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Factors Predisposing to Post Thyroidectomy Vocal Cord Paralysis at Ospital ng Maynila Medical Center

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ABSTRACT

Objective: To determine the prevalence of vocal cord paralysis among post thyroidectomy patients based on severity and laterality, and explore possible associations with age, sex, diagnosis and type of thyroid lesion and surgical procedure.

Methods:

Design: Cross-sectional study

Setting: Tertiary Government Training Hospital

Participants: Records of patients who underwent thyroidectomy under the Department of Otorhinolaryngology – Head and Neck Surgery of the *Ospital ng Maynila* Medical Center from January 1, 2014 to June 30, 2021.

Results: There were strong associations between the type of lesion and the presence of recurrent laryngeal nerve injury (V=.211, p=.001) and the diagnosis and the presence of RLNI (V=.245, p=.006). There were no significant associations between patient's sex, age, diagnosis, type of thyroid lesion, surgical procedure with laterality and severity of RLNI. It was notable that all cases of bilateral recurrent laryngeal nerve injury were due to carcinoma only. Patients with malignant tumors were 2.8x (95% CI: 1.48-5.29) as likely to develop post-surgical RLNI than those with benign tumors (p=.0015).

Conclusion: The factors that had a strong association with the presence of vocal cord paralysis among post-thyroidectomy patients were the diagnosis and type of thyroid lesion. Malignant thyroid lesions (specifically thyroid carcinoma) had a higher incidence of recurrent laryngeal nerve injury compared to benign thyroid lesions. More data from different institutions and including other predisposing factors may confirm our findings.

Keywords: *paralysis; vocal cord; thyroidectomy; recurrent laryngeal nerves; recurrent laryngeal nerve injury*

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The course of the recurrent laryngeal nerve predisposes it to damage and injury from many factors anywhere along its path resulting in impaired vocal function. One common cause of injury is surgical intervention, the most frequently studied of which is thyroidectomy.[1] Complications such as bleeding, hypoparathyroidism and recurrent laryngeal nerve injury (RLNI) represent nearly half of all the complications of thyroid surgery.[2] Because of their postoperative morbidity, recurrent laryngeal nerve (RLN) injuries are considered among the most feared complications.[3] Factors that were observed and related to this complication include the close anatomical proximity of the recurrent laryngeal nerves to the thyroid gland, unilateral or bilateral involvement, as well as temporary or permanent paralysis.[4]

Risk factors that contribute to morbidity following thyroid surgery are well-defined but their actual contribution is still open to question. Increased extent of dissection, surgeon experience, malignancy, underlying thyroid disease, and intraoperative technique have been shown to affect post-thyroidectomy morbidity.[5] The incidence of iatrogenic vocal cord paralysis secondary RLNI has been exclusively studied in recent and past literature. However, based on a search of MEDLINE (PubMed and PubMed Central), the Directory of Open Access Journals (DOAJ), ASEAN Citation Index (ACI), Western Pacific Region Index Medicus (WPRIM) and HERDIN Plus using the keywords "thyroidectomy," "vocal fold palsy," "vocal cord paralysis," and "recurrent laryngeal nerve injury," we only found limited studies on risk factors for iatrogenic RLNI.

This study aims to determine the prevalence of vocal cord paralysis among post thyroidectomy patients based on severity and laterality, and explore possible associations with age, sex, diagnosis, type of thyroid lesion, and surgical procedure in our institution.

METHODS

With Institutional Review Board approval from the San Juan de Dios Educational Foundation Institutional Review Board (SJIRB-2021-0027/ E-SRG), we searched hospital section archives for all available records of patients who underwent thyroidectomy under the Department of Otorhinolaryngology – Head and Neck Surgery of the *Ospital ng Maynila* Medical Center from January 1, 2014 to June 30, 2021.

The inclusion criteria were patients with a diagnosed case of benign or malignant lesion of the thyroid who underwent total thyroidectomy, subtotal thyroidectomy or unilateral total lobectomy, with no documented vocal cord paralysis on preoperative laryngoscopic evaluation, and if with postoperative vocal cord paralysis, documented through laryngoscopic evaluation. Excluded were patients who underwent reoperation/ completion thyroidectomy, diagnosed cases of malignancy where the RLN had to be intentionally sacrificed due to gross involvement of the nerve and patients with incomplete records.

The sample size of 242 was calculated using OpenEpi Version 3.01(Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version. www.OpenEpi.com), open source calculator for power of cross-sectional studies at 95% confidence interval.

