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The incidence and recovery rate of idiopathic vocal fold paralysis: a population-based study

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Abstract

Purpose To determine the incidence and spontaneous recovery rate of idiopathic vocal fold paralysis (IVFP) and paresis (IVFp), and the impact of steroid treatment on rates of recovery.

Methods This retrospective cohort study included all patients with IVFP or IVFp within a large integrated health-care system between January 1, 2008 and December 31, 2014. Patient demographics and clinical characteristics, including time to diagnosis, spontaneous recovery status, time to recovery, and treatment, were examined.

Results A total of 264 patients were identified, 183 (69.3%) with IVFP and 81 (30.7%) with IVFp. Nearly all cases (96.6%) were unilateral and 89.8% of patients were over the age of 45. The combined (IVFP and IVFp) 7-year mean incidence was 1.04 cases per 100,000 persons each year with the highest 7-year mean annual incidence in white patients (1.60 per 100,000). The total rate of spontaneous recovery was 29.5%, where 21.2% had endoscopic evidence of resolution and 8.3% had clinical improvement in their voice without endoscopic confirmation. The median time to symptom resolution was 4.0 months. Use of steroids was not linked with spontaneous recovery in multivariable analyses.

Conclusion The annual incidence of VFP (IVFP and IVFp) was 1.04 cases per 100,000 persons, with spontaneous recovery occurring in nearly a third of patients, regardless of steroid use.

Keywords Vocal fold paralysis · Vocal fold paresis · Idiopathic · Spontaneous recovery · Dysphonia · Steroids

Introduction

Vocal fold paralysis (VFP) can be classified as either iatrogenic, traumatic, malignant, inflammatory, or idiopathic [1]. Previous studies report idiopathic vocal fold paralysis (IVFP) to comprise 10–37% of VFP cases [2–7] and to have a better rate of spontaneous recovery than other types [8]. The population-based incidence of IVFP, however, is unknown. Furthermore, the literature does not consistently distinguish idiopathic paralysis (complete immobility, IVFP) from paresis (partial immobility, IVFp), which may hold prognostic and therapeutic implications [9]. The efficacy of systemic steroid use has also not been studied, even though some clinicians use this in IVFP as they would for other idiopathic cranial mononeuropathies such as Bell's palsy and sudden sensorineural hearing loss.

Using a large integrated health-care system consisting of over three million patients representative of the state of California, this study aims to determine the incidence of IVFP and IVFp, their respective rates of spontaneous recovery, and the association between recovery rates and the use of steroid treatment.

Materials and methods

In this retrospective cohort study of a health maintenance organization with a patient population of over three million, we reviewed the electronic medical records (EMR) of patients with IVFP and IVFp from January 1, 2008 to

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December 31, 2014. Patients with cases of VFP were identified using International Classification of Diseases, ninth revision (ICD-9) codes 478.3, 478.30, 478.31, 478.32, 478.33, and 478.34. To restrict to cases of VFP that were idiopathic in etiology, records were excluded using ICD-9 and Current Procedural Terminology, fourth edition (CPT-4) codes for diseases, conditions, or procedures that could explain the VFP, including those diagnoses and procedures indicating pathology or surgery of the thyroid, parathyroid, esophagus, and thoracic aorta, neoplasms of the thyroid, parathyroid, esophagus, trachea, and lung, as well as neurologic and autoimmune diseases such as amyotrophic lateral sclerosis, multiple sclerosis, and systemic lupus erythematosus. Patient demographic characteristics, including age, sex and race/ethnicity, were extracted from the EMRs. Chart review was then performed for the entire cohort to collect clinical characteristics, such as the presence of IVFp versus IFVP, laterality of the VFP, treatment through the use of steroids, speech therapy, vocal fold injection and thyroplasty, the time from symptom onset to diagnosis by an otolaryngologist and the time of diagnosis to recovery of vocal function.

