

**BREATHING, SWALLOWING AND VOICE
IN LARYNGEAL DISORDERS**

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Helsinki 2011

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Hanna Tervonen

ACADEMIC DISSERTATION

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ABSTRACT

Breathing, swallowing and voicing are the main laryngeal functions. The aim of this work was to examine how these three are affected in different laryngeal disorders. For this purpose, we examined four different patient groups: patients who had undergone total laryngectomy, anterior cervical decompression (ACD), or injection laryngoplasty with autologous fascia (ILAF), and patients with dyspnea during exercise.

We studied the problems and benefits related to the magnetic speech valve used for the rehabilitation of speech in laryngectomized patients (Provox® FreeHands). The device was given to 14 total laryngectomized patients whose speech production was especially good with the traditional Provox® heat and moisture exchanger (HME). The usefulness of voice and intelligibility of speech were assessed by speech pathologists. The results demonstrated better performance with the traditional HME in both of the dimensions. Most of the patients considered the FreeHands a helpful additional device, especially in social situations such as eating or in situations where both hands are needed for something else. Because of heavier breathing and the greater work needed for speech production, the FreeHands was not suitable as a sole device in speech rehabilitation after total laryngectomy.

Dysphonia and dysphagia are known complications of ACD. These symptoms are caused due to the stretching of tissue needed during the surgery, but their extent and the recovery from them was not well known before our study. We studied two patient groups, an early group with 50 patients who were examined immediately before and after the surgery and a late group of 64 patients who were examined 3–9 months postoperatively. Altogether, 60% reported dysphonia and 69% dysphagia immediately after the operation. Six (12%) patients were diagnosed with unilateral vocal cord paresis in the early group. All six paresis cases recovered during the follow-up, but two cases of permanent vocal cord paralysis were found in the late group. Intraoperative factors, age and the sex of the patients had no influence on the results. Even though dysphagia and dysphonia often appeared after surgery, permanent problems seldom occurred.

In our third study, the long-term results of ILAF in 43 patients with unilateral vocal cord paralysis were examined. The mean follow-up was 5.8 years (range 3–10). Perceptual evaluation demonstrated improved results for voice quality and videolaryngostroboscopy revealed complete or partial glottal closure in 83% of the patients. The voice handicap index (VHI) was below 30 (normal or near normal voice) in 56% of the patients, the mean VHI postoperatively being 35. The length

of the follow-up, the time between the onset of paralysis and the injection and the age of the patient did not significantly affect the results.

We developed a new diagnostic method for exertional laryngeal dyspnea by combining a cardiovascular exercise test with simultaneous fiberoptic observation of the larynx in our final study. With this method, it is possible to visualize paradoxical closure of the vocal cords during inspiration, which is a diagnostic criterion for vocal cord dysfunction (VCD). We examined 30 patients referred to our hospital because of suspicion of exercise-induced vocal cord dysfunction (EIVCD). Twenty-seven patients were able to perform the test, and EIVCD could be seen in five and highly suspicious findings for EIVCD in four patients. The test was well tolerated and it could be performed in patients between the ages of 10–69 years presenting various physiological conditions.

LIST OF ORIGINAL PUBLICATIONS

This study is based on the following publications, which are referred to in the text by their Roman numerals:

- I Tervonen H, Bäck L, Räsänen P, Mäkitie A A, Sintonen H, Roine R P, Vilkmann E, Aaltonen L-M: Automatic speaking valve as an additional speech device for selected laryngectomized patients. *European Archives of Oto-Rhino-Laryngology*, 262(10):816-20, 2005 Oct.
- II Tervonen H, Niemelä M, Lauri E-R, Bäck L, Juvas A, Räsänen P, Sintonen H, Roine R P, Salmi T, Vilkmann E, Aaltonen L-M: Dysphonia and dysphagia after anterior cervical decompression. *Journal of Neurosurgery: Spine*, 7(2): 124-130, 2007 Aug.
- III Reijonen P, Tervonen H, Harinen K, Rihkanen H, Aaltonen L-M: Long-term results of autologous fascia in unilateral vocal fold paralysis. *European Archives of Oto-Rhino-Laryngology*, 266(8): 1273-1278, 2009 Aug.
- IV Tervonen H, Niskanen M, Sovijärvi A, Hakulinen A, Vilkmann E, Aaltonen L-M: Fiberoptic videolaryngoscopy during bicycle ergometry: A diagnostic tool for exercise-induced vocal cord dysfunction. *Laryngoscope*, 19(9): 1776-1780, 2009 Sept.

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Publication III appears in Petri Reijonen's PhD thesis "Injection Laryngoplasty with Autologous Fascia for Treatment of Unilateral Vocal Fold Paralysis", and it has been published as part of this thesis with the permission of Dr Reijonen and the Faculty of Medicine of the University of Helsinki.

ABBREVIATIONS

ACD	anterior cervical decompression
CN (IX-XII)	cranial nerve (glossopharyngeal, vagus, accessory, hypoglossal)
DDI	dysphagia disability index
ECG	electrocardiography
EIVCD	exercise-induced vocal cord dysfunction
EMG	electromyography
ENT	Ear, Nose and Throat specialty of medicine
FEF ₅₀	forced expiratory flow at 50% of vital capacity
FEES	fiberoptic endoscopic evaluation of swallowing
FEV ₁	forced expiratory volume in 1 second
FIF ₅₀	forced inspiratory flow at 50% of vital capacity
FVC	forced vital capacity
GRBAS	scale for perceptual evaluation of voice
HME	heat and moisture exchanger
HNSCC	head and neck squamous cell carcinoma
HUCH	Helsinki University Central Hospital
HRQoL	health related quality of life
ILAF	injection laryngoplasty with autologous fascia
LEMG	laryngeal electromyography
PCA	posterior cricoarytenoid muscle
PTP	phonation threshold pressure
SaO ₂	oxygen saturation
TEP	tracheoesophageal puncture
UVCP	unilateral vocal cord paralysis
VAS	visual analogue scale
VHI	voice handicap index
VCD	vocal cord dysfunction

INTRODUCTION

The most primitive laryngeal function is the protection of the airway. However, in humans the larynx has evolved into a highly complex and specialized organ, not only for airway protection and the control of respiration, but also for sound and speech production.

The intrinsic laryngeal muscles (Fig. 1) are responsible for the size, shape, length, mass, stiffness, and tension of the vocal cords. These muscles are innervated by the recurrent laryngeal nerve, a branch of the vagal nerve (CN X), and all these muscles, with the exception of the posterior cricoarytenoid muscles (PCA, the only vocal cord abductor), are responsible for vocal cord adduction. During normal inspiration, the respiratory center in the medulla stimulates the laryngeal abductor muscle to contract, abducting the vocal cords and therefore widening the rima glottidis (the space between the vocal cords) (Brancatisano, Dodd et al. 1984).

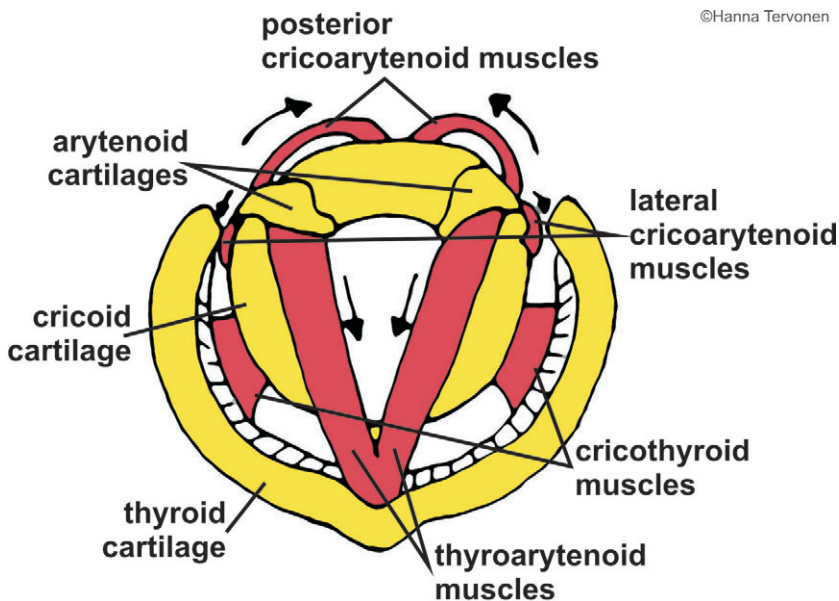


Figure 1. The intrinsic laryngeal muscles

The larynx has an important role in airway protection and control of the bolus during swallowing. Eating and swallowing are complex neuromuscular activities essentially consisting of three phases, an oral, pharyngeal, and esophageal phase.

The larynx plays a role in the pharyngeal phase of swallowing. The bolus prepared in the oral phase is advanced from the pharynx to the esophagus through sequential contraction of the constrictor muscles. The vagal nerve also has an important role in the swallowing process. Distension of this nerve often happens during anterior cervical decompression (ACD) surgery, and the patients complain of dysphagia in addition to dysphonia post-operatively (Bazaz, Lee et al. 2002, Ebraheim, Lu et al. 1996, Morpeth and Williams 2000). Some patients even report permanent swallowing difficulties after the surgical procedure (Daniels, Mahoney et al. 1998). The goal of our second study was to assess the prevalence of and recovery from dysphagia and dysphonia after ACD.

The most complex and highly specialized laryngeal function is sound production. The ability to couple phonation with articulation and resonance allows for human speech. Sound production requires several mechanical properties. Firstly, there must be adequate breathing to produce sufficient subglottic pressure. Secondly, there has to be adequate control of the laryngeal musculature to produce not only glottic closure, but also the proper length and tension of the vocal cords. Finally, there must be favorable pliability and vibratory capacity of the vocal cord tissues.

All four studies of this thesis included patients with voice symptoms. In the first study we examined patients who had undergone total laryngectomy, an alternative treatment modality for advanced laryngeal cancer. Post-operatively, these patients have a permanent tracheostoma, and the most significant change after removing the larynx is the loss of the voice. There are several methods for producing a voice after the surgery, such as esophageal and electrolaryngeal speech, and nowadays the increasingly used tracheoesophageal puncture (TEP) combined with a speech prosthesis. TEP is often already performed during the primary surgery. To produce a voice with this prosthesis, a speech valve is needed. The usual way of producing a voice is to use digital closure of the valve during speaking. At the time of our study, the Provox[®] FreeHands HME speech valve was a relatively new device, and we assessed its benefits and problems.

In the second and the third studies, the patients had hoarseness due to different diseases affecting the larynx or recurrent laryngeal nerve. Hoarseness is a well-known complication of anterior cervical decompression (ACD) surgery, where the distension, or in the worst case the transection of the recurrent laryngeal nerve can

occur. The second study was conducted to examine the appearance of and recovery from the known side effects after ACD, dysphonia and dysphagia.

The main complaint of unilateral vocal cord paralysis (UVCP) is a breathy, weak or aphonic voice. Failure to close the glottis can also lead to dysphagia and aspiration (Heitmiller, Tseng et al. 2000). Autologous fascia injection of the vocal cords is one of the possible surgical modalities in improving the voice in UVCP when spontaneous recovery of the nerve damage does not take place and speech therapy has failed. The third study investigated the long-term results of autologous fascia injection of the vocal cord, a method first introduced in 1998 (Rihkanen 1998).

Our final study included patients with dyspnea during physical exercise. Vocal cord dysfunction (VCD) is a condition where the vocal cords suddenly close during breathing, usually during inspiration, causing wheezing of the breath, dyspnea and sometimes hoarseness (Newman, Mason et al. 1995, Vertigan, Theodoros et al. 2006). Several stimuli can cause the attack, but the pathophysiology of this condition is poorly understood. If the trigger is exercise, the condition can be termed exercise-induced VCD (EIVCD). Diagnosis of EIVCD is very challenging, because the attacks in these patients only occur during strenuous exercise, and all the test results and laryngeal examination before and after are normal. Many patients are misdiagnosed and mistreated as exercise-induced asthma for years. The goal of our study was to develop a new diagnostic method for EIVCD.

In this thesis, the term “vocal cord” is used instead of “vocal fold” to avoid confusion. “Vocal cord” was also used in studies II and IV, and the term vocal cord dysfunction (VCD) is an established name for a condition.

REVIEW OF THE LITERATURE

Physiology of the normal larynx

The larynx serves three important functions in humans. In order of functional priority, they are protective, respiratory, and phonatory. Most importantly, the larynx protects the airway from swallowed material. It coordinates and optimizes the airway with respiration and provides controlled phonation. Voice production and therefore improved communication at the expense of airway protection offers a greater survival advantage in a highly interactive society.

The phylogenetically primary function of the larynx as a sphincter protects the lower airway from the intrusion of liquids and food (Thach 2001). Its secondary function, supported by the sequential phylogenetic acquisition of the cricoarytenoid complex, centers about its role in respiration governed by active muscular dilatation of the laryngeal aperture (Brancatisano, Dodd et al. 1984). The third function of the larynx, phonation, appears to be a late phylogenetic ability (Clarence and Sasaki 2006, Negus 1949).

Neuromuscular Physiology

The afferent system (Table 1)

Sensory innervation of the supraglottic larynx is derived from the internal branch of the superior laryngeal nerve. Each nerve innervates the ipsilateral half of the supraglottis. Below the vocal cords, in the subglottis, ipsilateral innervation is provided by each recurrent laryngeal nerve. It has been demonstrated that a diamond-shaped area in the anterior midline of the subglottic space is innervated by both external branches of the superior laryngeal nerves. Sensory impulses from deep muscle receptors and cricothyroid joints travel in this nerve branch (Suzuki and Kirchner 1968). Afferent impulses are delivered through the ganglion nodosum to the brainstem tractus solitarius (Bowden 1974).

The neural density of sensory innervation appears greatest in the laryngeal inlet (Koizumi 1953, Shin, Watanabe et al. 1987). This is logical, because the entrance to the larynx serves as a protective zone for distal parts of the respiratory system. The laryngeal surface of the epiglottis has the densest innervation, whereas the vocal cords exhibit fewer sensory receptors. Moreover, the posterior half of the vocal

cords has more sensory receptors than the anterior part, which may be of interest during endoscopy in regional or topic anesthesia (Shin, Watanabe et al. 1987).

