The Laryngoscope

Recurrent Laryngeal Nerve Monitoring Versus Identification Alone on Post-Thyroidectomy True Vocal Fold Palsy: A Meta-Analysis

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Objectives/Hypothesis: To compare by meta-analysis the effect of recurrent laryngeal nerve (RLN) monitoring versus RLN identification alone on true vocal fold palsy rates after thyroidectomy.

Study Design: Systematic review and meta-analysis.

Methods: A search of MEDLINE (1966–July 2008), EMBASE (1980–July 2008), Cochrane Central Register of Clinical Trials (CENTRAL), Cochrane Database of Systematic Reviews, clinicaltrials.gov, and The National Guideline Clearinghouse databases was performed. References from retrieved articles, presentation data, and correspondence with experts was also included. All authors used a detailed list of inclusion/exclusion criteria to determine articles eligible for final inclusion. Two authors independently extracted data including study criteria, methods of vocal fold function assessment, laryngeal nerve monitor type, and surgical procedure. Odds ratios (OR) were pooled using a random-effects model. Associations with patient and operative characteristics were tested in subgroups.

Results: One randomized clinical trial, seven comparative trials, and 34 case series evaluating 64,699 nerves-at-risk were included. The overall incidence of true vocal fold palsy (TVFP) was 3.52% for intraoperative nerve monitoring (IONM) versus 3.12% for nerve identification alone (ID) (OR 0.93; 95% confidence interval [CI], 0.76-1.12]. No statistically significant difference in transient TVFP (2.74% IONM vs. 2.49% ID [OR 1.07, 95% CI, 0.95-1.20]), persistent TVFP (0.75% IONM vs. 0.58% ID [OR 0.99, 95% CI, 0.79-1.23]), or unintentional RLN injury (0.12% IONM vs. 0.33% ID [OR 0.50, 95% CI, 0.15-1.75]) was found.

Conclusions: This meta-analysis demonstrates no statistically significant difference in the rate of true vocal fold palsy after using intraoperative neuromonitoring versus recurrent laryngeal nerve identification alone during thyroidectomy.

Key Words: Laryngeal, neuromonitoring, thyroid, thyroidectomy, recurrent laryngeal nerve, vocal fold, vocal cord, palsy, paralysis, paresis.

Level of Evidence: 2a.

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INTRODUCTION

True vocal fold palsy (TVFP) is one of most feared complications of thyroidectomy. The rate of TVFP has decreased over the past few decades, likely secondary to routine identification of the recurrent laryngeal nerve (RLN) during thyroidectomy.[1,2] Intraoperative neuromonitoring of the RLN (IONM) during thyroidectomy has been described since 1970.[3] However, there continues to be debate regarding neuromonitoring and its role in reducing the risk of TVFP. Although several studies have been published on this issue, it has been difficult to compile a large enough sample size in a single series to make a reasonable conclusion regarding such a rare complication.

The clinical and medicolegal implications of whether or not IONM reduces the risk of TVFP are substantial. Along with hypoparathyroidism, TVFP is one of the leading causes for litigation after thyroidectomy.[1] Impairment in voice can greatly affect quality of life with impact on daily and occupational function. Some individuals with unilateral TVFP may also have significant swallowing problems and aspiration. In addition, the dreaded bilateral TVFP can lead to airway obstruction, requiring tracheostomy. Variability in the RLN anatomic course led to advocates for routine identification of the nerve in the 1930s and 1940s, which has been shown to reduce TVFP rates and is now regarded as standard of care in thyroid surgery.[1] Although TVFP rates are lower with routine identification of the RLN, this complication still exists. IONM of the RLN has been advocated by some as a tool to further assist in limiting this complication. However, some surgeons opine that monitoring does not add to their capability to identify the nerve and could potentially increase risk to the nerve if relied on over the use of standard anatomic landmarks.

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The purpose of this study was to perform a systematic review and meta-analysis comparing the effect of RLN monitoring (IONM) and RLN identification alone (ID) on the rate of TVFP in thyroidectomy.

MATERIALS AND METHODS

Search Strategy

A systematic literature search of MEDLINE (1966–July 2008), EMBASE (1980–July 2008), Cochrane Central Register of Clinical Trials (CENTRAL), Cochrane Database of Systematic Reviews, clinicaltrials.gov, and The National Guideline Clearinghouse databases without language restriction was conducted for human studies evaluating recurrent laryngeal nerve monitoring in thyroid surgery. The search included combined key terms and exploded Medical Subject Headings (MeSH) *laryngeal, larynx, nerve,* and **monitor**. A concurrent search including *thyroid*, *surgery*, *identification*, and *identify* was also performed to capture reports evaluating RLN identification without monitoring during thyroidectomy. References from the retrieved articles were scanned, abstracts of selected scientific meetings (within the specialties of otolaryngology–head and neck surgery, surgery, and endocrine surgery) were reviewed, and experts in the field were contacted to identify all relevant articles.

