



Complete and incomplete recurrent laryngeal nerve injury after thyroid and parathyroid surgery: Characterizing paralysis and paresis

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ABSTRACT

Background: Injury of the recurrent laryngeal nerve and consequent disorder of vocal fold movement is a typical complication in thyroid and parathyroid surgery. During postoperative laryngoscopy we observed not only a complete standstill (vocal fold paralysis), but also a hypomobility (paresis). In this prospective study, we investigated the difference in incidence and prognosis as well as risk-factors, intraoperative neuromonitoring, and symptoms between vocal fold paralysis and vocal fold paresis.

Methods: Data were prospectively collected and analyzed in a single high-volume thyroid center between 2012 and 2016. Vocal fold paresis was defined as hypomobility in abduction or adduction, a reduction in range and speed of vocal fold movement. Vocal fold paralysis was defined as asymmetry and missing purposeful vocal fold movement.

Results: The study included 4,707 surgeries and 7,992 at-risk nerves at risk. Vocal fold paralysis was diagnosed in 374 patients (4.68% of 7,992 nerves at risk) and vocal fold paresis in 114 patients (1.43%). Exclusively in the paralysis group, 36 patients (0.45%) developed permanent loss of vocal fold function ($P < .001$). In follow-up, vocal fold paresis patients regain normal vocal fold function significantly earlier than vocal fold paralysis (mean duration: 6.96 ± 6.506 vs 10.77 ± 7.827 weeks) and presented with significantly less symptoms like hoarseness, diplophonia, dysphagia, and dyspnea (68.8% vs 95.9%). In intraoperative neuromonitoring, vocal fold paresis showed a significantly higher postresectional N. vagus amplitude than vocal fold paralysis patients (0.349 mV vs 0.114 mV, $P < .001$).

Conclusion: After thyroidectomy, vocal fold paresis must be distinguished from vocal fold paralysis and should be implemented as a separate outcome parameter in the postoperative quality assessment.

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Introduction

Paralysis of the recurrent laryngeal nerve (RLN) is a typical and occasionally permanent complication after thyroid surgery affecting patient's quality of life. The incidence of temporary (rehabilitation within 6 months) and permanent paralysis ranges from 1.4 to 38 and 0.3 to 3 percent respectively.^{1–8} Immobility of the vocal fold (VF) is defined as the absence of purposeful motion and is categorized as VF paralysis.^{9,10} Recently a reduced but still visible mobility of the VF (in contrast to paralysis) gained attention in laryngological research

owing to improved methods of diagnosis.^{11,12} This entity was first described by Koufman et al in 50 patients with symptoms such as dysphonia, vocal fatigue, and diplophonia.¹³

Hypomobility of the VF after thyroidectomy has still not been defined as an outcome parameter and has not been implemented in early routine postoperative evaluation, yet VF hypomobility was mentioned in a previous manuscript of our institution.¹⁴ However, for patients and for surgeons it is of major importance to distinguish between complete immobility (paralysis), incomplete or reduced mobility (paresis), and regular movement of the VF. The aim of the present study was to prospectively investigate the incidence, rate of recovery of VF paresis in comparison to VF paralysis after thyroid and parathyroid surgery and to evaluate contributing risks factors for these complications. Furthermore,

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intraoperative neuromonitoring data of surgeries and symptoms of VF paresis patients were compared with those with VF paralysis.

Methods

Data were prospectively collected and analyzed in a single high-volume thyroid center with the focus on postoperative VF function distinguishing paralysis, paresis, and regular mobility. These entities were recorded as separate outcome parameter in our database. Ethical approval was granted by the KAV review board (EK 15-128-VK). In the study, 4,715 patients (female and male) were prospectively included. All patients underwent thyroid and parathyroid surgery between January 2012 until December 2016 at our institution. Patients were excluded in case of preoperative RLN palsy or intended sacrifice of the nerve owing to invasive malignant disease.

During all surgeries, institutional guidelines of our department and the practice guidelines of the German Association of Endocrine Surgeons for the treatment of thyroid diseases were followed.^{6,15,16} Standard surgical technique in our department consists of routine identification and protection of the RLN including intraoperative neuromonitoring (IONM) of the RLN, superior laryngeal nerve, and vagal nerve. The same effort was made to save parathyroid glands.^{17–20}

Several thyroidectomies and lobectomies were combined with additional parathyroid surgery or central and lateral lymph node dissection. Sole lateral neck dissection was added to nerves at risk (NAR) calculation because of the risk of vagal injury. We did not include resection of thyroid isthmus or pyramidal lobe in NAR calculation.