Table 1. Sensory innervation of the larynx

Sensory Innervation	
Nerve	Distribution
Superior laryngeal (internal division)	Supraglottic mucosa Thyroepiglottic joint Cricoaarytenoid joint
Superior laryngeal (external division)	Anterior subglottic mucosa Cricothyroid joint
Recurrent laryngeal	Subglottic mucosa
Nerve of Galen (communicating branch between superior and recurrent nerves)	Aortic arch

The efferent system (Table 2)

Motor innervation of the intrinsic laryngeal muscles originates in the medullary nucleus ambiguus. Each recurrent laryngeal nerve ipsilaterally innervates all muscles except the cricothyroid, which receives motor impulses from the ipsilateral superior laryngeal nerve. The interarytenoid muscles, however, receive bilateral innervation from both recurrent laryngeal nerves (Bowden 1974). The only muscle that widens the glottis, as happens in inspiration, is the posterior cricoarytenoid muscle. Vocal cord adduction results from the contraction of all the other intrinsic musculature.

If the cricothyroid muscle is denervated by cutting the superior laryngeal nerve, the unopposed contraction of the contralateral muscle results in rotation of the posterior commissure towards the inactive site. On the other hand, unilateral recurrent laryngeal nerve injury results in the paramedian position of the vocal cord, because the unopposed action of the ipsilateral cricothyroid (innervated by an intact superior laryngeal nerve) produces adduction on the side of recurrent laryngeal nerve injury.

Table 2. Motor innervation of the larynx

Motor Innervation		
Nerve	Distribution	Action
Superior laryngeal (external division)	Cricothyroid muscle	Adductor, isotonic tensor
Recurrent laryngeal	Thyroarytenoid muscle	Adductor
	Lat. cricoarytenoid muscle	Adductor
	Interarytenoid muscle (bilat.)	Adductor
	Post. cricoarytenoid muscle	Abductor
Nerve of Galen	Tracheoesophageal mucosa	Autonomic (secretory)
	Tracheal smooth muscle	Autonomic

Laryngeal reflexes

The basic functions of the larynx (protective, respiratory, phonatory) are derived from a complex interrelationship of diverse polysynaptic brainstem reflexes. The protective function is entirely reflexive and involuntarily, whereas the respiratory and phonatory performances may be initiated voluntarily, but are regulated involuntarily through an array of feedback reflexes.

Neurophysiology of the protective function

The glottic closure reflex is a simple polysynaptic reflex producing glottic closure during swallowing. Electrostimulation of the superior laryngeal nerve produces a low threshold-evoked action potential in the adductor branches of the recurrent laryngeal nerve. In humans, the threshold of the adductor reflex measures 0.5 V and has a latency of 25 ms (Sasaki and Suzuki 1976).

Sphincteric closure of the upper airway occurs at three levels of the laryngeal framework. The highest level is at the level of aryepiglottic folds, which contain the most superior division of the thyroarytenoid muscle. With a contraction of these fibers, the aryepiglottic folds approximate to cover the superior inlet of the larynx. The anterior gap is filled by the epiglottic tubercle and the posterior gap by the arytenoid cartilages. The second level of protection is the level of false vocal cords. Laterally along both cords are fibers of thyroarytenoid muscles, capable of bringing the cords together in a reflex response to superior laryngeal nerve stimulation. Third level of protection is the level of vocal cords. The inferior part of each thyro-

arytenoid muscle forms the bulk of the cords and contributes to the strong reflex protective closure at this level. The passive valvular effect caused by the upturned border of the cord margin, combined with the capacity for forceful closure, makes the vocal cords the most effective of the three barriers to aspiration. A counter-productive exaggeration of this protective reflex is present in laryngospasm, in which a prolonged closure off larynx in response to noxious supraglottic or glottic stimulation persists beyond the duration of the stimulus (Sasaki and Suzuki 1977).

Neurophysiology of respiration

The discovery of central and peripheral chemoreceptors and vagally mediated thoracic stretch receptors in the regulation of breathing were among the great discoveries of the 19th century. The respiratory contribution of the larynx, however, was not appreciated until 1949, when it was noticed that the glottis opens a fraction of a second earlier, as the air is drawn in by the descent of the diaphragm (Negus 1949). The neurophysiology behind this was clarified by Suzuki, who also established this activity as a direct effect of the medullary respiratory center (Suzuki and Kirchner 1969). Having shown that widening of the glottis occurs with the rhythmic bursts of activity in the recurrent laryngeal nerve, he then demonstrated that, like phrenic activity, this rhythm is accentuated by hypercapnia and ventilatory obstruction, and depressed by hyperventilation and hypocapnia. This stimulus to contract is shown to occur through a graded posterior cricoarytenoid muscle (PCA) response to varying medullary stimuli, including serum carbon dioxide and oxygen levels and altered intrapulmonary pressure from thoracic airway obstruction (Brancatisano, Dodd et al. 1984).

From a structural perspective, the vocal cords passively act to obstruct the airflow to and from the lungs. To relieve this obstruction, active inspiratory abduction, caused by muscular contraction of the posterior cricoarytenoid muscle, has to happen. This activity has been demonstrated to be synchronous with inspiration. The degree of this activity depends on the ventilatory resistance (Sasaki, Fukuda et al. 1973). Vagotomy abolishes this response, and it is therefore considered that the regulation of inspiratory abduction lies within the ascending vagus nerve (Fukuda, Sasaki et al. 1973).

The larynx also has a role during expiration. At the beginning of normal expiration, a physiologic glottic narrowing can be seen. Most of this narrowing is caused through a decrease in the activity of PCA (Murakami and Kirchner 1972). The rima glottidis is estimated to narrow by 10–40% during expiration with a normal

tidal volume (Newman and Dubester 1994). It has been shown that the duration of expiration regulates the respiratory rate (Remmers and Bartlett 1977). In this regard, the larynx exerts a major valvular effect on ventilatory resistance, influencing the expiratory phase of respiration. By increasing and decreasing the diameter, the larynx plays an active role in the duration of the respiration cycle and in each subsequent resulting lung volume (Pierce and Worsnop 1999).

The cricothyroid muscle plays an important role in expiration. Its activity is evoked by a positive intratracheal pressure independent of the respiratory rate. In addition, the rate of change of intratracheal pressure appears important in triggering cricothyroid activity, with a critical level measured at 30 cm H₂O per second (Horiuchi and Sasaki 1978). Cricothyroid contraction results in vocal cord elongation, which increases the size of the glottal opening. Such an action reduces the airway resistance and shortens the expiration phase.

Neurophysiology of phonation

The phonatory function of the larynx is the most complex and least well understood. Speech results from the fundamental tone produced at the larynx and is modified by resonating chambers of the upper aerodigestive tract. Intelligible speech therefore represents the combined effect of the larynx, tongue, palate and related structures of the oral vestibule. The fundamental tone is produced by the vocal cords powered by the passage of air between them.

The phonatory process, or voicing, occurs when air is expelled from the lungs through the glottis, creating a pressure drop across the larynx. When this drop becomes sufficiently large, the vocal cords start to oscillate. The minimum pressure drop required to achieve phonation is called the phonation threshold pressure (PTP), and for humans with normal vocal cords, it is approximately 2–3 cm H₂O (Rieves, Regner et al. 2009). Surprisingly, it was recently shown that injection laryngoplasty does not significantly affect the PTP (Hoffman, Witt et al. 2010). The motion of the vocal cords during oscillation is mostly in the lateral direction, although there is also a superior component. However, there is almost no motion along the length of the vocal cords. The oscillation of the vocal cords serves to modulate the pressure and flow of the air through the larynx, and this modulated airflow is the main component of the sound of most voiced phones. The vocal cords do not oscillate if they are not sufficiently close to one another, are not under sufficient tension or are under too much tension, or if the pressure drop across the larynx is not large enough.

The sound that the larynx produces is a harmonic series. In other words, it consists of a fundamental tone (called the fundamental frequency, the main acoustic cue for the percept pitch) accompanied by harmonic overtones, which are multiples of the fundamental frequency (Titze 2008). According to the Source-Filter Theory, the resulting sound excites the resonance chamber, that is the vocal tract, to produce the individual speech sounds (Greene and Lesley 2001).

The fundamental frequency can be varied through a variety of means. Large-scale changes are accomplished by increasing the tension in the vocal cords through contraction of the cricothyroid muscle. Smaller changes in tension can be effected by contraction of the thyroarytenoid muscle or changes in the relative position of the thyroid and cricoid cartilages, as may occur when the larynx is lowered or raised, either voluntarily or through movement of the tongue, to which the larynx is attached via the hyoid bone (Zemlin 1998). In addition to tension changes, the fundamental frequency is also influenced by the pressure drop across the larynx, which is mostly affected by the pressure in the lungs, and will also vary with the distance between the vocal cords. Variation in the fundamental frequency is linguistically used to produce intonation and tone.

There are currently two main theories for how vibration of the vocal cords is initiated: the myoelastic theory and the aerodynamic theory (Van Den Berg 1958). These two theories are not in contention with one another, and it is quite possible that both theories are correct and operate simultaneously to initiate and maintain vibration. A third theory, the neurochronaxic theory, was in considerable vogue in the 1950s, but has since been largely discredited (Rubin, H. J. 1960).

Myoelastic and aerodynamic theory

The myoelastic theory states that when the vocal cords are brought together and breath pressure is applied to them, the cords remain closed until the pressure beneath them, the subglottic pressure, is sufficient to push them apart, allowing air to escape and reducing the pressure enough for the muscle tension recoil to pull the cords back together again. Pressure builds up once again until the cords are pushed apart, and the whole cycle keeps repeating itself. The rate at which the cords open and close, the number of cycles per second, determines the pitch of the phonation.

The aerodynamic theory is based on the Bernoulli energy law in fluids. The theory states that when a stream of breath is flowing through the glottis while the arytenoid cartilages are held together by the action of the interarytenoid muscles, a push-pull

effect is created on the vocal cord tissues that maintains self-sustained oscillation. The push occurs during glottal opening, when the glottis is convergent, whereas the pull occurs during glottal closure, when the glottis is divergent. During glottal closure, the air flow is cut off until the breath pressure pushes the cords apart and the flow starts up again, causing the cycles to repeat. The passive nature of vocal cord vibration forms the basis of the aerodynamic theory of sound generation. This is supported by a finding that a cadaver larynx is capable of producing sound when air is blown through it (Brunton and Cash 1883).

Prevalence of laryngeal cancer

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer in the world (Parkin, Bray et al. 2005), and approximately two-thirds of cases are in stage III/IV at presentation. In Finland, HNSCC represents 2.6% of all new malignancies (Finnish Cancer registry). The 5-year overall survival rate for stage III/IV disease remains between 30–50% (Chin, Boyle et al. 2006). Surgery and radiotherapy are the cornerstones of treatment in early stage I-II HNSCC, with locoregional control rates of 70–80%. Advanced-stage disease (III-IV), in turn, is treated with chemoradiation or a combination of surgery and radiation.

The age-adjusted incidence of laryngeal carcinoma in Finland is 3.5 per 100 000 person-years in males and females. Even though laryngeal carcinoma is the most common head and neck malignancy, it comprises approximately only one percent of all new cancer cases in Finland (Finnish Cancer Registry). Total laryngectomy is performed with large laryngeal carcinomas (T4) and sometime as salvage surgery after the failure of other treatment options. About ten total laryngectomies are performed yearly at Helsinki University Central Hospital (HUCH).

Reconstruction of speech after total laryngectomy

The procedure of total laryngectomy not only removes the phonatory source but also influences respiration, so that the patient breathes post-operatively via a permanent tracheostoma (Ackerstaff, Hilgers et al. 1998, Ackerstaff, Hilgers et al. 1995, Hess, Schwenk et al. 1999). Speech rehabilitation is one of the tasks post-operatively. There are three primary approaches to alaryngeal speech rehabilitation following a total laryngectomy: electrolaryngeal speech, esophageal speech and tracheoesophageal speech. In tracheoesophageal speech, a prosthesis is placed in a surgically created fistula between the trachea and esophagus (Fig. 2). The prosthesis directs

the pulmonary air into the oesophagus to vibrate the pharyngoesophageal segment following tracheostomal occlusion (Singer and Blom 1980). The occlusion can be accomplished digitally or via a hands-free valve (Blakley and Podraza 1987, van As, Hilgers et al. 1998). In Finland, the speech prosthesis is inserted between the trachea and esophagus at the time of the primary surgery in ca. 80% of the patients, allowing these laryngectomized patients to achieve an average to good voice (Makitie, Niemensivu et al. 2003). If total laryngectomy is performed as salvage surgery after primary chemoradiation, a secondary tracheoesophageal puncture is recommended because of the risk of pharyngocutaneous fistula formation (Emerick, Tomycz et al. 2009). A recent study has shown reflux to be a reason for failure in TEP voice production through granulation, and the usage of prophylactic antireflux therapy has been discussed (Pattani, Morgan et al. 2009).

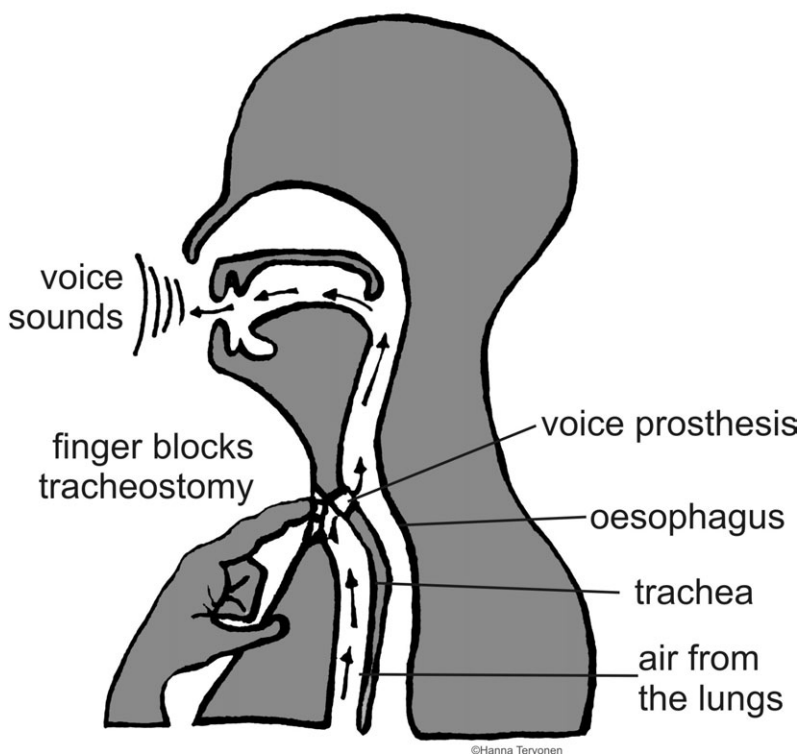


Figure 2. Principle of voice production with a tracheoesophageal prosthesis. Digital occlusion of the stoma can be replaced by an automatic speaking valve.

