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Recurrent Laryngeal Nerve Paralysis and Hypocalcemia in Superior to Inferior Compared to Inferior to Superior Dissection Approaches in Thyroidectomy

ABSTRACT

Objective: To compare the incidence of recurrent laryngeal nerve injury and hypocalcemia in patients who underwent thyroidectomy using a superior-inferior versus an inferior to superior approach in identifying the recurrent laryngeal nerve in a tertiary government hospital between January 2012 to December 2016.

Methods:

Design: Retrospective Cohort Study

Setting: Tertiary Government Hospital

Patients: Records of 241 adult patients who underwent surgery for thyroid diseases in the department of Otorhinolaryngology – Head and Neck Surgery between January 2012 and December 2016 were evaluated. Records of patients with postoperative hoarseness after total thyroidectomy or lobectomy with isthmusectomy and hypocalcemia after total thyroidectomy were reviewed, and operative techniques analyzed for the approaches to recurrent laryngeal nerve identification.

Results: Records of 119 patients (aged 20-73; median 41-years-old) meeting inclusion and exclusion criteria were analyzed. Of 57 thyroidectomies using a superior-inferior approach, 42 were bilateral, totaling 99; of 62 using an inferior-superior approach, 40 were bilateral, totaling 102. There was a higher incidence of post-operative complications among those who underwent inferior-superior dissection than those who underwent superior-inferior dissection. Chi square test showed the former approach (versus the latter) had 4.86 times the relative risk (RR) of permanent RLN injury (1.9%, 0.0475 to 5.5914, p=.3058), 1.62 times the RR of transient RLN injury (5%, 0.3971 to 6.5889, p=.5021), 1.92 times the RR of permanent hypocalcemia (1.9%, 0.0.1806 to 21.2838, p=.5910), and 2.06 times the RR of transient hypocalcemia (17%, 0.9055 to 4.4333, P=.0738). However, there was no significant difference between the two approaches with regard to hoarseness (independent t test, t value 0.90; p = .367) or hypocalcemia (t=0.428; p= .796).

Conclusion: There is no significant difference in the incidence of recurrent laryngeal nerve injury and hypocalcemia in patients who underwent thyroidectomy using a superior-inferior versus an inferior to superior approach in identifying the recurrent laryngeal nerve. Intraoperatively,

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surgeons may shift from one approach to the other as needed, and we recommend that they be well versed in both approaches and fully knowledgeable of the various anatomical courses of the recurrent laryngeal nerve and locations of parathyroid gland.

Keywords: *recurrent laryngeal nerve injuries, thyroid neoplasms, thyroidectomy, vocal cord paralysis, hypoparathyroidism, hypocalcemia*

Thyroidectomy remains the main source of iatrogenic recurrent laryngeal nerve (RLN) paralysis[1] and the most common complication after total thyroidectomy is still hypocalcemia with varied reported incidences for both transient and permanent hypocalcemia.[2] These injuries induce significant post-operative morbidities from hoarseness to more serious complications including aspiration and dyspnea which are potentially life threatening.[3,4] The management of such complications warrant hospitalization, and preventing them may help avoid further physical, emotional, social, psychological and financial burdens for the patient.

It is prudent for surgeons to identify the RLN during thyroidectomy[5] and different thyroidectomy dissection approaches have been advocated to facilitate this and prevent complications.[2,6-14,17-18] These include lateral-medial,[17] medial-lateral,[18] superior-inferior,[2,6-7,10-12] or inferior-superior dissection.[2,6,8-9,14] Some prefer a superior-inferior approach suggesting it may decrease the incidence of postoperative permanent and transient RLN injury and hypoparathyroidism[2,6] but evidence for this approach is limited.

This study aims to compare the incidence of RLN injuries and hypoparathyroidism in patients who underwent thyroidectomy using a superior-inferior approach versus those using an inferior-superior approach over 5 years in a single institution.

METHODS

With Institutional Ethics Review Board approval, this 5-year retrospective study of medical records of all adult patients who underwent thyroid surgery from January 2012 to December 2016 was conducted in the Otorhinolaryngology–Head and Neck Surgery department of a tertiary government hospital. There were a total of 241 adult patients who underwent thyroid surgery in our department from January 2012 to December 2016.

Records of patients with multinodular non-toxic goiter, nodular non-toxic goiter, colloid goiter, Grave disease and well-differentiated thyroid malignancy who underwent lobectomy with isthmusectomy or total thyroidectomy were considered for inclusion in the study. Of these, records of patients with post-operative hoarseness after total thyroidectomy or lobectomy with isthmusectomy and hypocalcemia after total thyroidectomy were retrieved for further analysis.

