Decision Making in Vocal Fold Paralysis

A Guide to Clinical Management

Milan R. Amin
Michael M. Johns
Editors

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To Kathy, Michael, William, and Catrina for their unconditional support.

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To Prina, Aashtha, and Aarav for providing balance to my work and to my parents, Ramesh and Kalpana, for their support through many years of school and training.

Milan R. Amin

Preface

Thank you for your interest in our book entitled *Decision Making in Vocal Fold Paralysis: A Guide to Clinical Management*. The intricate nature of laryngeal innervation, response to neural injury in the larynx, and variable presentation of symptoms set a landscape for a complex and nuanced decision-making process for the physician caring for patients with vocal fold paralysis. This text brings thought leaders and master clinicians together to share their wisdom and expertise regarding clinical decisions surrounding unilateral and bilateral vocal fold paralysis. Designed as a "what to do and why" as opposed to a "how to do" guide, the authors detail the reasoning process from work-up, through intervention, to posttreatment decision-making. We would like to thank the outstanding contributors to this effort, which we believe fills a unique gap in the medical literature, and we would like to thank you, the reader. We hope that you find this to be a valuable resource to you.

New York, NY, USA — Milan R. Amin
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Part I
Unilateral Vocal Fold Paralysis

Chapter 1
Diagnostic Studies in Workup for Vocal Fold Paralysis: When and Why

Shaum S. Sridharan and Clark A. Rosen

Introduction

Clinical evaluation of a patient with vocal fold immobility may often require further diagnostic testing to determine causation. In many cases, thorough history-taking and physical examination will determine the cause of vocal fold immobility. However, when a clear etiology does not exist, it is the responsibility of the physician to consider further testing.

Generally, absent vocal fold motion should be broadly categorized as vocal fold immobility. Vocal fold immobility can further be defined as (1) vocal fold paralysis, (2) cricoarytenoid joint mechanical impairment, and (3) vocal fold immobility due to cancer invasion. Investigating the cause of vocal fold immobility can improve overall patient care and treatment outcomes. This is especially true in cases of undiagnosed tumor burden in the neck or chest resulting in neurologic insult to the vagus (VN) or recurrent laryngeal nerve (RLN). Moreover, vocal fold immobility may be a result of undiagnosed neurologic or rheumatologic disease which would require appropriate multidisciplinary care of the patient. Only after a thorough negative workup has been completed should a patient be given the diagnosis of idiopathic vocal fold paralysis.

This chapter will discuss various tests which should be considered in patients presenting with vocal fold immobility as confirmed by direct or indirect laryngeal examination. These tests include computed tomography (CT) scan, magnetic resonance imaging (MRI), ultrasound (US), X-ray, laryngeal electromyography (LEMG), serologic studies, and in-office cricoarytenoid joint palpation.

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History and Physical Examination

Performing a history and physical exam for a new unilateral vocal fold paralysis (UVFP) patient is a vital component in the decision-making process for these patients. It is easy to say "take a complete history and perform a thorough physical exam" in patients with a new UVFP, but this is not realistic in a busy practice that requires efficiency. Thus the chapter will highlight essential components of history evaluation and physical exam methods that are driven based on possible etiologic entities of UVFP. Understanding the plethora of etiologic causes of UVFP can make the history and physical exam evaluation for UVFP streamlined and effective.

History for a Patient with Unilateral Vocal Fold Paralysis

When taking a history of UVFP patients, the *timing and onset of the symptoms* drive much of the further evaluation and treatment decision-making. The timing part is typically related when the patient first noticed sustained symptoms with their voice, cough, swallowing, and sometimes breathing (dyspnea with phonation). Documentation of the time period from onset of symptoms to present evaluation time point drives a variety of next steps in the evaluation and treatment process.

In addition to the duration of symptoms, associated medical care or bigger "picture" aspects are important to assess. Did the patient have *surgery*? Did the patient suffer from any *external trauma* to the neck or chest or have an *upper respiratory infection* (URI) at the onset of symptoms? Regarding the latter, when asked, patients frequent report that they thought they had a "cold" or "laryngitis," but this is only because they noticed a change in their voice. It is important to ask a follow-up question if they report a suspected URI and if they have any symptoms of an URI in addition to voice change. Common causes of external trauma that may result in UVFP (or more precisely an immobile vocal fold) include a fall with neck trauma, motor vehicle accident with trauma to the neck from the seatbelt or steering wheel, or strangulation. These etiologies tend to cause an injury to the cricoarytenoid joint resulting in an immobile vocal fold. Similarly it is important to ask about any history of "prolonged" intubation for anytime of medical illness (surgery, coma, trauma, etc.). Another historical inquiry should be a history of external beam radiation therapy; again this can cause a loss of vocal fold motion due to changes in the soft tissue of the posterior glottis and can occur many months/years following treatment.