Selection Criteria

Two authors (t.h. and j.s.) independently screened the titles and abstracts of the search results and identified articles eligible for further review. Inclusion criteria for obtaining the full-text article included original studies, systematic reviews, meta-analyses, or guidelines reporting on laryngeal nerve monitoring in neck surgery. Exclusion criteria included review articles, case reports, technical reports, editorials, and animal studies.

All authors critically appraised the full-text articles using the CONSORT checklist[4] for randomized controlled trials and the Meta-Analysis of Observational Studies in Epidemiology[5] checklist for observational studies. The studies included were either prospective or retrospective comparative trials, or case series evaluating the relationship of vocal fold paralysis or paresis with intraoperative recurrent laryngeal nerve monitoring. Exclusion criteria at this stage included studies that focused on laryngeal nerve stimulation alone, did not document preoperative and postoperative laryngoscopic true vocal fold function, or did not exclude patients with preoperative TVFP or intentionally resected nerves. Any disagreement was resolved by consensus. The authors of reviewed references were contacted when a need to clarify aspects of their articles arose.

Data Extraction

Primary outcome variables included transient and persistent TVFP. Also extracted were pertinent baseline characteristics for subgroup analyses and information on key indicators of study quality.

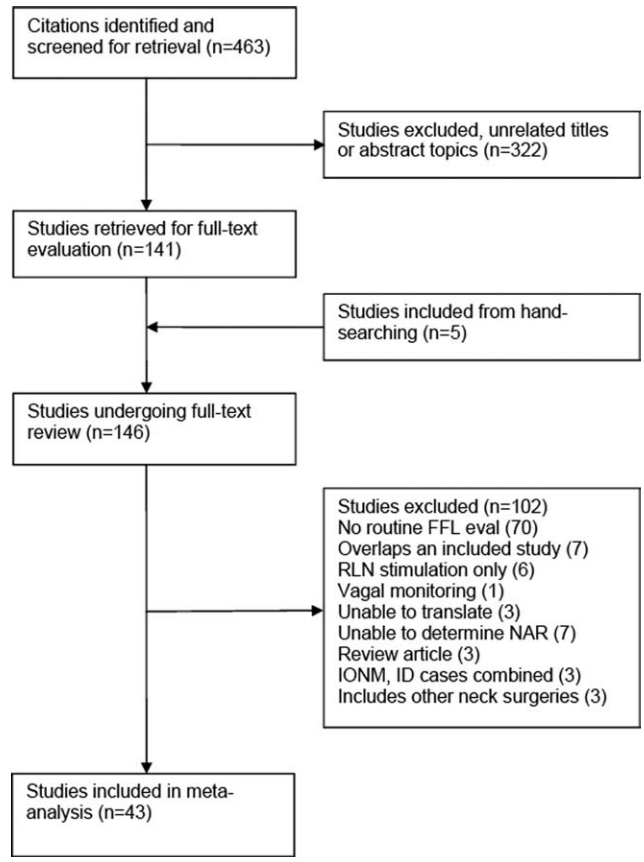

Fig. 1. Flowchart of article retrieval showing inclusion and exclusion criteria. FFL = laryngoscopy; RLN = recurrent laryngeal nerve; NAR = nerves at risk; IONM = intraoperative nerve monitoring, ID = nerve identification alone.

Statistical Analysis

The statistical analysis was performed after all authors had critically appraised the articles and decided on the final list of included articles. Sample size calculations were performed with OpenEpi statistical software[6] using a two-sided confidence level of 95%, odds ratio (OR) of 0.5, power of 80%, and TVFP rate in the ID group (control group). An OR of 0.5 was chosen to represent an estimate that could reasonably be considered clinically significant and may change management. The meta-analysis was performed using Review Manager 5,[7] using the random-effects Mantel-Haenszel model. OR was used to measure the association across studies. Statistical heterogeneity was calculated using the Cochrane Q statistic and the Tau^2 statistic. Forest plots were constructed to visually represent the OR with corresponding 95% confidence intervals (CI) across studies. A funnel plot was constructed to evaluate data symmetry and publication bias.

RESULTS

Literature Search

The search strategy retrieved 463 unique citations. Figure 1 shows the flowchart of inclusion and exclusion of studies. Review of the titles and abstracts resulted in

TABLE I.
Characteristics of Included Comparative Studies.

