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Voice Rehabilitation in an aquatic setting

Universidade Fernando Pessoa

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Dissertation presented to Universidade Fernando Pessoa as a requirement to obtain the doctoral degree in Desenvolvimento e Perturbações da Linguagem, under the supervision of Professor Fátima Maia and Professor Maria da Conceição Manso.

## **Abstract**

Voice disorders are any anatomical or functional issue that affects the vocal folds. Two of the more common voice disorders include bilateral vocal nodules (non-cancerous calluses) and vocal fold paralysis. The former related with voice abuse and misuse and the latter most often associated with surgery to the thyroid or thorax. In both pathologies, voice therapy has an important role in the treatment plan.

The characteristics of the aquatic environment through the properties of buoyancy/floating, hydrostatic pressure, viscosity (resistance) and thermodynamics may give a valuable setting for a therapeutic intervention at the level of the voice.

The purpose of this thesis is to provide a greater understanding of the assessment and voice therapy intervention in these two voice disorders, exploring the potential of its implementation in an aquatic environment.

A systematic review and a meta-analysis of visual-perceptual outcomes measures was performed and aimed to estimate with a high precision the efficacy of voice treatment on the vocal fold motility in adult patients with unilateral vocal folds paralysis. A total of 10 studies containing morphofunctional evaluation results were included in the analysis. The pooled data analysis of the visual-perceptual measures revealed that vocal fold motility improved in 72% (95% CI:64.0-80.0) of all patients after the therapeutic interventions.

A narrative review with a systematic search of the current literature about the effectiveness of voice therapy interventions in adults with vocal fold nodules was performed. The level of evidence based on the National Health and Medical Research Council guidelines, assessment, and critical appraisal were included. Regardless of receiving direct or indirect or a combination of both voice therapy contents, nearly all voice quality parameters were found to improve after treatment. Improved evidence is required to suggest that short period treatments are as beneficial as traditional therapy programs.

Moreover, another literature review was performed by searching studies in adults, with bilateral vocal fold nodules who received voice therapy, and where voice quality was evaluated quantitatively using acoustic analysis, before and after treatment. Meta-analysis was performed using random-effects model. A total of four studies were selected with 147 participants for the meta-analysis. The pooled results showed significant positive effect of voice therapy on: 1) increased  $f_0$  [mean difference post-therapy was 33.00Hz (95% CI:20.26-45.74,  $p < 0.001$ )]; 2) decreased jitter [mean difference post-therapy was 0.59% (95% CI:0.23%-0.94%,  $p = 0.0012$ )] and 3) a non-significant decreased shimmer [mean difference post-therapy was 2.98% (95% CI:-0.03-6.00,  $p = 0.052$ )].

A retrospective analysis was performed in 132 patients, mostly after thyroid surgery, who underwent voice therapy. Side and position of cord paralysis varied, 57.6% affecting the left vocal fold and 66.6% at the paramedian position. A significant improvement in voice and self-perceived quality of life after voice therapy was achieved.

A retrospective analysis of multidimensional voice outcomes was performed in 17 patients with bilateral vocal fold nodules, who presented dysphonia and received voice therapy in a water-based setting. Vocal fold lesions disappeared in 82.3% of the patients after voice therapy. Compared pre- and post-therapy audio-perceptual and aerodynamic parameters were significantly improved up to normal range values in all parameters. There is a need for more studies in aquatic environment to ensure that voice therapy delivered in this setting, in patients with vocal fold problems, can be effective and efficient.

The last study is a case report that looks at a voice therapy programme - delivered in a water-based setting - for a patient with unilateral vocal fold paralysis (UVFP) following surgery. Direct water-based exercises aimed to reduce vocal fold gap, reduce supra-glottic structures hyperfunction and improve voice quality. There was a positive change in the voice outcome measures after completion of treatment (visual perceptual, audio-perceptual, acoustic and self-perception).

Further studies with larger samples are needed to draw any realistic conclusions on the efficacy of water-based voice therapy in patients with UVFP.

## Resumo

As perturbações das pregas vocais são qualquer problema anatómico ou funcional que afetam as pregas vocais. Duas das perturbações mais comuns das pregas vocais incluem nódulos vocais bilaterais e paralisia das pregas vocais. A primeira relaciona-se com o abuso e mau uso da voz e a segunda está mais frequentemente associada à cirurgia da tiróide ou do tórax. Em ambas as patologias, a terapia vocal tem um papel importante no plano de tratamento.

As características do ambiente aquático através das propriedades de flutuação, pressão hidrostática, viscosidade (resistência) e termodinâmica podem dar um cenário valioso para uma intervenção terapêutica ao nível da voz.

O objetivo desta tese é proporcionar uma maior compreensão da avaliação e da intervenção terapêutica da voz nestas duas perturbações das pregas vocais, explorando o potencial da sua implementação num ambiente aquático.

Realizou-se uma revisão sistemática e uma meta-análise de medidas de avaliação vocal visual-perceptivas com o objetivo de estimar, com maior precisão, a eficácia da terapia vocal no movimento das pregas vocais, em pacientes adultos com paralisia unilateral das pregas vocais. Foram incluídos na análise um total de 10 estudos contendo resultados da avaliação da voz. A análise das medidas visual-perceptivas agrupadas revelou que a mobilidade das pregas vocais melhorou em 72% (IC 95%: 64,0-80,0) dos pacientes após as intervenções terapêuticas.

Simultaneamente foi realizada uma revisão da narrativa com pesquisa sistemática da literatura sobre a eficácia das intervenções da Terapia da Fala em adultos com nódulos nas pregas vocais. Foram incluídos artigos de acordo com os resultados da avaliação, avaliação crítica e níveis de evidência do National Health and Medical Research Council (NHMRC). Quase todos os parâmetros de qualidade de voz melhoraram após o

tratamento, independentemente de os pacientes terem terapia vocal direta ou indireta ou uma combinação de ambas. São necessárias mais pesquisas para sugerir que os tratamentos de curta duração são tão benéficos quanto os programas de terapia tradicional.

Foi efetuada uma revisão da literatura em estudos com adultos, com nódulos bilaterais nas pregas vocais que receberam terapia vocal, e onde a qualidade vocal foi avaliada quantitativamente por meio de análise acústica, antes e após o tratamento. A meta-análise foi realizada usando o modelo de efeitos aleatórios. Foram selecionados o total de quatro estudos com 147 participantes para a meta-análise. Os resultados combinados mostraram um efeito positivo significativo da terapia no: 1) aumento de  $f_0$  [diferença média pós-terapia de 33,00 Hz (IC 95%: 20,26-45,74,  $p < 0,001$ )]; 2) jitter diminuído [diferença média pós-terapia de 0,59% (IC 95%: 0,23% -0,94%,  $p = 0,0012$ )]. O shimmer também diminuiu, de modo não significativo [diferença média pós-terapia de 2,98% (95% CI: -0,03-6,00,  $p = 0,052$ )].

Também foi conduzida uma análise retrospectiva de 132 pacientes com paralisia unilateral de prega vocal, que realizaram terapia vocal, a maioria após cirurgia da tireóide. A lateralidade da paralisia e a posição das pregas vocais variaram, 57,6% afetando a prega vocal esquerda e 66,6% em posição paramediana. Foi alcançada uma melhora significativa na voz e na autopercepção do impacto da voz na qualidade de vida após a terapia vocal.

De seguida foi realizada uma análise retrospectiva dos resultados vocais multidimensionais em 17 pacientes com nódulos bilaterais das pregas vocais, que apresentavam disfonia e receberam terapia vocal em meio aquático. As lesões das pregas vocais desapareceram em 82,3% dos pacientes após terapia vocal. A maioria dos parâmetros áudio-perceptivos e aerodinâmicos pós-terapia melhoraram significativamente até valores normais. Há a necessidade de mais estudos em meio aquático para garantir que a terapia vocal realizada neste cenário, em pacientes com problemas das pregas vocais, possa ser eficaz e eficiente.

O último estudo é um relato de caso que analisa um programa de terapia vocal – em meio aquático - num paciente com paralisia unilateral de prega vocal (PUPV) após cirurgia. Os exercícios no meio aquático tinham como objetivos reduzir a fenda entre as pregas vocais,

diminuir a hiperfunção compensatória das estruturas supraglóticas e melhorar a qualidade vocal. Após o término do tratamento, houve mudança nos resultados vocais (perceptivo-visuais, perceptivo-auditivos, acústicos e na autopercepção do impacto da voz na qualidade de vida).

São necessários mais estudos com amostras maiores para tirar conclusões realistas sobre a eficácia da terapia vocal em meio aquático, em pacientes com PUPV.

## **Dedication**

To Ana.

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## List of Abbreviations and Symbols

<i>et al.</i>	and others	>	is greater than
AVA	acoustic voice analysis	<	is less than
C	conventional	IVT	intermediate therapy group
CG	control group	LVT	late voice therapy group
CI	confidence interval	(√)	low risk of bias
CSL	computerized speech lab	Me	median
CT	confidential therapy	M	male
PhD	Doctor of Philosophy	(x)	moderate risk of bias
$I^2$	degree of heterogeneity	MPT	maximum phonation time
EG	experimental group	MFR	mean airflow rate
EVT	early voice therapy group	n	samples size
$f_0$	fundamental frequency	NHR	noise-to-harmonic r
F	female	NNE	normalized noise energy
(□)	high risk of bias	ND	not described
=	is equal to	GIRBAS	perceptual rating scale
≥	is greater than or equal to	+	plus
≤	is less than or equal to	±	plus or minus

P	probability	RR	relative risk
POP	population	TVT	traditional voice therapy
PTP	phonation threshold pressure	t	t-test value
PQ	phonation quotient	VTI	voice turbulence index increased
PROEL	proprioceptive-elastic method	VHI	voice handicap index
PSR	Patient Satisfaction Ratings	VHI-10	voice handicap index 10
SNR	signal-to-noise ratio	VTC	video-teleconference
S.D.	standard deviation	T	Wilcoxon test value
SG	study group	IVT	intensive voice therapy

## **Chapter I – Introduction**

This thesis is part of the doctoral program in Development and Language Disorders at the Faculty of Health Sciences of Fernando Pessoa University.

The objective of this research was to systematize the procedures adopted by the speech-language therapy profession in an alternative to the traditional land-based environment, that is a water-based environment. The theoretical framework consisted of a literature review with a special emphasis on specific voice disorders. Unilateral vocal fold paralysis (UVFP) and vocal fold nodules (VFNs) were the two voice disorders chosen for this dissertation.

The starting point in the research was to review the literature on UVFP and VFNs pathologies and the voice therapy programs used, specifically regarding the efficacy of voice intervention, intensity, timing, and duration of the therapy programs. A systematic review and a meta-analysis on UVFP (Chapter II), plus a systematic search and narrative review on VFNs (Chapter III) were conducted. The idea after doing the systematic reviews was to perform two separate meta-analysis of the acoustic parameters assessment in both pathologies. The reason why acoustic analysis was chosen was to use a voice objective assessment that could monitor progress of voice therapy and enable comparison of voice therapy results delivered in-water and in-land. Unfortunately, during the systematic reviews it was clear that only a very small number of studies included voice acoustic assessments. A meta-analysis on acoustic voice parameters post voice therapy was only possible to be performed in VFNs (Chapter IV).

After the in-depth theoretical research of both pathologies, a more practical approach was taken. The plan was to carry out two retrospective studies by reviewing the clinical practice of the Speech Therapy Department of one of the main hospitals of Porto, Portugal, on UVFP and VFNs. These two studies would serve as baseline to compare with two additional prospective studies to be undertaken in a water-based environment. Nevertheless, only one retrospective study regarding multidimensional evaluation of patients with UVFP was conducted as insufficient data hindered the realisation of the retrospective study on VFNs. Hospital de Santo Antonio's Hospital Board of Directors and the University Research Ethics Committees (Appendix I) granted permission to

retrospectively review the clinical practice of the Speech Therapy Department on patients with UVFP (Chapter V).

The initial proposal for chapters VI and VII was to prospectively study 5 cases of UVFP and VFNs in a water-based environment and compare them with the land-based environment. Due to the constraints of COVID-19, recruitment of patients for water-based therapy was very limited (only one patient). The initial proposal was reviewed and modified for the following two studies, which approval was requested and granted by the Fernando Pessoa Research Ethics Committee (Appendix II). A retrospective study of private practice with 17 cases with VFNs on water-based environment was subsequently carried out in accordance with the guidelines of the Declaration of Helsinki on human studies (Chapter VI). Finally, an in-depth case study of a patient with UVFP treated in water-based environment was conducted (Chapter VII).

Moreover, an integrative discussion of the main thesis results is presented in chapter VIII, followed by a conclusion (Chapter IX).

## **1.1 Literature review**

The theoretical foundations that support the pertinence of the thesis have now been presented. From Chapter II to Chapter VII, detailed articles have been provided relating to each specific topic.

The complexity of realities that are the object of this scientific approach constitutes one of the main reasons, around which it was decided to further knowledge on the subject. Using aquatic settings for physical therapy is well documented (Brody & Geigle, 2009) throughout human existence traced through Roman spas, Egyptian water treatments such as healing waters in Bath United Kingdom, as mentioned in the ‘Canterbury Tales’. So, why not aquatic settings in relation to ‘breathing for speech’, or voice rehabilitation in warm ‘healing waters’?

It was with this presuppose of benefit that has led to deepen the dichotomy and the correlation, which might be established between both: speech therapy and water-based environment. To fully understand how this correlation can work in improving voice disorders, one needs to appreciate the properties of water, the water physics principles, and the human physiology.

### **i. Properties of Water**

It’s not possible to be a good therapist working in a water-based setting without having much knowledge on the effect of water in a body. A better job can be done when understanding the action and interaction of water on a submersed body, which needs to be in accordance with physics laws, because they rule everything that is inside water.

Fluids have unique hydrostatic and thermal properties (Kucher et al., 2015). In fact, to move, human beings take in, transforms, transports and uses energy, in a vital flow, which by itself constitutes a biophysics entity (Vilas-Boas, 2000). When projecting human being movement to a more specific domain, such as inside water, it is necessary to understand water-based environment characteristics and all the involved biophysics. According to Gaines (1998), the various techniques and exercises used in a water-based setting, make a creative usage of water physic properties, such as buoyancy/floating, hydrostatic pressure, viscosity (resistance) and refraction. Thus, in view of a better overall

understanding of this subject, it makes sense to present and systemize the fluid's properties (Gaines, 1998).

### *Density*

Pascal Law (1653) states that “pressure exerted anywhere in a confined incompressible fluid is transmitted equally in all directions throughout the fluid” (Baglio et al., 2011).

The human body is majorly consisted of water but, nonetheless, the body is slightly less dense than water, with a specific gravity of about 0.975, while that of men usually averages higher than women (Becker, 2009a). Muscles, bones, connective tissue and other lean body masses such as organs average a density of 1.1, while fat mass ranges at around 0.9. Highly lean, muscular and fit people have a specific gravity of more than one, while the obese can have considerably lower. As a result of immersion, the body will displace water volume weighing the same as the body, forcing the body upward in up-thrust.

### *Hydrostatic pressure*

Pressure varies proportionally with the depth of immersion and the density of a liquid when its incompressible. Water exerts 1mm Hg/1.36cm (0.540 in) pressure, or 22.4mm Hg/ft. Therefore, a human body dipped to 123cm experiences 88.9mmHg, which slightly exceeds normal diastolic blood pressure. This pressure aids in the resolution of edema in a wounded body part. Immediately after immersion, the effects of hydrostatic pressure begin to set in, leading to plastic deformation in the short term. Blood leads to cephalad displacement, then the rise of the right atrial pressure, the rise of the pressure on the pleural surfaces, the compression of the chest wall and the displacement of the cephalad diaphragm (Becker, 2009a).

### *Viscosity*

This refers to the level of internal friction of a fluid in motion. When a limb moves relative to water, the resistive effects of the liquid come to play, namely the turbulence and drag force. During turbulence flow situations, the resistance rises with respect to velocity as a long function (the faster they are, the greater is the turbulence which implies greater resistance). The viscous resistance rises with more force being exerted on it, while, when there's no force exerted, the resistance drops to minimum, since only an insignificant

magnitude of viscosity counters inertial momentum. Therefore, if a person feels pain while rehabilitating in water and stops motion, the force reduces impulsively and enhances the control of strengthening actions within the comfort of the patient (Becker, 2009a).

According to Vilas-Boas (2000), viscosity and other principles are used to enhance or minimize water resistance. In this context, and having this principle in mind, in water-based setting we need to consider: a) during movement, resistance is greater than on land setting; b) increase viscosity leads to raised resistance, and c) there is an increase in resistance when water surface is crossed through (air/water movements) (Vilas-Boas, 2000).

And, according to Kucher (2015), when movements are planned during a water-based therapy session, resistance can be manipulated, changing: movement's velocity, movement's amplitude, opposite inertia, inversion of movement's direction and using the swimming pool borders (Kucher et al., 2015).

### *Thermodynamics*

The heat capacity of water is equivalent to over 1000 times that of air for the same volume. The ability of water to both retain heat and transfer heat energy gives it great therapeutic capabilities. Water is also efficient at conducting heat, making it 25 times better than air. Together with the high water's specific heat capacity, the thermo-conductive properties render water rehabilitation highly versatile since water easily retains cold or heat and transfers it to the immersed body. Several therapeutic uses can be made of water at various temperature ranges, for instance, cold plunge tanks at around 9°-15°C enhances speed recovery and reduces muscle pains, despite studies (Becker, 2009a) contradicting this. Typical competitive and public pools at about 27°-30°C are generally too cool for rehab since the populations are generally less active. Therefore, most rehabilitative pools are maintained at about 33.5°-35°C, which allows lengthy immersion while exercising without being too cold or too hot. Hot tubs range from 37°C-41.5°C, although the higher temperature is barely comfortable for a long time (Becker, 2009a). As soon as one is immersed in the water, heat transfer commences, and, owing to the fact that the heat capacity of the body is lower (0.83) than that of the water (1.00) the body reaches equilibrium before the water does.

Maniu et al (2013) states that water temperature above 32°C is adequate for speech therapy with movements. During water sessions attention needs to be pay to hypothermia signs (tremor, cyanosed skin and wrinkled tissues) and hyperthermia signs (headaches, vomiting, extreme fatigue and blackouts) (Maniu et al., 2013). Thus, sessions should be less than 45 minutes (Kucher et al., 2015). Wittmer et al (2013) states those water-based therapy sessions should be no longer than 60 minutes. Water temperature is inverted relate to viscosity. That means, temperature can be adjusted to alter viscosity: warmer water makes it less viscous, which leads to less resistance. When planning a speech therapy session in a water-based environment we can set water characteristics to patient benefit (Wittmer & Maki, 2013).

## **ii. Physics Principles**

### *Buoyancy and Submersion*

Archimedes' principle states that 'any object that is completely or partially submerged in a fluid at rest is acted upon by an upward, or buoyant force, force the magnitude of which is equal to the weight of the fluid displaced by the body. The magnitude of this force is equal to the weight of the fluid displaced by the object'. This ascending force directly opposite to gravity force which supports the body, leads to a decreased weight, supported by the spine and lower limbs. Thus, a body submerged in water is acted on by two opposite forces: 1) gravity force, which is acted on the center of gravity of the object, and 2) buoyance force, which is acted on the center of buoyancy of the object (Vilas-Boas, 2000).

When the position of the forces is not lined up, a turn of the body will occur. Thus, an unbalance can happen to right/left and forward/backward (Barbosa, T; Magalhães, 2002). It's important to mention that human body is constituted by organs that float (such as lungs filled with air and lipid layers) and organs that sink (such as muscles and denser organs).

A person whose specific gravity is 0.98 gets to floating equilibrium once 98% of the total body volume is immersed. As the body gradually submerges, water gets displaced, bringing about the force of buoyancy, offloading immersed joints progressively. At neck depth submersion, close to 16lb in compressive force (approximately the head's weight) is wielded on the hips, spine and the knees. On average, a person submerged to the pubis

effectively offloads 40% of their weight, and 50% when further immersed to the umbilicus. Buoyancy is of significant therapeutic use, for instance, a strained pelvic bone may be unstable mechanically for full body loading for several weeks. When immersed in water, the gravitational forces are either partially or entirely offset so only muscle torque acts on the fractured area, enabling gentle building of strength, straight gait gain and even aided range of motion exercises. In the same way, patients with lower limit weight bearing restrictions can be placed in a water-based depths that allow them to regulate to those restrictions.

According to Kucher et al (2015), when a body is submerged in water there is a sensation of loss of weight leading to lesser pressure on joints and less contraction of postural muscles (anti-gravitational). A body submerged in water, in upright position, the total body weight reduction depends on the level submerged: a) body up to iliac crest - 20-30% reduction; b) body up to xiphoid appendix - 27 to 37% reduction, c) body up to clavicle - 50% reduction and d) body above clavicle (C7) – 90% reduction (Kucher et al., 2015). A submerged body, in horizontal plane, can lead to reduction of body weight up to a 100%, resulting in cancellations of forces (buoyancy and gravity).

Buoyancy, according to Kucher et al (2015) and Barbosa et al (2002), can give assistance, support or resistance to body movement, depending on the patient position and/or movement carried through, and being able to be adjusted in order to reach the exercise goals (Barbosa, T; Magalhães, 2002; Kucher et al., 2015). Thus, the therapist can adjust/use buoyancy as required to benefit the patient intervention, having present that: reduces weight supported by joints and work of anti-postural muscles; increases easiness of manipulation/mobilization for the therapist and freedom of movement of patient; assists upwards movements; and worsens downwards movements (Prins & Cutner, 1999; Wicker, 2007).

### **iii. Human Physiology**

#### *Importance of immersion*

The immersion of a body in water leads to a dramatic blood shift in the chest, with 2/3 of the volume in the lungs and the rest within the heart. The resultant increment in cardiac filling volume leads to an increase in cardiac output and consequently stroke volume. Therefore, the heart is able to pump the same blood volume per minute during rest as at

the start of aerobic exercises. This makes immersion useful at the start of recovery from extreme incapacity or cardiac rehabilitation. Also, it reduces peripheral resistance, thus decreasing the amount of work needed by the heart to move the blood. As the effort required to move a certain volume blood decreases, the cardiac efficiency rises (Becker et al., 2009). Following ischemic heart injuries, the benefit of aquatic exercise in cardiac rehab is highly rational. Additionally, there is a significant increment in blood circulation to deep muscle fibers following immersion, leading to the improved oxygen supply to the tissues and in turn facilitating the healing of injuries in muscle, joints and bones (Becker, 2009a). More efficient blood flow is also applicable to processes that change circulation in tissues, such as auto-immune diseases or diabetes. Neck depth immersion enhances brain blood flow by the improved cardiac output and lowering of peripheral vascular resistance. These lead to improved brain functions, such as cognition, memory, production of diuresis by increased potassium and sodium excretion, and helping to reduce edema in its presence (Becker, 2009a).

While stress and fear increase the sympathetic nervous system (SNS) action, activities such as meditation, relaxation and water immersion reduce SNS activity and improve Parasympathetic nervous systems (PNS) activities. The increase in SNS is associated with adverse cardiac functions, while the increase in PNS leads to a decline in adverse cardiac action (Becker et al., 2009).

#### **iv. Effects on Phonation**

Taking in consideration the above context, the combination of a submerged body with the water properties allows for certain speech therapy activities not normally achieved in land-based settings (Kucher et al., 2015). It enhances abdominal breathing support and phonation, facilitates greater posture balance and a range of positive mind effects (Schultz, 2013).

The correct postural alignment of the body promoted by the thermodynamic and buoyancy properties of the water, together with the proprioceptive feedback caused by the pressure of the water against the chest, support the respiratory effort and contraction of abdominal muscles in controlling exhaled airflow and consequently supra-glottic pressure. This correlation between body posture, abdominal muscle tone and breathing support will enhance, control, and stabilize voice projection (Ruoti et al., 2000).

Moreover, the hydrostatic pressure of water at shoulder-deep level provides resistance, strengthening the diaphragm, an important muscle that supports inhalation breathing muscles and assisted the exhalation movements, therefore, facilitates voice projection (Styer-Acevedo, 2004).

#### **v. Advantages of speech therapy in a water-based environment**

Despite our planet is cover 71% with water and be called Blue Planet, human beings did not develop in a biological way to be ready to live in water. Thus, a water-based environment stands differently from land-based environment, with specific physics characteristics that demand several adaptations from human being when he is inside water (Vilas-Boas, 2000).

The different characteristics of water and adaptations been hold by the body when submerged in it makes this environment appreciated and used for the following proposes:

1. Leisure: swimming pools, aquatic parks, where fun and leisure activities are expected;
2. Thermal: for relaxation, body's hygiene and revitalization;
3. Therapeutic: to minimize or to recovery normal functional status.

For human being, be in water means unsettling and perturbation of motor control. The permanent unbalances, the awful feeling of water in the eyes, mouth and ears, the constant searching of a stable aid (pool border), constitute evidence of changes in standardized water-related behaviors. Thus, only after the human being is well adapted to new environment that is possible, to know and control it, and gain confidence and comfort (Thomaz et al., 2010).

Usually, a speech therapy session is held on a land-base and aim to prevent, assess, and treat voice disorders, communication dysfunctions (language and speaking), feeding dysfunctions, oro-facial muscle function, fluency and reading and writing (American Speech-Language-Hearing, 2016).

Speech therapy performed in a water-based environment is defined by the use of activities associated with swimming, combined with the execution of specific exercises, which aim to improve a certain body function. Over time, health professionals have developed new

methods (Watsu, Halliwick; Bad Ragaz; Ai Chi) of a water-based therapy based on different philosophies and water properties, in order to rehabilitate functional disorders (Dull, 2004; Gamper & Lambeck, 2010; Gresswell, 2015). The combination of these aspects will have beneficial consequences for the individual's physical and psychological well-being, which have proved to be extremely important for users of all ages, from birth to adulthood (Ruoti et al., 2000).

Evidence in the literature of delivering speech therapy in an aquatic setting is sparse. Nevertheless, there is a recent study comparing in-classroom with in-water speech therapy intervention in two groups of children with autism spectrum disorders, which showed a significantly greater improvement of vocabulary measures in the water-based group (Sourvinos et al., 2021). To our knowledge there is not yet a study on water-based intervention to be reported in vocal pathologies.

## **1.2 Motivations**

The author of this thesis was a high-level competitive swimmer and started competing at the age of 8 and stopped at the age of 22 due to study commitments. She represented Portugal many times in international competitions including the Youth Olympic Games in Fukuoka 1992. With a strong background in swimming, she knows how body works and responds in a water-based environment and she uses her extensive experience to formulate a strategy to treat severe limitations of phonation, respiration and voice volume control, in adults with voice disorders and oral-sensory hypersensitivity, in children with autism.

For over 20 years, she has practiced speech therapy in a water-based environment in both private and public health sectors. This thesis intends to contribute to create scientific evidence about the benefits of speech therapy intervention in an water-based environment in vocal pathologies.

A PhD by publication as opposed to a dissertation was adopted with the aspiration of most researchers: to contribute and share results with the scientific community. She tried to compile the scientific articles and each one was aligned according to the precedent. In this way, the coherence of the thesis process is explained below.

### **1.3 Research goals**

The aim of this doctoral thesis was to systematize the procedures and results adopted by speech-language therapy in a different setting than the usual, the water. This environment has specific properties that give it characteristics different from land, conditioning human activity: making it more pleasant, motivating and stimulating. Thus, it presents an added value for the intervention, being able to provide singular results, when compared with those obtained in terrestrial environment.

Chapter II - The aim of the first study was to estimate the efficacy of voice treatment on the vocal fold motility in adult patients with unilateral vocal folds paralysis.

Chapter III - The aim of this study was to establish the evidence base for the general effectiveness of voice therapy programs in adults' patients with bilateral VFNs through critically reviewing the existing body of knowledge.

Chapter IV - The aim of this study was to present evidence based on literature regarding objective acoustic voice parameters changes, after voice therapy, in patients with bilateral VFNs.

Chapter V - The aim of this study was to analyze multidimensional voice evaluation outcomes in a group of patients with unilateral vocal fold paralysis.

Chapter VI - The aim of this study to analyze the results of voice therapy delivered in a water-based environment in patients who presented with bilateral vocal fold nodules.

Chapter VII - The aim of this study was to describe a voice therapy program delivered in a water-base setting to a patient with UVFP after thyroid surgery.

In Table 1, a summary of every scientific and/or academic activity is presented.

Table 1 – List of publications and communications related to the thesis

<b>Chapter II</b>	<b>Efficacy of speech language therapy intervention in unilateral vocal fold paralysis: a systematic review and a meta-analysis of visual-perceptual outcome measures</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2020). Efficacy of speech language therapy intervention in unilateral vocal fold paralysis – a systematic review and a meta-analysis of visual-perceptual outcome measures. <i>Logopedics Phoniatrics Vocology</i> 10.1080/14015439.2020.1762730
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2019). Efficacy of Speech Language Therapy Intervention in Unilateral Vocal Fold Paralysis (UVFP) - a Meta-Analysis. <i>In PEVOC - Pan-European Voice Conference, Copenhagen, Denmark (Oral communication)</i>
<b>Chapter III</b>	<b>Effectiveness of voice therapy in patients with vocal fold nodules: a systematic search and narrative review</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2020). Effectiveness of voice therapy in patients with vocal fold nodules: a systematic search and narrative review. <i>Journal of European Archives of Oto-Rhino-Laryngology</i> 277(11), 2951-2966. 10.1007/s00405-020-06059-8
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2019). Content and timing of speech therapy intervention for vocal fold nodules: a systematic review” e “Efficacy of Speech Language Therapy Intervention in Unilateral Vocal Fold Paralysis (UVFP) - a Meta-Analysis. <i>In PEVOC - Pan-European Voice Conference, Copenhagen, Denmark (Oral communication)</i>
<b>Chapter IV</b>	<b>Is there an improvement on acoustic voice parameters in patients with bilateral vocal fold nodules after voice therapy? a meta-analysis.</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2020). Is there an improvement on acoustic voice parameters in patients with bilateral vocal fold nodules after voice therapy? a meta-analysis. <i>Journal of European Archives of Oto-Rhino-Laryngology</i> 277(8), 2163-2172. 10.1007/s00405-020-05956-2
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2020). Is there an Improvement on Acoustic Voice Parameters in Patients with Bilateral Vocal Fold Nodules after Voice Therapy? A Meta-Analysis. <i>In 49th Congress of The Voice Foundation – Care of the Professional Voice, Philadelphia, EUA (Virtual Congress).</i>
<b>Chapter V</b>	<b>Unilateral vocal fold paralysis multidimensional assessment: before &amp; after speech and language intervention</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Unilateral vocal fold paralysis multidimensional assessment: before & after speech and language intervention. <i>Journal of Voice</i> . Submitted and under peer review.
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Vocal Fold Paralysis Multidimensional Assessment – Before & After Speech and Language Intervention. 2º Congresso Internacional da Sociedade Portuguesa de Terapia da Fala, 15-17 October, Lisbon, Portugal
<b>Chapter VI</b>	<b>Is an aquatic setting an alternative way to deliver speech therapy in patients with bilateral vocal fold nodules? a retrospective study</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Is an aquatic setting an alternative way to deliver speech therapy in patients with bilateral vocal fold nodules? a retrospective study. <i>Complementary Medicine Research</i> . Submitted and under peer review.
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Is an aquatic setting an alternative way to deliver speech therapy in patients with bilateral vocal fold nodules? a retrospective study. <i>In 50th Congress of The Voice Foundation – Care of the Professional Voice, Philadelphia, EUA (Virtual Congress).</i>
<b>Chapter VII</b>	<b>Voice therapy delivered in a water-based setting for unilateral vocal fold paralysis: a case report</b>
Publication	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Voice therapy delivered in a water-based setting for unilateral vocal fold paralysis: a case report. <i>Complementary Medicine Research</i> . Submitted and under peer review.
Presentation	Alegria, R., Vaz Freitas, S., Manso, C. M. (2021). Voice therapy delivered in a water-based setting for unilateral vocal fold paralysis: a case report. <i>In 50th Congress of The Voice Foundation – Care of the Professional Voice, Philadelphia, EUA (Virtual Congress).</i>

Voice Rehabilitation in an aquatic setting

<b>Other relevant publications during this period</b>	
Book	Vaz-Freitas, S, Alegria, R. (2021) <i>Terapia da fala: clínica e ocupacional a propósito de 20 anos de carreira, 10 temas contemporâneos</i> . Porto, Portugal: Publicações Universidade Fernando Pessoa.
Book Chapter	Alegria, R., Nachimson, S. (2021). <i>Terapia da Fala em Meio Aquático: uma experiência com adultos/idosos</i> . In Vaz Freitas, S, Alegria, R. (Ed) <i>Terapia da fala: clínica e ocupacional a propósito de 20 anos de carreira, 10 temas contemporâneos</i> . Porto, Portugal: Publicações Universidade Fernando Pessoa.
Book Chapter	Nachimson, S., Dull, C., Alegria, R. ( <i>in press</i> ). <i>Watsu® Voices in the Water: Speech Language Pathology and Communication Disorders</i> . In Dull, H. (Ed) <i>Watsu® Professional Path &amp; Clinical Applications an Integrative Approach Chapter Talking Points</i> . California, USA: Watsu Publishing.
Book Chapter	Vaz-Freitas, S., Alegria, R., Pestana, P.M. (2019) <i>Saúde Vocal e Prevenção de Alterações da Voz em Professores de desporto em Natação</i> . In Brasil, C., Catrib, A. and Caldas, J. (Eds.), <i>Tendências e Tecnologias na Promoção da saúde nos Espaços Educacionais</i> . Fortaleza: UNIFOR
<b>Other relevant presentations</b>	
Presentations	Alegria, R. (2018). <i>Speech Therapy in An Aquatic Setting: A New Intervention Approach - Case Report: 10 Children Diagnosed with Autismo Spectrum Disorder</i> . In CITA, Congresso Internacional Terapia Aquática em Coimbra, Portugal – POSTER (1° prize)

## **Chapter II - Efficacy of speech language therapy intervention in unilateral vocal fold paralysis: a systematic review and a meta-analysis of visual-perceptual outcome measures**

### **2.1 Abstract**

*Objective:* Unilateral vocal folds paralysis is a disorder that affects a patient's quality-of-life by disturbing their phonation, breathing, and swallowing activities. This systematic review aimed to estimate, with a higher precision (i.e., through meta-analysis of visual-perceptual measures), the efficacy of voice treatment on the vocal fold motility in adult patients with unilateral vocal folds paralysis.

*Methods:* PubMed, CINAHL, CENTRAL and Web of Science were searched for retrospective and prospective cohort, case-control, and cross-sectional with comparative studies with adults that were published between January 1, 2008 to December 31, 2018 and written in the English language. After applying the inclusion and exclusion criteria and removing of duplicates, a total of 10 studies containing morphofunctional evaluation results were included in the analysis. Pooled data analysis of the motility of the vocal folds before and after voice therapy allowed inferring about the efficacy of voice therapy intervention in patients with unilateral vocal folds paralysis. A random-effect model was used to estimate the effect size. Publication bias was considered.

*Results:* The pooled data analysis of the visual-perceptual measures revealed that vocal fold motility improved in 72% (95% CI:64.0-80.0) of all patients after the therapeutic interventions. The inconsistency index ( $I^2=18.35\%$ ) of the studies included in this meta-analysis revealed an extremely low heterogeneity. Funnel plot and Cochran's Q test showed no publication bias. The systematic review was limited to only English language articles.