Pre- and postoperative laryngoscopy

All patients were routinely examined pre- and postoperatively for VF function by an experienced otorhinolaryngology specialist. Our protocol required all patients to have preoperative laryngoscopy regardless of any symptoms. Patients with findings in the preoperative laryngoscopy were re-examined by one of our laryngologist experts. Patients with preoperative VF movement disorder were excluded from the study.

Postoperative assessment was performed on the first or second postoperative day by 1 of 2 laryngologists with special expertise in phoniatrics. In case of paresis or paralysis, examination was repeated after 3 weeks, 6 weeks, 12 weeks, 6 months, and occasionally at 1 year until complete recovery occurred or until persistent VF impairment was diagnosed. Examination was performed regularly by flexible laryngoscopy; VF movement was captured (video) for a detailed analysis and consecutive follow up exams. The laryngologists were not part of the surgical team and therefore not aware of intraoperative neuromonitoring signal or possible challenging anatomic complexity. Patients with VF movement disorder were appointed to the same laryngologist for further follow-up examinations. Time to restitution was only calculated for patients who attended thorough follow-up.

Definition of vocal fold paresis versus paralysis

VF paresis was defined as hypomobility in abduction or adduction, a reduction in range and speed of VF movement.^{9–11} VF paralysis was defined as asymmetry and missing purposeful VF movement in laryngoscopic examination.^{9,10} The recurrent nerve injury was considered as permanent if there was a VF movement disorder (paresis or paralysis) in the otorhinolaryngologic examination 6 months after surgery.

Data collection

Relevant clinical parameters were registered with ChirDok Software (MediCare ChirDok; Micom, Wiener Neustadt, Austria). The database is continuously updated by surgeons with information on diagnosis, procedure, complication, follow-up, and so on, and validated by ward physicians not involved in surgical treatment. Starting in 2012, VF paresis was encoded separately from VF paralysis.

IONM and postoperative vagal nerve

Intraoperative electromyography (EMG) is widely established in thyroid surgery. At our department IONM is used routinely following the standards of the International IONM guidelines with a sterile bipolar stimulation probe and laryngeal (endotracheal) tube-based surface electrodes positioned on the vocal cord (thyroarytenoid or vocalis muscle), and the signal is monitored on a display and computer system Avalanche XT (Dr Langer Medical, Waldkirch, Germany) on site in the operating theater.²¹ The intermittent nerve stimulation current is set to 2 milliamperes. IONM data were collected retrospectively and were not available for all patients because it is not archived digitally. For each group (VF paralysis and VF paresis), the recorded amplitude of the vagal nerve (V2) after thyroidectomy was obtained in 32 cases. In addition, 92 cases were evaluated in the control group, consisting of patients who underwent thyroid surgery and had postoperative normal VF function.

Symptoms

In the first postoperative ENT-report, detailed descriptions of symptoms were documented in 56.7% (277 out of 488) of patients, 197 out of 374 with postoperative VF paralysis and 80 out of 114 with postoperative VF paresis. The information included hoarseness, dysphagia, dyspnea, diplophonia, and incomplete glottic closure. If there was a subjective voice alteration, patients were offered voice therapy with a speech therapist. No interventions like temporary VF injections were used in the study population, neither for VF paralysis nor VF paresis patients.

Statistical analysis

For statistical analysis, we used SPSS (IBM Corp., Armonk, NY). The encoded string variable for time to restitution was transformed in a numeric variable. Continuous variables were calculated as mean \pm standard deviation (SD), categorical variables were shown as numbers (n) and proportions (%) of NAR. Descriptive analysis for time to restitution was calculated for both groups, VF paresis, and paralysis. A power analysis was performed to evaluate sample size. Time to restitution means of both groups were compared via skewness and Kolmogorov-Smirnov test for Gaussian distribution and showed a nonnormal distribution. The groups were considered independent variables. Time to restitution for the 2 groups was compared via Wilcoxon rank-sum test (Mann-Whitney U test). Effect size and statistical power were calculated post-hoc with open source software G*Power (Düsseldorf, Germany).²² Furthermore, Pearson's χ^2 test was calculated to investigate the connection between VF paresis and various independent variables. These variables were sex and diagnosis such as Graves disease, bilateral surgery, lymph node dissection and benign or malignant thyroid disease, recurrence, completion thyroidectomy for misdiagnosed malignancies in frozen section and duration of stay with early or late recovery. Differences in group mean for intraoperative neuromonitoring values were analyzed with a linear regression model, followed by direct group comparison using pair-wise t test, adjusted with bonferroni-method for multiple testing. The