Author (Year)	Study Type	RLN ID Method	Country	Dates	Pros/Retr	Allocation Method	Post-op FFL Timing	Persistent TVFP (mo)
Barczynski (2009)	A	IONM (voc bi)vs. ID	Poland	2006–2007	Pros	Random	<24 hr	12
Robertson (2004)	B	IONM (ETT)vs. ID	USA	1999–2002	Retr	Consecutive	NS	NS
Dralle (2004)	B	IONM (voc bi)vs. ID	Germany	1998–2001	Pros	Equipment/Surgeon	NS	6
Witt (2005)	B	IONM (ETT)vs. ID	USA	1998–2003	Retr	Consecutive	NS	12
Chan (2006)	B	IONM (ETT)vs. ID	China	2002–2005	Pros	Equipment/Surgeon	>24 hr	12
Shindo (2007)	B	IONM (ETT)vs. ID	USA	1998–2005	Retr	Consecutive	<24 hr	NS
Netto (2007)	B	IONM (ETT)vs. ID	Brazil	2003–2006	Pros	Convenience	>24 hr	3
Terris (2007)	B	IONM (ETT)vs. ID	USA	2004–2006	Pros	NS	<24 hr	6
Agha (2008)	B	IONM (NS)vs. ID	Germany	1992–2005	Retr	NA	NS	6

RLN = recurrent laryngeal nerve, ID = recurrent laryngeal nerve identification; Pros = prospective; Retr = retrospective; FFL = laryngoscopy; TVFP = true vocal fold palsy; A = randomized controlled trial; IONM = recurrent laryngeal nerve neuromonitoring; voc bi = bipolar electrode in vocalis muscle; B = nonrandomized comparative trial; ETT = monopolar endotracheal tube electrodes; NS = not stated; Equipment = equipment availability; Surgeon = surgeon preference; NA = not applicable.

exclusion of 322 titles. Hand searching the references of the included articles identified five additional studies. During full-text review, an additional 103 articles were excluded, resulting in 43 articles for final inclusion in the meta-analysis.

Study Characteristics

The characteristics of the 43 selected studies are shown in Table I through Table III.[8–51] Baseline characteristics are provided in Table IV. The search yielded one published randomized clinical trial and no guidelines. The accepted articles also included eight nonrandomized comparative trials and 34 case series evaluating 64,817 nerves-at-risk. The studies were published between 1991 and 2009. There were eight studies conducted in the United States, 15 in Germany, and 20 in other countries. Among the studies documenting demographic data, there were 77.9% females in the IONM group versus 79.3% in the RLN ID group. The mean age was 53.1 years in the IONM group versus 49.3 years in the RLN ID group.

Data were collected prospectively in 20 studies and retrospectively in 23 studies. Four studies were multi-institutional. The patient allocation method for comparative studies was specified in all studies and included consecutive allocation, surgeon preference, and equipment availability. A few studies mentioned the extent of resident surgical involvement. However, most studies did not specify the primary surgeon. Seven studies included data from multiple surgeons. The timing of the initial postoperative laryngoscopy varied from the immediate postoperative period to within 2 weeks of surgery. Persistent vocal fold palsy was defined as 3 months in two studies, 6 months in 16 studies, up to 9 months in

TABLE II.
Characteristics of Included Case Series Using Recurrent Laryngeal Nerve Neuromonitoring.

Author (Year)	Study Type	RLN ID Method	Country	Dates	Pros/Retr	Allocation Method	Post-op FFL Timing	Persistent TVFP (mo)
Horn (1999)	C	IONM (ETT)	Germany	1997–1998	Retr	NA	3 d	NS
Hemmerling (2001)	C	IONM (ETT)	Germany	NS	Pros	NA	3 d	NA
Hamelmann (2002)	C	IONM (voc mono)	Germany	1998–2001	Retr	NA	3–5	6
Meyer (2002)	C	IONM (ETT)	Germany	NS	Pros	NA	3–5	6
Tschopp (2002)	C	IONM (ETT/voc mono/bi)	Switzerland	2001	Pros	NA	1	NS
Kunath (2003)	C	IONM (voc/ mono)	Germany	1998–2000	Pros	NA	2–4	4–9
Marcus (2003)	C	IONM (ETT)	USA	1999–2001	Pros	NA	NS	12
Beldi (2004)	C	IONM (ETT)	Switzerland	1996–2002	Retr	NA	NS	NS
Barczynski (2006)	C	IONM (voc mono)	Poland	2004–2005	Retr	NA	2	6
Jonas (2006)	C	IONM (voc bi)	Germany	1999–2004	Pros	NA	3–4	24
Petro (2006)	C	IONM (voc bi)	USA	NS	Pros	NA	NS	NA
Moroni (2007)	C	IONM (voc bi)	Germany	1999–2005	Pros	NA	3–4	12
Ulmer (2008)	C	IONM (voc mono)	Germany	NS	Pros	NA	NS	24
Chiang (2008)	C	IONM (ETT)	Taiwan	2006–2007	Pros	NA	NS	6

RLN = recurrent laryngeal nerve; ID = recurrent laryngeal nerve identification; Pros = prospective; Retr = retrospective; FFL = laryngoscopy; TVFP =true vocal fold palsy; C = single arm case series; IONM = recurrent laryngeal nerve neuromonitoring; ETT = monopolar endotracheal tube electrodes; NA = not applicable; NS = not stated; voc mono = monopolar electrode in vocalis muscle; voc bi = bipolar electrode in vocalis muscle.