The population-based incidence of idiopathic VFP (IVFP/IVFp) was calculated as the number of cases per 100,000 patients annually. The primary outcome was spontaneous recovery of IVFP/IVFp, defined as either endoscopic confirmation of true vocal fold mobility and/or recovery of vocal function. We performed the two-group *t* test to compare the mean age in years of the study subjects between those who had a spontaneous recovery versus those who did not. Fisher's exact and Chi-square tests were used for comparisons of frequencies of demographic (age categories, sex, race/ethnicity) and clinical (e.g., treatment types) characteristics between those patients who experienced spontaneous recovery compared to those who did not. The Wilcoxon rank-sum test was employed to compare distributions of time between onset of symptoms and seeing a specialist. Chi-square tests were used to compare annual incidence rates of IVFP/IVFp by age groups (≤ 45 years old and >45 years old) and race (white versus non-white). To assess the adjusted association between treatments and spontaneous recovery, we employed multiple logistic regression to control for demographic and clinical characteristics.

All statistical analyses were performed using Statistical Analysis Systems (SAS) version 9.3 (SAS Institute Inc., Cary, North Carolina). A p value of <0.05 was considered statistically significant. The Institutional Review Board of our institution approved this study with waiver of consent.

Results

Our query of the EMRs using the inclusionary and exclusionary codes described in "Materials and methods" yielded 865 subjects. Chart review excluded 601 subjects who were determined to have VFP with a known etiology, did not have VFP, were diagnosed with IVFP/IVFp in the years preceding 2008, or had insufficient documentation to verify that they had IVFP/IVFp (Fig. 1). The resulting

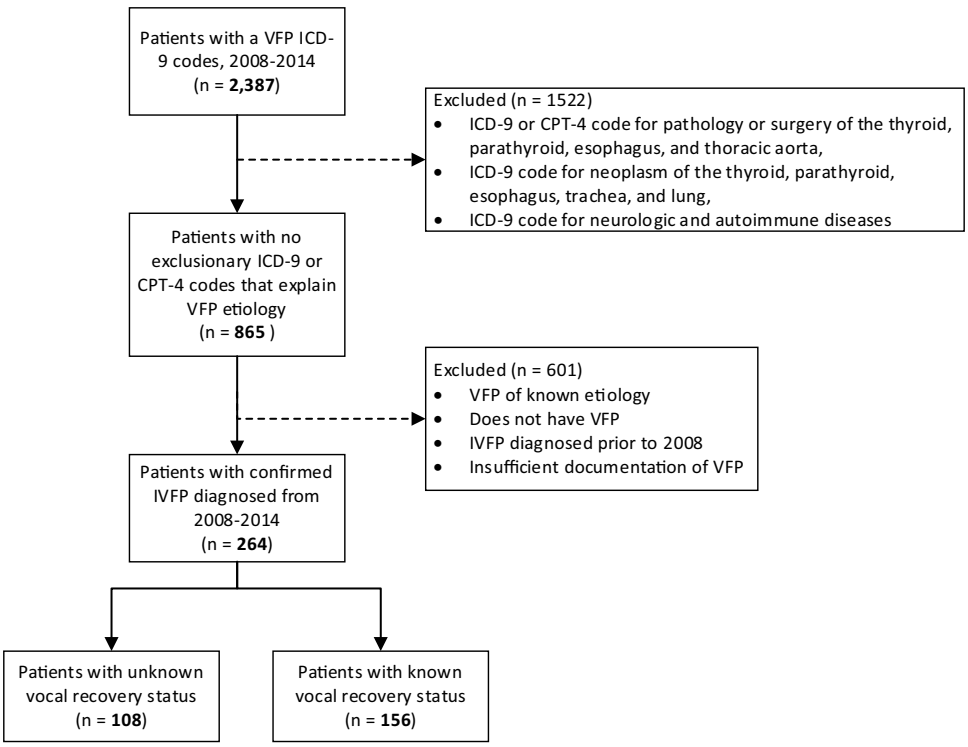

Fig. 1 Cohort selection

cohort consisted of a total of 264 patients: 81 (30.7%) with IVFp and 183 (69.3%) with IVFP.