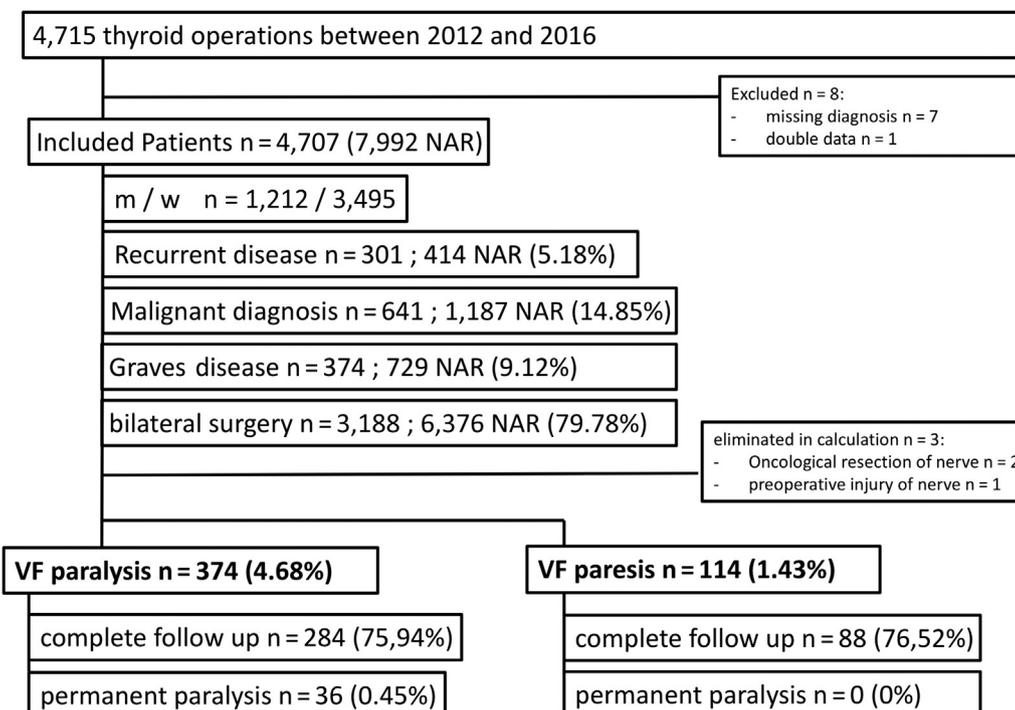


Fig 1. Consort diagram showing patient details (excluded patients; sex and diagnoses of included patients). Number of patients with complete follow-up (until restitution or permanent paralysis >6 months) and persistent impairment of vocal fold movement in comparison (recurrent laryngeal nerve paralysis versus paresis).

calculated Cohens' d effect size of 0.529 ($r = 0.26$) represents a small to moderate effect. The power of the statistical analysis was 0.992 and showed that the sample size was large enough to prove a significant difference.

Results

In the study, 4,707 patients were surgically treated for thyroid and parathyroid disease with 7,992 NAR; 3,495 were women and 1,212 men. Patients received bilateral surgery ($n = 3,302$) or unilateral surgery ($n = 1,388$), and 17 were sole resections of thyroid isthmus or pyramidal lobe.

Diagnoses were distributed as follows: malignant diagnosis in 641 patients (14.85%), Graves disease in 374 (9.12%), recurrent disease in 301 (5.18%), and hyperparathyroidism in 245 (4.09%) patients. The remaining subjects ($n = 3,146$; 66.75%) were treated for large endemic goiter or suspicious adenoma (Fig 1).

Among the 4,707 patients who underwent surgery, we found postoperative VF paralysis in 374 patients (4.68% of 7,992 NAR) and VF paresis in 114 patients (1.43% of NAR). In total, there were 488 patients with VF impairment postoperatively.