TABLE III.
Characteristics of Included Case Series Using Recurrent Laryngeal Nerve Identification Alone.

Author (Year)	Study Type	RLN ID Method	Country	Dates	Pros/Retr	Allocation Method	Post-op FFL Timing	Persistent TVFP (mo)
Herranz-Gonzalez (1991)	C	ID	Spain	1986–1988	Retr	NA	NS	6
Jatzko (1994)	C	ID	Austria	1984–1991	Retr	NA	3–5 d	6
Kasemsuwan (1997)	C	ID	Thailand	1993–1996	Retr	NA	NS	3
Runkel (1998)	C	ID	Germany	1995–1997	Retr	NA	3–5 d	6
Wahl (1998)	C	ID	Germany	NS	Retr	NA	NS	12
Andreassen (1999)	C	ID	Australia	1987–1996	Retr	NA	NS	NS
Sturniolo (1999)	C	ID	Italy	1997–1999	Retr	NA	NS	6
Lo (2000)	C	ID	China	1995–1998	Pros	NA	<2 wk	12
Brennan (2001)	C	ID	USA	1994–2000	Pros	NA	NS	6
Prim (2001)	C	ID	Spain	1982–1997	Retr	NA	NS	NS
Steinmuller (2001)	C	ID	Germany	1985–1999	Retr	NA	NS	6
Gergely (2002)	C	ID	Hungary	NS	Retr	NA	NS	4
Hermann (2002)	C	ID	Austria	1979–1990	Retr	NA	3–4	12
Steurer (2002)	C	ID	Austria	1996–1999	Pros	NA	3–7	24
Kotan (2003)	C	ID	Turkey	1998–2000	Retr	NA	NS	6
Ardito (2004)	C	ID	Italy	1990–2000	Pros	NA	2	12
Aytac (2005)	C	ID	Saudi Arabia	1989–2003	Retr	NA	2–3	6
Munks (2005)	C	ID	Germany	2002–2003	Retr	NA	2	18
Shindo (2005)	C	ID	USA	2003–2004	Pros	NA	NS	NS
Chiang (2005)	C	ID	Taiwan	1986–2002	Retr	NA	NS	6

RLN = recurrent laryngeal nerve, ID = recurrent laryngeal nerve identification; Pros = prospective; Retr = retrospective; FFL = laryngoscopy; TVFP = true vocal fold palsy; C = single arm case series; NA = not applicable; NS = not stated.

TABLE IV.
Baseline Characteristics of Included Studies.*

Characteristic	IONM	ID
Demographics		
Included studies (series/comparative)	14/9	20/9
Nerves at risk, no.	27,920	36,882
Age, yr	53.1	49.3
Females, %	77.9	79.3
Pathologies		
Benign disease, %	86.3	85.1
Malignancy, %	8.5	12.6
Nontoxic goiter, %	80.6	73.0
Toxic goiter/Graves, %	6.6	8.5
Thyroiditis, %	0.2	0.3
Retrosternal goiter, %	10.6	14.5
Surgery types		
Primary surgery, %	94.4	93.6
Revision surgery, %	5.7	9.4
Total thyroidectomy, %	6.5	28.4
Subtotal thyroidectomy (STL), %	30.1	23.3
Lobectomy, %	19.5	29.6
Lobectomy + contralateral STL, %	4.3	3.6
Other surgeries, %	6.1	2.5

*Not all studies provided demographic data; the results are a compilation of available data.

IONM = recurrent laryngeal nerve neuromonitoring; ID = recurrent laryngeal nerve identification; STL = subtotal thyroidectomy.

one study, 12 months in nine studies, and 18 to 24 months in three studies.

Internal Analyses

Cochrane Q statistic and the Tau^2 statistic, using $P < .05$, did not reveal significant statistical heterogeneity among the studies. The funnel plots, shown in Figure 2, indicate minimal influence of publication bias and a fairly symmetric distribution in total TVFP and persistent TVFP. There was mild asymmetry noted in the funnel plot of transient TVFP.