The mean age was 64.8 (standard deviation 15.1), with 237 (89.8%) patients over age 45. Additionally, 52.3% of our cohort was female and white non-Hispanics comprised the largest racial/ethnic group (65.5%). Unilateral IVFP/IVFp occurred in 96.6% of the patients (Table 1). The rate of spontaneous recovery was 29.5% ($n = 78$, with 21.2% having endoscopic confirmation of return of vocal fold motion and those remaining demonstrating documented improvement in their voice without endoscopic confirmation). The recovery status of 108 (40.9%) patients was unknown due to lack of follow-up. The presence of IVFP versus IVFp was not associated with spontaneous recovery status.

Regarding treatments, speech therapy was employed in 74 (28.0%) patients and 20 (25.6%) recovered from IVFP/IVFp; the association between speech therapy and recovery was not statistically significant ($p = 0.57$). Thirty-four (12.9%) patients underwent vocal fold injection and 13 (4.9%) thyroplasty. Among the 15 patients given steroids, 8 (53.3%) recovered from their IVFP/IVFp, compared to the 70 (28.1%) patients who were not given steroids ($p = 0.05$).

The median duration of time that patients waited to be seen by an otolaryngologist was 1 month, with 75% of patients seen within 4 months and nearly all within 1 year (Table 1). For 25 patients, a clear date of onset of symptoms was not discernible through chart review and, therefore, they were not included in these calculations. Among those who had a spontaneous recovery, the median time to recovery following a diagnosis from an otolaryngologist was 4 months, with 75% of spontaneous recoveries occurring within 1 year (Table 1). There were five patients whose recovery of vocal function was noted after 3 years, with the longest time being 8 years. For these patients, there was no interval re-examination of vocal function by an otolaryngologist and, therefore, their recovery of vocal function may have occurred earlier.

The annual incidence, the overall incidence rate, and the incidence rate according to age group and race are shown in Table 2. The average annual 7-year incidence rate was 1.04 new cases per 100,000 patients, with a higher incidence for those over age 45 years versus 45 years or younger (2.36 versus 0.18 new cases per 100,000) and for whites versus non-whites (1.60 versus 0.63 new cases per 100,000 patients).

In multivariate analysis, after adjusting for demographic and clinical characteristics, the presence of IVFP versus IVFp was not associated with spontaneous recovery status (OR 0.74, 95% CI 0.40–1.39) nor was the association between treatment with steroids and spontaneous recovery, (OR 2.62, 95% CI 0.85–8.13, Table 3).

Discussion

A previous population-based study from Germany found the incidence of IVFP to be 0.8 per 100,000 persons [10], with the caveat that transient palsies were excluded and only patients admitted to a hospital were included. Accounting for these differences, this incidence is comparable to the results presented here (1.04 per 100,000 persons), where we have used a population base of over 3.2 million patients that belong to our integrated healthcare system [11]. The reason for the variation in incidence that we have found between whites and non-whites is unclear. Bell's palsy, which is an idiopathic facial nerve palsy presumed to be virally mediated, has an annual incidence of 13–34 cases per 100,000 without a racial predilection [12]. Likewise, sudden sensorineural hearing loss, another idiopathic cranial mononeuropathy, has an annual incidence of five to 20 cases per 100,000 without racial variation [13].

Previous studies on the rate of spontaneous recovery of vocal function after IVFP report a wide range. A study from 1998 documented a recovery rate of 19% in a small group of 16 patients with IVFP [14]. Recently, a study of 55 patients found a higher recovery rate of 69% [15]. The cohort presented here is one of the largest to date ($n = 264$) and shows the rate to be 29.5%, but the vocal status of 40.9% of the cohort is unknown (due to poor documentation or absent reassessment by an otolaryngologist). It is possible that the actual rate is higher since patients whose voices improve are less likely to return for medical reassessment of their diagnosis.

The presence of paresis rather than paralysis is not associated with an increased rate of vocal recovery (OR 0.74, 95% CI 0.40–1.39). This may be due to several factors that are not accounted for in this study, including the position and muscle tone/bulk of the vocal fold. A paralyzed vocal fold in the paramedian position that does not regain mobility may give a better voice outcome than a paretic vocal fold in the lateralized position with partial recovery of mobility. Likewise, reinnervation that restores the muscle tone and bulk but not mobility of the paralyzed vocal fold may still produce an acceptable voice outcome [9].