Surgery is one of the most common causes of UVFP, and in many situations, the "search" for the etiology of the UVFP is quite obvious given the patient reports change in laryngeal function related to the surgery and/or an incision is found in the

head/neck/chest area during physical exam. The challenge comes when obvious "clue(s)" is not present. Given the prevalence of surgery involving the head, neck, or chest causing UVFP, it is imperative to inquire with every UVFP patient about past surgical history of the head/neck/chest and upon physical examination look and ask for explanation for every surgical scar found in the head/neck/chest region. It is not uncommon that a middle-aged UVFP patient may forget to disclose a head/neck/chest surgery that was done many years earlier. Common surgeries to ask regarding the patient are the following:

- Carotid surgery
- Thyroid and parathyroid surgery
- Anterior approach to spine surgery
- Mediastinal surgery
- Esophageal surgery
- Brain and skull base surgery
- Heart and lung surgery
- Cervical rhizotomy

Medical Conditions that Can Cause UVFP

One of the more common of the rare medical conditions causing a UVFP is an enlarged left atrium, Ortner's syndrome. There are a variety of cardiac/great vessel diseases that can result in significant enlargement of the left atrium causing a left vocal fold paralysis due to stretch and/or compression (cardiovocal syndrome). Malignant disease or metastatic disease involving the left upper lung or mediastinum can cause UVFP, and thus when an etiology is not apparent, imaging of the chest should be considered. Rarely a medical condition will cause UVFP, but it is important to ask historical questions regarding the below medical conditions when no other etiologic agent can be found for UVFP:

- Cardiac condition causing enlarged left atrium (Ortner's syndrome)
- Malignant disease of the left upper lung and/or mediastinum
- Diabetes mellitus
- Hypokalemia
- Lyme disease
- Rheumatologic disease (negative impact on the cricoarytenoid joint)
- Cerebral vascular accident (most notably a Wallenberg stroke)
- History of neurotoxic chemotherapy (vinca alkaloids, etc.)
- Neurologic conditions (Parkinson's disease, ALS, Arnold-Chiari syndrome, Guillain-Barre syndrome, Lambert-Eaton syndrome, Shy-Drager syndrome, progressive bulbar palsy, myasthenia gravis, multiple sclerosis, and post-polio syndrome)

Idiopathic Unilateral Vocal Fold Paralysis

Idiopathic UVFP is a common diagnosis made when evaluating a patient with a unilateral immobile vocal fold. It is a diagnosis of exclusion, and thus a careful history (see above) and detailed physical exam (see below) are required to make the diagnosis of idiopathic UVFP. Most often this diagnosis can be made with history and physical exam, but in select clinical situations, some radiologic imaging is also required (see below). When the history and physical evaluation identifies a reasonable etiology for the UVFP and the timeline of the etiology and patient's symptoms match, then further evaluation is typically required.

Physical Examination for Unilateral Vocal Fold Paralysis

The physical examination of a patient with new onset, unknown etiology of UVFP should include a complete head and neck examination with special emphasis related to (1) cranial nerve evaluation, (2) cervical lymphadenopathy, (3) thyroid disease, and (4) laryngeal assessment. Given that UVFP involves an abnormality of the vagus nerve (recurrent and possible superior laryngeal nerve(s)), looking for other possible cranial nerve abnormalities is essential (such as palate and tongue function). This is especially true for the lower cranial nerve functions of 9, 11, and 12. Findings in these nerves suggest an etiology at the level of skull base and will invoke further investigations in these areas. A careful examination of cervical neck masses/lymph nodes will assist with the identification of head and neck cancer as a cause for UVFP or distant malignant disease that has spread to Virchow's node (left supraclavicular node). Given the proximity of the recurrent laryngeal nerves to the thyroid gland, a careful thyroid exam is important. This exam should involve assessment of size and presence of fixation.