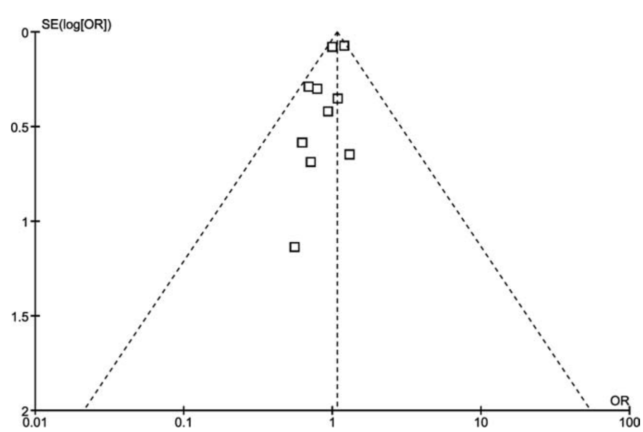

Fig. 2. Funnel plot depicting the odds ratios (OR) with 95% confidence intervals and standard error (SE) for overall true vocal fold palsy in all studies. Publication bias is minimal and data symmetry is adequate.

TABLE V.
Meta-Analysis of Subgroups Comparing Recurrent Laryngeal Nerve Neuromonitoring Versus Recurrent Laryngeal Nerve Identification Alone on the Rate of True Vocal Fold Palsy During Thyroid Surgery.

Subgroups	IONM Events/Total (%)	ID Events/Total (%)	OR [95% CI]	*P* Value
All groups				
All palsies	982/27,935 (3.52)	1,149/36,882 (3.12)	0.93 [0.77, 1.12]	.44
Transient palsies	755/27,762 (2.72)	885/36,204 (2.44)	1.07 [0.95, 1.20]	.26
Persistent palsies	208/27,762 (0.75)	212/36,204 (0.59)	0.99 [0.80, 1.24]	.94
Injury to RLN	3/2507 (0.12)	11/3340 (0.33)	0.50 [0.15, 1.75]	.28
Benign disease				
All palsies	175/6080 (2.88)	704/25,684 (2.74)	0.83 [0.57, 1.20]	.33
Transient palsies	142/6080 (2.34)	596/25,684 (2.20)	0.84 [0.59, 1.20]	.34
Persistent palsies	114/18,079 (0.63)	118/24,761 (0.48)	1.13 [0.78, 1.64]	.52
Malignancies				
All palsies	56/607 (9.23)	76/1057 (7.19)	1.37 [0.92, 2.04]	.12
Transient palsies	42/607 (6.92)	49/1057 (4.64)	1.51 [0.94, 2.44]	.09
Persistent palsies	33/1726 (1.91)	33/1489 (2.22)	1.11 [0.63, 1.94]	.72
Graves disease or toxic goiter				
All palsies	5/136 (3.68)	15/234 (6.41)	0.66 [0.07, 6.43]	.72
Transient palsies	5/136 (3.68)	13/234 (5.56)	0.81 [0.06, 10.76]	.88
Persistent palsies	2/1249 (0.16)	6/650 (0.92)	0.28 [0.07, 1.11]	.07
Retrosternal goiter				
All palsies	3/95 (3.16)	31/894 (3.47)	0.47 [0.12, 1.84]	.28
Transient palsies	1/95 (1.05)	26/894 (2.91)	0.27 [0.04, 1.63]	.15
Persistent palsies	2/95 (2.11)	5/894 (0.56)	1.56 [0.22, 10.87]	.65
Primary surgery				
All palsies	84/2108 (3.98)	579/20,103 (2.88)	1.02 [0.37, 2.80]	.97
Transient palsies	69/2108 (3.27)	484/20,103 (2.41)	1.05 [0.35, 3.09]	.94
Persistent palsies	126/18,961 (0.66)	138/26,181 (0.53)	0.92 [0.67, 1.27]	.63
Revision surgery				
All palsies	24/178 (13.48)	28/507 (5.52)	1.26 [0.14, 11.22]	.83
Transient palsies	15/178 (8.43)	20/507 (3.94)	1.16 [0.15, 9.23]	.89
Persistent palsies	43/1157 (3.72)	26/925 (2.81)	1.33 [0.44, 4.00]	.61
High risk surgery*				
All palsies	269/3469 (7.75)	110/1668 (6.59)	0.77 [0.32, 1.83]	.55
Transient palsies	209/3469 (6.02)	80/1668 (4.80)	0.77 [0.35, 1.67]	.50
Persistent palsies	81/4464 (1.81)	53/2831 (1.87)	1.04 [0.57, 1.89]	.90
Low risk surgery†				
All palsies	352/13,678 (2.57)	373/16,656 (2.24)	1.29 [0.48, 3.50]	.61
Transient palsies	277/13,678 (2.03)	316/16,656 (1.90)	1.35 [0.45, 4.02]	.60
Persistent palsies	92/15,398 (0.60)	84/21,020 (0.40)	1.00 [0.66, 1.50]	.99
Persistent palsy definition				
Persistent, defined as $<$6 mo	35/3302 (1.06)	41/3149 (1.30)	0.87 [0.55, 1.38]	.56
Persistent, defined as $\geq$6 mo	174/24,633 (0.71)	176/33,733 (0.52)	0.85 [0.66, 1.10]	.22
Comparative trials				
All palsies	729/20,500 (3.56)	325/7939 (4.10)	0.87 [0.73, 1.03]	.11
Transient palsies	552/20,500 (2.69)	234/7939 (2.95)	0.94 [0.80, 1.10]	.44
Persistent palsies	167/20,500 (0.81)	79/7939 (0.99)	0.88 [0.66, 1.16]	.36
Case series				
All palsies	253/7435 (3.40)	845/29,440 (2.87)	1.32 [0.77, 2.27]	.31
Transient palsies	213/7435 (2.86)	697/29,440 (2.37)	1.43 [0.86, 2.38]	.16
Persistent palsies	42/7,435 (0.56)	146/29,440 (0.50)	0.95 [0.43, 2.10]	0.90

