



Electromyographic Amplitude Changes in the Laryngeal Adductors during Thyroidectomy with Vagal Nerve Stimulation: A Marker of Tensile Stress in the Recurrent Laryngeal Nerve?

James C. Lee^{1,2}, Sze Ling Wong¹, William R. Johnson^{1,2}, Meei J. Yeung^{1,2}, Simon Grodski^{1,2}, Jonathan W. Serpell^{1,2*} and Michael Bailey³

¹Monash University Endocrine Surgery Unit, Alfred Hospital, Australia

²Department of Surgery, Monash University, Australia

³Department of Epidemiology and Preventative Medicine, Monash University, Australia

*Corresponding author: Jonathan W Serpell, The Alfred Hospital, Commercial Road, Prahran, Victoria 3181, Australia, E-mail: serpellj@bigpond.com

Abstract

Background: Most Recurrent Laryngeal Nerve Palsies (RLNP) occurs with visually intact nerves, indicating neurapraxia. However the mechanism of RLNP neurapraxia in intact nerves is not well understood. During thyroid surgery, Recurrent Laryngeal Nerve (RLN) palsy has occasionally been observed immediately following anteromedial rotation of the thyroid lobe (AMRT), upon identification but prior to dissection of the RLN. We postulated that traction placed on RLN during AMRT may lead to neurapraxia. This study aimed to describe these cases, and to measure Electromyographic (EMG) changes in the vocal cord adductors (VCA) with Vagus Nerve (VN) stimulation, before and after AMRT, and to correlate the EMG findings to prediction of RLN palsy.

Methods: Firstly, the cases of RLN palsy following AMRT are described. Secondly, in a prospective study, the EMG amplitudes of 138 VCA muscles following VN stimulation were measured using the Intraoperative Nerve Integrity Monitor (IONM) during thyroidectomy in 90 patients. The EMG amplitudes of VCA with VN stimulation were measured before and after AMRT. All data was collected during a 16-month period, between 2012 and 2013. Standard statistical methods were used to analyse the data.

Results: A retrospective series of 7 cases is described where EMG activity with VN stimulation was lost following AMRT upon identification but prior to dissection of the RLN.

In the prospective study of 90 patients, anteromedial rotation of the thyroid caused a significant increase in EMG amplitude on the right side ($p=0.02$) but not on the left ($p=0.44$). Multivariate analysis identified only extralaryngeal branching of the RLN to be associated with the EMG change.

Conclusion: The increase in EMG amplitude of the VCA with right VN stimulation is likely to represent hyper excitability of the RLN after AMRT. Further studies are required to explore the underlying mechanism of this finding, and correlate it to the development of nerve palsy.

Keywords

Vagus nerve, EMG, Recurrent laryngeal nerve palsy, Thyroidectomy, Nerve monitoring, Neurapraxia

Abbreviations

RLN: Recurrent Laryngeal Nerve, RLNP: Recurrent Laryngeal Nerve palsy, IONM: Intraoperative Neuromonitoring, VCA: Vocal Cord Adductor, VN: Vagus Nerve, AMRT: Anteromedial Rotation Thyroid, EMG: Electromyogram

Introduction

Vocal cord paralysis due to iatrogenic injury of the Recurrent Laryngeal Nerve (RLN) is one of the most serious complications in thyroid surgery [1,2]. Recurrent Laryngeal Nerve palsy (RLNP) may result in difficulties with phonation, respiration, and airway protection during swallowing, hence severely affecting a patient's quality of life. Although many surgical techniques have been described to prevent RLN injury, the incidence of permanent RLNP remains between 0 – 18.6 % of thyroidectomies, and temporary RLNP 1.4 – 38.4 % of cases [3].

Risk factors for RLNP in thyroid surgery include re-operative surgery, thyroid cancer, central compartment lymph node dissection, surgeon inexperience, retrosternal goitre, RLN bifurcation, RLN anatomical anomalies, and non-identification of the RLN [2]. The possible mechanisms of RLN injury during thyroidectomy include stretching or traction resulting in increased tensile stress within the nerve, transection, clamping, ligation, electro-thermal injury, ligature entrapment, and ischaemia [4].