Bivona I and II, the Blom-Singer Adjustable Tracheostoma Valve (Blom, Singer et al. 1982), the Eska-Herrmann (Herrmann 1987), and the Window (Hagen, Schwarz et al. 2001) are earlier automatic speaking valves, requiring no digital occlusion for speech production. The Provox[®] FreeHands HME was developed shortly before our study (Hilgers, Ackerstaff et al. 2003). The automatic valve remains open during calm breathing, but is closed by an increase in air pressure to produce speech. This device consists of a disposable heat and moisture exchanger (HME) cassette with a reusable multi-magnet automatic speaking valve on top. The same tracheo-esophageal prosthesis (Provox[®] or Provox[®] 2) and an adhesive base plate can be used with both the traditional HME and FreeHands HME. An earlier study reported that more air pressure is needed for speech, and breathing was stated to be heavier with the FreeHands HME compared with the traditional HME (Hilgers, Ackerstaff et al. 2003).

Impact of anterior cervical decompression (ACD) on swallowing and the voice

A cervical herniated disc and spondylosis are common cervical disorders causing pain and numbness of the upper extremities. Anterior cervical decompression (ACD), usually performed by neurosurgeons, is widely used for nerve root decompression for both of these conditions (Bailey and Badgley 1960, Cloward 1958, Robinson and Smith 1955). The anterior surgical approach necessitates distension of the soft tissue to reach the damaged anterior part of the cervical spine (Daniels, Mahoney et al. 1998, Martins 1976, Stewart, Johnston et al. 1995, Winslow, Winslow et al. 2001). Post-operative problems in swallowing or in voice caused by the distension of the cranial nerves in the neck area are usually reversible. One study compared swallowing difficulties in ACD, in posterior cervical decompression (PCD), and in posterior lumbar decompression (PLD) patients and showed that 47% had swallowing difficulties after ACD, 21% after PCD, but none after PLD. Most recovered within a few weeks. The same study also showed that intubation as such seems to have no adverse effect on the voice or on swallowing (Smith-Hammond, C. A., New et al. 2004). Another small series showed swallowing and speech dysfunction in ACD to correlate with the number of disc spaces operated on in one session, and these side-effects were mostly caused by swelling of soft tissue (Frempong-Boadu, Houten et al. 2002). Although the right-sided approach causes more recurrent nerve distension for anatomical reasons (Smith-Hammond, C.A., Davenport et al. 1997, Weisberg, Spengler et al. 1997), the side of the surgical approach does not seem to affect the incidence of dysphonia (Beutler, Sweeney et al. 2001).

Reconstruction of the voice in unilateral vocal cord paralysis

Unilateral vocal cord paralysis (UVCP) typically causes hoarseness, weakness of the voice and sometimes aspiration. Common causes for UVCP are operations and tumors in the head and neck area. Different methods are available to reduce the above-mentioned problems.

Voice therapy as a nonsurgical method often produces satisfactory vocal results, especially in patients who do not use their voice professionally. The literature considering the effectiveness of voice therapy in UVCP treatment is scarce. In a study on 41 patients, 68% of the female and 64% of the male patients did not elect to have surgery after voice therapy. The same study showed the self-reported satisfaction outcome after surgery and non-surgery to be similar, highlighting the importance of voice therapy before planning any surgical interference (Heuer, Sataloff et al. 1997). Comparing surgical and nonsurgical methods in therapy for UVCP is not simple, because patients with minor glottal insufficiency opt for conservative therapy, and no clear pre-operative signs exist for recognizing patients needing surgery (Miller, S. 2004). Post-operatively, a few sessions of voice therapy are recommended to help the patients to produce a voice with the new mechanical condition (Isshiki 1998).

Laryngeal reinnervation with the return of normal vocal cord function would be an ideal treatment for UVCP, but it has proved to be difficult. Several surgical procedures using anastomosis of the recurrent nerve to the ansa cervicalis, phrenic nerve, preganglionic sympathetic neurons, hypoglossal nerve and nerve-muscle pedicles have been introduced (Rubin, A. D. and Sataloff 2007). The results of reinnervation procedures currently remain at the level of atrophy prevention of laryngeal muscles caused by denervation rather than achieving vocal cord movement.

Laryngeal framework surgery including thyroplasty type I and arytenoid adduction/rotation (Isshiki, Morita et al. 1974, Isshiki, Tanabe et al. 1978) and injection laryngoplasty are the medialization methods in UVCP therapy. Thyroplasty type I involves the medialization of the vocal cord by its inward displacement through an implant placed in the thyroid cartilage lamina, and is generally considered suitable in large glottal insufficiencies. Several implant materials have been introduced over the years (Cummings, Purcell et al. 1993, Friedrich 1999, Koufman 1986, McCulloch and Hoffman 1998, McCulloch, Hoffman et al. 2000). Injection laryngoplasty, first introduced in 1911 with paraffin, can be used with minor gaps (Dursun, Boynukalin et al. 2008). Injection laryngoplasty can be carried out alone or after laryngeal framework surgery to optimize the degree of glottal closure achieved (Umeno, Chitose et al. 2008).

Various substances have also been used in injection laryngoplasty. The ideal soft

tissue filler substance should be safe, biocompatible, nonmigratory, resistant to phagocytosis, pliable, and should persist and maintain its volume without being absorbed. Although a growing number of injectable materials have been developed and tested, no single optimal material has been found (Broder and Cohen 2006). The materials used are categorized according to their origin: xenograft, homograft/allograft and autograft (Eppley and Dadvand 2006, Kwon and Buckmire 2004).

Initial trials with autologous fat injection reported promising short-term results (Brandenburg, Kirkham et al. 1992, Mikaelian, Lowry et al. 1991). However, a later study showed an unpredictable rate of absorption of fat after three months (Shindo, Zaretsky et al. 1996). The unpredictable long-term outcome has advocated opinions that fat injection is not a preferable method of surgery for UVCP (Laccourreye, Papon et al. 2003, McCulloch, Andrews et al. 2002).

Free fascia was proposed for injection laryngoplasty to overcome the poor persistence of fat in the larynx (Rihkanen 1998). Autologous fascia transplantation has been widely used in plastic, reconstructive and head and neck surgery for a long time (Boyce, Nuss et al. 1994). Fascia has proven to be a stable and predictable graft material for various head and neck indications and suitable for the augmentation of minor soft tissue defects (Miller, T. A. 1988).

Impact of vocal cord dysfunction (VCD) on breathing and the voice

Vocal cord dysfunction (VCD), also known as paradoxical vocal fold motion, is a condition with paradoxical closure of the vocal cords, typically during inspiration. This limits airflow, causing dyspnea and stridor, a condition very often misdiagnosed and mistreated as asthma (Newman, Mason et al. 1995). Dysphonia, dysphagia, and coughing are other typical symptoms in a VCD attack (Vertigan, Theodoros et al. 2006). Some VCD patients have symptoms in exercise, others in rest, and some both in exercise and rest (Morris, Deal et al. 1999, Newman, Mason et al. 1995, Wood and Milgrom 1996). The pathophysiology of VCD is not clear, and the etiology may be multi-factorial. Suggested etiological factors - alone or combined - include infections (Taramaraz, Grissel et al. 2004), physical exercise (Heimdal, Roksund et al. 2006, Rundell and Spiering 2003), laryngeal sensitivity to various stimuli (Ayres and Gabbot 2002), and psychosomatic and psychological stress (Rundell and Spiering 2003).

For the diagnosis of VCD, paradoxical adduction of the vocal cords has to be visualized (Heimdal, Roksund et al. 2006, Morris, Deal et al. 1999, Rundell and Spiering 2003). Flattening of the inspiratory curve in spirometry can sometimes

be seen during a VCD attack (Bucca, Rolla et al. 1991). The incidence of VCD in the general population is not widely established. A study on 1025 patients in which dyspnea was evaluated reported an overall VCD incidence of 2.8% (Kenn, Willer et al. 1997). One study with exercise-induced dyspnea patients showed an exercise-induced VCD incidence of 12% (Morris, Deal et al. 1999). Pathological vocal cord adduction was seen in 63% of the patients in a recent study on 166 young patients suffering from exercise-induced dyspnea (Roksund, Maat et al. 2009).

Shortness of breath and wheezing during exercise in generally healthy adolescents is often caused by exercise-induced asthma (EIA) (Abu-Hasan, Tannous et al. 2005). However, EIVCD alone or a combination of EIA and EIVCD can be behind these symptoms (Newman, Mason et al. 1995). VCD is also common among asthmatics. A study on 95 VCD patients showed coexistent asthma in 56% (Newman, Mason et al. 1995). EIVCD typically appears during very strenuous exercise, the symptoms resolving within a few seconds or minutes after stopping or just slowing down, and athletes have learned to limit their activity to avoid such attacks (Mathers-Schmidt and Brilla 2005). Being an episodic symptom that does not always appear in the same exercise surroundings (Wood and Milgrom 1996), a negative result in any provocation test does not preclude the diagnosis. Bent et al. published a study on 10 young healthy volunteers using a stationary bicycle combined with continuous laryngoscopy to determine the incidence of exercise-induced laryngomalacia. This test setting lacked a patient group, as well as ECG, blood pressure, heart rate, and respiratory rate monitoring (Bent, Kim et al. 1996). Other studies have reported promising results with a diagnostic method for EIVCD based on continuous laryngoscopy during treadmill exercise (Heimdal, Roksund et al. 2006, Roksund, Maat et al. 2009).

EVALUATION METHODS FOR LARYNGEAL DISORDERS

Videolaryngostroboscopy

The history of using a stroboscopic light source to examine the larynx is nearly as long as that of the continuous light source, dating back to the introduction of the laryngeal mirror by Manuel Garcia in 1855. In 1895, an internist named Oertel used a stroboscopic light source with a laryngeal mirror to investigate voice production in different registers.

In modern laryngological practice, videolaryngostroboscopy is an essential diagnostic procedure for the detection of vocal pathology and is considered routine (Bless, Hirano et al. 1987). A videostroboscopy unit consists of a stroboscopic unit (light source and microphone), a video camera, an endoscope, and a video recorder. Endoscopy is performed with a rigid 70° or 90° angled laryngoscope transorally, or a flexible fiberoptic nasolaryngoscope in patients with a hypersensitive gag reflex. Videolaryngostroboscopy produces intermittent light flashes in close relation to the frequency of the vocal cord vibration. A microphone picks up the frequency of the examinee's sustained voice, which triggers the stroboscopic light source. With the provision that the vocal vibrations are periodic, a frequency of light flashes equal to the vocal frequency produces a clear, still image of the same portion to the vibratory cycle.

When the frequency of the flashes is slightly less than the vibration of the vocal cord, it causes a delay in the portion of each vibratory cycle illuminated, and the illusion of slow motion is obtained. This wave like motion is then analyzed for its symmetry, regularity (periodicity), glottal closure, amplitude of vibration and stiffness (presence of immobility) (Bless, Hirano et al. 1987). Laryngostroboscopy does not demonstrate each individual vibratory cycle but it shows a pattern averaged over many successive nonidentical cycles. This means that it is not an illustration of the true vibratory nature, whereas high speed video makes each vocal cord cycle visible and allows vocal cord dynamics to be viewed, even when aperiodic.

Perceptual voice analysis

There is no simple association between voice production, objective acoustic data and subjective auditory perception, because they express different phenomena. Perceptual evaluation of the voice is usually performed by a panel of voice professionals, who listen to recorded voice samples. Standardized evaluation of the samples is challenging. The most widely used tool for this is the Japanese GRBAS (Hirano 1981). It consists of five voice quality dimensions (Grade, Roughness, Breathiness, Asthenia and Strain) with a score of 0 to 3 in each section (0 = normal voice, 1 = minor dysfunction, 2 = moderate dysfunction, 3 = severe dysfunction). Even this scale carries the problems of intra- and interrater reliability. The general "grade" value as well as "roughness" and "breathiness" of voice are evaluated by professionals with moderate reliability and interrater consistency (De Bodt, Wuyts et al. 1997).

Another tool is CAPE-V, a product of the American Speech-Language-Hearing Association, 2002 (http://www.asha.org/about/membership-certification/divs/div_3.htm). It provides a standardized framework and procedures for perceptual eva-

luation of abnormal voice quality that includes prescribed speech materials and visual analogue scaling of a closed set of perceptual vocal attributes: the severity of dysphonia, straining, pitch and loudness. Similar reliability problems to GRBAS are present in CAPE-V (Karnell, Melton et al. 2007, Kreiman and Gerratt 2000). The INFVo perceptual rating scale for substitution voicing was developed for those voices for which GRBAS cannot be accurately used. It consists of five new parameters: impression, intelligibility, noise, fluency and voicing, each to be scored between 0 (very poor score) to 10 (very good score for a substitution voice) (Moerman, M., Martens et al. 2006, Moerman, M. B., Martens et al. 2006)

Acoustic voice analysis

Objective multidimensional analysis of the voice is conceivable through several computer programs. The voice sample, usually consisting of sustained vowel phonation, is recorded in a silent non-reverberant room. The acoustic parameters analyzed are perturbation (irregularity of frequency and amplitude), fundamental frequency and the relation of noise components to the harmonic signal. Being non-invasive, rapid and providing objective data, acoustic analysis of the voice is a preferable method for perceptual evaluation of the pathological voice. However, perturbation measures rely on the inherent ability to accurately determine the fundamental frequency. This can be difficult or impossible to achieve with severely dysphonic voices, which are often only partly periodic (Kaszuba and Garrett 2007).

Jitter is the frequency variability between cycles of vibration. High jitter levels suggest that something is interfering with normal vocal cord vibration and the mucosal wave. Measurement of the cycle-to-cycle variability of vibration can allow the detection of changes in the neuromuscular function of the muscles controlling the vocal cords. Jitter is related to periodicity of the vocal cords. When elevated, it suggests an inability to maintain periodic vibration or the person's ability to vibrate cords rhythmically. Irregular glottal pulses are heard as roughness of the voice (Rontal, Rontal et al. 1983). Shimmer is the amplitude variability between cycles of vibration and it increases with poor and inconsistent contact between the vocal cord edges (Yumoto 1983). The noise-to-harmonic ratio (NHR) estimates the proportion of aperiodic noise to the periodic signal produced by the vocal cords. The NHR seems to combine breathiness and roughness, the principal components of hoarseness (Yumoto 1983). The reliability between different acoustic analysis programs has raised some criticism. In particular, perturbation values correspond poorly between programs, which can cause problems in comparing data from different institutions (Bielamowicz, Kreiman et al. 1996).