(*Continued*)

TABLE V.
(*Continued*).

Subgroups	IONM Events/Total (%)	ID Events/Total (%)	OR [95% CI]	*P* Value
Prospective Studies				
All palsies	875/25,880 (3.38)	447/11,921 (3.75)	0.86 [0.72, 1.03]	0.21
Transient palsies	684/25,880 (2.64)	355/11,921 (2.98)	0.84 [0.68, 1.04]	0.17
Persistent palsies	193/25,880 (0.75)	92/11,921 (0.77)	0.93 [0.72, 1.20]	0.79
Retrospective Studies				
All palsies	102/1972 (5.17)	697/24,854 (2.80)	1.00 [0.40, 2.45]	0.99
Transient palsies	78/1972 (3.96)	561/24,854 (2.26)	1.38 [0.68, 2.78]	0.37
Persistent palsies	14/1972 (0.71)	124/24,854 (0.50)	1.52 [0.85, 2.74]	0.16
Prospective, comparative, PTVFP $\geq$6 mo				
All palsies	678/19,425 (3.49)	274/7100 (3.86)	0.79 [0.55, 1.13]	0.20
Transient palsies	523/19,425 (2.69)	207/7100 (2.92)	0.79 [0.53, 1.20]	0.27
Persistent palsies	155/19,425 (0.80)	67/7100 (0.94)	0.86 [0.64, 1.16]	0.31

*High risk includes malignancies, retrosternal or toxic goiter, and revision surgeries.
†Low risk surgery include primary benign nontoxic goiters without retrosternal extension.
IONM = recurrent laryngeal nerve neuromonitoring; ID = recurrent laryngeal nerve identification alone; OR = odds ratio; CI = confidence interval; RLN = recurrent laryngeal nerve; PTVFP = persistent true vocal fold palsy.

Pooled Analyses

The calculated sample sizes required in each group to demonstrate a statistically significant difference with an OR of 0.5 were: 1,662 for all TVFP, 2,087 for transient TVFP, 8,523 for persistent TVFP, and 18,047 for unintentional RLN injury. Figure 3 shows forest plots for all included surgeries. The pooled adjusted OR for all TVFP, transient TVFP, persistent TVFP, and unintentional RLN injury, respectively, were 0.93 (95% CI, 0.76-1.12), 1.07 (0.95-1.20), 0.99 (0.79-1.23), and 0.50 (0.15-1.75); there was no statistically significant difference between the two groups. Table V summarizes the subgroup analyses. None of these comparisons demonstrated a statistically significant difference.

DISCUSSION

In this meta-analysis, IONM and ID did not demonstrate a statistically significant difference in rates of total TVFP, transient TVFP, or persistent TVFP with adequately-powered sample sizes for all thyroid surgeries, primary surgery, benign disease, and low-risk groups. Results were also similar within other risk-based subgroups, including revision surgery, malignant disease, as well as high-risk groups. However, sample size restrictions limit our ability to make statistical conclusions among these subgroups.

One randomized controlled trial (RCT) has been performed, and it compares 1,000 nerves at risk in each group.[9] This study found that the RLN monitoring group had a statistically significantly lower total and transient TVFP rate compared to the identification alone group. The "permanent" TVFP did not show a statistically significant difference. Although this is the highest-grade study performed to date, the results and conclusions can still be debated. The total TVFP rate in the RLN identification alone was 5.0%, which is substantially higher than most case series. One explanation could be that the surgeons in this study were more comfortable using IONM to identify the RLN. Further randomized controlled trials are needed to confirm these results, but such trials have difficulty in evaluating rare complications such as TVFP because exceptionally large numbers of subjects are required, surgical techniques can vary greatly, and surgeons may often be reluctant to agree to randomization protocol.[2] Dralle et al. reported that their initial goal of performing a randomized trial was prohibited because many institutions declined randomization.[2]

