Time Course of Recovery of Iatrogenic Vocal Fold Paralysis

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INTRODUCTION

Iatrogenic vocal fold paralysis (VFP) may follow a number of procedures in the central nervous system, neck, and chest, during which the vagus and recurrent laryngeal nerves are at risk for surgical injury. The pathophysiology of such injury encompasses the entire spectrum of neural disruption from stretch and compression to complete transaction. It is often not possible to know the precise mechanism of injury because the injury may not be recognized intraoperatively. Symptoms may be evident immediately after the surgery, or be temporarily masked by laryngeal edema from intubation, or simply go unnoticed for a time amid other immediate postoperative concerns.

Management is symptomatic. Patients may elect to await spontaneous recovery without treatment or to undergo injection augmentation for temporary relief of dysphonia and dysphagia. If recovery does not occur, or if the nerve is known to be transected, framework surgery may be pursued. In each case, the potential for recovery is of paramount clinical importance in guiding selection and timing of interventions.

A prior study described the time course of recovery in patients with idiopathic VFP. In this study, we aim 1) to describe the time course of recovery of voice as well as vocal fold movement in patients with iatrogenic VFP, 2) to evaluate the effect of side and site of injury, and 3) to use this information to generate treatment recommendations. We also seek to compare recovery of voice and movement in iatrogenic and idiopathic VFP, which may differ as a result of differences in pathophysiology.

MATERIALS AND METHODS

This study was approved by the institutional review board. Adult patients diagnosed with iatrogenic VFP between January 1, 2006, and May 12, 2016, were identified from the senior author’s (L.S.) database. The diagnosis was verified by review of videostroboscopic examination at the time of presentation. Patients were excluded if they presented more than 12 months from diagnosis, if they had bilateral disease, or if they underwent framework surgery prior to presentation or less than 1 year from onset. From the remainder, patients without follow-up to at least 1 year from onset or to resolution of symptoms were excluded for inadequate follow-up. Medical records were reviewed to identify demographic information including gender; age; date of onset of symptoms; date of presentation to clinic; date and type of treatment, if any; and date of recovery. The relevant dates are collected as a matter of routine at the time of the patient visit, and...
patients are asked to be as precise as possible. For purposes of this article, certain assumptions were made in case of approximate reporting. When recovery was reported in terms of weeks, for example, “2 weeks ago,” recovery was assumed to have occurred exactly 14 days ago. Similarly, “beginning of the month” was recorded as the first day of the month; “middle” was recorded as the 15th; and “end” was recorded as the last day of the month. Recovery was based on patient report of voice quality and does not refer to recovery of vocal fold motion, for which a separate determination was carried out.

Vocal fold movement was assessed from review of recorded stroboscopic examinations by two fellowship-trained laryngologists blinded to patient identity, examination audio, exam sequence (i.e. presentation or recovery examinations), and chart information. For each examination, vocal fold motion was graded in relation to the normal side on a 4-point scale. A score of 0 indicated 0% to 5% movement of the affected vocal fold compared to the unaffected side; a score of 1 indicated 5% to 50%; a score of 2 indicated 50% to 95% movement; and a score of 3 indicated 95% to 100% movement of the affected vocal fold compared to the normal vocal fold. The scores at presentation were compared to the scores at the recovery visit; patients who had an increase in score of 2 or greater were determined to have return of motion.

When raters’ assessments conflicted, both graders reviewed examinations together and made a consensus determination.

Patients whose vocal function recovered were compared to those who did not recover by age, gender, laterality of disease, time to presentation from onset of the disease, time to recovery, and site of injury. Patients in whom vocal fold motion returned were compared to those in whom it did not return by age, gender, laterality of disease, and time to recovery of vocal function. Age, time to presentation, and time to recovery of vocal function were compared using a Mann-Whitney test for independent samples. Gender and laterality of disease were compared using chi-squared analysis. Sites of injury were compared using analysis of variance (ANOVA) analysis.

The iatrogenic VFP and idiopathic VFP populations were compared by time to recovery. Mean time to recovery of iatrogenic and idiopathic VFP were compared using a Mann-Whitney Test for independent samples. A 20-bin histogram of iatrogenic and idiopathic VFP was created using Stata 14.2 (StataCorp LP, College Station, TX).

RESULTS

Two hundred and ninety-three patients with iatrogenic VFP were identified. After exclusion criteria were applied (Fig. 1), 114 patients remained in this study. Of these 114 patients, 102 (89.5%) recovered vocal function. Demographic and clinical characteristics of recovery and nonrecovery groups were compared in Table I; no significant difference was found. Precise determination of time of recovery could only be made in 39 patients who recovered but did not undergo injection augmentation (Fig. 2), which masks recovery until injectable material resorbs. The time course of recovery is shown in Figure 3. Left-sided iatrogenic VFP recovered in 166.4 ± 106.7 days, whereas right-sided iatrogenic VFP recovered in 221.8 ± 115.6 days (P value = 0.095).

