IS EARLY INITIATION OF VOICE THERAPY AFTER MICRO LARYNGEAL SURGERY BENEFICIAL?

A RANDOMIZED CONTROL TRIAL.

Dissertation submitted in partial fulfilment of the requirement for the M.S. Branch IV (Otorhinolaryngology) Examination of The Tamil Nadu Dr. M.G.R Medical University to be held in May 2019

DEPARTMENT OF OTORHINOLARYNGOLOGY

CHRISTIAN MEDICAL COLLEGE VELLORE

CERTIFICATE

I declare that this dissertation entitled "***Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial.***" submitted towards partial fulfillment of the requirements of the Tamil Nadu Dr. M.G.R. Medical University for the MS Branch IV, Otorhinolaryngology examination to be conducted in May 2019, is the bonafide work done by me, and due acknowledgements have been made in text to all materials used.

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DEPARTMENT OF OTORHINOLARYNGOLOGY

CHRISTIAN MEDICAL COLLEGE VELLORE

CERTIFICATE

This is to certify that the dissertation entitled "***Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial***" is a bonafide original work of **Dr. Titus Raju** , submitted in partial fulfillment of the rules and regulations for the M S Branch IV, Otorhinolaryngology examination of The Tamil Nadu Dr. M.G.R. Medical University to be held in May, 2019.

Dr. Anna B. Pulimood	**Dr. Rita Ruby Anbuselvi Albert**
Principal,	Professor and Head,
Christian Medical College,	Department of ENT,
Vellore.	Christian Medical College, Vellore.

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.

Dr. Suma Susan Mathews,

Professor and Guide,

Department of ENT,

Christian Medical College, Vellore

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I wish to express my heartfelt gratitude to my guide and mentor in ENT, Dr. Suma Susan Mathews, Professor of Unit 5, Department of ENT, Christian Medical College, Vellore for lending her wisdom, expert guidance and encouragement in conducting this study and preparing this dissertation.

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I also thank my co-guides Dr. Roshna Rose Paul, Dr. Philip George, Dr. Antonisamy and Mr R Thejesh for their help in collecting and analysing the data.

I am also extremely thankful to all my friends and colleagues, from the Department of ENT and the OPD and Ward nursing staff for helping me in collecting the cases and for their help in this study.

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I would like to thank the Fluid Research Committee, CMC Hospital for granting me permission for conducting this study and for the financial assistance.

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I am forever grateful to Lord Almighty for all the above mentioned people and for all the blessings that he has showered on me.

I am grateful to all the patients who participated in the study who took the effort to comply to the advices given regarding the intervention and the follow up.

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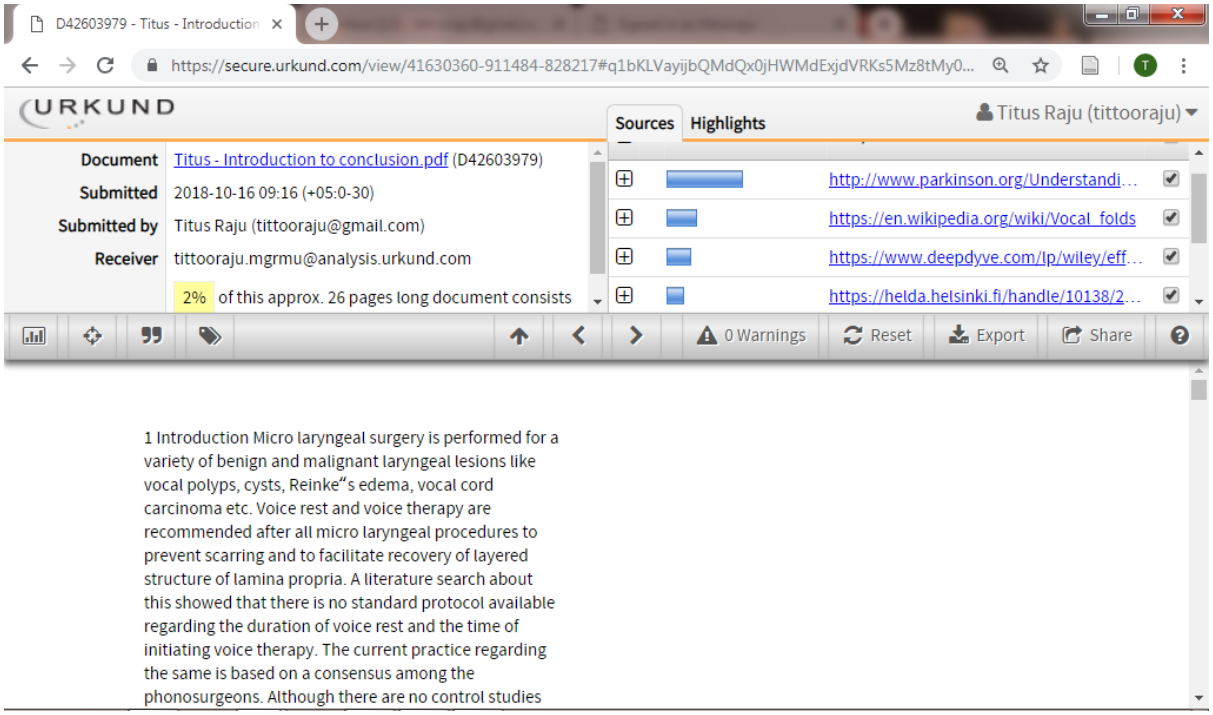

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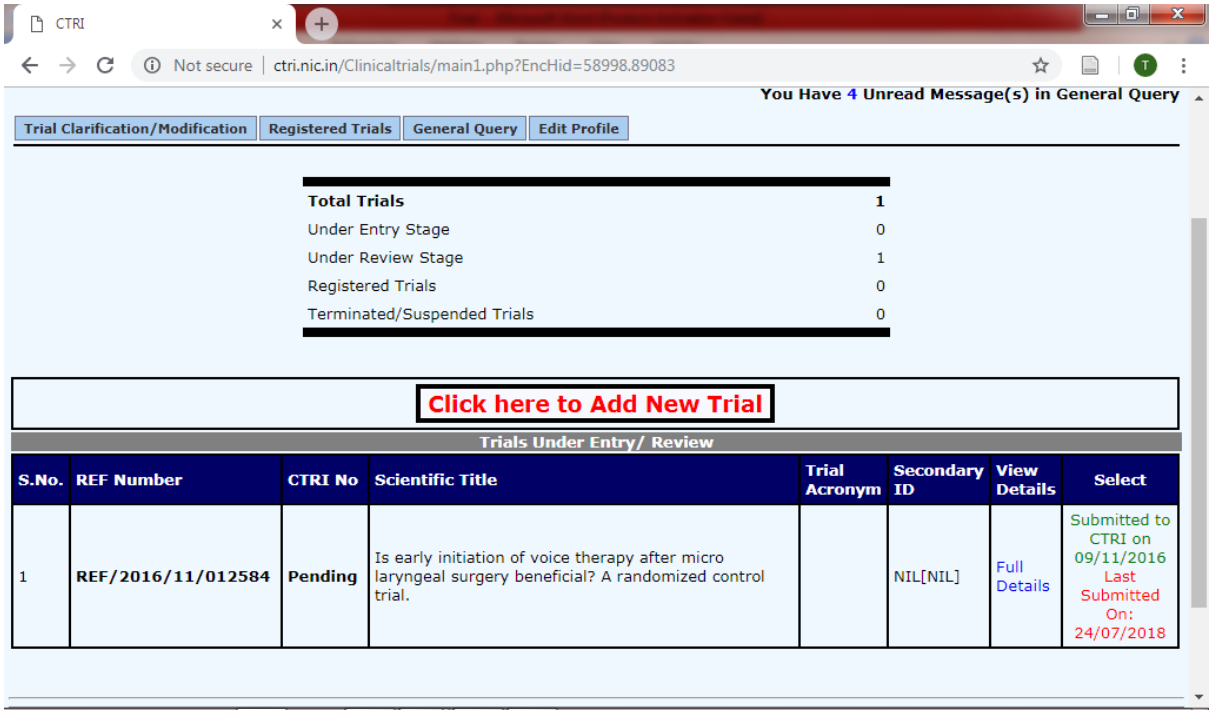

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January 03, 2017,

Dr. Titus Raju,
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Sub: **Fluid Research Grant:**
Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial.
Dr. Titus Raju, Employment Number: 21113, Dr. Suma Susan Mathews, Employment Number: 14423, Professor, Dr. Rita Ruby Anbuselvi Albert, Professor & HOD, Emp No: 10817, Dr. Roshna Rose Paul, Assistant Professor, Emp No: 28660, Dr. Philip George, Senior Resident, Emp No: 32676 , Department of ENT Unit 5, Mr. R Thejesh, Speech-language pathologist and Audiologist, Emp No: 33930, Dr. Antonisamy, Professor, Department of Biostatistics.

Ref: IRB Min No: 10328 [INTERVEN] dated 19.10.2016

Dear Dr. Titus Raju,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY - (ETHICS COMMITTEE)
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Christian Medical College, Vellore - 632 002.

Cc: Dr. Suma Susan Mathews, Dept. of ENT, CMC, Vellore

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Dear Dr. Titus Raju,

The Institutional Review Board (**Silver**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial" on October 19th 2016.

The Committee reviewed the following documents

1. IRB Application form
2. CV of Drs. Antonisamy, Philip George, Ramanathan, Rita Ruby, Roshna, Suma Susan and Raju Titus.
3. Patient Information Sheets and Consent Forms.
4. Permission Letter
5. Proforma
6. No. of documents 1-5

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Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

The following Institutional Review Board (**Silver**, Research & Ethics Committee) members were present at the meeting held on October 19th 2016 in the BRTC Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Affiliation
Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB, Chennai	External, Clinician
Dr. Vinod Joseph Abraham	MBBS, MD, MPH	Professor, Community Medicine, CMC, Vellore	Internal, Clinician
Dr. Suceena Alexander	MBBS, MD, DM	Associate Professor, Nephrology, CMC, Vellore	Internal, Clinician
Dr. Abhay Gahukamble	MS, D Ortho, DNB(Ortho)	Associate Professor, Paediatric Orthopaedics, CMC, Vellore	Internal, Clinician
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Rev. Dr. T. Arul Dhas	MSc, BD, DPC, PhD(Edin)	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Dr. Ashish Goel	MBBS, MD, DM	Professor, Hepatology, CMC, Vellore	Internal, Clinician
Dr. Denise H. Fleming	BSc (Hons), PhD	Honorary Professor, Clinical Pharmacology, CMC, Vellore	Internal, Scientist & Pharmacologist
Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB	External, Lay Person & Social Scientist
Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore	External, Clinician

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Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Shirley David	MSc, PhD	Professor, Head of Fundamentals Nursing Department, College of Nursing, CMC, Vellore	Internal, Nurse
Dr. Vinitha Ravindran	PhD (Nursing)	Professor & Addl. Deputy Dean, College of Nursing, CMC, Vellore	Internal, Nurse
Mrs. Ruma Nayak	M Sc (Nursing)	Professor, Head of Paediatric Nursing & Deputy Nursing Superintendent, College of Nursing, CMC, Vellore	Internal, Nurse
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Dr. Thambu David	MBBS, MD, DNB	Professor, Medicine, CMC, Vellore	Internal, Clinician
Dr. Jiji Elizabeth Mathews	MBBS, MD, DGO	Professor, Head of OG unit - 5, CMC, Vellore.	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

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Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 91,000/- INR (Rupees Ninety one thousand Only) will be granted for 18 months.

Yours sincerely

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
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CONTENTS

Introduction

Micro laryngeal surgery is performed for a variety of benign and malignant laryngeal lesions like vocal polyps, cysts, Reinke's edema, vocal cord carcinoma etc.

Voice rest and voice therapy are recommended after all micro laryngeal procedures to prevent scarring and to facilitate recovery of layered structure of lamina propria. A literature search about this showed that there is no standard protocol available regarding the duration of voice rest and the time of initiating voice therapy. The current practice regarding the same is based on a consensus among the phonosurgeons. Although there are no control studies looking at the role of voice rest in recurrence and healing, it is a generally accepted that 48 hours of absolute voice rest following a phonosurgical procedure is essential (1)

According to the guidelines given by Robert W. Bastian (2) there should be a period of absolute voice rest for 4 days after micro laryngeal surgery and on the 5th day, voice therapy need to be initiated under the supervision of a trained speech pathologist. Cho et al (3) concluded in their study on canine model that voice rest helps in re epithelialization and recommended voice rest of 2 weeks and vocal hygiene of 8 weeks following phonosurgery. A survey by the American Academy of Otolaryngology indicated that most otolaryngologists preferred a 7 day voice rest after surgery, however there was no evidence to back up this practice (4). There are very few RCTs comparing various voice rest protocols.

A recent study from Japan by Kaneko et al (5) concluded that 3 days of voice rest followed by voice therapy may lead to better wound healing of the vocal fold

compared to 7 days of voice rest and that appropriate mechanical stimulation during early stages of vocal fold wound healing may lead to favorable functional recovery.

In our institution the duration of voice rest advised varies from surgeon to surgeon and it range from 2 days to 2 weeks.

It has also been shown that there is only 35% compliance on the prescribed voice rest in patients even after proper counselling by a trained speech pathologist (6).

The current study proposed evaluation of the voice outcome after two different postoperative management protocols namely 2 day voice rest followed by voice therapy and 5 day voice rest followed by voice therapy in patients undergoing micro laryngeal surgery.

Aims and Objectives

Aim:

To study if early initiation of voice therapy after micro laryngeal surgery produces a better voice outcome in patients with benign vocal cord lesions

Objectives

1. To compare the voice outcome in patients undertaking two day voice rest followed by voice therapy and five day voice rest followed by voice therapy after micro laryngeal surgery for benign laryngeal pathologies

2. To compare the return of normal mucosal wave function in patients undertaking two day voice rest followed by voice therapy and five day voice rest followed by voice therapy after micro laryngeal surgery for benign laryngeal pathologies

3. To evaluate the compliance of patients in adhering to the instructions regarding voice rest after micro laryngeal surgery**.**

Review of Literature

Anatomy

Larynx is a structure suspended from the hyoid bone, supported by a fibrocartilaginous framework and lined by mucosa. The primary purpose of the larynx is to act as a sphincter. It is designed to protect the distal airway from ingested material and saliva, to regulate airflow into and out of the airway as well as maintain airway patency. Also the larynx functions in voice production. The laryngeal cartilages not only provide structural support for the larynx but also move relative to one another to control vocal fold position, length, and tension.

Embryology

Larynx develops from the midline ventral respiratory diverticulum of the foregut which is called as laryngotracheal groove. This groove is seen behind the hypobranchial eminence. The part of the foregut dorsal to this groove develops into esophagus. The groove deepens and its edges fuse to form a partition or septum to separate the groove from the esophagus. The upper end of the groove remains open as it develops to communicate to the pharynx. The lower end deepens and divides into two branches and develops into the bronchi. The part of this tube above the division forms the trachea and the uppermost part of the tube forms the larynx.

Epiglottis is developed from the hypobranchial eminence in its posterior most part. The thyroid cartilage is formed from the fourth arch cartilage. The other cartilages of larynx and the trachea are formed from the 5^{th} and 6^{th} arch cartilage. Nerve of the fourth arch is superior laryngeal nerve and the nerve of the 6^{th} arch is the recurrent laryngeal nerve(7).

Cartilages of the larynx

The thyroid cartilage is shaped like a shield with a right and left lamina and fused in the midline forming an angle of 90° degree in males and 120 degrees in females. It is covered by a thick perichondrium on its outer surface and a thin layer of perichondrium on the inner surface.

The cricoid cartilage sits inside the posterior aspect of the thyroid cartilage. The cricothyroid joint is a synovial joint. It allows the thyroid cartilage to rotate forward and backward on the attachment to the cricoid cartilage. The cricoid cartilage is shaped like a signet ring with the wide lamina located posteriorly and a thin arch anteriorly. The thyroid and cricoid cartilages are connected anteriorly by the cricothyroid membrane, the thickened anterior part of which is called cricothyroid ligament.

Sitting on the superior surface of the posterior cricoid lamina are the paired arytenoid cartilages. The arytenoid cartilages are pyramidal in shape with the vocal processes located anteriorly and the muscular processes located laterally.

The vocal ligament of the vocal folds attaches to the vocal processes of the arytenoids cartilages. The arytenoid cartilages articulate with the cricoid cartilage through a joint

that allows the arytenoids to both swivel and slide relative to the cricoid cartilage. Their movement is responsible for adduction and abduction of the vocal folds.

Finally, the epiglottis is a leaf-shaped, elastic cartilage that is attached to the inner surface of the thyroid cartilage just above the anterior attachment of the vocal folds. This attachment is known as the petiole or thyroepiglottic ligament. The epiglottis flips down to cover the entry to the larynx during swallowing.