Laryngeal Examination of the Unilateral Vocal Fold Paralysis

As mentioned earlier, UVFP by definition involves an immobile vocal fold to all volitional tasks (respiration, cough, and phonation). The next level assessment should involve the (1) characteristics of the contralateral vocal fold, (2) location and features of the immobile vocal fold, (3) closure pattern of the vocal folds, and (4) nature of the hypopharynx. The first assessment of the larynx should involve the mucosal surfaces to identify potential malignant processes. The contralateral vocal fold assessment is often forgotten due to the focus applied to the unilateral immobile vocal fold but can have a major impact on clinical treatment options including managing the airway with surgery and the patient's ability to tolerate temporary vocal fold edema from surgery or inflammatory conditions. It is wise to assess and

document the range of motion and speed of motion of the contralateral vocal fold. The most important aspects to describe the immobile vocal fold include (1) position, (2) length, and (3) tone. All of these assessments are subjective and based on an assessor's internal evaluation system. The position of the vocal fold is classically described as being (1) midline/median, (2) paramedian, and (3) lateral/cadaveric. These are reasonable descriptors, but they are not objective nor has inter-rater reliability been determined. In a similar manner, the "length" of the immobile vocal fold is helpful to document if the vocal fold is "shortened" presumably due to an anteriorly displaced/canted arytenoid that is teleologically present due to the UVFP causing a loss of innervation to the vertical belly of the posterior cricoarytenoid muscle. The clinical impacts of this finding are (1) there is a great likelihood of vocal fold level mismatch and (2) the need for an arytenoid repositioning surgery (i.e., arytenoid adduction). The tone of the unilateral vocal fold is a very subjective assessment and typically comes from assessing the vocal fold during quiet respiration, active respiration, and during stroboscopy (if possible). The clinical impact of this assessment involves the degree of improvement with static medialization and the role of vocal fold atrophy as a comorbid condition. The literature is replete with studies showing that many aging vocal fold surgeries are not successful and that this may be due to poor vocal fold "tone." This similar problem with tone may negatively impact the degree of improvement with surgical repositioning of the immobile vocal fold of the UVFP. This assessment may play a role in counselling the UVFP patient regarding surgical outcomes. Lastly it is wise to assess the presence or absence of retained secretions/food material in the pyriform sinuses. This assessment coupled with a "gestalt" of laryngeal sensory function can alter management of UVFP-related dysphagia and subsequent decision-making for this vital patient complaint.

Imaging Studies for Unilateral Vocal Fold Paralysis

Imaging studies to determine the etiology of vocal fold paralysis is often employed when head and neck examination, laryngeal visualization, and clinical history do not reveal a clear etiology. Paradigms for ordering imaging studies in the treatment of vocal fold paralysis are widely varied as demonstrated by a survey of members of the American Broncho-Esophagological Association [1]. Treating physicians should keep in mind the course of the recurrent laryngeal nerve when considering imaging studies. Right-sided vocal fold paralysis would warrant studies which would rule out lesions affecting the vagus nerve or recurrent laryngeal nerve (RLN) from the skull base down to the thoracic inlet. Left-sided vocal fold paralysis requires consideration of lesion from the skull base down to the aortic triangle due to the course of the left RLN.

Computed tomography (CT) is the most common imaging modality utilized to determine the etiology of vocal fold paralysis [1]. CT neck with contrast should be ordered with detailed history and laterality of vocal fold immobility provided to the

radiologist to ensure the proper exam is performed. In left-sided VFP, CT scan should encompass the course of the vagus/RLN from the base of skull down to the mid-chest or aortic triangle. This approach has the advantage of subjecting the patient to a single exam rather than CT of the neck and chest. In this chapter, laterality-based CT scan (skull base down to appropriate level) as described above will be referred to as a *modified CT neck*. The rate of detecting lesions on CT neck/chest varies widely from 6% to 47% [2–5]. Kang et al. [5] showed that etiology was discovered on CT scan in 23.5% of the time in a 153 patients, while Chin et al. [4] reviewed 40 patients and found the lesion 15% of the time. Alternatively, Chen et al. [3] reviewed over 400 patients with idiopathic vocal fold paralysis and demonstrated that CT neck and chest did not show a lesion responsible for vocal fold paralysis in 94% of patients. Recently, a cost-effectiveness study was conducted comparing screening CT scan vs physical exam alone [6]. When the detection rate for CT neck was set at 15%, CT was more cost-effective than clinical exam alone with 99.5% certainty.