Data collected included age, sex, type of lesion (benign or malignant), histopathologic diagnosis, and type of operative procedure (total thyroidectomy, subtotal thyroidectomy or lobectomy) which were considered to be the independent variables. While the presence of postoperative vocal cord paralysis, laterality of vocal cord paralysis (unilateral or bilateral), and severity of vocal cord paralysis (temporary or permanent) were the dependent variables. All collected data was tabulated using Microsoft Excel 2016 MSO 16.0.4266.1001 (Microsoft Corporation, Redmond, WA, USA).

Data Analysis

Descriptive statistics were used to summarize demographic variables. Assumption of normality of age was assessed using Shapiro-Wilk test. Chi-square test was used to determine if a significant association between the independent variables with the dependent variables. Cramer's V quantified the association detected. Cramer's V (V) was calculated by dividing the chi-square ($\chi 2$) value by sample size and taking the square root of this value. The evaluation matrix of Cramer's V was used;[6] values >0.25 are very strong; 0.15–0.25 are strong; 0.10–0.15 are moderate; 0.05–0.10 are weak and 0–0.05 are interpreted as having no association or very weak association. Risk ratio was used for significant associations that could be shown as 2 x 2 contingency tables. Post-hoc tests using z-test for column proportions with Bonferroni correction were then conducted on significant associations in tables with >2 rows or columns. A p-value $< .05$ was considered statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) ® IBM version 27 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 242 participant records were included in the study. The majority of patients were female (87.2%). Most were in the 35 to 49-year-old age group with the youngest being 13 years old and the oldest 78 years old, having a median age of 44 and IQR of 22. More than half of the total sample were noted to have benign lesions (67.4%) and 32.6% were carcinomas. Furthermore, 29 (12%) had unilateral RLNI while only 4 (1.7%) were bilateral. Based on severity of RLNI, 13 (5.4%) participants had temporary RLNI while 20 (8.3%) were permanent. The types of surgical procedure (lobectomy, subtotal thyroidectomy and

total thyroidectomy) were almost equally distributed at 61 (25.2%), 87 (36%) and 94 (38.8%), respectively.

A Shapiro-Wilk test showed a significant departure of the age distribution from normality, W (242) = 0.982, p = .003. There were strong associations between the type of lesion with the presence of RLNI (V = .211, p = .001) and the diagnosis and the presence of RLNI (V = .245, p = .006). Though there were no significant associations between patient's sex, age, diagnosis, type of thyroid lesion, surgical procedure with whether RLNI was unilateral or bilateral and temporary or permanent, it was notable that all cases of bilateral RLNI were due to carcinoma only. Patients with malignant tumors were 2.8x (95% CI: 1.48-5.29) as likely to develop post-surgical RLNI as those with benign tumors (p = .0015).

The z test with Bonferroni correlation showed that among patients without RLNI, the proportion of those with NNTG (93.8%) was higher than the proportion of those with carcinoma (75.9%) while among patients with RLNI, the proportion of those with carcinoma (24.1%) was higher than the proportion of those with NNTG (6.2%). Furthermore, among patients with NNTG, the proportion of those without RLNI (36.4%) was higher than the proportion of those with RLNI (15.2%). And lastly, among patients with carcinoma, the proportion of those with RLNI (57.6%) was higher than the proportion of those without RLNI (6.2%).

DISCUSSION

In this study, we determined the prevalence of vocal cord paralysis in post thyroidectomy patients based on severity and laterality, and found significant associations between diagnosis and type of thyroid lesion with the presence of vocal paralysis. However, there were no significant associations between age, sex, diagnosis, type of thyroid lesion and surgical procedure with laterality and severity of RLNI.

With regards to type of thyroid pathology, the incidence of RLNI has been reported at 2.9% for benign and 12.8% for malignant.[2] This trend was similarly found in our study, where there was a higher incidence of RLNI among malignant than among benign tumors. Despite this statistical association, causality cannot be established in our current study because of its retrospective nature and other variables which were not accounted for. Other factors which can contribute to the increased risk for RLNI such as size of the lesion, approach in dissection and intraoperative identification of RLN were not included. The injury resulting in vocal cord paralysis may not be due to the thyroidectomy per se, but due to pressure or pathology damaging the nerve or due to invasion of the recurrent laryngeal nerve by malignant neoplasms which can be manifested pre-operatively.[7]

Damaging the recurrent laryngeal nerve is one of most dreaded complications of thyroidectomy.[8] Different mechanisms of injury to the RLN ranging from simple traction or misplaced ligature to complete dissection of the nerve may lead to RLNI.[9] This can cause vocal cord dysfunction resulting in dysphonia, dysphagia and aspiration problems.[10] While the incidence of temporary dysfunction ranges from 0% to 12% based on our references, the incidence of permanent dysfunction ranges from 0 % to 3.5%.[11] In contrast, our study found a higher incidence of permanent RLNI than temporary RLNI.