IONM

IONM showed a significant difference in vagal nerve amplitude after resection when comparing VF paralysis, VF paresis, and the control group (0.114 mV, 0.349 mV and 0.449 mV, $P < .001$; Fig 2).

Symptoms

There was a significant difference between the amount of symptoms in the VF paralysis compared with the VF paresis group.

Patients with postoperative VF paralysis developed any kind of symptoms in 95.9% ($n = 189$; $P < .001$), 93.9% ($n = 185$; $P < .001$) showed hoarseness, 16.2% ($n = 32$; $P < .027$) dysphagia, 2.5%

dyspnea ($n = 5$; $P = .505$), and 22.8% ($n = 45$; $P = .051$) had incomplete glottic closure. Of patients with postoperative VF paresis, 68.8% ($n = 55$) presented with symptoms. In addition, 52.5% ($n = 42$) had hoarseness, 13.8% ($n = 11$) had diplophonia, and 6.3% ($n = 5$) had dysphagia. Furthermore, 12.5% ($n = 10$) showed incomplete glottic closure at the first follow-up exam.

Follow-up

Complete follow-up (attendance at all appointments) until restitution or permanent paralysis was achieved in 372 of 488 patients (76.07%). In the paralysis group, 36 patients (0.45% of NAR) still showed immobility at the 6-month follow-up examination and were subsequently defined as permanent paralysis (9.7% of 372 injured nerves, ie, 90.3% recovery rate). No patient with VF paresis presented with VF impairment at the 6-month follow-up appointment ($P < .001$). Recovery was significantly faster in the paresis compared with the paralysis group. Arithmetic mean for recovery period in weeks was 6.96 ± 6.506 in patients with VF paresis compared with 10.77 ± 7.827 in patients with VF paralysis ($P < .001$). Time to rehabilitation is presented in Fig 3.

Risk factors

We could not identify a significant correlation comparing variables that may represent possible risk factors for the occurrence of iatrogenic VF injury like sex, recurrent disease (benign or malignant thyroid disease), malignancy, Graves' disease, bilateral surgery, or lymph node dissection (Table I).

Discussion

The aim of this study was to investigate incidence and prognosis of VF hypomobility (ie, paresis) versus complete VF immobility (ie, paralysis) after thyroid and parathyroid surgery in routine

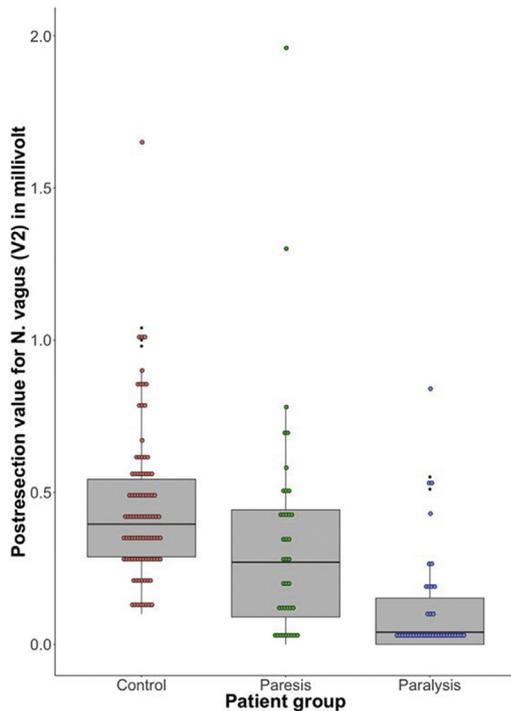


Fig 2. Postresection value of the intraoperative neuro-monitoring of the V2 in comparison. Control group ($n = 92$ patients who underwent thyroid surgery and had postoperative normal VF function), paresis group ($n = 32$, patients with hypomobility of vocal fold movement), and paralysis group ($n = 32$, patients with asymmetry and missing purposeful vocal fold movement).