Most RLN palsies occur with visually intact RLNs (85-90%). Division and crushing injuries of the RLN are uncommon. Most RLNPs are temporary, and recover rapidly, suggesting neurapraxia of the RLN. However, the pathophysiology of these nerve injuries resulting in neurapraxia, with intact RLNs is not well understood [4-6].

In our institution, we routinely use Intraoperative Neuromonitoring (IONM) in all thyroidectomy cases as an aid to identification and preservation of the RLN. The technique of IONM

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involves a number of steps, but essentially uses a stimulation current of 1.0mA applied to the RLN, which when conducted by the nerve results in contraction of the ipsi lateral Vocal Cord Adductor muscle (VCA). This contraction is detected by surface electrodes on the endotracheal tube which is positioned between the vocal cords. The surface electrodes record the EMG waveform of contraction from the laryngeal adductors, allowing measurement of EMG amplitude. The electrodes record events with a threshold set at 100 micrvolts. At operation, to test the IONM is functioning satisfactorily, identification and stimulation of the vagus nerve (VN) is first performed to establish integrity of the entire circuit, allowing subsequent stimulation of the RLN, a branch of the VN, as dissection of the RLN proceeds during thyroidectomy [7].

We have occasionally noted during thyroidectomy loss of EMG signal from the VCA upon VN stimulation, immediately following delivery of the thyroid lobe anteriorly by rotation into the wound, a manoeuvre we term - Anteromedial Rotation of the Thyroid Lobe (AMRT), upon identification but prior to dissection of the RLN. In these cases the VN initially stimulated the VCA, but signal was lost following AMRT upon identification but prior to dissection of the RLN. There are similar cases described in the literature, however, the precise underlying mechanism of neurapraxia in those cases is unknown [4-6]. The manoeuvre of AMRT results in a longitudinal traction force on the RLN. It is possible that longitudinal traction placed on the RLN during AMRT resulting in increased tensile stress in the RLN, may lead to RLN neurapraxia.

Further, a change in EMG amplitude during IONM may be a surrogate marker of traction and tensile stress, and therefore the development of RLN neurapraxia. It is known that with initial neural injury, hyper excitability may lead to increased EMG amplitude, whereas with progressive neural injury, EMG amplitude will decrease and ultimately be lost.

Therefore, the aims of this study were twofold. Firstly, to document the cases where the EMG from the VCA with VN stimulation was lost following AMRT, and secondly, to undertake a prospective study to determine if AMRT alone results in EMG amplitude changes in the VCA with VN stimulation, and to determine if the AMRT-associated EMG amplitude changes are a predictor of RLN palsy.

Patients and Methods

This study was approved by the Human Research and Ethics Committee of The Alfred Hospital, Melbourne.

This study is in 2 parts:

Part 1 – Case series

The Monash University Endocrine Surgery Unit (MUESU) Database (1171 thyroidectomy cases, between January 2012 and November 2013) was searched for cases where VCA signal was lost with VN stimulation sometime between AMRT and before RLN dissection. Demographic and surgical data were collected and presented for these cases. EMG values were not recorded routinely for these retrospective cases. Therefore, these cases were not included in the second part of this report.

Part 2 – VCA EMG changes with AMRT

A total of 90 consecutive patients undergoing thyroidectomy

at The Alfred Hospital were prospectively recruited between August 2012 and November 2013. Fifty patients underwent total thyroidectomy, and 40 underwent hemi-thyroidectomy, resulting in 140 RLNs studied. Of these, 2 were excluded due to missing data, resulting in 138 RLNs available for analysis. All patients had pre- and postoperative laryngoscopy to assess vocal cord function [8].