Self-perceived handicap measures of the voice

The perceptual evaluation of voice and acoustic measurements provide objective data, but cannot assess the level of disability a person experiences as a result of a voice disorder (Benninger, Ahuja et al. 1998). Although the perceived disability is related to many factors, such as the patient's psychosocial traits and education, patient-based outcome measurements can potentially provide useful information to be added to the biological and physiological variables related to the voice (Dejonckere, Bradley et al. 2001). The Voice Handicap Index (VHI) was developed to demonstrate treatment effectiveness by relating clinical and objective results to the subjective experience of patients (Jacobson, Johnson et al. 1997). The VHI questionnaire has 30 statements reflecting experiences faced by the patient with a voice disorder. The statements are divided into three subscales (functional, emotional and physical), each having 10 questions. The VHI has been translated into and validated in several languages, and it is widely applied throughout the world (Amir, Tavor et al. 2006, Hsiung, Lu et al. 2003, Nawka, Wiesmann et al. 2003). The VHI-10, an abbreviated version of the VHI comprising the 10 most robust questions, is in wide clinical use, demanding less time without loss of validity (Rosen, Lee et al. 2004). There is also another 10-item questionnaire for evaluating the voice-related quality of life (V-RQOL). It performs well in tests of reliability, validity, and responsiveness. Measurement of V-RQOL is a valuable addition to the evaluation of dysphonic patients and their treatment outcomes (Hogikyan and Sethuraman 1999). The Voice Activity and Participation Profile (VAPP) is a 28-item assessment tool developed for evaluating the impact of voice disorders on daily activities (Ma and Yiu 2001).

Maximum phonation time (MPT)

MPT is the maximum time (in seconds) for which a person can sustain a vowel sound (usually /a/) when produced following one deep breath at a relatively comfortable pitch and loudness. Being non-invasive and requiring no special equipment, other than a stopwatch, MPT can be obtained in a variety of settings. With an easy measure, it provides the clinician with the phonation duration, which correlates with the completeness of glottal closure. Normal mean values for adults are 26 seconds for men and 20 seconds for women (Colton and Casper 1996). The validity and stability of this measure on repeat trials has been questioned, since age, sex, size, general health condition, cooperation, and instructions have an influence on the result (Behrman 2004). However, follow-up data from the same patient can be analyzed (Hirano 1989).

Forced expiratory volume in one second (FEV₁)

The forced expiratory volume in one second is the volume that a subject can exhale in the first second during a forced expiration test. FEV₁ is the most frequently used index for assessing airway obstruction, bronchoconstriction, or bronchodilatation; FEV₁ expressed as a percentage of the vital capacity is the standard index for assessing and quantifying airflow limitation (Johannessen, Lehmann et al. 2006). Spirometry is performed to measure this parameter. The result can be affected by restrictions at the level of the larynx or distal to it (for example UVCP, VCD, asthma). Spirometry may be useful in discerning VCD from asthma. In asthma, the defect is in expiration and the typical finding is a reduced FEV₁ or lowered FEV₁/FVC (forced vital capacity). In contrast, VCD results in the patient having difficulty with inhalation, so the ratio of forced expiratory to forced inspiratory flow at 50% of vital capacity (FEF₅₀/FIF₅₀) is usually elevated from the normal value of <1. Therefore, a truncated or flattened inspiratory curve is suggestive of VCD. Again, it has to be considered that VCD and asthma may exist concurrently, making the diagnosis more complex.

Evaluation of swallowing with videofluorography and FEES

Bedside observation while the patient is swallowing is the most often used evaluation method, although its reliability is not optimal. X-ray examination, videofluorography, provides information on the anatomy and the motility of upper digestive tract, including the esophagus, detects possible aspiration, and can be performed with different bolus consistencies (Skolnick 1970). Videofluorography has become the gold standard examination for the assessment of aspiration in patients with clinically diagnosed dysphagia due to neurological causes. Major limitations of videofluorography include poor detection of mild cases of esophagitis and an occasional lack of specificity in diagnosing esophageal motor dysfunction (Ott, Gelfand et al. 1986). The acquired video film can be observed after the procedure, the method is not invasive, and the required amount of radiation is within acceptable limits, i.e. 0.2–0.4 mSv (Zammit-Maempel, Chapple et al. 2007) (Wright, Boyd et al. 1998).

Functional endoscopic evaluation of swallowing (FEES) (Langmore, Schatz et al. 1988) can be performed at the bedside or in an outpatient clinic. In FEES, a flexible fiberoptic endoscope is introduced transnasally close to the patient's hypopharynx, where the clinician can clearly view the laryngeal and pharyngeal structures. The patient is then led through various tasks to evaluate the sensory and motor status of the pharyngeal and laryngeal mechanism. Boluses of different consistencies are then given to the patient so that the integrity of the pharyngeal swallow can be de-

terminated. Information obtained from this examination includes the ability to protect the airway, to sustain airway protection for a period of several seconds, and to initiate a prompt swallow without spillage of material into the hypopharynx, as well as the timing and direction of movement of the bolus through the hypopharynx, the ability to clear the bolus during the swallow, the presence of pooling and residue of material in the hypopharynx, the timing of bolus flow and airway protection, the sensitivity of the pharyngeal/laryngeal structures and the effect of anatomy on the swallow. Appropriate postural changes and swallowing maneuvers are attempted to detect problems and enable the examiner to make recommendations regarding optimal interventions to improve the safety and efficiency of the swallow, the advisability of oral feeding, and use of appropriate behavioral strategies that facilitate safe and efficient swallowing. The most critical finding during examination is aspiration. FEES is able to detect post-swallow phase aspiration more than videofluorography with no difference in the pre-swallow phase, whereas videofluorography detects aspiration during the swallow phase (Singh, Berry et al. 2009).

Laryngeal electromyography (LEMG)

Electromyography (EMG) is a technique for evaluating and recording the electrical activity produced by skeletal muscles. An electromyograph detects the electrical potential generated by muscle cells when these cells are electrically or neurologically activated. The signals can be analyzed to detect medical abnormalities, the activation level, the recruitment order, or to analyze the biomechanics of human or animal movement.

The first documented experiments dealing with EMG started with Francesco Redi's works in 1666. Redi discovered that a highly specialized muscle of the electric ray fish (electric eel) generated electricity. The first actual recording of voluntary muscle contraction activity was made by Marey in 1890, who also introduced the term electromyography.

Laryngeal EMG (LEMG) is useful to assess the nature and extent of neurogenic pathology after vocal cord paresis and to determine the prognosis for recovery of an affected vocal cord. It can also be used to verify vocal cord paresis in cases with symptoms fitting vocal cord paresis with limited clinical findings in videolaryngostroboscopy or fiberoptolaryngoscopy (vocal cord bowing, reduced/asymmetric abduction-adduction motion or lack to lengthen the vocal cords). LEMG recording is made through a fine needle electrode inserted into various muscles bilateral in the larynx through the skin. The patient is asked to perform several vocal functions

while a computer-controlled machine records activities from laryngeal muscles. The reported prognostic value varies widely in the literature, but the utilization of discreet EMG criteria improves the utility in assessing the recovery of vocal cord motion (Munin, Rosen et al. 2003, Wang, Chang et al. 2008). Serial LEMG examination over time may be helpful in predicting the recovery of vocal cord paresis. A study on 31 patients showed that a poor prognosis was defined as reduced motor unit recruitment with acute or chronic spontaneous activity. In the same study, an excellent prognosis included a normal motor unit recruitment pattern with only a slightly decreased interference pattern and no fibrillation potentials or positive sharp waves. LEMG was performed between 21 days and six months after the onset of the paralysis (Munin, Rosen et al. 2003).

Health related quality of life (HRQoL) using the 15D instrument

15D is a generic 15-dimensional, standardized, self-administered HRQoL instrument useful both as a profile and a single index score measure (Sintonen 1995). The 15D questionnaire consists of 15 dimensions: moving, seeing, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity. For each dimension, the respondent must choose one of the five levels that best describes his/her state of health at the moment (best level = 1; worst = 5). The valuation system of the 15D is based on an application of the multi-attribute utility theory. A set of utility or preference weights, elicited from the general public through a 3-stage valuation procedure, is used in an additive aggregation formula to generate the utility score, i.e., the 15D score (single index number) over all the dimensions. The maximum score is 1 (no problems in any dimension) and the minimum score 0 (deceased). A minimally important difference (MID) ≥ 0.03 is considered clinically significant or important. In most of the important properties, the 15D compares favorably with other instruments of its kind (Sintonen 1995, 2001, Stavem 1999).

AIMS OF THE STUDY

The aim of this work was to evaluate different laryngeal functions and functional problems in four independent patient groups with laryngeal disorders.

Specific aims were:

1. To evaluate the benefits and problems of an automatic speaking valve used for rehabilitation of speech in laryngectomized patients. The patients' health related quality of life (HRQoL) was also assessed. (I)
2. To evaluate the appearance, duration and the severity of dysphonia and dysphagia after anterior cervical decompression. HRQoL was additionally measured. (II)
3. To present the long-term results of injection laryngoplasty with autologous fascia. (III)
4. To develop a new diagnostic tool for exercise-induced laryngeal dyspnea. (IV)

PATIENTS AND METHODS

The individual studies of this thesis are identified with Roman numerals. All patients in studies I-IV were examined at the Department of Otorhinolaryngology - Head and Neck Surgery, of Helsinki University Central Hospital (HUCH), Helsinki, Finland, which is a tertiary referral center.

In the clinical trials, informed consent was obtained from all individuals, and the human experimentation guidelines of HUCH were followed. The study protocols were approved by the Ethics Review Board of the Helsinki and Uusimaa University Hospital District.

Study I

At the Department of Otorhinolaryngology - Head and Neck Surgery, HUCH, between the years 1995 and 2002, 103 patients underwent total laryngectomy. Of these patients, 19 whose speech with HME was especially easy and clear received the Provox® FreeHands HME. In November 2003, three of them had died, one lived far away, and one refused to participate, so 14 patients entered our study. These were all males, mean age 62 years (range 40–85), and the median follow-up time after total laryngectomy was 5.8 years (range 2.3–9.3).

All patients had received radiation therapy, six as a primary treatment and eight post-operatively. Total laryngectomy was performed on six patients as a primary treatment and on eight patients as salvage surgery. In addition to total laryngectomy, two of the patients underwent radical neck dissection and one patient modified radical neck dissection. The patients were examined by an ENT specialist and a speech pathologist.

Videolaryngoscopy was performed and tracheostomas were evaluated (possible granulation tissue, distance of the prosthesis from the skin-mucosal border, muscular symmetry around the tracheostoma). Structured questionnaires containing both free-text questions and VAS scales (Price, McGrath et al. 1983) served in collecting data on voicing and breathing, skin adhesion and the subjective quality of voice and speech. In the voice laboratory, the vowel /a/ was sustained as long as possible for assessment of the maximum phonation time, and its dynamic loudness range (minimum and maximum). A text was read aloud and recorded for perceptual evaluation by five speech pathologists, who evaluated parameters such as the

intelligibility of the speech and usefulness of the voice. All tests were performed blinded, both with the traditional HME and with the FreeHands HME. HRQoL was measured using the 15D questionnaire.

Study II

The first 100 consecutive ACD patients operated on at the Department of Neurosurgery, HUCH, in 2004 were invited by letter for a post-operative visit 3 to 9 months (median 6.1) after the operation. Of these, 64 agreed and entered the study (late group). Their mean age was 51 years (range 29–84, median 51). To evaluate the immediate pre- and post-operative symptoms and signs, later in 2004 we invited by letter another series of consecutive ACD patients ($n = 196$), operated on at HUCH, and 50 of them entered the study (early group). Their mean age was 52 years (range 23–80, median 53). The pre-operative examination was performed one day before or on the day of the surgery and the post-operative examination on the day of discharge, usually on the first post-operative day (median 1, range 1–7). Moreover, a questionnaire was sent to these patients 3 months post-operatively. The patients with clinical findings at the first post-operative visit, and those who reported persistent dysphonia or dysphagia in the questionnaire were invited for a second visit (Fig. 3).

As a control group for the patients examined pre- and post-operatively (early group), we examined 50 age- and gender-matched patients visiting the Department of Otorhinolaryngology - Head and Neck Surgery, HUCH, for reasons other than dysphagia or dysphonia and who had not been intubated during the previous 5 years. Patients with acute infection or head and neck malignancy were excluded. The control group comprised mainly vertigo, nasal polyposis, cholesteatoma, and sleep apnea patients.

Videolaryngostroboscopy was performed, and the function of cranial nerves IX-XII was clinically tested for all. Data on voicing, swallowing, subjective quality of the voice and speech, and surgery results were collected with structured questionnaires also containing visual analogue scales (VAS). Moreover, late-group patients were examined by a neurosurgeon. Patients having dysphonia 3 to 9 months post-operatively were referred for laryngeal EMG and phoniatric examination, again including videolaryngostroboscopy, and those with dysphagia were examined together with a speech pathologist. Structured questionnaires were used, and transoral endoscopic evaluation of swallowing was performed. Patients with pathological findings or severe subjective symptoms were referred to videofluorography. Control group

subjects underwent the same examinations as the patients in the early group during pre-operative visit. HRQoL was measured using the 15D questionnaire.

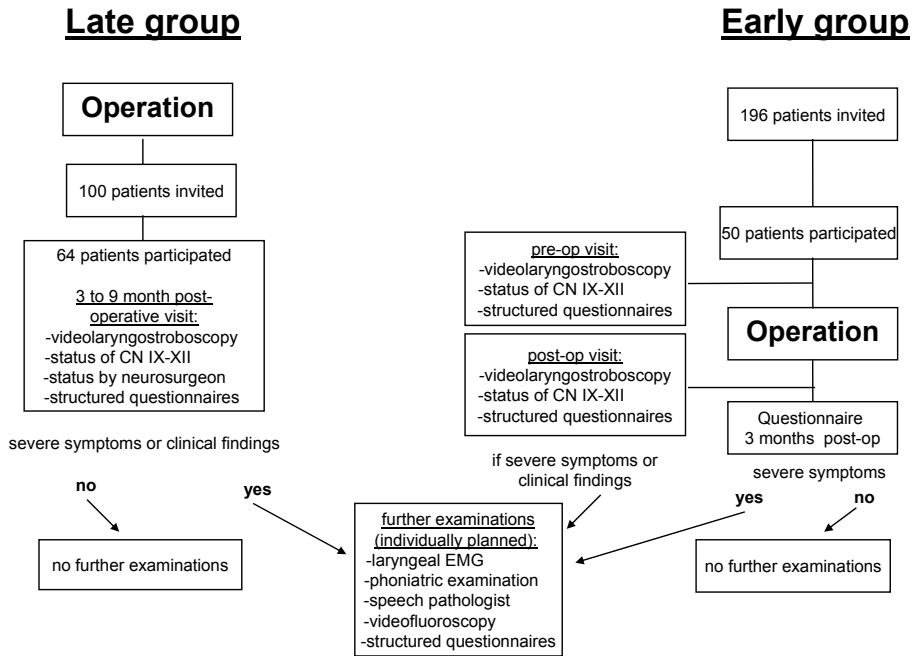


Figure 3. Flow chart of the patients and performed examinations

Study III

Ninety-four patients underwent ILAF for UVCP between 1996 and 2006 at Jorvi Hospital and the Department of Otorhinolaryngology - Head and Neck Surgery, HUCH. Five patients were lost to follow up and 19 had died. Our goal was to evaluate patients whose primary and only phonosurgical procedure was ILAF, and 13 further patients were therefore excluded for the following reasons: re-fasciainjection (N = 7), arytenoid adduction (N = 2) and additional lipoinjection (N = 1). Three patients had a mother tongue other than Finnish. After these exclusions, 57 patients were invited to participate in the study and 44 patients entered it. In one female patient the paralysis had recovered, and 43 patients were therefore included.