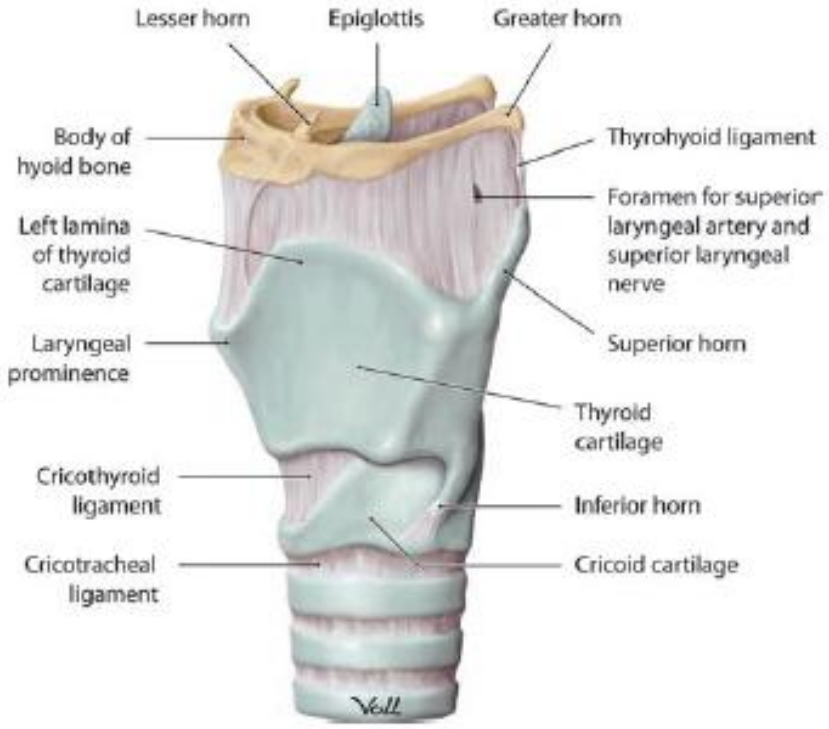


Fig 1: Anatomy of larynx (adapted from Laryngeal Evaluation – Kendall and Leonard)

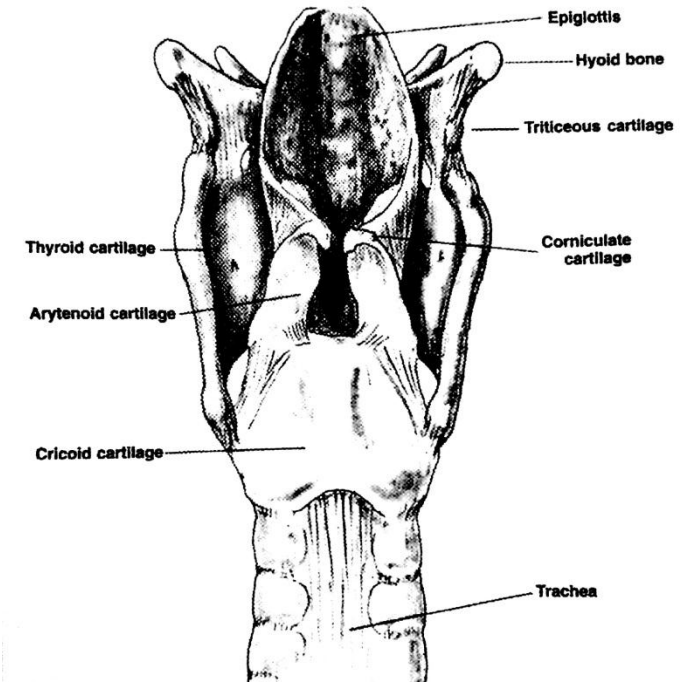


Figure 2: Posterior view of larynx (adapted from Laryngeal Evaluation – Kendall and Leonard)

Ligaments of the larynx

The quadrangular membrane extends from the lateral edge of the epiglottis to the arytenoid cartilage on either sides of the larynx. The superior free border corresponds to the aryepiglottic folds and the inferior free border corresponds to the false cords or ventricular folds. These superior and inferior borders of the membrane are thickened to form the aryepiglottic ligament and the vestibular ligament.

The Conus Elasticus and the Vocal Ligament

The true vocal folds contain connective tissue known as the vocal ligament. The vocal ligament is the superior margin of another sheet of connective tissue known as the conus elasticus. The conus elasticus is attached to the inner surface of the cricoid cartilage and fans superiorly and medially to provide shape and contour to the under

surface of the vocal folds. It runs deep to the epithelial covering of the vocal fold and superficial to the deep musculature of the larynx. The ligament makes up the deep layer of the lamina propria and is involved in the attachment of the thyroarytenoid muscle to the connective tissue, that is, the lamina propria.

Laryngeal musculature

The laryngeal muscles can be classified as:

- Intrinsic
- Extrinsic
- Accessory

Intrinsic muscles of larynx can again be divided based on their action on the glottis into

- Adductors
- Abductors
- Relaxers
- Tensors

The intrinsic laryngeal musculature attaches to the laryngeal cartilages, moving them relative to one another and thereby controlling the position, tension, and the length of the vocal folds.

The lateral cricoarytenoid muscle is the primary adductor of the vocal folds. The fibers of this muscle attach to the muscular process of the arytenoid cartilages and run anteriorly and inferiorly to insert in the superior aspect of the cricoid cartilage. Muscle contraction pulls the muscular process of the arytenoids cartilages forward (and slightly downward), which, in turn, rotates the vocal processes of the arytenoids cartilages medially, closing the vocal folds

Abduction of the vocal folds results from contraction of the posterior cricoarytenoid muscles. These muscles also attach to the muscular process of the arytenoid cartilages and then run posteriorly to fan out and insert near the midline on the posterior aspect of the cricoid lamina. Shortening of the posterior cricoarytenoid muscle fibers moves the muscular process of the arytenoid cartilages postero medially. This results in movement of the vocal processes laterally and abduction of the vocal folds.

The thyroarytenoid muscles attach to the anterior surface of the arytenoid cartilages and insert into the inner surface of the thyroid cartilage. They make up the "body" of the true vocal folds and are responsible for control of "tension" in the folds. In other words, contraction of these muscles results in greater resistance to airflow through the glottis during phonation allowing the build-up of subglottic pressure and subsequent increases in vibratory amplitude and vocal volume. These muscles are also likely involved in pitch regulation as their contraction may lead to "shortening" of the vocal fold length. The medial belly of the thyroarytenoid muscle is also known as the 'vocalis' muscle.

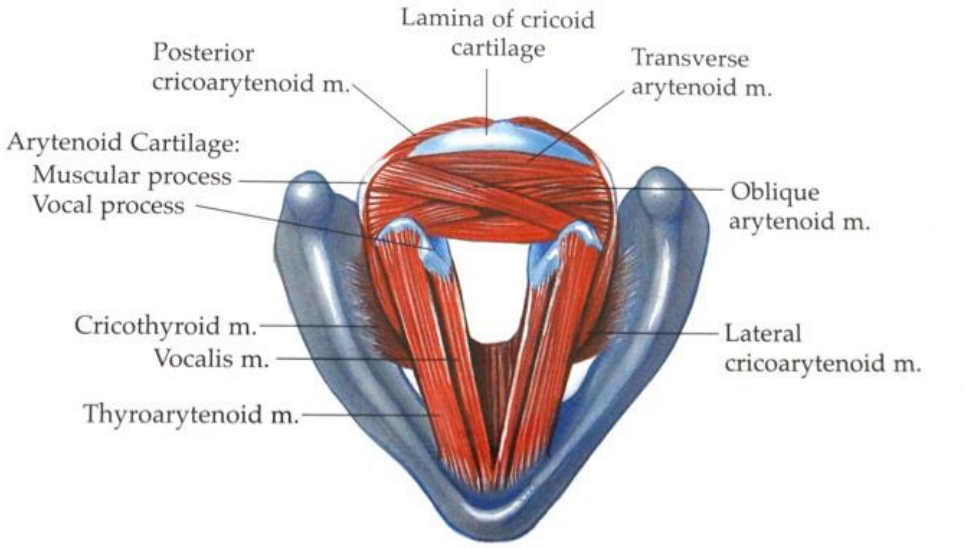


Figure 3: Intrinsic muscles of larynx (adapted from www.ohniww.org)

The muscles considered the most important in pitch regulation are the cricothyroid muscles. These muscles attach to the outer surface of the inferior margin of the thyroid cartilage and insert on the anterior and aspect of the cricoid cartilage. Contraction of the cricothyroid muscles causes the thyroid cartilage to rock forward on the cricoid cartilage. This movement increases the distance between the vocal processes of the arytenoid cartilages and the thyroid cartilage, lengthening and tensing the vocal folds. The interarytenoid muscles run between the arytenoid cartilages and help to close the posterior glottis during voicing. Contraction of the interarytenoid muscles approximates the arytenoid cartilages.

Function of laryngeal muscles on glottis					
	Cricothyroid	Vocalis	Lateral cricoarytenoid	Inter arytenoid	Posterior Cricoarytenoid
Position	Paramedian	Adducts the membraneous part	Adducts entire fold	Adducts cartilaginous part	Abduct
Level	Lower	Lower	Lower	--	Elevate
Length	Elongate	Shorten	Elongate	--	Elongate
Thickness	Thin	Thicken	Thin	Thicken	Thin
Edge	Sharpen	Round	Sharpen		Round
Cover	Stiffen	Slacken	Stiffen	Slacken	Stiffen
Transition	Stiffen	Slacken	Stiffen	Slacken	Stiffen
Body	Stiffen	Stiffen	Stiffen	Slacken	Stiffen

The sensory supply of the larynx is via the internal branch of the superior laryngeal nerve and the recurrent laryngeal nerve both of which are branches of the Vagus nerve. Internal laryngeal nerve supplies the area above the level of the glottis and the recurrent laryngeal nerve supplies the area below the glottis.

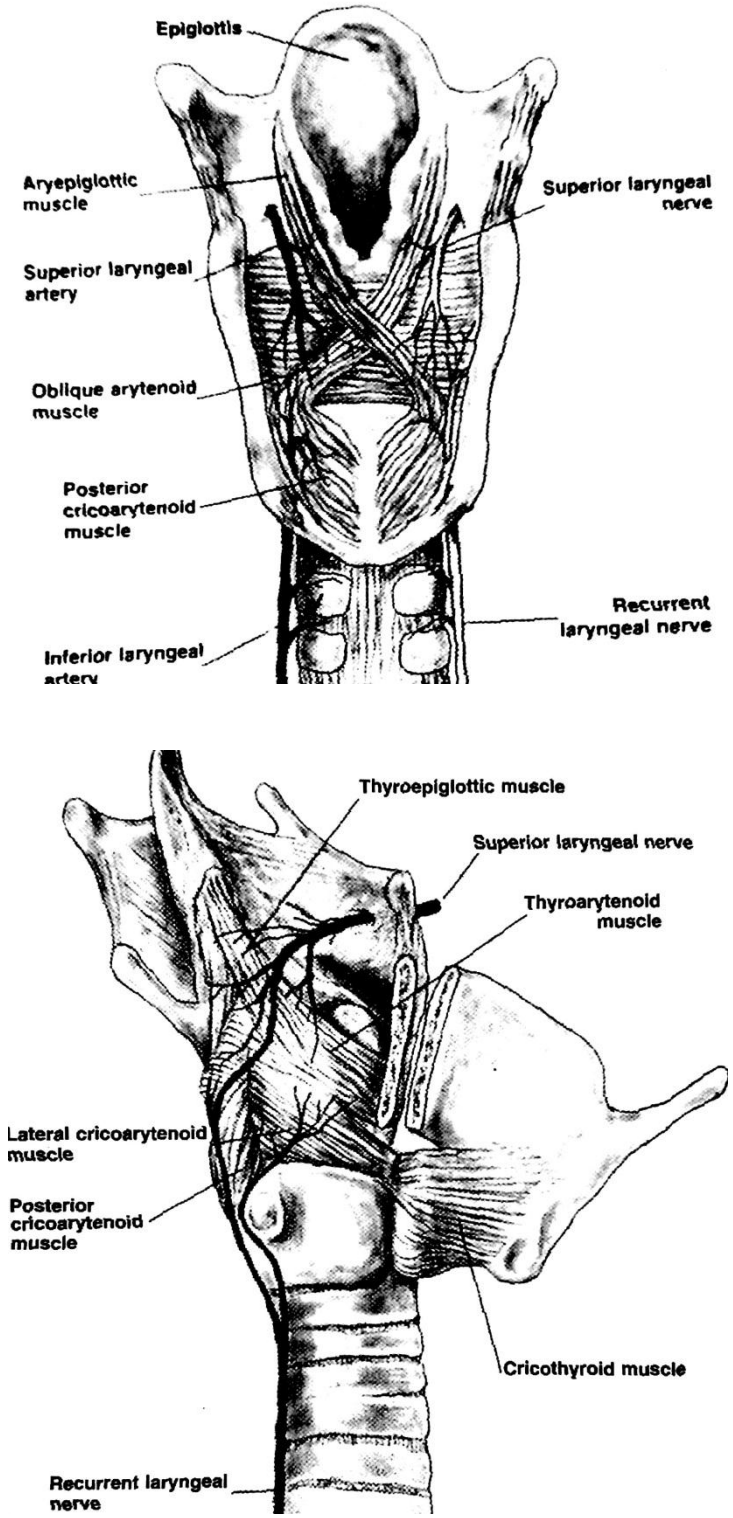


Fig 4,5: Nerve supply of larynx(8) (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

Anatomy of the glottic region

The opening between the vocal folds during abduction is referred to as the glottis or the glottic opening. The margin of the glottic opening created by the edges of the vocal folds is called the rima glottidis. The membranous portion of the vocal folds accounts for the anterior $3/5^{th}$ of the margin of the rima glottis, and the cartilaginous portion of the vocal folds makes up the posterior $2/5^{th}$ of the margin of the rima glottis(8). The membranous portion of the vocal folds is the portion of the vocal folds that vibrates during phonation and consists of the thyroarytenoid muscle and overlying lamina propria and epithelial covering. Healthy membranous vocal folds usually appear white in colour and glistening with moisture. The membranous portion of the vocal folds inserts anteriorly in the midline into the thyroid cartilage. This area is referred to as the anterior commissure. Posteriorly, the membranous portion of the vocal folds inserts into the vocal process of the arytenoid cartilage. The cartilaginous portion of the vocal folds is created by the medial surface of the arytenoid cartilage and the overlying mucosa. The interarytenoid portion of the rima glottis refers to the area between the arytenoid cartilages.

The length of adult human vocal folds are approximately 12 to24 mm and thickness is 3 to 5 mm(9). Infant vocal folds do not demonstrate a distinct layered structure(10).

Fig 6: Endoscopic appearance of Larynx

Vocal Fold Histology

The vocal fold consists of five histologic layers: epithelium; superficial, intermediate, and deep layers of the lamina propria; and the vocalis muscle. The surface epithelium contains stratified squamous cells devoid of mucous glands, unlike the pseudo-stratified ciliated, columnar epithelium found in the remaining respiratory tract. This modification allows the vocal fold to maintain shape and undulate freely over the underlying vocalis muscle.

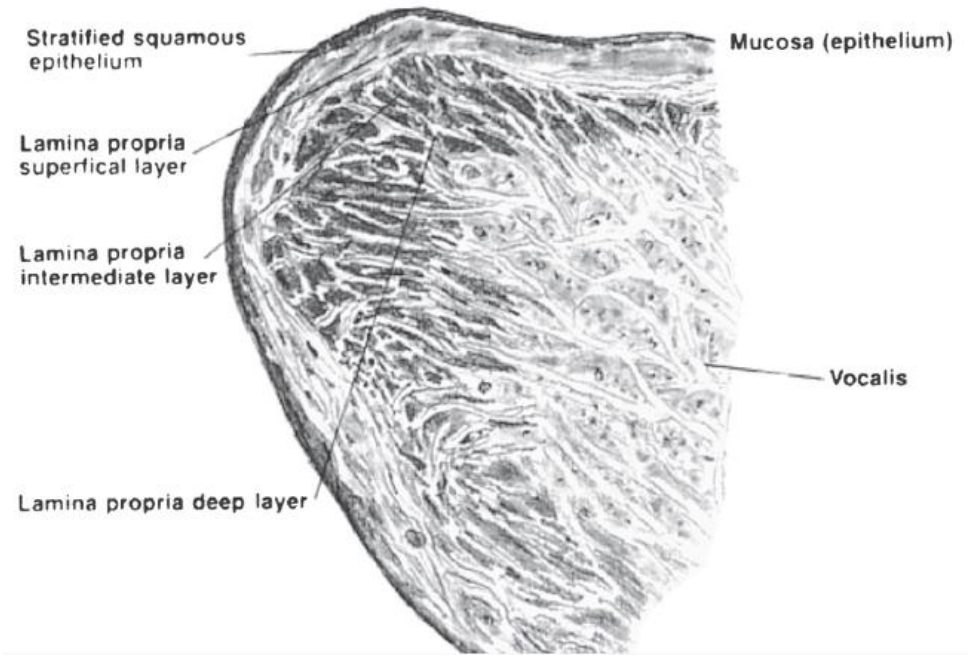


Fig 7: Layered ultrastructure of vocal fold (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

A complex basement membrane zone connects the epithelium of the vocal fold to the superficial lamina propria (SLP). The basement membrane zone contains a delicate network of proteins and collagen fibers that allow the epithelium to adhere to the gelatinous SLP.

The SLP is also known as Reinke's space and lies immediately deep to the surface epithelium. The SLP layer contains loose fibrous tissue and a network of hyaluronic acid, mucopolysaccharides, decorin, and other extracellular matrix (ECM) components. The SLP contains very few fibroblasts and is primarily devoid of both elastic and collagen fibers. It provides little resistance to vibration and is very flexible,

characteristics that are required for proper phonation to occur. Any change in the composition of the ECM can lead to a loss of vibratory function.