The small number of patients in our cohort treated with systemic steroids ($n = 15$) shows a higher rate of spontaneous recovery (53.3% vs 28.1%, $p = 0.05$ in univariate analysis), but after adjusting for demographic and clinical characteristics in a multiple logistic regression analysis, this association was no longer statistically significant (OR 2.62, 95% CI 0.85–8.13). The literature is silent on this treatment, and there are no guidelines advocating for its use. Given that IVFP/IVFp is postulated to be a virally mediated inflammatory process akin to Bell's palsy or

Table 1 Demographic and clinical characteristics of patients with idiopathic vocal fold paralysis/paresis by spontaneous recovery status

	Patient total ($N=264$)	Spontaneous recovery status		
		Yes ($n=78$, 29.5%)	No ($n=186$, 70.5%)	Chi-square p value
Demographic characteristics				
Age, mean (SD) (years)	64.8 (15.1)	61.4 (14.9)	66.2 (15.0)	0.02*
Age categories, *n* (%)				0.18
≤45	27 (10.2)	11 (14.1)	16 (8.6)	
>45	237 (89.8)	67 (85.9)	170 (91.4)	
Sex, *n* (%)				0.55
Female	138 (52.3)	43 (55.1)	95 (51.1)	
Male	126 (47.7)	35 (44.9)	91 (48.9)	
Race/ethnicity, *n* (%)				0.75[1], 0.99[2]
White	173 (65.5)	50 (64.1)	123 (66.1)	
Non-white	91 (34.5)	28 (35.9)	63 (33.9)	
Black	18 (6.8)	5 (6.4)	13 (7.0)	
Hispanic	37 (14.0)	12 (15.4)	25 (13.4)	
Asian	24 (9.1)	7 (9.0)	17 (9.1)	
Other/missing	12 (4.6)	4 (5.1)	8 (4.3)	
Clinical characteristics				
Paralysis/paresis, *n* (%)				0.37
Paralysis (IVFP)	183 (69.3)	51 (65.4)	132 (71.0)	
Paresis (IVFp)	81 (30.7)	27 (34.6)	54 (29.0)	
Laterality, *n* (%)				0.06‡
Unilateral	9 (3.4)	78 (100.0)	177 (95.2)	
Bilateral	255 (96.6)	0 (0.0)	9 (4.8)	
Treatment, *n* (%)				
Steroids				0.05‡
No	249 (94.3)	70 (89.7)	179 (96.2)	
Yes	15 (5.7)	8 (10.3)	7 (3.8)	
Speech therapy				0.57
No	190 (72.0)	58 (74.4)	132 (71.0)	
Yes	74 (28.0)	20 (25.6)	54 (29.0)	
Vocal injection				N/A
No	230 (87.1)	N/A	N/A	
Yes	34 (12.9)			
Thyroplasty				N/A
No	251 (95.1)	N/A	N/A	
Yes	13 (4.9)			
Time from symptom onset to specialist visit (months), median (IQR) (missing = 25)	1.0 (1.0–4.0)	1.0 (0.0–2.0)	2.0 (1.0–5.0)	<0.01†
Time from diagnosis to spontaneous recovery (months), median (IQR)	N/A	4.0 (1.0–12.0)	N/A	N/A

SD standard deviation, *IQR* interquartile range (25th and 75th percentiles)

*p value for comparison calculated by t test

†p value for comparison calculated by Wilcoxon rank-sum test

‡p value for comparison calculated by Fisher's exact test

[1]Chi-square test comparing white and non-white by spontaneous recovery status

[2]Chi-square test comparing all racial/ethnic categories by spontaneous recovery status

Table 2 Annual incidence and incidence rate per 100,000 patients of IVFP/IVFp from 2008 to 2014, overall and by year, age and race