Some clinicians have advocated for alternative paradigms for the workup of vocal fold paralysis. Chest X-ray alone may be used as a screening test, but, if negative, patients would likely undergo CT neck and chest. This is due to higher sensitivity of CT to identify lesions as compared to X-ray. A large series by Benninger and colleagues showed chest X-ray to be very effective as a screening tool [7]. In 47 patients, chest X-ray not only identified all patients with chest lesions (28), but these findings were confirmed on further workup. Moreover, all patients with negative chest X-ray were not found to have undetected lesions on chest CT. This author argues for chest X-ray alone for screening with follow-up modified CT neck in cases of negative chest X-ray. Others have argued against X-ray alone due to their higher published rates of false negative. A retrospective series, published by Glazer et al., noted that lesions were missed often in the aortopulmonary window [8]. In their series, 13 of 18 patients with mediastinal disease on CT chest had negative chest X-ray. Song et al. reviewed 19 patients with thoracic disease-related vocal fold paralysis showing that 8 of 19 showed no lesions on chest X-ray [9]. Upfront modified CT neck may be advantageous over X-ray alone given increased sensitivity of CT scans and potential to limit the number of tests for the patient.

Ultrasound (US) of the neck has also been suggested for screening exam often in combination with chest X-ray. US of the neck is highly sensitive and offers the advantage of immediate US-guided fine needle aspiration (FNA) of concerning lesions. It should be noted that skull base lesions would not be adequately evaluated using US neck alone. CT scans may be considered in patient with negative US neck and chest X-ray. Bilici et al. reviewed a series of 202 patients and recommended diagnostic chest CT with US of the neck as initial imaging modalities [2]. Ultrasound of the neck was recommended over CT neck due to exposure to radiation and high incidence of thyroid malignancy in their patient population. It should be noted that in this review, diagnostic yield for CT chest was 30.9%, while yield for CT neck and US neck were 24.5% and 26.2%. Of course, if modified CT neck were available, diagnostic yield would certainly be improved over any one modality alone.

Though initial screening tests may have shown no lesions, clinicians may consider surveillance studies of patients with idiopathic vocal fold paralysis. Several

studies have not shown a benefit to repeat imaging with the majority of patients retaining the diagnosis of idiopathic vocal fold paralysis [10, 11]. Willatt et al. had extended follow-up for 34 patients for idiopathic vocal fold paralysis who had neither concerning findings on head and neck exam nor imaging modalities [11]. In this cohort, four patients were eventually found to have a carcinoma responsible for their vocal fold paralysis either on clinical exam or repeat imaging study. The author advocates for continued follow-up for patients labeled as having idiopathic vocal fold paralysis with consideration of repeat imaging studies.

Damrose and colleagues reviewed 29 patients with idiopathic vocal fold paralysis and repeat imaging showing that 8 of these patients developed a new lesion which could explain vocal fold paralysis [12]. In the same review, 90% of patients maintained a diagnosis of idiopathic vocal fold paralysis, though repeat imaging was not performed in the majority of these patients.

Most imaging study paradigms are based on retrospective series making their level of evidence level IV. The only consensus among most clinicians seems to be that imaging of some type is needed in cases of new onset idiopathic vocal fold paralysis.

Specialized Evaluations for Assessment of Unilateral Vocal Fold Paralysis

Palpation of CA Joint: In Office vs in OR

Palpation of the vocal process to assess the mobility of the arytenoid can be a useful adjunct when a clinician is attempting to differentiate between vocal fold paralysis and CA joint fixation. This method may serve as a substitute for laryngeal electromyography (LEMG) to rule out CA joint fixation, especially when LEMG is not available. It should be noted that LEMG also provides prognostic information regarding the degree of nerve injury. CA joint palpation may not be required if there is a clear etiology of vocal fold immobility.

In-office palpation of the CA joint is usually performed trans-orally with concurrent flexible laryngoscopy. The patient is first prepared for the procedure by placing nasal packing with topical anesthetic and a nasal decongestant. The patient is then given a nebulized lidocaine treatment, and, subsequently, a catheter is introduced via the laryngoscope working channel to topically anesthetize the base of the tongue and larynx with topical lidocaine. A curved instrument such as an Abraham cannula is then used trans-orally to palpate the CA joint during trans-nasal flexible laryngoscopy.