The median age of the patients at surgery was 55 years (range 14–72). Nine patients were male, 34 female. The median duration from the paralysis to laryngoplasty was 1.1 years (range 0.2–46.7), and the median duration of the post-operative follow-up was 5.8 years (range 3.3–10.0).

A standard text of six Finnish sentences read aloud was recorded (mean duration 22.4 s) and perceptual evaluation using the GRBAS scale (Grade, Roughness, Breathiness, Asthenia, Strain) was carried out by a panel of three speech therapists. Pre- and post-operative samples were arranged in a file in random order and the panel listened to them with closed earphones from a portable computer.

Acoustic parameters (jitter, shimmer and NHR) were calculated from sustained vowel /a/, samples produced on a comfortable pitch and loudness level using Kay Elemetrics Corp. Multidimensional Voice Program Model 4305. Pre- and post-operative videolaryngostroboscopy recordings were archived and the video recordings were evaluated by two phoniatricians not involved in operative treatment. The analyzed parameters were glottal closure, phase symmetry and mucosal wave amplitude. The VHI questionnaire was returned only at the post-operative visit, because it was first presented in 1997.

Study IV

We examined 30 consecutive patients referred to the Department of Otorhinolaryngology - Head and Neck Surgery, HUCH, because of a suspicion of EIVCD. The median age of the patients was 27.8 years (range 10.6–69.2) and 24 (80%) of them were female. There were 13 (43%) patients with co-existing asthma. Twenty-five patients had symptoms only during strenuous exercise.

As controls we examined 15 healthy volunteers. In the control group the median age was 33.4 (range 20.9–54.1) and of them 10 (67%) were female.

All patients and controls underwent the same research protocol. The protocol was tested with one volunteer staff member before starting the study. Data on the medical history of the patients were collected with a questionnaire. After baseline measurements (FEV₁, SaO₂, ECG, blood pressure, heart rate, and respiratory rate), topical anesthesia was applied inside the patient's nostril to prevent irritation by the fiberoptic videolaryngoscope, which was then inserted in the optimal position for visualizing the larynx. Thereafter, the patient started to pedal, beginning with a work load of 40 W (watts) for women and 50 W for men. The load was then increased every 4 minutes by 40 W/50 W increments supervised by an anesthesiologist. The pedaling speed was held constant at 60 rpm. Blood pressure, heart rate, and respiratory rate were regularly measured. Subjects continued pedaling until the typical symptom of dyspnea appeared or until exhaustion.

STATISTICAL METHODS

Differences in mean values between two groups of observations for continuous variables were tested with non-parametric or parametric tests, depending on distribution assumptions. For non-parametric data, the Mann-Whitney test (I, III, IV) was chosen for unpaired group comparisons and the Wilcoxon test (I, III) for paired groups. In addition, the Student's t-test for unpaired groups (II) and for paired groups (I) served for parametric analysis.

Spearman's rank correlation coefficient was used to measure the degree of associations between different voice parameter values (III).

Differences in categorical variables between cases and controls were studied with Fisher's exact test (IV). The Kolmogorov-Smirnov test (IV) was performed to determine whether the distributions of some continuous variables differed between patients and controls.

Two-way analysis of variance ANOVA (I) was used to study the relationship between continuous dependent and two categorical independent variables. When studying several continuous dependent variables, multivariate analysis of variance MANOVA (III) was used.

Logistic regression analysis (II) allowed analysis of the association between dichotomous dependent and continuous independent variables.

RESULTS

Table 3. Summary of the patients and main outcomes

	Study I	Study II	Study III	Study IV
Patients	14 total laryngectomized patients, who used the traditional speaking valve especially well	<u>Early group</u> : 50 ACD patients, examined pre-and post-operatively <u>Late group</u> : 64 ACD patients, examined only post-operatively	44 patients who had undergone autologous fascia injection of the vocal cord as a treatment for unilateral vocal cord paralysis 3.3–10 years earlier	30 patients with a suspicion of EIVCD. (27 patients completed the test)
Controls		50 to early group age- and gender-matched subjects		15 healthy volunteers
Main outcomes	<ul style="list-style-type: none"> - Automatic speaking valve was a useful additional device, but not suitable as the sole device - speaking and breathing were reported to be heavier with an automatic speaking valve - HRQoL did not differ significantly from the normal population 	<ul style="list-style-type: none"> - Dysphonia and dysphagia were common immediate post-operative problems. Most of these were transient - 6 transient vocal cord paresis were diagnosed in the early group - 2 permanent vocal cord paralysis were detected in the late group patients 	<ul style="list-style-type: none"> - Complete or partial vocal cord closure was seen in most of the patients - most of the patients were satisfied with their voice - fascia injection was considered a suitable method in less severe glottic insufficiencies -the long term results remained stabile 	<ul style="list-style-type: none"> - Dyspnea could be induced in 15 patients - 5 patients had EIVCD and 4 high suspicion of EIVCD - subjective feeling of laryngeal dyspnea was often false → visualizing the vocal cords during dyspnea attack remains a "gold standard" for diagnosing EIVCD

I Speaking, breathing and health-related quality of life in patients with a Provox® FreeHands HME

The aim of the study was to evaluate the benefits and problems related to the Free-Hands HME. The health related quality of life (HRQoL) and voice of these total laryngectomized patients were also surveyed.

Of 14 patients, 12 (86%) used the FreeHands HME for special social occasions. One patient (7%) used it continuously and 1 patient (7%) did not find the device useful because of problems with skin adherence of the base plate.

ENT examination and videolaryngoscopy produced no distinctive findings other than those related to the surgery. All patients had a well-functioning Provox® 2 prosthesis, except for one that leaked and needed to be changed. The median distance of the prosthesis from the skin-mucosal border was 10 mm (range 3–20).

Granulation tissue appeared around the prosthesis in one patient. Musculature around the tracheostoma was asymmetrical in two patients, in both cases due to surgery on the neck.

Of the 14 patients with a FreeHands HME, breathing was reported to be heavier in nine (64%), speaking more difficult in seven (50%) and subjective voice quality worse in four (29%). However, two (14%) found breathing easier, three (21%) reported speaking easier, and the self-reported voice quality was better in three (21%). Despite the problems related to the FreeHands HME, most patients considered it a useful additional device and easy to use.

The softest phonation was softer ($t = 2.795$, $df = 13$, $p = 0.015$) with a HME, but the loudest phonation was louder with the FreeHands HME ($t = 2.795$, $df = 13$, $p = 0.015$, paired samples test).

A text was read aloud and recorded for perceptual evaluation by a panel of five speech pathologists. Among the aspects evaluated were the usefulness of the voice ($p < 0.001$) and intelligibility of speech ($p = 0.007$, two-way analysis of variance test), both of which were better when using a HME.

The 15D score reflecting overall HRQoL was 0.877 in our patients and 0.884 in age- and gender-matched controls from the general Finnish population (n.s.). Compared to the controls, total laryngectomy patients had more problems with breathing ($p = 0.006$), eating ($p < 0.001$), speaking ($p = 0.019$), and sexual activity ($p = 0.022$, Mann-Whitney test).

II Swallowing, hoarseness and health-related quality of life before and after anterior cervical decompression

The aim of the study was to evaluate the appearance, duration and severity of dysphonia and dysphagia after ACD. Altogether, 114 patients entered the study, 50 of whom were examined immediately pre- and post-operatively (early group) and 64 at 3–9 months post-operatively (late group). As controls for the early group, we examined 50 age- and gender-matched subjects.

Pre-operative findings

No marked dysphonia, dysphagia, or pathological clinical signs appeared in either patient or control groups. The function of cranial nerves IX–XII was normal in all subjects.

Immediate post-operative results, median first post-operative day (early group)

Of the 50 patients, 30 (60%) reported dysphonia and 69% (34 of 49) dysphagia in the immediate post-operative examination (measured by VAS, results under 20 considered non-significant and eliminated). Unilateral vocal cord paresis was found in six (12%). All the pareses occurred on the operated right side. In the control group, 12 (24%) reported dysphonia and four (8%), dysphagia. A significant difference appeared in both dysphonia ($p < 0.0005$, Fisher) and dysphagia ($p < 0.0001$, Fisher) between the early group and controls.

Results 3 to 9 months post-operatively

Patients in the early group received a questionnaire 3 months after the operation. Those with clinical findings in the first post-operative visit or who reported severe subjective symptoms in the questionnaire were invited for another visit. All patients in the late group were examined 3 to 9 months post-operatively.

Seven percent (3/44) of those in the early group and 21% (13/62) of the patients in the late group reported persistent dysphonia. In the early group, all six vocal cord pareses had recovered both clinically and in videolaryngostroboscopy. In the late group, two patients (3%) had a unilateral right-sided vocal cord paralysis. One was well compensated in videolaryngostroboscopy and the patient was satisfied with his voice, but the other required phonosurgery.

Twelve percent (5/43) of those in the early group and 15% (9/62) of patients in the late group had persistent dysphagia.

Surgical Results

The median duration of the operation was 80 minutes (range 35–205). The right-sided approach was used in 75 (68%) operations and the left in 32 (29%). Eighty-one (74%) operations were performed in one disc space.

No statistically significant difference appeared between immediate or persistent dysphonia or dysphagia and the disc space level, number of disc spaces, approach side of the surgery, duration of the operation, the surgeon, the age or gender of the patient, or whether the diagnosis was spondylosis or disc herniation. This was also true for the patients with vocal cord paralysis.

Post-operative laryngeal EMG and videolaryngostroboscopy findings

Laryngeal needle EMG of both thyroarythenoid muscles was successfully performed on all 16 patients with dysphonia. A moderate neurogenic abnormality in EMG existed in nine patients (including two patients with permanent vocal cord

paresis), and some neurogenic signs and asymmetry in five. Two results were graded as normal.

A phoniatician performed videolaryngostroboscopy in nine patients with hoarseness but no clinical paresis. Of these, the findings from seven patients were normal, and two showed very mild vocal cord movement asymmetry. Of these two patients, one was in the group of “moderate” and the other in “some neurogenic abnormality” in laryngeal EMG. Grading of the damage in EMG was based on a quantitative turn analysis (Stalberg, Chu et al. 1983) and visual scale.

Swallowing

Functional studies of swallowing were performed on two early-group and six late-group patients of the 14 who reported persistent dysphagia 3 to 9 months post-operatively. The dysphagia disability index (DDI) questionnaire (Silbergleit, Jakobson et al. 1997) for evaluation of the subjective dysphagia complaints showed pathological results in only one patient. Six patients had normal and two had pathological findings in transoral endoscopic evaluation of swallowing. Videofluorography was performed on four patients (all from the late group). The results were normal in three patients, and one patient’s bolus movement was slightly slowed.

Health related quality of life assessed by the 15D

In the early group, the mean (SD) 15D score increased from the preoperative stage to 3 months post-operatively, but not significantly ($p = 0.199$, Student’s t-test). For the dimension of discomfort and symptoms, however, the patients experienced significant ($p = 0.017$) improvement. At the 3-month follow-up, the improved 15D score of the patients no longer differed significantly from that of the general population or controls ($p = 0.519$).

In the late group, the mean 15D score was significantly worse ($p < 0.001$) than for the age- and gender-matched general Finnish population. Questionnaires with three or more unanswered questions were eliminated.

III Voice quality and videolaryngostroboscopy: long-term results after injection laryngoplasty with autologous fascia

The aim of the study was to evaluate the long-term stability of the single fascia injection of the vocal cord as a treatment for unilateral vocal cord paralysis. Patients with fascia injection as the first and only phonosurgical procedure were included. Forty-three patients entered the study and the median duration of the follow-up was 5.8 years (range 3.3–10.0 years).

The improvement after the phonosurgery was statistically significant ($p < 0.01$, Wilcoxon) in all domains except strain in GRBAS, perceptually evaluated. In acoustic analysis, the average proportion of jitter was significantly reduced from 5.25% to 2.61% ($p < 0.01$, Wilcoxon). There was no statistically significant change in the average shimmer or in NHR. Post-operative videolaryngostroboscopy revealed completed or partial glottal closure in 83% of patients. Mucosal wave symmetry was seen in every cycle or in most of the cycles in 74% of patients, and the mucosal wave amplitude symmetry in 58% of patients. The mean post-operative VHI score was 35 (median 29). The VHI was below 30 in 24/43 patients (56%) and 9/43 patients considered their voice to be poor (VHI over 60). The VHI scale ranges from 0 to 120.

Analysis of single acoustic and perceptual parameters and VHI scores showed that delay from the onset of paralysis to injection laryngoplasty and the length of the follow-up had no effect on the results. Neither had the age any influence on the results. In perceptual evaluation, a severely disturbed pre-operative voice correlated with a poor outcome (Spearman 0.404, $p < 0.05$). The patients whose paralysis was caused by chest surgery ($N = 7$) showed results clearly below the average.

IV Dyspnea during an exercise test

The aim of the study was to develop a new tool for the challenging diagnostics of exercise-induced dyspnea, appropriate for a laryngeal out-patient department and suitable for patients of various ages and physical conditions by combining fiberoptic videolaryngoscopy with a bicycle exercise test. Thirty patients with a suspicion of EIVCD entered the study.

For all age groups, the test was relatively easy to perform and well tolerated. We had 3 patients in the age group ≥ 60 years and 8 patients ≤ 16 years, and the youngest one was a 10-year-old female. The test was successfully performed by 27 (90%) patients and all controls. Three of the 30 patients interrupted the test: one patient's laryngeal spasm was triggered by FEV1 measurement, another experienced a panic attack during the preparation phase, and the third patient's test was interrupted by vasovagal collapse during local anesthesia of the nose.