*Conclusion:* This meta-analysis supports the evidence that voice therapy intervention can have a positive effect on the vocal fold motility, that is, they can improve the glottal gap closure, irrespective of the exercises and techniques used. As the data indicated an increase efficacy of voice therapy, early voice therapy in patients with unilateral vocal folds paralysis should be considered.

## 2.2 Introduction

Unilateral vocal fold paralysis (UVFP) is the term used to describe dysfunction in one vocal fold, which may affect patients' ability to phonate, breathe, swallow and cough (Myssiorek, 2004). Vocal fold motility is controlled by intrinsic laryngeal muscles, which are largely innervated by the recurrent laryngeal nerves (the branches of the proximal vagus nerves) (Dankbaar & Pameijer, 2014; Myssiorek, 2004). An injury along these nerves can result in vocal folds paralysis, which is the most frequently reported etiology post-surgery (46%), followed by idiopathic nature (18%) or cancer (13%) according to the 2009 study by Rosenthal, Benninger and Deeb who reviewed the etiologies of UVFP (Mehlum et al., 2009; Rosenthal et al., 2007).

Patients with UVFP normally seek medical help when their voice becomes hoarse and breathy. Vocal fold paralysis makes vocal communication difficult, interferes with the patients' social and work lives, and creates emotional and psychological distress, thus negatively impacting their quality-of-life (QoL) (M S Benninger et al., 1994; Kuhn et al., 2013; Francesco Mattioli et al., 2017; Walton et al., 2017; Watterson et al., 1990). The position of the affected vocal fold and the degree of glottal gap relates to the severity of dysphonia, and these factors should be considered when deciding the appropriate treatment options (Chen et al., 2014; Fang et al., 2014; Schwarz et al., 2011; Siu et al., 2016).

The therapeutic approach for a patient who presents with UVFP is usually composed of 3 initial strategies:

- 1) observation for spontaneous neural recovery or compensation, which can occur for up to 9-12 months after the onset of injury (M S Benninger et al., 1994; Sulica, 2009; Watterson et al., 1990);
- 2) voice therapy, often the recommended primary approach, to facilitate achieving adequate contralateral vocal fold compensation; therefore, improving the voice quality and maximizing the chance of natural recovery (Cohen et al., 2016);
- 3) and transcutaneous injection laryngoplasty of a biocompatible augmentation material to ameliorate the glottal closure by moving the affected vocal fold towards the midline

during the time when spontaneous compensation and recovery happen (Chen et al., 2014; Fang et al., 2014; R. C. Nelson et al., 2019; Siu et al., 2016).

Siu et al (Siu et al., 2016) reported the voice outcomes after interventions for UVFP and showed that injection laryngoplasty (IL) improved the acoustic and aerodynamic voice outcomes in almost all measures of the reviewed studies. Furthermore, voice improvement was sustained for as long as 4 years and comparable results were obtained when a medialization thyroplasty (MT) was performed. The timing of the intervention seems to significantly affect the effect size of the intervention in patients with UVFP after thyroidectomy, according to Chen et al (Chen et al., 2014). The authors recommend that reversible interventions, such as IL and MT, be performed within the first 12 months of the onset of paralysis to augment the natural healing process.

Direct voice therapy alone or a combination of indirect and direct voice therapy strategy to be effective in patients with UVFP. This is particularly true when the length of time with paralysis has been less than a year. Direct voice therapy focuses on voice-production elements such as breathing, phonation and musculoskeletal function, while indirect voice therapy focuses mainly on education and prevention (e.g. vocal hygiene and vocal rest) of risk factors that aggravate the disorder (Ruotsalainen et al., 2008). According to the current review, there is lack of consensus regarding which type of voice techniques are more beneficial because most therapies are based on patients' individual symptoms of voice use and clinical judgment of the speech-language pathologists (or therapists).

Only a few research studies and systematic reviews have been published to determine the effect of vocal therapy on the glottal gap closure in UVFP. In addition, there is no clear framework of assessment and measurement of vocal and laryngeal outcomes. To the best of our knowledge, no meta-analysis has been published on these topics. Against this backdrop, in order to evaluate more precisely the success of voice therapy intervention in patients with UVFP, we performed a systematic review of the literature on this subject and statistically analyzed its resulting impact on the voice visual-perceptual outcome measures. More specifically, this research examined the laryngoscopy findings observed before and after voice therapy with an emphasis on the vocal fold closure.

### **2.3 Methods**

The guidelines mentioned in the Preferred Reporting Items for Systematic Review and

Meta-Analysis were applied to conduct the systematic review of the literature – PRISMA (Shamseer et al., 2015).

### **i. Eligibility Criteria**

To elaborate the inclusion and exclusion criteria, the first and second authors performed a lengthy exchange of views regarding the main goal of the study, and any disagreements were discussed and resolved before creating the initial search strategy took place.

#### *Report Characteristics*

1. Only those articles that were peer reviewed and published in indexed scientific journal were included.
2. Only those articles that were written in English and published during January 2008 to December 2018 were included.
3. Gray literature was not included.

#### *Study Characteristic*

1. Participants
  - a. Patients diagnosed with UVFP.
  - b. Patients age  $\geq 18$  years; excluded articles using only pediatrics' samples.
  - c. Patients who had received only pharmacological and surgical treatments for their UVFP were excluded.
  - d. Studies conducted on animals or cadavers were excluded.
2. Voice therapy program
  - a. Direct voice therapy alone or direct plus indirect voice therapy were included.
  - b. Direct voice intervention combined with transcutaneous electrical nerve stimulation (TENS) were included.
  - c. Indirect voice therapy alone or in combination with TENS were excluded.

- d. TENS alone was excluded.
- e. No restriction regarding the timing of initiation of treatment after diagnosis, the type of techniques used, the duration and intensity of voice intervention;
- f. Voice training programs for voice professionals without vocal fold disorders were excluded;
- g. Studies in which the intervention was conducted or supervised by a SLPs were included.

### 3. Outcome measures

- a. Only visual-perceptual outcome measure, that is studies reporting pre- and post-treatment data on visual examination of the vocal fold function, were included.
- b. Visual-perceptual outcome measure and any other voice outcome measure, that is, studies documenting pre- and post-treatment data on auditory-perceptual, aerodynamic, acoustic, and self-assessment of voice function, were included.

### 4. Study type and design

- a. Retrospective and prospective cohort, case-control and cross-sectional with comparative studies documenting pre- and post- intervention voice outcomes were included.
- b. Randomized controlled trials and controlled trials without randomization reporting pre- and post-voice outcomes were included.
- c. Systematic reviews, editorial articles, and meta-analysis were excluded.
- d. Studies describing the visual-perceptual assessment of the vocal folds (before and after voice intervention) that were performed during a laryngoscopic or stroboscopic examination were included.
- e. Studies that had clearly described the voice intervention strategy, including the types of techniques, frequency, and duration of intervention, were included.

- f. Studies reporting complete pre and posttreatment voice outcomes data were included only when the if visual-perceptual outcome data was comprised.
- g. Studies in which the interventions had to involved at least five participants in each group were included.
- h. No other restrictions were considered on the study design, geographical location, or the duration of follow-up.

## **ii.Information Source**

In order to gather all the studies on voice intervention in patients with UVFP, the first author executed an electronic search from PubMed, CINAHL, CENTRAL and Web of Science search databases. During this search, no restriction to language and publication date were applied (search performed on January 5<sup>th</sup>, 2019).

## **iii.Search Strategy**

Table 2 lists the search standardized terms and keywords that were used to identify potentially relevant studies in the databases.

**Table 2 - Search strategy terms used**

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((vocal[Title/Abstract] OR voice[Title/Abstract])) AND (paralysis[Title/Abstract] OR palsy[Title/Abstract] OR immobility[Title/Abstract]) AND (therapy[Title/Abstract] OR intervention[Title/Abstract])  
((voice[Title/Abstract] OR vocal[Title/Abstract] OR larynx[Title/Abstract] OR laryngeal[Title/Abstract]))  
AND (paralysis[Title/Abstract] OR palsy[Title/Abstract] OR immobility[Title/Abstract]) AND  
(therapy[Title/Abstract] OR intervention[Title/Abstract])

((voice OR vocal)) AND (palsy OR paralysis OR immobility)) AND (therapy OR intervention) (((voice OR vocal OR larynx OR laryngeal)) AND (palsy OR paralysis OR immobility)) AND (therapy OR intervention)

---

## **iv.Study Selection**

A study selection was performed after the initial search, in the following stepwise order:

- 1) Duplicate references were removed using the Mendeley Desktop ®Version 1.19.2. (Zaugg et al., 2011);
- 2) Title and abstract of the remaining articles, were screened against the eligibility criteria by the first two authors, independently. At this stage studies were excluded if the sample of the studies comprised of the following:

- a. only children, animals or cadavers;
- b. vocal fold pathology not related to paralysis;
- c. no voice intervention;
- d. not written in English;
- e. systematic reviews and editorials; and
- f. published outside of the inclusion criteria period (i.e., 2008-2018).

3) if the reference lists of the selected studies from the previous step were title screened by the first author;

4) full text review of the included studies from the title and abstract stage and reference lists screening were evaluated independently by the first author for eligibility against inclusion and exclusion criteria. Studies were removed if they did not have an adequate design, description of the voice therapy intervention and voice function assessment; if the outcome measures did not include a laryngoscopic or stroboscopic examination, and the results data were inexistent or incomplete. Moreover, one study retrieved from the reference lists was excluded due to the lack of voice therapy intervention. To assess the screening reliability of the studies selected for a full-text review, 20% were screened independently by the second author for evaluation against eligibility criteria. In case of disagreements with respect to the screening and categorization between the two first authors, a third independent reviewer was assigned to resolve the dispute.

#### **v.Data Entry Extracted from Reviewed Studies**

The first and second authors built an entry list using data that were considered significant to achieve a reliable systematic review. The data from each selected study included the following:

1. Study: publication year, study place, study design, and sample size.
2. Participant: sex, age (range or mean), and etiology of vocal fold paralysis.
3. Voice therapy: timing of initiation of therapy in relation to the with onset of paralysis, type of intervention and frequency, and intensity and duration of therapy.

4. Outcome measures that compared the pre- and post-treatment voice outcomes.
5. Results with statistical significance, where the *p* value was reported.

#### **vi. Quality of Evidence**

National Health and Medical Research Council (NHMRC) level of evidence (Glasziou et al., 2000) was used to lay out a structure for deciding the level of evidence. The two authors reviewed the quality of evidence of each included study, according to the NHMRC, and granted one level of evidence to each study. Conflicts and disagreements between the authors were argued and resolved by a third author.

#### **vii. Data analysis**

To summarize the characteristics and main findings of the 10 selected articles, a systematic narrative synthesis was conducted as per the direction of the Conduct of Narrative Synthesis in Systematic Reviews (Popay et al., 2006).

The heterogeneity of the studies was assessed with Cochran's Q-test and the inconsistency index measure ( $I^2$ ) (Higgins et al., 2011; Sheskin, 2003). A random-effect model and a standardized mean difference of 95% CI (confidence interval) was used to conduct the meta-analysis. The risk ratios and the respective 95% CI were recorded. The meta-analysis was conducted using the MedCalc software for Mac (version 14.8.1.0). A forest plot graph was created to demonstrate the estimated results (effect on the glottal closure) from each study, along with the overall result. Existence of publication bias was evaluated using a funnel plot graph (Egger et al) (Haidich, 2010). The samples size, effect size, and standard errors were eliminated from the selected studies.

## **2.4 Results**

### **i. Study selection**

As illustrated in Figure 1, the PRISMA adaptation flow chart diagram shows the result of the study selection process which encompasses an initial search and the filtering stages. The number of citations identified after the initial search and the number of studies selected and removed at each stage of the screening are also presented, in addition to the reasons for exclusion after title and abstract review as well as after a full-text examination review. Finally, a total of 10 studies met all eligibility criteria and were assessed in this study.

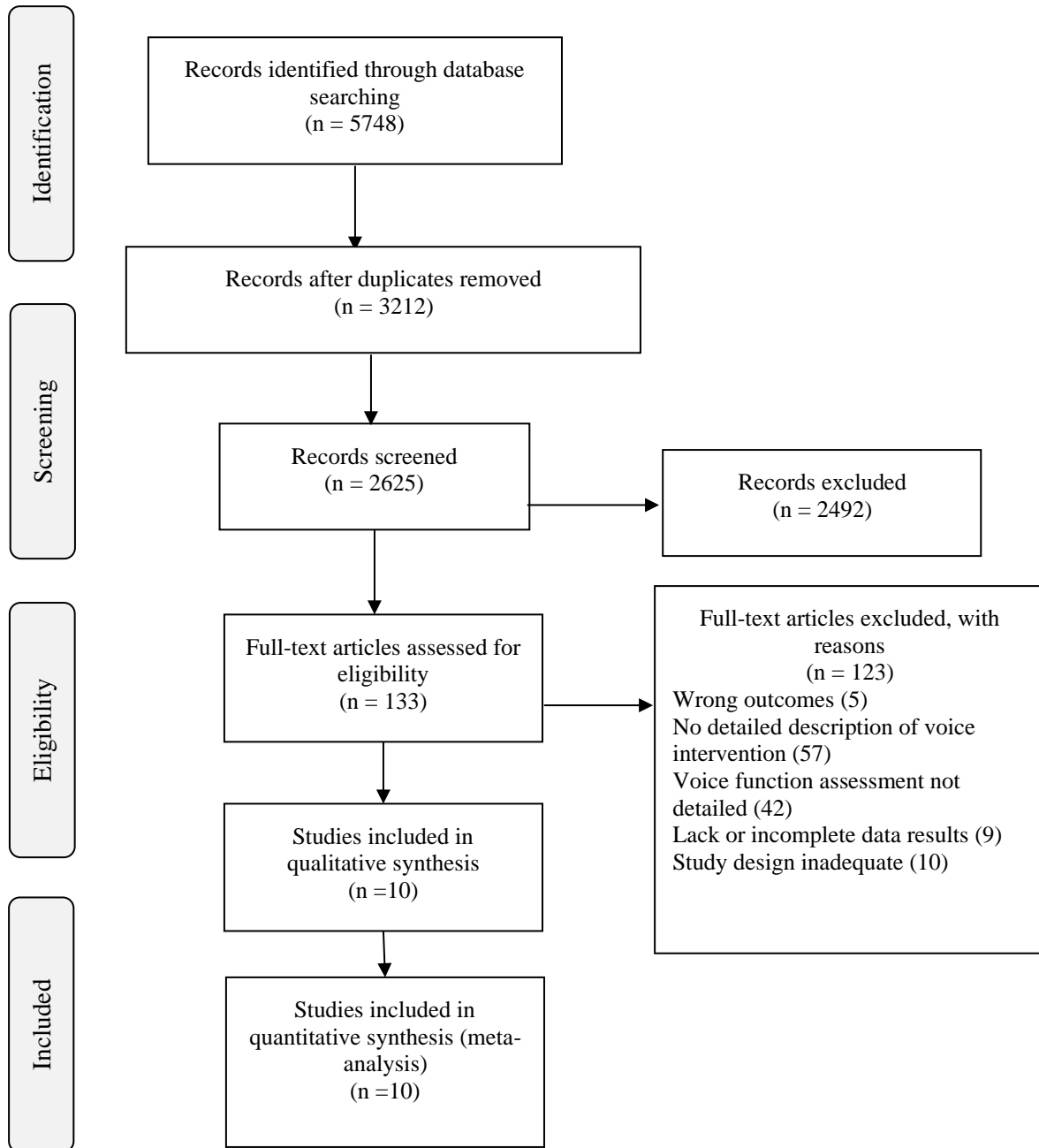
### **ii. Systematic Narrative Synthesis of the Selected Studies**

A description of the 10 studies and the characteristics of the participants included for critical appraisal has been listed in Tables 3 and Table 4.

#### *Participants characteristics*

Nearly twice as many women as men enrolled in the studies (women=314 vs men=163). D'Alatri et al (D'Alatri et al., 2008) and Vij et al (Vij et al., 2017a) did not document the gender of participants. Only Cantarella et al (Cantarella et al., 2010) included more male than female participants. With regard to the participants' age, at least four studies (Schindler et al (Schindler et al., 2008), Cantarella et al (Cantarella et al., 2010), Mattioli et al (Francesco Mattioli et al., 2011), Mattioli et al (F Mattioli et al., 2015a) included patients aged < 18 years. The data documented in these studies included patients in the age range stated in the inclusion criteria, which were important for the overall results analysis of the intended aim of this review. The age range was also found to be diverse across the studies. UVFP diagnosis was confirmed in all studies through a videolaryngoscopy or videostroboscopy. Except for three studies (Cantarella et al (Cantarella et al., 2010), El-Banna et al (El-Banna & Youssef, 2014) and Barcelos et al (Barcelos et al., 2017) that included only iatrogenic or malignancy as the etiology for UVFP, the remaining studies included at least two origins for the paralysis (i.e., iatrogenic, idiopathic, or others).

Figure 1 - PRISMA-P Study flow diagram



**Table 3 - Participants Characteristics**

Authors	Sample Size	Female/Male	Age Range/Mean Age	Etiology UVFP
Schindler et al (Schindler et al., 2008)	40	F/M=26/14	Age Range=12-82	Iatrogenic Idiopathic Other
D'Alatri et al (D'Alatri et al., 2008)	91	F/M=ND	Age Range=31-68	Iatrogenic Idiopathic
Cantarella et al (Cantarella et al., 2010)	30	F/M=14/16	Age Range=15-80	Iatrogenic
Mattioli et al (Francesco Mattioli et al., 2011)	74	F/M=49/25	Age Range=14-86	Iatrogenic Idiopathic Other
El-Banna et al (El-Banna & Youssef, 2014)	30	F/M=18/12	Age Range=22-52	Iatrogenic
Mattioli et al (F Mattioli et al., 2015a)	171	F/M=116/55	Age Range=17-87	Iatrogenic Idiopathic Other
Busto-Crespo et al (Busto-Crespo et al., 2016)	70	F/M=45/25	Age Range=ND Mean Age=54	Iatrogenic Idiopathic Other
Kao Y-C et al (Kao et al., 2017b)	19	F/M=15/4	Age Range=32-68	Iatrogenic Idiopathic Other
Vij S. et al (Vij et al., 2017a)	20	F/M=ND	Age Range=20-50	Iatrogenic Idiopathic Other
Barcelos et al (Barcelos et al., 2017)	43	F/M=31/12	Mean Age=52.4	Malignancy

**Abbreviations:** ND – not described; F – female; M - male

### *Voice Therapy program*

The selected studies demonstrated appreciable heterogeneity with regard to the voice therapy content, timing of initiation of intervention, and the intensity and duration of therapy. Table 5 provides a concise description of the main findings.

#### a. Therapy Content

The voice therapy used in all studies was the direct voice therapy, except in three studies (Kao et al (Kao et al., 2017b), Barcelos et al (Barcelos et al., 2017) and D'Alatri et al (D'Alatri et al., 2008)) where indirect voice therapy was also delivered. In three studies (El-Banna et al (El-Banna & Youssef, 2014), Busto-Crespo et al (Busto-Crespo et al., 2016) and Kao et al (Kao et al., 2017b)), the treatment program was controlled through a protocol-based therapy, while the majority of the studies utilized a patient-based approach. A great variability in the direct voice techniques was used across the studies.

### b. Timing, Duration and Intensity of Therapy

Table 5 describes the main characteristics of voice therapy. The early and late voice therapy relate to the timing when the treatment was initiated after the diagnosis of UVFP was made. There was no consensus regarding the exact meaning of early voice therapy in the included studies, which had varied onset of symptoms from < 3 weeks in Vij et al (Vij et al., 2017a) to < 1 year Busto-Crespo et al (Busto-Crespo et al., 2016). Schindler et al (Schindler et al., 2008), Mattioli et al (Francesco Mattioli et al., 2011), El-Banna et al (El-Banna & Youssef, 2014), and Mattioli et al (F Mattioli et al., 2015a) defined early voice therapy as < 4 weeks, Kao et al as < 6 weeks, and finally, Cantarella et al (Cantarella et al., 2010) < 3 months. In four studies (Cantarella et al (Cantarella et al., 2010), El-Banna et al (El-Banna & Youssef, 2014), Mattioli et al (F Mattioli et al., 2015a) and Busto-Crespo et al (Busto-Crespo et al., 2016)) compared the voice function outcomes in both early and late interventions groups. The duration of therapy provided varied in both among studies and within each study. Only five studies (D'Alatri et al (D'Alatri et al., 2008), El-Banna et al (El-Banna & Youssef, 2014), Busto-Crespo et al (Busto-Crespo et al., 2016), Vij et al (Vij et al., 2017a) and Barcelos et al (Barcelos et al., 2017)) reported the duration of each session, varying from 20 min in El-Banna et al (El-Banna & Youssef, 2014) to 30 min in the other studies. The remaining studies did not mention the session duration at all. In the studies that did not include protocol-based therapy, the number of total therapy sessions were different within the same study, and it appeared to change according to the clinical recovery and severity of symptoms. For instance, the sessions ranged between 6 and 20 min in Schindler et al; between 8 and 35 minutes in D'Alatri et al (D'Alatri et al., 2008), between 10 and 40 minutes in Cantarella et al (Cantarella et al., 2010), and between 14 and 20 min in Mattioli et al (Francesco Mattioli et al., 2011). In three studies (Cantarella et al (Cantarella et al., 2010), Mattioli et al (Francesco Mattioli et al., 2011) and Mattioli et al (F Mattioli et al., 2015a)), daily homework sessions were also included as a part of their voice therapy program. With regard to the intensity of treatment, eight studies documented a twice-a-week schedule, Kao et al (Kao et al., 2017b) reported a weekly session and Cantarella et al (Cantarella et al., 2010) adjusted the intensity of the therapy depending on the severity of paralysis.

**Table 4 – Description Visual perceptual measurement**

<b>Authors</b>	<b>Assessment</b>	<b>Number of Raters</b>	<b>Blind Raters</b>	<b>Glottal Gap Rating</b>	<b>Proportion Patients that Improved VF motility</b>
Schindler et al (Schindler et al., 2008)	Videolaryngoscopy	ND	ND	Subjective: Complete and Incomplete (posterior glottal chink, posterior membranous portion and entire glottis)	95% (n= 38)
D'Alatri et al (D'Alatri et al., 2008)	Videolaryngoscopy	ND	ND	Subjective: Complete and Incomplete (posterior glottal chink, posterior membranous portion and entire glottis)	63% (n= 57)
Cantarella et al (Cantarella et al., 2010)	Videostroboscopy	ND	ND	Unclear	100% (n= 30)
Mattioli et al (Francesco Mattioli et al., 2011)	Videostroboscopy	ND	ND	Subjective: Complete and Incomplete (anterior glottal chink, posterior glottal chink and irregular)	69% (n= 51)
El-Banna et al (El-Banna & Youssef, 2014)	Videostroboscopy	3	Yes, but inter or intra-rater data not available	Subjective: Reduced glottal gap No change glottal gap Increased glottal gap	67% (n= 20)
Mattioli et al (F Mattioli et al., 2015a)	Videostroboscopy	ND	ND	Unclear	62% (n= 106)
Busto-Crespo et al (Busto-Crespo et al., 2016)	Videostroboscopy	ND	No, but Intra-rater data available	Subjective: Complete and Incomplete (posterior membranous portion and irregular)	77% (n= 54)
Kao Y-C et al (Kao et al., 2017b)	Videostroboscopy	1	Yes, and with intra-rater data available	Objective: Six-point scale from “0” normal to “5” severe.	100% (n= 10)
Vij S. et al (Vij et al., 2017a)	Videostroboscopy	ND	ND	Objective: Glottal gap measured in millimeters	100% (n= 10)
Barcelos et al (Barcelos et al., 2017)	Videolaryngoscopy	1	Yes, but intra-rater data not available	Subjective: Adapted protocol	77% (n= 33)

*Voice Outcome Measurements*

A summary of the voice outcomes measures used in the selected studies are presented in Table 6. All ten studies used a holistic multidimensional approach to assess the voice function before and after the therapy.

- Visual-Perceptual Outcomes

One of the outcomes measures included in all studies was the visual-perceptual one that used laryngoscopic or stroboscopic examination. All selected studies used a video to record the images as well as to assess the glottal closure changes before and after treatment. The way vocal fold motility and glottal closure were measured varied with the use either subjective or objective approach in most of the studies. In El-Banna et al (El-Banna & Youssef, 2014), the authors rated glottal gap in the following three subjective categories: reduced, no change, and increased. They also reported using three blinded assessors for rating the glottal gap; nevertheless, they did not provide inter-rated reliability. Kao et al (Kao et al., 2017b) used an objective 6-point scale to measure the glottal closure ranging from “0 – normal” to “5 – severe”, with only one blinded rater (laryngologist). In Mattioli et al (F Mattioli et al., 2015a; Francesco Mattioli et al., 2011), the glottal closure was subjectively rated as either complete or incomplete; the latter was divided further in anterior and posterior glottal chink and there was no documentation regarding the number of assessors. D’Alatri et al (D’Alatri et al., 2008) and Schindler et al (Schindler et al., 2008) used the same subjective categories for glottal closure, that is, incomplete entire glottis closure; incomplete closure of the membranous part vocal folds; posterior glottal chink; and complete glottal closure. Finally, Vij et al (Vij et al., 2017a) objectively measured the glottal gap distance before and after therapy. In these last three studies, no details were provided on the number of raters. No data regarding inter- and intra-rater reliability was available in any of these studies. In general, all selected studies reported that, in a proportion of the patients, the vocal fold motility was improved after voice therapy. In other words, not all patients showed improvement in all the studies. Only Cantarella et al (Cantarella et al., 2010) and Vij et al (Vij et al., 2017a) reported 100% improvement.

**Table 5– Voice Therapy Program Characteristics**

Authors	Sample Size	Description of Intervention	Timing	Intensity	Duration
Schindler et al (Schindler et al., 2008)	40	Direct voice therapy included: Abdominal breathing training; Resonance Voice Therapy; sustain vowel.	Early (<4 weeks)	2 sessions/week 6 to 20 sessions	6 to 20 sessions
D'Alatri et al (D'Alatri et al., 2008)	91	Indirect voice therapy (Vocal Hygiene) Direct voice therapy included: Abdominal breathing training; half-swallow boom technique; Lip and tongue trill; nasal twang, speaking on inhalation, Laryngeal manipulations techniques	Early (<6 weeks)	2x30 min session/week	8 to 35 sessions
Cantarella et al (Cantarella et al., 2010)	30	Direct Voice Therapy included: Abdominal breathing training; Resonance Voice Therapy; Digital manipulation; strengthening adductor muscles and Thyroid manipulations techniques	Early (<3 months) vs Late (>3 months)	Depending on severity	10 to 40 sessions 2 to 3x daily homework for 10 to 15 min
Mattioli et al (Francesco Mattioli et al., 2011)	74	Direct Voice Therapy included: Cough attack; Cough with vowel; Vocal Functional Exercise; Pushing exercises; Laryngeal manipulations techniques; Resistance maneuvers	Early (<4 weeks)	2 sessions/week	14 to 20 sessions Daily homework
El-Banna et al (El-Banna & Youssef, 2014)	30	Direct Voice Therapy included: Modified pushing exercises and Smith accent method	Early (<4 weeks) vs Late (>6 weeks)	2x 20 min session/week	Early group: 16 sessions Late group: ND
Mattioli et al (F Mattioli et al., 2015a)	171	Direct voice therapy includes: Cough attack, cough with vowel, Vocal Functional Exercise; chest compression, Laryngeal manipulations techniques, resistance maneuvers.	Early (<4 weeks) vs Intermediate (8 weeks) vs Late (>8 weeks)	2 session/week	12 to 18 sessions Daily homework
Busto-Crespo et al (Busto-Crespo et al., 2016)	70	Direct voice therapy: Correcting posture; Abdominal breathing; Resonance Voice Therapy; Vocal exercises; Cough attack; Lip and tongue trill; vocal and singing exercises; auditory masking.	Early (< 1 year) vs Late (>1 year)	2x 30 min session/week	15 sessions
Kao Y-C et al(Kao et al., 2017b)	19	Indirect voice therapy (Vocal Hygiene) Direct voice therapy included: Breathing control; relaxation exercise, Vocal Functional Exercise; Hard glottal attack and Resonance Voice Therapy)	Early (<6 Months)	1 session/week	16 sessions Daily homework
Vij S. et al (Vij et al., 2017a)	20	Direct voice therapy included: Pushing-pulling exercises; Half-swallow boom; Head tilt method; Digital manipulation; Neck relaxation exercises; Laryngeal manipulations.	Early voice therapy (< 3 weeks) vs surgical therapy	2x 25-30 min session/week for 1 month and gradually called once a week	16 sessions
Barcelos et al (Barcelos et al., 2017)	43	Indirect voice therapy (Vocal Hygiene) Direct voice therapy included: Pushing-pulling exercises; Laryngeal manipulations; Auditory and proprioceptive biofeedback training.	Unspecified	2x 30 min session/week	12 sessions

The meta-analysis revealed a significant improvement, although it was not more than 80% of the cases. The result of five (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; D'Alatri et al., 2008; Kao et al., 2017b) of these ten studies yielded significant statistical results, indicating the success of the voice therapy.

- Auditory-Perceptual Outcomes

Auditory-perceptual voice analysis was measured in six studies (Schindler et al (Schindler et al., 2008), D'Alatri et al (D'Alatri et al., 2008), Cantarella et al (Cantarella et al., 2010), El-Banna et al (El-Banna & Youssef, 2014), Kao et al (Kao et al., 2017b) and Barcelos et al (Barcelos et al., 2017)). A modified scale (Grade, Roughness, Breathiness, Asthenia and Strain (GRBAS)) was used in each of the studies ; D'Alatri et al (D'Alatri et al., 2008) and Cantarella et al (Cantarella et al., 2010) did not use blinded raters; Kao et al (Kao et al., 2017b) used only one speech language pathologist for rating, whereas all other studies used at least two raters. Cantarella et al (Cantarella et al., 2010) was the only study that reported inter-observer variability data, and it was evaluated to be low. To summarize, all studies described at least four auditory-perceptual voice qualities with a statistically significant improvement after the voice therapy. Altogether, the visual-perceptual and audio-perceptual results should be decoded with prudence, as there is an important risk for measurements bias, because of the lack of data on inter- and intra-observer agreement.

- Acoustic Outcomes

Acoustic voice analysis was performed in nine (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; D'Alatri et al., 2008; Kao et al., 2017b; F Mattioli et al., 2015a; Francesco Mattioli et al., 2011; Schindler et al., 2008; Vij et al., 2017a) out of the ten studies; the most frequent acoustic parameters included were shimmer (%), jitter (%), Noise-Harmonic-Ratio (NHR, dB), and fundamental frequency ( $f_0$ ). Overall, improvements with statistical significance were observed in jitter in all studies as a decrease in values of jitter from pre-treatment to post-treatment (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; D'Alatri et al., 2008; El-Banna & Youssef, 2014; Kao et al., 2017b; F Mattioli et al., 2015a; Francesco Mattioli et al., 2011; Schindler et al., 2008; Vij et al., 2017a). In addition, improvements with statistical significance were observed in shimmer in seven studies; HNR dB in eight studies; as well

as  $f_0$  in four out of six studies (Busto-Crespo et al., 2016; F Mattioli et al., 2015a; Francesco Mattioli et al., 2011; Vij et al., 2017a).

- Aerodynamic Outcomes

Aerodynamic voice measurement was performed in all studies except in El-Banna et al (El-Banna & Youssef, 2014). All studies used the maximum phonation time (MPT) as an indirect measure of airflow; the MPT used was the best among all three attempts. In general, most studies (eight out of nine) described MPT improvements with a statistical significance after voice therapy.

- Self-Assessment Outcomes

The patients' self-assessment of the effect of the UVFP on their QoL was evaluated in eight (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; D'Alatri et al., 2008; El-Banna & Youssef, 2014; Kao et al., 2017b; Francesco Mattioli et al., 2011; Schindler et al., 2008) out of the ten studies; of these, seven (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; D'Alatri et al., 2008; Kao et al., 2017b; Francesco Mattioli et al., 2011; Schindler et al., 2008) studies used the Voice Handicap Index (VHI) questionnaire, and, one study (31) used the Voice Problem Self-Assessment Scale-20 questionnaire (VPSS-20). In summary, all studies reported improvement with statistically significant in patients' QoL after voice therapy.

**Table 6 - Summary of outcomes measurements, evaluation techniques and results of the Included Studies**

Authors, Year	Therapy Program	Evaluation Outcomes	Main findings
Schindler et al (Schindler et al., 2008), 2008	Total: 40 Voice therapy Patient-based	Morphofunctional Acoustic (F $f_0$ , jitter, shimmer, HNR)	95% of patients improved vocal motility. Statistically significant in mean values of jitter (p=0.001), shimmer (p<0.0001) and NHR (p=0.003). Statistically significant improvement after voice therapy (p<0.0001).
		Aerodynamic (MPT) Perceptual (GIRBAS) Self-Assessment (VHI)	Statistically significant in all parameters except strain domain (p<0.02). Statistically significant for the total values and subscales (physical, functional, and emotional) (p<0.0001).
D'Alatri et al (D'Alatri et al., 2008), 2008	Total: 91 Voice therapy Patient-based	Morphofunctional Acoustic (jitter, shimmer, HNR, VTI)	Significant Increase in glottal motility (p<0.05). Statistically significant in all parameters (p<0.05) except VTI. Statistically significant improvement p<0.05).
		Aerodynamic (MPT) Perceptual (GIRBAS) Self-Assessment (VHI)	Statistically significant improvement in mean values for grade, instability, breathiness and asthenia (p<0.05) except roughness. Statistically significant improvement in mean values for total and subscales (physical, functional and emotional) (p<0.05).
Cantarella et al (Cantarella et al., 2010), 2010	Total: 30 EVT: 14 Voice therapy LVT: 16 Voice therapy Patient-based	Morphofunctional Acoustic (jitter, shimmer, HNR)	Statistically significant improvement in glottal competence in all patients of both groups (p=0.011). Statistically significant improvement in both groups for the parameters of frequency instability (jitter, $f_0$ ) and for the HNR.
		Aerodynamic (MPT) Perceptual (GIRBAS) Self-Assessment (VHI)	Statistically significant improvement in both groups (p< 0.0001). Statistically significant improvement in all except for strain in the EVT. Statistically significant improvement in mean values for total and subscales in both groups (p<0.0001).
Mattioli et al (Francesco Mattioli et al., 2011), 2011	Total: 74 Voice therapy Patient-based	Morphofunctional Acoustic (jitter; shimmer; HNR, $f_0$ )	68,9% of patients recovered vocal fold motility. No statistical significance related with initial vocal fold position. Statistically significant improvement in all parameters (p<0.001). Statistically significant improvement in all parameters (p<0.001).
		Aerodynamic (MPT) Self-Assessment (VHI)	Statistically significant for the total values and subscales (physical, functional, and emotional) (p<0.0001)
El-Banna et al (El- Banna & Youssef, 2014), 2014	Total: 30 EVT: 22 Voice therapy LVT: 8 Voice therapy Protocol-based	Morphofunctional Perceptual (GIRBAS)	A reduction in gap size in the majority of the studied groups, more evident in the EVT. Statistically significant improvement in all parameters except asthenia for EVT. Statistically significant improvement only in strain for LTV (p=0.011).
		Self-Assessment (VPSS-20)	Statistically significant improvement in total VPSS-20 score and its clusters for the EVT. Statistically significant improvement in total VPSS-20 score (p = 0.017) and in the phonasthenic clusters in the LVT (p=0.022).

