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ORIGINAL ARTICLE

Effectiveness of intraoperative neuromonitoring of the recurrent laryngeal nerve with intermittent vagal nerve stimulation

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Abstract

Introduction: Vocal fold paralysis due to recurrent laryngeal nerve (RLN) injury during thyroidectomy occurs in 1-5% of patients, but it can reach up to 15% in reoperations. Intraoperative neuromonitoring (IONM) during thyroidectomy was first described in 1970, and has been widely used by surgeons. However, data on the IONM capacity to predict inferior laryngeal nerve function are still lacking. **Objective:** To evaluate the effectiveness of IONM of the RLN using intermittent stimulation of the vagus nerve during thyroidectomy to predict post-operative vocal fold function. **Methods:** Retrospective cohort analysis of 104 patients undergoing thyroidectomy with IONM of the RLN through intermittent vagal nerve stimulation. IONM response and vocal fold mobility were evaluated utilizing the McNemar's test associated with the Kappa agreement coefficient. **Results:** The final response of RLN stimulation showed 69.23% sensitivity and 93.79% specificity (p=0.180). **Conclusion:** IONM of the RLN through intermittent vagal nerve stimulation during thyroidectomy is effective to predict post-operative vocal fold function.

Keywords: intraoperative neuromonitoring; laryngoscopy; thyroidectomy.

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Introduction

Thyroidectomy is one of the most common endocrine procedures performed by head and neck (H&N) surgeons, presenting relatively low complication rates. Although these complications are infrequent, they can significantly compromise the quality of life (QoL) of patients. Recurrent laryngeal nerve (RNL) paralysis occurs in approximately 5% of primary thyroidectomies, but it can reach up to 15% in reoperations[1,2].

Surgical technique and anatomical knowledge to visually identify the RNL remain the gold standard; however, direct and indirect intraoperative methods to assess vocal fold function have been increasingly used by surgeons[1,2].

Endotracheal tube-based surface electrodes that respond to intermittent vagal nerve stimulation are the most common method used in intraoperative neuromonitoring (IONM) of the RNL because of their safety, simplicity, and applicability. Nevertheless, there are controversial data in the literature regarding their capacity to predict inferior laryngeal nerve function[3,4].

This study aimed to analyze the effectiveness of IONM of the RLN through intermittent vagal nerve stimulation to accurately predict post-operative vocal fold function.

Methods

Study design and location

This is a retrospective, descriptive, cohort study based on the analysis of patients' records that underwent thyroidectomy with IONM of the RNL through intermittent vagal nerve stimulation in a private clinic in the city of São Paulo between January 2011 and January 2014.

The study was exempted from informed consent since there were no ethical impediments according to the Ethics Research Committee of the University of São Paulo Medical School (FMUSP) on 26 June 2014.

Inclusion and exclusion criteria

Patients with thyroid disease undergoing surgical treatment with IONM of the RNL through intermittent vagal nerve stimulation were included in the study. The surgical treatment criteria included suspected or confirmed malignancy diagnosis after fine-needle aspiration (FNA) biopsy, signs or symptoms of compression, substernal goiter, toxic goiter refractory to medical treatment, and esthetic complaints reported by the patient. Patients with thyroid neoplasm and/or hyperparathyroidism were excluded from the study.

Intraoperative vagal nerve monitoring method

Pre- and postoperative assessments of vocal fold mobility were performed. The post-operative evaluation was conducted on the 7th, 14th and 30th days. Patient vocal fold evaluation was classified accordingly to mobility:

1. Vocal fold paralysis - absence of movement;
2. Partial vocal fold immobility - partial movement;
3. Normal vocal folds.

All vocal fold mobility tests were performed by the same evaluator.

Anesthesia was induced with neuromuscular blocking agents with rapid onset of action and metabolism. Endotracheal tube-based surface electrodes connected to the NIM 3.0 system (Medtronic™) were used. Assisted mechanic ventilation along with anesthesia with propofol were maintained until the end of surgery. The endotracheal tubes were carefully selected according to the size of the patient, thus avoiding airway trauma, and the cannula electrodes were positioned at the level of the vocal folds confirmed by laryngoscopy.

Vagal nerve stimulation was performed according to a standard procedure:

1. Dissection followed by stimulation of the vagus nerve (V1);
2. Middle thyroid vein was ligated during thyroid lobe exposure;
3. Superior thyroid vessels were ligated before releasing the upper pole, always performed as close to the gland as possible in order to prevent injuries to the superior laryngeal nerve external branch;
4. Visual identification and stimulation of the RLN (R1);
5. Dissection of the RLN;
6. Branches of the inferior thyroid artery were ligated, preserving the parathyroid glands;
7. Resection of the thyroid lobe and isthmus;
8. Hemostasis during intraoperative Valsalva maneuver;
9. Final stimulation of the RLN (R2);
10. Final vagal nerve stimulation (V2).