Records of patients with pre-operative vocal fold paralysis, intrathoracic goiters, re-operation or completion thyroidectomy, or with gross involvement of the RLN by malignant tumor, as well those with incomplete data were excluded.

Pre-operative evaluations considered included thyroid ultrasound results, thyroid stimulating hormone (TSH) and free T4 values, fine needle aspiration biopsy results, documentation of vocal cord mobility by flexible or rigid laryngoendoscopy, and serum calcium determination. Parathyroid hormone assays were not used to evaluate parathyroid hormone levels in our institution.

Operative techniques were scrutinized. All thyroidectomies were performed by third year and fourth year residents with RLN identification utilizing superior-inferior or inferior-superior dissection approaches, as documented in the operative records. Intraoperative tumor size was also recorded, as it may have been a confounding factor. The superior-inferior dissection involved identifying the RLN as it enters the cricothyroid articulation, followed by superior pedicle ligation, while inferior-superior dissection involved identifying the RLN as it coursed through the tracheoesophageal groove after inferior pedicle ligation.

Postoperative evaluations recorded in the charts included vocal cord function assessed by flexible nasopharyngolaryngoscopy or 70˚ rigid laryngoendoscopy in all patients on the first post-operative day, and serum calcium levels determined 24 hours after surgery with a reference range of 2.10 – 2.55 mmol/L. Post-thyroidectomy hypocalcemia was defined as levels below 2.00 mmol/L.

Patients were followed-up after one month then at three-month intervals for the first post-operative year. Vocal cord function and serum calcium levels were assessed using flexible nasopharyngolaryngoscopy or 70˚ rigid laryngoendoscopy and serum calcium determination was repeated. Permanent vocal cord paralysis was diagnosed when vocal fold mobility did not return 6 months after surgery and permanent hypocalcemia was considered when it persisted beyond 1 year.

Data Analysis

Data (age, gender, tumor size, diagnosis, temporary and permanent post-operative vocal cord paralysis and hypocalcemia, inferior-superior and inferior-superior approach) were tabulated by the author using Microsoft Excel 2013 version 15.0.5041.1000 (Microsoft Corporation, Redmond, WA, USA) and analyzed by a statistician. The incidence of permanent and temporary RLN injury and hypoparathyroidism were expressed in percentages of the total number of RLN identification per dissection approach. Inferential statistics included the Chi-square

test to compare the superior-inferior and inferior-superior approaches with outcomes, independent t test to determine whether there was a significant difference between the two approaches, and Pearson Correlation Coefficient to determine any relationship between tumor size and technique performed. IBM SPSS version 21.0 (IBM Corporation, Armonk, NY, USA) was used for statistical computations.

RESULTS

A total of 119 records of patients meeting inclusion and exclusion criteria were included. The age range was 20 to 73 years-old (median age 41-years-old). There were more females (85, 71%) than males (34, 29%) with a F:M ratio of 2.5:1.

The thyroid tumor size range was 1 to 8cm for inferior to superior approach with a mean tumor size of 3.31cm and 1 to 6cm for superior to inferior approach with a mean tumor size of 3.16cm. There was no correlation between the size of the predominant mass and the approach of choice in RLN identification (Pearson *r*=-0.0576, n=119, p=.278).

There were 57 thyroidectomies performed using a superior-inferior approach and 62 performed using an inferior-superior approach. Among the 57 superior-inferior approaches, 42 involved total thyroidectomy and 15 underwent lobectomy with isthmusectomy for a total of 99 superior-inferior approaches. Among the 62 inferior-superior approaches, 40 underwent total thyroidectomy and 22 had lobectomy with isthmusectomy for a total of 102 inferior-superior approaches.