postoperative laryngoscopy. The discrepancy between these 2 diagnoses has not been evaluated as an independent parameter after thyroid surgery to the best of our knowledge. There was a significant difference between the 2 groups in the rate of recovery, time to restitution, and IONM vagal nerve amplitude (V2) after resection. VF paresis recovers significantly faster and in all cases, as opposed to patients with VF paralysis, and developed significantly less symptoms, such as hoarseness and dysphagia. The results presented in this study show that it is of great importance to include the diagnosis of incomplete recurrent laryngeal nerve injury (VF paresis) in quality control. Furthermore, we strongly recommend performing routine pre- and postoperative laryngoscopy. Early examination is necessary, as Dionigi et al presented.²³ Most VF movement disorders are diagnosed in the first 2 postoperative days.²³ Especially in the absence of symptoms, VF movement disorder can be overlooked. Laryngoscopy therefore represents an essential tool for quality management as postulated in the German thyroid surgery guidelines.¹⁶ In addition, in the rare case of late occurrence of VF movement disorder, it is beneficial to have an early postoperative report for comparison.^{5,6}

Up to now there is no final consensus on the definition of VF paresis and VF paralysis. Bruce et al suggested to use the terms paralysis and palsy for a complete immobility of the VF and to use descriptive terms like decreased movement for hypomobility.²⁴ In a study by Rubin and Sataloff, a now widely accepted definition was established by characterizing VF paralysis as an immobile VF except for a slight respiratory motion and the maintained ability to alter longitudinal tension and VF paresis as hypomobility.²⁵ In an effort to standardize the nomenclature Rosen et al also defined VF paresis as a VF hypomobility if the underlying etiology is caused by the RLN.⁹ Definite signs of VF paresis in laryngoscopy are still being discussed. Our definition is in line with studies mentioned earlier describing paresis as an asymmetrical VF movement where the

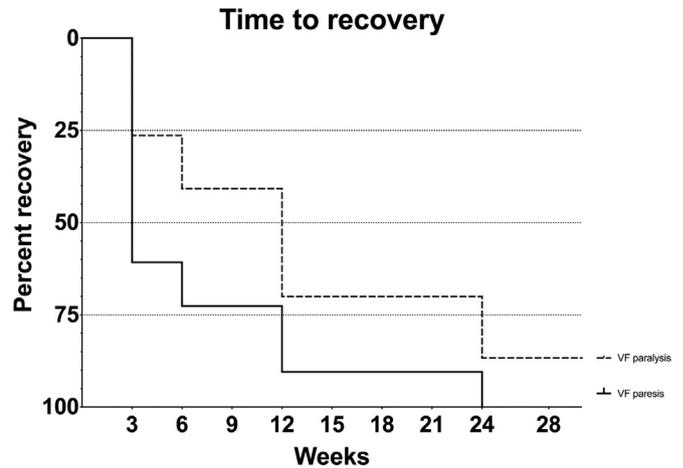


Fig 3. Kaplan-Meier plot showing the cumulative rehabilitation rate of the 2 groups, VF paresis and VF paralysis, at the follow-up examination intervals.

affected side shows a slow or sluggish motion, decreased range of adduction or abduction, and decreased tone of the VF.^{10,13,26,27} Paralysis was defined as asymmetry and missing purposeful VF movement.

Postoperative examinations of VF movement were performed by experienced otorhinolaryngology specialists at our center. A recent study by Madden and Rosen showed that there is a high intra- and inter-rater reliability for the diagnosis of VF paralysis and paresis.²⁸ Koufman et al suggested that laryngeal electromyography (LEMG) is necessary to diagnose VF paresis¹³; however, other authors outline the difficulties in application and interpretation of LEMG.^{11,29} LEMG was not used in the present study. Previous research on the entity of VF paresis did not focus on patients who underwent thyroid surgery because only a minor role was attributed to this cause. A study by Koufman et al on 50 patients with VF paresis concluded that the presumed causes were distributed as follows: idiopathic (44%), postviral neuropathy (24%), iatrogenic (20%), 2 patients had had thyroid surgery, malignancy (6%), multiple sclerosis (4%), and chemotherapy induced peripheral neuropathy (2%).¹³ In other studies investigating VF paresis, iatrogenic nerve injury accounted for 4% to 36%.^{12,30} VF paresis has to be distinguished from synkinesis, a pathology which can also present with VF hypomobility.¹⁰ Laryngeal synkinesis is a result of variable reinnervation occurring about 3 months after a RLN injury.^{31,32} Because all our patients were diagnosed 1 or 2 days after surgery synkinesis can be ruled out in the population of this study. Further correlations between VF paresis and paralysis and different variables were analyzed in this study. Statistical analyses showed no significant correlation with sex. This is in line with a study by Heman-Ackah investigating the connection between thyroid disease and VF paresis with no significant difference for sex.²⁷ Potential risk factors like recurrent disease (benign or malignant thyroid disease), malignancy, Graves disease, bilateral surgery, and lymph node dissection did not show a significant correlation with VF paresis.