All procedures were performed under general anaesthesia, and using the Xomed Nerve Integrity Monitor (NIM; Medtronic) with the accompanying Standard Reinforced EMG Endotracheal Tube [7]. At induction, 4 mg of dexamethasone was routinely administered [9]. Short-acting muscle relaxants (suxamethonium, cisatracurium, or rocuronium) were used in some of cases at the discretion of the anesthetists. If muscle relaxants were used, adequate return of muscular function was confirmed prior to vagal stimulation, or reversal of the relaxant was given to ensure absence of neuromuscular blockade.

Thyroidectomy was performed according to our previously described technique [10]. We ligate, rather than use vessel sealing devices for superior pole vessels, hence avoiding the possibility of heat injury to the RLN prior to AMRT. During each lobectomy, the evoked EMG in the VCA, as detected by the surface electrodes, was recorded at 2 time points – before (designated “V1”) and after (designated “V2”) anteromedial rotation of the thyroid lobe (AMRT) with VN stimulation. All EMG amplitudes recorded were the median peak values of the evoked EMG activities. The time lapsed between each of the recordings during a single lobectomy was also recorded.

The VN was stimulated with a handheld neuro-stimulatory probe set at 1.0mA. This results in supra-maximal stimulation of the nerve. The EMG amplitudes generated from the VCA with VN stimulation were recorded by the EMG endotracheal tube, with the detection threshold set at 100µV. Other data collected included age, gender, and the weight and dimensions of the resected thyroid lobe.

Statistical Analysis

All variables were assessed for normality with normally distributed variables reported as means and Standard Deviations (± SD) and non-parametric variables reported as medians and Interquartile Ranges (IQR). A paired t-test was used to compare V1 and V2.

Relationships between EMG amplitude change and other variables were determined using multiple linear regression and reported as parameter estimates ± Standard Errors (SE). A two-sided p-value of 0.05 was considered to be statistically significant. All analysis was performed using SAS version 9.3 (SAS Institute Inc., NC, USA), and were undertaken by a (MB).

Results

Part 1 – Case series

We encountered 7 cases of temporary RLNP where IONM showed neurapraxia at the level of the VN after AMRT. In all 7 cases the VN initially stimulated, but signal was lost after AMRT, upon identification but prior to dissection of RLN. In each case once the RLN was identified it did not stimulate, and postoperatively RLNP was confirmed with naso endoscopy. Further details of these cases are shown in Table 1.

Table 1: Case series of RLNP with AMRT

No	Age (year)	Gender	Procedure	Indication for Surgery	Affected side	Bifid RLN	Preoperative vocal cord movement	Postoperative vocal cord movement	Postoperative Hoarseness	Duration of RLNP recovery (month)
1	62	M	TT	MNG	Left	Yes	Normal	Left palsy	Presence	3
2	64	M	TT	MNG	Left	No	Normal	Left palsy	Presence	2
3	55	M	HT	Thyroid nodule	Right	No	Normal	Right palsy	Presence	6
4	79	F	TT	MNG	Left	No	Normal	Left palsy	Presence	1
5	66	F	HT	MNG	Left	Yes	Normal	Left palsy	Presence	2
6	56	F	TT	MNG	Right	No	Normal	Right palsy	Presence	1
7	75	M	TT	Toxic MNG	Right	No	Normal	Right palsy	Presence	2

Abbreviations: M: Male, F: Female, TT: Total Thyroidectomy, HT: Hemithyroidectomy, MNG: Multinodular Goiter

Table 2: Median EMG amplitudes from vocal cord adductors (VCA) following vagus nerve stimulation, and the difference of pre-to-post AMRT (V1 – V2) EMG amplitude

Measurement	Left			Right		
	Median EMG amplitudes (µV)	IQR	P-value	Median EMG amplitudes (µV)	IQR	P-value
EMG from VCA pre-AMRT (V1)	519	316 to 857		522	367 to 811	
EMG from VCA post-AMRT (V2)	612	368 to 905		698	453 to 1048	
Difference in EMG amplitude of VCA before (V1) and after (V2) AMRT	10.5	-135 to 169	0.44	77	-93 to 1597	0.02