Adopted stimulation response criteria:

A. Positive response: Final R2 and V2 stimulus with electromyographic response >100 V, increased latency up to 20% and amplitude <30% from the initial response;
B. Negative response: Final R2 and V2 stimulus with electromyographic response <100 V, or latency >20% and amplitude <30% from the initial response.

If there was no response to vagal stimulation, the cannula placement was verified, a warm saline solution was poured over the surgical area, and a new stimulation was performed after 20 min:

A. If a positive vagal nerve response was obtained, a total thyroidectomy was performed on the contralateral side following the aforementioned steps;
B. If a negative vagal nerve response was obtained, the procedure was interrupted.

Statistical analysis

Categorical variables were descriptively presented in tables containing absolute (n) and relative (%) frequencies. Normality of the quantitative variables was assessed using the Kolmogorov-Smirnov test. The variables were descriptively presented as median and interquartile range. The nonparametric McNemar's test associated with the Kappa agreement coefficient[5] were applied to analyze data from IONM through intermittent vagal nerve stimulation during thyroidectomy and its correlation with post-operative vocal fold function. To this end, contingency tables were built between the times R2, V2 and laryngoscopy on the 7th postoperative day using the null hypothesis that there is no difference between the methods.

Results

This study analyzed a cohort of 104 patients aged 17-72 years (88, 84.6% male; 16, 15.4% female) undergoing surgical treatment for thyroid disease.

Regarding thyroid function, thyroid stimulating hormone (TSH) was normal in 99 (95.2%) cases, high in one (1%) case, and low in four (3.8%) cases. Free thyroxin values were normal in 102 (98.1%) cases and high in two patients. Antithyroid antibodies were negative in 90 (86.5%) cases.

In the sonographic evaluation, 38 (36.9%) patients had single nodules and 66 (63.1%) presented multiple nodules.

Considering the preoperative indication for surgical treatment, 58 (58.7%) patients had carcinoma, 26 (25%) presented follicular lesion, 13 had substernal goiters, two showed toxic goiters, and one patient had a nodule with benign cytopathological evaluation, but with increasing size.

Surgery extent according to intermittent IONM of the vagus nerve is described in Table 1.

There were 174 recurrent laryngeal nerves at risk: 85 on the right side and 89 on the left side. V1 and R1 showed that all nerves had a positive response in the beginning. The standard R2-V2 electromyographic responses are described in Table 2.

Laryngoscopy performed on the 7th day after surgery showed normal vocal folds in 88 (85.7%) cases, partial vocal fold immobility in 14 (13.4%) cases, and vocal fold paralysis in two (1.9%) cases. On the 14th day after surgery, 92 (88.4%) patients had normal vocal folds, 12 (11.6%) presented partial vocal fold immobility, and no patients showed vocal fold paralysis. On the 30th postoperative day, 101 (97.1%) patients had normal vocal folds, three (2.9%) showed partial vocal fold immobility, and no patients presented vocal fold paralysis.

Correlation between laryngoscopy on the 7th postoperative day and R2 and V2 is presented in Table 3 in order to assess the accuracy of the method in predicting vocal fold function.

Table 1. Surgery extent.

Surgery	n
Total thyroidectomy (TT)	58 (55.8%)
Partial thyroidectomy	28 (26.9%)
TT plus unilateral central neck dissection	5 (4.8%)
TT plus bilateral central neck dissection	7 (6.7%)
TT plus central and lateral neck dissection	1 (1%)
Completion thyroidectomy	3 (2.9%)
Lobectomy with central neck dissection	1 (1%)
Central neck dissection	1 (1%)

Table 2. Electromyographic response according to side and RLN stimulation.

	Pre-lobectomy	Post-lobectomy
Right vagus nerve response (V)		
Positive	85 (100%)	77 (90.5%)
Negative	0 (0%)	8 (9.5%)
Right RLN response (R)		
Positive	85 (100%)	73 (85.8%)
Negative	0 (0%)	12 (14.2%)
Left RLN response (R)		
Positive	89 (100%)	78 (87.6%)
Negative	0 (0%)	11 (12.4%)
Left vagus nerve response (V)		
Positive	89 (100%)	74 (83.2%)
Negative	0 (0%)	15 (17.8%)

Table 3. Correlation between laryngoscopy on the 7th postoperative day.

