RLN was undoubtedly one of the greatest achievements in thyroid surgery in the 20th century. Intraoperative neural monitoring (IONM) has many advantages (*Table 1*), but primarily it allows surgeons to monitor the functioning of the nerve, which has significantly affected surgical techniques, intraoperative strategy and the quality of treatment of thyroid pathologies.

In 1848, Emil du Bois-Reymond first noticed electromyographic (EMG) activity from muscles after stimulation of a nerve (25). One hundred years later, Foerster and Alternberger used the EMG in practice (25). The primary purpose of neural monitoring was to identify changes in nerve function before inadvertent damage to the nerve. Its use also helped to find neural structures before their visual identification in the operating field (25). At first IONM was used mainly by neurosurgeons, vascular surgeons, orthopedists and otolaryngologists. In thyroid surgery, neural monitoring of the RLN and EBSLN was first described by Shedd in 1966 in a canine model using endolaryngeal balloon spirography (26). He observed changes in a pressure recording from a balloon in the dog's larynx upon electrical stimulation of the RLN. This was the first method described for electrical identification of

the RLN. However, Shedd didn't succeed in identifying the EBSLN by this method. Shedd's method was later tested during thyroid operations in humans with good results. Riddell in 1970 (27) and Gavilán and Gavilán in 1986 (28) presented the use of nerve stimulation in RLN identification, but both reports emphasized that extensive knowledge of RLN anatomy is still the basis of safe thyroid operations. In subsequent years of the second half of the 20th century, various invasive and noninvasive neural monitoring techniques were presented: laryngeal palpation, glottic pressure monitoring, glottic observation, endoscopically placed intramuscular vocal cord electrodes, endotracheal tube-based surface electrodes (1,15,29). The post popular and easiest to use turned out to be the system equipped with surface electrodes fixed to an endotracheal tube, which works better than intramuscular electrodes, which could be implanted in the wrong location or migrate in any direction.

The next step in the development of IONM and its dissemination was the standardization of this technique (1,2). In 2011, guidelines for RLN monitoring were published (1) and in 2013 Barczyński and the Neural Monitoring Study Group standardized EBSLN monitoring in thyroid surgery (2). These recommendations normalized the technique of neuromonitoring and greatly influenced its spread around the world (29-31). The technique of IONM quickly evolved, leading to the use of new systems capable of continuous monitoring (C-IONM) (32). C-IONM is an advanced tool to improve risk management of the RLN through ongoing determination of vagus amplitude and latency during thyroid surgery. C-IONM provides immediate alerts throughout the thyroid operation being performed. This technique is better than intermittent neural monitoring, which recognizes RLN malfunctions only after the damage has happened (33). At present we are observing rapid growth of the use of IONM in thyroid surgery all over the world, and its benefits for both patients and surgeons.

The impact of functional assessment of laryngeal nerves on thyroid surgery

Intraoperative nerve monitoring increases the rate of early and definitive RLN identification, because it locates the nerve before visual confirmation (34). The nerve can be mapped out by a step-by-step probe stimulation in the area of its potential course, usually the paratracheal region. Neural mapping is of great of importance in difficult thyroid operations such as secondary thyroidectomies,

where the nerve is distorted after the first intervention on the neck (34,35). Moreover, IONM can distinguish between nerves and blood vessels or other structures in the operating field. According to the literature, the rate of RLN identification with IONM is almost 99% versus about 90% identification without IONM (36,37). IONM is used not only in RLN identification, but is also helpful in safely dissecting the nerve while monitoring its function. Traction of the RLN is one of the main causes of injury to it, and IONM, particularly C-IONM, can protect the nerve from extensive traction caused overstretching (38).

The application of IONM in thyroidectomy has influenced surgical strategy. Monitoring the neural function of the RLN has great prognostic significance for the postoperative function of the nerve. This prognostication is possible intraoperatively, not postoperatively, which protects patients from bilateral vocal cord palsy (39). This is important during total thyroidectomy, which is always associated with a risk of bilateral paresis. In case of a loss of signal on the first side operated on, the surgeon should consider stopping the procedure. With the introduction of IONM the concept of staged thyroidectomy has emerged. Staged thyroidectomy is defined as thyroid/neck resection performed at two different times: the first operation is limited to excision of the dominant lobe, and the second is operated on later (40,41). Before the surgical procedure, the possibility of undertaking a staged thyroidectomy should be discussed with the patient, the anesthesiologist and the endocrinologist in order to reach an optimal decision in case of complications. According to Goretzki's study, in 85% of patients with known nerve injury, and in 56% with negative IONM stimulation on the first operated side, the surgical strategy was changed to avoid potential bilateral RLN palsy (42). This was in contrast to a 17% rate of bilateral vocal cord palsy when the surgeon continued the operation after a loss of signal on the first resected side. The decision to undertake a staged thyroidectomy can be taken into consideration only if the surgeon is perfectly experienced in loss-of-signal troubleshooting algorithms (1). In the future the use of neuromonitoring could eliminate bilateral vocal cord palsy, the most frightening complication of thyroid surgery, and one which significantly influences the quality of life.

Functional RLN assessment should decrease the rate of RLN injuries. But this thesis is difficult to confirm for two reasons: first, the rate of incidence of transient and permanent RLN injury is relatively low, so a large study group of patients needs to be enrolled in order to reach

an adequate statistical power; second, not all patients undergo postoperative laryngoscopies following thyroid operations. However, in a study involving more than 850 patients, Barczyński concluded that IONM could reduce the prevalence of neural injury (43). In this study transient RLN injuries were found in 2.6% and permanent injuries in 1.4% of the RLNs in procedures with IONM *vs.* transient paresis in 6.3% and permanent paresis in 2.4% of the nerves in procedures without IONM.

Progress in mapping RLN anatomy with the use of IONM

Functional assessment of the RLN during thyroid surgery has made it possible to find out more about its anatomy. Extralaryngeal branches of the RLN, non-recurrent RLNs and the nerve's relationship with the inferior thyroid artery could be precisely confirmed with the use of IONM (21).

Extralaryngeal branches of the RLN are a common variant. The rate of RLN branching identified with IONM is 28% *vs.* 17% in patients operated on without IONM (44). Moreover, IONM makes it possible to distinguish the anterior (motor) branch from the posterior (sensory) branch of the RLN. An electromyography signal and twitching of the larynx can be induced through IONM stimulation of the anterior branch; neither an EMG signal nor a laryngeal twitch results from stimulation of the posterior branch (45).

IONM is especially useful in identifying non-recurrent inferior laryngeal nerves (NRLN)—a rare but asymptomatic anomaly. After IONM was introduced, an algorithm for identifying NRLNs was developed. 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 NRLNs (46).

Conclusions

Over the centuries our knowledge of the anatomy and electrophysiology of laryngeal nerves has evolved from visual identification to functional assessment of the nerve. The introduction of intraoperative nerve monitoring was undoubtedly the biggest achievement in recent years.

Acknowledgments

Footnote

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