Table 3: Linear Regression analysis of factors influencing the pre-to-post AMRT (V1 – V2) difference in Electromyogram (EMG) amplitude of the left and right VCA

Factor	Right VCA		Left VCA	
	Parameter Estimate +/- S.E.	p-value	Parameter Estimate +/- S.E.	p-value
Extralaryngeal branching of ipsilateral RLN	176 ± 363	0.62	-588 ± 281	0.04
Suxamethonium	-128 ± 137	0.35	-314 ± 112	<0.01
Rocuronium	121 ± 0.574	0.57	155 ± 98	0.12
Cistracurium	235 ± 0.923	0.92	-43 ± 239	0.86
Age	3.61 ± 0.512	0.51	-2.8 ± 2.75	0.3
Weight	-0.61 ± 1.48	0.68	1.04 ± 1.23	0.4
Thyroid size (medial to lateral dimension)	-2.1 ± 4.65	0.65	2.37 ± 3.27	0.47
Thyroid size (anterior to posterior dimension)	-4.1 ± 5.49	0.64	2.03 ± 4.79	0.41
Thyroid size (superior to inferior dimension)	-1.6 ± 3.34	0.64	-2.4 ± 2.68	0.06

Part 2 – VCA EMG changes with AMRT

The mean age of the 90 patients studied was 53 ± 16.7 years (range 17–86), and the female-to-male ratio was 4:1. No preoperative vocal cord palsy was identified.

The initial EMG amplitudes of VCA, following stimulation of the left and right VNs were similar prior to AMRT; the left VCA had a median of 519µV (IQR 316 to 857) and the right VCA had a median of 522µV (IQR 367 to 811), p=0.49. After AMRT, the right VCA median EMG amplitude increased significantly by 77µV (IQR -93 to 1597, p=0.02), while the left VCA median EMG amplitude did not show a significant change (p=0.44), (Table 2).

On multiple linear regression analysis, there were no significant associations between the differences in EMG amplitude of the right VCA with AMRT. On the left, the difference in EMG amplitude of the VCA was associated with extralaryngeal branching of the RLN, and the use of suxamethonium. Other factors, including age, thyroid lobe size, and the use of rocuronium or cistracurium as a muscle relaxant were not found to correlate with the change in the EMG amplitude of the VCA during AMRT (Table 3).

In this prospective series, the temporary RLN palsy rate was 2.2 % (3 out of 138 nerves). The median increase from V1 to V2 in these 3 cases was 418µV (IQR -479 to 538), while the median increase from V1 to V2 in the remaining, non-palsied RLNs was 30.5µV (IQR -138 to 290). The small number of RLNs with palsy precluded these figures from further statistical analysis. There was no permanent RLN palsy and RLN recovery occurred within 2 months in all 3 cases.

Discussion

Routine intraoperative identification of the RLN has resulted in a lower incidence of RLN injury as reported in multiple studies. Hermann et al. studied over 27,000 nerves at risk and showed the risk of permanent RLN injury reduced from 1.1% to 0.4% when the nerve was completely visualized compared to when it was not [11]. The study of Jatzko et al. which combined over 12,000 thyroidectomies, also revealed a lower incidence of RLN palsy in the group where the nerve was identified compared with the group where it was not identified (2.7% vs 7.9% temporary RLN palsy, and 1.2% vs 5.2% permanent RLN palsy) [12]. Hayward et al. from the authors' institution recently reported a rate of permanent RLNP in primary thyroidectomies at 0.13% between 2007 and 2011 with 3,736 RLNs at risk [2].

Despite visual identification and preservation of the RLN, some patients still develop postoperative RLN palsy. The underlying mechanism of RLN injury in the scenario of RLN neurapraxia with an intact RLN is not fully understood. However, explanations for the

mechanisms of RLN palsy, with an intact RLN, have progressively been reported.