Laryngeal anatomy and function before exercise test was normal in all patients. During the test, the typical dyspnea in their history could be induced in 15 (56%) of the patients. Of these, 9 (60%) had EIVCD ($n = 5$) or a high suspicion of EIVCD ($n = 4$), showing collapse of arytenoids and aryepiglottic folds toward the aditus of the larynx; in 5 EIVCD patients, this supraglottic collapse was followed by adduction

of the vocal cords. Inspiratory stridor was audible during the subjective symptom of dyspnea in all these 9 patients. In addition, our test identified one patient with ST-level changes in the ECG, which revealed a cardiovascular disease in further examinations. In 13/15 (87%) controls, slight and fast physiological adduction of the vocal cords without respiratory symptoms was observed during expiration soon after starting the test. This was only briefly seen and did not narrow the glottic level considerably.

DISCUSSION

In this work we studied breathing, swallowing and the voice in four patient groups with different laryngeal disorders. The basis of this work was purely clinical, and through it we obtained many answers to questions of interest in a laryngeal outpatient clinic. In addition, we developed a new diagnostic method for exercise-induced dyspnea. Our four study groups consisted of patients who had undergone total laryngectomy, ACD or ILAF, and patients with suspected EIVCD.

Breathing (I,IV)

Breathing was affected in two of our studies (I, IV). In study I, the patients reported breathing to be heavier with the Provox FreeHands HME in comparison to the normal HME. In study IV, we provoked a dyspnea attack in 15/27 patients using an ergometer test. Five of these patients were diagnosed as having EIVCD, and four patients showed pathological findings related only to supraglottical structures during exercise.

Breathing after total laryngectomy with the Provox FreeHands HME (Study I)

Breathing physiology radically changes after total laryngectomy due to the loss of nasal and laryngeal functions. The inhaled air goes directly to the trachea via a permanent tracheostomy, and it is recommended to be moisturized and warmed through a HME device.

All but one of our patients reported the FreeHands HME to be useful and an easy-to-use additional device for special occasions when both hands were needed for tasks other than closing the stoma (e.g. fishing, driving a car, dining). These patients represented only 18% of the laryngectomized patients operated on over a period of 8 years at Helsinki University Central Hospital. However, these selected patients with a history of successful use of a traditional speaking valve often reported problems associated with the FreeHands HME, mainly reflecting the heavier work in breathing and speaking.

In line with earlier studies (Armstrong, Isman et al. 2001, Schuster, Lohscheller et al. 2003), the overall HRQoL in our patients was not notably reduced. Parameters

concerning eating, speaking, breathing and sexual activities showed significantly lower scores in patients than in controls. In our study, the 15D questionnaire (Sintonen 2001) was used because it has been extensively validated in Finland. Being a general questionnaire, it allows comparison of the results with other disease groups, and it also contains questions especially relevant to laryngectomized patients.

The reasons for the good outcome with the FreeHands HME and the HRQoL among the patients can be related to the better adhesion of the base plate due to a symmetrical neck (only two patients had undergone radical neck dissection), the optimal size and position of the prosthesis, and a good general condition: five (36%) of the patients were still working and nine (64%) actively participated in the activities of the organization of laryngectomees.

The manufacturer's recommendation for the distance between the center of the tracheo-esophageal fistula and skin-mucosal border is 5 mm. In our patients, this distance varied considerably, but did not seem to have an effect on prosthesis function.

A weakness of our study was the small and selected patient population, and the overall result could be weaker if the patients were unselected. On the other hand, our results concerning speaking and breathing were in line with a previous study (Hilgers, Ackerstaff et al. 2003).

Our review of the literature in 2005 revealed very few publications concerning automatic speaking valves, and this is still true in 2011. Because the existing "hands-free" devices in speech rehabilitation after total laryngectomy are far from optimal, but still appreciated by the patients, further product development is necessary.

Exercise-induced breathing difficulties: presentation of a new diagnostic method (Study IV)

Continuous transnasal fiberoptic videolaryngoscopy during bicycle ergometry proved a well-tolerated and relatively easily performed diagnostic method for exercise-induced dyspnea. It could be performed on patients in different age groups (10–69 years) and with different physical conditions. It is possible to establish a test setting in an ordinary laryngeal out-patient department at the relatively low extra cost of a stationary bicycle, ECG monitor and FEV₁ measuring equipment. Our protocol with a slowly increasing work load was suitable for elderly patients, but younger and more athletic patients needed the fast unlimited pedaling at the end of the test to generate the work load at which the symptoms typically occur. In comparison with the test of Heimdal et al. (Heimdal, Roksund et al. 2006), the benefit of our test is

that it can be performed on patients of different age groups and physical conditions. In addition, the set-up is technically less demanding, and space requirements favor an ergometer as compared with a treadmill in often-crowded facilities.

In line with previous studies, our patients stated that exercise-induced dyspnea does not appear identically every time, even if the level, mode, and the surroundings of the exercise are the same (Wood and Milgrom 1996). This leads us to the conclusion that most probably no single optimal way to test EIVCD exists, and variations in the testing method in different surroundings might be required for this complicated diagnostics. Therefore, in this series a negative test result did not rule EIVCD out, but a positive result ruled it in.

In line with previous reports, EIVCD findings resolved within a few seconds when the exercise slowed or stopped (Rundell and Spiering 2003). This again confirms the value of direct visualization of the vocal cords during the symptoms in the diagnosis of laryngeal dyspnea (Heimdal, Roksund et al. 2006, Morris, Deal et al. 1999, Rundell and Spiering 2003, Wood and Milgrom 1996). On the other hand, the patient's subjective feeling of dyspnea at the laryngeal level was not always accurate: 6 (40%) of the patients who reported subjective laryngeal dyspnea had a wide-open larynx, visualized simultaneously in fiberoptic videolaryngoscopy.

In all five confirmed EIVCD patients, the laryngeal signs began with the collapse of the posterior supraglottic structures and aryepiglottic folds, followed by adduction of the vocal cords. Four other patients, considered highly suspicious of EIVCD, also showed supraglottic adduction without progression to vocal cord adduction. A large study (Roksund, Maat et al. 2009) using a treadmill test with successful laryngeal observation in 151 patients showed similar supraglottic adduction followed by glottic adduction in 88/109 (81%) patients, and in 21/109 (19%) patients adduction was confined to supraglottic structures only. Slight medial rotation of the cranial edge of the cuneiform tubercles without respiratory symptoms was observed in 8/20 (40%) healthy control group subjects at maximum exercise and classified as negative test result. In our study, 87% of the controls showed mild physiological adduction of the vocal cords without respiratory symptoms during expiration at the beginning of test, but no findings during inspiration could be seen. Our study lacked a scoring system introduced by Roksund et al. (Roksund, Maat et al. 2009)

In line with previous studies, we had a dominance of female patients, and co-existing asthma was diagnosed in almost half the patients (Altman, Mirza et al. 2000). The figure of 19% (5/27) of patients with established EIVCD in our study represented a low prevalence. However, the typical symptom of dyspnea only appeared in 15

patients during the test. This result may reflect the limited sensitivity of our test, but perhaps also the difficulties in diagnosing exercise-induced dyspnea. It is also possible that some of those 12 patients without symptoms during the test could have been diagnosed with a treadmill test. It would be interesting to examine a larger series of patients, with a more individual protocol, and even by performing both tests on each patient.

Although examined by many physicians specialized in airway problems, those with exercise-induced dyspnea, not being asthma or EIA, often remain without an accurate diagnosis.

There was no clinically relevant test method for EIVCD before the one introduced by Heimdal et al. Using their test set-up or ours will definitely improve the diagnostic accuracy of EIVCD. Moreover, while many EIVCD patients have been misdiagnosed as having asthma, the severe side effects of high dose corticosteroids and other asthma drugs can through these tests be avoided.

Swallowing (II)

Swallowing was affected in studies I,II, and IV. Dysphagia was our main interest in study II, in which it was triggered by ACD surgery. In studies I and IV, swallowing difficulties were rather a side finding that was not further investigated.

Dysphagia after anterior cervical decompression (II)

Consistently with earlier studies, the incidence of dysphagia after ACD ranged from 12% to 69%. Functional studies of swallowing showed good results, with only minor findings in DDI, videofluorography, and transoral endoscopic evaluation and no signs of aspiration could be detected. Immediately after surgery, the number of patients complaining of dysphagia was large (69%), and this was unquestionably partly caused by the tissue swelling, as also suggested by Frempong-Boadu et al. (Frempong-Boadu, Houten et al. 2002). A population-based study found the overall prevalence of dysphagia to be 13.5% (Locke, Talley et al. 1997). Considering this, the prevalence of 8% in the control group and 12–15% in the patient groups during the later examination were in line with the overall prevalence of dysphagia in the population.

Evaluated with the VAS, the subjective handicap caused by dysphagia varied widely. The use of the VAS has been confidently recommended as a reliable method for reporting pain and other symptoms (Price, McGrath et al. 1983), and has earlier been used to evaluate swallowing and hoarseness (de Swart, van der Sluijjs et al. 2006, Uloza, Pribuisiene et al. 2005).

In line with many previous studies, none of the surgical variables evaluated such as the operated disc level, number of disc spaces operated on, laterality, surgeon, operation time, patient age or sex, or the diagnosis had a significant impact on risk of dysphagia. Moreover, the majority of the patients were satisfied with the surgical results. Unlike the overall health related quality of life measured by 15D, the dimension “discomfort and symptoms” improved significantly.

Voice (I-III)

The voice was a focus of our interest in all the studies (I-IV). In study IV, hoarseness during a dyspnea attack was reported by half of the patients, but this finding was not further examined in this study setting.

Rehabilitation of speech with the Provox FreeHands HME after total laryngectomy (I)

All but one of the patients reported the FreeHands HME to be a useful and easy-to-use additional device, even though half of the patients found speaking with it to be heavier. This finding is in line with a previous study (Hilgers, Ackerstaff et al. 2003).

The handicap caused by a persistent tracheostoma and prosthetic voice in our series was limited, perhaps partly due to the fact that all our patients were males. Female features of the voice are reported to be even harder to produce with a voice prosthesis (Eadie and Doyle 2004). Our patients were able to communicate on the telephone and in noisy surroundings, but their ability to shout was limited. However, the loudest phonation was louder with the FreeHands HME than with the traditional HME.

Dysphonia after anterior cervical decompression (II)

To our knowledge, this study was the largest one concerning the incidence and appearance of, and recovery from dysphonia and dysphagia after ACD. Moreover,

the health related quality of life was assessed. The literature on this topic is scarce; many of the previous studies have been retrospective, had small patient groups, and lacked controls. None of the previous studies used laryngeal EMG to identify the degree of nerve damage. A weakness of our study is that the early and late group patients were not the same, although they were operated on in the same hospital by the same surgeons. Perhaps the worse results in the late group were caused by possible under-representation of patients satisfied with the surgical outcome.

Earlier studies have shown that the prevalence of permanent dysphonia after ACD ranges from 0.07% to 11% (Beutler, Sweeney et al. 2001), whereas in our study the range was from 7% to 21%. It was recently reported that the incidence of dysphonia in the general population is 6.6% (Roy, Merrill et al. 2005). In our control group, 24% of the patients reported dysphonia. This prevalence was high, and the reason is unclear, but one explanation may be that our controls were hospital outpatients. Moreover, in the early group, none of the patients reported pre-operative dysphonia. We assume that immediately before the surgery, such mild dysphonia may have been overwhelmed by pain and other more severe symptoms.

The degree of recurrent nerve damage evaluated by laryngeal EMG varied widely in patients with clear clinical symptoms. Moreover, the clinical relevance of the minor EMG changes is unknown. It would be interesting to repeat this examination in a larger series, also including EMG in the pre-operative protocol.

The incidence of vocal cord paresis in our series was 12% (6/50). In all of the cases the paresis was on the right side, supporting previous findings of anatomical factors increasing the risk for damage on the right-sided recurrent nerve (Smith-Hammond, C.A., Davenport et al. 1997, Weisberg, Spengler et al. 1997). On the other hand, most of the surgeons also preferred the right-sided approach (approach from the right was used in 68% of the operations). All the six vocal cord paresis found in the early group recovered during the follow-up period of 3 months. In the late group, two cases of permanent right-sided vocal cord paralysis occurred. Both of these patients had been operated on 9 months earlier. One patient's paralysis was well compensated, whereas the other's needed a vocal cord medialization to improve voice quality. These two patients had not been examined pre-operatively, but neither had reported hoarseness before the operation.

In line with many previous studies, none of the surgical variables, patient age or sex, or the diagnosis had a significant impact on the risk of dysphonia.

Vocal cord paresis is also a well-known complication in thyroidectomy. The incidence of permanent paresis after thyroidectomy ranges from 0% to 5.8%, and that of temporary paresis from 1.5% to 14% (Doikov, Yovchev et al. 2001, Lo, Kwok et al. 2000). It was reported that many patients with vocal cord paresis had only very mild symptoms, and concluded that the incidence may be higher if thyroidectomy patients are examined routinely (Lo, Kwok et al. 2000). In a recent study that evaluated vocal cord motion before thyroid surgery, 32% of the patients with vocal cord motion impairment were asymptomatic, and pre-operative examination of the vocal cords was strongly recommended (Farrag et al. 2006). Because the incidence of vocal cord paresis in our study was similar to that reported in thyroidectomy, laryngeal examination pre- and post-operatively should possibly be considered.

Reconstruction of the voice in unilateral vocal cord paralysis by injection laryngoplasty with autologous fascia (III)

In our series of 43 patients, the perceptual assessment of the voice showed a significant improvement in grade, roughness, breathiness and asthenia. This is in line with earlier short-term studies on injection laryngoplasty with fascia (Saarinen, Sovijarvi et al. 2007). In our study, the long-term result could be considered successful in 60% (26 of 43) of the patients when subjective (VHI) and objective (GRBAS) auditive voice assessments were combined.

Subjectively, 56% of patients reported their handicap due to voice disorder to be near normal (VHI <30), the mean VHI score at the follow-up visit being 35. This agrees with another series with fascia, where patients assessed a mean VHI score of 69 preoperatively and 38 seven months after the procedure (Saarinen, Sovijarvi et al. 2007).

However, measured by acoustic analysis, the results were not as good as those reported earlier in short-term studies with autologous fascia. The earlier study showed a statistically significant improvement in jitter, shimmer and the noise-to-harmonic ratio 9 months after a similar procedure (N = 40) (Duke, Salmon et al. 2001). Good acoustic results were also shown in another series of UVCP patients (N = 11) treated with fascia, analyzed 7 months after the procedure (Saarinen, Sovijarvi et al. 2007). In our study, jitter was significantly better at the follow-up visit 5.8 years later, but shimmer and the noise-to-harmonic ratio did not show an improvement. In elderly patients, the acoustic characteristics of the voice may have naturally ceased during the follow-up. Moreover, the two different recording facilities (booths, microphones, digital tape recorders) and different instructors

(nurses, speech-language pathologists) when taping the voice samples may also have had an impact on the results of acoustic analysis.