With the instrument between the vocal folds, the arytenoid can be manually abducted in cases of vocal fold paralysis. In contrast, in CA joint fixation, the arytenoid will have little to no movement with instrumentation. This finding may also be seen in conjunction with scar tissue in the posterior glottis (posterior glottis stenosis with involvement of the cricoarytenoid joint(s)).

Laryngeal Electromyography for Unilateral Vocal Fold Paralysis

Laryngeal electromyography has the two main objectives for the evaluation and care of UVFP patients, diagnostic and prognostic. The former is rarely a situation after a thorough history and physical exam (see above). The diagnostic utility of LEMG is of valve in the uncommon situation that a patient with a recent onset unilateral immobile vocal fold that a suspected etiology can be of neurogenic or a mechanical (injury to the CA joint) etiology. Rarely a patient will present with a recent onset vocal fold immobility following general anesthesia involving orotracheal intubation and no surgery that put the vagus/recurrent laryngeal nerve at risk, and thus the differential diagnosis is neurogenic etiology due to endotracheal cuff compression of the RLN versus injury to the CA joint associated with the intubation/tube placement. If the clinical care or prognostic outcome will be changed knowing the exact etiology (neurogenic versus CA joint abnormality), then an LEMG can be useful.

LEMG of UVFP for prognostic purposes is more commonly the reason to consider LEMG. Much of this indication is based on the duration of onset. In cases of "early" UVFP (1–3 months since onset) and "late" UVFP (8 months or more), there is limited value to LEMG. Patients being evaluated and willing to "act" on the outcome of the LEMG results can benefit significantly from a properly performed LEMG. The latter generally involves a team approach to performing LEMG using an experienced laryngeal surgeon and a board-certified electrodiagnostic physician. Ingle et al. performed a prospective study on the clinical impact of LEMG and found that the diagnosis was altered in 10% of the cohort, and the clinical plan was altered in 36% of the patients [13]. As important as these findings, the study also reported that the period of "clinical observation prior to permanent treatment" was shorted in 36% of the patients by an average of 2.5 months. Regarding prognostic accuracy LEMG has significantly improved its ability to predict recovery of motion or lack thereof. Smith et al. reported a positive predictive value of 100%, negative predictive value of 90%, and an accuracy rate of 91% [14]. This is in stark contrast to LEMG studies of 20 years ago which were in the 50% range. The major difference in prognostic accuracy is the implementation of quantified LEMG and use of synkinesis testing in LEMG [14–16].

Serologic Studies for the Evaluation of Unilateral Vocal Fold Paralysis

Historically there has been much debate about the utility of serological testing in the evaluation of the new onset UVFP patient. Common lab tests included in this debate include rheumatoid factor, Lyme titer, erythrocyte sedimentation rate, antinuclear antibody, complete blood count, and serology for syphilis. A survey of the American Broncho-Esophagological Association reported that 65% of the participants

performed serum testing often or occasionally. In this same paper, Merati et al. elegantly dissects the past literature on this type of testing and determines that "the practice of serum testing" for the evaluation of idiopathic vocal paralysis is not supported by any level I or II evidence…there is only anecdotal or case series information to support this practice [1].

Editors' Comments

In cases of unilateral vocal fold paralysis associated with surgical dissection or retraction around the RLN, the etiology is straightforward, and minimal workup is required. Some controversy remains around the need for imaging along the course of the RLN for vocal fold paresis when partial mobility of the vocal fold remains intact. One study suggests that imaging is very low yield and may not be necessary [17]. Another remaining question is the question of need for serial imaging in cases of idiopathic vocal fold paralysis with negative initial imaging studies as highlighted above. While laryngeal EMG can be a useful adjunctive procedure for sorting neurogenic vs mechanical etiologies for vocal fold immobility, detailed and up close flexible laryngoscopy aided by topical laryngeal anesthesia usually reveals signs of trauma/scar around the region of the cricoarytenoid joint in cases of fixation.