Until further RCTs can be performed, data from published nonrandomized studies can be used for such comparisons as listed above. Case series and nonrandomized comparative trials have demonstrated fairly accurate results, and their use has been advocated for rare conditions in which randomized trials are difficult to perform.[10]

Most articles neglected to mention or describe the circumstances of any unintentional RLN injury, making this comparison difficult to assess. The meta-analysis demonstrated that no statistically significant difference between the groups in unintentional RLN injury existed, although the OR was 0.5. The sample size of 5,845 was far below the 36,094 required to determine if there would be a true difference. Similar statistically nonsignificant OR results are noted in the subgroup analyses of malignancies, retrosternal goiter, revision surgery, and toxic goiter. The difference may disappear or become significant with larger numbers of subjects and could be related to multiple biases, including selection, technology, and publication biases. In addition, most articles reviewed did not adequately distinguish partial paresis from full paralysis, thus preventing proper analysis. Any future RCTs should include these commonly neglected characteristics.

This study includes biases inherent in a meta-analysis of case series: selection bias (limited by including

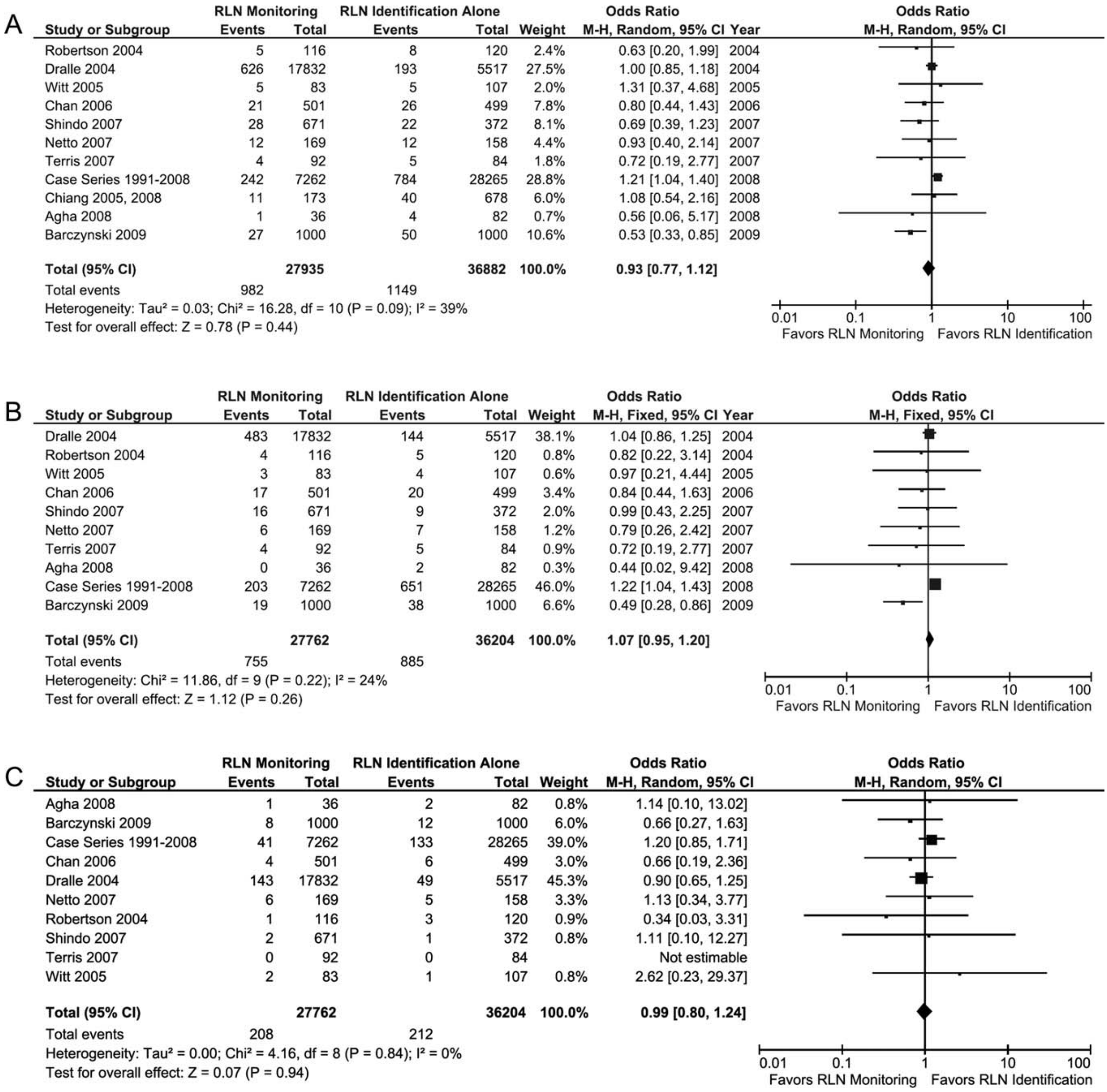

Fig. 3. Forest plots showing the distribution of (A) overall true vocal fold palsy (TVFP). (B) Transient TVFP. (C) Persistent TVFP. RLN = recurrent laryngeal nerve; CI = confidence interval.