Several patients (20%) had died of causes other than injection laryngoplasty during the long follow-up. A similar amount of patients (19%) refused to participate or were lost to follow-up. It is also possible that patients who attended the follow-up visit years after the surgery were patients with voice problems, and the ones without problems did not participate.

Thyroplasty type I can be considered as the gold standard for UVCP. However, long-term studies with a follow-up period longer than 12 months are also scarce for this procedure. A study with 26 UVCP patients treated with thyroplasty type I compared short-term 1-month and long-term 12-months results. Based on significant differences in the mean glottal flow rate, maximum phonation time (MPT) and acoustic parameters, it was concluded that maximum improvement was attained within 1 month of surgery (Lundy, Casiano et al. 2000). Another study reported results from 16 patients with UVCP treated with thyroplasty type I. The patients were followed for 1–7 years (mean 26 months). The results measured by perceptual evaluation, acoustic analysis and MPT were excellent and continued to improve after 6 months (Dursun, Boynukalin et al. 2008). Dursun et al. also reported a mean grade reduction (GRBAS) of 1.68 points, while in our series with fascia it was 0.6 points.

In our series with fascia, the result in an individual patient was hard to predict, even if the mean vocal parameters evaluated showed improvement. This could be due to fact that even patients with severe glottal insufficiency were not excluded from the study, but also partly because of the variable graft yield. Injection laryngoplasty with fascia is not suitable for wide glottal gaps, especially those related to intrathoracic lesions.

CONCLUSIONS

Based on studies I-IV, the following conclusions were drawn:

1. The automatic speaking valve was a useful additional device for selected patients. Taking into account breathing- and speaking-related problems, and also the relatively high cost of this automatic speaking valve, it seems to be unsuitable as the sole speech-rehabilitation tool for laryngectomized patients. The overall health related quality of life of the patients was not significantly lower than in the normal population.
2. Swallowing and voice problems related to anterior cervical decompression were common but usually transient complications, often present even months after surgery. The majority of the patients were satisfied with their neurological outcome. The health related quality of life in early group patients after the surgery did not differ from that in the general population. In the late group, the mean 15D score was significantly worse than that of the age- and gender-matched general population
3. The long-term follow-up results of autologous fascia injection of the vocal cord remain stable over 3-10 years. The results were not dependent on the delay from the onset of paralysis to the surgery, or the length of the follow-up period after the surgery. Wide glottal insufficiencies were not suitable for fascia injection, whereas minor glottal gaps can be well treated with it.
4. Fiberoptic videolaryngoscopy during bicycle ergometry was a well tolerated and relatively easily established diagnostic tool for laryngeal dyspnea. It induced dyspnea in more than half of the patients examined. If the symptom of dyspnea appeared, the most frequent finding was exercise-induced vocal cord dysfunction. The test was suitable for a laryngeal outpatient department and applicable to patients of various ages and physical conditions.

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REFERENCES

- Abu-Hasan, M., Tannous, B., et al. (2005). "Exercise-induced dyspnea in children and adolescents: if not asthma then what?" *Ann Allergy Asthma Immunol* 94(3):366-71
- Ackerstaff, A. H., Hilgers, F. J., et al. (1998). "Long-term compliance of laryngectomized patients with a specialized pulmonary rehabilitation device: Provox Stomafilter." *Laryngoscope* 108(2):257-60
- Ackerstaff, A. H., Hilgers, F. J., et al. (1995). "Long-term pulmonary function after total laryngectomy." *Clin Otolaryngol Allied Sci* 20(6):547-51
- Altman, K., Mirza, N., et al. (2000). "Paradoxical vocal fold motion: Presentation and treatment options." *J Voice* 14(1):99-103
- Amir, O., Tavor, Y., et al. (2006). "Evaluating the validity of the Voice Handicap Index-10 (VHI-10) among Hebrew speakers." *Otolaryngol Head Neck Surg* 135(4):603-7
- Armstrong, E., Isman, K., et al. (2001). "An investigation into the quality of life of individuals after laryngectomy." *Head Neck* 23(1):16-24
- Ayres, J. and Gabbot, P. (2002). "Vocal cord dysfunction and laryngeal hyperresponsiveness: a function of altered autonomic balance?" *Thorax* 57(4):284-85
- Bailey, R. and Badgley, C. (1960). "Stabilization of the cervical spine by anterior fusion." *J Bone Joint Surg Am* Volume 42(A):565-94
- Bazaz, R., Lee, M. J., et al. (2002). "Incidence of dysphagia after anterior cervical spine surgery: a prospective study." *Spine* 27(22):2453-8
- Behrman, A. (2004). "Evidence-based treatment of paralytic dysphonia: making sense of outcomes and efficacy data." *Otolaryngol Clin North Am* 37(1):75-104
- Benninger, M. S., Ahuja, A. S., et al. (1998). "Assessing outcomes for dysphonic patients." *J Voice* 12(4):540-50
- Ben, J., Kim, J., et al. (1996). "Pediatric exercise-induced laryngomalacia." *Ann Otol Rhinol Laryngol* 105(3):169-75
- Beutler, W. J., Sweeney, C. A., et al. (2001). "Recurrent laryngeal nerve injury with anterior cervical spine surgery risk with laterality of surgical approach." *Spine* 26(12):1337-42
- Bielamowicz, S., Kreiman, J., et al. (1996). "Comparison of voice analysis systems for perturbation measurement." *J Speech Hear Res* 39(1):126-34
- Blakley, B. W. and Podraza, B. L. (1987). "Acoustic and perceptual assessment of speech using a voice-prosthesis with valvular and manual occlusion." *Otolaryngol Head Neck Surg* 97(6):552-7
- Bless, D. M., Hirano, M., et al. (1987). "Videostroboscopic evaluation of the larynx." *Ear Nose Throat J* 66(7):289-96
- Blom, E. D., Singer, M. I., et al. (1982). "Tracheostoma valve for postlaryngectomy voice rehabilitation." *Ann Otol Rhinol Laryngol* 91(6 Pt 1):576-8
- Bowden, R. (1974). "Innervation of intrinsic laryngeal muscles. In: Wyke B, ed." *Ventilatory and Phonatory Control Systems*. London: Oxford University Press
- Boyce, R. G., Nuss, D. W., et al. (1994). "The use of autogenous fat, fascia, and nonvascularized muscle grafts in the head and neck." *Otolaryngol Clin North Am* 27(1):39-68
- Brancatisano, T. P., Dodd, D. S., et al. (1984). "Respiratory activity of posterior cricoarytenoid muscle and vocal cords in humans." *J Appl Physiol* 57(4):1143-9
- Brandenburg, J. H., Kirkham, W., et al. (1992). "Vocal cord augmentation with autogenous fat." *Laryngoscope* 102(5):495-500
- Broder, K. W. and Cohen, S. R. (2006). "An overview of permanent and semipermanent fillers." *Plast Reconstr Surg* 118(3 Suppl):7S-14S
- Brunton, T. L. and Cash, T. (1883). "The Valvular Action of The Larynx." *J Anat Physiol* 17(Pt 3):363-78
- Bucca, C., Rolla, G., et al. (1991). "Histamine hyperresponsiveness of the extrathoracic airway in patients with asthmatic symptoms." *Allergy* 46(2):147-53
- Chin, D., Boyle, G. M., et al. (2006). "Head and neck cancer: past, present and future." *Expert Rev Anticancer Ther* 6(7):1111-8
- Clarence, T. and Sasaki, M. D. (2006). "Anatomy and development and physiology of the larynx." *GI Motility online*
- Cloward, R. B. (1958). "The anterior approach for the removal of ruptured cervical disks." *J Neurosurg* 15(6):602-17
- Colton, R. and Casper, J. (1996). "Understanding voice problems: a physiological perspective for diagnosis and treatment." Philadelphia, Lippincott Williams & Wilkins 358

- Cummings, C. W., Purcell, L. L., et al. (1993). "Hydroxylapatite laryngeal implants for medialization. Preliminary report." *Ann Otol Rhinol Laryngol* 102(11):843-51
- Daniels, S. K., Mahoney, M. C., et al. (1998). "Persistent dysphagia and dysphonia following cervical spine surgery." *Ear, Nose, & Throat Journal* 77(6):473-5
- De Bondt, M. S., Wuyts, F. L., et al. (1997). "Test-retest study of the GRBAS scale: influence of experience and professional background on perceptual rating of voice quality." *J Voice* 11(1):74-80
- de Swart, B. J. M., van der Sluijs, B. M., et al. (2006). "Ptosis aggravates dysphagia in oculopharyngeal muscular dystrophy." *J Neurol Neurosurg Psychiatry* 77(2):266-68
- Dejonckere, P. H., Bradley, P., et al. (2001). "A basic protocol for functional assessment of voice pathology, especially for investigating the efficacy of (phonosurgical) treatments and evaluating new assessment techniques. Guideline elaborated by the Committee on Phoniatrics of the European Laryngological Society (ELS)." *Eur Arch Otorhinolaryngol* 258(2):77-82
- Doikov, I. Y., Yovchev, I., et al. (2001). "Microsurgical technique as a method for prevention of recurrent laryngeal nerve injury in thyroid surgery. Review of seven consecutive cases." *Folia Medica* 43(4):5-9
- Duke, S. G., Salmon, J., et al. (2001). "Fascia augmentation of the vocal fold: graft yield in the canine and preliminary clinical experience." *Laryngoscope* 111(5):759-64
- Dursun, G., Boynukalin, S., et al. (2008). "Long-term results of different treatment modalities for glottic insufficiency." *Am J Otolaryngol* 29(1):7-12
- Eadie, T. L. and Doyle, P. C. (2004). "Auditory-perceptual scaling and quality of life in tracheoesophageal speakers." *Laryngoscope* 114(4):753-9
- Ebraheim, N. A., Lu, J., et al. (1996). "Vulnerability of vertebral artery in anterolateral decompression for cervical spondylosis." *Clinical Orthopaedics & Related Research* Jan(322):146-51
- Emerick, K. S., Tomycz, L., et al. (2009). "Primary versus secondary tracheoesophageal puncture in salvage total laryngectomy following chemoradiation." *Otolaryngol Head Neck Surg* 140(3):386-90
- Eppley, B. L. and Dadvand, B. (2006). "Injectable soft-tissue fillers: clinical overview." *Plast Reconstr Surg* 118(4):98e-106e
- Frempong-Boadu, A., Houten, J. K., et al. (2002). "Swallowing and speech dysfunction in patients undergoing anterior cervical discectomy and fusion: a prospective, objective preoperative and postoperative assessment." *J Spinal Disord Tech* 15(5):362-8
- Friedrich, G. (1999). "Titanium vocal fold medializing implant: introducing a novel implant system for external vocal fold medialization." *Ann Otol Rhinol Laryngol* 108(1):79-86
- Fukuda, H., Sasaki, C. T., et al. (1973). "Vagal afferent influences on the phasic activity of the posterior cricoarytenoid muscle." *Acta Otolaryngol* 75(2):112-8
- Greene, M. and Lesley, M. (2001). "The Voice and its Disorders." John Wiley&Sons; 6th Edition 13, 978-
- Hagen, R., Schwarz, C., et al. (2001). "[Tracheostomy valve with integrated cough flap for improving hands-free speech in laryngectomized patients-development and clinical applications]." *Laryngorhinootologie* 80(6):324-8
- Heimdal, J.-H., Roksund, O., et al. (2006). "Continuous laryngoscopy during exercise test: A method for visualizing laryngeal dysfunction during exercise." *Laryngoscope* 116(1):52-57
- Heitmiller, R. F., Tseng, E., et al. (2000). "Prevalence of aspiration and laryngeal penetration in patients with unilateral vocal fold motion impairment." *Dysphagia* 15(4):184-7
- Herrmann, I. F. (1987). "[Secondary surgical voice rehabilitation]." *Hno* 35(8):351-4
- Hess, M. M., Schwenk, R. A., et al. (1999). "Pulmonary function after total laryngectomy." *Laryngoscope* 109(6):988-94
- Heuer, R. J., Sataloff, R. T., et al. (1997). "Unilateral recurrent laryngeal nerve paralysis: the importance of "preoperative" voice therapy." *J Voice* 11(1):88-94
- Hilgers, F. J., Ackerstaff, A. H., et al. (2003). "Development and clinical assessment of a heat and moisture exchanger with a multi-magnet automatic tracheostoma valve (Provox FreeHands HME) for vocal and pulmonary rehabilitation after total laryngectomy." *Acta Otolaryngol* 123(1):91-9
- Hirano, M. (1981). "Clinical Examination of Voice." New York Springer-Verlag
- Hirano, M. (1989). "Objective evaluation of the human voice: clinical aspects." *Folia Phoniatr (Basel)* 41(2-3):89-144
- Hoffman, M. R., Witt, R. E., et al. (2010). "Multiparameter comparison of injection laryngoplasty, medialization laryngoplasty, and arytenoid adduction in an excised larynx model." *Laryngoscope* 120(4):769-76
- Hogikyan, N. D. and Sethuraman, G. (1999). "Validation of an instrument to measure voice-related quality of life (V-RQOL)." *J Voice* 13(4):557-69
- Horiuchi, M. and Sasaki, C. T. (1978). "Cricothyroid muscle in respiration." *Ann Otol Rhinol Laryngol* 87(3 Pt 1):386-91
- Hsiung, M. W., Lu, P., et al. (2003). "Measurement and validation of the voice handicap index in voice-disordered patients in Taiwan." *J Laryngol Otol* 117(6):478-81