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Authors, Year	Therapy Program	Evaluation Outcomes	Main findings
Mattioli et al (F Mattioli et al., 2015a), 2015	Total: 171 EVT: 78 Voice therapy IVT: 49 Voice therapy LVT: 44 Voice therapy Patient-based	Morphofunctional  Acoustic (jitter; shimmer, HNR, $f_0$ )  Aerodynamic (MPT)	62% of patients recovered vocal fold motility. No statistical significance related with timing of initiation of therapy. Statistically significant improvement in $f_0$ , mean values of Jitter, Shimmer and NHR (P<0.001) in early and intermediate groups. Statistically significant improvement only in NHR in the late group (p<0.001). Statistically significant improvement in the early and intermediate groups (p<0.0001). No statistical significance in the late group.
Busto-Crespo et al (Busto-Crespo et al., 2016), 2016	Total: 70 EVT: 47 Voice therapy LVT: 23 Voice therapy Protocol-based	Morphofunctional  Acoustic (jitter; shimmer, HNR, $f_0$ )  Aerodynamic (MPT) Self-Assessment (VHI-10)	Statistically significant glottal motility improvement in the EVT group (p<0.001). No statistical significance in LVT. Statistically significant improvement in jitter parameter only in EVT group (p<0.006). No statistical significance in LVT. No statistical significance in both groups. Statistically significant improvement in the total score (P<0.001) in both groups.
Kao Y-C et al (Kao et al., 2017b), 2017	Total: 19 EG: 10 Voice Therapy CG: 9 Vocal Hygiene Protocol-based	Morphofunctional Acoustic (jitter; shimmer, HNR) Aerodynamic (MPT, PTP, PQ)  Perceptual (GIRBAS)  Self-Assessment (VHI)	Statistically significant improvement in glottal closure in EG (p<0.05). Statistically significant improvement in all parameters in EG. No statistical significance in the CG. Statistically significant improvement in all parameters in EG (p<0.005). No statistical significance in the CG. Statistically significant improvement in grade, loudness, pitch, breathiness, aphonia, monotone, and resonance in EG (p<0.05). Statistically significant improvement only in loudness and breathiness in the CG (p<0.05). Statistically significant improvement for the total values and subscales in the EG (p<0.005). Statistically significant improvement only in the physical domain in the CG (p<0.05).
Vij S. et al (Vij et al., 2017a), 2017	Total: 20 EG: 10 Voice Therapy CG: 10 Surgical Therapy Patient-based	Morphofunctional Acoustic (jitter; shimmer, HNR, $f_0$ )  Aerodynamic (MPT)	All patients improved after 3 months of therapy in both groups. Statistically significant improvement in the mean values of $f_0$ (p<0.0001) in both groups at 1 month and 3 months. Statistically significant improvement in jitter %, shimmer % and HNR at 3 months in both groups Statistically significant improvement in the mean values of MPT (p<0.0001) in both groups at 1 month and 3 months.
Barcelos et al (Barcelos et al., 2017), 2017	Total: 43 Voice therapy Patient-based	Morphofunctional  Acoustic (jitter; shimmer, HNR, PPQ) Aerodynamic (MPT)	Statistically significant vocal improvement, 69.2% reached full glottal motility (p=0.001). Statistically significant vocal improvement in jitter (p=0.016) and PQ (p=0.006) in pre, short, medium and long term. Statistically significant improvement in pre and short-term time points.

## Voice Rehabilitation in an aquatic setting

Authors, Year	Therapy Program	Evaluation Outcomes	Main findings
		Perceptual (GIRBAS)	Statistically significant improvement in all parameters in pre and short-term time points (p<0.005).
		Self-Assessment (VHI)	Statistically significant improvement in mean values for total and all subscales (p<0.001).

**Abbreviation:** VTI- Voice turbulence index increased; MPT - Maximum phonation time; AVA - Acoustic voice analysis; GIRBAS, perceptual rating scale (grade (G), instability (I), roughness (R), breathiness (B), asthenia (A), and strain (S)); CSL - Computerized Speech Lab; VHI – Voice Handicap Index; DSI - Dysphonia Severity Index; NHR - noise-to-harmonic ratio; NNE - normalized noise energy; VHI-10 - Voice Handicap Index 10; SNR - signal-to-noise ratio; F0 - fundamental frequency; DS - deviation standard; PTP, phonation threshold pressure; PQ, phonation quotient; EVT - early voice therapy group; IVT - intermediate therapy group; LVT - late voice therapy group; EG – experimental group; CG – control group.

*Study Design*

Regarding the location, most of the studies were from Italy (n=5), and the remaining were from Egypt, Taiwan, Brazil, Spain, and India (one each). The sample size varied across the studies, with Vij et al (Vij et al., 2017a) including the smallest sample size (n=10) and Mattioli et al (F Mattioli et al., 2015a) including the largest sample size (n=171).

The study design and the levels of evidence of the included studies was diverse: five case series (level IV) (Barcelos et al., 2017; D'Alatri et al., 2008; F Mattioli et al., 2015a; Francesco Mattioli et al., 2011; Schindler et al., 2008), three comparative studies with concurrent controls (III-2), (El-Banna & Youssef, 2014; Vij et al., 2017a) and two comparative studies without concurrent controls (III-3) (Busto-Crespo et al., 2016; Cantarella et al., 2010) (see Table 7). With regard to the study type, eight studies were prospective and two studies (F Mattioli et al., 2015a; Schindler et al., 2008) were retrospective.

**Table 7 – Studies Characteristics**

<b>Authors, Year</b>	<b>Country</b>	<b>Sample</b>	<b>Level of Evidence</b>	<b>Study Type</b>
Schindler et al (Schindler et al., 2008), 2008	Italy	40	IV Case series	Retrospective
D'Alatri et al (D'Alatri et al., 2008), 2008	Italy	91	IV Case series	Prospective
Cantarella et al (Cantarella et al., 2010), 2010	Italy	30	III-3 Comparative study without concurrent controls	Prospective
Mattioli et al (Francesco Mattioli et al., 2011), 2011	Italy	74	IV Case series	Prospective
El-Banna et al (El-Banna & Youssef, 2014), 2014	Egypt	30	III-2 Comparative study with concurrent controls	Prospective
Mattioli et al (F Mattioli et al., 2015a), 2015	Italy	171	IV Case series	Retrospective
Busto-Crespo et al (Busto-Crespo et al., 2016), 2016	Spain	70	III-3 Comparative study without concurrent controls	Prospective
Kao Y-C et al (Kao et al., 2017b), 2017	Taiwan	19	III-2 Comparative study with concurrent controls	Prospective
Vij S. et al (Vij et al., 2017a), 2017	India	10	III-2 Comparative study with concurrent controls	Prospective
Barcelos et al (Barcelos et al., 2017), 2017	Brazil	43	IV Case series	Prospective

### **iii. Level of Evidence**

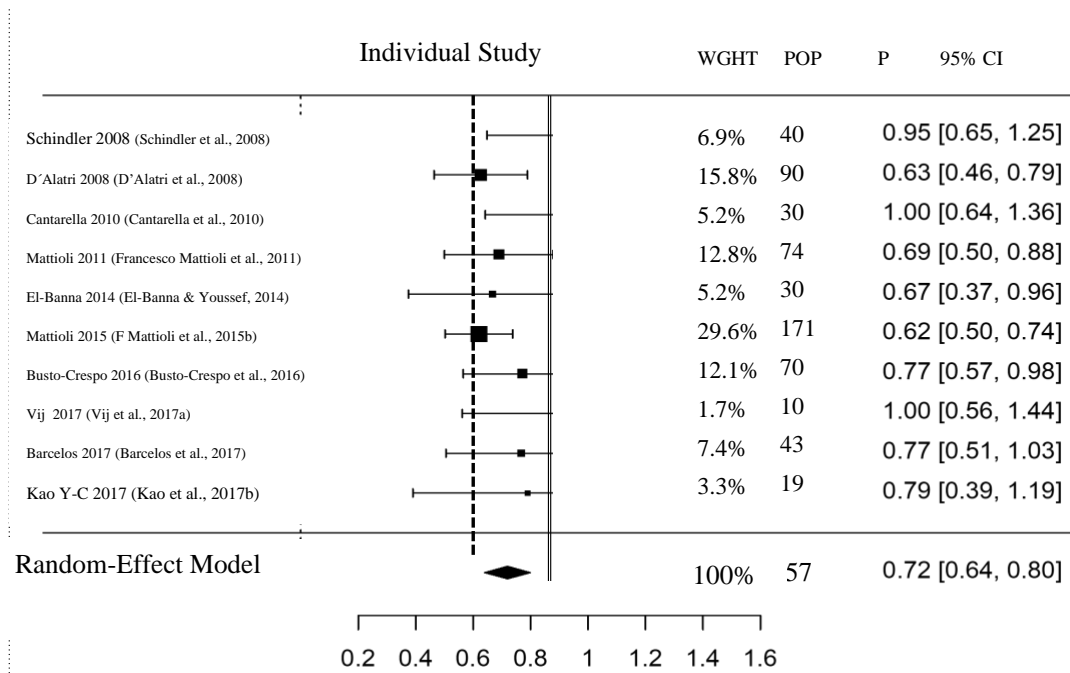
The quality of evidence of each included study, according to their methodology, was granted to one of the NHMRC levels of evidence. To summarize, the level of evidence of the included studies was low, due to the reduced sample sized, population differences, lack of randomization and characteristics of intervention-yielding risks of error, and moderate bias.

Results of the effects of voice therapy intervention on voice function outcomes were assessed for risk of bias using ROBINS-I tool (J. A. Sterne et al., 2016) which was applied in the five level III studies that used comparative groups. To concise, these studies were rated as having ‘moderate’ risk in the pre-intervention stage, and ‘low’ risk in the intervention and post-intervention stages.

### **iv. Meta-analysis of Visual-Perceptual Outcome**

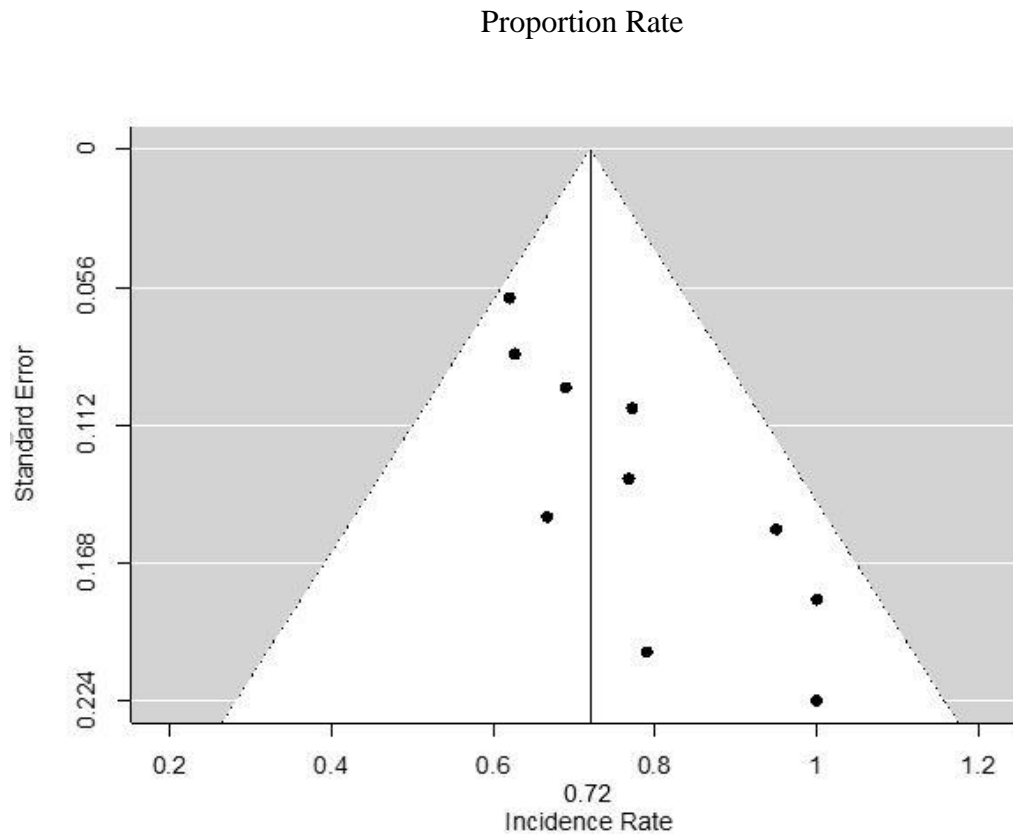
The changes visualized through the laryngo or stroboscopic examination was reported before and after the voice therapy. As mentioned above, a positive effect was observed on the vocal fold motility and, consequently, on the glottal closure after the voice therapy. The figure 2 demonstrates the pooled analysis of the 1117 results from all studies, with random-effect model, demonstrated that 72% of the patients (95% CI: 64.0%-80.0%) had improved glottal gap after the therapy. According to Higgins et al (Higgins et al., 2003; Higgins & Thompson, 2002), the inconsistency index of the different studies included in this meta-analysis was 18.35%, indicating a low heterogeneity. The statistical assessment of publication bias (Cochran’s Q test,  $Q=10.65$ ;  $p=0.300$ ) was non-significant, that is, it was found to be absent. Figure 3 shows a funnel plot in a shape of a symmetric inverted funnel, which is consistent with the absence of publication bias, although a slight lack of studies with a low proportion of successful of voice therapy and a small sample size (bottom-left panel in the graph) was denoted.

**Figure 2 – Forest Plot**



**Forest plot** - Illustration of results (proportion of patients with improved vocal fold motility after voice therapy) of different studies, with 95% CI, and the overall effect (random-effect model) with 95% CI. Studies are presented in order of year of publication (older to newer). Every study is represented by a filled square (denoting its risk ratio estimated and size vary according to weights accredited to the study; the size of square corresponds to the sample size/ study weight on the analysis) and the horizontal line denotes the corresponding 95% confidence interval. Studies that intersect the vertical line (incidence rate or proportion=1.0) indicate that all patients in that study improved their vocal fold motility after voice therapy. Pooled results from all studies are shown at the bottom, in diamond shape, with the random-effect model.

Figure 3 - Funnel Plot



**Funnel Plot** - symmetrical scatterplot of treatment efficacy against a measure of study size. Each dot represents a study; y-axis represents study standard error (precision); the weight of the study in the analysis is related with the inverse of the standard error (and therefore indirectly to the size of the sample); x-axis represents the voice therapy effect (vocal fold motility) proportion rate. Vertical line represents the summary estimated derived using random-effect meta-analysis. Diagonal lines represent 95% confidence limits (effect  $\pm 1.96$  SE) around for each standard error on the vertical axis.

## 2.5 Discussion

In this systematic review, ten studies were included after the search strategy was applied in four electronic databases. In all selected studies, a multidimensional voice assessment was used, in addition to an elementary voice therapy program that provided a comprehensive, decisive, and essential data regarding pre- and post-treatment evaluation of patients with UVFP. Study design included in this systematic review and meta-analysis was prospective or retrospective, with low level of evidence (III-2, III-3 and IV) (Shamseer et al., 2015).

The variability of the study design, the sample size, and the methodology used was an important rationale for statistical heterogeneity. Clinical diversity across the studies was an important source of variability, thus resulting in differences in the participants' characteristics and voice intervention program. With respect to the participant's characteristics, there was an important lack of homogeneity in the sample size, age ranges, gender, etiology, and side of paralysis. One comparative study (El-Banna et al (El-Banna & Youssef, 2014)) documented homogeneity between groups correlated with age range, gender and etiology of paralysis, but there was no relation with the gender and side of paralysis. In Cantarella et al (Cantarella et al., 2010) performed a comparative study of only the cause of the paralysis and found it to be homogeneous across the two groups. According to Robey's (Robey, 2004) framework, all studies are in phase one, because they do not control the participants' variables. There needs to be a better definition of both inclusion and exclusion criteria to allow for a more precise comparison among participants. This approach will minimize the risk of distortion of the voice therapy outcomes and help create a greater certainty of the types of patients who benefit from voice therapy intervention. Nevertheless, the proportion of patients who showed improved VF motility in the included studies for meta-analysis may vary independently with age heterogeneity across studies, as demonstrated in Kao et al (Kao et al., 2017b) and D'Alatri et al (D'Alatri et al., 2008) studies, where the age range of participants was similar (32-68 years and 31-68 years, respectively), but different proportions of patients improved their VF motility (100% vs 63%; Table 3). It is notable that although a similar age range would be advisable to enable comparison among studies, it would lead to a problem of applicability of results in the clinical world.

Concerning the voice program, most of the studies used an individualized voice therapy that matched the participants' clinical need, and the voice intervention was found to change even within the same study. Only three out of the ten included studies (Busto-Cespo et al (Busto-Crespo et al., 2016), El-Banna et al (El-Banna & Youssef, 2014) and Kao et al (Kao et al., 2017b)) used a voice therapy protocol for the patients, preventing comparison of specific therapy techniques across and within the studies. Moreover, having a structured framework therapy program enables control of the intensity and duration of therapy, the results of which could have an important role in clinical practice (phase 2 of Robey's (Robey, 2004) model). There is some evidence that higher intensity of voice therapy in patients with other types of dysphonia may help achieve overall success (Ramig et al., 1995; Wenke et al., 2014). The noteworthy point relates to the timing of initiation of therapy following the diagnosis of UVFP. All studies, with the exception of Barcelos et al (Barcelos et al., 2017), demonstrated that "early" intervention in patients with UVFP may be desirable to attain the optimal results. However, understanding what is considered as the early treatment is ambiguous in the studies, because there was a significant variance from < 3 weeks to < 1 year.

Although all studies used a multidimensional approach, there were restrictions on how the voice assessments were conducted. For instance, with regard to visual-perceptual evaluation using an endoscopic examination, three studies (Barcelos et al., 2017; El-Banna & Youssef, 2014; Schindler et al., 2008) used a videolaryngoscopy to record the change in glottal closure, while the other seven studies utilized a videostroboscopy. Only Barcelos et al (Barcelos et al., 2017) followed an adapted protocol for glottal examination. Except for Vij et al (Vij et al., 2017a), who used an objective measurement rating of glottal closure, all the other studies used a varied of subjective descriptive terms to rate the glottal changes. Another problem was the lack of inter- or intra-rater reliability data reported in all studies, against the recognized standard practice of reporting variability data between at least two raters. El-Banna et al (El-Banna & Youssef, 2014), Barcelos et al (Barcelos et al., 2017), and Kao et al (Kao et al., 2017b) used blinded raters, but there was no documentation on either inter or intra-rated variability data. The development of a protocol for use across studies would decrease the potential of bias, permit estimation of similarities among studies, and ameliorate the quality of evidence for the treatment of UVFP.

The positive effect of voice intervention on the glottal gap (which was statistically quantified by pooling the results' data from the included studies) determined the consistency of treatment effect across studies and the strength of evidence presented in the literature. In this regard, any improvement was considered as a positive effect in the glottal gap, irrespective of how glottal incompetence was rated in the different studies. From the meta-analysis for random-effects model, 72% of the patients from all the studies demonstrated a reduced glottal gap. Heterogeneity in the studies was found to be minimal ( $I^2=18.35\%$ ).

As stated by Robey (Robey, 2004), unidimensional measurement of voice outcomes limits the validation of vocal change over a period of time, whereas examining two or more areas (such as visual-perceptual assessment of glottal aspect; auditory-perceptual assessment of voice function, and impact on QoL) improves the validity as well as sensibility of identifying the nature and severity of UVFP. Overall, the majority of voice outcomes measures were improved, with statistical significance across the selected studies.

## **2.6 Limitations of the Systematic Review**

One limitation of this study is that the systematic review was restricted to articles in English language. In addition, the gray literature, such as conference papers, articles in obscure journals, research reports, dissertations, and some online journals have been excluded in the present review.

Interpretation of the results of the meta-analysis is limited by the quality of measurement outcome in the selected studies, which post a major risk of bias. Moreover, the positive effect of the voice intervention on the glottal gap could not be linked to any specific voice program due to its clinical diversity across the studies.

Another limitation was that studies were restricted to adults, which reduced the sample size, thus increasing the likelihood of study variability and adversely impacting the validity and credence of this article's conclusions.

## **2.7 Conclusion**

This meta-analysis supports the evidence that voice therapy has a significant positive effect on the glottal gap closure in patients with UVFP, irrespective of the technique of direct voice therapy. Nevertheless, a worldwide consensus protocol for glottal examination (which includes similar rating scale) in clinical practice is required, to enable robust comparison among studies as well as to improve the quality of evidence of impact of voice therapy in patients with UVFP.

In this systematic review, the sources of bias of the ten selected studies could not be controlled; therefore, it may not forecast the results of a single randomized well-designed large study. Early voice therapy and high-intensity program should be considered to accomplish optimal results. Nonetheless, a better understanding and clearer definition of what is “early therapy” and “high-intensity therapy” is essential in the future researched to establish the adequate outcome measures and treatment strategy.

Better study design and methodology in the future studies are needed to improve the quality of data for evidence-based use in clinical decision-making

## **Chapter III – Effectiveness of voice therapy in patients with vocal fold nodules: a systematic search and narrative review**

### **3.1 Abstract**

*Background/Objective:* An adult with vocal fold nodules can suffer from hoarseness, breathiness and vocal fatigue, which, in turn, significantly affects their vocal participation as well as activities. A well-designed voice therapy program improves the quality of life and vocal functionality. This is a narrative review with a systematic search of the current literature about the effectiveness of voice therapy interventions in adults with vocal fold nodules.

*Methods:* Several key terms were used for the database electronic search of articles. Strict inclusion criteria were used, and a broad evaluation of the studies performed. This included the level of evidence based on the National Health and Medical Research Council levels of evidence, assessment, and critical appraisal.

*Results:* Nine out of 30 reviewed articles met the criteria of inclusion and reported positive effects of voice therapy intervention in adult patients with vocal fold nodules. The vast majority of the reviewed studies reported multidimensional voice measures outcome data, most of them containing visual-perceptual, auditory-perceptual, acoustic and self-assessment results. Regardless of receiving direct or indirect or a combination of both voice therapy contents, nearly all voice quality parameters were found to improve after treatment. Short-term treatment (<3 weeks) may be as beneficial as longer traditional voice therapy programs, and using telepractice voice therapy may be an achievable and practical way of delivering treatment and enhance adherence in order to therapy. The study design and the evidence levels of the included studies were low ( $\leq$  III-2) and the risk of bias of the comparative studies was moderate.

*Conclusion:* This narrative review cannot conclude the general effectiveness of voice therapy programs. Further research and understanding of what specific parameters (exercise and techniques) of a therapy's content, will improving voice outcome measures. More studies are required to investigate whether or not voice therapy benefits are sustainable six months after ending therapy. However, improved evidence is required to

suggest that short period treatments are as beneficial as traditional therapy programs. Telepractice voice therapy may be an achievable and practical way of delivering treatment and enhance adherence to therapy.

### **3.2 Introduction**

Vocal fold nodules (VFNs) are bilateral benign growths that vary in size and occur in the middle part of the membranous vocal folds (Kunduk & McWhorter, 2009; Mette Pedersen & McGlashan, 2001). Histologically, they are described as thickened epithelium associated with a varying degree of an inflammatory reaction in the superficial lamina propria (Rosen et al., 2012).

Patients commonly seek medical attention when they experience ‘fatigue’, their voices become ‘rough’, and have reduced pitch range. The symptoms of dysphonia include: a disorder characterized by altered vocal quality, pitch, and loudness that impairs a patient’s ability to communicate and reduces the voice-related quality-of-life (QoL) (Birchall & Carding, 2019b).

The prevalence of VFN’s was found to be 1.31% in a large Korean sample (n=19636) of men and women aged >19years (4). In treatment-seeking populations with dysphonia, Houte et al reported a prevalence of 9.5% of VFNs, in a Belgian population of aged 15 years and older, whereas Coyle et al reported a prevalence of 8.2%, in a population in southwestern Ohio, USA, for the same age range (Coyle et al., 2001; Van Houtte et al., 2010a).

Women and type of occupation appear to be risk factors in the development of vocal fold lesions due to voice overuse, misuse or abuse that traumatizes the vocal fold tissue (Coyle et al., 2001; Van Houtte et al., 2010a; Zhukhovitskaya et al., 2015). Potentially, women are at a higher risk of developing nodules because they have less amount of hyaluronic acid (HA), in their superficial layer of the lamina propria of the vocal folds, when compared with men (3:1 male: female). HA levels affect the vocal fold tissue hydration, viscosity, and thickness which influence the biomechanics of voice production and voice quality. Less HA may suggest reduced protection from vibratory trauma and overuse (Casper & Leonard, 2006). Another factor differentiating gender is that women have

higher pitch (frequency) voices, which in theory, may result in an increase repetitive vocal fold collision and therefore, phonotrauma (Tae et al., 2012).

According to Vilkman et al (2000), some professions are considered to be at risk of developing vocal fold nodules, namely those that involve teaching activities for large groups of students and workplaces with high environmental noise (e.g. teacher) (Vilkman, 2000). Similarly, Jones et al (2002), stated that vocal nodules are frequent in vocally and environmentally demanding occupations or stressful lifestyles (e.g. aerobics instruction and singers) (Jones et al., 2002).

The treatment options for managing VFNs include voice therapy, pharmacotherapy (corticosteroids), and surgery (Chernobelsky, 2007). Evidence suggests the use of speech language pathology intervention as a preferred treatment option for VFN and surgical intervention should be considered in patients who do not exhibit signs of improvement after voice therapy (Syed et al., 2009). The usual surgical option comprise excision of the nodules with microsurgical techniques (Hsiung & Hsiao, 2004).

Standard clinical practice for voice therapy programs in patients with bilateral VFNs entail a combination of direct and indirect methods. Direct intervention - focus on controlling voice-producing mechanism (phonation, respiration and musculoskeletal function) by voice retraining (Casper & Leonard, 2006; R. Nelson et al., 2001); Indirect intervention - focus on patient education including counseling regarding vocal hygiene, voice rest and vocal abuse (R. Nelson et al., 2001; M Pedersen et al., 2004). Currently, there is lack of consensus regarding the best voice therapy plan. This implies that some authors concentrate on directly modifying the specific symptoms (i.e., symptomatic voice therapy) of the inadequate voice, whereas others, adopt a more holistic approach (physiologic voice therapy), i.e., when voice therapy techniques attend to the three subsystems of voice production (reparation, phonation and resonance) (Stemple, 2005). Several voice exercises, techniques, and programs described in the literature, where the selection was based on the type and severity of patients' dysphonia as well as their communication needs (Stemple et al., 2018). Moreover, consensus is also lacking between authors in terms of the intensity of voice therapy – this alludes to the duration and frequency of sessions, the dose of the teaching episodes within a session, and the total number of sessions ( or time period) required to achieve a desirable clinical outcome (Warren et al., 2007). Traditionally, the duration of a voice therapy program spanned over

period of 6 to 12 weeks, as long as improvement was observed in the patients' voice quality. Additionally, each therapy session, the frequency of which would be weekly, would last on average thirty minutes (Chagnon & Stone, 1996; Pannbacker, 1999).

The purpose of this systematic search and narrative review is to establish the evidence base for the general effectiveness of voice therapy programs in adults' patients with bilateral VFNs through critically reviewing the existing body of knowledge. A detailed critical appraisal, evaluation of the risk of bias and a rating of the studies in accordance with the evidence levels specified by the National Health and Medical Research Council (NHMRC) (Council, 2009) will be performed to assess the relevant literature on this subject.

### **3.3 Methods**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2015) was utilized to oversee the systematic literature review.

#### **i. Setting Eligibility Criteria**

The first and second authors developed the inclusion and exclusion criteria guided by the research question and objective, by the context and by the outcome measures considered in order to answer the research question, including study design, methodology, and analysis methods of the studies. The authors exchanged their viewpoints concerning the primary aim of the systematic review, subsequent to which any conflicts were discussed and dealt with before conducting the initial search strategy.

*Publication:* Only English written articles, published between January 1995 and May 2019 were included in the study. Only those publications were included that were peer-reviewed and published in an indexed scientific journal. Masters, doctorates, editorials, and grey literature were excluded due to the barrier in accessing them, which would have added time and expense to the process of the systematic review.

*Participant characteristics:* The participants included only those that were diagnosed with bilateral VFNs. Patients age  $\geq 18$  years. The study excluded articles that used only paediatrics' samples. Participants with bilateral VFNs who had received voice therapy in

the past were excluded. Similarly, studies conducted on animals or cadavers were also excluded.

*Therapy:* All voice therapies were included except if they were used in conjunction with a medical, pharmacological, or surgical therapeutic intervention. Even then, these interventions were only included if they were compared to a group that only received voice therapy. Furthermore, only those studies whose intervention was conducted by a SLP or by a Speech-language Pathologist Assistant (SLPA) supervised by a SLP were included, so as to ensure adherence to standard quality practice. No restrictions were imposed with regard to the content (techniques and exercises), duration, and intensity of voice therapy.

*Study design:* Retrospective and prospective cohort, case-control, and cross-sectional comparative studies documenting pre- and post-intervention voice outcomes were included. Additionally, controlled trials with and without randomization reporting pre and post voice outcomes were included as well. Studies were required to clearly report the voice therapy plan that should have included at least the types of techniques or exercises used, as well as the frequency, intensity, and duration of therapy received.

*Outcome measures:* Studies documenting any pre- and post-intervention, that is, either objective or subjective voice-function outcome measures were included. These could be inclusive of any of the following dimensions of outcome data: perceptual analysis of voice quality, visual examination of vocal fold anatomy and function, aerodynamic and acoustic measurements of the voice, and finally, the patient's self-assessment of voice function.

## **ii. Search Strategy**

In order to retrieve all the studies on Speech Language Pathology (SLP) intervention in patients with bilateral VFNs, the first author performed an electronic search on February 20th, 2019, in the following six databases: Embase, Web of Science, Pubmed, CINAHL, CENTRAL, and Google search. The initial search was not restricted to language, date of publication or age of the participants. The terms and keywords used to identify likely pertinent studies are listed in the Table 8.

**Table 8 - Search strategy terms used**

Population	Intervention
1. "vocal"	8. "therapy"
2. "Larynx"	9. "voice assessment"
3. "laryngeal"	10. "voice outcome"
4. "voice"	11. "intervention"
5. "nodules"	12. Combine 8-11 using "OR"
6. "nodule"	
7. Combine 1- 6 using "OR"	
Combine 7+12 using "AND"	

### ***Study Selection***

Upon the finalizing of the initial search strategy, a study selection was carried out following a step-by-step process, as illustrated in figure 4. Duplicated references were deleted using Mendeley Desktop ®Version 1.1., and the remaining studies for review were included for screening stages by the first author. However, in wake of its potential time intensiveness, hand-searching, that is a manual method of scanning select journals from cover to cover, page-for-page for relevant articles in case they were missed during indexing, was not performed for this systematic review. The screening process of these studies was conducted in three stages:

*1) Title and Abstract Screening* - the first and second authors screened the studies acquired from the database search in an independent manner before applying the predefined inclusion and exclusion criteria. A third independent reviewer resolved any divergence between the authors. At this stage, studies were excluded if the sample of the studies were found to include the following:

- a) only children (not the population of interest of this review), animals or cadavers;
- b) vocal fold pathology unrelated to nodules;
- c) voice therapy intervention not performed;
- d) not written in English;
- e) editorials, and
- f) published outside of the inclusion criteria period (i.e., 1995-2019).

2) *Full-text Screening* - the selected studies from the title and abstract phase were reviewed independently by the first and second authors, in order to ascertain the eligibility of articles against the decided inclusion criteria. Studies were excluded if:

- a) A description was made about the voice therapy intervention and voice function assessment, or
- b) Resultant data was non-existent or incomplete.

3) *Reference list Screening* - the reference list of identified articles in the full-text review stage was screened as another method using which the two authors retrieved the studies.

An independent third reviewer evaluated 20% of the articles selected from the title/abstract screening phase in order to assess the reliability of the screening. After examining the articles against the eligibility criteria, it was found that there was very minimal disagreement was found between the three authors.

### ***Critique procedures***

Essential data features from each selected study were extracted in order to help provide a critical appraisal of what was thought to be important to accomplish this systematic review. The data of this study are presented in Tables 2 to 5 and include the following:

- a) Study: publication year, study place, study design, and sample size.
- b) Participants' characteristics: gender, and age (range or median).
- c) Voice therapy: type of intervention, content, and intensity.
- d) Outcome measures that compared pre- and post- voice treatment.
- e) Results with statistical significance, where  $p$  value was reported.

### **iii. Methodology quality assessment**

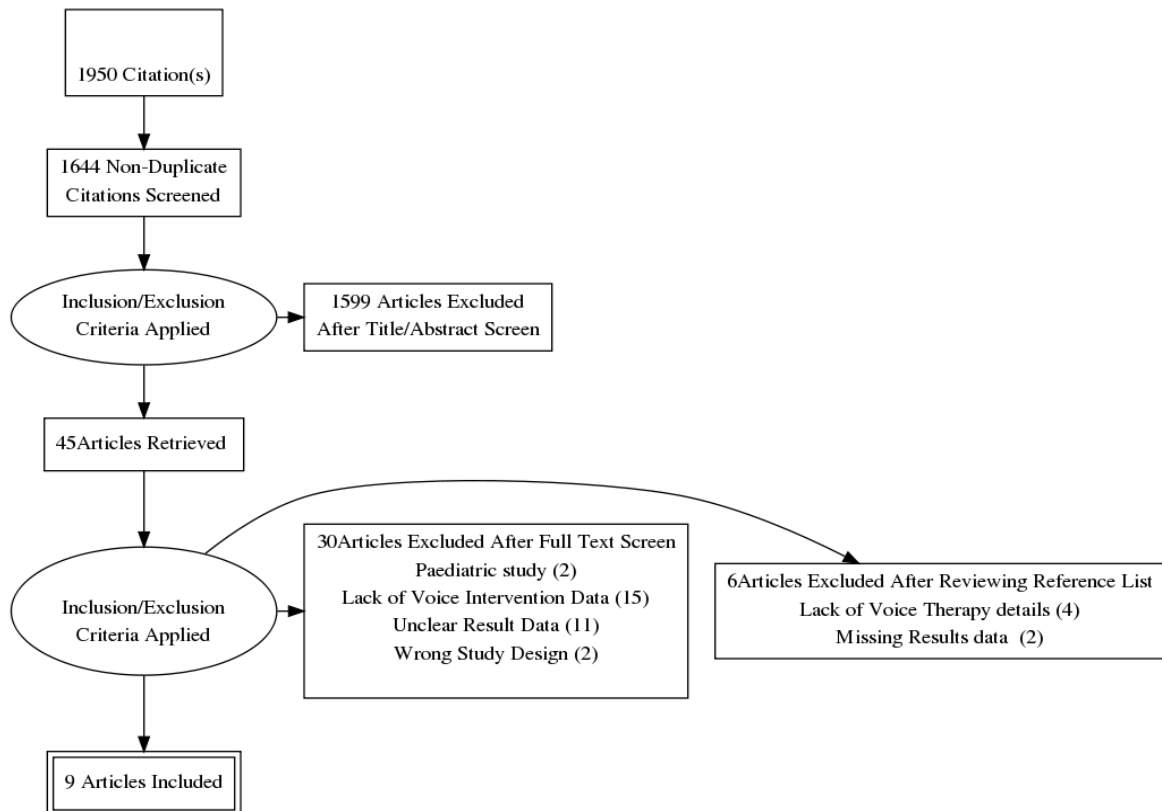
The first and second authors applied two tools independently in order to classify the selected studies with regard to speech therapy in patients with VFNs:

Level of evidence based on the framework provided by NHMRC (Council, 2009) was used to grade the studies based on the quality of the methodology used (design, validity, and applicability to patients).