	7th postoperative day laryngoscopy		
	Normal vocal fold	Partial vocal fold immobility/Vocal fold paralysis	Total
RLN response (R2)			
Normal vocal fold	151 (86.8%)	4 (2.3%)	155 (89.1%)
Partial vocal fold immobility / vocal cord paralysis	10 (5.7%)	9 (5.2%)	19 (10.9%)
Total	161 (92.5%)	13 (7.5%)	174 (100%)
Vagus nerve response (V2)			
Normal vocal fold	146 (83.9%)	0 (0%)	146 (83.9%)
Partial vocal fold immobility/ Vocal fold paralysis	15 (8.6%)	13 (7.5%)	28 (16.1%)
Total	161 (92.5%)	13 (7.5%)	174 (100%)

R2 showed 69.23% sensitivity and 93.79% specificity, and the results were concordant using the McNemar's test (p=0.180). V2 showed sensitivity of 100.0% and specificity of 90.68%, but the results were not concordant using the McNemar's test (p<0.001) (Table 4).

Discussion

Thyroidectomy IONM has been standardized since 2012, leading to better and more uniform data; however, controversy regarding the effectiveness of IONM to predict RLN injury and post-operative vocal fold function still remains.

Table 4. McNemar's test.

Statistics	RLN response (R2)	Vagus nerve response (V2)
Sensibility	69.23	100.00
Specificity	93.79	90.68
Accuracy	91.95	91.38
Kappa coefficient	0.52	0.59
p-value (McNemar's test)	0.180	<0.001

The most recent studies have shown excellent negative predictive values despite intermediate positive predictive values. Absence of response after nerve stimulation can occur not only because of nerve injury, but also as a result of apparatus malfunction, displacement of the endotracheal electrode tube and non-neural stimulation, thus making it unclear whether there was, in fact, nerve injury[6-14].

Many authors have recommended interruption of the procedure after absence of response to nerve stimulation, especially in benign diseases[15-18], hence impacting on the surgeon's decision on the surgery extent.

In the present study, a patient with papillary carcinoma underwent lobectomy, but R2 and V2 presented decreased responses. As the tumor was a T1 according to the histopathological frozen section, it was decided to interrupt the procedure. The patient presented vocal fold immobility for 45 days. Therefore, by adopting the standard care for IONM of the RLN, a possible bilateral paralysis was avoided.

Laryngoscopy on the 7th postoperative day performed in all cases showed a paresis index in 14 (13.4%) cases and paralysis in two (1.9%) cases.

R2 presented sensitivity of 69.2% and specificity of 93.8%, which makes the test concordant (p=0.180). However, for V2, sensitivity (100.0%) and specificity (90.7%) were not concordant using the McNemar's test (p<0.001). This is probably due to the false-negative cases that showed non-responses to vagal nerve stimulation, but later presented with a normal laryngoscopy on the 7th postoperative day. Descriptive analysis of the association between V2 responses of neuromonitoring and laryngoscopies showed that 6% were false-negatives.

Therefore, in order to evaluate the accuracy of the method, the Kappa coefficient was applied and showed moderate accuracy, corroborating the findings of other studies[13,16-21]. Although the patients with false-negative responses of IONM of the RLN underwent reoperation, a possible bilateral vocal fold paralysis was completed avoided[22].

As shown in previous studies, IONM can change the operative management, resulting in fewer complications[11,23-29]. Despite the small number of patients associated with low incidence of vocal fold paralysis, this study shows that IONM of the RLN with intermittent vagal nerve stimulation can accurately evaluate vocal fold function, and thus predict the post-operative function.

Due to the increasing number of thyroidectomies, this technology is of great significance in the effort to predict vocal fold function and, in some cases, even prevent the surgery.

Conclusion

Intraoperative monitoring of the vagus nerve during thyroidectomy is an effective method to predict post-operative vocal fold function.

References

1. Cernea CR, Brandão LG, Brandão J. Neuromonitoring in thyroid surgery. Curr Opin Otolaryngol Head Neck Surg. 2012;20(2):125-9. **http://dx.doi.org/10.1097/MOO.0b013e32834fa8e6**. PMid:22327789.

2. Hermann M, Hellebart C, Freissmuth M. Neuromonitoring in thyroid surgery: prospective evaluation of intraoperative electrophysiological responses for the prediction of recurrent laryngeal nerve injury. Ann Surg. 2004;240(1):9-17. **http://dx.doi.org/10.1097/01.sla.0000132260.34503.02**. PMid:15213612.

3. Pisanu A, Porceddu G, Podda M, Cois A, Uccheddu A. Systematic review with meta-analysis of studies comparing intraoperative neuromonitoring of recurrent laryngeal nerves versus visualization alone during thyroidectomy. J Surg Res. 2014;188(1):152-61. **http://dx.doi.org/10.1016/j.jss.2013.12.022**. PMid:24433869.