The intermediate layer of the lamina propria is similar to the SLP but contains higher amounts of collagen and mature elastin fibers arranged longitudinally. It is a highly hydrated structure, rich in fibrous and interstitial proteins as well as glycosaminoglycans and proteoglycans. The intermediate layer of the lamina propria also contains large quantities of hyaluronic acid that may act as a shock absorber.

The deep layer of the lamina propria is dense and contains the highest concentration of fibroblasts and collagen fibers. The properties of collagen limit its ability to stretch; therefore, the presence of this layer prohibits overextension of the vocal fold. The deep layer of the lamina propria is 1 to 2 mm thick. Together with the intermediate layer of the lamina propria, the deep layer forms the vocal ligament. The vocal ligament also forms the uppermost portion of the conus elasticus.

The deepest layer of the vocal fold consists of intrinsic laryngeal muscle, namely the vocalis muscle formed by the medial part of thyroarytenoid muscle.

Anteriorly, the intermediate layer of the lamina propria thickens to form an area called the anterior macula flava. This structure connects to the anterior commissure tendon, also known as Broyle's tendon, which provides a transition zone from the inner perichondrium of the thyroid cartilage. Similarly, posteriorly, the intermediate layer of the lamina propria of the vocal fold thickens again to form the posterior macula flava, which transitions into the arytenoid cartilage. These modifications are thought to facilitate a transition from the membranous vocal fold to the stiffer thyroid and

arytenoid cartilage. In addition, they may serve to protect and cushion the vocal fold from damage during phonatory vibration. The biomechanics of fold vibration is intimately associated with the fold's layered structure.

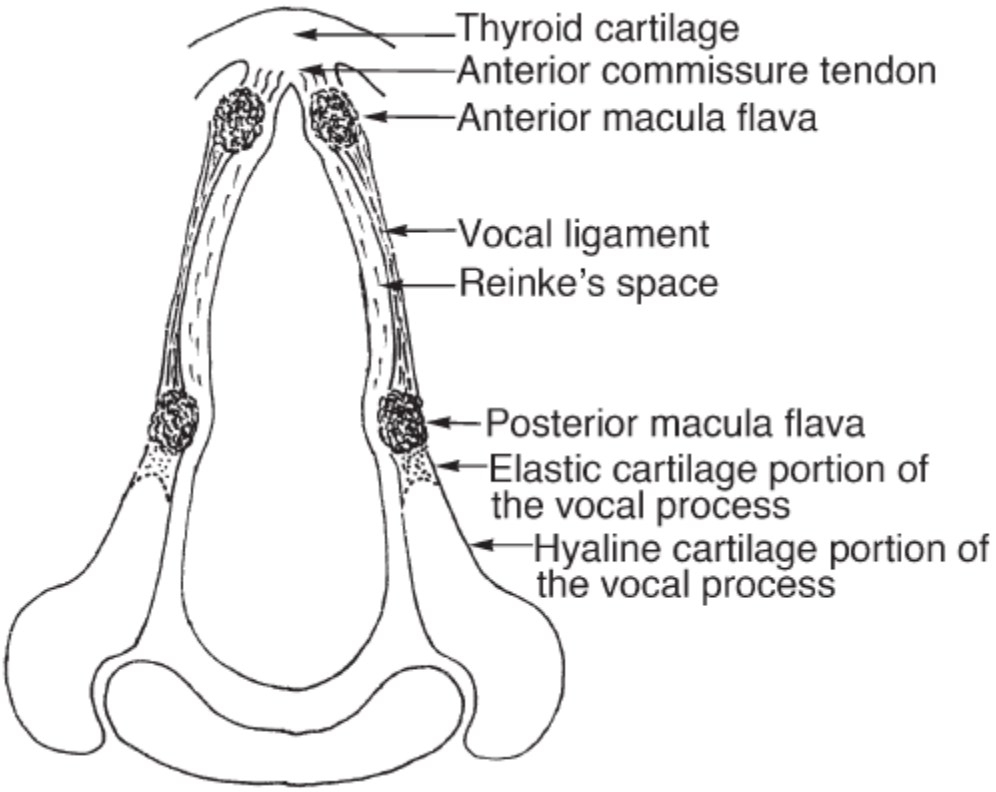


Figure 8: Parts of Vocal cord (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

Cover- transition - body concept

The five histologic layers of the vocal fold function as three different mechanical groups. The epithelium and SLP make up the cover of the vocal fold; the intermediate and deep layers of the lamina propria make up the vocal ligament or the transition;

and the vocalis muscle makes up the body of the vocal fold. The relationship between the three layers and the gradient of increasing stiffness provides the mechanics for the complex mucosal wave (8).

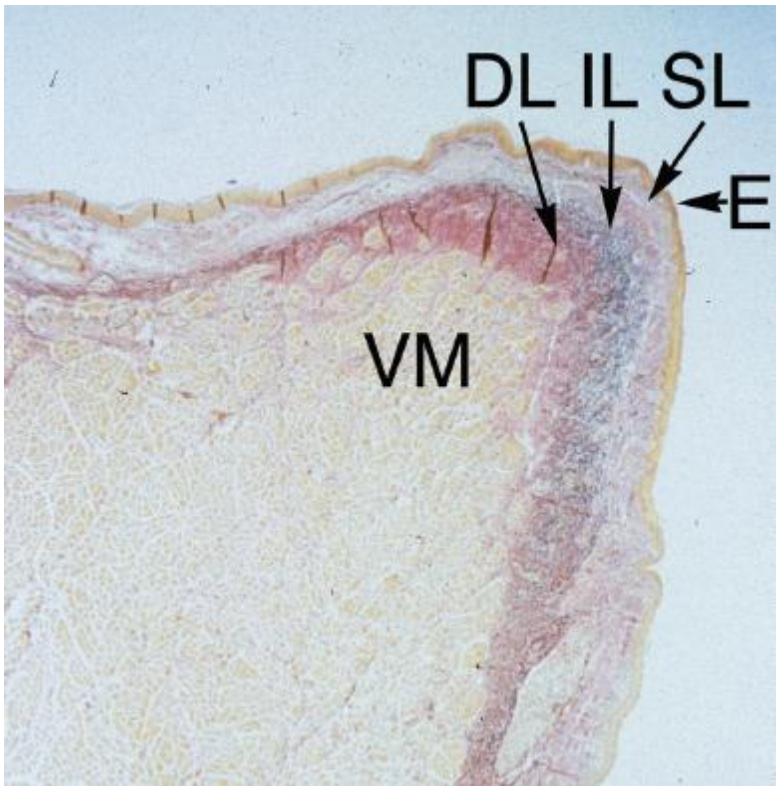


Figure 9: Histology of vocal fold(Cover: E- Epithelium, SL- Superficial Lamina propria, Transition: IL- Intermediate lamina propria, DL- Deep lamina propria, Body: VM- Vocalis muscle) (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

Vibration of the vocal fold cover (epithelium and SLP) results in the rhythmic opening and closing of the folds, which is critical to the creation of the intermittent pulses of air that we perceive as sound. Stiffness in the cover will result in impairment of vibration and hoarseness. The special components (cells, proteins, matrix scaffolding)

and organization of the lamina propria layers (superficial, intermediate, and deep) are all crucial in vocal fold vibration.

Physiology of phonation

The normal vibratory-phonatory cycle is regulated by several principles that include adequate breath support, approximation of vocal folds, favorable vibratory properties, favorable vocal fold shape and control of length and tension of vocal folds(11). Voice is achieved by a complex repeating cycle in which glottal opening and closing modulates the transglottic air-stream at anywhere from 50 to 1000 cycles per second.

Each cycle begins with the subglottic pressure pushing against the under surface of the closed vocal folds. The medial closing force holding the vocal folds together is called as phonatory threshold pressure. The pressure from the lungs eventually overcomes the phonatory threshold pressure, and pushes the vocal folds apart. The inferior-most part of the folds opens first, and the tissue is progressively compressed as an "air bubble" rises to the superior surface of the folds. This compression from inferior to superior is called a travelling wave. When the "bubble" or wave reaches the superior portion of the folds, they start to unzip, and pressurized air begins to escape from the folds as a jet. This mucosal wave thus starts in the infero-medial part of the vocal cords and proceeds in a rostral direction(11). This jet can attain velocities of 50 or more meters per second. The vocal folds open first anteriorly. At the superior portion of the folds, the tissue wave propagates out laterally. While this lateral propagation of the wave occurs, the inferior most edges of the vocal folds begin to approximate

together. There are many factors involved in this medial movement of the vocal folds which include fall in subglottic pressure due to escape of air, recoiling force because of the elasticity of the vocal folds and the Bernoulli effect which is the negative pressure created by high velocity of the escaping air. The vocal folds approximate inferiorly, and this closure then progresses superiorly and anteriorly until the vocal folds close completely, leading to repetition of the cycle. Sound is produced during fold oscillation by the inertial interaction of the pulsating jet against the air columns above and below the folds creating an air pressure wave that then interacts with the resonators of the vocal tract before exiting the lips.

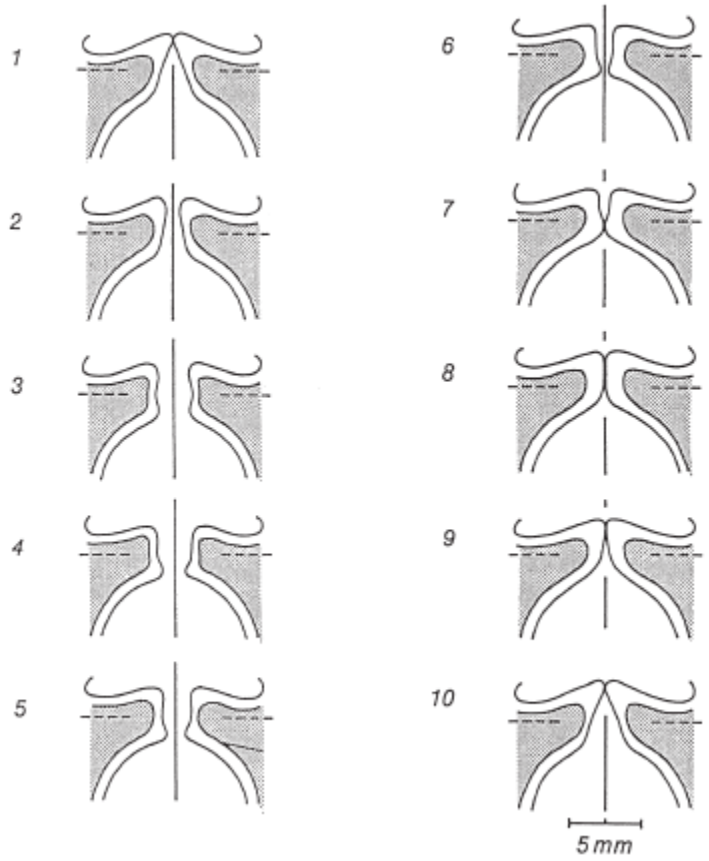


Figure 10: Aerodynamic theory of phonation (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

The simplest models of phonation are based on the principle that pitch depends on the frequency of vocal fold vibration, which is related to the vocal fold length, whereas loudness is the result of subglottic pressure and the amplitude of vibration of the vocal folds.

The three main types of vibratory patterns that exist are modal, falsetto, and glottal fry. In the modal register, the vocal folds exhibit a normal vibratory topography as the mucosa vibrates independently of the muscle. In falsetto, glottal closure is incomplete, and only the uppermost free edges of the folds are involved in vibration, creating a high-pitched voice. Glottal fry is characterized by an excessively low-pitched voice with the vocal folds tightly approximated for a longer than normal duration during the vibratory cycle.

Levels of voice usage:

Level 1: Elite vocal performer: For this class slight aberration of voice may have dire consequences. Eg: singers and actors, opera singer

Level 2: Professional voice user: This group of people includes those in whom a moderate vocal problem may prevent adequate job performance. Eg: Clergy , teachers, Lecturers

Level 3: Non Vocal professional: Only severe vocal problem would prevent adequate job performance in this group of people. E.g. Lawyers, Physicians, businessmen

Level 4: Non vocal Non-professionals: The voice quality is not a pre requisite for adequate job performance in them. E.g. Clerks, Labourers

Benign Lesions of the Vocal cord

Benign lesions of the vocal cord can be divided into two types:

-Neoplastic

-Non-neoplastic

Benign non-neoplastic lesions form the majority of vocal fold lesions. Vibratory injury of the vocal fold is the most common cause of majority of these lesions. However multiple other causative factors also have been attributed to the formation of these types of lesions(12).

The most common risk factors include occupations with high voice demands. The other risk factors that can cause vibratory injury include acid reflux, smoking, uncontrolled allergies, and infections.

Vocal nodules:

Vocal cord nodules appear as bilateral swellings at the junction of the anterior and middle membranous portion of vocal folds. This is the region of the maximal shearing and collision forces between the vocal cords. The nodules can be different in size, symmetry, contour, and colour.

The size of the nodule may not always correspond to the effect on voice- some singers may have vocal nodules with no voice complaints. Nodules develop in stages. Forceful or prolonged vibration at the membranous (vibratory) portion of the vocal cords lead to sub mucosal oedema and vascular congestion followed by healing and remodelling of the superficial lamina propria. Prolonged voice abuse leads to hyalinization of the superficial lamina propria, which in turn results in nodule formation. On laryngeal stroboscopy, vocal cord nodules form an hourglass closure pattern with a relatively normal mucosal wave.

Treatment of vocal nodule should be tailored for each patient based on voice demands. The primary mode of treatment is voice therapy. A key to successful treatment is optimisation of the laryngeal environment. This includes eliminating behaviour causing phono trauma, setting guidelines for voice use, and optimizing hydration. If any medical problems are diagnosed associated with vocal cord irritation, they should be treated promptly. If conservative therapy fails to improve symptoms, surgery may be indicated. The other options that have been suggested for treatment of vocal nodules include intra lesional steroid therapy and Botox injections.

Vocal Polyp:

Vocal polyps are mostly unilateral lesions, but can present bilaterally. They can be broad based or pedunculated. Their colour may vary and can be red, white, or translucent and are located usually on the anterior third of the true vocal cord. As with vocal nodules, polyps are associated with vocal abuse and are also associated with anticoagulant use. There are two types of polyps: hemorrhagic and non hemorrhagic.

Hemorrhagic polyps often are of sudden onset following extreme vocal effort or voice overuse. Non hemorrhagic polyps result due to outpouchings of the inflamed superficial lamina propria.

Polyp development is believed to be caused by shearing forces during voice exertion, which results in capillary rupture and focal accumulation of blood or hematoma in the superficial lamina propria. This results in oedema followed by infiltration of inflammatory cells, which ultimately results in the formation of a new matrix. (13)

Vocal cord polyps on video stroboscopy have intact mucosal waves sometimes with phase asymmetry due to impaired glottic closure.

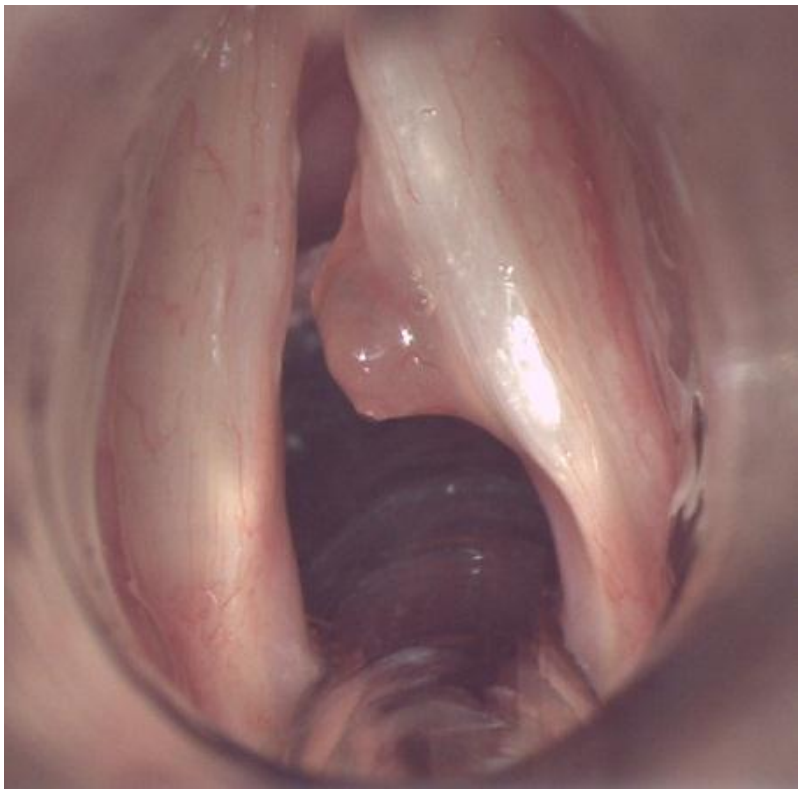


Figure 11: Vocal cord polyp

The management of vocal polyps differs according to the size of the polyp. Small polyps will mostly resolve with conservative management alone whereas larger polyps require surgical intervention. Anticoagulants must be discontinued and acid reflux should be controlled to prevent hyperaemia and vessel dilations associated with it. Voice therapy is beneficial to patients with vocal polyps and sometimes is the only management necessary in treating small polyps. Surgical removal is necessary when conservative therapies fail (14).