Results of the effects of voice therapy intervention on voice function outcomes were assessed for potential bias of risk using the Cochrane Risk of Bias Assessment Tool for non-randomized studies of Interventions (ROBINS-I) (J. A. C. Sterne et al., 2016). This tool, which includes the risk assessment in the results of studies in seven bias domains, and are categorized into the following three groups: 1) two pre-treatment features (confounding and selection of participants into the study); 2) one intra-treatment feature (classification of intervention); and 3) four post-treatment features (deviations from intended interventions, missing data, measurement of the outcome and selection on the reported result). The risk of each bias domain was judged by the authors as being 'low', 'moderate', 'severe' or 'unclear'. At the end, an overall grade was given based on the lowest quality outcome among the individual domains. A lack of agreement and conflicts between the first two authors were discussed before being resolved by a third author.

### **3.4 Results**

Our search strategy identified 1950 citations, among which 1644 were excluded after the duplicates were removed and extensive title/abstract screening were performed. Thereafter, the remaining 33 articles were selected for full-text assessment for eligibility, based on the inclusion criteria. Finally, nine studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) met all the eligibility criteria and were evaluated in this systematic review. The reasons for excluding the other 36 citations in addition to the entire study selection process are presented in Figure 4 (PRISMA adaptation flow chart diagram).

**Figure 4 – Flow diagram following PRISMA guidelines for the selection of papers**

### **i. Level of Evidence**

According to the methodology used in each selected study, the authors granted their level of evidence using its recommended grading based on the NHMRC levels of evidence. In general, the level of evidence of the studies was found to be low ( $\leq$  level III-2). Table 9 summarizes the NHMRC level of evidence, study type, and the main intervention outcomes of the intervention of each included study.

### **ii. Risk of Bias**

Using the ROBINS-I (J. A. C. Sterne et al., 2016) tool (Figure 5), which was conducted on all the studies included in this review, results of the effects of intervention in non-randomized studies were assessed for risk of bias (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995).

### **iii. Critical appraisal of identified studies**

Tables 10 and 11 elucidate the study and the participants' characteristics of each study that was included for critical appraisal.

#### *Study characteristics*

The nine studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) varied in both level and design: five of these were case series (level IV) (Chhetri & Gautam, 2015; Fu et al., 2015b; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018) and four were comparative studies with concurrent controls (level III-2) (Fu et al., 2015a, 2016; Mashima et al., 2003; Verdolini-Marston et al., 1995). Regarding the study type and country of origin, all studies were prospective: three (Fu et al., 2015a, 2015b, 2016) of them were from Australia, whereas the remaining ones were from Nepal (Chhetri & Gautam, 2015), Italy (Lucchini et al., 2018), Sweden (Holmberg et al., 2003), Iran (Khoramshahi et al., 2018), Hawaii (Mashima et al., 2003), and United States (Verdolini-Marston et al., 1995) (one each).

**Table 9- Identified Relevant Studies and its Main Findings**

Authors, year	Country	Study Type	Level of Evidence	Study Design	Main Findings
Verdolini-Marston et al (Verdolini-Marston et al., 1995), 1995	USA	Prospective	III-2	Comparative study with concurrent controls	A greater proportion of therapy subjects improved on all measures (effort, perceptual and visual) over the initial 2 week-period when comparing with control group. Subjects' compliance with utilization of technique following therapy termination appears to affect the outcome of therapy at 4 weeks.
Mashima et al (Mashima et al., 2003), 2003	Hawaii	Prospective	III-2	Comparative study with concurrent controls	Voice therapy provided by videoconference had similar positive effects to the conventional model. No statistical differences were found between the 2 groups.
Holmberg et al (Holmberg et al., 2003), 2001	Sweden	Prospective	IV	Case series with pretest-posttest outcomes	None of the nodules disappeared after voice therapy protocol. However, edema and nodule size reduce in 9/10 patients.
Fu et al (Fu et al., 2015b), 2014	Australia	Prospective	IV	Case series with pretest-posttest outcomes	Telepractice as a feasible and potentially effective mode of delivering intensive voice therapy. There were positive changes in physiologic parameters and in the participants' perception of voice.
Fu et al (Fu et al., 2015a), 2014	Australia	Prospective	III-2	Comparative study with concurrent controls	Intensive voice therapy improved physiologic voice parameters of the participants and is as beneficial in treating vocal nodules as traditional voice therapy.
Chhetri et al (Chhetri & Gautam, 2015), 2015	Nepal	Prospective	IV	Case series with pretest-posttest outcomes	Voice therapy had good effect on glottal closure and positive changes of acoustic parameters.
Fu et al (Fu et al., 2016), 2016	Australia	Prospective	III-2	Comparative study with concurrent controls	Intensive voice therapy improved physiologic voice parameters and patient's perception of voice quality, and those findings were maintained up to 6 months post-therapy and comparable with TVT.
Lucchini et al (Lucchini et al., 2018), 2017	Italy	Prospective	IV	Case series with pretest-posttest outcomes	PROEL method improved the voice quality of patients with VFNs.
Khatoonabadi et al (Khoramshahi et al., 2018), 2018	Iran	Prospective	IV	Case series with pretest-posttest outcomes	VHI subscales and total scores improved after voice therapy.

**Abbreviation:** PROEL, Proprioceptive-Elastic Method; TVT, traditional voice therapy

**Figure 5 - ROBINS-I Summary of RoB judgment of the 4 included studies**

Level of evidence	Authors	Overall Risk of Bias	Confounding	Selection of participants into study	Classification of interventions	Deviations from intended Interventions	Missing data	Measurement of outcomes	Selection of reported results
III-2	Verdolini-Marston et al (Verdolini-Marston et al., 1995)	X	X	X	√	√	√	√	√
III-2	Mashima et al (Mashima et al., 2003)	X	X	X	√	√	√	√	√
IV	Holmberg et al (Holmberg et al., 2003)	□	□	□	√	√	√	√	√
IV	Fu et al (Fu et al., 2015b)	□	□	□	√	√	√	√	√
III-2	Fu et al (Fu et al., 2015a)	X	X	X	√	√	√	√	√
IV	Chhetri et al (Chhetri & Gautam, 2015)	□	□	□	√	√	√	√	√
III-2	Fu et al (Fu et al., 2016)	X	X	X	√	√	√	√	√
IV	Lucchini et al (Lucchini et al., 2018)	□	□	□	√	√	√	√	√
IV	Khatoonabadi et al (Khoramshahi et al., 2018)	□	□	□	√	√	√	√	√

**key:** (√) = low risk of bias; (x) = Moderate risk of bias (□) = High risk of bias

*Participant characteristics*

The studies exhibited a show a considerable level of heterogeneity as far as the characteristics of the participants were concerned (Table 10). Chhetri et al (Chhetri & Gautam, 2015) and Mashima et al (Mashima et al., 2003) did not describe or specify the gender in their respective nodules group. In the remaining studies, the vast majority of the participants were women (2% male and 98% female). Concerning age, two studies (Chhetri & Gautam, 2015; Mashima et al., 2003) did not reveal details about the average age of participants. Despite the stated inclusion criteria of participants of only if 18 years and older, Chhetri et al (Chhetri & Gautam, 2015) included participants who were even 16 years old. The reason why they were included in this review was because the data reported included participants in our stated age range and the studies reported significant data on voice therapy in patients with VFNs.

**Table 10- Participants' characteristics**

Authors, year	Sample size	Male/Female	Average age (range)
Verdolini-Marston et al (Verdolini-Marston et al., 1995), 1995	Total: 13 CT:5 RT:3 CG:5	0/13	20 (18-22)
Mashima et al (Mashima et al., 2003), 2003	Total: 18 C: 9 VTC: 9	ND	≥ 18 years
Holmberg et al (Holmberg et al., 2003), 2001	10	0/10	23.3 (19-35)
Fu et al (Fu et al., 2015b), 2014	10	0/10	33.7 (19-49)
Fu et al (Fu et al., 2015a), 2014	Total: 53 TVT 29 IVT 24	0/53	37.5 (20-54) 37.52 37.54
Chhetri et al (Chhetri & Gautam, 2015), 2015	27	ND	>16 years
Fu et al (Fu et al., 2016), 2016	Total: 36 TVT 20 IVT 16	0/36	(18-55) 36.4 38.5
Lucchini et al (Lucchini et al., 2018), 2017	15	0/28	42.5 (25-66)
Khatoonabadi et al (Khoramshahi et al., 2018), 2018	11	1/10	37 (25-51)

**Abbreviation:** ND, not described; IVT, Intensive voice therapy; TVT, traditional voice therapy; C, Conventional; VTC, video-teleconference; CT, Confidential therapy; RT, Resonant therapy; CG, control group

**Table 11- Details of Therapy Plan applied in each study**

Authors	Sample	Voice Therapy Content	Duration of Intervention		Intensity of intervention
Verdolini-Marston et al (Verdolini-Marston et al., 1995)	Total: 13 CT: 5 RT: 3 CG: 5	Vocal Hygiene and Direct voice therapy (Confidential Colton and Casper vs Lessac Resonant) Protocol-based	2weeks	9 sessions	Therapy groups (CT and RT): 8 individual sessions of 1h and one final group session of 1h. 4 to 5 sessions /G week. Control group: had vocal hygiene counseling with the therapy groups before treatment started.
Mashima et al (Mashima et al., 2003)	Total: 18 C: 9 VTC: 9	Vocal Hygiene and Direct voice therapy Protocol-based	9 weeks	5 to 6 sessions	One 30 min/session every week and a half
Holmberg et al (Holmberg et al., 2003)	10	Vocal Hygiene and Direct voice therapy Protocol-based	16 weeks 24 weeks	15 sessions	One 80 min session/week 2x15min session a day (homework)
Fu et al (Fu et al., 2015b)	10	Lessac-Madsen Resonant Voice Therapy included: Vocal hygiene and Direct voice therapy Protocol-based	3 weeks	9 sessions	IVT: 3 sessions/week. Two 15 min telepractice sessions/day on a non-treatment day One 15 min telepractice session on a treatment day (homework)
Fu et al (Fu et al., 2015a)	Total: 53 TVT 29 IVT 24	Lessac-Madsen Resonant Voice Therapy included: Vocal Hygiene and Direct voice therapy Protocol-based	8 weeks 3 weeks	8 sessions	TVT (control) group: One 45 min session/week for 8 weeks The IVT group: Three 45 min sessions/week in the first 2 weeks followed by Two 45 min sessions/week in the third week
Chhetri et al (Chhetri & Gautam, 2015)	27	Unspecified Voice Therapy	12 weeks	16 sessions	Two 30 min session/week 1st month One 30 min session/week 2nd month onwards
Fu et al (Fu et al., 2016)	Total: 36 TVT 20 IVT 16	Lessac-Madsen Resonant Voice Therapy included: Vocal Hygiene and Direct voice therapy Protocol-based	8 weeks 3 weeks	8 sessions	TVT (control) group: One 45 min session/week for 8 weeks The IVT group: Three 45 min sessions/week in the first 2 weeks followed by Two 45 min sessions/week in the third week
Lucchini et al (Lucchini et al., 2018)	28	PROEL method includes: Vocal Hygiene and Direct voice therapy Protocol-based	8 weeks	15 sessions	Two 45-60 min session/week
Khatoonabadi et al (Khoramshahi et al., 2018)	11	Vocal Hygiene and Direct voice therapy Protocol-based	9 weeks	16 sessions	Two 50 min sessions/week

**Abbreviation:** ND – not described; TENS - Transcutaneous electrical nerve stimulation; PROEL, Proprioceptive-Elastic Method; TVT, traditional Voice Therapy; IVT, Intensive Voice Therapy; C, Conventional; VTC, Videoteleconference; CT, Confidential therapy; RT, Resonant therapy; CG, control group

The total number of participants was found to be similar in level III and IV studies. In totally, 169 participants were included across all the studies, with 83 participants in level III studies, with a range of 13-52 participants within the studies. Meanwhile, the average age in the level III studies and level IV studies ranged from 20 to 37.5 years and 23.3 to 42.5 years, respectively.

In all the studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995), an otolaryngologist confirmed the diagnosis of VFNs based on a laryngostroboscopy examination, The findings of the visual examination were video-recorded in seven out of the nine studies (all except Fu et al (Fu et al., 2015b) and Fu et al (Fu et al., 2016)).

### ***Details of therapy***

Table 11 illustrates considerable variability in voice therapy content and intensity.

### **Therapy content**

There is no consensus regarding the best voice therapy option. Put differently, some authors tend to focus on directly modifying specific symptoms (i.e. interventions target at modifying abnormal perceptual voice components with facilitating techniques). On the other hand, others adopt a more holistic approach (physiologic voice therapy), which directly modifies the physiology of the vocal mechanism, i.e., when voice therapy techniques attend to the three subsystems of voice production (reparation, phonation, and resonance) (Stemple, 2005).

A varied combination of direct and indirect voice therapy was used in all the studies (Table 11) except the one that was conducted by Chhetri et al (Chhetri & Gautam, 2015). In this study, all the details of voice intervention used were not documented.

At least eight of the nine studies reviewed used a pre-defined voice therapy program - a treatment-protocol - in order to minimize the variance of care delivered to patients. Most treatment plans in the selected studies adopted a holistic approach (physiologic voice therapy) as opposed to a symptoms-relief approach.

In the studies conducted by Fu et al (Fu et al., 2015a, 2015b, 2016), the therapeutic plan involved the combination of general voice hygiene method (indirect approach) with a direct approach by adapting the Lessac-Madsen resonant therapy, which encompassed exercises for rebalancing the three subsystems of the voice production: resonance, phonation, and breathing (physiologic voice therapy).

On the other hand, Lucchini et al (Lucchini et al., 2018) applied a treatment plan focusing on education and counseling of participants that was combined with another approach to rebalance the phonatory system by eliminating muscle tension (PROEL method, which is a physiologic voice therapy).

In the comparative study conducted by Verdolini-Marston et al (Verdolini-Marston et al., 1995), one group received a resonant voice therapy method adapted from Lessac-Madsen, which included exercises to produce a vibratory sensation on the anterior palate during phonation and relaxing the upper body. Meanwhile, the group received a confidential voice therapy method modeled after Colton and Caspar (Casper & Leonard, 2006), which comprised of techniques to produce a phonation mode that was slightly breathy and loud, required minimal effort, and required the whole body to relax (symptomatic voice therapy).

Moreover, in the study by Holmberg et al (Holmberg et al., 2003), the voice therapy protocol consisted of five rudimentary behaviorally approaches: the therapy began with vocal hygiene, followed by respiration, relaxation, and direct facilitation. The approach used included the following: loudness reduction and yawn-sigh exercises, before being finalized with an attempt to transfer the “newly learned” vocal behaviors to “real life” situations outside of therapy setting. The study conducted by Holmberg et al (Holmberg et al., 2003) was the only one that described the utilization of a transfer tasks to the patients’ daily life environment.

In the study conducted by Mashima et al (Mashima et al., 2003), both the groups (conventional and video teleconference) received the same voice therapy that incorporated other than vocal hygiene counseling, facilitating voice therapy techniques such as focus, establishing a new pitch, glottal attach changes, as well as a confidential voice therapy method (symptomatic voice therapy) adapted from Colton and Caspar (Casper & Leonard, 2006). Furthermore, in research conducted by Khatoonabadi et al

(Khoramshahi et al., 2018) direct voice therapy consisted of chewing, yawn-sigh, correction of general body posture and training in abdominal breathing (physiologic voice therapy) .

### ***Intensity of intervention***

#### *Therapy program period of time or total number of sessions*

Meanwhile, the time period required to deliver the treatment program differed across and within studies. For example, the studies conducted by Fu et al (Fu et al., 2015a, 2015b, 2016) and Verdolini-Marston et al (Verdolini-Marston et al., 1995) had the shortest duration of therapy programs (less than 3 weeks), as compared to the one carried out by Holmberg et al (Holmberg et al., 2003) where participants had the longest therapy program (24 weeks). Similarly, the total number of sessions in the therapy program also varied according to the study. The study conducted by Mashima et al (Mashima et al., 2003) incorporated the least number of sessions in their therapy program (five or six). Contrastingly, Khatoonabadi et al (Khoramshahi et al., 2018) and Chhetri et al (Chhetri & Gautam, 2015) included the greater number of sessions, which was 16.

#### *Duration and frequency of sessions*

In the studies conducted by Fu et al (Fu et al., 2015a, 2015b, 2016), the participants with a more intensive voice therapy schedule had sessions that occurred three times a week during the first two weeks before reducing to two in the last week of treatment, with each session lasting up to 45 minutes. In a study by Fu et al (Fu et al., 2015b), a 15-minutes online session (telepractice) was provided for the convenience of participants. Similarly, in studies by Chhetri et al (Chhetri & Gautam, 2015) and Khatoonabadi et al (Khoramshahi et al., 2018), participants had a total of 16 sessions, and a 30 min session was delivered twice per week in the first month that then was reduced to once a week in the former study, whereas twice-weekly 50 min sessions were given in the later study. In studies by Lucchini et al (Lucchini et al., 2018) and Holmberg et al (Holmberg et al., 2003), where 15 sessions were received by the patients, a 45 to 60-minutes session per week as well as an and an 80 min session were conducted. In the study by Verdolini-Marston et al (Verdolini-Marston et al., 1995), the participants in two groups had nine sessions, with each lasting for an hour and being conducted individually eight times. One session was conducted in a group, with an intensity of four to five times per week. Finally, in the study

carried out by Mashima et al (Mashima et al., 2003), the patients had the least number of sessions of all included studies, varying between 5 and 6 sessions. On average, patients received one session of 30 min every week and a half.

Studies conducted by Holmerg et al (Holmberg et al., 2003) and Fu et al (Fu et al., 2015b) were the only ones that included homework to patients as part of their therapeutic plan. In the study carried out by Holmerg et al (Holmberg et al., 2003) patients were requested to complete 15-minutes of homework twice a day. Similarly, in the Fu et al study (Fu et al., 2015b), participants were asked to participate in a 15 minute a week home practice session.

### ***Voice outcome measurement***

A summary of the voice outcome measures used in the included studies and their results following the voice therapy have been elucidated in Table 12. In the current review, a multidimensional voice assessment is defined as the assessment of three or more of the following parameters of voice that could be potentially affected by the presence of VFNs: visual-perceptual; auditory perceptual, acoustic, aerodynamic and self-assessment of the voice.

Seven of the nine studies (Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) used a minimum of two dimensions to evaluate voice function before and after the voice therapy. Five studies (Fu et al., 2015a, 2015b, 2016; Lucchini et al., 2018; J. K. de O. Santos et al., 2016) used a multidimensional approach to measure the outcome, with being visual-perceptual, auditory-perceptual and self-assessment explorations being the most common assessed areas of the voice. Chhetri et al (Chhetri & Gautam, 2015) and Khatoonabadi et al (Khoramshahi et al., 2018) only measured one dimension each: acoustic and self-assessment, respectively.

Concerning the visual-perceptual outcome measure, seven studies (Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) assessed the vocal folds pre- and post-therapy, using a videolaryngostroboscopic examination, which specifically examined the morphology and function of the vocal folds. Studies carried out by Fu et al (Fu et al., 2015a, 2015b, 2016) Verdolini-Marston et al (Verdolini-Marston et al., 1995), Holmberg et al (Holmberg et

al., 2003), Mashima et al (Mashima et al., 2003) and Lucchini et al (Lucchini et al., 2018) documented the inclusion of ratings from more than one otolaryngologist. Individual video recordings were randomized before being rated by the otolaryngologists. In the studies by Fu et al (Fu et al., 2015a, 2016), the authors reported good inter-rater reliability between the raters (ICC=0.88) and excellent intra-rater reliability (ICC=0.91) in the former study. Furthermore, the authors reported good inter-rater reliability between the raters and intra-rater reliability, (ICC=0.75) and (ICC=0.77) in the latter study. For example, in the study carried out by Fu et al (Fu et al., 2016) study, inter-rater agreement measurements between the raters and intra-rater reliability were good, (ICC=0.77) and (ICC=0.75), respectively. Similarly, the study from Mashima et al (Mashima et al., 2003) reported a good inter-rater agreement of (ICC=0.72). In the studies carried out by Verdolini-Marston et al (Verdolini-Marston et al., 1995), Holmberg et al (Holmberg et al., 2003) and Lucchini et al (Lucchini et al., 2018) there was lack of documentation in terms of whether or not inter- and intra-rater reliability were evaluated. Overall, the visual-perceptual results should be read with some degree of caution, given that there is a considerable risk for measurement bias due to the lack of inter- and intra-rater agreement data in some of the studies.

The auditory perceptual rating of voice quality was another feature of the multidimensional outcome measurement used in the studies. In this regard four more recent studies (Fu et al., 2015a, 2015b, 2016; Lucchini et al., 2018) were found to use GRBAS or GIRBAS scale, which consists of five or six voice parameters: grade (G), instability (I), roughness (R), breathiness (B), asthenia (A), and strain (S). Studies carried out by Fu et al (Fu et al., 2015a, 2015b) studies reported randomization of paired samples before getting rated by more than one SLP, but in one of the authors' studies (Fu et al., 2016), the rater was also blind to the assessment time points. The authors reported fair inter-rater reliability between the raters (ICC=0.64) and good intra-rater reliability (ICC=0.85) in a study conducted by Fu et al (Fu et al., 2015a) study; and an excellent inter-rater reliability between the raters and intra-rater reliability, both presented ICC=0.90 in Fu et al (Fu et al., 2015b). In a study conducted by Fu et al (Fu et al., 2016), reported good inter-rater and intra-rater agreement measures (ICC=0.83 and ICC=0.86, respectively). In a study carried out by In Lucchini et al (Lucchini et al., 2018), the two raters judged the randomized samples but there is no documentation regarding intra- inter-rater reliability scores. The three older studies that included auditory perceptual rating

were those conducted by Holmberg et al (Holmberg et al., 2003), Mashima et al (Mashima et al., 2003), and Verdolini-Marston et al (Verdolini-Marston et al., 1995). The parameters measured in these studies were found to be very different from the recent studies; for example, in the study conducted by Verdolini-Marston et al (Verdolini-Marston et al., 1995), four independent raters rated the voice using an ordinal scale with 1=healthy voice to 5= severely impaired voice, and there was no report regarding the rater agreement between judges. In the study undertaken by Holmberg et al (Holmberg et al., 2003), multi-parameters were used (Table 12) with a high Cronbach's coefficient alpha value for inter-listener reliability in some parameters, such as press, breathing, lack of sonority, scrape and dysphonia. Finally, in the study conducted by Mashima et al (Mashima et al., 2003) study the perceptual voice evaluation was on voice quality, but there is no documentation available regarding the scale that was used. However, the authors did report that the samples were randomized and paired with two SLPs judging them, and that an excellent inter-rater reliability scores was achieved.

In general, all studies reported improvement with statistical significance in most of the auditory-perceptual parameters after therapy.

Aerodynamic analysis of voice was performed in just two studies (Fu et al., 2015a, 2015b), which only included the mean airflow rate (MFR) measurement that was found to improve with statistical significance in only one of them (Fu et al., 2015b).

Acoustic analysis of the voice was included in six studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Mashima et al., 2003) and some parameters were consistently assessed across studies: vocal fundamental frequency ( $f_0$ ) (Hz), jitter (%), shimmer (%), and noise-to-harmonics ratio (NHR) (dB). Chhetri et al (Chhetri & Gautam, 2015) added the normalize noise energy (NNE) parameter to the study, while and Holmberg et al (Holmberg et al., 2003) incorporated the Sound Pressure Level (SPL). Overall, most of the acoustic parameters improved with statistical significance across the studies.

The Voice Handicap Index (VHI) was used to quantify self-assessment of voice-related quality of life in four of the aforementioned studies (Fu et al., 2015b, 2016; Khoramshahi et al., 2018; Lucchini et al., 2018). The VHI assesses the impact of voice in three domains of participants' life: emotional, physical and functional. Mashima et al (Mashima et al.,

2003) used a Patient satisfaction rating (PSR) for the process and outcome of voice therapy. The rating was done on a 5-point scale (being 1= positive response to 5=negative response); and lastly, Verdolini-Marston et al (Verdolini-Marston et al., 1995) used a 12-questions questionnaire with regard to patients' perceptions about the therapy. According to three studies, voice therapy improved the participants' quality of life, with a statistical significance.

### ***Summary of voice therapy results***

All nine studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) reported positive changes in participants' voice domains following a treatment plan for VFNs, irrespective of whether the voice therapy consisted of only an indirect or direct approach, or a combination of both. With the exception of the ones conducted by Chhetri et al (19) and Khatoonabadi et al (21), all studies used more than two dimensions (P H Dejonckere, 2000) to measure their treatment effects on the voice. In addition, all studies presented a statistical analysis of an outcome measures, thus providing some methodological robustness to the study's findings.

As previously described, visual-perceptual and auditory-perceptual outcome measures were limited by the lack of inter and intra-rater reliability data documentation, except for studies conducted by Fu et al (Fu et al., 2015a, 2015b, 2016) and Holmberg et al (Holmberg et al., 2003). In the other studies (Chhetri & Gautam, 2015; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) where the validity tests were not applied, care should be exercised when analyzing the results, because there is the possibility of outcome measurement bias, as assessed with the ROBINS-I tool (Carding et al., 2004). In general, improvement or positive change is observed in the implemented outcome measures across the included studies

**Table 12 - Voice Therapy: Outcomes, Assessments and Results**

Authors	Outcome Measurements	Assessments	Results
Verdolini-Marston et al (Verdolini-Marston et al., 1995)	Multidimensional	Visual-perceptual (5-point scale) Auditory-perceptual (ordinal scale) Phonatory Effort Rating (magnitude scale) Self-Assessment (Questionnaire)	Not statistically significant for the three groups but majority of subjects regardless the group improved their score. Not statistically significant for the three groups but majority of subjects from therapy groups improved their score. Not statistically significant for the three groups but majority of subjects from therapy groups improved their score. Patients 'perceptions regarding therapy were positive for both therapy groups but without statistical significance.
Mashima et al (Mashima et al., 2003)	Multidimensional	Visual-perceptual Auditory-perceptual (GRBAS) Acoustic (jitter, shimmer) Self-Assessment (PSR)	Unclear results regarding vocal nodule group. Unclear measures. Statistically significant in both groups $p < 0.0001$ . Statistically significant improvement in both groups in jitter ( $p < 0.0001$ ) and shimmer ( $p < 0.001$ ) Both groups felt their voices improved considerably with therapy.
Holmberg et al (Holmberg et al., 2003)	Multidimensional	Visual-perceptual Auditory-perceptual (P.B.A.L.I.G.R.V.P.B.S.O.) Acoustic ( $f_0$ , SPL)	After therapy none of the nodules had disappeared (0%). Vocal nodules size and edema reduced 9 at bilaterally and 1 unilaterally. Statistically significant in P, I, G, R, V, S, O parameters ( $p < 0.05$ ) Statistically significant to $f_0$ ( $p < 0.05$ ) only.
Fu et al (Fu et al., 2015b)	Multidimensional	Visual-perceptual Auditory-perceptual (GRBAS) Aerodynamic (MFR) Acoustic ( $f_0$ , jitter, shimmer, HNR) Self-Assessment (VHI)	Statistically significant ( $p < 0.05$ ) for mucosa wave, glottal closure and edge smoothness. Statistically significant in grade, roughness and asthenia ( $p < 0.005$ ). No statistical report on breathiness. Statistic improvement in MFR ( $p < 0.05$ ) Statistically significant in all parameters ( $p < 0.02$ ) Statistic improvement in physical and functional domains ( $p < 0.05$ ).
Fu et al (Fu et al., 2015a)	Multidimensional	Visual-perceptual Auditory-perceptual (GRBAS) Aerodynamic (MFR) Acoustic ( $f_0$ , jitter, shimmer, HNR)	Statistically significant in TVT and IVT groups ( $p < 0.001$ and $p < 0.002$ ) for mucosal wave, edge smoothness and glottal closure. Statistically significant in all parameters ( $p < 0.002$ ) for both for IVT and TVT. Not statistic significant in IVT or TVT groups. Statistic significant in all parameters in TVT and IVT ( $p < 0.02$ ) except for NHR ( $p < 0.02$ )
Chhetri et al (Chhetri & Gautam, 2015)	Unidimensional	Acoustic ( $f_0$ , jitter, shimmers, HNR, NNE)	Statistically significant in jitter and shimmer ( $p < 0.05$ ) and HNR ( $p < 0.001$ ). Not statistically significant in NNE ( $p = 0.40$ )
Fu et al (Fu et al., 2016)	Multidimensional	Visual-perceptual Auditory-perceptual (GRBAS) Acoustic ( $f_0$ , jitter, shimmer, HNR) Self-Assessment (VHI)	Statistically significant in TVT and IVT groups ( $p < 0.001$ and $p < 0.002$ ) for mucosal wave, edge smoothness and glottal closure after treatment. Statistically significant in all parameters ( $p < 0.05$ ) for both for IVT and TVT. Statistically significant in all parameters ( $p < 0.02$ ) for both for IVT and TVT. No statistically significant changes in both groups across all acoustic parameters at 6 months follow up. Not statistic significant in IVT or TVT groups and no interaction with time of assessment.

**Table 12 - Voice Therapy: Outcomes, Assessments and Results**

Authors	Outcome Measurements	Assessments	Results
Lucchini et al (Lucchini et al., 2018)	Multidimensional	Visual-perceptual Auditory-perceptual (GIRBAS) Self-assessment (VHI)	Not statistically significant (p=0.51) Statistically significant improvement (p<0.001) in all parameters except for Instability (p=0.008) Statistically significant improvement (p<0.001)
Khatoonabadi et al (Khoramshahi et al., 2018)	Unidimensional	Self-assessment (VHI)	Statistically significant improvement in all subscale's parameters (p<0.05) after voice therapy.

**Abbreviation:** NHR, noise-to-harmonics ratio; NNE, normalized noise energy;  $f_0$ , Fundamental frequency; CG, control group; GRBAS, perceptual rating scale (grade (G), roughness (R), breathiness (B), asthenia (A), and strain (S)); MFR, mean airflow rate; VHI, voice handicap index; GIRBAS, perceptual rating scale (grade (G), instability (I), roughness (R), breathiness (B), asthenia (A), and strain (S)); SPL, sound pressure level; P.B.A.L.I.G.R.V- press (P), breathiness (B), aphonic (A), lack of sonority (L), instability (I), gratings (G), roughness (R), vocal fry (V); P.B.S.O - press (P), breathiness (B), scrape (S), overall dysphonia.

### **3.5 Discussion**

Using clear search term and inclusion/exclusion criteria, the electronic database search review led to the final validation of nine studies. Altogether, the studies had a low level of evidence with an overall risk of bias judged as moderate for the comparative studies. Nevertheless, the positive findings after voice therapy consistently reported across the studies may motivate speech therapy pathologists to follow a recommendation for clinical practice. However, it would do well to remain alert to new information and sensitive to patients' voice evolution.

#### **i. Methodological quality assessment**

As opposed to medical and pharmacological research, Pring (Pring, 2005) suggests that achieving a high level of evidence is challenging for behavioral research. As an example of behavioral treatment, voice therapy is commonly individual, since it is based on diagnosis and patient's symptoms, thus underpinning the need for a pragmatic, eclectic, and holistic approach is required.

An NHMRC level of evidence classification was used to score the included studies. Five were classified as level IV and four studies as level III-2. Level IV studies fall under phase one of the Robey research model (Robey, 2004), which focuses on the determination of therapy effects using pre- or post-treatment measurements, despite presenting a high risk of bias and lacking a non-treatment group comparator. In order to provide a better definition of the participants' characteristics and voice therapy protocols, Level III studies selected for this review started using inclusion and exclusion criteria

#### **ii. Treatment Plan and Treatment Content**

A voice therapy strategy usually takes into considerations, both the 'condition' and the 'individual'. The content of treatment plan in all included studies involved the combination of direct and indirect approaches. The indirect therapy consisted of a variety of tasks that were designed to eliminate negative vocal behavior and to shape healthy vocal use. On the other hand, direct therapy incorporated exercises or techniques to help establish normal voice-production mechanisms, that is, musculoskeletal function, phonation, and respiration (physiologic approach) or a variety of voice facilitating techniques specific to tackling abnormal vocal symptoms (symptom approach). Based on

the findings of this systematic review, it is unclear as to what specific techniques/components of the direct therapy are effective.

Two widely recognised limitations of any type of behaviour rehabilitation study published, such as voice therapy study, are the lack of specification of the therapy content and the lack of clarity in determining which active ingredients (techniques/components) of the intervention are integral to their success (Cherney, 2012; Hart et al., 2014).

All included studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) did not provide a specific description of the delivered treatment, which is in consonance with Ruotsalainen et al (Jani et al., 2008) systematic review findings on the treatment of functional dysphonia and prevention of voice disorders .

A better understanding of which physiological mechanism of the voice that is being targeted by a specific voice technique or component will facilitate the linkage between clinical practice and outcome measures. Dijkers et al (Hart et al., 2014), posit that the behaviour rehabilitation is fraught with many greys areas, and one of them being the unclear process that links clinical intervention with functional outcomes. In order to address this issue, Van Stan et al (Van Stan et al., 2015) have proposed a taxonomy that subdivides further direct voice interventions into five categories: vocal function, respiratory, musculoskeletal, auditory and somatosensory, and indirect voice therapy in pedagogy and counselling sections. This classification intends to facilitate outcome research and communication among clinical practitioners, practice, and training.

In this systematic review, eight of the nine studies (Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) documented a predefined therapy strategy plan, which can be viewed as a step forward to help determine a definitive and consensual intervention for patients with VFNs in the future. All the eight studies that used a treatment-protocol strategy included different voice techniques and exercises, thus making it difficult to compare results and to provide evidence for a definitive treatment plan for VFNs. However, despite using a treatment-protocol, it is generally accepted in clinical practice parlance that some components of therapy program (such as specific

exercise variations or modelling techniques) are adapted based on the patients' specific needs (i.e. providing patient-centre care). Another important factor is the patient's perception of what therapy works, supported by an improvement or positive changes in outcome measures (Togher, 2012). Here again, these factors will reduce the likelihood of pinpointing which components of an intervention plan are successful for a positive outcome (Cherney, 2012; Kamhi, 2012; Roy, 2012). Despite that serious limitation, using a treatment-protocol decreases intervention bias and can (in theory) provide better evidence of the quality for VFNs for that specific treatment (Robey, 2004; J. A. C. Sterne et al., 2016).