Patients were stratified anatomically based on site of the surgical intervention resulting in VFP. Four patients had surgery at the skull base; four patients had carotid endarterectomy (considered separately from patients with neck surgery as it is a more proximal injury); five patients had thoracic surgery; and 22 patients had surgery in the neck (hemi- or complete thyroidectomy, parathyroidectomy, neck dissection). In four patients, VFP followed intubation. Mean time to recovery was determined, and ANOVA analysis demonstrated no difference in time to recovery between any of the sites of injury (P value = 0.60).

Twelve out of 39 patients (30.8%) who recovered vocal function were determined to have return of vocal

| TABLE I. Comparison of Iatrogenic VFP Patients Who Recovered Voice to Those Who Did not. |
|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|---------------------------------------------------|
| | Total Recovered | Total Not Recovered | |
| | n = 102; 89.5% | n = 12; 10.5% | |
| Age | 58.0 ± 14.7 years | 59.1 ± 8.6 years | P value = 0.75 |
| Gender | Male: 40 (39.2%) Female: 62 (60.8%) | Male: 5 (41.7%) Female: 7 (58.3%) | P value = 0.169 |
| Laterality of paralysis | Right: 29 (28.4%) Left: 73 (71.6%) | Right: 4 (33.3%) Left: 8 (66.7%) | P value = 0.983 |
| Time to presentation | 69.4 ± 65.1 days | 82.6 ± 77.9 days | P value = 0.584 |
| Injection augmentation | 63 patients (61.8%) | 3 patients (25.0%) | P value = 0.112 |

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fold movement. Figure 3 shows the distribution of these patients, marked by arrows, among all who recovered. Table II compares characteristics of this group to the 27 patients who recovered vocal function without return of vocal fold motion; the two groups were not significantly different, except that recovery of motion favored females.

For each month after onset of disease, the percent of patients who eventually recovered vocal function was calculated (Fig. 4). For example, of patients presenting at 1 month after onset of disease, 81% eventually recovered. Of patients who presented at 6 months with still-unresolved disease, 65% eventually recovered. At 11 months, less than 35% of patients presenting with unresolved disease eventually recovered.

Comparison of mean time to recovery between iatrogenic VFP and idiopathic VFP demonstrated no significant difference (idiopathic: 152.7 ± 109.3 days; iatrogenic: 181.8 ± 109.3 days; \( P \) value = 0.32).

**DISCUSSION**

Probabilities of recovery of VFP are commonly expressed as an aggregate rate for all similar patients—for example, for all patients who have had VFP after thyroidectomy—followed for a certain period of time, without further details. Such probabilities are often disparate, even when they concern similar groups of patients, because definitions of recovery vary from study to study.\(^4\) Surprisingly often, formal definitions are entirely absent from relevant studies. The potential for recovery is generally considered to be exhausted in about 1 year, a time interval apparently based on expert consensus rather than any physiologic basis or principle.\(^5\)

Clinical observation reveals recoveries in a population with laryngeal nerve injury to occur sporadically over many months. Factors determining the duration of a case of VFP are not defined but probably include severity and site of injury. Wallerian degeneration describes the mechanism of regeneration and reinnervation in peripheral nerve discontinuity injuries.\(^6\) This process includes the demyelination and degradation of the axon distal to the site of injury, and then subsequent regrowth of axon from the proximal stump. The rate of regrowth from the proximal stump is approximately 1 mm/day; reinnervation of the nerve is dependent on the distance from the neuronal injury from its target muscle.\(^7\) We hypothesized that patients whose surgical intervention occurred more proximally along the course of the recurrent laryngeal nerve (assuming that injury occurred at the site of the surgical intervention) would take longer to recover compared to those with more distal surgeries. However, in our cohort there was no significant difference in time to recovery based on surgical site. Along similar principles, we also hypothesized that patients with injuries of the longer left recurrent nerve might take longer to recover than those with right-sided injuries; again, this proved not to be the case. This is consistent with Paniello et al.’s work in the animal model suggesting that the 1 mm/day rate of nerve regeneration is not significantly different.
regrowth may not apply to the recurrent laryngeal nerve. The principal confounder in this population was most likely variation in the severity of injury.

Functional recovery may occur without the return of vocal fold motion, the consequence of improved glottic competence from return of muscle bulk and tone from reinnervation which is not specific or sufficient enough to restore physiologic motion. In studies that distinguish recovery of motion from recovery without return of motion, the percentage of patients who recover motion ranges from 23% to 75%. The wide range is explained by inconsistent definitions of return of motion. We hypothesized that iatrogenic VFP patients with recovered vocal fold motion represented a milder neuropraxic injury and would recover faster than those with more dysfunctional reinnervation. In our study, only 30% of patients recovered motion. Of those, nine patients recovered within the first 6 months; however, the overall time to recovery was not different from that of patients who did not recover motion. A larger sample size may be more revealing.