Vocal cord Cyst:

Vocal cord cysts are usually unilateral but can also be bilateral. They are sac like structures within the lamina propria, yellow or white in colour, and have a distinct border. They are true cysts with the cyst being covered by an epithelial lining. There are two subtypes: epidermoid and mucus retention cyst. The epidermoid cysts contain keratin and are covered by stratified squamous epithelium whereas mucus retention cysts contain mucus and are covered by cylindrical epithelium. Epidermoid cysts result from vocal abuse and mucous retention cysts usually develop spontaneously. Both the cysts differ in their pathogenesis. Epidermoid cysts arise in one of two ways. They can develop when epithelial cells are buried congenitally in the sub epithelial layer or from the healing of mucosa from voice abuse over buried epithelial cells. Mucous retention cyst form when mucous gland ducts become obstructed from conditions such as upper respiratory infections, voice overuse, and acid reflux. The video strobe of a patient with a vocal cord cyst will have an asymmetrical mucosal wave at the site of the lesion. The side with the cyst will have a decreased wave and the wave on the unaffected side is often normal. Glottic closure depends on the size of

the cyst and can vary. The primary management option for cysts consists of surgical removal because vocal cysts do not resolve with conservative management alone. Supportive measures can help but will not resolve these lesions. Voice therapy plays a limited role in treatment of these lesions but it can be useful in the epidermoid variety, which are more likely to be due to vocal abuse.

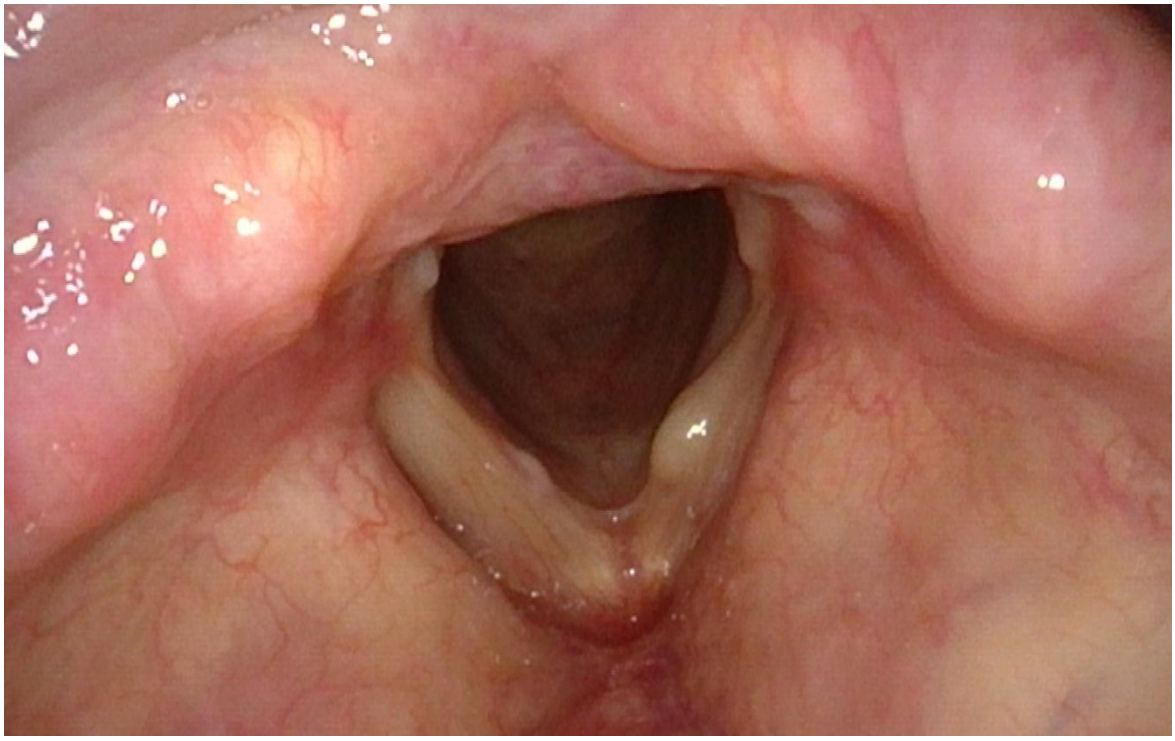


Figure 11: Vocal cord cyst

Evaluation of Voice

Stroboscopy

The evaluation of vocal fold anatomy, mucosal colour, and gross movement can be performed while illuminating the vocal folds with a constant light source. The typical fundamental frequency of the vocal cords is above 100 Hz(15). This speed of vibration is not perceivable to the human eye. Hence the evaluation of vocal fold vibration

requires special imaging technology to "slow down" vibration for assessment. Currently, the most widely used technique for assessing the vibratory characteristics of the vocal folds is videostroboscopy, which has become an accepted and essential component of the comprehensive evaluation of voice disorders.

Stroboscope was invented by Oertel in 1895, but it became popular in clinical use in second half of 20th century. Videostroboscopy has been attributed to work based on the principle of Talbot's law which states that images linger on the human retina for 0.2 seconds after exposure(16). Recently Mehta et al(17) debunked this concept and stated that two different visual perception phenomena actually play critical roles in laryngeal stroboscopy: 1) the perception of a flicker-free, uniformly-illuminated image (satisfied at strobe rates above 50 Hz) and 2) the perception of apparent motion from sampled images when no real motion exists (satisfied at display rates above 17 Hz).

Videostroboscopy is indicated when a detailed visual analysis of vocal fold vibration is desired. It is usually performed in addition to an indirect or flexible examination of the larynx. Videostroboscopy is indicated in any patient who complains of hoarseness but has an otherwise normal indirect or flexible laryngoscopic examination. The advantage of videostroboscopy over laryngeal video endoscopy is that in addition to providing information regarding vocal fold vibration, the image obtained with videostroboscopy is magnified, allowing a more detailed assessment of the vocal fold anatomy than is possible with indirect or flexible laryngoscopy. In addition to being an aid in the diagnosis of voice disorders, videostroboscopy is indicated to document vocal fold function prior to any treatment and to evaluate the outcomes of various interventions.

The European Laryngological Society cites videostroboscopy as being integral to the protocol because they believe that "Videostroboscopy is the main clinical tool for the etiological diagnosis of voice disorders"(18). Because videostroboscopy provides the benefit of documenting the examination findings, subsequent examinations can be compared, so that the results of treatment can be studied. Indeed, videostroboscopy has been used successfully to document the results of certain surgical interventions by demonstrating an improvement in the vocal fold vibratory characteristics after the treatment.

Videostroboscopy is performed with a rigid endoscope of 4mm diameter with a 70-degree or 90-degree angle of view. It is passed through the mouth, into the back of the pharynx, to visualize the larynx. A microphone on the patient's neck measures the frequency of vocal fold vibration and sets the frequency of strobe flashing to a frequency slightly off and several multiples slower than vocal fold vibration allowing images from sequential parts of the vibratory cycle to be recorded and viewed as a "virtual" slow-motion movie of vocal fold vibration.

The following parameters are assessed on Stroboscopy:

1.Symmetry

Symmetry of vibration refers to the movement of the right and left vocal folds relative to each other. The right and left folds normally vibrate as mirror images of one another. They begin to move laterally at the same time and at the same speed. They are displaced laterally to the same extent and reach maximal lateral displacement at the same time. They then begin to close together at the same time and at the same

speed. Differences in the mechanical properties of the two vocal folds, however, will result in asymmetric movements. Symmetry of vibration is influenced by differences in the position, shape, mass, stiffness, elasticity, and tension of the vocal fold tissues.

2. Periodicity

Periodicity of vibration refers to the relative length of the glottal cycle, and this should be stable from cycle to cycle. Use of the synchronized strobe setting can confirm that vibration is periodic. If the length of the vibratory cycle is stable from cycle to cycle, then a static image will persist with the strobe set to the synchronized mode. If changes in the length of the vibratory cycle are present, there will appear to be movement of the vibratory edge in the synchronized mode. Periodicity depends on the mechanical properties of the vocal folds and the expiratory force applied to them.

3. Phase closure

Phase closure refers to the percentage of time that the vocal fold edges are open and/or closed during a single cycle of vibration. The phase characteristics are normally influenced by the mode of phonation (falsetto, modal phonation, and glottal fry) and the pitch and loudness of phonation.

4. Amplitude of vibration

Amplitude of vibration refers to the amount of lateral movement of the vocal folds during vibration. Amplitude of vibration normally increases with increases in subglottic pressure, such as occurs during loud phonation. Amplitude of vibration also increases as the pitch or frequency of phonation decreases.

5. Glottic configuration

Glottic configuration refers to the shape or contour of the glottic opening, if there is one, at the point of maximal closure during the vibratory cycle. Other terms for this characteristic include the “contour of the glottal margin” and the “vocal fold closure pattern.”

6. Mucosal wave

Mucosal wave refers to the movement of the superficial tissues over the vocal fold as the air moves through the glottis. The mucosal wave can be seen as a traveling wave in the superficial tissues over the top of the vocal fold surface from medial to lateral. Slow-motion or frame-by-frame analysis of the video stroboscopic recording is usually required for an adequate evaluation of the mucosal wave. The mucosal wave is interrupted with abnormalities of the vocal fold mucosal cover such as scarring, lesions, inflammation, and oedema.

Being a perceptive analysis, one of the disadvantages of stroboscopic examination is the inter-rater variability. Poburka (19) designed a Stroboscopy evaluation rating form for this purpose.

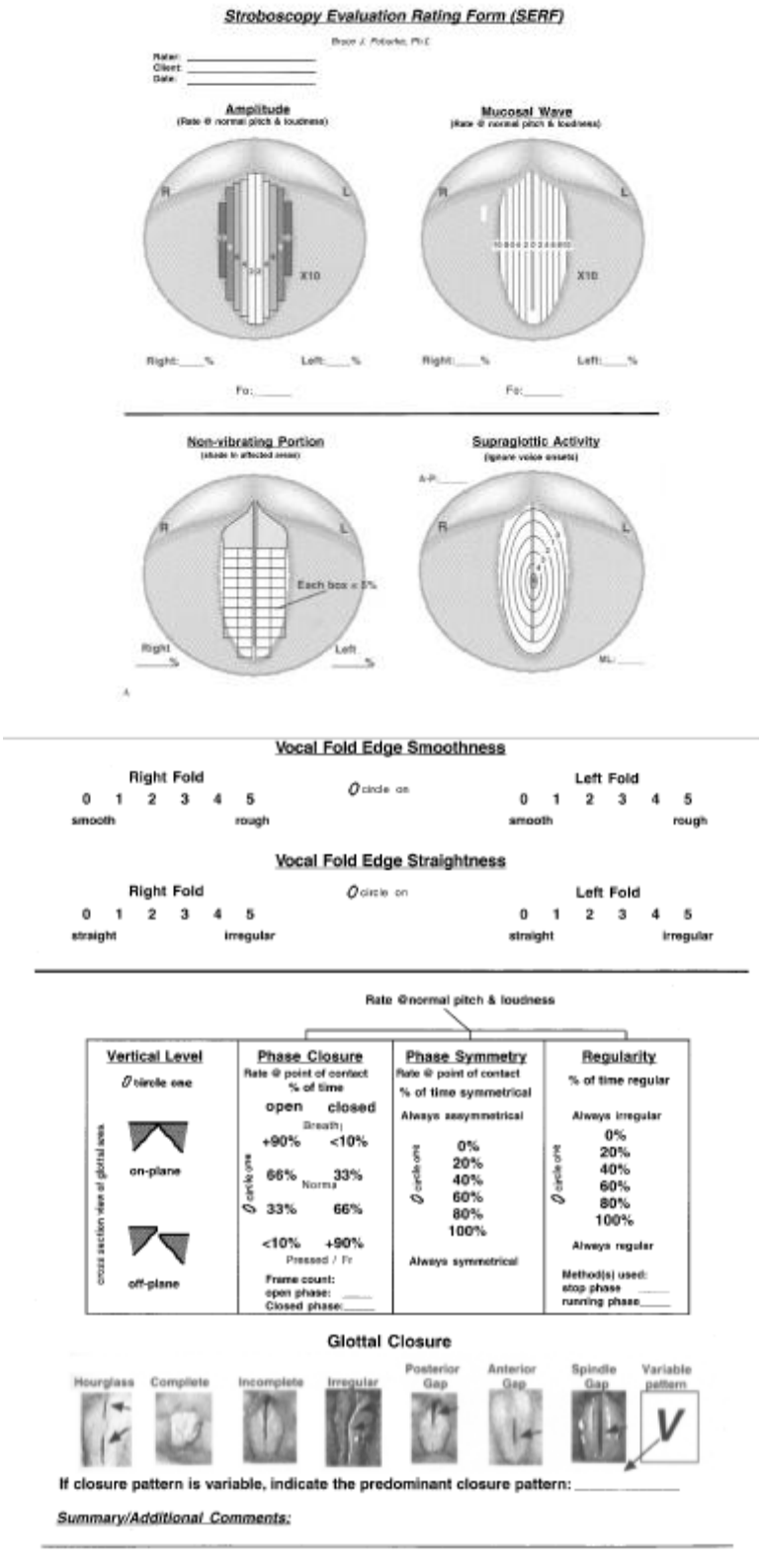


Figure 12: Stroboscopy rating form (19)

Acoustic Voice Analysis

The voice recording system remains the most valuable basic tool for the voice laboratory. Analog recordings can be converted to digital, which can then be used for data storage. Digital recording has almost completely replaced the use of the standard analog system. It is arguably more precise and of longer lasting, higher quality, although some investigators remain concerned about distortion introduced by the digitization and compression process. Data from digital recording are immediately computer compatible allowing online analysis. Alternatively, data can be stored for use at a later date.

The stopwatch is another simple tool in the voice laboratory. The maximum phonation time and the "s/z" ratio are both simple measures to obtain, with useful clinical correlations. The s/z ratio is the ratio between the maximum phonation time for the sound |s| to that of |z|. The site of resistance in phonating |s| is at the teeth, whereas for |z| it is at the glottis. In a normal speaking subject the s/z ratio is approximately 1.0. However in cases of pathology that affect glottic closure, the s/z ratio goes over 1.4 (20).

Jitter is the term given for frequency (period) perturbation. It is the variability of the fundamental frequency (F0). Jitter measurements tend to be concerned with short term F0 variation. Jitter, then, is a measure of frequency variability not accounted for by voluntary changes in F0 (fundamental frequency).

Measures of amplitude perturbation (shimmer) serve to quantify short-term instability of the vocal signal. Amplitude perturbation is a measure based on the peak amplitude of each phonatory cycle.

Harmonic-to-noise ratio is the mean amplitude of the average wave divided by the mean amplitude of the isolated noise components for the train of waves. If we assume that the pure (average) periodic wave is increasingly contaminated by random noise as hoarseness worsens, this degree of contamination can be expressed as a periodic harmonic-to-noise amplitude ratio. For convenience, it is expressed in decibels. A characteristic feature of hoarseness is the replacement of harmonics by noise energy.

Voice handicap index

In 1997, Jacobson et al. proposed a measure of voice handicap known as the Voice Handicap Index (VHI). This patient-based self-assessment tool consists of 30 items. These items are equally distributed over three domains: functional, physical, and emotional aspects of voice disorders.

Rosen et al later came up with a shortened form of the VHI, the VHI-10. There is no loss of utility or validity of VHI-10 compared with the VHI for assessing initial patient-based voice handicap evaluation and longitudinal follow-up after treatment. The VHI-10 is a powerful representation of the VHI that takes less time for the patient to complete. The VHI-10 can be easily and promptly self-administered and scored quickly at the time of evaluation.

Question	0	1	2	3	4
My voice makes it difficult for people to hear me.					
People have difficulty understanding me in a noisy room.					
My voice difficulties restrict personal and social life.					
I feel left out of conversations because of my voice					
My voice problem causes me to lose income					
I feel as though I have to strain to produce voice.					
The clarity of my voice is unpredictable.					
My voice problem upsets me.					
My voice makes me feel handicapped.					
People ask, “What’s wrong with your voice?”					

Micro laryngeal surgery

Micro laryngeal surgeries are high precision surgeries and are done under general anaesthesia. As in any other surgery exposure and adequate visualisation are paramount in this procedure too. There are multiple designs of laryngoscopes that are available to help in exposing the larynx for micro laryngeal surgery. Largest laryngoscope available is used to visualise the larynx. However in case of lesions close to the anterior commissure, smaller or narrow laryngoscopes are used.

Patient is positioned supine on the operating table with the head supported on a head ring in the Boyce’s position. Intubation is done with a small sized endotracheal tube preferably of size 5.0 to 6.0 thus providing adequate space for the surgeon to work. The teeth of the patient are protected using a tooth guard. The laryngoscope is

connected with a light source and inserted to the oral cavity and advanced to the oropharynx and further to visualise the larynx. Once adequate visualisation is obtained the laryngoscope is suspended using a Benjamin Parson Chest suspension. The chest piece is rested on a board kept above the chest of the patient or on a plate attached to the operating table.

Hitherto the operating microscope is used to provide binocular vision and to provide magnification. The working distance of the operating microscope for micro laryngeal surgeries is 40cm. The lesion is visualised and 1 cc of 1:10 000 saline adrenaline solution is injected in the superficial lamina propria with a No. 27 micro laryngoscopy needle. Either the medial micro flap technique or the lateral micro flap technique can be used to excise the lesion preserving the 'cover' of the vocal fold(21). In lateral micro flap technique, incision is made with a sickle knife over the superior surface of the vocal fold lateral to the lesion. With careful dissection, using a micro flap elevator, the epithelial cover is freed from the lesion (22). The lesion is then held using forceps like the Kleinsasser forceps with cup shaped jaws and Kleinsasser micro grasping forceps or the Bouchayer's forceps; and dissected from the underlying vocal ligament, removed and sent for histopathological examination. Redundant epithelium is trimmed and the flap is then reposited back. At all times during handling, care is taken to prevent a tear in the flap.