Year	Incident cases	Incidence rate*	Age ≤ 45 years		Age > 45 years		*p* value†	White		Non-white		*p* value
			Incident cases	Incidence rate*	Incident cases	Incidence rate*		Incident cases	Incidence rate*	Incident cases	Incidence rate*	
2008	36	1.01	4	0.18	32	2.36	< 0.01	25	1.70	11	0.53	0.0006
2009	34	0.97	3	0.14	31	2.27	< 0.01	20	1.37	14	0.69	0.0443
2010	26	0.74	5	0.24	21	1.51	< 0.01	13	0.88	13	0.64	0.4181
2011	23	0.65	1	0.05	22	1.56	< 0.01	18	1.20	5	0.24	0.0005
2012	32	0.89	3	0.14	29	2.01	< 0.01	18	1.17	14	0.68	0.1189
2013	56	1.53	4	0.18	52	3.54	< 0.01	36	2.27	20	0.96	0.0015
2014	57	1.48	7	0.31	50	3.23	< 0.01	43	2.61	14	0.64	< 0.0001
7-year	-	1.04	–	0.18	–	2.36	–	–	1.60	–	0.63	–

*Incidence rates are per 100,000 patients

†*p* value based on Chi-square tests

Table 3 Multivariable logistic regression to model predictors of spontaneous recovery in IVFP/IVFp patients, adjusted odds ratios (OR), 95% confidence intervals (CI)

	OR	95% CI
Demographic characteristics		
Age (reference ≤ 45 years)		
> 45	0.65	(0.27, 1.57)
Sex (reference = female)		
Male	0.84	(0.47, 1.51)
Race/ethnicity (reference = white)		
Asian	1.08	(0.41, 2.88)
Black	0.91	(0.28, 3.05)
Hispanic	1.35	(0.59, 3.10)
Other	1.21	(0.27, 5.37)
Clinical characteristics		
Paralysis/paresis (reference = paresis)		
Paralysis	0.74	(0.40, 1.39)
Speech therapy (reference = untreated)		
Treated	0.90	(0.47, 1.73)
Steroid treatment (reference = untreated)		
Treated	2.62	(0.85, 8.13)
Months between symptoms and specialist visit (per month)	0.93	(0.86, 1.01)

sudden sensorineural hearing loss [9], it is not surprising that some clinicians decide to use steroids. Unlike Bell's palsy or sudden sensorineural hearing loss, where the nerve palsy produces readily recognizable deficits to the patient and clinician, the dysphonia resulting from IVFP/IVFp often presents itself insidiously, resulting in a significant delay in diagnosis [9]. This delay can then render the use of steroids ineffective as the period of inflammation has passed. Further research in this area may shed light on the role of steroid treatment.

Patients are often advised to wait 1 year after the onset of IVFP/IVFp before considering laryngeal framework surgery to improve the voice. This recommendation is not grounded in clinical studies but rather expert opinion [9, 16] based on the understanding that axonal regrowth of an injured recurrent laryngeal nerve occurs slowly over 6–12 months [17]. The data presented here support this long-held view. Of the patients who had recovery of vocal function, 75% did so within 12 months, and the median length of time was 4 months. Husain et al.'s recent study also supports this position, where 77% of the patients who recovered did so within 9 months [15].

There are several limitations to this study. Given that the patient data for this study came from a health-care system that includes a health maintenance organization, certain populations may be underrepresented. Retrospective studies are inherently vulnerable to selection and information biases, and in our study this resulted in an unknown vocal

status of 40.9% of the cohort. Lastly, the determination of spontaneous recovery was based on chart documentation of either laryngoscopic findings or voice improvement, rather than the authors' assessment of recordings of laryngoscopy or videostroboscopy.

Conclusions

The mean annual 7-year incidence of IVFP/IVFp is 1.04 per 100,000 persons, with a higher incidence in those over age 45 (2.36 new cases per 100,000 patients) and in whites (1.60 new cases per 100,000 patients). The rate of spontaneous recovery was 29.5%, with the majority of these obtaining recovery within 12 months. The rate of recovery did not vary between patients with IVFp versus IVFP or according to steroid treatment.

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