Iatrogenic VFP differs from idiopathic VFP in that its pathophysiology encompasses a greater variety of peripheral nerve injury. The Seddon classification categorizes such injury into three groups: Neuropraxia, the mildest form, refers to injury of nerve conduction without disruption of the axon or perineurium. Axonotmesis refers to a loss of continuity of the nerve without rupture of the connective nervous tissue, the endoneurium, perineurium, or epineurium, most commonly seen in crush injuries. The most severe form of peripheral nerve injury is neurotmesis, or complete transaction of the nerve and its connective tissue. The severity of injury corresponds with the rate of recovery: neuropraxia recovers in days to weeks, whereas neurotmesis recovers in months to years, if at all. The variation in nerve injury in iatrogenic VFP may by itself undermine expectations regarding recovery time based on nerve length or site of injury.

In idiopathic VFP, the nerve is necessarily in continuity. A previous study yielded a curve illustrating the recovery of idiopathic VFP over time. A similar curve of iatrogenic VFP recovery was derived from the date in the current study and compared to the idiopathic VFP recovery curve (Fig. 5). Statistical analysis revealed no significant difference in mean time to recovery. However, visual inspection reveals that recovery of iatrogenic VFP was more evenly distributed over the time of study than idiopathic VFP. Idiopathic cases, in contrast, appear to recover briskly over the first 5 months, followed by a decreased incidence of recovery. These differences may reflect the greater heterogeneity in injury severity among patients with iatrogenic VFP, including a more time-dependent process such as regrowth of the axon.

Mau et al. have proposed a time to recovery model created with the assumption that recovery in VFP occurs
via two distinct recovery mechanisms (“early” and “late”) derived from the Seddon classification. The resulting bimodal distribution of recovery fits the VFP population of combined iatrogenic and idiopathic etiology in their study. The first peak represents neuropraxic injury, which recovers quickly due to the preserved nerve axon. The second, later peak represents patients with axonotmesis and neurotmesis, which have a lower probability of recovery and a longer time course due to required regrowth of the axon. In this model, severity is the principal determinant of recovery time as opposed to site of injury. Combining our idiopathic VFP and iatrogenic VFP populations yields a histogram of recovery that is not inconsistent with Mau et al.’s hypothesis regarding recovery (Fig. 6).

Although robust for a study on iatrogenic VFP, this study remains limited by the number of patients, which limits the resolution of differences in variables such as laterality and site of surgical intervention. In the latter instance in particular, the small number of patients with extracervical surgery presents a significant challenge. Ironically, the availability of ready symptomatic treatment in the form of office injection augmentation negatively affects such a study because injection augmentation serves to reduce the number of patients in which accurate observations about time to recovery can be made. In our population, 66 patients (58%) who otherwise met inclusion criteria underwent such treatment. The aggregate recovery rate of patients in this study (89%) is somewhat higher than usually reported. We believe that some patients with known nerve transection are offered prompt framework surgery, thereby eliminating a large number of patients (73 of 293, 25%) (Fig. 1) who do not recover from the study population. Although the total recovery rate thus may not be generalizable to other populations of iatrogenic VFP due to selection bias, this does not alter data regarding time to recovery.

Based on the results of this study, we now incorporate the data in Figure 4 in our discussions with patients. Because aggregate recovery rates do not account for the “age”—or time from onset—of the vocal fold paralysis; they consistently overstate probability of recovery and are thus less precise guides to treatment selection. In contrast to patients with idiopathic VFP, these data have not led us to recommend framework surgery to patients with iatrogenic VFP earlier than we have in the past because the recovery appears to occur more evenly over time, with significant potential for recovery retained later in the course of the condition.

CONCLUSION

Analysis of recovery in a population of patients with untreated iatrogenic VFP reveals the possibility of recovery to extend to slightly more than 1 year. Thirty-one percent of those with recovery of vocal function had return of vocal fold motion; the rest did not. Examination of patients by site of surgical intervention and by laterality of paralysis yielded no difference in the overall rate of recovery. The mean time to recovery of iatrogenic VFP did not differ significantly from that in idiopathic VFP in this population. The shape of the curve of recovery, however, suggests that idiopathic VFP recovery is more robust over the first 6 months than iatrogenic VFP, but iatrogenic VFP is more constantly sustained. Because it accounts for the effect of time from onset, data from our study may be a better guide to clinical decision making than aggregate recovery rates commonly found in the literature.

BIBLIOGRAPHY