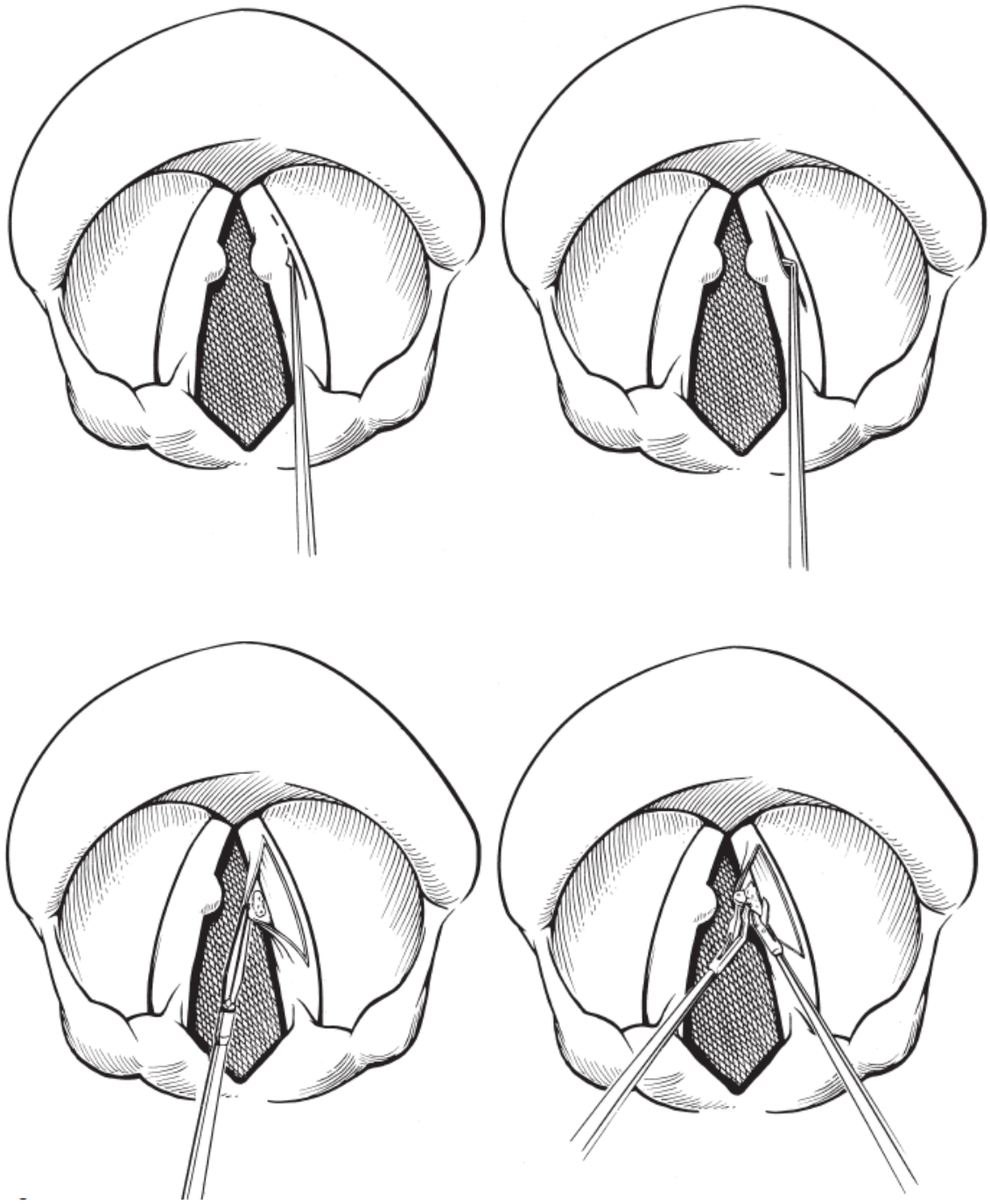


Figure 13: Micro flap technique (adapted from Diagnosis and Treatment of voice disorders- Rubin, Sataloff. Korovin)

Wound healing of vocal cord

The various factors contributing to vocal fold injury are

-Mechanical trauma

- Thermal trauma

- Chemical trauma

- Overuse or misuse

-Combination of these factors.

Wound healing, is the well regulated process of tissue repair and regeneration occurring after tissue injury. Insufficient tissue repair leads to formation of granulation tissue and excessive tissue repair leads to vocal fold scarring. Vocal fold scarring results in loss of mucosal pliability, thereby affecting the cover-body relationship and resulting in an altered acoustic signal. The normal wound-healing process comprises of four phases which are integrating and overlapping namely:

-hemostasis

-inflammation

-proliferation

-remodelling

Hemostasis is nothing but arrest of the flow of blood. This can be broken down into 3 phases. During the initial vascular phase, which may last up to 30 minutes, there occurs vascular spasm of the smooth muscle in the vessel wall leading to vasoconstriction to slow or stop blood flow. The damaged endothelial cells of the blood vessels produce von Willebrand factor which make the endothelium sticky causing the adhesion of platelets to its surface. This is called the platelet phase. The platelets which adhered to the vessel wall will start secreting adenosine diphosphate (ADP), causing further free platelets to come and attach and aggregate together leading to the formation of a platelet plug. The platelet plug secretes a vasoconstrictor called thromboxane and together may cause sealing of the break in the vessel wall. Coagulation phase begins 30 seconds to several minutes after these two phases and is initiated by two methods. It could be either be due to platelet thromboplastin secreted by the platelet plug in case of extrinsic pathway or due to blood coming in contact with the exposed collagen in the wall of the blood vessel in case of intrinsic pathway. Coagulation results in the formation of fibrin, which produces a network of fibres to trap blood cells and platelets, thereby forming a thrombus or clot. Inflammatory and mesenchymal cells migrate to this fibrous matrix which functions like a scaffold.

The cardinal signs of inflammation at the site of a wound include rise in temperature, redness, swelling, pain, and loss of function. These occur as a result of 3 processes: vasodilation, increased vascular permeability, and migration of neutrophils out of the blood to the damaged area.

After hemostasis is completed, dilatation of blood vessels occurs allowing for movement of essential molecules to the area. This vasodilation results in increased

blood flow to the site of injury. Blood vessel permeability increases as a result of chemical mediators that cause retraction of endothelial cells, leaving intercellular gaps. Water, salts, and some small proteins into the damaged area through these intercellular gaps. These proteins include plasma proteins that constitute the complement system, clotting proteins like fibrinogen, fibrinolytic proteins like plasminogen, and kinins. Chemotactic signals from chemotaxins such as bacterial components, complement, fibrin, and interleukin-8 (IL-8) will attract and draw the neutrophils into the injured area. Neutrophils squeeze through the endothelium and migrate toward the area of injury by diapedesis. These neutrophils then mature into phagocytes and engulf micro-organisms that may be present in the wound.

Proliferation is characterized by

-angiogenesis

-collagen synthesis

-formation of ECM

-epithelialization and

-tissue contraction.

Angiogenesis is the process by which endothelial cells produce new vasculature. This process is driven by chemotaxis and endothelial cell proliferation. The endothelial cells digest and penetrate the basement membrane of the blood vessels to enter into the stroma and forms tube like structures which branch and form networks. The fibroblasts are attracted to the wound by chemotactic signals like

platelet derived growth factor and endothelial growth factor. They come into the wound after 2- 3 days and degrade the fibrin clot and deposits hyaluronan and fibronectin which lead to the formation of granulation tissue. Subsequently a provisional extra cellular matrix is formed by the fibroblasts by production of type 1 and 3 collagen.

The epithelial cells begin to proliferate, migrate, and cover the exposed area to restore tissue integrity within hours of tissue injury. MMPs and plasmin are produced by the cells in the basal layer, causing them to separate from the basement membrane and migrate into the wound via chemotaxis. Migration of epithelial cells continues until contact is made with other basal cells.

Tissue contraction is a process by which the dimension of the wound is reduced because of the edges of a wound moving toward each other in a centripetal fashion. Contraction begins 4 to 5 days after injury and peaks at 14 days. It contributes to reduction of healing time by reducing the requirement of granulation tissue and ECM needed for reconstruction. The result of tissue contraction is scarring, which can have detrimental effects on the appearance and function of the tissue.

The final stage of wound healing is the scar remodelling or maturation phase. This stage begins approximately after 8 days following the injury and may continue for months. It is characterized by a change in ECM composition. The tensile strength of the tissue increases by approximately 70% of pre injury levels because of the cross links forming between the collagen fibers, This leads to decreased tissue elasticity(23).

Human vocal fold injury and repair

Although dermal and mucosal tissues undergo the same phases of wound healing, there is evidence from research examining the oral palatal mucosa in humans that mucosal wounds heal more rapidly and with minimal scar formation(24). This difference is understood to be due to the neural crest origin of oral mucosa as opposed to the mesenchymal origin of skin(25). Studies of vocal fold injury in humans are limited to normal cadaver tissue and excised surgical lesions due to the communicative deficits that would arise secondary to a disruption of this specialized vibratory mucosa.

Effect of voice rest in vocal cord wound healing:

Experts have a varied opinion on the matter of duration of voice rest after micro laryngeal surgery in the available published literature. Cho et al concluded in their study on a canine model that voice rest helps in re epithelialization and recommended voice rest of 2 weeks and vocal hygiene of 8 weeks following phonosurgery(3). Absolute voice rest is commonly prescribed after micro laryngeal surgery even though there is no available data to indicate a significant benefit for such voice rest over other vocal conservation techniques in the postoperative period. The problems with evaluating the efficacy of voice rest as an adjunct treatment tool are:

-patients usually ignore advices regarding voice rest due to their professional or cultural demands

- There is no standard voice rest treatment available in published literature. The duration of voice rest prescribed varies from surgeon to surgeon.

Behrman and Sulica(4) surveyed 1208 laryngologists in the United States of America regarding their preferences in advising absolute voice rest and relative voice rest after micro laryngeal surgery for benign lesions of vocal cord like polyps, nodules and cysts and also regarding the duration of voice rest advised. They found that 51% of the surgeons favoured absolute voice rest whereas 62% favoured relative voice rest. 15 % of the surgeons didn't recommend any type of voice rest after surgery. The most common duration of absolute voice rest that most otolaryngologists preferred was for 7 days after surgery, however there was no evidence to back up this practice(4).

Coombs et al(26) conducted a survey among the otolaryngologists in the UK and found that in case of benign lesions like vocal cord polyps, cysts and nodules, 45% of the surgeons advised complete voice rest and only 8% didn't recommend any type of voice rest in the post-operative period. However the most preferred duration of voice rest was 1-2 days (35%) followed by 3-5 days(23%), 5-7 days(24%) and 18% of the surgeons advised a voice rest period of more than 7 days.

A recent study from Japan by Kaneko et al(5) concluded that 3 days of voice rest followed by voice therapy may lead to better wound healing of the vocal fold compared to 7 days of voice rest and that appropriate mechanical stimulation during early stages of vocal fold wound healing may lead to favourable functional recovery.

Koufman et al(27) did a retrospective analysis of 127 patients who underwent micro laryngeal excision for lesions like polyps, nodules, granulomas, cysts, Reinke's edema, carcinoma in situ and leukoplakia. 26% of these patients were advised complete voice rest after the surgery and the others were advised relative voice rest for

varying periods of time. They found that 27% of the patients who were recommended complete voice rest had developed persistent post-operative dysphonia lasting more than 4 weeks. In the other group of relative voice rest 41% developed the same. However the results were not statistically significant. They concluded that relative voice rest is as effective as absolute voice rest in the post-operative period in preventing post- operative dysphonia(27). However this was not a randomised controlled trial and the patient compliance to the voice rest recommendations were varying in both the groups.

Reactive oxygen species (ROS) is an important factor that decides the course of wound healing and connective-tissue healing (28). For proper wound healing to take place a balance between oxidative and anti-oxidative forces is needed. Mizuta et al(29) suggested that a large amount of ROS is produced during the early phase of vocal fold wound healing until post injury day 3, and this period maybe crucial for regulating ROS levels (30). Therefore, **rest of injury** should be required for a certain period particularly during the inflammatory phase to avoid additional tissue damage caused by ROS.

Rousseau et al studied the impact of voice rest on the quality of life of patients and also the compliance of patients to the voice rest recommendations. 84 patients undergoing voice rest for various conditions were included in the study and the duration of voice rest recommended varied from 3-28 days. The type of voice rest was not specified. They concluded that voice rest had an adverse impact on the quality of life of the patients with longer periods having a worse effect. Half of the patients had to skip work due to the voice rest recommendations. They felt frustrated, found it

difficult to communicate and kept themselves away from interactions with other people during the period of voice rest. The interesting finding was that the self-reported compliance of the patients to the recommendations of voice rest was only 34.5%(6).

Effect of mechanical stimulation on vocal fold wound healing:

The effect of rest or exercise has been a controversial topic in orthopedic rehabilitation field for more than a century. However, controlled remobilization during the early stages of healing is believed to lead to favorable functional recovery. The improved healing response is thought to be the result of an exercise-induced anti-inflammatory response in the wound(31). Long-term immobilization is even considered to be detrimental to the recovery; therefore, it is not generally recommended in orthopaedic rehabilitation(32). Immobilization slows down turnover of ECM constituents, and leads to more disorganized ECM arrangement(33).

Tension applied on wounds may stimulate collagen synthesis and help align collagen fibres in the direction of force applied, but prolonged application of tension may also result in hypertrophic scarring(16).

The wound healing process in the vocal fold and the effect of mechanical stress/phonation on the wound healing process has been studied using animal models. The studies conducted in canine, rat and rabbit models show that re-epithelialisation and the beginning of collagen production occurs between 5^{th} and 7^{th} day after the injury(3) (35) (36). This would lead to the assumption that voice rest should last this

long. Titze and Gray(37) demonstrated in a canine model that hyperphonation can be detrimental to the vocal fold by causing destruction of basement membrane zone and the lamina propria.(37) The extrapolation of data from animal models of wound healing of vocal folds is limited by the variations in vocal fold microanatomy between humans and animals.

In vitro studies published recently have shown that cells in vocal fold are responsive to mechanical stress. Rabbit models were studied for mRNA expression of matrix metalloproteinases occurring as a result of induced phonation by Rousseau et al. They found that phonation induced expression of genes coding for matrix metalloproteinase-1 when compared to controls(38). These matrix metalloproteinases play a role in maintaining the connective tissue of the vocal folds. Another in vitro study by Kutty et al (39) investigated the effect of physiologically relevant vibratory stimulation on ECM gene expression and synthesis by fibroblasts which were encapsulated within hyaluronic acid hydrogels that resembled the viscoelastic properties of vocal mucosa.

Their results indicate that vibration is a critical factor that regulates the extra cellular matrix of the vocal fold and suggest that rapid restoration of the phonatory microenvironment may contribute a basis for reducing the scarring of vocal folds, restoring native ECM composition and improving vocal quality(39).

Post- operative voice therapy

Fibroblasts migrate to the wound area during the proliferative stage and produce large amounts of extracellular matrix which include elastin, collagen, proteoglycan and

glycosaminoglycan. It is thought that fibroblasts will be affected by mechanical stimulation during wound healing. Hence, early phonatory stimulation during the proliferative phase of wound healing may promote wound healing of the vocal cord. Several studies have reported the utility of post-operative voice therapy after micro laryngeal surgery.

Koufman and colleagues(27) have reported that preoperative voice therapy has a significant role in reducing the incidence of prolonged post-operative dysphonia. They also concluded that post-operative voice conservation techniques like soft glottal attack, loudness monitoring, and avoiding voice abuse are as effective as absolute voice rest for preventing prolonged postoperative dysphonia. (27)

Ju et al (40) studied 55 patients retrospectively for the effect of voice therapy after micro laryngeal surgery for vocal polyp removal. They had a control group of 63 patients who hadn't received voice therapy after same procedure. The study group had significantly improved VHI scores when compared to the control group but the acoustic analysis and GRBAS scale didn't show any significant difference. They concluded that post-operative voice therapy can improve patients' vocal discomfort, emotional responses and everyday self-perception.

Bequignon et al (41)evaluated the long-term outcome of patients with vocal fold nodules treated by surgery alone, or by a combination of surgery and voice therapy at a mean interval of 9.5 years after the surgery. They found that in the group without voice therapy there was 55% incidence of recurrent dysphonia and in the group with voice therapy the incidence of the same was 22% (p value = 0.02).

Kaneko et al (5) published the first randomized controlled trial that investigated the optimal duration and vocal stimulation post vocal fold surgery. Patients undergoing micro laryngeal surgery for vocal cord polyps, nodules, cysts, Reinke's edema, leukoplakia and carcinoma in situ were chosen and randomised to two groups: the first getting 3 days of voice rest and the second getting 7 days of voice rest. Following voice rest, both the groups received voice therapy. Preoperative and post-operative analysis of voice using subjective and objective parameters and stroboscopy were used to compare the two groups. Jitter, shimmer, and VHI-10 were significantly better in the 3-day group at 1 month post operation. GRBAS was significantly better in the 3-day group at 1 and 3 months post operation, and return of normal mucosal wave amplitude was significantly better in the 3-day group at 1, 3, and 6 months post operation compared to the 7-day group. They concluded that appropriate mechanical stimulation of the vocal folds during early postoperative period can lead to favourable functional outcomes.