The total incidence for postoperative VF impairment of 6.11% and 0.45% permanent paralysis is in line with complication rates of other specialized surgical centers.^{1–8} Studies have shown that centers with a low volume of thyroid surgeries have a significant increased risk for recurrent laryngeal nerve injury.^{2,14,33} Permanent VF impairment was diagnosed only in patients with VF paralysis. There were no patients with permanent VF paresis. Not only did all patients with VF paresis recover, rehabilitation was significantly faster than in the VF paralysis group (6.96 vs 10.77 weeks). In

Table 1
Clinical variables of patients with vocal fold paralysis, paresis, and control group after thyroid surgery

Nerves at risk (n = 7,992)	VF paralysis (n = 374)	VF paresis (n = 114)	P value	Control (7,504)
Sex (F)	261 (69.8)	75 (65.8)	.42	5,698 (75.9)
Recurrent disease	32 (8.6)	5 (4.4)	.141	377 (5.0)
Malignant diagnosis	61 (16.3)	16 (14.0)	.56	1,110 (14.8)
Graves disease	36 (9.6)	9 (7.9)	.576	684 (9.1)
Bilateral surgery	237 (63.4)	75 (65.8)	.638	6,064 (80.8)
Lymph node dissection	37 (9.9)	12 (10.5)	.844	551 (7.3)
Permanent NLR injury	36 (9.6)	0	<.001	
Mean recovery in weeks	10.77 ± 7.827	6.96 ± 6.506	<.001	

Values in parentheses are percentages. Mean recovery is presented in weeks ± standard deviation.

addition, fewer patients had dysphonia in the VF paresis group. These differences in symptoms, rate, and time to recovery is clinically relevant for the prognosis of patients with VF paresis. In addition, we think that the distinction between VF paresis and paralysis plays an important role when counselling patients on interventions aiming at voice improvement such as fillers. Following the data of our study patients with VF paresis should not be offered invasive treatments because it is a self-limiting disease. The IONM findings showed a significant difference in vagal amplitude (V2) after resection. V2 was lower than in the control group but higher than in the VF paralysis group. A hypothetical damage of a fraction of the nerve fibers in VF paresis resulted in a mildly decreased amplitude compared with the control group, but with sufficient conductive capability, contrary to the VF paralysis group. These results are applicable to prior laryngeal EMG studies, where VF paresis was associated with decreased recruitment, abnormalities in motor unit action potentials, and decreased duration of the waveform or polyphasic motor unit potentials.^{29,34} To this point, we use V2 in combination with laryngeal twitch as contributing information for patient counselling in case of postoperative VF paresis. Additional studies are needed to assess if these 2 parameters alone are predictive for VF paresis in comparison with VF paralysis after thyroidectomy.

Limitations

VF paresis, paralysis, and full range of VF motion were diagnosed via flexible laryngoscopy in this study. Laryngoscopy is a subjective examination method and therefore may represent a limitation of this study; however Madden et al showed a high inter- and intraobserver reliability in diagnosing VF paralysis and paresis.²⁷ No objective measurement such as LEMG, standardized voice assessment tests, or quality of life questionnaires were completed by the patients, which may also represent a limitation of this study. An additional important issue is that IONM data was only available for a limited number of patients and collected retrospectively. Additional research and standardized follow-up protocols including voice assessment are necessary to confirm the findings presented in this study.

In conclusion, our study shows a statistically significant difference in prognosis, symptoms, and outcome of VF paresis in comparison with VF paralysis, with a better prognosis for VF paresis in terms of earlier recovery and restitution in all cases. The results show that VF paresis, that is, incomplete injury of the RLN, is an important entity accounting for almost a third of postoperative VF impairments. We therefore propose to establish VF paresis as a separate outcome parameter in thyroid and parathyroid surgery.

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Conflict of interest/Disclosure

All authors declare no conflict of interest.

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