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Chapter 2
Timing of Intervention for Unilateral Vocal Fold Paralysis

Ted Mau

Introduction

The question of when to intervene in unilateral vocal fold paralysis (UVFP) is most pertinent if a reasonable potential for spontaneous recovery still exists. If the potential has been exhausted, then the time to intervene is advanced. The potential for recovery at a given time has two determinants: time from the onset of paralysis and prognosis of eventual recovery. Prognosis can be assessed by laryngeal electromyography (LEMG). However, since LEMG is not widely available nor a definitive tool for prognosis, the time from onset of paralysis becomes the chief determinant. It has long been assumed that reasonable potential for recovery exists up to 12 months following the onset of the paralysis. In this chapter, new clinical and research evidence is used to update the traditional 12-month time frame. In addition, the role of early vocal fold injection augmentation in the final functional outcome will be discussed with a thorough and critical review of the evidence. The goal of the chapter is to impart the reader with the necessary tools and knowledge to conduct an informed discussion with the patient with UVFP in shared decision-making on the timing of intervention. This chapter will address the question of *when* to intervene. The question of *what* to do, i.e., which medialization procedure to perform or what other interventions to pursue, is addressed in other chapters of the book.

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Terminology

Recovery

Functional recovery from UVFP most often refers to improvement in voice or return of vocal fold motion. The two are related but not equivalent. Return of vocal fold motion should guarantee improvement of voice. However, the voice can improve without return of active vocal fold motion. This occurs through synkinetic reinnervation that results in a more medial position of the immobile vocal fold and/or improved tone of the thyroarytenoid muscle. Recovery of voice without recovery of motion is more common than recovery of motion [1, 2]. In this chapter, whether functional recovery refers to improvement in voice or return of vocal fold motion will be specified where pertinent, but otherwise recovery is implied to mean vocal recovery.

Prognosis Versus Probability of Recovery

The prognosis for recovery refers to the likelihood of *eventual* recovery determined at the time of presentation. Prognostic information does not tell us *when* recovery will take place. In contrast, probability is time-specific. For a patient with a good LEMG-based prognosis determined at 4 months from symptom onset, the probability of recovery at 6 months is not the same as the probability of recovery at 8 months. This chapter is concerned with the timing of intervention, which is intimately tied to the *residual* probability of recovery at the time of decision-making. This chapter does not address prognosis. If the prognosis is poor to begin with, for example, based on LEMG or known complete recurrent laryngeal nerve (RLN) transection, then the question of when to intervene becomes much less medically relevant and is a matter of convenience.

Functional Status for Voice, Airway Protection, and Respiratory Valving

The functional status of the patient along with the time from the onset of paralysis and prognosis of eventual recovery comprise the triad in decision-making on whether and when to intervene. Three domains of glottal function should be considered: vocal function, airway protection for swallowing, and respiratory valving. These will only be briefly discussed here because they pertain more to the question of *whether* to intervene than *when* to intervene. For most patients with UVFP, vocal function will dominate the decision-making process. For patients with high vocal demand, early injection laryngoplasty with a temporary material can improve quality of life and level of function before making a decision regarding permanent

intervention. Aspiration that could impair pulmonary function in a patient whose UVFP is a large contributor to aspiration (as opposed to generalized dysphagia) is a strong indication for immediate medialization [3]. Finally, shortness of breath due to impaired glottal valving function is another relative indication for medialization. Poor function in any domain will trump other considerations. A timely injection can be carried out regardless of time from onset or prognosis because it can be done quickly and with minimal risk, in the era of in-office vocal fold injections.

Benefits of Early Intervention

The short-term benefits of early intervention in UVFP are well established. Long before in-office injections became commonplace and shifted the paradigm of UVFP care in the acute setting, immediate surgical medialization was deemed appropriate for patients who are aspirating and have low potential for spontaneous recovery [3]. For UVFP caused by thoracic surgery, patients who underwent medialization within 4 days had far lower rates of pneumonia and shorter lengths of stay than those who were medialized 5 days or later [4]. Injection within a week of thoracic surgery also enabled earlier resumption of an oral diet [5]. The benefits of early intervention for UVFP of all causes became apparent once in-office or bedside injections became widely performed. Aside from the expected improvement in short-term voice and swallowing function, early injection laryngoplasty is associated with improvement in long-term emotional and social functioning and mental health [6, 7]. Early injection with a temporary material has also been theorized to actually reduce the need for permanent medialization procedures. This notion, however, merits further scrutiny and will be discussed in detail later in the section "Does Early Injection Improve Eventual Functional Outcome?"