Voice therapy sessions are aimed at a general approach towards vocal hygiene. This includes adequate hydration, avoidance of laryngeal irritants, reducing voice abuse, reducing vocal loudness and avoiding throat clearing. The other constituent of voice therapy is vocal resonance exercise.

Voice therapy exercises

Semi occluded vocal tract exercises are used by voice therapists to decrease the excessive tension on the vocal folds to facilitate postoperative wound healing. These

exercises facilitate a voice quality which is neither breathy nor pressed. They also promote a gentle vibration of the vocal folds. Many benefits are attributed to this group of semi-occluded vocal tract exercises. One of them is increase in vocal tract impedance leading to change in inertive reactance which is the inertia of the air column in the vocal tract. This increase in vocal tract impedance may favourably impact vocal fold vibration. Other benefits are decrease in phonation threshold pressure, decreased trans glottal pressure, increased skewing of the glottal flow waveform, more resonant voice quality, easier voice production and decrease in laryngeal muscle activity. There are different types of semi occluded vocal tract exercises with variations in the method of exercise and physiology (42).

-exercises providing a constant frontal obstruction of the vocal tract

Eg: humming and hand over mouth

-exercises that lengthen the vocal tract using a resonance tube coupling

Eg: tube phonation, Lax-vox

-exercises that introduce a secondary source of vibration into the vocal tract

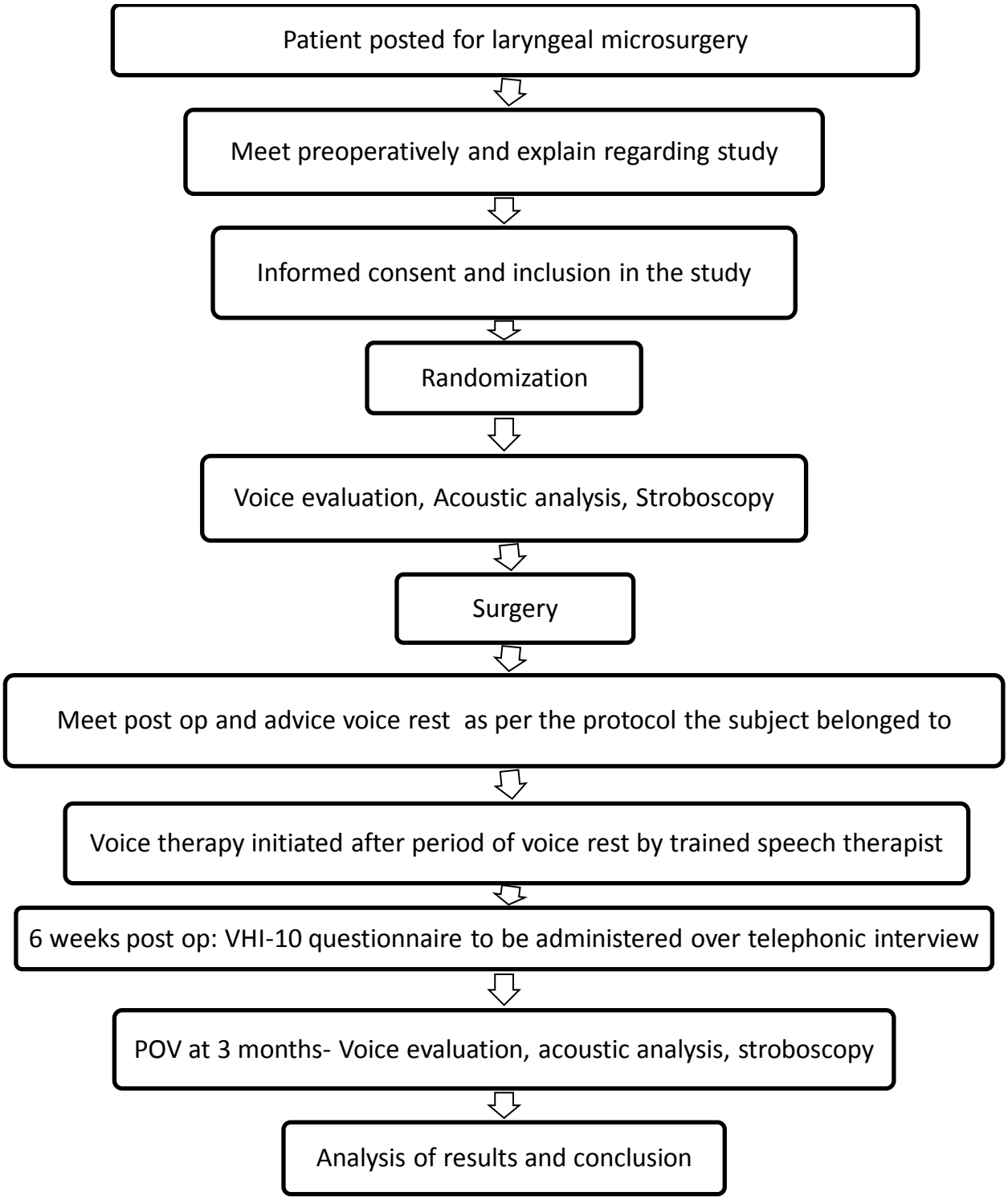
Eg: lip and tongue trills

Tube Phonation

Resonance tubes are narrow glass tubes of 8-9 mm diameter and approximately 25-28 cm long which are used in speech therapy. These were introduced by Professor Sovijärvi in 1960s(43). Phonation through a resonance tube is thought to be therapeutic and is used by speech therapists for vocal warm up exercises or for voice rehabilitation exercises. The tubes are placed between patient's lips and the other end

either in water or in air. The tube effectively lengthens the vocal tract. These are given the name resonance tubes because of the strong feeling of vibration sensed during phonating through these tubes on the lips and face(44).

Materials and Methods



1. **Study design**

This study was designed as a single blinded prospective randomised controlled trial with two arms and an allocation ratio of 1:1

Approval was obtained from the institutional review board with IRB no. 10328 dated January 3, 2017.

2. **Setting**

Department Of ENT unit 5, Christian Medical College and Hospital, a tertiary hospital in southern India.

3. **Participants**

Inclusion criteria

All consecutive patients above 18 years of age undergoing micro laryngeal surgery for benign looking laryngeal lesions in the department of ENT unit 5 were recruited for the study.

Exclusion criteria

- patients who were having coexisting vocal cord palsy
- Patients who were undergoing revision surgeries
- Patients who were on tracheostomy
- Patients not cooperating for stroboscopic examination

4. Intervention and comparison

a. Intervention: 2 days of absolute voice rest after micro laryngeal surgery followed by tube phonation

b. Comparator: 5 days of absolute voice rest after micro laryngeal surgery followed by tube phonation

5. Outcome measures

Preoperatively all patients underwent assessment of voice by voice handicap index (VHI-10), GRBAS scale and acoustic analysis followed by laryngeal videostroboscopy.

(a) Laryngeal video stroboscopy

It is a procedure which facilitates slow motion recording of the vocal fold movements during phonation. It uses a 90 degree Hopkins telescope and strobe light.

The procedure was explained to the patient, especially the need to keep the mouth open and to avoid swallowing. The throat was anesthetized by using 10% lignocaine topical spray. After giving a few minutes for the topical anesthetic to act, the patient was asked to protrude his tongue, which was held by the examiner with a gauze piece. The 90 degree telescope facing downwards was introduced into the oropharynx to visualise the larynx. A microphone was kept on the neck of the patient to detect the fundamental frequency of the patient. The patient was asked to phonate and the stroboscope produced strobe

light in accordance with the patient's fundamental frequency. The video was recorded on the computer.

The videos were analysed by two consultants in the department of ENT. The evaluators were blinded to the randomisation arm. The parameters assessed were

1. Mucosal wave- normal/reduced/ absent
2. Adynamic segments- present/ absent
3. Amplitude of the mucosal wave- normal/ abnormal
4. Glottic closure- present/ absent
5. Symmetry- present/absent

(b) Voice handicap index 10

It is a questionnaire for subjective assessment of the voice. There were 10 questions in the questionnaire and each question was answered on a scale of 0-4. VHI-10 questionnaire was administered by the principal investigator. The possible scores ranged from 0 to 40. A VHI-10 score more than 11 was considered abnormal (45).

(c) GRBAS

This is a score used for perceptive assessment of voice. The parameters used were grade, roughness breathiness asthenia and strain. This scoring was done by the speech language pathologist. We used a composite score for analysis by

summing the scores for each subscale and comparing between the two groups (5).

(d) Acoustic analysis

Each patient was evaluated in a sound treated room by recording their voice using a low impedance commercial microphone. The patient was asked to phonate continuously for 10-15 seconds and the voice was recorded. Voice analysis was performed using PRAAT software version 4.3.22 which is an open access software available for free in internet.

The parameters assessed were

- Jitter
- Shimmer
- Harmonics to noise ratio

The maximum phonation time was assessed for |s| and |z| consonants and the s/z ratio also was calculated.

Preoperative counselling was given to patients regarding need of voice rest in the post op period and the schedule of voice therapy.

The patients underwent micro laryngeal surgery for removal of the lesion using the standard laryngeal micro flap technique.

Post operatively the instructions for voice rest were reinforced. The patients were advised absolute voice rest for the prescribed period according to the randomisation and then they were sent to the speech language pathologist for initiating tube phonation.

Tube phonation

A 20cm long stainless steel pipe of 1cm inner diameter was given to the patient for tube phonation. The patient was advised to phonate |o:| through the pipe for a sustained period multiple times for 5 minutes thrice daily.

This was reinforced again on post-operative day 7 and the patient was advised to continue it for 1 month.

Post op evaluation

1. The patient was contacted over phone at the end of 6 weeks from the date of surgery and VHI-10 questionnaire was administered.
2. The patients reported for postoperative follow up after completion of 3 months from date of surgery.

   All the parameters assessed during the pre operative visit were repeated (GRBAS, VHI-10, acoustic analysis and laryngeal videostroboscopy.

6. **Randomisation**

a. Method of randomization:

Simple randomization based on computer generated code.

b. Method of allocation concealment:

Sealed envelope that will be opened only at the time of allocation after randomization, to which the evaluators are blinded.

c. Implementation :

After the preoperative evaluation was completed, the patients were randomised to two groups A and B. Envelopes provided were opened to reveal the randomisation.

Group A: 2 days (minimum 48 hours) of voice rest after micro laryngeal surgery followed by voice therapy (tube phonation)

Group B: 5 days (minimum 120 hours) of voice rest after micro laryngeal surgery followed by voice therapy (tube phonation)

7. Sample size

The primary outcome was voice quality of patients measured by a score GRBAS after phonomicrosurgery. A sample of size 36 (18 in each group)was required to detect a mean difference of 1.9 in the voice quality score between the two groups of subjects following initiation of voice therapy after 2 days and 5 days of voice rest with 80% power and 5% level of significance.

Assuming a dropout rate of around 20%, the sample size required was 50 (25 in each group).

8. **Blinding**

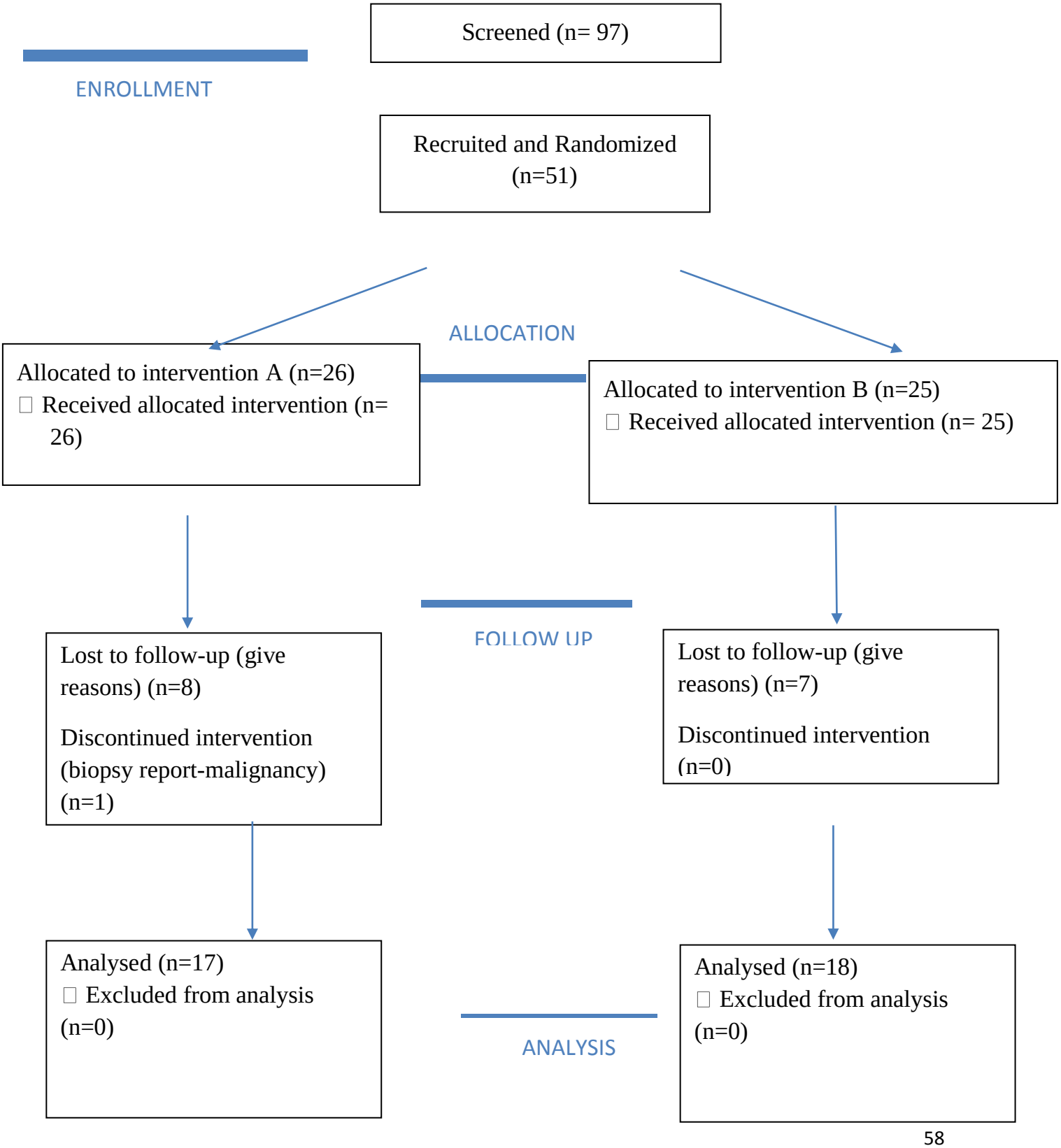
The investigators assessing the parameters were blinded to the randomisation code allotted to the patient. However the patient was not blinded

9. Statistical methods

Data was collected and entered into Microsoft excel worksheet and results were analysed. For normally distributed variables, the descriptive statistics n, Mean, SD was presented. For the categorical data, the number and percentage was presented. The t test was used to find the two group difference. The non-parametric Mann Whitney test was used to find the difference between two groups. All analyses were done using Statistical Package for Social Services (SPSS) software Version 21.0 (Armonk, NY: IBM Corp).

Results

Patient flow:



RECRUITMENT:

a. Period of recruitment and follow-up:

The study was conducted from February 2017 to June 2018

b. Trial ended:

The trial ended as the sample size initially calculated was reached and the period of study was completed.

This study was conducted in the Department of ENT of a Tertiary Teaching hospital in Southern India.

A total of 51 subjects were recruited for the study and were assigned to the two arms of the trial.

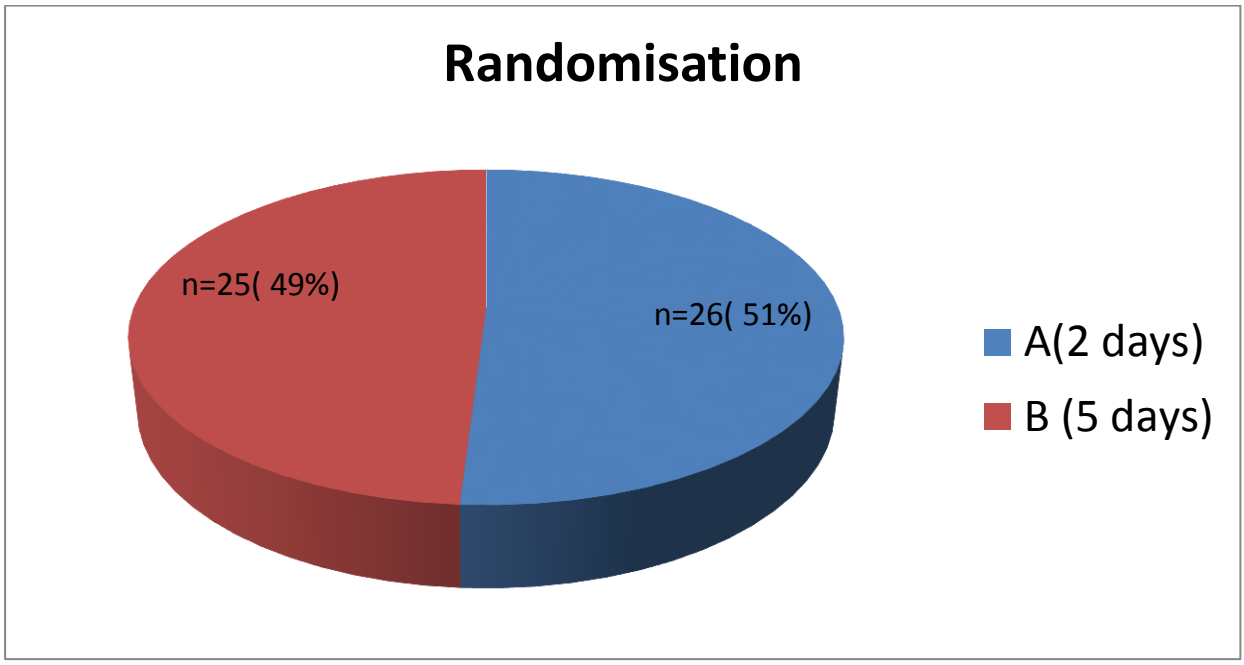


Figure 14: Distribution into the arms of the trial

Lost to follow up and exclusions:

One patient who was diagnosed as benign vocal cord polyp pre operatively and was included in the study, on histopathological evaluation was diagnosed to have a malignant lesion. Hence he was excluded from the study. Among the other 50 participants, 10 could not be contacted over phone for the 6 week follow up. They didn't report for the 3 month follow up also. Another 5 participants who responded to the 6 week follow up , didn't turn up for the 3 month post-operative visit. So the exclusion at 3 month follow up was 16 out of 51 who were randomized.