4. Rulli F, Ambrogi V, Dionigi G, Amirhassankhani S, Mineo TC, Ottaviani F, Buemi ADI, Stefano P, Mourad M. Meta-analysis of recurrent laryngeal nerve injury in thyroid surgery with or without intraoperative nerve monitoring. Acta Otorhinolaryngol Ital. 2014;34(4):223-9. PMid:25210215.

5. Siegel S, Castellan NJ Jr. Nonparametric statistics for the behavioral sciences. 2nd ed. New York: McGraw-Hill Humanities; 1988.

6. Randolph GW, Dralle H, Abdullah H, Barczynski M, Bellantone R, Brauckhoff M, Carnaille B, Cherenko S, Chiang FY, Dionigi G, Finck C, Hartl D, Kamani D, Lorenz K, Miccolli P, Mihai R, Miyauchi A, Orloff L, Perrier N, Poveda MD, Romanchishen A, Serpell J, Sitges-Serra A, Sloan T, Van Slycke S, Snyder S, Takami H, Volpi E, Woodson G. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. Laryngoscope. 2011;121(Suppl 1):S1-16. **http://dx.doi.org/10.1002/lary.21119**. PMid:21181860.

7. Tschopp KP, Gottardo C. Comparison of various methods of electromyographic monitoring of the recurrent laryngeal nerve in thyroid surgery. Ann Otol Rhinol Laryngol. 2002;111(9):811-6. **http://dx.doi.org/10.1177/000348940211100909**. PMid:12296336.

8. Otto RA, Cochran CS. Sensitivity and specificity of intraoperative recurrent laryngeal nerve stimulation in predicting postoperative nerve paralysis. Ann Otol Rhinol Laryngol. 2002;111(11):1005-7. **http://dx.doi.org/10.1177/000348940211101110**. PMid:12450175.

9. Snyder SK, Hendricks JC. Intraoperative neurophysiology testing of the recurrent laryngeal nerve: plaudits and pitfalls. Surgery. 2005;138(6):1183-91, discussion 1191-2. **http://dx.doi.org/10.1016/j.surg.2005.08.027**. PMid:16360407.

10. Chan WF, Lang BH, Lo CY. The role of intraoperative neuromonitoring of recurrent laryngeal nerve during thyroidectomy: a comparative study on 1000 nerves at risk. Surgery. 2006;140(6):866-72, discussion 872-3. **http://dx.doi.org/10.1016/j.surg.2006.07.017**. PMid:17188132.

11. Loch-Wilkinson TJ, Stalberg PL, Sidhu SB, Sywak MS, Wilkinson JF, Delbridge LW. Nerve stimulation in thyroid surgery: is it really useful? ANZ J Surg. 2007;77(5):377-80. **http://dx.doi.org/10.1111/j.1445-2197.2007.04065.x**. PMid:17497981.

12. Barczyński M, Konturek A, Cichoń S. Cichon' S randomized clinical trial of visualization versus neuromonitoring of recurrent laryngeal nerves during thyroidectomy. Br J Surg. 2009;96(3):240-6. **http://dx.doi.org/10.1002/bjs.6417**. PMid:19177420.

13. Cernea CR, Brandão LG, Hojaij FC, Carlucci D Jr, Brandão J, Cavalheiro B, Sondermann A. Negative and positive predictive values of nerve monitoring in thyroidectomy. Head Neck. 2012;34(2):175-9. **http://dx.doi.org/10.1002/hed.21695**. PMid:21413099.

14. Calò PG, Pisano G, Medas F, Tatti A, Pittau MR, Demontis R, Favoriti P, Nicolosi A. Intraoperative recurrent laryngeal nerve monitoring in thyroid surgery: is it really useful? Clin Ter. 2013;164(3):e193-8. PMid:23868637.

15. Thomusch O, Sekulla C, Machens A, Neumann HJ, Timmermann W, Dralle H. Validity of intra-operative neuromonitoring signals in thyroid surgery. Langenbecks Arch Surg. 2004;389(6):499-503. **http://dx.doi.org/10.1007/s00423-003-0444-9**. PMid:14722777.

16. Goretzki PE, Schwarz K, Brinkmann J, Wirowski D, Lammers BJ. The impact of intraoperative neuromonitoring (IONM) on surgical strategy in bilateral thyroid diseases: is it worth the effort? World J Surg. 2010;34(6):1274-84. **http://dx.doi.org/10.1007/s00268-009-0353-3**. PMid:20143072.