- http://www.asha.org/about/membership-certification/divs/div_3.htm. "American Speech-Language-Hearing Association: Consensus auditory-perceptual evaluation of voice (CAPE-V)."
- Isshiki, N. (1998). "Mechanical and dynamic aspects of voice production as related to voice therapy and phonosurgery." *J Voice* 12(2):125-37
- Isshiki, N., Morita, H., et al. (1974). "Thyroplasty as a new phonosurgical technique." *Acta Otolaryngol* 78(5-6):451-7
- Isshiki, N., Tanabe, M., et al. (1978). "Arytenoid adduction for unilateral vocal cord paralysis." *Arch Otolaryngol* 104(10):555-8
- Jacobson, B. H., Johnson, A., et al. (1997). "The voice handicap index (VHI). Development and validation." *Am J Speech Lang Pathol* 6:66-70
- Johannessen, A., Lehmann, S., et al. (2006). "Post-bronchodilator spirometry reference values in adults and implications for disease management." *Am J Respir Crit Care Med* 173(12):1316-25
- Karnell, M. P., Melton, S. D., et al. (2007). "Reliability of clinician-based (GRBAS and CAPE-V) and patient-based (V-RQOL and IPVI) documentation of voice disorders." *J Voice* 21(5):576-90
- Kaszuba, S. M. and Garrett, C. G. (2007). "Stroboscopy and laboratory voice evaluation." *Otolaryngol Clin North Am* 40(5):991-1001
- Kenn, K., Willer, G., et al. (1997). "Prevalence of vocal cord dysfunction in patients with dyspnea. First prospective clinical study." *Am J Respir Crit Care Med* 155:965
- Koizumi, H. (1953). "On sensory innervation of larynx in dog." *Tohoku J Exp Med* 58(3-4):199-210
- Koufman, J. A. (1986). "Laryngoplasty for vocal cord medialization: an alternative to Teflon." *Laryngoscope* 96(7):726-31
- Kreiman, J. and Gerratt, B. R. (2000). "Sources of listener disagreement in voice quality assessment." *J Acoust Soc Am* 108(4):1867-76
- Kwon, T. K. and Buckmire, R. (2004). "Injection laryngoplasty for management of unilateral vocal fold paralysis." *Curr Opin Otolaryngol Head Neck Surg* 12(6):538-42
- Laccourreye, O., Papon, J. F., et al. (2003). "Intracordal injection of autologous fat in patients with unilateral laryngeal nerve paralysis: long-term results from the patient's perspective." *Laryngoscope* 113(3):541-5
- Langmore, S. E., Schatz, K., et al. (1988). "Fiberoptic endoscopic examination of swallowing safety: a new procedure." *Dysphagia* 2(4):216-9
- Lo, C.-Y., Kwok, K.-F., et al. (2000). "A prospective evaluation of recurrent laryngeal nerve paralysis during thyroidectomy." *Archives of Surgery* 135(2):204-07
- Locke, G. R., 3rd, Talley, N. J., et al. (1997). "Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota." *Gastroenterology* 112(5):1448-56
- Lundy, D. S., Casiano, R. R., et al. (2000). "Thyroplasty type I: short- versus long-term results." *Otolaryngol Head Neck Surg* 122(4):533-6
- Ma, E. P. and Yiu, E. M. (2001). "Voice activity and participation profile: assessing the impact of voice disorders on daily activities." *J Speech Lang Hear Res* 44(3):511-24
- Makitie, A. A., Niemensivu, R., et al. (2003). "Postlaryngectomy voice restoration using a voice prosthesis: a single institution's ten-year experience." *Ann Otol Rhinol Laryngol* 112(12):1007-10
- Martins, A. N. (1976). "Anterior cervical discectomy with and without interbody bone graft." *J Neurosurg* 44(3):290-5
- Mathers-Schmidt, B. and Brilla, L. (2005). "Inspiratory muscle training in exercise-induced paradoxical vocal fold motion." *J Voice* 19 (4):635-44
- McCulloch, T. M., Andrews, B. T., et al. (2002). "Long-term follow-up of fat injection laryngoplasty for unilateral vocal cord paralysis." *Laryngoscope* 112(7 Pt 1):1235-8
- McCulloch, T. M. and Hoffman, H. T. (1998). "Medialization laryngoplasty with expanded polytetrafluoroethylene. Surgical technique and preliminary results." *Ann Otol Rhinol Laryngol* 107 (5 Pt 1):427-32
- McCulloch, T. M., Hoffman, H. T., et al. (2000). "Arytenoid adduction combined with Gore-Tex medialization thyroplasty." *Laryngoscope* 110(8):1306-11
- Mikaelian, D. O., Lowry, L. D., et al. (1991). "Lipoinjection for unilateral vocal cord paralysis." *Laryngoscope* 101(5):465-8
- Miller, S. (2004). "Voice therapy for vocal fold paralysis." *Otolaryngol Clin North Am* 37(1):105-19
- Miller, T. A. (1988). "Temporalis fascia grafts for facial and nasal contour augmentation." *Plast Reconstr Surg* 81(4):524-33
- Moerman, M., Martens, J. P., et al. (2006). "The INFVo perceptual rating scale for substitution voicing: development and reliability." *Eur Arch Otorhinolaryngol* 263(5):435-9
- Moerman, M. B., Martens, J. P., et al. (2006). "Perceptual evaluation of substitution voices: development and evaluation of the (I)INFVo rating scale." *Eur Arch Otorhinolaryngol* 263(2):183-7

- Morpeth, J. F. and Williams, M. F. (2000). "Vocal fold paralysis after anterior cervical discectomy and fusion." *Laryngoscope* 110(1):43-46
- Morris, M., Deal, L., et al. (1999). "Vocal cord dysfunction in patients with exertional dyspnea." *Chest* 116(6):1676-82
- Munin, M. C., Rosen, C. A., et al. (2003). "Utility of laryngeal electromyography in predicting recovery after vocal fold paralysis." *Arch Phys Med Rehabil* 84(8):1150-3
- Murakami, Y. and Kirchner, J. A. (1972). "Mechanical and physiological properties of reflex laryngeal closure." *Ann Otol Rhinol Laryngol* 81(1):59-71
- Nawka, T., Wiesmann, U., et al. (2003). "[Validation of the German version of the Voice Handicap Index]." *Hno* 51(11):921-30
- Negus, V. (1949). "The comparative anatomy and physiology of the larynx." London: Heinemann
- Newman, K. and Dubester, S. (1994). "Vocal cord dysfunction: masquerader of asthma." *Seminars in Respiratory and Critical Care Medicine* 152(4 Pt 1):161-67
- Newman, K., Mason, U., et al. (1995). "Clinical features of vocal cord dysfunction." *Am J Respir Crit Care Med* 152(4 Pt 1):1382-86
- Ott, D. J., Gelfand, D. W., et al. (1986). "Radiological evaluation of dysphagia." *Jama* 256(19):2718-21
- Parkin, D., Bray, F., et al. (2005). "Global cancer statistics, 2002." *CA Cancer J Clin* 55(2):74-108
- Pattani, K. M., Morgan, M., et al. (2009). "Reflux as a cause of tracheoesophageal puncture failure." *Laryngoscope* 119(1):121-5
- Pierce, R. J. and Worsnop, C. J. (1999). "Upper airway function and dysfunction in respiration." *Clin Exp Pharmacol Physiol* 26(1):1-10
- Price, D., McGrath, P., et al. (1983). "The validation of visual analogue scales as ratio scales measures for chronic and experimental pain." *Pain* 17(1):45-56
- Remmers, J. E. and Bartlett, D., Jr. (1977). "Reflex control of expiratory airflow and duration." *J Appl Physiol* 42(1):80-7
- Rieves, A. L., Regner, M. F., et al. (2009). "Phonation threshold pressure estimation using electroglottography in an airflow redirection system." *Laryngoscope* 119(12):2378-83
- Rihkanen, H. (1998). "Vocal fold augmentation by injection of autologous fascia." *Laryngoscope* 108(1 Pt 1):51-4
- Robinson, R. A. and Smith, G. W. (1955). "Anterolateral cervical disc removal and interbody fusion for cervical disc syndrome." *Bull Johns Hopkins Hosp.* 96(1):223-24
- Roksund, O. D., Maat, R. C., et al. (2009). "Exercise induced dyspnea in the young. Larynx as the bottleneck of the airways." *Respir Med* 103(12):1911-8
- Rontal, E., Rontal, M., et al. (1983). "Quantitative and objective evaluation of vocal cord function." *Ann Otol Rhinol Laryngol* 92(5 Pt 1):421-3
- Rosen, C. A., Lee, A. S., et al. (2004). "Development and validation of the voice handicap index-10." *Laryngoscope* 114(9):1549-56
- Roy, N., Merrill, R. M., et al. (2005). "Voice disorders in the general population: prevalence, risk factors, and occupational impact." *Laryngoscope* 115(11):1988-95
- Rubin, A. D. and Sataloff, R. T. (2007). "Vocal fold paresis and paralysis." *Otolaryngol Clin North Am* 40(5):1109-31
- Rubin, H. J. (1960). "The neurochronaxic theory of voice production-a refutation." *AMA Arch Otolaryngol* 71(Jun):913-20
- Rundell, K. and Spiering, B. (2003). "Inspiratory stridor in elite athletes." *Chest* 123(2):468-74
- Saarinén, A., Sovijärvi, A. R., et al. (2007). "Medialization of paralyzed vocal fold does not increase respiratory resistance measured by impulse oscillometry." *Eur Arch Otorhinolaryngol* 264(11):1323-7
- Sasaki, C. T., Fukuda, H., et al. (1973). "Laryngeal abductor activity in response to varying ventilatory resistance." *Trans Am Acad Ophthalmol Otolaryngol* 77(6):ORL403-10
- Sasaki, C. T. and Suzuki, M. (1976). "Laryngeal reflexes in cat, dog, and man." *Arch Otolaryngol* 102(7):400-2
- Sasaki, C. T. and Suzuki, M. (1977). "Laryngeal spasm: a neurophysiologic redefinition." *Ann Otol Rhinol Laryngol* 86(2 pt. 1):150-7
- Schuster, M., Lohscheller, J., et al. (2003). "Quality of life in laryngectomees after prosthetic voice restoration." *Folia Phoniatr Logop* 55(5):211-9
- Shin, T., Watanabe, S., et al. (1987). "Sensory nerve endings in the mucosa of the epiglottis-morphologic investigations with silver impregnation, immunohistochemistry, and electron microscopy." *Otolaryngol Head Neck Surg* 96(1):55-62
- Shindo, M. L., Zaretsky, L. S., et al. (1996). "Autologous fat injection for unilateral vocal fold paralysis." *Ann Otol Rhinol Laryngol* 105(8):602-6
- Silbergleit, A. K., Jakobson, B. H., et al. (1997). "Dysphagia Disability Index: Development, Design and Validation." American Speech Language Hearing Association

- Singer, M. I. and Blom, E. D. (1980). "An endoscopic technique for restoration of voice after laryngectomy." *Ann Otol Rhinol Laryngol* 89(6 Pt 1):529-33
- Singh, V., Berry, S., et al. (2009). "Investigation of aspiration: milk nasendoscopy versus videofluoroscopy." *Eur Arch Otorhinolaryngol* 266(4):543-5
- Sintonen, H. (1995). "The 15-D measure of health-related quality of life: Feasibility, reliability and validity of its valuation system. Working paper 42. National Center for Health Program Evaluation. National Health and Medical Research Council. Melbourne."
- Sintonen, H. (2001). "The 15D instrument of health-related quality of life: properties and applications." *Ann Med* 33(5):328-36
- Skolnick, M. L. (1970). "Videofluoroscopic examination of the velopharyngeal portal during phonation in lateral and base projections--a new technique for studying the mechanics of closure." *Cleft Palate J* 7(Oct):803-16
- Smith-Hammond, C. A., Davenport, P. W., et al. (1997). "Motor innervation of the cricopharyngeus muscle by the recurrent laryngeal nerve." *J Appl Physiol* 83(1):89-94
- Smith-Hammond, C. A., New, K. C., et al. (2004). "Prospective analysis of incidence and risk factors of dysphagia in spine surgery patients: comparison of anterior cervical, posterior cervical, and lumbar procedures." *Spine* 29(13):1441-6
- Stalberg, E., Chu, J., et al. (1983). "Automatic analysis of the EMG interference pattern." *Clin Neurophysiol* 56(6):672-81
- Stavem, K. (1999). "Reliability, validity and responsiveness of two multiattribute utility measures in patients with chronic obstructive pulmonary disease." *Quality of Life Research* 8(1-2):45-54
- Stewart, M., Johnston, R. A., et al. (1995). "Swallowing performance following anterior cervical spine surgery." *Br J Neurosurg* 9(5):605-9
- Suzuki, M. and Kirchner, J. A. (1968). "Afferent nerve fibers in the external branch of the superior laryngeal nerve in the cat." *Ann Otol Rhinol Laryngol* 77(6):1059-70
- Suzuki, M. and Kirchner, J. A. (1969). "The posterior cricoaryteoid as an inspiratory muscle." *Ann Otol Rhinol Laryngol* 78:849-64
- Taramarcaz, P., Grissel, T., et al. (2004). "Transient postviral vocal cord dysfunction." *J Allergy Clin Immunol* 114(6):1471-72
- Farrag, T.Y., et al. (2006). "The utility of evaluating true vocal fold motion before thyroid surgery." *Laryngoscope* 116(2):235-38
- Thach, B. T. (2001). "Maturation and transformation of reflexes that protect the laryngeal airway from liquid aspiration from fetal to adult life." *Am J Med* 111 (Suppl 8A):69S-77S
- Titze, I. R. (2008). "The human instrument." *Sci Am* 298(1):94-101
- Uloza, V., Pribuisiene, R., et al. (2005). "Multidimensional assessment of functional outcomes of medialization thyroplasty." *Eur Arch Otorhinolaryngol* 262(8):616-21
- Umeno, H., Chitose, S., et al. (2008). "Efficacy of additional injection laryngoplasty after framework surgery." *Ann Otol Rhinol Laryngol* 117(1):5-10
- van As, C. J., Hilgers, F. J., et al. (1998). "The influence of stoma occlusion on aspects of tracheoesophageal voice." *Acta Otolaryngol* 118(5):732-8
- Van Den Berg, J. (1958). "Myoelastic-aerodynamic theory of voice production." *J Speech Hear Res* 1(3):227-44
- Wang, C. C., Chang, M. H., et al. (2008). "Prognostic indicators of unilateral vocal fold paralysis." *Arch Otolaryngol Head Neck Surg* 134(4):380-8
- Weisberg, N. K., Spengler, D. M., et al. (1997). "Stretch-induced nerve injury as a cause of paralysis secondary to the anterior cervical approach." *Otolaryngol Head Neck Surg* 116(3):317-26
- Vertigan, A., Theodoros, D., et al. (2006). "The relationship between chronic cough and paradoxical vocal fold movement: A review of the literature." *J Voice* 20(3):466-80
- Winslow, C. P., Winslow, T. J., et al. (2001). "Dysphonia and dysphagia following the anterior approach to the cervical spine." *Arch Otolaryngol Head Neck Surg* 127(1):51-5
- Wood, R. and Milgrom, H. (1996). "Vocal cord dysfunction." *J Allergy Clin Immunol* 98(3):481-85
- Wright, R. E., Boyd, C. S., et al. (1998). "Radiation doses to patients during pharyngeal videofluoroscopy." *Dysphagia* 13(2):113-5
- Yumoto, E. (1983). "The quantitative evaluation of hoarseness." *Arch Otolaryngol* 109(1):48-52
- Zammit-Maempel, I., Chapple, C. L., et al. (2007). "Radiation dose in videofluoroscopic swallow studies." *Dysphagia* 22(1):13-5
- Zemlin, W. (1998). "Speech and hearing science: anatomy and physiology." Allyn and Bacon; 4th Edition

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