Given the low risk of in-office or bedside injection laryngoplasty and the resulting improvement in laryngeal function, weighed against the reduced function over an uncertain period of observation, there are very few reasons *not* to do early injection:

- Good likelihood of spontaneous recovery within a few weeks
- The need to do the injection under general anesthesia in the operating room due to patient intolerance of office-based injection, with less favorable risk/benefit ratio compared to office-based injection
- Medically unfit for any procedure
- Patient declining the treatment for any reason, including cost

By this point, the value of early injection should be apparent. So why not just inject everyone at the time of presentation? The answer has to do with the likelihood of recovery. If there is a high likelihood of recovery within a time frame that is acceptable to the patient, then the patient may elect to wait. So the likelihood of recovery and the time course of spontaneous recovery become important considerations. Let's start with the traditional "12-month rule."

The 12-Month Rule

It is instructive to conceptually divide UVFP patients into two groups: those who will eventually recover and those who will not. Simplistically, the first group corresponds to those with good prognosis, and the second group corresponds to those with poor prognosis. The trouble is that in the absence of definitive LEMG data or clear knowledge of the state of the involved RLN (e.g., total severance vs. 100% retention of physical integrity), we do not know to which group a particular patient belongs at the time of presentation. So we assume the potential for recovery is present and, in the past, have asked the patient to wait.

How long are patients to wait for possible spontaneous recovery of vocal function? The conventional wisdom and generally accepted consensus has been 12 months. This time frame, in Dr. Lucian Sulica's words, had been "established by convention, hardening into fact by means of repetition over years" [1]. This "12-month rule" has dominated decision-making about timing for permanent intervention, with most surgeons advising against thyroplasty within 12 months. In addition to being somewhat arbitrary, the 12-month rule is flawed because it implies that, from a decision-making standpoint, the potential for recovery remains constant through the 12-month period. In other words, a patient who presents at 7 months is counseled in the same manner as another who presents at 4 months. This traditional view can be expressed by the probability function in Fig. 2.1, where the probability for recovery remains at a constant value then suddenly drops to zero at 12 months. In reality, most surgeons probably have the intuition that the probability drops toward the latter part of the 12 month period, but how quickly the probability declines has been unknown until relatively recently. If the natural history of recoverable UVFP is known, it would replace the boxcar function in Fig. 2.1 with a more

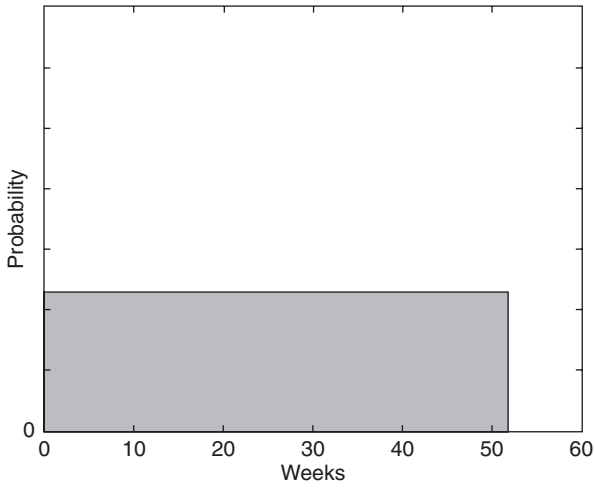

Fig. 2.1 A unit step function denoting the equivalent of the traditional view of probability of recovery, where the probability becomes essentially zero past 12 months

realistic probability function that declines with time. Let us now review the data on the time course of recovery.

The Natural History of Recoverable UVFP

Consideration of the natural time course of recovery is highly relevant to the question of when and whether to intervene. The natural time course provides a likelihood of eventual recovery at the time of decision-making. If a patient is seen early in the time course of possible recovery, the residual probability of recovery remains high (assuming the prognosis is favorable). However, if the patient is seen late in the time course, the residual probability of recovery would be lower. If the prognosis for eventual recovery is good but is unlikely to happen soon, then early injection will improve vocal function for a "worthwhile" period of weeks to months. However, if recovery may happen soon, then the risk/benefit ratio of an intervention may not be favorable enough to justify the cost and hassle of the intervention, however low they may be.

