## Types and Timing of Therapy for Vocal Fold Paresis/Paralysis After Thyroidectomy: A Systematic Review and Meta-Analysis

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**Summary: Objectives.** To perform a systematic literature review to evaluate the type and timing of therapy for vocal fold paresis/paralysis after thyroidectomy and develop a primary decision-making pathway. **Study Design.** Meta-analysis.

**Methods.** Four databases and one journal were searched using the key words of "thyroidectomy," "vocal cord paresis/paralysis," and "therapy." Study quality was evaluated using the Cochrane Collaboration's risk of bias tools. Data regarding type and timing of therapy were extracted from 39 articles. Odds ratios (ORs), relative risk (RR), 95% confidence interval, and heterogeneity were recorded. Logistic regression analysis was performed to determine the relationships between timing and OR/RR.

**Results.** Among the 13 studies investigating unilateral paresis/paralysis, five focused on early therapy (0–6 months). In these studies, the OR for clinical heterogeneity was significantly higher after neurolysis than after injection laryng-oplasty and voice training (Q = 17.002,  $I^2 = 78\%$ , P = 0.000), and the RR for heterogeneity was significantly higher after injection laryngoplasty at  $\geq 12$  months than <12 months (Q = 9.984,  $I^2 = 89.9\%$ , P = 0.002). In the 26 studies that investigated bilateral paresis/paralysis, the OR for heterogeneity was significantly higher for bilateral posterior cordectomy than for endolaryngeal laterofixation (Q = 3.510,  $I^2 = 71.5\%$ , P = 0.061) and laser arytenoidectomy with posterior cordectomy (Q = 2.90,  $I^2 = 65.6\%$ , P = 0.088).

**Conclusions.** For unilateral vocal fold paresis/paralysis after thyroidectomy, we recommend absorbable mass injection laryngoplasty, voice training, and neurolysis during the first 12 months but laryngeal reinnervation after 12 months. For bilateral vocal fold paresis/paralysis, we recommend early laterofixation and combined laser arytenoidectomy with posterior cordectomy after 12 months.

Key Words: Thyroidectomy–Vocal fold paresis/paralysis–Therapy.

#### INTRODUCTION

Voice symptoms such as hoarseness, fatigue, and abnormal loudness and pitch are common after thyroid and parathyroid surgery, with reported rates ranging from 0% to 87%.<sup>1</sup> Some patients also experience aspiration and apneas, which severely affect the quality of life. Such symptoms usually result from damage to the recurrent laryngeal nerve that innervates the larynx. Patients may experience unilateral or bilateral paresis/paralysis of the vocal folds after thyroidectomy, which may be temporary paresis/paralysis and permanent paralysis reflected preservation and severance of the recurrent laryngeal nerve during surgery, respectively. Lo et al<sup>3</sup> reported a temporary paresis/paralysis rate of 5.2% (3.3% due to recurrent laryngeal nerve damage) and a permanent paresis/paralysis rate of

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1.4% (0.9% due to recurrent laryngeal nerve damage). It is very important to treat vocal fold paresis/paralysis promptly and effectively to restore respiration, phonation, and swallowing functions.<sup>4</sup> Watt-Boolsen et al<sup>5</sup> reported that early voice training can reduce the rate of voice problems in patients with either temporary or permanent paresis/paralysis. Aaron et al<sup>6</sup> reported that early vocal fold medialization procedure performed within 6 months created a more favorable vocal fold position for phonation than medialization performed after 6 months. The type and timing of therapy affect clinical outcomes, and treatment decisions should consider both the natural healing process and options for intervention. Although it is true that the selection of therapy is often driven by individual deficits demonstrated by the client, the aim of this study was to provide a pathway for selecting therapeutic options and their timing based on findings of a meta-analysis.

#### MATERIALS AND METHODS

We searched four databases for abstracts published in any language between 1950 and June 2012, using the Cochrane Stroke Group Database Search Protocol. The databases searched were Science Citation Index, MEDLINE with full text, China National Knowledge Infrastructure, (CNKI), Wanfang, and the *Journal of Voice*. The key words used in the search were "thyroidectomy," "vocal cord paresis/paralysis," and "therapy". A total of 3703 articles were identified. There were no related articles found in the Cochrane Library using the same search key words.

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#### Definitions

The positions of the vocal folds (median, intermediate, and lateral), profiles of the vocal folds (concave and rectilinear), glottic closure (complete and incomplete), vibrations of the vocal folds (wide, narrow, and absent), and mucosal wave propagation (normal, small, and absent) on strobovideolaryngo-scopy were assessed. Paresis was diagnosed if movement was sluggish, and paralysis was diagnosed if no volitional movement was observed. A decrease in movement by 1–30% was defined as mild paresis, 31–60% was defined as moderate paresis, 61–99% was defined as severe paresis, and no observable movement was defined as paralysis.<sup>7</sup>

#### Article selection

Articles that mainly focused on treatment of patients with vocal fold paresis/paralysis after thyroidectomy were selected. The following articles were included in the analysis: (1) case series with at least 10 consecutively enrolled patients with vocal fold paresis/paralysis after thyroidectomy; (2) prospective or retrospective cohort studies with consecutive patient enrollment; and (3) randomized and nonrandomized controlled trials. The following articles were excluded: (1) editorials and review articles; (2) studies without extractable vocal fold paresis/paralysis outcomes according to findings on laryngoscopy, laryngeal electromyography, voice assessment, or voice handicap index; and (3) studies without consistent pre- and post-therapy evaluations.

#### **Data retrieval**

All selected articles were rated for blinding and completeness of data regarding vocal fold paresis/paralysis outcomes. Study design, consistency of assessment of all patients, and use of operational definitions for vocal fold paralysis were also recorded. Two authors (X.C. and Y.Y.) then extracted the data of the reported patients, the time interval between the onset of vocal fold paralysis and therapy, follow-up, and the effectiveness of therapy. Another author (P.W.) independently checked the accuracy of the extracted data for 15% of the articles.

#### **Statistical analysis**

The types and timing of therapy were extracted from the selected articles. The timing of therapy was defined as the period from the onset of vocal fold paresis/paralysis after thyroidectomy to initiation of therapy and was classified as early (0-6 months), intermediate (6–12 months), or late ( $\geq$ 12 months). The effect size was extracted using Comprehensive Meta-analysis, Version 2 (a computer program for meta-analysis developed by a team of experts in the United States and United Kingdom developed by Michael Borenstein, Larry Hedges, Julian Higgins, Hannah Rothstein; this project was funded by the National Institutes of Health). The odds ratio (OR), relative risk (RR), and 95% confidence interval were recorded. Logistic regression analysis was performed to determine the relationships between the timing of therapy and OR/RR. The effect size reflects the cases with unsatisfactory therapy outcomes (such as ongoing hoarseness or dyspnea). The smaller the effect size, the better the therapy.

### RESULTS

A total of 3703 citations were identified by searching the databases and journal using the terms "thyroidectomy," "vocal cord paresis/paralysis," and "therapy." Of these, 3569 did not meet our study inclusion criteria based on the title retrieved; and the remaining 134 articles were reviewed based on the review of their abstracts. After a preliminary review, 84 articles that did not meet our inclusion criteria were eliminated, the remaining 50 articles were fully reviewed, along with 11 articles about therapy for vocal fold paralysis after thyroidectomy, including seven case studies, one article with nonthyroidectomy, and three articles with either unclear diagnosis of vocal fold paresis/paralysis or inconsistent pre- and post-therapy evaluations. The remaining 39 articles were selected for systemic review, which had a total of 1798 patients (Figure 1).



FIGURE 1. Article selection process.

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