Unilateral RLNI makes the voice hoarse, husky or breathy while bilateral RLNI can additionally cause airway obstruction. A previous study among patients who underwent thyroidectomies reported about 10% (63 out of 653 sample population) had vocal cord paresis/palsy with 9.4% unilateral and 0.6% bilateral involvement,[3] which is similar to our results of 12% unilateral and 1.7% bilateral RLNI. However, the lack of specification and association of unilateral or bilateral RLNI with the type of thyroidectomy limits interpretation. Our current study found that unilateral or bilateral RLNI was not associated with the type of procedure. This supports another study that demonstrated no significant association between laterality of RLNI with type of surgical procedure.[12]

Majority of the patients that were included in our study had either subtotal or total thyroidectomy, while the rest underwent lobectomy. Similarly, Iyomasa *et al.* had more patients who underwent total thyroidectomy compared to lobectomy with isthmusectomy, (74% and 26%, respectively), and 34% of their patients had vocal cord paralysis with 79.4% having undergone total thyroidectomy.[13] In contrast, the study of Dutta *et al.* reported that more than half underwent lobectomy while the rest were distributed among total thyroidectomy, subtotal and completion thyroidectomy, with about 13% RLNI.[14] The majority were patients who underwent total thyroidectomy; 3x higher than patients who underwent subtotal thyroidectomy and 1.5x higher than those who underwent lobectomy.[14] Our current study attempted to determine the association between type of surgery and the presence of RLNI. However, there was no significant association found between these two variables.

According to Santosh *et al.*, RLNI after thyroidectomy was more prevalent in women than men because thyroid diseases are more common among women.[15] Similarly, according to Chen *et al.*,[16] females have a higher risk of RLNI compared to males because of the higher incidence of thyroid pathologies and subsequent thyroidectomies among women. However, Zakaria *et al.* showed a similar incidence of RLNI with regard to sex of about 4% for both males and females.[2] In our study, sex was not found to be statistically associated with the presence of RLNI including its severity and if it is unilateral or bilateral.

Regarding age, most of the literature reported the incidence of thyroid lesions among 20 – 50 year-olds followed by patients 51 - 60 years old which is consistent with our study. However, according to Sarma *et al.* and Smith *et al*., thyroid lesions are more common in those less than 50 years of age but this is not a predictor of RLN dysfunction.[9,17] In contrast Chen *et al.* reported that thyroid surgery–related unilateral RLNI was higher in older patients, averaging of 57 years of age.[16]

Joliat *et al*. tried to associate Graves' disease, goiter and malignancy with RLNI.[3] However, after univariate and multivariate analysis, a previous history of thyroid surgery and intraoperative injury were the only factors that were found to have a significant association with permanent RLNI after thyroid surgery.[3] In our study, the different thyroid pathologies included (NNTG, MNTG, thyroiditis, adenoma and carcinoma) had no association with RLNI, both in severity and laterality. However, we also found that RLNI was more common in thyroid carcinoma compared to benign thyroid lesions.

This study has several limitations. We did not identify size of the lesion or patients who underwent reoperation or completion thyroidectomy, nor did we investigate malignancies where the RLN had to be sacrificed, the approach in dissection (superior to inferior or vice versa), and intraoperative identification and non-identification of RLN. Moreover, the study was only done in one hospital, and collecting data from multiple centers is recommended to have more significant results. Despite the limitations of the current study, our findings may be useful for identifying patterns. For future studies, it is recommended to employ a prospective design and conduct preoperative RLN assessment to establish any causal association.

In conclusion, the factors that had a strong association with the presence of vocal cord paralysis among post-thyroidectomy patients were the diagnosis and type of thyroid lesion. No significant association was found with regards to severity of vocal cord paralysis and if it was unilateral or bilateral. Malignant thyroid lesions (specifically thyroid carcinoma) had a higher incidence of recurrent laryngeal nerve injury compared to benign thyroid lesions.

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