Firstly, AMRT of the thyroid lobe results in a longitudinal traction force on the RLN which may result in neurapraxia. Transient loss of nerve conduction signal due to stretch has been demonstrated in vivo with rabbit tibial nerves by Wall et al. [13]. In that study, 24 rabbit tibial nerves were stretched by 6% or 12% for 1 hour, and given another hour for recovery. Nerve conduction was measured before stretching, after stretching, and after recovery. They found that at 6% stretch for an hour, conduction decreased by 70%, but returned to normal after the recovery period. However, at 12% stretch, conduction was completely blocked, and minimal recovery was demonstrated in the experimental time frame [13]. Whilst the Wall et al. study was performed using rabbit tibial nerves, the principle of the relationship between the risk of nerve palsy and the extent of stretch should be applicable to the human RLN. Approximately 25% of RLNs show extra laryngeal bifurcation, and the motor fibres have been shown to be in the anterior branch. For the same traction force, a branch because of its smaller size compared to the trunk will be more susceptible to increased tensile stress, providing an explanation for bifid RLNs being at greater risk of RLNP [14,15].

In human thyroidectomy studies, Snyder et al. and Chiang et al. have both recently identified that excess traction on the RLN is a factor in the development of palsy in visually intact nerves [4,6]. Snyder et al. prospectively evaluated 666 at risk RLNs in thyroid or parathyroid procedures, documenting the visual and functional identification of the RLN, persistent loss of RLN function, the mechanism and location of injury, and anatomical or technical factors that might have contributed to the risk of RLN injury. They found that the most common cause of RLN injury resulted from traction near the ligament of Berry, particularly of the anterior motor branch of a bifurcated RLN [6]. Similarly, in a study of 173 at risk RLNs, using IONM, Chiang et al. reported that of the 16 nerves that lost EMG signal after thyroid dissection, 12 were due to apparent overstretching of the nerve in the region of the ligament of Berry [4]. Other identified causes of loss of EMG signal in that study included transection, a constriction band, and clamping. All these additional causes are usually associated with visible damage to the nerve, and are uncommon.

Secondly, as alluded to in the study by Chiang et al. the RLN can sometimes sustain an injury due to a tissue band causing constriction [4]. The superficial facial layer containing the tertiary branches of the inferior thyroid artery is anterolateral to the RLN when the thyroid lobe is anteromedially rotated [16]. While under tension, this fascial layer can compress the RLN against the more rigid ligament of Berry. Division of this superficial constricting fascial layer releases

the compressive effect. Therefore, the longer it takes to free the nerve from this layer, the longer the RLN is under compression.

Thirdly, it has more recently been demonstrated that the RLN increases in diameter after surgical manipulation as part of the thyroidectomy [17]. Nerve oedema was thought to be the likely cause, which was associated with increased recorded EMG in VCA following NIM stimulation in swollen nerves which did not develop a palsy; but associated with decreased or loss of EMG in the VCA from nerves that developed a temporary palsy. This finding was unexpected, as a decrease of EMG signal would be expected with stretch and oedema, preceding a loss of signal. However, it is possible the initial stretch and oedema resulted in an increased excitability of the nerve, with increased amplitude, prior to a reduction and finally loss of signal [17].

Normative data for amplitude, latency and threshold for VN and RLN stimulation resulting in an EMG from the VCA are yet to be fully defined. The amplitude of the evoked EMG response following stimulation of VN and RLN represents the summated motor action unit potentials of the ipsilateral VCA. The measure of amplitude therefore correlates with the number of motor fibres participating in depolarization. Baseline values for EMG from the VCA vary between 100 and 800 microvolts [7].