only studies evaluating consecutive patients), publication bias (positive results are more likely to be published), allocation bias (possible surgical reasons for authors' decisions to use neuromonitoring, such as difficult dissection), measurement bias (surgeons in favor of monitoring may be influenced when determining TVFP on equivocal flexible laryngoscopic examinations), and intervention bias (interventions or treatments are not applied equally to subjects due to skill/training differences among personnel and/or differences in resources or procedures used at different sites). Heterogeneity is an inherent limitation to meta-analysis and was addressed using standard meta-analytic techniques, including: 1) Cochrane Q and Tau^2 statistics, 2) sensitivity analysis, 3) random-effects analysis, 4) subgroup analysis, and 5) standardized article selection criteria.

There are advantages and disadvantages of each method of identifying the RLN in thyroid surgery. Some authors think that IONM allows quicker nerve dissection and can alert the surgeon to the nerve location before visual identification. Disadvantages may include the cost and setup time of the system. One potentially devastating risk of IONM is RLN injury due to reliance on a signal, presuming that the monitor is adequately functioning, when in fact it is not. The sensitivity of the monitor is only 63%[9]; thus, many authors discourage sole reliance on the monitor to identify the nerve. Proponents of identification alone point to the fact that false negatives can actually increase the risk of RLN injury if the surgeon relies on the monitoring system.

These results indicate that RLN neuromonitoring is not the standard of care in routine thyroid surgery. However, the available data are unable to address certain factors in which neuromonitoring may theoretically be beneficial, including when the surgeon was trained to perform thyroidectomies with IONM or feels more comfortable using IONM, or in high-risk cases.

Our consensus based on the results of this study include:

- IONM should not be considered standard of care. However, surgeons should use IONM if they feel more comfortable using the device during thyroidectomy.
- IONM should not supplant anatomical identification of the nerve.
- The use of IONM should not play a role medicolegally.
- Future studies should include prospective double-blinded randomized controlled trials in which both the subject and the laryngoscopist are blinded to the subject allocation.
- The term *persistent* TVFP should be used instead of *permanent*. We recommend the definition of *persistent* TVFP as no resolution after at least 6 months, although 12 months is preferable. This recommendation is based on the authors' experiences and literature reports of resolution of TVFP after long-term follow-up.[52]

In evaluating TVFP following thyroidectomy, one must consider several caveats. Postoperative hoarseness can have other causes, such as vocal fold edema or endotracheal injury, and thus should always be evaluated with a laryngoscopic examination. In addition, iatrogenic RLN injury is not the only reason for postoperative TVFP. For example, one study found that intubation-related injury represented 4% of TVFP in a recent series of 827 TVFPs.[1] Transient TVFP may be underestimated due to lack of blinding. The surgeon who performs the operation may be biased against documenting vocal fold palsy, especially in the case of partial palsy.

Important elements of an ideal design for RCT comparing RLN monitoring and RLN identification alone on TVFP would include:

- Sample size calculation.
- Complete demographics (e.g., age, gender, pathology, surgery)
- Description of standardized nerve dissection technique or IONM type.
- Documentation of unintentional RLN injury.
- Documentation of complete vocal fold paralysis and partial vocal fold paresis.
- A blinded, experienced laryngoscopist to perform preoperative and postoperative laryngoscopic examinations. Some investigators could consider laryngovideostroboscopy to provide highly sensitive outcome data, although there are currently no available validated measures. Preoperative TVFP and intentional resections of RLN should be excluded from the analysis. Postoperative laryngoscopic examination should be performed within 24 hours of the surgery and then periodically until paralysis resolves. The suggested definition for persistent vocal fold palsy is palsy lasting more than 12 months.
- Documentation of symptomatology, such as hoarseness and dysphagia, using validated outcome measures.
- Analysis should include subgroup stratification.

CONCLUSION

This meta-analysis demonstrates no statistically significant difference in the rate of true vocal fold palsy after using intraoperative neuromonitoring versus recurrent laryngeal nerve identification alone during routine thyroidectomy. IONM is a tool that surgeons can consider using to assist in identification of the recurrent laryngeal nerve during thyroidectomy. However, IONM should not be considered the standard of care and should not supplant anatomical identification of the RLN. Future studies are warranted to evaluate the benefit of IONM in thyroidectomy, especially in conditions in which the RLN is at high risk of injury.

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