In summary, it has been suggested that clinicians prefer to use in their practice a structured treatment-protocol voice therapy program in their practice. Another important aspect is that clinicians' standard practice is to combine a direct and indirect approach as part of their therapeutic strategy. Finally, it needs to be acknowledged that voice therapy content, specifically the ingredients (exercises and techniques) that collectively make up an intervention, is a complex area that requires further research and understanding before a clear specific treatment can be recommended.

### **iii. Intervention Intensity**

The intensity of therapy is normally determined in advance. Typically, this decision is influenced by the standard practice in the health service offering the therapy for patients with vocal fold nodules, by the skill mix of the staff delivering the service, and by the workplace restrictions (Enderby, 2012; Robey, 2004; J. A. C. Sterne et al., 2016).

All the aforementioned studies (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) explicated on the intensity of the therapy. Fu et al (Fu et al., 2015b, 2016), suggest that intensive voice therapy (three weeks duration and a total of eight sessions) may be as effective as traditional voice therapy (eight weeks) for patients with VFNs. In comparison, in their study, Verdolini-Marston et al (Verdolini-Marston et al., 1995) demonstrated positive improvement of voice quality outcome measures in the intensive voice therapy group (two weeks duration and a total of nine sessions). In this regard, the apparent lack of uniformity and clarity in defining what is

and what is not intense between authors, interferes with the interpretation of the results and encapsulates the challenges of establishing an optimal voice therapy intensity.

Another important aspect pointed out by Yoder et al (2012) is that optimal voice intensity therapy may be better understood in the context of the patients' characteristics (Yoder et al., 2012). Cherney et al (2012) underscore the fact that some patients may benefit from more sessions as compared to others (Cherney, 2012; Schmitt & Justice, 2012). Some patients may benefit from a different approach, such as delivering intensive voice therapy using telepractice, as observed in the studies conducted by Fu et al (Fu et al., 2015b) and Mashima et al (Mashima et al., 2003). Telepractice, which uses a secure standard-based technology, may be a feasible way of delivering voice therapy in clinical practice. In addition, it may be an effective strategy to improve some patients' availability and commitment to voice therapy. Nevertheless, there is a need for future studies involving the management of patients with VFNs using telepractice, in order to further explore the benefits of this promising alternative way of delivering voice therapy.

#### **iv. Outcome measures**

Therapy outcome should consist of examining the change in two or more of the following areas; quality of life according to Robey's model (Robey, 2004), physiological features, and impairment level outcomes. The application of multidimensional measures is known to improve the validity and sensitivity (Carding et al., 2004) in detecting the magnitude and nature of the treatment's efficaciousness in patients with VFNs. In general, extant literature shows that the most recent studies have adopted objective and subjective voice outcome measures practices to provide evidence of the effectiveness of the treatment in patients with VFNs (P H Dejonckere, 2000). The selected studies clearly indicate a positive effect on several outcome measurements of voice quality after voice therapy. Nevertheless, a large amount of inconsistency still exists among the outcome measure used in the studies. To that end, the need to define a standardized 'recipe' of the best combination of outcome measures to assess voice therapy effectiveness, would be useful not only in clinical practice, but also in research studies.

Evidence of treatment benefits on voice quality parameters was best provided in studies carried out by Fu et al (Fu et al., 2015a, 2015b, 2016) and Mashima et al (Mashima et al., 2003), where a low risk of biases and robust methodologies were applied. Four of these

studies (Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003) also used best practice techniques for rating visual-perceptual and auditory-perceptual parameters by utilizing more than one rater evaluating the inter and intra-rater reliability, increasing scoring accuracy, thus explaining the results' validity (Carding et al., 2004). In the other studies, the outcomes should be analyzed cautiously, owing to the possibility of measurement bias.

Laryngoscopic or stroboscopic examination of the vocal folds is fundamental for diagnosing VFNs and for assessing response to voice therapy because it can objectively compare the vocal nodules sizes (or their disappearance) before and after the therapy. Thus, it is not surprising that the majority of the seven studies (Fu et al., 2015a, 2015b, 2016; Holmberg et al., 2003; Lucchini et al., 2018; Mashima et al., 2003; Verdolini-Marston et al., 1995) included the voice outcome.

Enhancing the validity of the results, the study from Fu et al (Fu et al., 2015a) suggested that intensive vocal therapy (IVT) delivered over a shorter period of time (three weeks) was as effective as its traditional (voice therapy model) counterpart delivered over eight weeks. Furthermore, in the most recent study undertaken by Fu et al (Fu et al., 2016), these positive changes in the voice were sustained until after six months post-treatment. Similarly, the study from Mashima et al (Mashima et al., 2003) also suggests that there was no statistical difference was observed in the outcomes measured between voice therapy delivered conventionally and through video teleconference.

It is noteworthy that none of the studies used a multiparametric outcome measure, such as the Acoustic Voice Quality Index (AVIQ) or Dysphonia Severity Index (DSI). Both indexes have been successfully validated to quantify voice quality as well as to objectively evaluate the severity of the dysphonia (Barsties v. Latoszek et al., 2019; Uloza et al., 2018). As such, both AVIQ and DSI could have been useful in assessing therapy progress in the dysphonic participants and ameliorating the results' validity and sensitivity (Carding et al., 2004) in detecting the effectiveness of the treatment in patients with VFNs (Wuyts et al., 2000).

### **v. Long-term outcomes**

Follow-up assessments were performed in studies conducted by Fu et al (Fu et al., 2016) and Verdolini-Marston's (Verdolini-Marston et al., 1995). Fu et al (Fu et al., 2016) performed a follow-up study six months after the termination of voice therapy and found that its positive effects were still visible. Meanwhile, in Verdolini-Marston's (Verdolini-Marston et al., 1995) study, a re-evaluation was carried out two weeks after concluding the therapy. The subjects' compliance with the utilization of learned voice techniques/exercises appeared to affect the outcome of the therapy. There is a general lack of long-term follow-up in seven (Chhetri & Gautam, 2015; Fu et al., 2015a, 2015b; Holmberg et al., 2003; Khoramshahi et al., 2018; Lucchini et al., 2018; Mashima et al., 2003) of the nine studies selected in this review. More studies are required to investigate whether or not patients will benefit, in continuing vocal hygiene and vocal exercises routines, after concluding the voice therapy program. This assumes even more significance if we consider that a significant number of patients across the studies lacked a complete resolution of the nodules by the end of the therapy.

### **3.6 Study Limitations**

In the present review, some limitations that need to be taken into consideration while analyzing the findings. The conclusions of this systematic review are limited to articles in English language. Furthermore, gray literatures were not considered for this review. Moreover, those that were included in this article were heterogeneous concerning research design; thus, a narrative synthesis was used to outline the level of evidence. Additional limiting factors include the small number of studies under review, the heterogeneity across studies in terms of the specific content of voice therapy and the lack of standardization in outcome measures, which prevents meaningful comparisons between studies. Moreover, even when the outcome measures are the same, major inconsistencies can be found in the manner in which the results are reported. This makes it impossible to perform a pooled meta-analysis to increase the validity of any observed differences after voice therapy.

Finally, there is a general lack of long-term follow up in seven of the nine studies selected. This, in turn, stymies the analysis of the results obtained immediately after the completion of the voice therapy program.

### **3.7 Conclusion**

After exploring nine studies in this systematic search and narrative review we cannot conclude the general effectiveness of voice therapy programs because 1) the sample is small; 2) the studies have low level of evidence according to NHMRC and, 3) the fact that a variety of therapy techniques/exercises were used across the selected studies. This review also reinforces the need to conduct further research, develop a better understanding of what specific ingredients (exercise and techniques) of a therapy's content are responsible for improving the voice outcome measures and, in effect, to recommend a specific therapy program in the future.

There is a need to provide a more precise definition of what 'intensive therapy' is and entails. In addition, more evidence is required, to suggest that short intensive voice therapy may be as beneficial as longer traditional voice therapy.

More studies are also required to investigate whether or not voice therapy benefits are sustainable six months after completing therapy. Similarly, the use of telepractice as a means of delivering voice therapy, underscores the need for further research to explore its benefits, practicability, and achievability in clinical practice.

One of the key objectives of level III and IV studies is the establishment of treatment protocols to provide more reliable evidence on outcome measures and treatment effect, which can subsequently be used in more advanced research designs (clinical trials). However, there is a need to conduct future studies in order to improve the current methodological limitations by 1) ensuring that a voice therapy plan is clearly predefined and does not change once the therapy begins; 2) making sure that the assessment of intervention uses a multidimensional approach and; 3) incorporating statistical analysis in the objective and subjective outcome measures.

In conclusion, further studies on a phased approach for conducting rehabilitation (clinical outcome) research, are necessary in order to establish appropriate voice outcome

measures, treatment protocol (content), duration, and intensity of therapy for patients with VFNs.

For the purpose of strengthening the findings of future studies, it is necessary to have bigger sample sizes, intervention control group, and experimental control group to rule out placebo effect of voice exercises or techniques, long-term follow-up evaluations, as well as adherence to voice exercise routines after ending therapy

## **Chapter IV – Is there an improvement on acoustic voice parameters in patients with bilateral vocal fold nodules after voice therapy? a meta-analysis**

### **4.1 Abstract**

*Background/objective:* The aim of this study is to estimate the effect of voice therapy intervention in adults with vocal fold nodules, on three acoustic voice parameters (fundamental frequency, jitter and shimmer).

The purpose of this meta-analysis is to present evidence based on literature regarding objective acoustic voice parameters changes, after voice therapy, in patients with bilateral VFNs. A pooled statistical analysis comparing pre- and post-therapy measurements of three acoustic voice parameters (average  $f_0$ , % jitter and % shimmer) were performed.

*Methods:* A literature review was performed by searching studies in adults, with bilateral vocal fold nodules whom received voice therapy, and where voice quality was evaluated quantitatively using acoustic analysis, before and after treatment. Meta-analysis was performed using random-effects model. PubMed, CINAHL, CENTRAL and Web of Science were searched for retrospective and prospective cohort, cross-sectional and case-control with comparative studies in adults published between January/1995 and March/2019 and English written. Search terms used were: intervention, therapy, vocal, voice, nodules, bilateral, multidimensional assessment, acoustic and analysis.

*Results:* Overall 1950 articles were identified. After removing repeated articles and conducting screening stages using inclusion and exclusion criteria, a total of four studies were selected with 147 participants for the meta-analysis. The pooled results analysis showed a statistically significant effect in 2 acoustic parameters after voice therapy: (1)  $f_0$  [increased mean difference post-therapy was 33.00Hz (95%CI:20.26-45.74,  $p<0.001$ )] and (2) jitter (%) [decreased mean difference post-therapy was 0.59% (95%CI:0.23%-0.94%,  $p=0.0012$ )]. In addition, a non-statistically significant effect in shimmer (%) [decreased mean difference post-therapy was 2.98% (95%CI:-0.03-6.00,  $p=0.052$ )].

*Conclusion:* Acoustic analysis has a clinical role in patients with vocal fold nodules, by objectively assessing and providing data on the effect of voice therapy in voice acoustic

parameters. This meta-analysis has showed that patients with vocal fold nodules improved their acoustic voice parameters after receiving voice therapy.

## 4.2 Introduction

Vocal fold nodules (VFNs) are non-cancerous growths on the vocal folds, which are usually bilateral and roughly symmetrical (Martins et al., 2011; Verdolini et al., 2014).

Predisposing factors related to the development of vocal fold lesions comprise: 1) young age; 2) higher level of education; 3) occupational voice demands and 4) voice disorders. Common features among these factors are chronic overuse and abuse/misuse (stress or injury) of the voice, which can cause inflammation, and consequently, VFNs (Johns, 2003).

VFNs prevent full glottal closure, interfering with vocal fold vibration (Martins et al., 2011). As a result, patients seek medical attention when the quality of their voice changes. Patients may perceive their voice as ‘hoarse’, ‘breathy’ or ‘rough’, which may vary in severity, depending on the size and firmness of the nodules. Patients may also complain of physical and voice fatigue and reduced capability to change vocal pitch (Holmberg et al., 2003). The degree of dysphonia may negatively influence their quality of life and mental health (Hogikyan et al., 1999; Hsiung & Hsiao, 2004).

Accurate diagnosis is the key to initiating the correct therapy strategy. The primary diagnostic method is a direct visualization of the vocal fold through a laryngostroboscopy, usually performed by an otolaryngologist. Subtle differences among polyps, cysts and nodules – especially when swelling is present – can make diagnosis challenging (Dickers & Nikkels, 1999). Moreover, a thoughtful evaluation of the patient’s voice history, medical background, and physical examination of the neck and head are also important. Given that voice is a multidimensional phenomenon, a set of basic minimal measurements of voice function are normally performed in order to assist diagnosis, which includes a subjective perceptual and objective acoustic evaluation of the voice (P H Dejonckere, 2000). There is no agreement within the literature regarding the clinical purpose of acoustic analysis in helping to make a differential diagnosis. Moreover, there is a lack of consistent evidence across studies that one single parameter or a combination of acoustic

parameters can, with precision offer a diagnosis (Hillenbrand, 2011; Minoru Hirano et al., 1988).

Even though objective measurements of the voice do not substitute subjective evaluation, these measurements provide a quantitative and precise evidence of treatment outcomes and monitor progress of patients throughout therapy (Hillenbrand, 2011).

In general, acoustic measures of vocal function involve techniques to assess: 1) periodicity; 2) intensity; and 3) spectral shape of the voice signal. Since Lieberman et al (Lieberman et al., 1992) reported observations where laryngeal pathologies had a tendency for frequent and rapid changes in the regularity of the vibratory pattern of the voice, disturbances in periodicity measures have been used extensively in clinical and research settings (Vaz-Freitas et al., 2018).

Common acoustic parameters used in clinical practice over the last decades comprised: 1)  $f_0$  (Hz) – average fundamental frequency; and 2) periodicity perturbation measures such as: jitter (%) – variability in fundamental frequency; shimmer (%) – variability in amplitude; and HNR (dB) – harmonics-to-noise ratio.

The purpose of this meta-analysis is to present evidence based on literature regarding objective acoustic voice parameters changes, after voice therapy, in patients with bilateral VFNs. A pooled statistical analysis comparing pre- and post-therapy measurements of three acoustic voice parameters (average  $f_0$ , % jitter and % shimmer) were performed.

### **4.3 Materials and Methods**

The Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines were applied in order to conduct a systematic review of the literature – PRISMA (Moher et al., 2015).

#### **i. Eligibility Criteria**

The first and second authors exchanged their views with regard to the main aim of the study, and to develop the inclusion and exclusion criteria. Any disagreements were discussed and solved before the initial search strategy took place.

***Inclusion and Exclusion Criteria***

*Publication:*

- a. Only articles that were peer reviewed and published in an indexed scientific journal were included.
- b. Only articles written in English and published from January 1995 until March 2019 were included.
- c. Gray literature, master and doctorate thesis, systematic reviews, meta-analysis, editorials, expert opinion and case reports were not included.

*Participant characteristics:*

- a. Patients had to have been diagnosed with VFNs.
- b. Only adult patients ( $\geq 18$  years and older) were included.
- c. Articles using only pediatrics' samples were not selected.
- d. Studies conducted on animals or cadavers were excluded.

*Therapy:*

- a. Only direct voice therapies alone or used jointly with indirect therapies were included.
- b. Direct voice therapies combined with transcutaneous electrical nerve stimulation (TENS) were not included.
- c. Voice training programs for voice professionals without vocal folds disorders were excluded.
- d. Therapy had to be conducted or supervised by SLP.

*Study type and design:*

- a. Randomized controlled trials, comparative studies with concurrent controls (cohort or case-control), comparative studies without concurrent controls (retrospective) or case series with pre- and post-outcomes were included.
- b. Studies that had clearly described the voice therapy strategy (content, duration, and intensity) were included.
- c. Studies reporting complete quantitative voice quality assessment outcomes pre- and post-treatment, and which included at least one of the three following acoustic parameters analyses: *f<sub>0</sub>* (Hz), jitter (%) and shimmer (%) were considered.

*Outcome measures:*

- a. Studies reporting pre- and post-therapy voice acoustic assessments alone or in combination with any other voice-function outcome measures were included

**ii. Search Strategy**

Studies assessing voice quality or voice outcomes in patients with VFNs (after receiving Speech Language Pathology (SLP) orientation) were retrieved from four electronic databases search, which included PubMed, CINAHL, CENTRAL, and Web of Science. The initial search was performed by the first author and was not restricted to the participants' age, date of publication and language. Furthermore, search was carried out without time limits until the 1<sup>st</sup> of April 2019. Table 13 lists the search terms used to identify potentially relevant studies in the databases.

**Table 13- Search strategy terms used in association with the Boolean term OR/AND for the search on PubMed and equivalent terms on the other databases.**

<b>Population</b>	<b>Intervention</b>
1. "vocal"	8. "therapy"
2. "Larynx"	9. "voice assessment"
3. "laryngeal"	10. "acoustic analysis"
4. "voice"	11. "intervention"
5. "nodules"	12. Combine 8-11 using "OR"
6. "bilateral"	
7. Combine 1- 6 using "OR"	
Combine 7+12 using "AND"	

### *Study Selection*

A study selection was conducted after the initial search in a stepwise manner as illustrated in figure 6.

1) Duplicate references were removed by the first author using Mendeley Desktop ®Version 1.19.2. (Zaugg et al., 2011).

2) Titles and abstracts of the remaining articles were screened against eligibility criteria by the first two authors independently. At this stage, studies were ruled out if a sample from the studies comprised of: a) animals, cadavers or only children; b) studies on dysphonia not related with VFNs; c) studies without voice therapy intervention; d) studies not written in English; e) studies that were systematic reviews and editorials; and f) studies with year of publication falling outside the inclusion criteria period.

3) Reference lists of selected studies from the previous step were screened with respect to titles by the first author in order to identify additional studies that could meet the eligibility criteria.

4) Full text review of the included studies from the title and abstract stage and reference lists of screening were evaluated independently by the first author for eligibility against inclusion and exclusion criteria. Studies were removed if they did not have an adequate design, a description of the voice therapy intervention, and a voice function assessment; or if the outcomes did not include acoustic assessment and the results were inexistent or incomplete. Unfortunately, one study (Chhetri & Gautam, 2015) did not present all data required for statistical analysis and although the correspondent author of the study was contacted, no reply was obtained. Therefore, data from only four studies were included for the final meta-analysis.

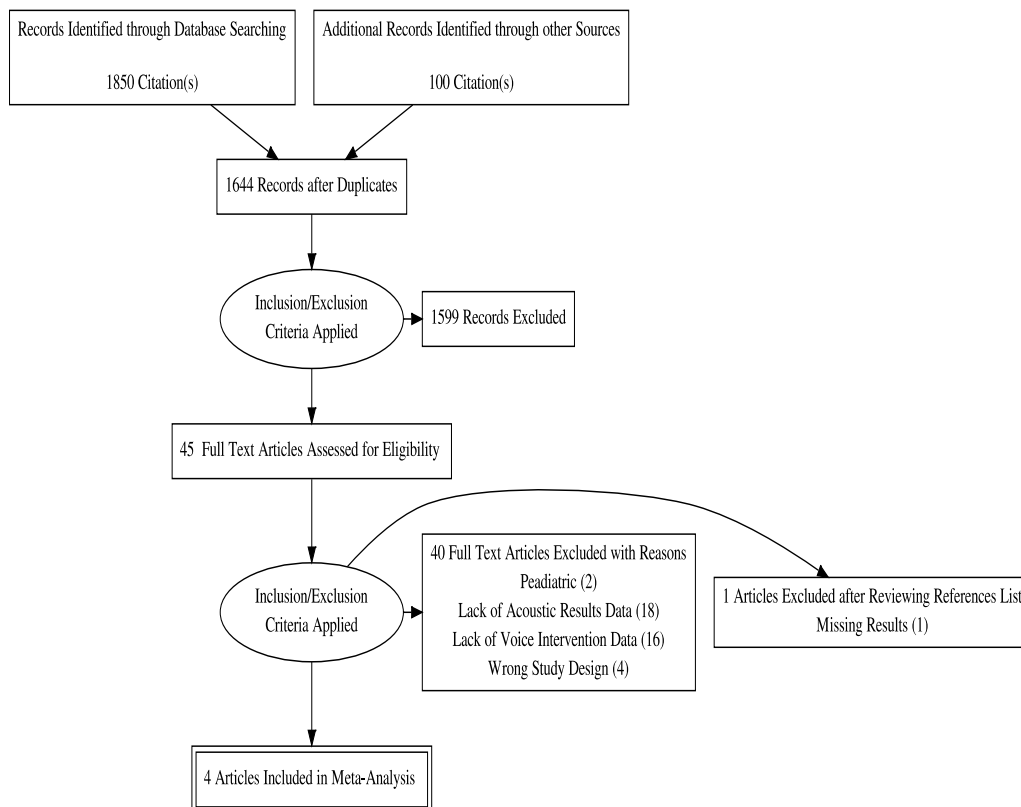
To assess screening reliability of the studies selected for full text review, an independent third reviewer appraised 20% of the included articles against eligibility criteria and consented study selection. Moreover, this third reviewer also resolved disagreements between the first two authors on the screening and categorization of the selected articles.

### iii. Data Entry Extracted from Selected Studies

Relevant data features were extracted from each included study in order to assist in the goal of a critical appraisal of this article. Data entries are shown in tables 2 to 4:

- a) Study: publication year, study place, study design and sample size
- b) Characteristics of participants: gender and age (range or median)
- c) Voice therapy: content, duration, and intensity
- d) Outcome measures: comparison of pre and post voice therapy intervention
- e) Acoustic assessment: software used and parameters measured
- f) Results: documented *p* value documented and statistical significance

**Figure 6: PRISMA – Flow diagram for study selection.**



#### **iv. Quality of Evidence**

The National Health and Medical Research Council (NHMRC) level of evidence (Glasziou et al., 2000) was used to lay out a structure in order to decide the studies' level of evidence. The first two authors reviewed the quality of evidence of each included study, according to their methodology, and assigned to it one specific NHMRC levels of evidence (Glasziou et al., 2000). An independent third reviewer solved any conflicts and disagreements between the authors.

#### **v. Data Analysis**

The acoustic voice parameters measurements before and after voice therapy ( $f_0$ , jitter and shimmer) in each of the selected studies enabled pooling of combined data that were analyzed for each of the three acoustic outcomes. Statistical software R (CRAN R) (Ripley, 2001) was used to analyze the data. The inconsistency index ( $I^2$ ) and the Cochran's Q-test measured the heterogeneity of the studies. A random effect model and a standardized mean difference 95% CI (confidence interval) were used to perform the meta-analysis. Forest plot graphs were generated to estimate the effect of voice therapy in each acoustic parameter, from each article, and from the overall combined result. Presence of publication bias in this meta-analysis was assessed, illustrated in funnel plot graphs, and argued using the Egger et al (J. A. C. Sterne & Egger, 2001) details.

### **4.4 Results**

#### **i. Search Strategy**

Figure 6 illustrates the flow diagram of study selection and the exclusion reasons at each stage of screening. The initial search terms strategy used enabled the identification of studies from 1950. After careful screening, a total of four studies met all eligibility criteria for inclusion in this meta-analysis (Fu et al., 2015a, 2015b; Holmberg et al., 2003; Saltürk et al., 2018).

## **ii. Critical Appraisal of Selected Studies**

Different acoustic software was used for voice analysis across the studies. Table 14 demonstrates the type of software, the number of performed measures and the parameters assessed in each study by the authors.

The summary of each of the four (Fu et al., 2015a, 2015b; Holmberg et al., 2003; Saltürk et al., 2018) included studies is available in Table 15, which includes authors name, year of publication, type and study level of evidence, participants' characteristics and sample size, voice therapy content, duration, and intensity.

Two studies were from Australia (Fu et al., 2015a, 2015b) and the remaining were from Sweden (Holmberg et al., 2003) and Turkey (Saltürk et al., 2018). Every single study was prospective, with two comparative studies including concurrent controls (level III-2) (Fu et al., 2015a; Saltürk et al., 2018) and two case series (level IV) (Fu et al., 2015b; Holmberg et al., 2003). All participants were women. In total, 129 participants were included, with the average age ranging from 23.3 to 37.5 years.

With respect to voice therapy, a protocol-based approach was applied in all included studies that used a variation of direct and indirect voice techniques. Holmberg et al (Holmberg et al., 2003), Fu et al (Fu et al., 2015b) and Saltürk et al (Saltürk et al., 2018) also included homework as part of their voice therapy plan. In Fu et al (Fu et al., 2015b) voice therapy was given by video-teleconference and in the remaining studies, in the conventional face-to-face setting. Duration of therapy program and intensity of each session were different across the studies and within the same study. It extended from a three week therapy plan in Fu et al (Fu et al., 2015b) to a 24 week program in Holmberg et al (Holmberg et al., 2003), which affected the intensity of the sessions from three times a week to once every week, respectively.

A multidimensional voice assessment (more than 3 dimensions) was performed in all selected studies. Table 16 summarizes the number of voice dimensions measured and the type of assessments performed in each study, and their respective result after voice therapy. Visual-perceptual outcome measure, using a videolaryngostroboscopic examination, was consistently done in all studies. General studies reported at least some degree of regression or even complete regression of vocal fold nodules in the majority of the participants. Regarding auditory-perceptual assessment, half of the studies (19,20)

used this voice outcome and results showed improvement after voice therapy, with statistical significance for most of the parameters. Aerodynamic analysis of the voice was also included in three studies (Fu et al., 2015a, 2015b; Saltürk et al., 2018) and parameters also ameliorated after therapy, with statistical significance. Finally, Fu et al (Fu et al., 2015a) and Saltürk et al (Saltürk et al., 2018) used the Voice Handicap Index for participants' self-assessment of the impact of voice on quality of life, and the results were also positive with statistical significance.

### **iii. Meta-analysis of Acoustic Parameters**

In this meta-analysis the pooled data analysis of the change in  $f_0$  (Hz) after voice therapy in patients with VFNs was 33.00Hz (95% CI: 20.26-45.74 Hz) for the random-effects model (Figure 7A) and showed statistical significance ( $p < 0.001$ ). Moderate heterogeneity was obtained for the different studies included in the meta-analysis ( $I^2 = 69.26\%$ ). The statistical assessment of publication bias (Cochran's Q test,  $Q = 14.81$ ;  $p = 0.005$ ) was shown to be significant, i.e., that it was present, which can be observed in Figure 8. Furthermore, this scatterplot shows asymmetry, which is consistent with presence of publication bias.

Regarding jitter after voice therapy, the combined data analysis value was 0.59% (95% CI: 0.23%-0.94%) lower than pre-therapy for the random-effects model and was statistically significant ( $p = 0.001$ ) (Figure 7B). Heterogeneity was significant for the studies selected in the meta-analysis ( $I^2 = 63.39\%$ ). Assessment of presence of publication bias showed statistical significance (Cochran's Q test,  $Q = 9.73$ ;  $p = 0.021$ ).

The combined results analysis of shimmer (%) after voice intervention was 2.98% (95% CI: -0.03-6.00%) lower than pre-therapy for the random-effects model and was not statistically significant ( $p = 0.052$ ) (Figure 7C). Heterogeneity was severe for the studies selected in the meta-analysis ( $I^2 = 96.60\%$ ). Assessment of presence of publication bias showed statistical significance (Cochran's Q test,  $Q = 81.19$ ;  $p < 0.001$ ).

**Table 14- Acoustic software's and parameters**

Authors, year	Country	Acoustic Software	Acoustic Parameters	Repeated Measures	Sample Material Analyzed
Holmberg et al (Holmberg et al., 2003), 2003	Sweden	SOUNDSWELL	<i>f<sub>0</sub></i>	3	Standard text (Rainbow passage)
Fu et al (Fu et al., 2015b), 2015	Australia	CSL	<i>f<sub>0</sub></i> , jitter, shimmer, HNR	3	Sustained vowel /a/
Fu et al (Fu et al., 2015a), 2015	Australia	CSL	<i>f<sub>0</sub></i> , jitter, shimmer, HNR	3	Sustained vowel /a/
Saltürk et al (Saltürk et al., 2018), 2018	Turkey	PRAAT	<i>f<sub>0</sub></i> , jitter, shimmer, HNR	ND	Sustained vowel /a/

**Abbreviation:** CSL, computerized speech lab

**Table 15. Characteristics of included Studies**

STUDY				THERAPY		
First Author	Study Level of Evidence	Sample size	Age/gender	Voice Therapy Content	Voice Therapy Plan	Session Intensity
Holmberg et al (Holmberg et al., 2003)	Prospective IV	Total: 10	Average/range 23.3 (19-35) F/M=10/0	Vocal Hygiene and Direct voice therapy Protocol-based	16 weeks 24 weeks (15 sessions)	One 80 min session/week 2x15min session a day (homework)
Fu et al (Fu et al., 2015b)	Prospective IV	Total: 10	Average/range 33.7 (19-49) F/M=10/0	Lessac-Madsen Resonant Voice Therapy included: Vocal hygiene and Direct voice therapy	3 weeks (9 sessions)	IVT: 3 sessions/week. Two 15 min telepractice sessions/day on a non-treatment day One 15 min telepractice session on a treatment day (homework)
Fu et al (Fu et al., 2015a)	Prospective III-2	Total: 53 TVT 29 IVT 24	Average/range 37.5 (20-54) 37.52 37.54 F/M=53/0	Lessac-Madsen Resonant Voice Therapy included: Vocal Hygiene and Direct voice therapy	8 weeks (8 sessions)  3 weeks (8 sessions)	TVT (control) group: One 45 min session/week for 8 weeks The IVT group: Three 45 min sessions/week in the first 2 weeks followed by Two 45 min sessions/week in the third week
Saltürk et al (Saltürk et al., 2018)	Prospective III-2	Total: 56 CG: 30 SG: 26	Average 29.86 32 F/M=56/0	Lessac-Madsen Resonant Voice Therapy included: Vocal Hygiene and Direct voice therapy	6 to 8 weeks  (6 to 8 sessions)	One session/week for 6 to 8 weeks (plus, repeat exercises at least five times a day at home)

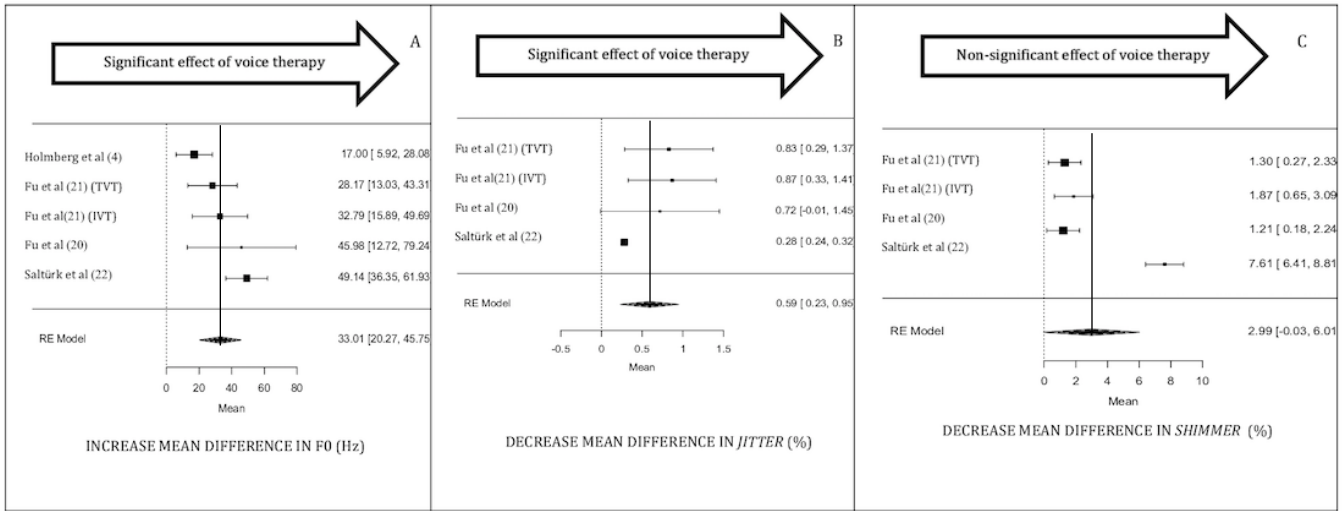
**Abbreviation:** ND, not described; F, female; M, male; TVT, traditional voice therapy; IVT, intensive voice therapy; CG, control group; SG, study group.

**Table 16- Voice-function: Outcomes, Assessments and Results**

First Author	Outcome Measurements	Assessments	Results
Holmberg et al (Holmberg et al., 2003)	Multidimensional	Morphofunctional	After therapy none of the nodules had disappeared (0%). Vocal nodules size and edema reduced 9 at bilaterally and 1 unilaterally.
		Perceptual (P.B.A.L.I.G.R.V.P.B.S.O.) Acoustic ( $f_0$ , SPL)	Statistically significant in P, I, G, R, V, S, O parameters ( $p < 0.05$ ) Statistically significant to $f_0$ ( $p < 0.05$ ) only.
Fu et al (Fu et al., 2015b)	Multidimensional	Morphofunctional	Statistically significant ( $p < 0.05$ ) for mucosa wave, glottal closure and edge smoothness.
		Perceptual (GRBAS)	Statistically significant in grade, roughness and asthenia ( $p < 0.005$ ). No statistical report on breathiness.
		Aerodynamic (MPT, MFR) Acoustic ( $f_0$ , jitters, shimmers, NHR)	Statistic improvement in MFR ( $p < 0.05$ ) Statistically significant in all parameters ( $p < 0.02$ )
		Self-Assessment (VHI)	Statistic improvement in physical and functional domains ( $p < 0.05$ ).
Fu et al (Fu et al., 2015a)	Multidimensional	Morphofunctional	Statistically significant in TVT and IVT groups ( $p < 0.001$ and $p < 0.002$ ) for mucosal wave, edge smoothness and glottal closure.
		Perceptual (GRBAS)	Statistically significant in all parameters ( $p < 0.002$ ) for both for IVT and TVT.
		Aerodynamic (MPT, MFR)	Not statistical significance in IVT or TVT groups.
Saltürk et al (Saltürk et al., 2018)	Multidimensional	Acoustic ( $f_0$ , jitters, shimmers, HNR)	Statistically significant in all parameters in TVT and IVT ( $p < 0.02$ ) except for NHR ( $p < 0.02$ )
		Morphofunctional	Complete regression of the VFNs in 14 patients, partial regression in 9 patients, and no regression in 3 patients after voice therapy.
		Aerodynamic (MPT)	Statistically significant in SG ( $p < 0.0001$ ) but not in CG after voice therapy.
		Acoustic ( $f_0$ , jitters, shimmers, HNR)	Statistically significant in all parameters in SG ( $p < 0.0001$ ) but not in CG after voice therapy.
		Self-Assessment (VHI)	Statistically significant in SG ( $p = 0.001$ ) but not in CG ( $p = 0.783$ ) after therapy.

**Abbreviation:** NHR, noise-to-harmonics ratio;  $f_0$ , fundamental frequency; GRBAS, perceptual rating scale (grade (G), roughness (R), breathiness (B), asthenia (A), and strain (S)); MPT, maximum phonation time; MFR, mean airflow rate; VHI, voice handicap index; PSR, Patient Satisfaction Ratings; VHI, voice handicap index; TVT, traditional voice therapy; IVT, intensive voice therapy; CG, control group; SG, study group.