Those who underwent inferior-superior approaches had a higher incidence of postoperative complications: temporary RLN injury (5, 4.9%); permanent RLN injury (2, 1.96%); transient hypocalcemia (17, 16.67%); and permanent hypocalcemia (2, 1.96%) compared to those who underwent superior-inferior approaches: temporary RLN injury (3, 3.03%); permanent RLN injury nil; transient hypocalcemia (8, 8.08%); and permanent hypocalcemia (1, 1.01%). (*Table 1*)

Compared to the superior-inferior approach using chi square test with the confidence interval of 95%, the inferior to superior approach had 4.86 times the relative risk of permanent RLN injury (1.9%, 0.0475 to 5.5914, p=.3058), 1.62 times the relative risk of transient RLN injury (5%, 0.3971 to 6.5889, p=.5021), 1.92 times the relative risk of permanent hypocalcemia (1.9%, 0.0.1806 to 21.2838, p=.5910), and 2.06 times the relative risk of transient hypocalcemia (17%, 0.9055 to 4.4333, P=.0738). Compared to the inferior-superior approach, the relative risks of the superior to inferior approach were 0.21 times for permanent RLN injury (0%, 0.1771 to 20.8776, p=.3058), 0.62 times for temporary RLN injury (3%, 0.1518 to 2.5179, p=0.5021), 0.52 times for permanent hypocalcemia (1%, 0.2193 to 1.0721, p=0.5856) and 0.48 times for transient hypocalcemia (8%, 0.0100 to 4.2378, p=0.0738).

Table 1. Outcomes of RLN paralysis and hypocalcemia (number, n and %)

Outcomes	Superior-Inferior *(n=99)*	Inferior-Superior *(n=102)*	P value
	N(%)	*N(%)*	
Temporary RLN injury	3(3.03)	5(4.9)	.4984587
Permanent RLN injury	0(0.00)	2(1.96)	NAN
Transient hypocalcemia	8(8.08)	17(16.67)	.032924
Permanent hypocalcemia	1(1.01)	2(1.96)	.5793469

Utilizing the independent T-test to determine whether there is significant difference between the two approaches, there was no significant difference in inferior-superior (M: 1.07; SD: 0.319) and with superior-inferior (M:1.29; SD: 0.462) with a t value of 0.905 and a p value of .367.

Despite the apparent trends, there was no significant difference between the two approaches with regard to hoarseness (independent t test, t value 0.90; p = .367). With regard to the hypocalcemia, there was also no significant difference between the two approaches (t=0.428; p= .796).

DISCUSSION

Our findings suggest that both thyroid surgical approaches in identifying the RLN and preserving the parathyroid glands are comparable in terms of complications of temporary and permanent RLN injury and hypoparathyroidism.

Of the 2 approaches to identifying the recurrent laryngeal nerve during thyroidectomy mentioned in the literature, Veyseller *et al.* state that "the first identifies the nerve where it penetrates the larynx, following superior pedicle ligation, and the other traces the nerve in the superior direction after locating it in the tracheoesophageal groove."[11] Also cited by Babu *et al.*,[2] both studies claim the superior-inferior approach was safer compared to the inferior-superior approach and had less complications of recurrent laryngeal nerve injury and hypocalcemia.[2,11]

Several others state that the superior-inferior thyroidectomy approach allows the surgeon to reach the region directly involving less dissection with lower rates of RLN injury and hypocalcemia.[2,6,13] In this regard, Rimpl et al. demonstrated that postoperative hypocalcemia was caused by extensive thyroid resection and parathyroid gland manipulation.[13]

On the other hand, Lai *et al*.[8] agree with Loré *et al*. that "identification of the RLN is best achieved through an inferior approach in a space

defined by Lore and colleagues as the retrolaryngeal node triangle."[14]

Despite proper technique and identification of the recurrent laryngeal nerve and parathyroid gland, postoperative hoarseness and hypocalcemia can ensue. Dy and Lapeña reported a case of transient bilateral vocal fold paralysis after total thyroidectomy and asked whether branched recurrent laryngeal nerves may be a risk factor for transient and permanent vocal cord paresis after surgery.[19]

We set out to address the divergence between superior-inferior and inferior-superior approaches. However, our study cannot favor either approach as it showed no significant difference between both approaches in terms of postoperative hoarseness and hypocalcemia and the status quo remains.

This study has several limitations. It was unable to account for variability among surgeons and surgical skills, mastery and experience for each surgical approach. Tumor size was another possible confounding factor but it was not statistically significant.

We recommend a larger population size and a prospective study design to address the limitations of a retrospective study and having a team of surgeons that is well versed in both approaches and mastery of various anatomical variations of the recurrent laryngeal nerve and location of the parathyroid glands and its blood supply.

In conclusion, our study showed no significant difference between both thyroidectomy approaches in terms of postoperative hoarseness and hypocalcemia. Surgeons may intraoperatively shift from one approach to the other as needed, and we recommend that surgeons should be well versed in both approaches and fully knowledgeable of the various anatomical courses of the recurrent laryngeal nerve and location of parathyroid glands and their blood supply.

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