Two converging lines of work in the late 2010s shed light on the time course of recovery. Husain et al. reviewed UVFP patients who presented over a 10-year period and analyzed the time to vocal recovery in patients who presented within 12 months of symptom onset [8, 9]. Their findings are shown in Fig. 2.2. These data are valuable because these authors were among the few to carefully document the date of recovery for each patient. In doing so, they generated data for recovery times with a fine enough temporal resolution (with increments in weeks) to provide fairly precise likelihoods for patient counseling. For example, a patient with iatrogenic UVFP who presents at 3–4 months after symptom onset can be told that the likelihood of vocal recovery is around 70% (Fig. 2.2, solid line), whereas a patient with idiopathic UVFP who presents at 8–9 months has a recovery likelihood of only about 30% (Fig. 2.2, dash line). This type of quantitative prognostic information based on probability is more precise for patient counseling than the binary prognosis of "probably will recover" vs. "probably will not recover."

A second line of work came from Mau et al. [10], who collected similar data in UVFP patients who eventually recovered voice. In addition, the time course of recovery was mathematically modeled to generate a probability function. The modeling was based on four assumptions: (1) patients can be divided into an "early" recovery group, corresponding to those with neurapraxia, and a "late" recovery group, corresponding to axonal disruption; (2) for the late group, RLN reinnervation involves two stages – a first stage in which the regenerating axons have to cross the site of injury and a second stage in which the axons then grow unimpeded to the larynx; (3) the first stage is probabilistic and can be modeled by a decaying exponential; and (4) the second stage is deterministic and can be modeled by a Gaussian. The clinical data on recovery times were then fitted to this mathematical model to

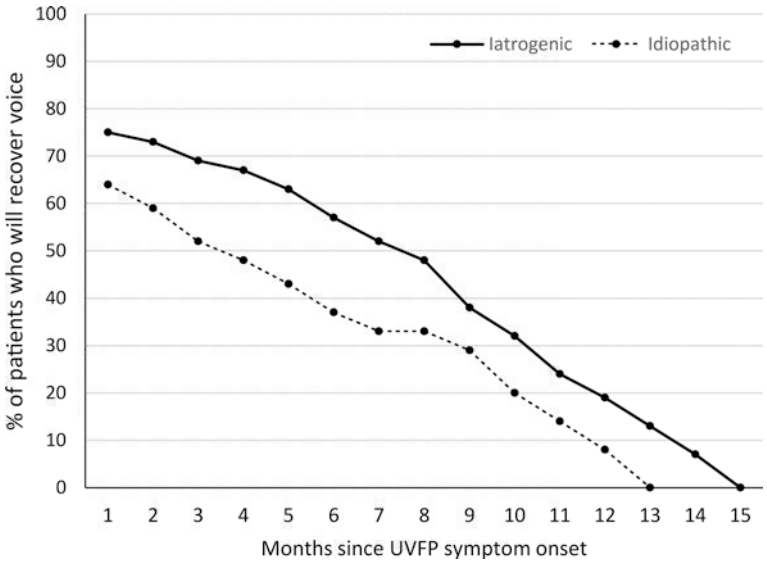

Fig. 2.2 Percentage of patients who will eventually recover voice but have yet to recover, as a percentage of the total number of patients who have yet to recover by that time. For example, at month 4, just under 50% of those still with symptoms of idiopathic UVFP will eventually recover. By month 12, less than 10% of those still with idiopathic UVFP will recover voice. Graph based on data from Hussain et al. [8, 9]. Note that unlike Fig. 2.3, this graph does not represent a probability distribution

generate the probability distribution shown in Fig. 2.3. The graph can be used for patient counseling by providing the cumulative probability for recovery at any point in time. A lookup table is provided in Table 2.1.

There is an important difference between how Figs. 2.2 and 2.3 are used for patient counseling. Figure 2.2 includes patients who will recover voice and also those who will not, whereas Fig. 2.3 is only concerned with those who will recover voice. For example, for a patient who presents at 4 months after symptom onset of idiopathic UVFP, she can be told, based on Fig. 2.2, that her probability of eventual recovery is about 50%. At the same time, according to Fig. 2.3 and Table 2.1, 66% of those who will eventually recover voice would have recovered by 4 months, so her likelihood of recovery is more like 33%. The discrepancy between the information from the two figures can be attributed to two factors. First, data on which Fig. 2.3 was based contained both idiopathic and iatrogenic UVFP, whereas Fig. 2.2 separated the two groups. Second, in all three studies [8–10], the recovery time estimates were based on a relatively small number of patients (fewer than 50 in each study), which corresponded to relatively poor monthly sampling over a 12-month time frame, so the study samples were not large enough to be comparable. Nevertheless, the information provided by Figs. 2.2 and 2.3 finally offers some evidence-based, probabilistic information for the patient and the physician to make