The major reason for loss of follow up was patient's inability to come to the institution of study from other states.

Harms:

No harms or unintended effects or adverse reactions occurred as a direct consequence of the study.

Baseline Data:

Age distribution

In the group of 51 patients, the minimum age was 19 years and the maximum age was 66 years. The mean age was 41.4.

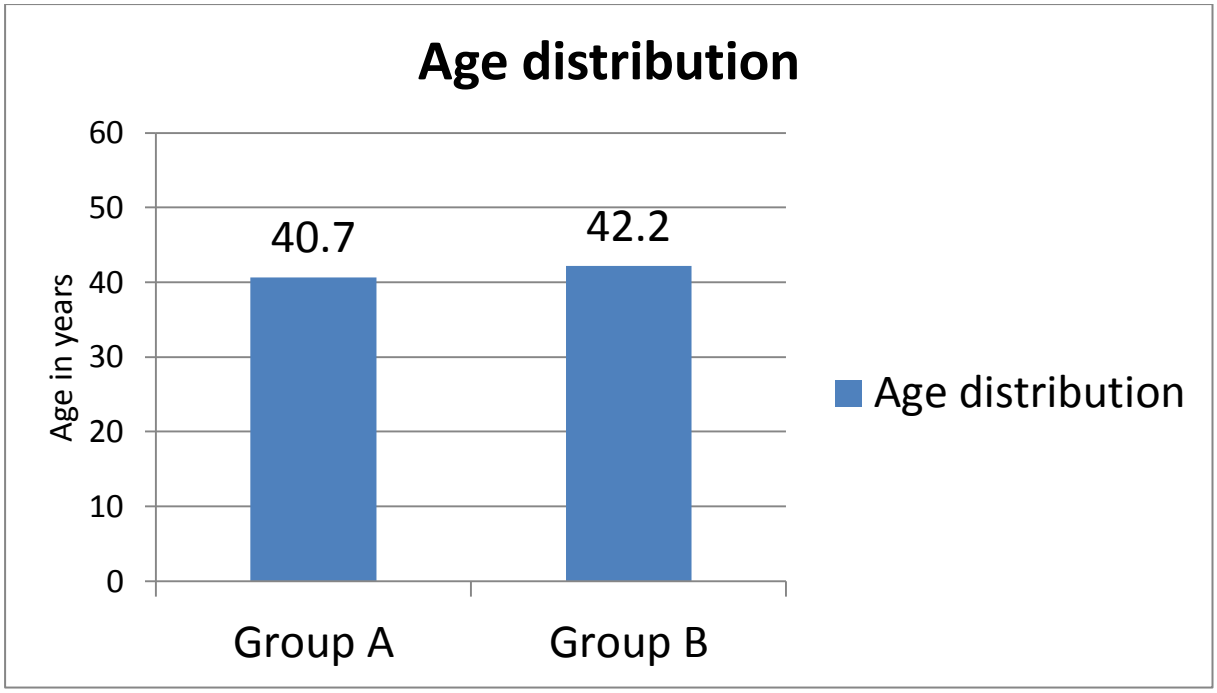


Figure 14: Age distribution across the two arms of the trial

Sex distribution

Among the total 51 patients recruited, there was a male preponderance. (n=45)

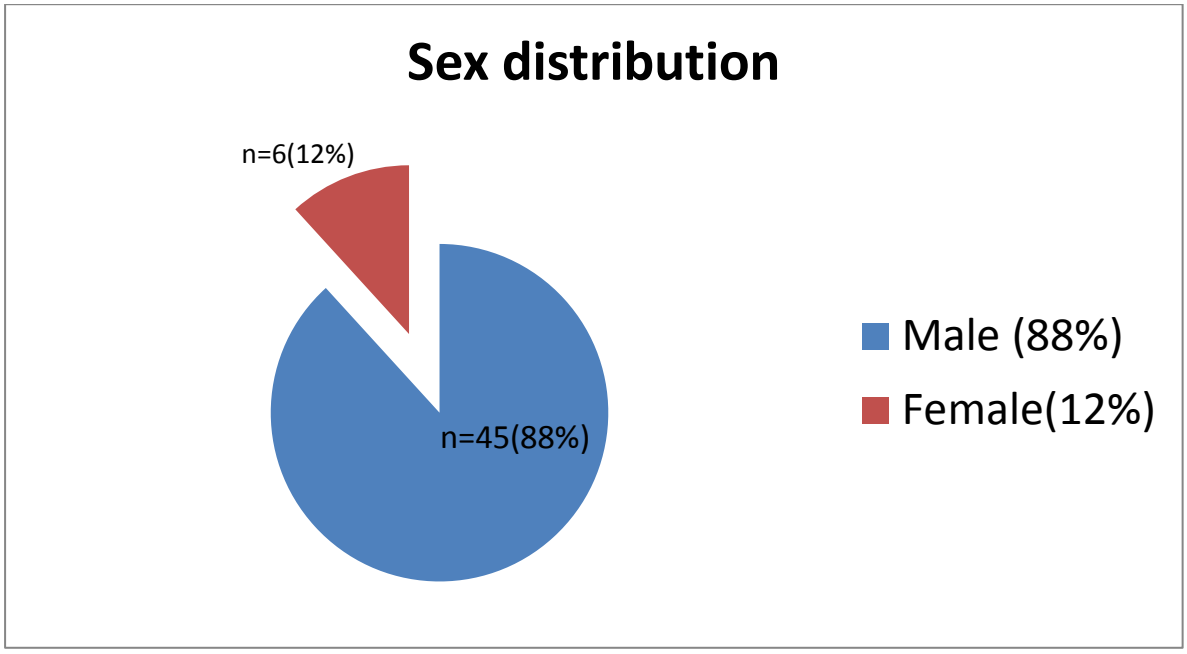


Figure 15: Sex distribution across the study group

Place of Residence

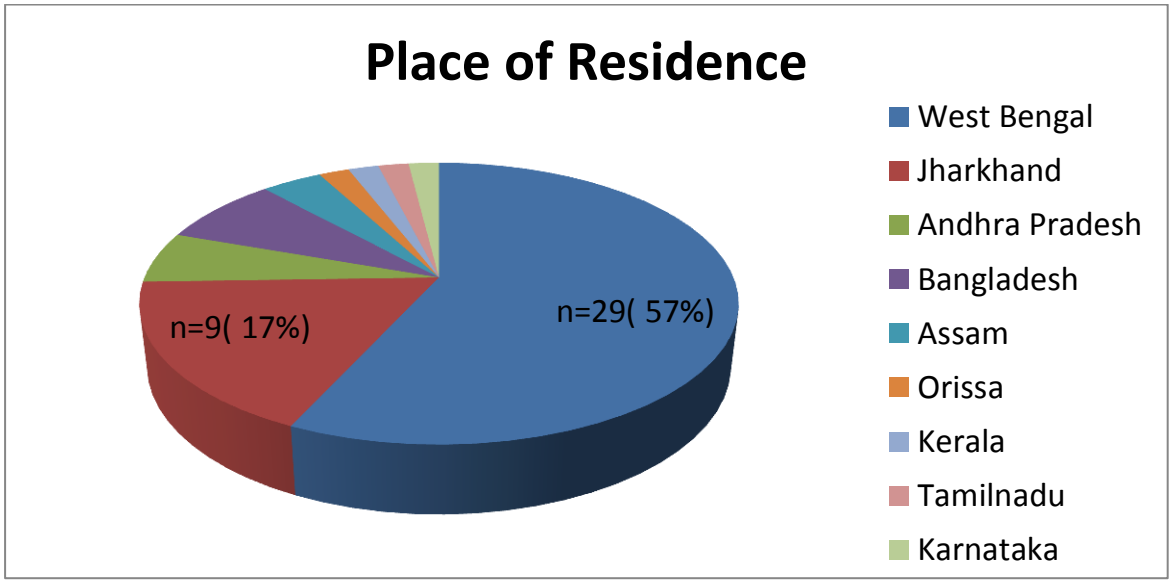


Figure 16: State of residence of participants

Level of Voice use

The recruited patients were categorized according to their voice demands. There were 3 elite voice users (level 1-singers/preachers), 4 professional voice users (level 2 – teachers), 24 non vocal professionals (level 3- doctors, clerks, salesmen) and 20 non vocal non-professionals (level 4- carpenters, masons, drivers).

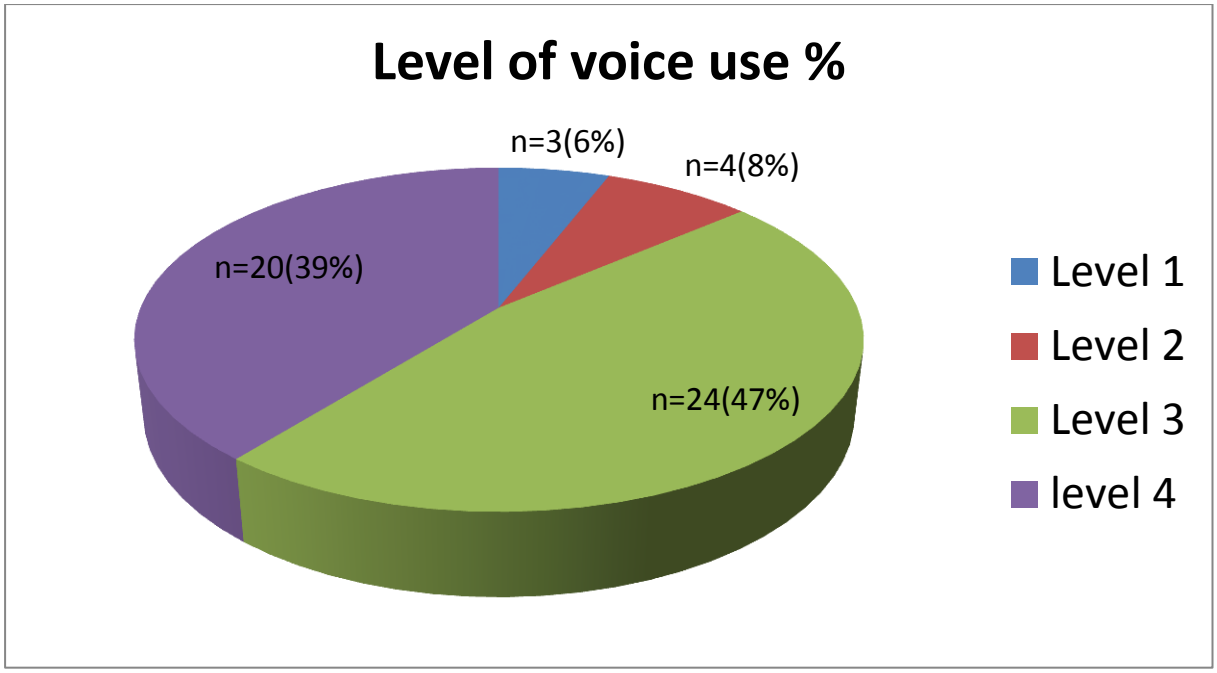


Figure 17: Level of voice use among the study group

Diagnosis

The inclusion criterion of this study was specifically limited to benign lesions of the vocal cord. The different types of lesions which were seen in the subjects recruited were vocal cord polyps and vocal cord cysts. However there was a patient with a suspected vocal cord polyp, which turned out to be a malignant lesion after the histopathological examination.

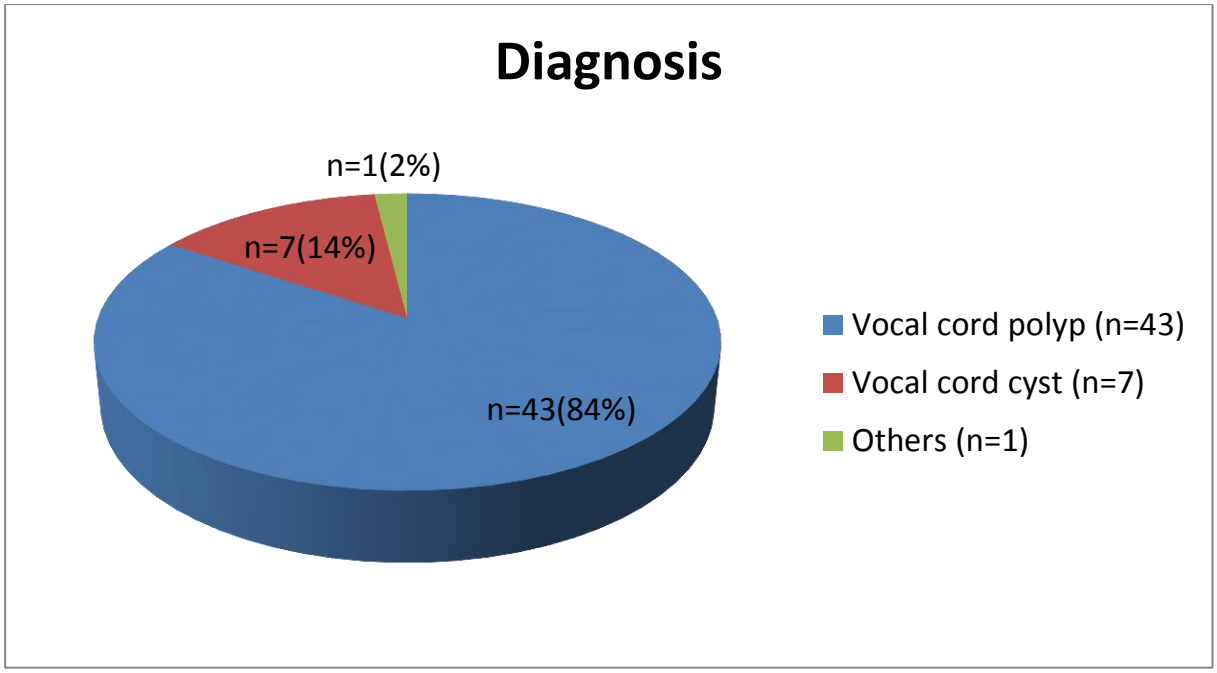


Figure 18: Types of diagnoses among the participants

Side of lesion

Of the 51 lesions assessed, 46 were unilateral and 5 were bilateral lesions

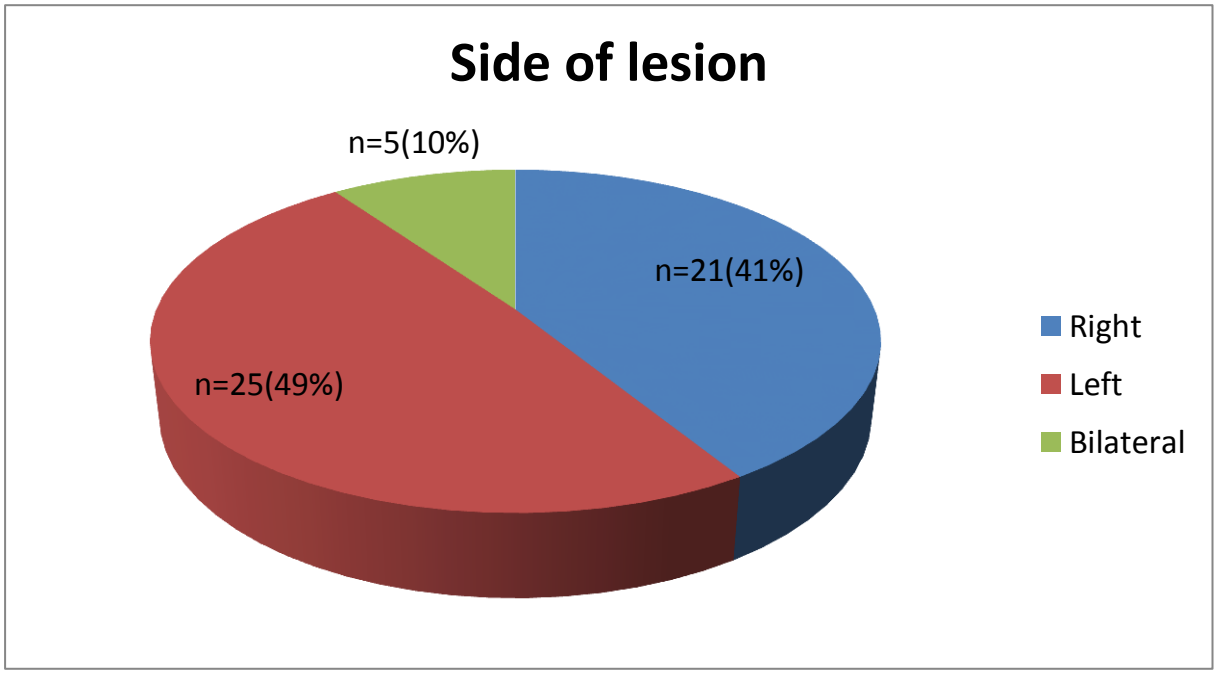


Figure 19: Side of lesion among the participants

The recruited patients underwent micro laryngoscopy and excision of the lesion under general anesthesia. They were advised on periods of absolute voice rest as per the randomization code allotted.