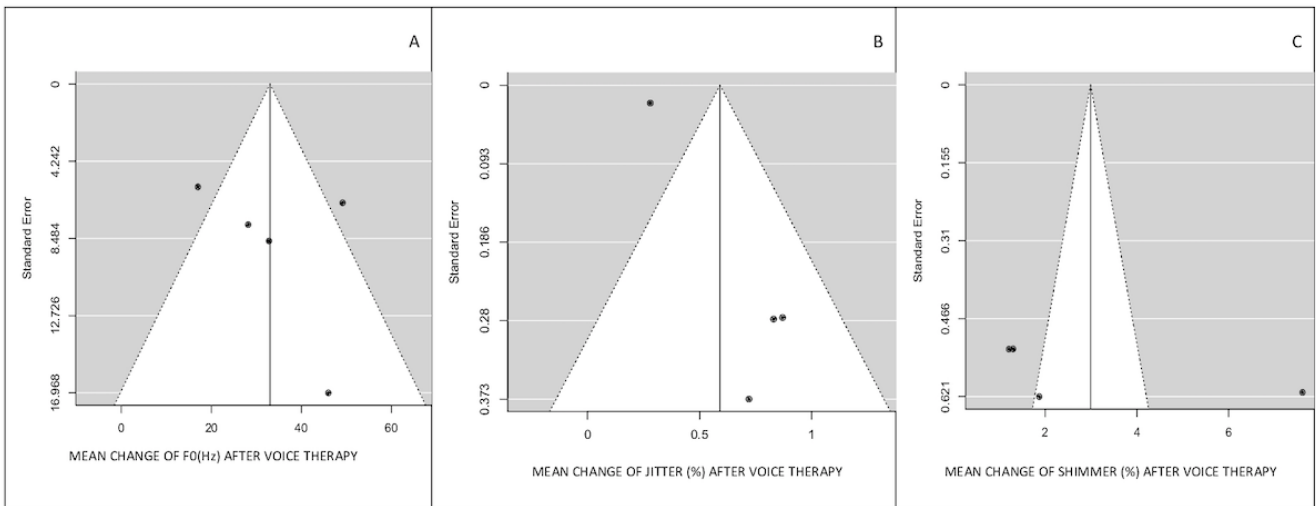
**Figure 7 - Forest Plot illustrating change of  $f_0$  (Hz), jitter (%) and shimmer (%) after voice therapy in patients with VFNs.**



Abbreviation: TVT, traditional voice therapy; IVT, intensive voice therapy

A: Forest plot of change of  $f_0$ . B: Forest plot of change of jitter. C: Forest plot of change of shimmer. Every study is represented by a filled square (denoting its risk ratio estimated and size vary according to weights accredited to the study) and the horizontal line denotes the corresponding 95% confidence interval (CI). Studies that intersect the vertical dotted line (0) indicate null mean difference between post-therapy and pre-therapy values. Pooled results from all studies are shown at the bottom of the forest plot, in diamond shape, using the random-effect model

**Figure 8 - Funnel Plot: asymmetrical scatterplot, consistent with presence of publication bias.**



A: Funnel plot of change of  $f_0$ . B: Funnel plot of change of jitter. C: Funnel plot of change of shimmer. Every study is represented by a black dot. The vertical full-line in each funnel plot (on the horizontal axis) represents the result estimated derived using random-effect meta-analysis for the measured acoustic parameter. The diagonal dot-lines represent 95% confidence limits around each standard error on the vertical axis by a black dot. The vertical full-line in each funnel plot (on the horizontal axis) represents the result estimated derived using random-effect meta-analysis for the measured acoustic parameter. The diagonal dot-lines represent 95% confidence limits around each standard error on the vertical axis.

## 4.5 Discussion

There are several multinational computer programs available for acoustic analysis of voice in clinical and research setting, and this is the most mentioned feature in the literature such as the *Computerized Speech Lab*, Multi-Dimensional Voice Program (CSL; Kay Elemetrics Corporation, Lincoln Park, NJ), *Dr. Speech* (DRS - Tiger Electronics, Neu-Anspach, Germany) and PRAAT (Oral Dynamics Lab, Amsterdam, The Netherlands) (Amir et al., 2009; Godino-Llorente et al., 2008; Smits et al., 2005). Two of these computer software programs were used in the selected studies, except in the Holmberg et al (Holmberg et al., 2003) study where a lesser known software named Soundswell – Signal Workstation (Hitech Development AB, Stockholm, Sweden) (Ternström, 1991) was utilized to analyze acoustic data.

The main indications for utilization of voice acoustic analysis in clinical practice usually include assessment of effectiveness of different therapeutic options, monitoring progress of ongoing course of therapy, and diagnostic aid (Laver et al., 1992). The inability of using acoustic measurements to provide noninvasive quantitative indices in order to help differentiate among laryngeal pathologies have narrowed its clinical utility (Minoru Hirano et al., 1988). Nevertheless, many techniques, including methods to measure disturbances in periodicity, have been described as capable of discriminating normal from abnormal voices with reasonably good accuracy (Hadjitodorov & Mitev, 2002; Peppard et al., 1988).

In patients with VFNs, the ability to control the vibration of the cords is affected reducing the pitch range that they can produce. Furthermore, the presence of vocal nodules decreases the resistance of glottal closure, compromising the intensity of the voice (related with loudness or amplitude of the voice), and the range of amplitude the patient can produce (Rosen, Lombard, et al., 2000). The voice average  $f_0$ , an acoustic measure of voice pitch, may be within the normal range; however, the pitch range and amplitude may be decreased. Jitter, defined as cycle-to-cycle perturbation in fundamental frequency, may be enhanced due to the lack of control of vibration of the vocal folds (Koike, 1973; Lieberman, 1961). The intensity of voice, an acoustic measure of voice loudness or amplitude, may also be normal, yet patients' amplitude range may be reduced. Shimmer, defined as variability in amplitude, may also be increased due to lower resistance of glottal closure in patients with VFNs (Koike et al., 1977).

In the included studies (Fu et al., 2015a, 2015b; Holmberg et al., 2003; Saltürk et al., 2018), all  $f_0$  values were within normal range (according to software used) before treatment. Jitter (%) and shimmer (%) values were increased in all studies at pre-therapy stage. This corroborates with the expected acoustic parameters that are derived from the pathophysiological changes imposed by the presence of the nodules.

This meta-analysis has shown that patients with VFNs who received voice therapy had an effect (reduced mean value) on the disturbance periodicity measures [jitter (%) and shimmer (%)], with statistical significance difference. The inconsistency in the results of the studies was moderate for  $f_0$  ( $I^2=69.26\%$ ) and jitter ( $I^2=63.39\%$ ) but was severe for shimmer ( $I^2=96.60\%$ ). Regarding shimmer, an attempt to reduce inconsistency was undertaken and the Saltürk et al study (Saltürk et al., 2018) was removed. However, although inconsistency reduced, the non-statistically significant effect still remained. We decided to maintain the study due to that and to the fact that this study (Saltürk et al., 2018) was being used for both jitter (%) and shimmer (%) meta-analysis.

Jitter can be calculated using five different algorithms. The Fu et al (Fu et al., 2015a, 2015b) studies used jitter, which represents the average absolute difference between two consecutive periods, divided by the average period (Teixeira et al., 2013). The threshold limit to be considered pathologic is 1.04%, which in these studies was above this value, and therefore abnormal. In the Saltürk et al (Saltürk et al., 2018) study, RAP (relative average perturbation) represents the average of the period with its two neighbors, divided by the average period (Teixeira et al., 2013). The threshold limit to be considered pathologic is 0.68%. In this study, both the control group and the study group had values under this limit before and after voice therapy. Therefore, it can be argued that in this study, the RAP was not a sensitive indicator to differentiate between people with and without vocal folds nodules. Nevertheless, despite the RAP values being under the pathologic threshold, there was a statistically significant improvement after therapy, which indicates its usefulness in detecting the patients' progress with the voice therapy.

Additionally, voice therapy also had a statistically significant effect (an increase) in the mean difference value of  $f_0$  pre and post therapy. There was no inconsistency in the studies' results ( $I^2=0.00\%$ ), and therefore no presence of publication bias for this acoustic parameter.

Heterogeneity among studies was a problem in the results of all the acoustic parameters results presented in this meta-analysis, caused by clinical and methodological diversity (Table 3). With respect to clinical diversity, the variety of voice therapy' contents, plan and intensity were a decisive source of heterogeneity across the studies. The Fu et al studies (Fu et al., 2015a, 2015b) and Saltürk et al (Saltürk et al., 2018) studies used similar treatment intervention, which included voice hygiene and direct voice therapy for at least eight sessions when compared with Holmberg et al (Holmberg et al., 2003) (15 sessions). Other clinical variations that could have led to heterogeneity were the participants' average age, despite all participants being women, the nodules sizes and time periods since the onset of voice problems at start of voice therapy, which were varied within and between the included studies.

Respecting methodological diversity, varied factors can be taken into consideration such as variability of the study design, sample size, methodology and the risk of bias in each study. The design of all included studies (Fu et al., 2015a, 2015b; Holmberg et al., 2003; Saltürk et al., 2018) was prospective with similar moderate risk of bias. With respect to study design and level of evidence, according to NHMRC, two studies were level III-2 (Fu et al., 2015a; Saltürk et al., 2018), a comparative study with controls and two studies (Fu et al., 2015b; Holmberg et al., 2003) were case series with pretest-post-test outcomes (Table 4); therefore, results should be read with some caution.

Even though significant statistical heterogeneity arose from differences in the methods used, this does not necessarily suggest that the true intervention effect was altered (increased mean  $f_0$ , decreased jitter (%) and shimmer (%)).

Some factors can be taken into account from this systematic review, such as voice intervention in patients with VFNs is an effective and noninvasive treatment choice, and should be considered as the first option in most cases (Fu et al., 2015a, 2015b; Holmberg et al., 2003; Mashima et al., 2003; Saltürk et al., 2018) (Table 4). Furthermore, acoustic parameters, specifically periodicity perturbation measures, require more than one voice therapy session to produce changes. Moreover, short, intensive voice therapy may be as beneficial as longer, traditional voice therapy, however, further studies are required (Fu et al., 2015b; Mashima et al., 2003).

#### **4.6 Conclusion**

In the selected studies, two of the acoustic voice parameters were abnormal [jitter (%) and shimmer (%)], before voice therapy. These were expected acoustic changes associated with the presence of nodules in the vocal folds and their pathophysiological consequences on the vocal phonation.

This meta-analysis has showed that patients with VFNs improved their acoustic voice parameters measurements after receiving voice therapy. There was an effect on the disturbance periodicity measures (jitter (%) and shimmer (%)) \_ reduced mean value, and on the pitch range measure ( $f_0$ ) \_ increased mean value, with statistical significance difference for jitter (%) and  $f_0$ . Finally, acoustic analysis plays a clinical role in patients with VFNs, by objectively assessing and providing data on the effect of voice therapy in voice acoustic parameters.

## **Chapter V – Unilateral vocal fold paralysis multidimensional assessment: before & after speech-language pathology intervention**

### **5.1 Abstract**

*Objective:* Unilateral vocal fold paralysis can have a significant impact on a patient's breathing, swallowing, phonation and overall quality of life. This study aims to analyze multidimensional voice evaluation outcomes in a group of patients with unilateral vocal fold paralysis.

*Methods:* A retrospective analysis was performed in 132, mostly after thyroid surgery, who underwent voice therapy. Data were collected from January 2000 to December 2019. Data analysis were performed with non-parametric tests ( $\alpha=0.05$ ).

*Results:* A total of 132 patients (57.1±12.9 years (range 27-86); 74% female) with unilateral vocal fold paralysis, were included in the study. Side and position of cord paralysis varied, 57.6% affecting the left vocal fold and 66.6% at the paramedian position. Voice therapy with an experienced speech-language pathologist once or twice a week, with 10±4.9 appointments (range 4-41). The overall vocal fold motility recovery rate was 57.6% (95%CL:49.0%-65.7%); and regarding etiology; 55.3% (95%CL:44.7%-65.4%) for post-total thyroidectomy patients, 44.4% (95%CL:24.5%-66.3%) for recovering from other surgeries, 75% (95%CL:56.4%-87.6%) for idiopathic paralysis. A significant improvement in the multidimensional measures were obtained ( $p<0.01$ ) in all parameters. Early onset showed significant improvement for Grade post-treatment results ( $p=0.047$ ).

*Conclusion:* A significant improvement in voice and self-perceived quality of life after voice therapy was achieved. Idiopathic paralysis presented a significant higher vocal fold motility recovery rate compared to post-surgical. Early therapy after onset of vocal fold paralysis seems to have some importance in the response to the intervention, however, more studies are required.

## 5.2 Introduction

Vocal fold paralysis can occur due to peripheral damage to the recurrent laryngeal nerves, superior laryngeal nerve (SLN), and inferior laryngeal nerve (ILN) or by involvement of the vagus nerve pathway (Sataloff, 2017).

The origin of the nerve injury falls into three categories: injury due to surgery or trauma, impairment from some medical conditions or a dysfunction caused by unidentified or characterized factors – and thus of an “idiopathic” nature (Sulica et al., 2006). Vocal fold paralysis caused by surgical intervention can, according to some authors, spontaneously regenerate till one year after the surgery (Marina et al., 2011; Verdolini et al., 2014). However, in cases of section, that is, nerve rupture, paralysis is usually permanent (Arnold, 1962).

The position assumed by the paralyzed vocal fold can vary from median to lateral, determining the type of folds adduction and the degree of symptoms. The functional impairment of vocal fold mobility affects both biological functions - breathing and swallowing - and phonation (De Biase et al., 2003).

Dysphonia, ‘weak’ or ‘breathy voice’ and effortful speaking are some of the symptoms that makes patients seek medical help, and those arise from the glottic incompetence, resulting from the lateral displacement of the paralyzed cord. Some authors point out that the presence of breathiness and the inability to communicate effectively are the greatest losses presented by patients with unilateral vocal fold paralysis (UVFP) (Alves et al., 2002).

Normally, patients with UVFP report decreased quality of life, especially in physical, social and emotional domains. The impact of these changes can vary according to the personal characteristics of each individual and their need to use the voice for social, family and professional interaction (Fang et al., 2008).

Pitch of the voice deserves special attention since, although affected individuals usually acquire a high pitch, in some people (especially women), a phenomenon called “paralytic falsetto” may occur. This symptom is characterized by an average increase of 85 Hz above of what is expected for each gender (Simpson & Cheung, 2006).

Breathiness and asthenia are the most striking perceptual aspects in UVFP (due to the perception of airflow turbulence) (Hartl et al., 2003; Minoru Hirano & Mori, 2000). In a study by Hirano (1989), hoarseness was reported in approximately 25% of cases (Minoru Hirano, 1989).

In dysphonia and dysphagia, speech therapy accelerates rehabilitation and enables the production of a functional or even (almost) normal voice and swallowing pattern (Boone & McFarlane, 1994; LF, 2000). Phonotherapy treatment aims to provide endolaryngeal compensation, being based on the principle of compensatory glottic closure by effortful vocal activity (Arnold, 1962). In cases of unilateral paralysis, the healthy vocal fold is stimulated to cross the midline and approach the paralyzed vocal fold, providing better adduction and, consequently, greater balance between the aerodynamic and myoelastic forces of the larynx (Maia, 2010).

Some authors (D'Alatri et al., 2008; Heuer et al., 1997) recommend that speech therapist should provide the patient with information about phonatory physiology, data about his specific pathology and vocal hygiene. Voice therapy should lead the patient to avoid behaviors of hyper-functional compensations (e.g. ventricular folds hyperfunction) often responsible for discomfort in the neck and tense voice, to optimize breathing and abdominal support and increase strength and mobility of the intrinsic muscles of the larynx (Cantarella et al., 2010; D'Alatri et al., 2008; Schindler et al., 2008). Strengthening of the abdominal and thoracic muscles, attention to breathing and vocal variation are some of the techniques that are described in the literature. Resistance exercises should be used with care so as to avoid damaging the vocal folds or the development/worsening of hyper-functional compensations (F Mattioli et al., 2015a; Francesco Mattioli et al., 2011). Heuer et al (1997) also point out that the use of specific singing techniques can also help in the rehabilitation of patients, particularly in muscular support, breathing coordination, resonance and vocal efficiency (Castro et al., 2014; López et al., 2020).

The aim of the present study is to analyze the results achieved with speech therapy over a 19-year period, in patients with UVFP, by reviewing the voice multidimensional assessment measures administered before and after the speech therapy program.

### **5.3 Material and Methods**

Ethics approval for the study was granted by the Hospital Board of Directors and the University Research Ethics Committees.

#### **i. Patients**

A total of 132 patients with UVFP were involved in this retrospective study. From January 2000 to December 2019, 172 patients diagnosed with UVFP in the ENT outpatient Department were referred to the Speech-Language Pathology (SLP) Department for voice therapy.

Patients were included in this study if they: (1) were adults of either gender, aged 18 years and above; (2) were diagnosed with UVFP; and (3) had a multidimensional voice assessment. Exclusion criteria comprised patients who: (1) had previous speech therapy or laryngeal surgical intervention; (2) had associated severe dysphagia; (3) had previous professional singing or speaking training; (4) had ongoing psychiatric and neurological disease; and (5) had other concomitant vocal fold pathology. We excluded from the analysis 40 patients who had one or more of the exclusion criteria or did not complete the multidimensional assessment.

The study group was composed of 34 males (25.8%) and 98 females (74.2%). The average age of participants was  $57.1 \pm 12.9$  years (range 27-86 years), revealing a great variability. It was decided not to match the sample by gender, as no significant differences were found in the literature for the variable in question.

Table 17 shows the etiologies found for vocal fold paralysis. Most of them were related to surgery, particularly on the thyroid gland. There were 28 patients in whom the cause of the paralysis was unknown; thus, their condition was classified as idiopathic.

The time elapsed from the onset of UVFP to the beginning of voice therapy ranged from 7 days to 36 months; the average time was  $1.8 \pm 3.5$  months.

**Table 17- Unilateral Vocal Fold Paralysis etiology**

Cause	n (132)	Cases	
			%
Thyroidectomy Total	85		64.4
Idiopathic	28		22
Other surgeries	18		12.8
Other causes	1		0.8

## ii.Procedure

Patients received a comprehensive initial assessment of their voice, speech production and self-perceived quality of life. Afterwards, they completed a therapy program, which was customized to the participants. Finally, a reassessment of voice was performed after completion of the therapy. Details of the overall procedure is as follow:

### *Baseline and post-therapy voice assessment*

A phoniatic consultation was conducted by a senior ENT. The clinical evaluation of the voice included the collection of information through the following actions: clinical interview, audio-perceptual evaluation, musculoskeletal and aerodynamic functional examination, and self-assessment of the impact of the voice in quality of life. Visual-perceptual evaluation was performed by an Ear, Nose and Throat consultant, who was independent and blinded to this study.

Patients were submitted to the following voice evaluations, before and after voice therapy:

### *Visual-perceptual*

Videolaryngostroboscopic evaluation was conducted by an ENT consultant, using a rigid or flexible laryngoscope (Karl Storz, Germany), depending on the patients' degree of comfort and tolerance.

### *Auditory-perceptual voice analysis*

Audio-perceptual evaluation was based on a modified Grade, Instability, Roughness, Breathiness, Asthenia, and Strain (GIRBAS) scale (Philippe H Dejonckere et al., 2001) and was performed by the senior SLP. The speech samples of sustained vowel, counting,

and reading passage were used for assessment of voice quality with auditory perceptual judgements. All samples were recorded and copied onto a compact disc (CD).

#### *Aerodynamic analysis*

Maximum phonation time (MPT) was obtained during a sustained /a/ at comfortable pitch and loudness, after a profound inspiration. A prior demonstration was necessary in few cases, and three trials were required, the longest time being selected.

#### *Self-assessment*

A self-assessment perception of voice impairment was completed using the Voice Handicap Index (VHI-30) (Jacobson et al., 1997). This is a 30-item test divided into 3 subscales that measure the functional, physical, and emotional aspects of the handicap caused by voice impairment. The subscale scores range from 0 to 40 and the cumulative total ranges from 0 to 120; a higher score indicating a greater degree of disability.

### **iii. Voice therapy**

The purpose of the voice therapy plan for each patient was to provide laryngeal compensation, based on the principle of compensatory glottic closure by vocal effort activity (recruiting the action of the rest of the intrinsic and extrinsic healthy size muscles of the larynx). Even though the intervention followed a structured voice therapy program, it was individualized; therefore, the percentage of time allotted to a given technique or exercise of a particular method varied according to each patient's characteristics and progress in therapy. Table 18 illustrates the voice rehabilitation structured sessions, with a reference to the methods and techniques used in all patients. SLP was always on alert to avoid erroneous compensations such as ventricular fold hyperfunction and concomitant ventricular phonation.

The therapy program period of time, the onset, the number and frequency of the sessions and the type of intervention varied across the patients, depending on the patients' characteristics, commitment, and response to the therapy plan. The onset was  $1.75 \pm 3.46$  months, varying from 0.25 up to 36 months. For results' presentation, this onset was dichotomized into  $\leq 1$  month (early intervention) and  $> 1$  month (late intervention). Patients, on average, had  $10 \pm 4.9$  sessions, ranging from 4 to 41 sessions in total. On average, each participant involved in the current study underwent one or two voice

therapy sessions per week in the beginning of the therapy plan. Each session lasted for 45 minutes. In addition to the therapy sessions, all patients were asked to do daytime home exercises on weekdays (every two hours for 5-10 minutes) during the period of intervention. A reduction of this home exercises was implemented in last weeks of therapy and substituted by functional conversation, in more ecological communication settings aiming the generalization of the learned/acquired changes.

#### **iv. Statistical analysis**

Statistical analysis was conducted using the statistical software package IBM SPSS Statistics vs.25 software (IBM Corp. released 2017, Armonk, NY: IBM Corp.). Descriptive statistical analysis was performed, and categorical variables described using absolute and relative counts (n and%) and quantitative using median values and respective interquartile range (depicting 1<sup>st</sup> and 3<sup>rd</sup> quartile values) as well as average and standard deviation. Recovery rates were presented using both counts (n and %) and the respective confidence limits interval percentage values calculated using the adjusted Wald method. The level of significance was set at *p* value lower than 0.05. In inferential statistics, the Wilcoxon test was selected to compare pre- and post-treatment paired median results of the quantitative variables (the visual-perceptual parameter, the audio-perceptual parameters of grade, instability, roughness, breathiness, asthenia, and strain, the aerodynamic parameter (MPT) and also the VHI-30) due to lack of normalcy in their frequency distribution. Median post intervention differences for early (onset $\leq$ 1 month) and late (onset $>$ 1 month) intervention were assessed according to the Mann-Whitney test for independent groups.

**Table 18- Voice rehabilitation structured sessions**

Session	Content
1	<p>Clinical history                      Voice assessment                      Voice physiology education: diagnosis explanation and understanding; relation between therapy and laryngeal physiology; voice prognosis.</p>
2	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training of head position changes in inspiratory apnea, without sound production; pushing exercises with reflex laryngeal sphincter movement.</p>
3	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training of head position changes in inspiratory apnea, with sound production (voiced sibilants); different head position with sound production in maximum phonation time.                      Review patient understanding and mastery of session 2 techniques                      Patient-specific feedback and continued training to consolidate techniques.                      Phonation with correct vocal techniques to a greater extent; voiced sounds.</p>
4	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training of pushing exercises with syllables starting with unvoiced and voiced plosives after.                      Review foundation exercises                      Expand on vocal techniques and phonation exercises.                      Repeated syllables, short words.</p>
5	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training of pushing exercises with short words and pseudowords starting with unvoiced and voiced plosives after.                      Review provide feedback and continue training.                      Expand on session 4: focus on intonation and stressed syllables                      Commence generalization with short phrases</p>
6	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training based on reading text, using voiced (sibilant and plosive) sounds (effort phonation and control of vocal attacks).                      Review provide feedback and continue training.                      Expand on session 5 and begin generalization of phonation with correct vocal techniques with a focus on longer phrases and with different static head position.</p>
7	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training based on glottic resistance exercises (finger kazoo) and semi-occluded vocal tract exercises, using mesa di voce and melodic variations (musical scales).                      Review provide feedback and continue training.                      Repetition of most patient-relevant techniques                      Continue generalization exercises with a focus on resonance and also phrases of increasing length</p>
8	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training based on reading text, using intonation, nasal, basal and hyperacute sound.                      Review provide feedback and continue training.                      Repetition of most patient-relevant techniques.                      Focus on voice stability and control, volume and voice projection</p>
9	<p>Voice physiology education - Foundation exercises consisting of indirect and direct techniques:                      Education and training based on reading text, using inspiratory phonation, whisper and expand the techniques used in session 8.                      Review provide feedback and continue training.                      Repetition of most patient-relevant techniques</p>

## Voice Rehabilitation in an aquatic setting

	Generalization exercises: maintaining optimal phonatory control in reading of dialogues and also in conversation.
10	Voice assessment Outcome's analysis and discharge.

The sessions took place 2 times/week during the first 2 weeks, once a week during weeks 3-6, and once every second week during the last 2 weeks: a total of 10 sessions. After each session the patients were encouraged to exercise at home (schematics drawings given by the SLP) with focus on the techniques taught.

## 5.4 Results

The pre- and post-therapy results of each voice dimension assessment are presented according to the onset of symptoms before starting voice therapy. For this study purpose, ‘early’ and ‘late’ intervention, are defined as patients having symptoms less or more than a month before the initiation of therapy, respectively.

### i. Visual-perceptual

Table 19 presents data regarding the side and the position of the paralyzed vocal folds of the sample. In relation to the side of paralysis, 57/132 (43.2%) were on the right and 75/132 (56.8%) were on the left. With regard to the position of the paralyzed cord, data were only available in 81 patients; in 54/81 (40.9%), the vocal fold was in a paramedian position, while, in the remaining 27 patients (20.5%), the cord was found to be in an intermediate position (larger glottal gap).

Out of 132 patients with UVFP, 76 (57.6%; 95%CL: 49.0%-65.7%) had a full vocal fold motility recovery (total closure of glottal gap). Of these patients, no statistically significant difference was observed in terms of motility recovery related to the position of the vocal fold before voice therapy: Vocal fold paralysis in a paramedian (adduction) position recovered in 31/54 (57.4%; 95%CL: 44.2%-69.7%) cases while paralysis in an intermediate position was seen in 8/27 (29.6%; 95%CL: 15.7%-48.7%) patients.

In relation to etiology, vocal fold motility recovery was observed in 47/85 (55.3%; 95%CL: 44.7%-65.4%) post-total thyroidectomy patients, in 8/18 (44.4%; 95%CL: 24.5%-66.3%) patients recovering from other surgeries, and in 21/28 (75%; 95%CL: 56.4%-87.6%) of patients with idiopathic paralysis.

**Table 19- Position and size of paralyzed vocal fold**

Variables	Patient (n=132)	onset ≤1	onset >1	p*
		month n=97 (73.5%)	month n=35 (26.5%)	
Position, n=82 (%)	Hemi-larynx	1 (0.8)	1 (1.8)	0 (0)
	Intermediate	27 (20.5)	19 (33.3)	8 (32)
	Paramedian	54 (40.9)	37 (64.9)	17 (68)
Side, n=132 (%)	right	57 (43.2)	44 (45.4)	13 (37.1)
	left	75 (56.8)	53 (54.6)	22 (62.9)
Mobility pre, n=132 (%)	Incomplete closure	132 (100)	97 (100)	35 (100)
	Total closure glottal gap	76 (58.5)	59 (61.5)	17 (50)
Mobility post, n=130 (%)	Partial closure glottal gap*	35 (26.9)	27 (28.1)	8 (23.5)
	No change of glottal gap	19 (14.6)	10 (10.4)	9 (26.5)

\*when compared with pre-mobility

### ii. Auditory-perceptual ratings

Table 20 illustrates the GIRBAS values before and after voice therapy (average and SD; median and interquartile range), and the associated *p* value of the paired comparison rating. No single patient had all 6 parameters (Grade, Instability, Roughness, Breathiness, Asthenia and Strain) evaluated. Grade (n=74), Instability (n=75) and Roughness (n=60) were the most common measured across all patients.

Overall, all measures in all the parameters significantly reduced (e-g., improved) after voice therapy ( $p < 0.01$ ). Nevertheless, when taking in consideration timing of onset of symptoms before starting therapy, while grade (GIRBAS) showed a significant improvement in the post-treatment results for ‘early’ intervention, the asthenia and strain scales were not statistically significant in patients who had ‘early’ intervention. In a similar way, in the patients who had ‘late’ intervention, voice roughness and asthenia scales were also non-significant.

### iii. Aerodynamic analysis

Table 21 presents the results of the average and median values of aerodynamic assessment before and after speech therapy. One hundred and four patients had the MPT reported.

The median MPT was 6.15 (Q1-Q3: 4.55-9.21) before therapy and increased to 9 (Q1-Q3: 6.26-12.91), showing a significant improvement ( $p < 0.001$ ). These results were significant regardless if patients had an 'early' or 'late' intervention.

#### **iv. Self-assessment**

The overall average VHI-30 pre- therapy total was  $54.16 \pm 21.81$ , while after voice therapy, the encountered score had an average of  $20.87 \pm 15.51$ . Table 22 illustrates this significant positive change for all three quality of life domains ( $p \leq 0.001$ ). When considering the timing of onset of symptoms prior to the start of therapy, only the VHI emotional dimension improvement was not statistically significant, for the patients who had 'early' intervention patients.

**Table 20- GIRBAS statistical results before and after the Voice Therapy program and considering early and late intervention**

		All			onset ≤1 month			onset >1 month			Post: p (≤1 vs. >1 month)
		Pre	Post	p*	Pre	Post	p*	Pre	Post	p*	
<b>Grade</b>	n	74	74		49	49		25	25		
	av ± sd	1.99 ± 0.49	1.34 ± 0.46		1.93 ± 0.53	1.28 (0.43)		2.12 ± 0.36	1.48 ± 0.49		
	Me (Q1-Q3)	2.00 (1.88-2.13)	1.00 (1.00-1.5)	<0.001	2 (1.5-2)	1.0 <sup>b</sup> (1-1.5)	<0.001	2 (2-2.5)	1.5 <sup>a</sup> (1-2)	<0.001	0.047
<b>Instability</b>	n	75	75		48	48		27	27		
	av ± sd	1.58 ± 0.47	1.23 ± 0.40		1.53 ± 0.49	1.25 (0.41)		1.67 ± 0.44	1.2 ± 0.37		
	Me (Q1-Q3)	1.50 (1.00-2.00)	1.00 (1.00-1.50)	<0.001	1.5 (1-2)	1 (1-1.5)	0.001	2 (1.5-2)	1 (1-1.5)	<0.001	0.465
<b>Roughness</b>	n	60	60		45	45		15	15		
	av ± sd	1.93 ± 0.72	1.26 ± 0.52		2.08 ± 0.71	1.27 (0.5)		1.47 ± 0.58	1.23 ± 0.59		
	Me (Q1-Q3)	2.00 (1.13-2.50)	1.00 (1.00-1.50)	<0.001	2 (1.5-2.75)	1 (1-1.5)	<0.001	1 (1-2)	1 (1-1.5)	0.196	0.538
<b>Breathness</b>	n	55	55		32	32		23	23		
	av ± sd	1.94 ± 0.57	1.46 ± 0.58		1.92 ± 0.62	1.45 (0.63)		1.96 ± 0.5	1.48 ± 0.53		
	Me (Q1-Q3)	2.00 (1.50-2.50)	1.50 (1.00-2.00)	<0.001	2 (1.5-2.38)	1 (1-2)	0.001	2 (1.5-2.5)	1.5 (1-1.5)	0.001	0.532
<b>Ashtenia</b>	n	43	43		27	27		16	16		
	av ± sd	1.73 ± 0.67	1.48 ± 0.45		1.67 ± 0.71	1.43 (0.45)		1.84 ± 0.6	1.56 ± 0.44		
	Me (Q1-Q3)	2.00 (1.00-2.00)	1.50 (1.00-2.00)	0.014	2 (1-2)	1.5 (1-1.5)	0.076	2 (1.5-2.38)	1.5 (1-2)	0.090	0.266
<b>Strain</b>	n	27	27		17	17		10	10		
	av ± sd	1.24 ± 0.42	0.98 ± 0.29		1.06 ± 0.35	0.91 (0.26)		1.55 ± 0.37	1.1 ± 0.32		
	Me (Q1-Q3)	1.00 (1.00-1.50)	1.00 (1.00-1.00)	0.005	1 (1-1)	1 (0.75-1)	0.160	1.5 (1.38-2)	1 (1-1.5)	0.007	0.129

Data are shown as average (standard deviation) and median and interquartile range. \*Comparison of median values performed using the Wilcoxon test. <sup>a,b</sup>- different letters show significant median post intervention differences for early and late intervention according to Mann-Whitney test [p (≤1 vs. >1 month)].

**Table 21- Maximum Phonation Time statistical results before and after the Voice Therapy program**

		All		p*	onset ≤1 month		p*	onset >1 month		p*	Post: p (≤1 vs. >1 month)
		Pre	Post		Pre	Post		Pre	Post		
	n	104	104		69	69		35	35		
MPT /a/	av (sd)	7.3 ± 4.55	10.03 ± 5.57		7.24 ± 4.16	9.99 ± 5.58		7.41 ± 5.32	10.11 ± 5.62		
	Me (Q1-Q3)	6.15 (4.55-9.21)	9 (6.26-12.91)	<0.001	6.4 (4.37-9.18)	9 (6.02-12.77)	<0.001	5.79 (4.71-9.29)	8.62 (6.42-12.96)	0.002	0.970

Data are shown as average (standard deviation) and median and interquartile range. \*Comparison of median values performed using the Wilcoxon test. p (≤1 vs. >1 month) comparison of median values performed using the Mann-Whitney test.

**Table 22- VHI domains statistical results before and after the Voice Therapy program**

		All		p*	onset ≤1 month		p*	onset >1 month		p*	Post: p (≤1 vs. >1 month)
		Pre	Post		Pre	Post		Pre	Post		
VHI Functional	n	29	29		15	15		14	14		
	average (sd)	17.62 ± 8.67	6.59 ± 4.77		15.87 ± 6.53	7.6 ± 5.28		19.5 ± 10.42	5.5 ± 4.07		
	Me (Q1-Q3)	15 (11-22)	5 (3-10)	<0.001	15 (10-22)	7 (3-13)	0.001	15.5 (12.5-25.5)	4 (2-9.5)	0.001	0.240
VHI Organic	n	38	38		20	20		18	18		
	average (sd)	23.03 ± 7.21	10.84 ± 6.83		22.25 ± 7.04	11 ± 6.21		23.89 ± 7.51	10.67 ± 7.64		
	Me (Q1-Q3)	24 (17.75-28.25)	9.5 (5-17)	<0.001	24 (16-26.75)	11.5 (7-16.5)	<0.001	22.5 (18-30)	8.5 (4.75-17.5)	<0.001	0.675
VHI Emotional	n	31	31		18	18		13	13		
	average (sd)	13.94 ± 8.76	8.29 ± 8.82		9.44 ± 4.78	9 ± 10.67		20.15 ± 9.35	7.31 ± 5.62		
	Me (Q1-Q3)	11 (7-18)	6 (2-11)		9 (5.75-11.25)	6 (2-11.25)	0.085	18 (14.5-26)	6 (3.5-10)	0.001	1.000
VHI total	n	38	38	0.001	20	20		18	18		
	average (sd)	54.16 ± 21.81	20.87 ± 15.51		49.3 ± 18.27	21.45 ± 14.78		59.56 ± 24.58	20.22 ± 16.68		
	Me (Q1-Q3)	50 (38.75-66)	26 (8.75-32.25)	<0.001	49 (34.5-60.75)	18.5 (10-32.75)	<0.001	52.5 (43.75-68.75)	17 (7.75-30.75)	<0.001	0.914

Data are shown as average (standard deviation) and median and interquartile range. \*Comparison of median values performed using the Wilcoxon signed-ranks test. p (≤1 vs. >1 month) comparison of median values performed using the Mann-Whitney test.