17. Sadowski SM, Soardo P, Leuchter I, Robert JH, Triponez F. Systematic use of recurrent laryngeal nerve neuromonitoring changes the operative strategy in planned bilateral thyroidectomy. Thyroid. 2013;23(3):329-33. **http://dx.doi.org/10.1089/thy.2012.0368**. PMid:23249377.

18. Melin M, Schwarz K, Lammers BJ, Goretzki PE. IONM-guided goiter surgery leading to two-stage thyroidectomy--indication and results. Langenbecks Arch Surg. 2013;398(3):411-8. **http://dx.doi.org/10.1007/s00423-012-1032-7**. PMid:23179319.

19. Shindo M, Chheda NN. Incidence of vocal cord paralysis with and without recurrent laryngeal nerve monitoring during thyroidectomy. Arch Otolaryngol Head Neck Surg. 2007;133(5):481-5. **http://dx.doi.org/10.1001/archotol.133.5.481**. PMid:17520762.

20. Cavicchi O, Caliceti U, Fernandez IJ, Macrì G, Di Lieto C, Marcantoni A, Ceroni AR, Piccin O. The value of neurostimulation and intraoperative nerve monitoring of inferior laryngeal nerve in thyroid surgery. Otolaryngol Head Neck Surg. 2009;140(6):866-70. **http://dx.doi.org/10.1016/j.otohns.2008.12.047**. PMid:19467405.

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21. Alesina PF, Rolfs T, Hommeltenberg S, Hinrichs J, Meier B, Mohmand W, Hofmeister S, Walz MK. Intraoperative neuromonitoring does not reduce the incidence of recurrent laryngeal nerve palsy in thyroid reoperations: results of a retrospective comparative analysis. World J Surg. 2012;36(6):1348-53. **http://dx.doi.org/10.1007/s00268-012-1548-6**. PMid:22411090.

22. Duclos A, Lifante JC, Ducarroz S, Soardo P, Colin C, Peix JL. Influence of intraoperative neuromonitoring on surgeons' technique during thyroidectomy. World J Surg. 2011;35(4):773-8. **http://dx.doi.org/10.1007/s00268-011-0963-4**. PMid:21267565.

23. Chiang FY, Lu IC, Kuo WR, Lee KW, Chang NC, Wu CW. The mechanism of recurrent laryngeal nerve injury during thyroid surgery - The application of intraoperative neuromonitoring. Surgery. 2008;143(6):743-9. **http://dx.doi.org/10.1016/j.surg.2008.02.006**. PMid:18549890.

24. Donnellan KA, Pitman KT, Cannon CR, Replogle WH, Simmons JD. Intraoperative laryngeal nerve monitoring during thyroidectomy. Arch Otolaryngol Head Neck Surg. 2009;135(12):1196-8. **http://dx.doi.org/10.1001/archoto.2009.167**. PMid:20026815.

25. Dionigi G, Bacuzzi A, Boni L, Rovera F, Rausei S, Frattini F, Dionigi R. The technique of intraoperative neuromonitoring in thyroid surgery. Surg Technol Int. 2010;19:25-37. PMid:20437342.

26. Frattini F, Mangano A, Boni L, Rausei S, Biondi A, Dionigi G. Intraoperative neuromonitoring for thyroid malignancy surgery: technical notes and results from a retrospective series. Updates Surg. 2010;62(3-4):183-7. **http://dx.doi.org/10.1007/s13304-010-0036-5**. PMid:21153003.

27. Barczynski M, Konturek A, Stopa M, Hubalewska-Dydejczyk A, Richter P, Nowak W. Clinical value of intraoperative neuromonitoring of the recurrent laryngeal nerves in improving outcomes of surgery for well-differentiated thyroid cancer. Pol Przegl Chir. 2011;83(4):196-203. **http://dx.doi.org/10.2478/v10035-011-0030-8**. PMid:22166358.

28. Silva IC, Pedro I No, Vartanian JG, Kowalski LP, Carrara-de Angelis E. Prevalence of upper aerodigestive symptoms in patients who underwent thyroidectomy with and without the use of intraoperative laryngeal nerve monitoring. Thyroid. 2012;22(8):814-9. **http://dx.doi.org/10.1089/thy.2011.0118**. PMid:22780215.

29. Dionigi G, Chiang FY, Dralle H, Boni L, Rausei S, Rovera F, Piantanida E, Mangano A, Barczyński M, Randolph GW, Dionigi R, Ulmer C. Safety of neural monitoring in thyroid surgery. Int J Surg. 2013;11(Suppl 1):S120-6. **http://dx.doi.org/10.1016/S1743-9191(13)60031-X**. PMid:24380543.