In the current study, RLN activity increased with AMRT, evidenced by the increased EMG signal amplitudes from the VCAs, but the significance of this finding is not well understood. While the increase was only statistically significant on the right side, both sides demonstrated increased EMG amplitudes with AMRT. This finding is perhaps counterintuitive, as the proposed mechanics of traction and constriction would be expected to cause a decrease in EMG amplitude. However, the finding is similar to that reported in a series of anterior cervical operations where the RLN is commonly at risk, especially on the right side. In cadaveric studies of anterior neck surgery, the right RLN incurs a stretch of 24% with 4 cm of lateral retraction, whereas the left nerve is more redundant and shows less change [18]. Jellish et al. documented EMG amplitudes from the posterior laryngeal muscles during neck surgery where a lateral retractor was used resulting in stretch on the RLN [19]. In all cases they found the EMG amplitude increased with traction, and reduced to baseline when it was released. They concluded that irritation of the RLN due to traction results in increased spontaneous activity of the nerve, reflected in increased EMG amplitude; however with ongoing traction they found failure of the nerve and loss of EMG activity.

We have previously reported an increase in tension of the right compared to the left RLN for the same degree of traction applied to the nerve, based on a hypothetical engineering model and a mathematical model, using the differing lengths of the right (6cm) and left (12cm) RLNs. The study showed with 2cm of lateral traction, tension within the right nerve was 30 MPa, compared to 15 MPa in the left, and mathematically tension in the right was 21.7% compared to 8.5 % in the left [20]. The current finding of presumed hyperexcitability of the right RLN but not the left, resulting in an increased EMG amplitude with AMRT, may be explained by and is consistent both the findings of the engineering and mathematical model, and the monitoring study of Jellish et al. [19].

Therefore, this bipolar response, of initial hyperexcitability (increased EMG), followed by loss of signal (reduced EMG), may explain why in the retrospective series of 7 cases of RLN palsy, EMG was completely lost with VN stimulation, whereas in the prospective study, where amplitudes were being monitored immediately following AMRT, there was an increase in initial amplitude.

In contrast, others have shown in a series of 52 cases of continuous Intraoperative Vagal Neuro-monitoring, that reduction in EMG amplitude during thyroidectomy was predictive of postoperative RLNP, and that releasing the traction resulted in recovery of the EMG amplitude change, a result we have not been able to reproduce with intermittent neuro-monitoring [21].

In summary, the 3 factors – stretch, external compression and oedema – albeit temporary, seem to be acting in concert to cause RLN palsy [22]. Two of these factors, stretch and external compression, can occur as soon as the thyroid lobe is anteromedially rotated. Therefore, they are the postulated mechanisms underpinning the observation that AMRT alone can result in RLN palsy.

From this set of data, no reliable predictor of RLN palsy can be found from the change in EMG pre- and post-AMRT. The difference in the degree of EMG amplitude increase between nerves with and without palsy may be due to differences in time under tension, anatomy, nerve diameter, or other surgical factors. Association with each of those would need to be further studied.

As muscle relaxants were used in some of the cases, there is a potential for the neuromuscular blockade to interfere with the EMG amplitudes [23]. Although only short acting muscle relaxants were used, and reversal was given, this may be one of the limitations of the study. Another limitation is the relatively small number of RLNs included in the study. Due to the low rate of RLN palsy, a much larger sample size is necessary for a representative comparison of EMG amplitude changes between the palsy and non-palsy groups. With the ongoing development of the technique of IONM, analysis of latency as well as EMG amplitude may help explain our observations.

Overall, an understanding of the RLN anatomy is vital in preventing RLN injury. In addition, this study adds to the evidence that excessive traction placed on the thyroid lobe during anteromedial rotation can cause stretch injury to the nerve. Therefore, the clinical relevance of this finding is that surgeons need to be constantly aware of the amount of traction being applied to the RLN and the degree of the rotation of the thyroid lobe during thyroidectomy to reduce risk of RLNP. We therefore recommend being aware of the need to reduce the force of RLN with anterior elevation of the thyroid lobe, and to create a tunneling plane immediately anterior to the nerve upon identification, to prevent compression.

In conclusion, this study has shown that AMRT causes an initial increase in signal EMG amplitude in the VCA with VN stimulation. However, further studies are required to elucidate underlying mechanisms of development of neurapraxia as a result of AMRT.

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