## 5.5 Discussion

With respect to gender, it was possible to verify the dominance of females in the study sample, constituting 74.2% of the subjects. The researched literature did not indicate prevalence of gender regarding alteration of vocal fold mobility. However, in this study, the majority of the causes of vocal fold paralysis were related to the treatment of thyroid disorders, which is more prevalent in women, as found by other researchers (Mangilli et al., 2008).

In respect to the etiology of the UVFP, this study mostly focused on post-surgery cases. When analyzing the types and locations of tumors, it was possible to determine that the most prevalent were thyroid tumors (64.4%), differing in their histological diagnoses. The findings are in line with the literature (Wang et al., 2012) that points out that neck surgery, particularly thyroid, can cause trauma to the recurrent laryngeal nerve. Another study (Hartl et al., 2005) also reveals that unilateral recurrent laryngeal nerve palsy is a known complication of thyroid surgery, with 3.5% of patients having permanent paralysis. As for the affected side, the left side was slightly more prevalent (56.8%) and it is in accordance with the findings of Gaëtan-Romain Joliat et al study (Joliat et al., 2017) In regard to position of paralyzed vocal fold before voice therapy, patients with paramedian (adduction) position recovered in 31/54 (57%) cases while those with intermediate position recovered in 8/27 (29.6%). Even though, this result did not show statistical significance they are in line with Schindler et al study, which may suggest that voice therapy is not as effective if a more lateral position of the paralyzed vocal fold is present, before initiation of voice intervention. This is related to the lack of full compensation of the contralateral vocal fold and position change of the affected vocal fold (Schindler et al., 2008).

Solomon Husain et al 2018 study reported that almost 69% of the patients with idiopathic vocal fold paralysis recovered vocal function within 6 months spontaneously. In 64% of these patients the paralyzed vocal fold became mobile. In this study, 27 out of 28 patients had their vocal fold gap reduced and some vocal fold mobility of the affected side regained (Husain et al., 2018). It seems that the combination of spontaneous recovery and voice therapy has had a synergic positive effect, in patients with vocal fold paralysis resulting from an idiopathic cause.

This study has shown that speech therapy intervention, when started early (two months after the appearance of the vocal alteration) is successful in patients with UVFP. In our sample, all patients avoided the need for surgical laryngeal treatment for compensation of vocal alteration.

The methods and techniques, as adopted for this study, proved to be effective, corroborating the evidence of their application in this pathology. Even though there was a structured plan of the exercises and techniques that all patients should go through, the intensity of which was individualized, and the frequency of appointments adjusted, that limits which active components of the intervention are responsible for its success.

In regards to the average number of sessions per patient, this study shows a significant lower number ( $p < 0.001$ ) compared to studies such as Vij et al (Vij et al., 2017b), 11.7 sessions; Schindler et al (Schindler et al., 2008) 12.6 consultations; El-Banna et al (El-Banna & Youssef, 2014) 16 sessions; Barcelos et al (Barcelos et al., 2017) 12 sessions and Kao et al (Kao et al., 2017b) 16 sessions. The reason for this is that therapy was stopped once the SLP felt that a good voice improvement was achieved, regardless of the number of sessions completed by the patient, but majorly coinciding with 10 appointments.

The current study shows that a multiple dimension voice assessment was used. The fact that objective parameters, that is, quantitative data, were collected makes the results less prone to bias and more statistically robust, than if qualitative data would have been used. The maximum phonation time (MPT) mean values in pre-therapy (7.3 seconds) and post-therapy (10.03 seconds) are similar with studies found in the literature, which state that the MPT is shorter in patients with vocal fold paralysis (average between 4 to 5 seconds) (Colton et al., 1996) and with an average of 7 seconds for the vowels (Steffen et al., 2004). The increased maximum phonation time values after speech therapy suggests that the intervention was effective in adapting vocal physiology and developing adequate and necessary compensations for a louder voice production and voice clarity of patients (Boone & McFarlane, 1994; LF, 2000).

Therapy outcomes tackle the physical, emotional, and social well-being of a patient. Assessing patient's perspective of the condition using a self-assessment questionnaire provides an important outcome data, which is particularly sensitive to quality of life

changes caused by dysphonia (Michael S Benninger et al., 1998). Besides, the patient's perception of the severity of the dysphonia may impact the type of therapy required and results. The voice handicap index has been shown to have test– retest reliability and to be sensitive for a wide variety of voice disorders (Jacobson et al., 1997). Rosen et al (Rosen, Murry, et al., 2000) study argue that the patient's voice handicap index score may be more important than the absolute score, when used to check the treatment progress (or lack of it) during and after completed. The voice handicap index score of patients with untreated UVFP tends to reveal greater perceived vocal dysfunction, especially in the physical dimension, when compared with patients with dysphonia from other causes (El-Banna & Youssef, 2014). This finding is not evident in this study, as all dimensions were greatly perceived as affected by the patients, probably because the acute onset of voice dysphonia experienced by them. Another characteristic of this group of patients is that they generally preserve a good auditory and proprioceptive biofeedback which enables good treatment compliance, which is important to the success of voice therapy.

It would have been interesting to give continuity to this study by following-up on these patients, to confirm the functional stability of the results, including the laryngeal condition, 12, 24 or more months after completing voice therapy. It would also be recommended to start including other forms of vocal assessment, namely the acoustic analysis, to have a more comprehensive voice evaluation.

Further studies are needed in the area of intervention, especially with regard to therapy content, with emphasis on the physiological mechanism of the voice that is being targeted by a specific voice technique or component, to facilitate association between clinical practice and voice outcome measures, which supports the clinical rational to select rehabilitation programs or exercises, and its customization to each patient voice gains.

In regards to the timing of initiation of therapy following the onset of symptoms, El-Banna et al (El-Banna & Youssef, 2014), Mattioli et al, Busto-Crespo et al (Busto-Crespo et al., 2016) and Cantarela et al (Cantarella et al., 2010) studies suggest that 'early' intervention in patients with UVFP may be preferable to achieve best results. Nevertheless, these studies' results are difficult to interpret because there is an important variance on how authors define 'early' and 'late' intervention, with periods ranging from as minimal as less than 3 weeks to as maximal as more than 1 year. This

study results are in accordance with Barcelos et al (Barcelos et al., 2017) study that failed to evidence advantage of ‘early’ intervention on voice outcome measures improvement.

## **5.6 Conclusion**

The comparison of objective outcome parameters, before and after SLP intervention, have shown that voice therapy was effective with a strong statistical significance.

The costs and risks associated with a surgical laryngeal treatment for patients with UVFP are not to be underestimated, therefore, more studies are required to confirm the efficacy of speech therapy and a role as the first treatment approach.

Timing to initiate voice therapy after onset of symptoms/diagnosis seems to have no relationship with patients’ quality of life and voice response to therapy, in some of the assessed parameters.

This study adds to the existing scientific evidence that speech therapy intervention is effective to improve some voice parameters in patients with unilateral vocal fold paralysis, especially if started early after the onset of vocal symptoms.

Again, more studies are required to create scientific evidence, before best timing to initiate voice therapy can be agreed amongst medical community members and, consequently, incorporated in clinical practice.

## **Chapter VI - Is an aquatic setting an alternative way to deliver speech therapy in patients with bilateral vocal fold nodules? a retrospective study**

### **6.1 Abstract**

*Introduction:* Vocal fold nodules are bilateral lesions that can have an important negative impact in a person's job performance, social interaction, and quality of life. Voice therapy in an aquatic setting is a well-established but less revealed practice.

*Objective:* The aim of this study was to analyze the results of voice therapy delivered in water environment in patients who presented with vocal fold nodules.

*Methods:* A retrospective analysis of multidimensional voice outcomes was performed in 17 patients with vocal fold nodules, who presented dysphonia and received voice therapy in aquatic setting with an experienced speech-language pathologist once a week. Patients were referred by Ear Nose and Throat consultation. Data was collected from January/2001 to December/2017. The median of the pairwise pre- and post-treatment data was compared with non-parametric tests (Wilcoxon test) using  $\alpha=0.05$ .

*Results:* A total of 17 patients (female n=15) with bilateral vocal fold nodules were included in the study. Average age was  $33.7\pm 9.7$  years (range 27-86 years). The average number of appointments was  $9.8\pm 5.2$  (range 8-26 appointments). Vocal fold lesions disappeared in 82.3% of the patients after voice therapy. Late initiation of treatment presents worse prognosis (small sample size for statistical comparison). Compared pre- and post-therapy audio-perceptual and aerodynamic parameters showed significant improvement.

*Conclusion:* Voice therapy delivered in aquatic environment may be a valid and effective way to treat patients with vocal fold nodules. Early timing to initiate voice therapy after onset of symptoms/diagnosis seems to be a significant factor for the therapy outcomes (effectiveness).

## 6.2 Introduction

Vocal fold nodules (VFN) are whitish or reddish, mainly bilateral benign mass lesions that develop in the middle area of the anterior region of the vocal folds, after repetitive glottal trauma (vibration) (Saran et al., 2019).

Injuries to the vocal fold tissue, and subsequently the development of lesions (nodules), are due to voice overuse, misuse or abuse and seem to be associated with the type of occupation and gender (women) (Coyle et al., 2001; Van Houtte et al., 2010b; Zhukhovitskaya et al., 2015).

According to Jones et al (2002), vocal fold nodules are frequent in vocally and environmentally demanding professions or stressful lifestyles (e.g. aerobics instructors and singers) (Jones et al., 2002). Additionally, Behlau et al (2008) stated that people involved in teaching activities for big groups and workplaces with noisy environments (e.g. lecturers and professors) are regarded to be at higher risk of developing vocal fold nodules (M Behlau, 2008).

Hoarseness is the symptom that most commonly makes patients seek medical help, especially when it starts interfering with their professional activities, social integration, and consequently their overall quality of life (Kasper et al., 2011).

Speech therapy intervention is generally recommended as a preferred treatment option, due to several studies having shown its efficacy in treatment for VFN (Mansuri et al., 2018; Syed et al., 2009). Established challenges in effectively delivering behavioral interventions (Behlau, Madazio, Pacheco, Vaiano, Badaró & Barbara, 2021), such as voice therapy intervention, include high rates of therapy dropouts, patients' resistance to vocal behavioral change, and their lack of motivation (Portone-Maira et al., 2011; L. R. Santos et al., 2013).

Despite several reasons for patients to be non-compliant with therapy, a patient's motivation plays an important role (Behrman, 2006; Behrman et al., 2008). When combining speech therapy and a water-based environment, combined goals of speech therapy and advantages of an aquatic environment are provided. Water, in this setting, is considered as a meeting between a 'pleasure' environment and a therapeutic environment. Speech therapy in an aquatic setting utilizes the properties of water to provide a safe and

effective means to address impairments and improve functional skills. The properties of water include buoyancy, viscosity, and hydrostatic pressure (Becker, 2009b). Using an aquatic setting for speech and language therapy is a well-established but relatively unknown practice with a lack of documented literature. Consequently, there is a need for aquatic speech language pathologists to share the results of their clinical practice, and to raise awareness of the benefits of delivering voice therapy in an aquatic setting.

In this study, we aimed to evaluate a group of patients with bilateral VFNs who underwent voice therapy in an aquatic setting and analyze the multidimensional voice assessment measures before and after intervention, comparing them to the published expected outcomes.

### **6.3 Material and methods**

#### **i.Ethics**

This study was granted with ethics approval by the Fernando Pessoa Research Ethics Committee (FCS/PLS – 74/20) and was carried out in accordance with the guidelines of the Declaration of Helsinki on human studies. Participants' confidentiality and privacy of personal data were ensured.

#### **ii.Participants**

A total of 17 patients with bilateral VFNs were involved in this retrospective study. Data was collected from the participants' clinical notes. From January 2001 to December 2017, 25 patients diagnosed with bilateral VFNs by an Ear, Nose and Throat (ENT) consultant were referred for voice therapy.

Patients were included in this study if they were: (1) Adults aged 18 or over; (2) Diagnosed with bilateral VFNs; (3) Had no infection or inflammation of the upper airway at the time of speech and language therapy evaluation; and (4) Had a multidimensional voice assessment.

The exclusion criteria were: (1) Previous speech therapy; (2) Previous professional singing or voice coaching; (3) Presence of severe cardiovascular and respiratory diseases;

(4) Wounds or bedsores, skin diseases, urinary incontinence, or fear of water; (5) Ongoing psychiatric or neurological disease; and (6) Other concomitant vocal fold pathology.

Participants' occupation was categorized according to Koufman and Isaacson's (1991) (Koufman & Isaacson, 1991) classification: professional voice users – elite (e.g. singer, actor), professional voice users – non-elite (e.g. educator, teacher); non-professional voice users (e.g. lawyer, dentist, business person) and other non-professional non-voice users (e.g. student, agriculture/farmer, unemployed).

### **iii.Procedure**

A speech language pathologist (SLP) performed a comprehensive initial clinical history and assessment of patients' voice and speech production. Afterwards, the participants completed a voice therapy program in an aquatic setting, which was tailored. After completion of voice therapy, a reassessment of voice function was executed, which included an ENT re-evaluation. Details of the overall procedure are as follows.

### **iv.Baseline and post-therapy voice assessment:**

The clinical evaluation of the voice included the collection of information through clinical interview, and visual-perceptual, audio-perceptual and aerodynamic examination.

The voice assessment performed before and after voice therapy consisted of the following:

#### ***Visual-perceptual Evaluation***

A video-laryngostroboscopic evaluation was conducted by ENT consultants, using a rigid or flexible laryngoscope, depending on the patients' degree of comfort and tolerance (Milstein et al., 2005).

ENT consultants did not use any specific protocol to report laryngoscopic findings. Subjects were instructed to breathe through the mouth and produce the sound /i/ effortlessly with constant, comfortable intensity and frequency (Philippe H Dejonckere et al., 2001). The ENT consultants analyzed the laryngeal appearance with respect to three parameters: lesion size (increased, decreased, maintained), involvement of the

laryngeal vestibule (present, absent), and glottal gap (increased, decreased, and maintained) (M Hirano, 1981; Minoru Hirano & Bless, 1993).

### ***Audio-perceptual Evaluation***

An audio-perceptual evaluation was based on a modified Grade (G), Roughness (R), Breathiness (B), Asthenia (A) and Strain (S) - (GRBAS) scale (Philippe H Dejonckere et al., 2001), and was performed by a single senior SLP. The speech samples of sustained vowel production, counting, and reading a passage were used for the assessment of voice quality with auditory perceptual judgements. All samples were recorded and copied onto a compact disc (CD) (Sony® MDS-JE 500, mini-disk Sony®) and a microphone professional microphone (Le Son®). The senior SLP analyzed the samples, which were blinded in terms of timepoint (pre- and post-therapy), and rated each voice sample on a three-point scale, where “0 = normal,” “1 = mild,” “2 = moderate,” and “3 = severe,” (Nemr et al., 2012; Yu et al., 2001). After all of the samples were rated, five pairs were randomly selected to evaluate intra-rater reliability, using the intraclass correlation coefficient (ICC).

### ***Aerodynamic Evaluation***

Maximum phonation time (MPT) is a frequently used clinical tool for voice evaluation and the most common aerodynamic measure for assessing glottal sufficiency (Patel et al., 2018).

MPT was obtained during a sustained /a/, /s/ and /z/ at comfortable pitch and loudness, after a profound inspiration. After providing a prior demonstration, three trials were carried out with the longest time selected. Being considered a reliable measure in the evaluation of glottic efficiency, the s/z ratio is a fast, practical and non-invasive measure that provides interesting data on the dynamics of phonation (Van der Meer et al., 2010).

## **v. Voice therapy program**

Participants were initially scheduled for a set of 6–10 voice therapy appointments, according to the number recommended by the ENT. After completion of the sessions, participants were re-assessed by the ENT, and another set of appointments was recommended if nodules were still present.

The therapy was conducted once a week and each session lasted around 45 minutes. Participants were encouraged to exercise at home (indirect voice therapy) for 10 minutes every day (using schematics drawings given by the SLP), with focus on the techniques taught.

The water pool was maintained at a constant temperature of 33°C. The program was guided by the SLP, who was qualified and experienced in both aqua therapy and monitoring patients with voice problems.

A combined indirect and direct voice therapy approach was used. Even though the voice program was tailored to each participant's needs and progress during the treatment, a general 'structured' program, which focused on meeting key objectives, was followed:

Session 1– clinical history taken to identify participant's risk factors and behaviors leading to development of vocal nodules. Voice assessment performed and voice physiology education and voice hygiene given.

Session 2 and 3 – participant's adaptation to aquatic setting. Exercises to relax shoulder blade muscles. Vocal exercises to reduce laryngeal effort and improve resonance (e.g. nasal sounds). Vocal techniques to redirect airway flow, enhance maximum phonation time and control (reduce/soften) vocal attacks (inspiratory control with and without sound production during expiration – unvoiced sibilants).

Session 4 and 5 – Expand session 2 and 3 vocal techniques, based on reading text, using unvoiced (sibilant) sounds (control of vocal attacks). Techniques to improve normotensed coaptation of vocal folds and voice quality (tongue and lips trill).

Session 6 and 7 – Expand session 4 and 5 using repetition of the most patient-relevant techniques and generalization exercises to reach the level of conversational speech. Additionally, transfer “newly-learned” vocal behaviors to “real-life” situations outside the therapy setting.

Session 8 or up to 10 – Expand the previous and the last sessions with voice re-assessment and voice outcomes analysis.

When needed, extra sessions were undertaken – Restart/start over or continue the process if necessary.

## **vi. Statistical analysis**

Statistical analysis was performed using the software IBM SPSS® Statistics v. 26.0 (IBM Corp. released 2017, Armonk, NY: IBM Corp.). Descriptive statistical analysis of the quantitative variables included both mean average and standard deviation, and median and interquartile range (IQR: 1st and 3rd quartiles), while the categorical variables were described using counts and percentages (n and %). For inferential statistics, the Wilcoxon test was used to compare pre- and post-therapy results of the quantitative variables, as data showed a non-normal distribution. Post-visual-perceptual evaluation distribution results of the outcome groups (no nodules and the nodules reduced groups), as well as comparison with normal range published values, was performed using the Mann-Whitney U test. The level of significance was set at a p value lower than 0.05.

## **6.4 Results**

Only 17 out of the 25 participants completed the scheduled voice therapy program and were re-assessed at the end of therapy (32% dropout), therefore only 17 were considered for this study/analysis. Five participants were unable to complete the voice therapy program due to lack of time and the three other participants decided to quit for other reasons.

Participants' group characteristics according to gender, age, occupation, symptoms, time elapsed before beginning voice therapy, and number of sessions are presented in the Table 23. A large majority were women (n=15, 88.2%). The average age of participants was  $33.7 \pm 9.7$  years (range 18-55 years), revealing a large amount of variability. Most participants sought medical attention presenting with dysphonia (n = 12, 70.6%), and the three patients who presented with aphonia, had symptoms for a long time (6, 12, and 14 months). The average time elapsed from the onset of bilateral VFNs symptoms to the beginning of voice therapy was  $1.8 \pm 3.5$  months, ranging from 7 days to 14 months. Patients were enrolled initially with a first set of therapy sessions, which ranged between 8 and 10 sessions. Those patients who did not improve after this first set of sessions were submitted to additional therapy. Patients, had an average of  $9.8 \pm 5.2$  sessions, ranging from 8 to 26 sessions in total.

**Table 23- Study group characteristics**

<b>Gender</b>	F, n (%)	15 (88.2)
	M, n (%)	2 (11.8)
<b>Age (years)</b>	Average (sd)	33.7 (9.7)
	min-max	18-55
<b>Occupation Category</b>	Professional voice users – elite, n (%)	1 (5.9)
	Professional voice users – non-elite, n (%)	9 (52.9)
	Non-professional voice users, n (%)	3 (17.7)
	Non-professional non-voice users, n (%)	4 (23.5)
<b>Symptoms</b>	Dysphonia, n (%)	14 (82.3)
	Dyspnea, n (%)	1 (5.9)
	Phonoasthenia, n (%)	1 (5.9)
	Aphonia, n (%)	1 (5.9)
<b>Time elapsed to begin voice therapy (months)</b>	Average (sd)	1.8 (3.5)
	min-max	0.25-14
	Time=1 week (0.25 months)	14 (82.4)
	Time> 1 month	3 (17.6)
<b>Number of sessions</b>	Average (sd)	9.8 (5.2)
	Me (P25-P75)	8 (8-10)
	min-max	8-26

**Abbreviation:** sd, standard deviation

### **i. Visual-perceptual evaluation**

Documentation of the laryngoscopic examination findings by the ENT consultants was very scarce, and mostly limited to the presence or absence of VFNs.

Pre- and post-therapy visual examinations of vocal folds were compared, and the vocal fold nodules disappeared in 82.3% of the participants after the first set of voice therapy sessions. Three participants, who began therapy when they had shown symptoms for more than one month (presenting with aphonia), did not recover, even after having a second set of therapy sessions. The lack of improvement was significantly associated with the elapsed time before beginning therapy and with the number of sessions required, were with statistical significance ( $p < 0.001$  and  $p = 0.017$ , respectively). In two of the participants the nodules were only reduced in size even after a second set of therapy sessions (14 and 16 sessions in total), and in one participant no change was observed, but the patient refused extra treatment. Table 24 demonstrates a summary of the visual-perceptual results (pre- and post-therapy), along with participants' professional category, their vocal symptoms and post-therapy evaluation comparisons for the different outcome groups.

**Table 24- Visual-perceptual evaluation**

		<b>Pre-therapy</b>	<b>Post-therapy</b>		
			<b>No Nodules</b>	<b>nodules reduced</b>	<b>No change</b>
<b>Gender</b>	F, n (%)	15 (88.2)	12 (85.7)	2 (100)	1 (100)
	M, n (%)	2 (11.8)	2 (14.3)	0 (0)	0 (0)
<b>Professional category</b>	Professional voice users – elite, n (%)	1 (5.9)	1 (7.2)	0 (0)	0 (0)
	Professional voice users – non-elite, n (%)	9 (52.9)	8 (57.1)	1 (50)	0 (0)
	Non-professional voice users, n (%)	3 (17.7)	2 (14.3)	1 (50)	0 (0)
	Non-professional non-voice users, n (%)	4 (23.5)	3 (21.4)	0 (0)	1 (100)
<b>All</b>		<b>17 (100)</b>	<b>14 (82.3)</b>	<b>2 (11.8)</b>	<b>1 (5.9)</b>
<b>Time Elapsed to begin therapy (months)</b>	Average (sd)		0.25 (0)	13 (1.4)	6 (0)
	Me (P25-P75)		0.25 (0.25-0.25)	13 (12-14)	6
			<b>p-value&lt;0.001</b>		<b>-</b>
<b>Number of sessions</b>	Average (sd)		8 (1.6)	23 (4.26)	8 (0)
	Me (P25-P75)		8 (8-85)	23 (20-26)	8 (0)
			<b>p-value=0.017</b>		<b>-</b>

**Abbreviation:** F, female, M, male; sd, standard deviation; p-value comparing median values of quantitative variables for the post Visual-perceptual Evaluation distribution results of the no nodules and the nodules reduced groups using the Mann-Whitney test.

## ii. Audio-perceptual evaluation

There was a statistical significance improvement in all parameters after voice therapy, with strong agreement between the first and second ratings performed by the SLP (ICC=0.92). The metric describes how strongly units in the same group resemble each other. A summary of the audio-perceptual results is presented in Table 25.

**Table 25- Audio-perceptual results (n=17)**

		<b>Pre-therapy</b>	<b>Post-therapy</b>	<b>p-value</b>
<b>Grade</b>	Average (sd)	1.53 (0.62)	0.74 (0.59)	
	Me (Q1-Q3)	1.5 (1-2)	1 (0-1)	<b>0.002</b>
<b>Roughness</b>	Average (sd)	1.44 (0.7)	0.44 (0.56)	
	Me (Q1-Q3)	1.5 (1-2)	0 (0-1)	<b>0.001</b>
<b>Breathness</b>	Average (sd)	0.79 (0.75)	0.32 (0.53)	
	Me (Q1-Q3)	1 (0-1.5)	0 (0-1)	<b>0.016</b>
<b>Ashtenic</b>	Average (sd)	0.68 (0.86)	0.29 (0.59)	
	Me (Q1-Q3)	0 (0-1.5)	0 (0-0.5)	<b>0.042</b>
<b>Strain</b>	Average (sd)	0.65 (0.68)	0.24 (0.44)	
	Me (Q1-Q3)	1 (0-1)	0 (0-0.5)	<b>0.023</b>

**Abbreviation:** sd, standard deviation; p-value comparing the median of the difference of pairwise values using the Wilcoxon test.

### iii. Aerodynamic evaluation

Pre- and post-therapy aerodynamic measures were obtained from all participants (Table 26). There was a statistically significant improvement after voice therapy in the median MPT /a/ ( $p < 0.001$ ) and s/z ratio ( $p = 0.046$ ).

**Table 26- Aerodynamic evaluation summary (n=17)**

		<b>Pre-therapy</b>	<b>Post-therapy</b>	<b>p-value</b>
<b>MPT /a/</b>	Average (sd)	10.81 (3.03)	13.39 (4.07)	
	Me (Q1-Q3)	10.80 (9.05-12.1)	13 (11.1-14.65)	<b>&lt;0.001</b>
<b>MPT /s/</b>	Average (sd)	10.94 (2.58)	11.92 (2.76)	
	Me (Q1-Q3)	11.45 (9.35-12.28)	12.8 (9.14-14.12)	0.052
<b>MPT /z/</b>	Average (sd)	9.56 (2.72)	10.85 (2.51)	
	Me (Q1-Q3)	10.06 (7.74-11.34)	11.88 (8.45-12.95)	0.072
<b>s/z ratio</b>	Average (sd)	1.19 (0.25)	1.06 (0.15)	
	Me (Q1-Q3)	1.08 (1-1.39)	1.01 (1-1.09)	<b>0.046</b>

**Abbreviation:** sd, standard deviation; p-value comparing the median of the difference of pairwise values using the Wilcoxon test.

### iv. Comparison of post-therapy results with normal range parameters

Despite the statistically significance improvement in all audio-perceptual parameters after therapy, only the parameter asthenia returned to normal when compared to previously reported values ( $p = 0.059$ ) (Table 27). On the other hand, in the group of participants who started therapy within 1 week of symptoms onset (0.25 months), three parameters returned to normal voice values (breathiness  $p = 0.083$ , asthenia  $p = 0.083$  and strain  $p = 0.157$ ).

Regarding the aerodynamic evaluation, MPT/a/ and the s/z ratio improved after voice therapy, reaching values within the normal range (Table 27), regardless of the time between symptom onset and starting treatment. The median value of the s/z ratio was within the normal range and the median MPT /a/ value was not significantly different from the lower bound of the normal range.

**Table 27– Comparison of post-therapy results with normal range parameters**

Parameter		Median result Post-therapy	Normal range <sup>*,**</sup>	n=17 Comparison	n=14 (onset=0.25 months) Comparison
Audio-perceptual*	Grade	1	0	<b>p=0.002</b>	<b>p=0.005</b>
	Roughness	0	0	<b>p=0.011</b>	<b>p=0.020</b>
	Breathiness	0	0	<b>p=0.034</b>	p=0.083
	Asthenia	0	0	p=0.059	p=0.083
	Strain	0	0	<b>p=0.046</b>	p=0.157
Aerodynamic**	MPT/a/ (F)	(n=15) 12.9	15-25	F – with 15: p=0.126	F – with 15: p=0.136
	MPT/a/ (M)	(n=2) 14.8	25-35	M – n.a.	M – n.a.
	s/z ratio (F/M)	1.01	0.8-1.2	with < 0.8: <b>p&lt;0.001</b> with > 1.2: <b>p=0.002</b>	with < 0.8: <b>p=0.001</b> with > 1.2: <b>p=0.001</b>

**Abbreviation:** F- female; M- Male; n.a. not applicable; \* Audio-perceptual (Minoru Hirano, 1989) ; \*\* Aerodynamic evaluation (Beber et al., 2009; Cielo et al., 2008, 2011; Fabron et al., 2011; Rossi et al., 2006)

## 6.5 Discussion

The vocal demand of each individual is associated with an increased risk of developing vocal problems (Cutiva et al., 2013; Przysieszny & Przysieszny, 2015). Although professional use of the voice usually occurs in about 1/3 of the working population, phonatory requirements vary according to the occupation (Mota, 2017). Several studies describe that the most frequent complaint of teachers is vocal fatigue, and that at least 80% presented with vocal complaints in a specific period of their career (Cutiva et al., 2013; Przysieszny & Przysieszny, 2015). In our study group, the majority of the participants (52.9%) belonged to the group of professional voice users – non-elite, which included six schoolteachers and two kindergarten teachers. 17.7% (n=3) were classified as belonging to the group of non-professional voice users and 23.4% (n=4) belonging to the group of non-professional non-voice users. There is an accumulation of factors that increased the risk of vocal alterations, and a dysphonia cannot be explained by a single cause (Mara Behlau et al., 2018). In 2009, Spina et al used a protocol to assess the relationship between quality of life and voice with the degree of dysphonia in 101 patients with vocal complaints in an outpatient department of otorhinolaryngology. The sample consisted of 46 male and 55 female individuals. Only 37 of the 101 participants were voice professionals (Spina et al., 2009).

Mara Behlau (2018) argues that the appearance of vocal fold changes and dysphonia cannot be explained only by the degree voice use/misuse or abuse, but instead is the accumulation of a variety of factors. In our study sample, two of three patients classified as non-professional voice users and three out of the four non-professional non-voice

users, found that their vocal nodules disappeared after voice therapy. These positive results of therapy in the groups of patients at less risk of developing vocal nodules, are in accordance with the results observed in the study by Spina (2009), where the majority of the participants were non-voice professionals (Spina et al., 2009).

In this study, the sample shows a female dominance, constituting 88.2% of the participants. The literature is unanimous in describing a higher incidence of vocal disorders in women (Birchall & Carding, 2019a). Smith et al (1996) at University in Iowa, showed a 2:1 woman-to-man ratio in vocal disorder treatments (Smith et al., 1996).

Despite this, the multidimensional voice outcome measures were generally positive in this group. The rate of therapy dropouts (32%) was still considered moderate, despite being below some rates reported in the literature. In a study by Portone-Maira et al (2011), 120 out of 197 patients (60%) with dysphonia who were referred for voice therapy by an ENT dropped out of treatment (Portone-Maira et al., 2011). In comparison, a meta-analysis of 110 studies of adults requiring psychotherapy (behavioral change therapy) showed an average dropout rate of 35.2%. In our study, three participants (12%) dropped out of therapy because they found it difficult to change their vocal habits and voice behavior, and were not motivated to complete the therapy. It would have been interesting to hear participants' feedback regarding aquatic therapy, by collecting data through a survey to better understand if the water-based environment enhanced their engagement and self-motivation surrounding the therapy.

With respect to the visual-perceptual evaluation, 82.3% of the participants had no vocal fold nodules at the end of the first set of voice therapy sessions. This result suggests that the voice therapy delivered in the aquatic setting was effective. When taking into consideration the time elapsed since the onset of vocal symptoms, it seems that delivering therapy early (< 1 week after onset) was a significant factor associated with a good response to the treatment. All participants who had a shorter history of symptoms found that their vocal nodules disappeared during therapy. In contrast, three of the participants who had vocal symptoms for a longer period, required a second set of voice therapy sessions. Despite this, the vocal nodules only reduced in size or were unchanged at the end of treatment. One of the reasons that may explain the lower effectiveness of speech therapy was the participants' constant vocal use on their jobs, not allowing vocal rest (an integral part of the therapy). Another aspect that could have helped in the interpretation

of this result, was knowledge of the degree of keratosis of the vocal nodules before starting therapy; however, this information was not documented by the ENT doctor in the patients' clinical notes. More fibrotic vocal nodules are less likely to disappear after therapy (Calado, 2010).

Regarding the audio-perceptual evaluation, the pre-therapy results of this study were in accordance with findings from other studies (Rodríguez-Parra et al., 2009; Speyer et al., 2004). Furthermore, all parameters were statistically significantly improved after voice therapy. These results are comparable with the systematic review on the effectiveness of voice therapy in patients with vocal fold nodules by Alegria et al (2019), where a significant improvement in the overall audio-perceptual parameters was observed (Rita Alegria et al., 2020b).

The measurement of MPT is one of the procedures used frequently in the aerodynamic evaluation of the voice. The presence of a nodule on the vocal folds edge creates air leak during phonation (Mara Behlau, 2005; Cielo et al., 2015; Colton et al., 1996). In the present study, the participants' MPT/a/ was significantly increased at the end of therapy, reflecting previous results in literature. In a survey carried out by Kurtz et al (2010), the authors stated that the MPT/a/ was reduced in all 38 female participants with vocal nodules (Kurtz & Cielo, 2010). In another study by Cielo et al (2015), a total of 54 subjects, predominantly women (n=46, 85%) with a diagnosis of vocal fold nodules, showed increased MPT/a/ values increased after voice therapy (Cielo et al., 2015).

The average pre-therapy s/z ratio of our cohort was within the normal range (1.19), but the participants' MPT averages for /s/ and /z/ were 10.94 and 9.56, respectively, both lower than the normal range. The non-significant difference in the median values of the pre- and post- treatment measurements may be due to type II errors (most probably due to the low sample size). Nevertheless, these results are in line with a study by Cielo et al. (2008) (Cielo et al., 2008), in which 70 individuals with dysphonia were evaluated. In this study, although the s/z ratio is within the normal range, the individual MPTs of /s/ and /z/ are reduced suggesting lack of coordination in expiratory control and/or lack of glottal coaptation (Casper et al., 2006) (Casper & Leonard, 2006), which can be associated with vocal fold lesions.

## **6.6 Limitations and future projects**

Despite evidence of the overall benefits of voice therapy delivered in an aquatic setting, care should be taken when interpreting these results, due to the small sample size. Thus, further studies with higher sample sizes are required to avoid the risk of overestimating the effect on the outcome. Another limitation of the results is the considerable risk for of measurement bias, as there were no procedures put in place to reduce measurements errors in the different assessment methods used.

It is important to state that the fact that a single evaluator performed the perceptual evaluation of the voice increased the risk of the bias in the results and decreased their robustness.

The lack of other objective voice measurements such as acoustic or aerodynamic analysis, along with the absence of subjective self-assessment of voice quality by the participants, limits the validity and quality of the voice therapy results (therapeutic effect). Another important factor is that the data analysis is limited by the quality and accuracy of documentation in the participants' clinical notes and, therefore, the data needs to be analyzed with prudence.

In this study, the therapeutic strategy aimed for a holistic approach to the vocal problem, combining a direct and indirect therapeutic approach. Although there was a similar “structured” treatment plan for each participant, the intensity and duration of each exercise and technique was adapted to the individual, depending on their progress during therapy sessions and comfort with the water-based environment. In addition, the voice therapy program changed and evolved over the past 17 years, underpinned by obvious advances in techniques and exercises, and the experience working in aquatic setting gained by the SLP. Further studies are needed to better understand which components of the intervention were responsible for the clinical improvement.

It would also have been interesting to give continuity to this study by following-up on these patients, to confirm the functional stability of the results 6 or 12 months after completing voice therapy, but the retrospective nature of the present study precludes this possibility.

## **6.7 Conclusion**

The highlight of this study is that this is the first study that associates speech-language pathology in water-base milieu and voice disorders.

Voice therapy delivered in an aquatic environment seems to be a valid and effective way to treat patients with vocal fold nodules. The results of voice outcome measures in this study are comparable with similar studies where voice therapy was delivered in a land-based environment.

Early initiating of voice therapy after the onset of symptoms/diagnosis seems to be a significant factor in the success of voice therapy.

There is a need for more studies in an aquatic environment to further ensure that voice therapy delivered in this setting can be effective and efficient in patients with vocal fold problems.

## **Chapter VII - Voice therapy delivered in a water-based setting for unilateral vocal fold paralysis: a case report**

### **7.1 Abstract**

*Introduction:* voice therapy programs – in a water-based setting – can lead an improved quality of life for individuals with various conditions. This case report looks at a specific voice therapy program – delivered in a water-based setting – for a patient with unilateral vocal fold paralysis following surgery.

*Case report:* Sixty-four years old man, professional voice user (teacher), ex-smoker, who underwent a total thyroidectomy for a thyroid cancer. He participated in a voice therapy program in a water-based setting once a week, for 8 weeks. Voice therapy strategy included a combination of direct and indirect techniques. Direct water-based exercises aimed to reduce vocal fold gap, reduce supra-glottic structures hyperfunction and improve voice quality. A pre- and post-therapy multidimensional assessment and a six-month follow-up were performed.

*Results:* There was a change in the voice outcome measures after completion of treatment (visual perceptual, audio-perceptual, acoustic and self-perception). At six-month follow-up assessment, patient reported a return to its almost normal – professional and social – voice use.

*Conclusions:* Water-based therapy can create a gentle, engaging, motivational and supportive context for voice treatment. The properties of water create an environment for safe practice of skills. Advantages of combining water-based therapy with voice therapy are promoting communication and improving breathing and phonation control. Further studies with larger samples are needed to draw any realistic conclusions on the efficacy of water-based voice therapy in patients with unilateral vocal fold paralysis..

## 7.2 Introduction

The branches of the proximal vagus nerves and the recurrent laryngeal nerves control the intrinsic laryngeal muscles responsible for the vocal fold motility; therefore, any injury along these nerves can result in vocal folds paralysis (Dankbaar & Pameijer, 2014; Myssiorek, 2004). In a study conducted by Rosenthal et al (2007), where the etiologies of unilateral vocal fold paralysis were reviewed, 46% of the injuries were related to surgery of the head and neck (Rosenthal et al., 2007).

Voice therapy is generally recommended as part of the primary therapeutic strategy to maximize the chance of spontaneous contralateral vocal fold compensation, which can occur up to one year after nerve injury (Cohen et al., 2016; Sulica, 2009). In Alegria et al (2020), a systematic review on the efficacy of voice therapy delivered in unilateral vocal fold paralysis (VFP), 72% of the patients showed a positive effect (reduced glottal gap) regardless of the voice techniques or exercises used (R. Alegria et al., 2020).

Usually, a speech therapy appointment is conducted ‘on land’; however, holding sessions in a water-based setting is relatively unknown. In general land and water-based environments differ in that they have different physical characteristics, requiring a human being to adapt differently in each. Water physical characteristics are often referred to as ‘the principles of water’ including (but not limited to) hydrostatic pressure, buoyancy and viscosity. The depth of submersion affects the force exerted on the body, known as hydrostatic pressure. As a consequence of the hydrostatic pressure, constant muscle activation ensues to maintain stability (Park & Roh, 2011). A fluid’s pressure is exerted equally around all the body’s surface that is submerged. When submerged in an aquatic setting, one is in the presence of a group of equal external forces that compress the body. Compression can cause various changes to be considered when an intervention takes place in a water-based setting, such as: effects on circulation, increase or decrease of muscle strength, relaxation, increased aerobic capacity, increased resistance to chest wall expansion, and ease of postural and balance reactions, among others (Park & Roh, 2011). Bodyweight and balance receive greater support the more the body is immersed in water. The support of the body weight develops the ease of movement, thereby allowing for the practice and refinement of increasingly difficult skills compared to their land-based abilities (Becker, 2009a; Becker et al., 2009). The internal friction of water creates a drag force, also known as viscosity. The effects of viscosity and hydrostatic pressure in water

are reported by individuals to have created an environment associated with an increased sense of security and ease of movement when undertaking harder tasks (Park & Roh, 2011; Stowell et al., 2001).

There is a lack of evidence in the scientific literature of delivering voice therapy in a water-based setting. To the best of our knowledge, no study thus far has been published investigating the effect of the aquatic environment on an individual with unilateral VFP. Taking the above into consideration, the need for further investigation of water-based intervention programs becomes evident.

The purpose of this case report was to describe a voice therapy program performed in a water-based setting in a patient with unilateral VFP after thyroid surgery.

### **7.3 Case description**

This study was granted with ethical approval by the Hospital de Santo Antonio's Hospital Board of Directors. It was carried out by the guidelines of the Declaration of Helsinki on human studies. Participants' confidentiality and privacy of personal data were ensured.

#### **i. History**

The patient was a 64-year-old man, teacher, ex-smoker for more than 24 years and used to regularly drink a glass of wine during meals. The patient was submitted to a total thyroidectomy for thyroid cancer in a public tertiary hospital in Portugal. No iodine therapy was required after surgery.

A first surgical follow-up was performed two weeks after surgery, and, at that time, the patient did not report any symptoms. During his second surgical follow-up, six months after surgery, the patient complained of worsening dysphonia, which was limiting his professional activity the point that the assistance of another teacher was required to deliver most of his lectures. The patient also mentioned that he was seen by a speech therapist and enrolled in land-based speech therapy. However, after two sessions, he dropped out of therapy, reporting a lack of engagement and motivation as the primary reasons for that outcome.

## **ii.Examination**

A comprehensive voice evaluation was conducted by a senior speech-language pathologist eight months after surgery, and in addition to their clinical history, a visual-perceptual examination, audio-perceptual, acoustic, aerodynamic and self-perception of the voice impact in quality-of-life assessments were carried out.

### ***Visual-perceptual Evaluation***

An experienced Otorhinolaryngologist performed a video-laryngostroboscopic evaluation, using a flexible laryngoscope. The visual-perceptual exam was performed during a sustained vowel /i/ and /ε/ and during respiration. A video-laryngostroboscopic evaluation was essential to document the vocal fold position, motility, and morphology and observe its prolonged vibratory characteristics.

### ***Audio-perceptual Evaluation***

Voice quality was assessed based on a modified Grade, Instability, Roughness, Breathiness, Asthenia and Strain (GIRBAS) scale (Philippe H Dejonckere et al., 2001). Samples of sustained vowel /a/, counting and reading passage were recorded and copied onto a compact disc (CD). All of the voice samples were scored in a four-point interval scale (0 = normal, 1 = slight disturbance, 2 = moderate disturbance, 3 = severe disturbance).

### ***Acoustic Analysis***

The Praat program (Phonetic Sciences, University of Amsterdam) was used for acoustic voice analysis. Speech was recorded in a room without acoustic room treatment but with a noise level inferior to 40dB SPL. A unidirectional microphone Philips SBC ME 400, positioned at a 45° angle and 10 cm from the patient's mouth was used. The patient was asked to repeat two times a sustain a vowel /a/ at a comfortable pitch and loudness for at least five seconds. The samples were assessed from the 2<sup>nd</sup> second of vowel production, which is considered the most stable spectrum zone for an acoustic assessment. The acoustics measures analyzed were:

- 1) Average pitch ( $f_0$ , Hz): patient repeats sustained vowel /a/ three times;

- 2) Jitter (local, %): the cycle-to-cycle pitch period;
- 3) Shimmer (local, %): the cycle-to-cycle amplitude variation;
- 4) Harmonic to noise ratio (HNR, dB): the amount of signal that is coming from voicing versus noise.

### ***Aerodynamic Analysis***

A maximum phonation time (MPT) is a frequently used clinical tool for voice evaluation and is also the most common aerodynamic measure for assessing glottal sufficiency (Patel et al., 2018). MPT was obtained by asking the patient to sustain the vowels /a/ and the consonants /s/ and /z/ for as long as possible on a single breath. The longest of three attempts was considered as the maximum phonation time. The s/z ratio was determined using the /s/ and /z/ MPT (Van der Meer et al., 2010).

### ***Self-perception Evaluation***

The voice handicap index (VHI) (Jacobson et al., 1997) questionnaire was used to assess the patient's self-perception of the voice impairment impact on his functional, physical and emotional - sub-domains – aspects of life. This is a 30-item test divided into three subscales that measure the functional, physical and emotional aspects of the disability caused by voice impairment. The participants rated each statement based on the frequency of occurrence on a five-point interval scale: 0 = never, 1 = almost never, 2 = sometimes, 3 = almost always, and 4 = always. An increase in score represents an increase in voice severity (Azevedo et al., 2020).

### **iii. Voice therapy Intervention**

The therapy program was adapted according to the patient's needs and voice impairment, and also to the progress during treatment. The aquatic sessions were delivered by an experienced aquatic SLP in a private pool, where water temperature was maintained around 33°C.

The patient underwent eight voice therapy sessions, seven in the water. To perform a voice re-assessment, the final one was on land.

Sessions were delivered once a week and lasted around 40 to 45 minutes. After each water session, the patient was encouraged to exercise at home, 'on land', 2-3 times a day for 10-15 minutes (Cantarella et al., 2010), using schematic drawings provided by the SLP, focusing on the techniques taught.

The overall goals of the voice therapy program were to: (1) reduce the vocal folds gap by strengthening adductor muscles, based on the contralateral vocal fold hyper-adduction; (2) reduce compensatory vocal effort of supra-glottis structures and (3) improve voice steadiness, endurance and loudness (Boone et al., 2005).

The voice therapy program included a combination of direct and indirect techniques. Indirect techniques use with the participant consisted in explaining the condition's diagnosis and prognosis and educating about voice physiology and its relationship with the therapy goals.

The direct therapy developed throughout the seven appointments, was reinforced during the homework-therapy, and consisted of the following techniques to achieved therapy program goals:

Goal 1 and 2 - reduce the vocal fold gap and supra-glottis hyperfunction.

- Emission of sustained voiced sibilants (/z/, /v/, /ʒ/) on exhalation, while feeling by one hand movements of the anterior neck region and contraction of the abdominal wall (Cantarella et al., 2010);
- Education and training of pushing exercises with syllables starting with unvoiced and voiced plosives and open vowels (/a/, /ε/, /ɔ/) after (Yamaguchi et al., 1993).
- Education and training of pushing exercises with short words and pseudowords (reduplication of the previous syllables) starting with unvoiced and voiced plosives after (Yamaguchi et al., 1993).
- Education and training based on reading text using voiced (sibilant and plosive) sounds (effort phonation and control of vocal attacks).

Goal 3 – improve voice steadiness, endurance, and loudness

- Therapy based on glottic resistance exercises (finger Kazoo) and semi-occluded vocal tract exercises using *messa di voce* and melodic variations (musical scales) (Cielo et al., 2013);
- Controlled reading while using inspiratory phonation, whisper and focusing on voice stabilization and control, volume and voice projection;
- Maintaining optimal phonatory control in conversation. At the end of therapy, a special attention was paid to achieving and maintaining optimal coordination between breathing and phonation during spontaneous speech so that it can be generalized to the day-by-day lectures of the patient.

Table 28 displays the interrelationships between the therapy program goals, water-based exercise goals, and description of the aquatic therapy exercises correlated with its aquatic principles.

**Table 28 - Interrelationships between the therapy program goals, water-based therapy goals, water-based exercises & water characteristics**

Voice Therapy Goals	Water-based therapy goals	Water-based exercises & water characteristics
<p><b>Appropriate breath Support for phonation</b></p>	<ul style="list-style-type: none"> <li>• Warm-up, correct body position and laryngeal position shifts.</li> <li>• Self-awareness of body, abdominal breathing training aimed to optimize breath support and to obtain a steady subglottic pressure.</li> </ul>	<ul style="list-style-type: none"> <li>• Warm-up exercises: movement activities in deep water (shoulder level): running on the spot, jumping jacks, and reciprocal arm and leg movements, jumping on the spot and jumping forwards, backwards and sideways. (<b>thermodynamic</b>).</li> <li>• Movement activities in deep water (shoulder level): self-awareness of breathing pattern and body posture (<b>hydrostatic pressure and viscosity</b>).</li> <li>• Movement activities in deep water (shoulder level): Hip flexion bilaterally while supported on an aquatic noodle to work on lower abdominals and supine, float to upright sitting as modified sit-ups. Control of body posture and abdominal muscles tone. The breathing exercises included abdominal control and diaphragmatic breathing. Progression: no noodle needed (<b>thermodynamic, hydrostatic pressure and buoyancy</b>).</li> <li>• Activity in the deep water (shoulder level): simulation of the patient’s working environment with exercises (reading, declamation, appealing) focusing on voice’s loudness and pitch variations and speed of voice, required for fulfilment of patient’s job.</li> </ul>
<p><b>Reduce vocal gap and supra-glottic hyperfunction</b></p>	<ul style="list-style-type: none"> <li>• Interplay between airflow, vocal fold vibration and supraglottic structures.</li> </ul>	<ul style="list-style-type: none"> <li>• Movement activities in deep water (shoulder level): education and training of head position changes in inspiratory apnea, with sound production (voiced sibilants); different head position with sound production in maximum phonation time (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> <li>• Activity in the deep water (shoulder level): phonation with straw exercises. Progression: drinking straw with a narrower diameter (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> </ul>
<p><b>Strengthen of intrinsic adductors muscles</b></p>	<ul style="list-style-type: none"> <li>• Strengthen and coordinate laryngeal musculature.</li> </ul>	<ul style="list-style-type: none"> <li>• Movement activity in the deep water (shoulder level): repetitions with elastic bands while saying syllables starting with unvoiced and voiced plosives after. Progression: extend 10cm of elastic bands to increase resistance (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> <li>• Activity in the deep water (shoulder level): pushing a ball (volleyball size) while saying short words and pseudo-words starting with unvoiced and voiced plosives after. Progression: larger ball to increase resistance and increase number of words and sentences (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> <li>• Movement activity in the deep water (shoulder level): repetitions with elastic bands while on reading text, using voiced (sibilant and plosive) sounds (effort phonation and control of vocal attacks). Progression: extend 10cm of elastic bands to increase resistance (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> <li>• Movement activity in the deep water (shoulder level): marching on the spot holding a ball (volleyball size) while reading sentences written on the pool wall/mirror. Progression: larger ball to increase resistance (<b>viscosity, hydrostatic pressure, and buoyancy</b>).</li> </ul>

#### **iv. Outcomes**

The patient undertook a multidimensional assessment before and after the therapy plan. The visual and perceptual examination of vocal folds were compared pre- and post-therapy (Table 29). The vocal fold gap was reduced from a moderate to a minimal size gap, and at the end of therapy a maximal contralateral compensation was observed on the non-injured vocal fold.

Regarding audio-perceptual evaluation there was an improvement in the grade, roughness breathiness and strain parameters after voice therapy. Harshness, asthenia and instability parameters maintained the same values pre- and post-therapy. In general, audio-perceptual voice quality improved to a slight disturbance (Table 29).

Concerning the aerodynamic measures, there was a mild improvement after voice therapy on the average MPT/a/, MPT/s/, and MPT/z/ (Table 29), without reaching normal values (>25 sec). Concerning the s/z ratio, there was a slight decrease, which is considered in the pathologic range (<0.8 sec).

With respect to acoustic assessment (Table 29), the patient exhibited an improvement in all parameters after therapy and the values indicate a healthy voice according to PRAAT program thresholds ( $f_0$  85-195Hz; Jitter  $\leq$  1.04%; Shimmer  $\leq$  3,810%; HNR  $\geq$  7dB) (Boersma, 2011).

For self-perception of the voice impairment, the patient exhibited considerable improvement after therapy in all three dimensions (physical, functional, and emotional parameters), and therefore, the total VHI score (Table 29). Before therapy the patient felt that his voice impairment had a low impact on his quality of life, and after completing treatment there was no negative impact.

**Table 29 - Summary of the multidimensional assessment before and after treatment**

<b>Visual Perceptual</b>	<b>Pre-therapy</b>	<b>Post-therapy</b>
Glottal Gap & Degree of contralateral compensation	Moderate Glottal gap Minimal contralateral compensation	Minimal Glottal gap Maximum contralateral compensation
<b>Audio perceptual</b>	<b>Pre-therapy</b>	<b>Post-therapy</b>
Grade	2.0	1.0
Roughness	2.0	1.5
Breathiness	2.5	1.0
Asthenia	0.0	0.0
Strain	1.5	0.0
Harshness	1.5	1.5
Instability	1.5	1.5
<b>Maximum Phonation Time</b>	<b>Pre-therapy</b>	<b>Post-therapy</b>
MPT/a/	18.28	19.83
MPT/s/	16.72	16.99
MPT/z/	21.73	23.05
S/Z Ratio	0.76	0.73
<b>Acoustic</b>	<b>Pre-therapy</b>	<b>Post-therapy</b>
$f_0$ (SD), Hz	94.043 (2.152)	140.101 (1.669)
Jitter, %	1.855	0.298
Shimmer, %	1.801	2.571
HNR, dB	6.384	12.212
<b>Voice Handicap Index</b>	<b>Pre-therapy</b>	<b>Post-therapy</b>
Functional	5	2
Organic	12	3
Emotional	4	0
VHI Total	21	5

### v. Follow-up

A telephone follow-up was performed six-months after the patient completed the voice therapy program, and a group of questions was made to address the following areas: vocal abilities, voice quality and social situations - Does your voice sound very deviant (e.g., breathy or rough)? Do you encounter problems holding a conversation or socializing due to your voice? Do you encounter problems shouting? Do you have to strain to produce voice?

The patient reported that, at school, he is working full-time and able to deliver all the lectures without requiring an assistant. He also mentioned that his social life had improved remarkably because he enjoyed singing (with an audible and more endurance voice) along with his friends again. In summary, he felt that his voice was clear most of the time, with occasional dysphonia episodes when he misused or abused his voice for

longer periods. Overall, he had a better vocal self-control and self-perception of his voice quality.

#### **7.4 Discussion**

In this case report, a multidimensional approach was used to evaluate the voice impairment, which is in line with many studies in the research literature (Barcelos et al., 2017; Busto-Crespo et al., 2016; El-Banna & Youssef, 2014). About visual-perceptual assessment a subjective description was used to define the glottal changes. This practice is similar to other studies (Busto-Crespo et al. 2016; Cantarella et al. 2010; Kao et al. 2017; F Mattioli et al. 2015; Francesco Mattioli et al. 2011; Lucchini et al. 2018) where no standard protocol was followed to document the observed glottal changes.

In this case report, although voice therapy was started eight months after the onset of symptoms, there was an improvement in the parameters of grade, roughness, breathiness, and strain. Comparable results were found in the 'on land' studies of D'Alatri et al (D'Alatri et al., 2008) and Schindler et al (Schindler et al., 2008) in the group of patients that received therapy after six months of symptoms.

Concerning the aerodynamic evaluation assessment, the results of this case report were by most studies where improved MPT/s/ were observed after voice therapy (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; Kao et al., 2017b; Lucchini et al., 2018; F Mattioli et al., 2015b; Francesco Mattioli et al., 2011; Vij et al., 2017b).

In the acoustic voice analysis, the parameters chosen were the most frequent acoustic parameters used in the literature and included fundamental frequency ( $f_0$ ), shimmer (%), jitter (%) and noise-harmonic-ratio (NHR, dB) (Barcelos et al., 2017; Busto-Crespo et al., 2016; Cantarella et al., 2010; Kao et al., 2017b; Lucchini et al., 2018; F Mattioli et al., 2015b; Francesco Mattioli et al., 2011; Vij et al., 2017b). In this case, all parameters improved after therapy and this was in accordance with multiple studies results (Busto-Crespo et al., 2016; F Mattioli et al., 2015a; Francesco Mattioli et al., 2011; Vij et al., 2017b).

And finally, the patient's self-assessment of the impact of the unilateral VFP on his QoL was assessed. Even though, the level of impact was mild before therapy, it was reduced

after therapy. This result is also in accordance with all studies included in the systematic review and meta-analysis on the efficacy of unilateral VFP by Alegria et al (Rita Alegria et al., 2020a).

The main aim of this case report was to describe a voice therapy program performed on a patient with unilateral VFP in a water-base setting. According to Gaines (1998), an aquatic setting is a appealing environment, which motivates one to accomplish exercises since it is stimulating and fun, and turns up as a pleasant and comfortable experience (Gaines, 1998). In this case, before enrolling with this speech therapy program, the patient had a brief experience of land-based voice therapy, which he dropped out of because he found them ‘boring and not engaging ‘. In the Portone-Maira et al (2011) study, 120 out of 197 patients (60%) who had dysphonia (paralysis) and were referred for voice therapy by an Otorhinolaryngologist dropped out of treatment (Portone-Maira et al., 2011). In our case study, the patient enjoyed the aquatic setting and was always motivated to attend the sessions.

Combining an aquatic environment with voice therapy has some advantages for breathing and phonation. Kucher et al (2015) mentioned that an aquatic setting presents as a unique therapeutic environment, allowing for certain activities not normally achieved in land-based settings (Kucher et al., 2015). This therapy gives visual, hearing, and perception stimuli. It also improves abdominal breathing support and phonation, facilitates better posture balance, and a range of positive mind effects (Schultz, 2013). The correct postural alignment of the body promoted by the thermodynamic and buoyancy properties of the water, together with the proprioceptive feedback caused by the pressure of the water against the chest, support the respiratory effort and contraction of abdominal muscles in controlling exhaled airflow and consequently supra-glottic pressure. This correlation between body posture, abdominal muscle tone, and breathing support will enhance, control, and stabilize voice projection (Ruoti et al., 2000). In this case report, water was usually maintained above 33°C, and the duration of each session was 45 minutes, and it is in accordance with Kucher et al (2015) study (Kucher et al., 2015). The benefits of warm water were evident in helping the patient to get the right posture for the exercises. On the other hand, the water temperature had an inverse correlation with the related viscosity, meaning that temperature can be adjusted to alter viscosity: warmer water makes it less viscous, which leads to less resistance (Wittmer & Maki, 2013). To take advantage of this water property, the last three sessions of the water-based therapy were

delivered in a pool with lower water temperature (30°C) to promote further muscle strength by using greater resistance to motion.

The hydrostatic pressure of water at shoulder-deep level provides resistance, strengthening the diaphragm, an important muscle that supports breathing and, therefore, facilitates phonation. Water can give more support to the trunk, head, and neck, offering better positioning for the jaw and tongue. In this case, when the patient's body was submerged (below shoulder level), the hydrostatic pressure of the water strengthened the inhalation breathing muscles and assisted the exhalation movements, and therefore voice projection (Styer-Acevedo, 2004).

### **7.5 Limitations**

There are limitations inherent to any case report. The validity of the results depends on the accuracy and availability of data records. There is a lack of ability to generalize the results and to establish a cause-effect relationship. Results should be interpreted cautiously as there is a high risk of results and selection bias. To enhance robustness of the results, a randomized study with comparison groups is required to determine treatment effects and generalizability to the unilateral VFP population. The development of a protocol for use across studies would decrease the potential of bias, allow estimation of similarities among studies, and enhance the quality of evidence for the treatment of unilateral VFP treatment.

Regarding the auditory-perceptual voice results, only one speech therapist language was used for rating, increasing the risk of bias. Further research is also needed to compare water and land-based interventions on voice in patients with unilateral VFP.

### **7.6 Conclusion**

The findings from this case report suggested that an individualized water-based therapy program changed some assessed voice parameters.

Even though the voice outcome measures were improved in some parameters after therapy in this case report, including the self-perception of the voice impairment, it is impossible to determine whether the outcomes derived from the voice therapy in a water-based setting. Further studies with an increased population size are needed to draw any realistic and permanent conclusions.

## Chapter VIII - Discussion

When the author decided to embark upon this research, she was presented with two major challenges: the availability and quality of published literature to support the research and the recruitment of patients to be treated in the pool instead of a land-based (traditional) therapy.

Chapters II, III and IV constituted the theoretical framework that underpinned the key concepts of this research study and was based on two literature reviews and one meta-analysis.

In **Chapter II**, the systematic review aimed to identify, evaluate, and summarize the findings of all relevant studies over the efficacy of voice treatment on the vocal fold motility in adult patients with UVFP. The meta-analysis of the visual-perceptual outcome measures of the 10 eligible studies provided a more reliable and with an increased accuracy of the estimated effect of voice therapy on this group of patients. The vocal fold motility improved in 72% of all patients after voice therapy intervention and a positive effect of therapy was considered as any improvement observed in the glottal incompetence, regardless of how this was rated in the studies. The absence of a worldwide consensus protocol for glottal examination limits comparison among studies and weakens quality of evidence of impact of voice therapy in patients with UVFP. Moreover, therapy effect could not be linked to any specific voice program due to its clinical diversity across the studies. A broader information search strategy could have been adopted through searching in more electronic databases, narrower time intervals, and using a full text rather than only the title and abstract for study selection. Because of the low level of evidence (III and IV) of the included studies and the small sample size, the likelihood of study variability was increased adversely impacting the validity and credence of the study conclusions. This systematic review is intended to be reproduced in the future so comparisons can be made.

In **Chapter III**, the systematic search and narrative review of the effectiveness of voice therapy interventions in adults with VFNs aimed to create a summary of the current knowledge that can contribute to evidence-based practice. The paucity of articles in the literature about this subject is important to note and the ones available to be analyzed had

low levels of evidence ( $\leq$  III-2) and the comparative studies had a moderate risk of bias. Therefore, it is without surprise that there is insufficient evidence in the literature review to conclude the effectiveness of voice therapy in patients with VFNs, even though most voice dimensions outcome measurements across the included studies improved after therapy. There is a clear need for better quality studies that should incorporate bigger sample size, experimental and intervention control groups to rule out placebo effect of voice exercises or techniques, long-term follow-up evaluations and adherence to voice exercise routines after ending therapy. This systematic review is also expected to be replicated in the future to assess the progress on the quality of level of evidence of the studies.

In **Chapter IV**, the meta-analysis of the acoustic voice parameters in patients with bilateral vocal fold nodules aimed to determine whether there was an effect on the vocal quality after voice therapy. The pooled statistical analysis comparing pre- and post-therapy measurements of three acoustic voice parameters (average  $f_0$ , % jitter and % shimmer) showed a statistically significant effect in the first two acoustic parameters after voice therapy but not in the shimmer. The main indications for utilization of voice acoustic analysis in clinical practice usually include assessment of effectiveness of different therapeutic options, monitoring progress of ongoing course of therapy and diagnostic aid. Nevertheless, the inability of using acoustic measurements to provide noninvasive quantitative indices to help differentiate among laryngeal pathologies have narrowed its clinical utility. This meta-analysis is intended to be used as an example for future meta-analysis to estimate the effect of voice therapy in other voice dimension outcomes.

After the in-depth theoretical research, two retrospective studies (Chapter V and VI) were undertaken to assess and review the clinical practice of the Speech Therapy Department of one of the main hospitals in Porto and of the author's private practice, in UVFP and VFNs respectively. The study presented in Chapter VI was fundamental because it looked back at the author's clinical practice on delivering voice therapy in an aquatic setting, which gave a preliminary indication that water-based voice therapy could have an improved outcomes when comparing with land-based therapy.

In **Chapter V**, the retrospective study of patients with unilateral vocal fold paralysis was important to assess the practice of a Speech Therapy Department in a tertiary hospital in

the north of Portugal. The sample of study had a reasonable size (n=132) and most patients developed UVFP after surgery (mainly thyroid) and some had idiopathic etiology, and their voices were assessed in multi-dimensions outcomes before and after voice therapy intervention. In this study, voice therapy efficacy was 82.3%, which is slightly higher than the 72.0% reported in the 2020 meta-analysis of visual-perceptual outcome measures after voice therapy intervention in UVFP. Furthermore, the findings seemed to be depended on the initial position of the vocal fold, etiology of vocal paralysis and timing to initial therapy. Lateral vocal fold position before treatment may predict a worse response to therapy and an idiopathic etiology and early intervention after onset of symptoms may anticipate a better recovery. It would have been interesting if this study had included voice acoustic parameters as well as follow-up of the patients.

In **Chapter VI**, is one of the most important studies in this thesis because it is to the best of our knowledge the first voice-related study in a water-based setting. The findings of this retrospective study of 17 patients with VFNs who had voice therapy in an aquatic setting are comparable with similar studies where voice therapy was delivered on traditional setting. Vocal fold nodules disappeared in 82.3% of patients after therapy and late initiation of voice treatment after onset of symptoms carried a worse prognosis in terms of recovery. An important limitation of this study was the small sample size therefore care should be given when interpreting results and avoid the risk of overestimating the outcome effects. Future studies should include increase sample size, more objective voice measurements (acoustic or aerodynamic analysis) and subjective voice self-perception questionnaires to improve the validity and quality of the voice therapy results.

Finally, in **Chapter VII**, the study case report aimed to provide information on clinical practice of delivering voice therapy to a patient with UVFP in an aquatic setting. The main purpose of this case report was to outline a voice therapy program by describing the inter-connections between the voice therapy objectives, the water-based therapy goals and the water-based exercises and water characteristics. There was a positive change in the patient's voice outcome measures after completion of treatment (visual perceptual, audio-perceptual, acoustic and self-perception) and at a six-month follow-up assessment, patient reported a return to its almost normal professional and social voice use. Further studies with larger samples are needed to draw any realistic conclusions on the efficacy of water-based voice therapy in patients with UVFP.

## Chapter IX - Conclusion

The major conclusions of this thesis are as follows:

- There is evidence that voice therapy has a significant positive effect on the glottal gap closure in patients with UVFP, irrespective of the technique of direct voice therapy.
- Voice therapy is potentially an effective treatment choice for patients with VFNs, despite the fact that a variety of therapy techniques/exercises were used across the selected studies. There is a paucity in articles about this topic and more further studies with less bias and a better methodological design are required.
- Patients with VFNs improved their acoustic voice parameters after receiving voice therapy. There was a combined positive effect on the disturbance periodicity measures (jitter (%) and shimmer (%)) - reduced mean value, and on the pitch range measure ( $f_0$ ) increased mean value, with statistical significance difference.
- Evidence suggested that speech therapy intervention is effective to improve some voice parameters in patients with unilateral vocal fold paralysis, especially if started early after the onset of vocal symptoms.
- A voice therapy delivered in a water-based environment may be a valid and effective way to treat patients with VFNs. Timing to initiate voice therapy after onset of symptoms/diagnosis seemed to be a significant factor for the success of voice therapy.
- The findings from the case report suggested that an individualized water-based therapy program changed some voice assessed parameters. At six-month follow-up assessment, patient reported a return to its almost normal – professional and social – voice use.
- More research is needed to show possible benefits of water-based speech therapy for voice pathology, particularly in terms of impact of the water characteristics in patients' physiology and motivation for therapy.

## **9.1 Recommendations for Future Work**

Recommendations for future studies include case-series of patients with UVFP and VFNs treated with speech therapy in a water-based setting. Results should be based on multi-dimensional voice assessments and voice outcome measures should be compared before and after therapy. Afterwards, develop better-designed observational studies such as cohort and case-control studies to assess associations between speech therapy in a water-based setting in both vocal conditions. In addition, an appropriate sample size is fundamental to draw precise and accurate conclusions from future studies.

Therefore, future investigation to study the effects of voice therapy in a water-based environment would require a mixed method research study. By joining the benefits of quantitative and qualitative approaches, a more comprehensive understanding of the impact of water-based speech therapy in vocal pathologies would be achieved. On one hand, a qualitative approach by gathering data through patients' interviews before and after therapy would explore the patients' views, perceptions, and attitudes towards acceptance and benefit of a water-based speech therapy. On the other hand, a quantitative approach by using large, detailed sample sizes, gather data from multidimensional voice assessments and protocol-based voice programme (exercises) would objectively explain to what extent water-based therapy improve voice outcomes measures.

The scope of speech therapy given in a water-based setting can go beyond vocal pathologies, such as in people that pursue better voice quality or performance (e.g., singers, teachers).

Finally, speech therapy in a water-based therapy is not known to the Portuguese speech therapy community, therefore, an awareness campaign is recommended by lecturing in courses and seminars.

## Chapter X - References

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**Appendix I - Hospital Board of Directors and the University Research Ethics  
Committees**

Exma. Sra. Dra. Rita Alegria  
Rua Calouste Gulbenkian 53 P4H5  
4050-145 Porto

**ASSUNTO:** Trabalho Académico - Doutoramento - "Reabilitação vocal e meio aquático: estudo longitudinal" – N/ REF.º 2019.078(066-DEFI/067-CE)

O Conselho de Administração do CHUP autoriza a realização do estudo acima mencionado, a realizar no Serviço de ORL desta Instituição e tendo como Investigador Principal a Dra. Rita Alegria, estudante da Universidade Fernando Pessoa - Faculdade de Ciências da Saúde.

O estudo foi previamente analisado pela Comissão de Ética CHUP|ICBAS, pelo Serviço de Investigação Clínica, pela Direção do Departamento de Ensino, Formação e Investigação do CHUP e pelo Presidente do Conselho de Administração, tendo obtido parecer favorável.

Cumprimentos,

CONSELHO DE ADMINISTRAÇÃO  
3/7/2019

Jr. PAULO BARBOSA	Dr.ª ÉLIA GOMES
Presidente	Vogal Executiva
Prof. Doutor JOSÉ BARROS	Dr.ª RITA ANDREIRA
Deputado	Vogal Executiva
Enf.ª EDUARDO ALVES	
Enf.ª Gestor	

\* Em todas as eventuais comunicações posteriores sobre este estudo é indispensável indicar a nossa ref.º.

**Appendix II - Fernando Pessoa Research Ethics Committee**



Universidade Fernando Pessoa  
www.ufp.pt

Exma. Senhora  
Prof. Doutora Sandra Gavinha  
Diretora da FCS

Nº	Data
FCS/PLS – 74/20	25 de Junho de 2020

Exma. Senhora Prof. Doutora,

A Comissão de Ética, depois de apreciar o projeto de doutoramento em Desenvolvimento e Perturbações da Linguagem de Rita Alegria, intitulado "Terapia da Fala em meio aquático nos profissionais de voz: estudo retrospectivo", considera nada haver a opor ao mesmo.

Com os melhores cumprimentos.

A Presidente da  
Comissão de Ética da UFP

  
Teresa Toldy

*Autenticação*



Fundação Frelino e Cultura "Fernando Pessoa"

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