Compliance on voice rest

The compliance on voice rest was assessed using a simple scale

Never – I didn't speak during the time of voice rest

Almost never - I spoke less than 10 times during the period of voice rest

Used voice - I spoke more than 10 times during the period of voice rest

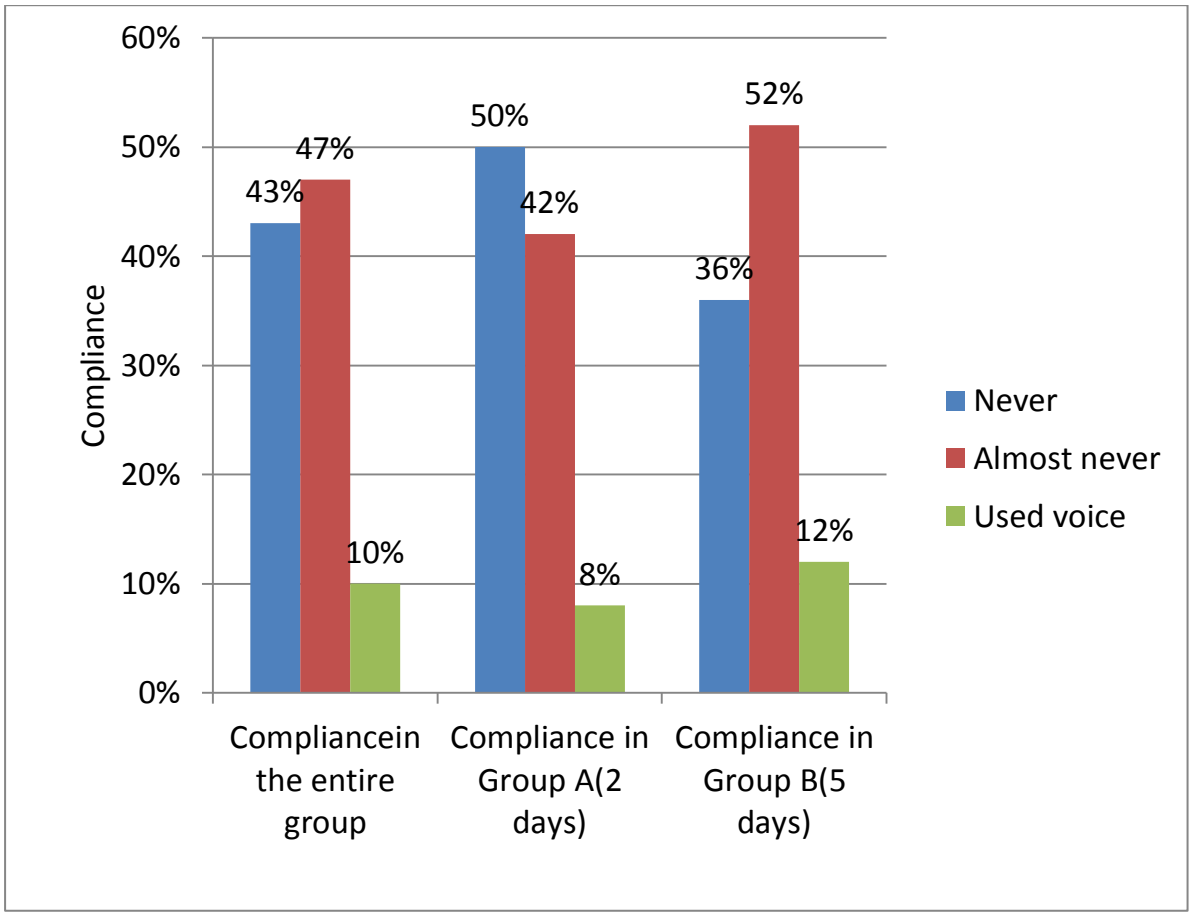


Figure 20: Compliance to advice regarding voice rest.

The compliance to the advice regarding absolute voice rest after surgery was 43%. The shorter voice rest group had a compliance of 50% and the longer voice rest group had 36%. The difference in compliance across the two arms of the study was not statistically significant.

Pre-operative voice evaluation

All the 51 subjects underwent preoperative voice evaluation by the speech pathologist. The parameters assessed were:

-GRBAS scale

-Voice Handicap Index-10

-Jitter

- Shimmer

- s/z ratio

- Harmonics to noise ratio

Table 1: The preoperative baseline data

Parameter	**Group A**		**Group B**		**P value**
	Mean	SD	Mean	SD	
GRBAS	4.8	1.7	5.6	1.6	0.09
VHI-10	12.7	7	15.2	5.1	0.14
Jitter (dB)	1.01	1.03	1.33	1.31	0.34
Shimmer(Hz)	6.45	5.03	6.95	3.57	0.69
s/z ratio	2.35	1.93	2.61	1.73	0.62
Harmonics to noise ratio	15.72	5.8	14.29	5.27	0.37

Of all the 51 patients recruited for the study, we were able to contact 40 patients over phone at 6 weeks after surgery, for a telephonic interview to administer the VHI-10 questionnaire. 35 of them reported to the hospital back for follow up which was scheduled after 3 months.

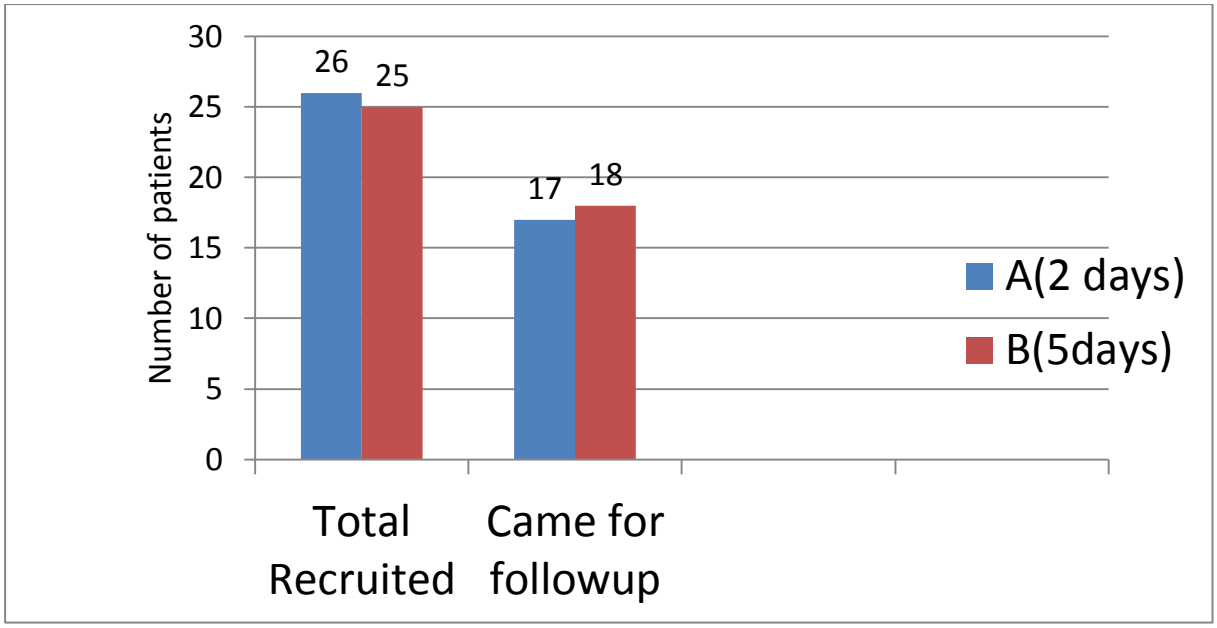


Figure 21: Follow up among the two groups

Mean duration of follow up

The mean duration from the date of surgery to the date of telephonic interview was 6.5 weeks where as for the post-operative visit the mean duration from the date of surgery was 17.9 weeks.

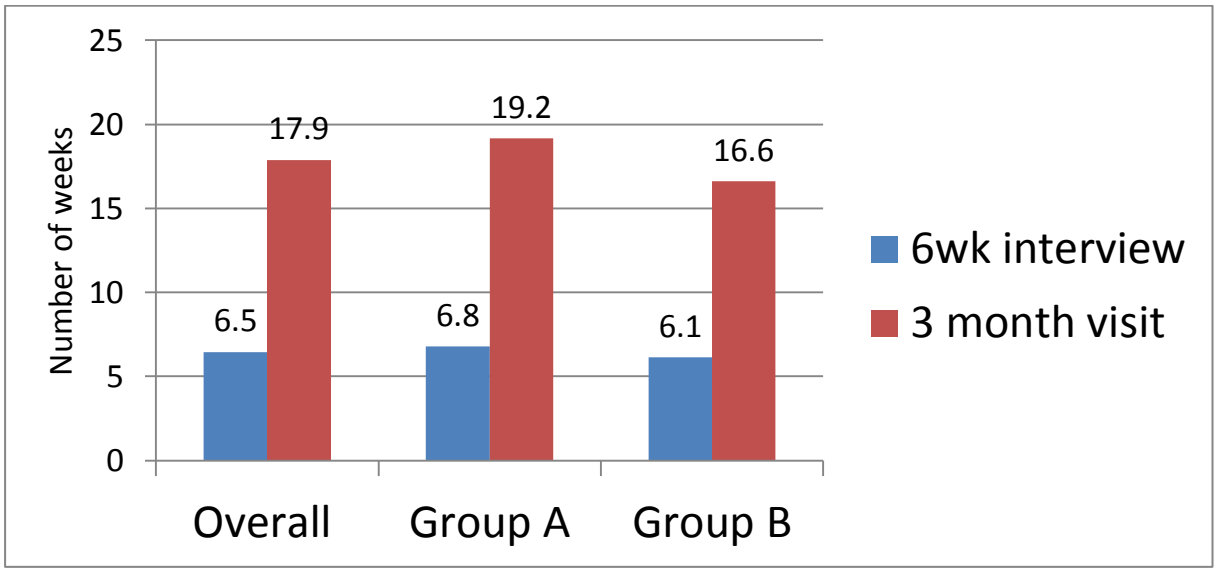


Figure 23: Duration between surgery and follow up

Post-operative voice evaluation

The 35 patients who reported for follow up underwent the same pre-operative evaluation.

Table 2: Post-operative data of voice evaluation

Parameter	**Group A**		**Group B**	
	Mean	SD	Mean	SD
GRBAS	1.17	1.7	1.5	1.58
VHI-10	0.78	1.86	0.39	0.92
Jitter (dB)	0.57	0.72	0.48	0.31
Shimmer(Hz)	2.91	2.08	3.19	2.19
s/z ratio	1.17	0.26	1.20	0.19
Harmonics to noise ratio	21.08	5.47	22.48	4.73

Difference between pre and post op values at 3 months

There was a significant improvement inVHI-10 at 6 wks. The mean improvement in the shorter voice rest group was 10.89, whereas the mean improvement in the longer voice rest group was 15.23. This result was statistically significant.

Table 3: Improvement in VHI 10 scores at 6 weeks follow up

Difference between post op and preop	**Group A**		**Group B**		**P value**
	Mean	SD	Mean	SD	
6 wk VHI - 10	-10.89	6.30	15.23	5.35	**0.022**

Difference between pre and post op values at 3 months

The difference between the preoperative value and the post-operative value was assessed in each of the subjects and comparisons were drawn between both the groups. There was significant improvement in jitter in the longer voice rest group compared to the shorter voice rest group (p=0.017). In the other parameters like GRBAS, VHI-10, shimmer, s/z ratio and harmonics to noise ratio, the longer voice

rest group fared slightly better compared to the shorter voice rest group, but the results were not statistically significant.

Table 4: Difference in the preoperative and post-operative values of voice evaluation (median and interquartile range are used instead of mean and SD as the SD values were more than half of that of mean)

Difference between post op and preop	**Group A**		**Group B**		**P value**
	Median	**IQR**	**Median**	**IQR**	
GRBAS	3.0	(2,5)	3.5	(2.75,6)	0.525
VHI-10	11.5	(5.5,15.0)	14.0	(11.75, 19.25)	0.064
Jitter (dB)	0.13	(0.01,0.45)	0.34	(0.21,1.53)	**0.017**
Shimmer(Hz)	1.91	(0.58,4.24)	2.21	(0.92,6.05)	0.546
s/z ratio	0.49	(0.13,1.55)	0.58	(0.09,2.22)	0.883
Harmonics to noise ratio	4.13	(2.15, 7.71)	7.64	(3.34, 9.73)	0.143

Rate of Improvement

We also calculated the rate of improvement using the formula:

Rate = (Difference between post op and pre-op value)/ Pre-op value x 100

When rate of improvement was analysed, there was no significant difference between the two arms of the study at 6 weeks follow up using VHI-10. At 3 month follow up, the improvement in jitter was significantly better in the longer voice rest group compared to the shorter voice rest group. However the rate of improvement of other parameters assessed were not significantly different.

Table 5: Rate of improvement of voice evaluation parameters across the two arms (median and IQR are used wherever SD is more than half of the value of mean).

Rate of Improvement	**Group A**		**Group B**		**P value**
	Mean	Standard deviation	Mean	Standard deviation	
VHI-10 (6WKS)	88.22	18.37	95.56	7.84	0.143
GRBAS	76.57	35.56	72.36	31.63	0.714
VHI-10 (12WKS)	91.92	18.29	97.32	6.37	0.262

	Median	IQR	Median	IQR	
Jitter (dB)	37.25	(2.28,56.06)	47.08	(29.23,76.84)	**0.038**
Shimmer(Hz)	44.66	(23.21,68.53)	48.29	(20.37,67.77)	0.782
s/z ratio	30.56	(10.95,58.16)	32.47	(8.19,65.81)	1.00
Harmonics to noise ratio	29.84	(17.32,50.41)	61.42	(17.10,81.03)	0.143

Stroboscopic assessment

The stroboscopy videos were graded by 2 evaluators.

1. Glottic closure

Improvement in glottic closure was compared across the groups. When glottic closure was analyzed, we found that the shorter voice rest group fared better compared to the longer voice rest group. But the results were not statistically significant.

Table 6: Improvement in glottic closure

Glottic Closure	Group A	Group B	P value
Rater 1	13/17(76%)	8/15(53%)	0.169
Rater 2	13/16 (81%)	9/15 (60%)	0.193

2. Mucosal wave

Stroboscopy videos were evaluated to assess if the mucosal wave function improved postoperatively. Analysis was done to assess the worsening of mucosal wave function in the two arms of the study. The analysis was done for both the vocal cords separately. We found that the worsening of mucosal wave function was not significant between the two arms of the study.

Table 7: Number of participants with worsening of mucosal wave on right vocal cord

Right VC	Group A	Group B	P value
Rater 1	2/16 (12%)	1/15(6%)	0.58
Rater 2	1/16 (6%)	1/14(7%)	0.92

Table 8: Number of participants with worsening of mucosal wave on left vocal cord

Left VC	Group A	Group B	P value
Rater 1	0/16 (0%)	1/14(7%)	0.46
Rater 2	0/16(0%)	1/14(7%)	0.46

3. Adynamic segments

Preoperative and post-operative stroboscopy videos were compared for favorable outcomes of adynamic segments. Favorable outcomes were resolution of preoperative adynamic segments if any, and non-development of new adynamic segments on the vocal folds postoperatively. Analysis showed that the shorter voice rest group fared slightly better with regard to this parameter, but the results were not statistically significant.

Table 9: Favorable outcomes with regard to adynamic segments on right vocal cord

Right VC	Group A	Group B	P value
Rater 1	13/15 (86%)	10/13 (77%)	0.5
Rater 2	13/16 (81%)	9/13 (69%)	0.45

Table 10: Favorable outcomes with regard to adynamic segments on left vocal cord

Left VC	**Group A**	**Group B**	**P value**
Rater 1	12/16 (75%)	10/13 (77%)	0.9
Rater 2	16/16 (100%)	12/14 (86%)	0.23

4. **Amplitude**

Favorable outcome with regard to amplitude were: improvement from the preoperative amplitude and non-worsening of preoperative amplitude. The results were almost similar across the two arms of the study. There was no difference which was statistically significant.

Table 11: Favorable outcomes with regard to amplitude of right vocal cord

Right VC	**Group A**	**Group B**	**P value**
Rater 1	14/15 (93%)	13/13 (100%)	0.54
Rater 2	13/14 (93%)	13/13 (100%)	0.51

Table 12: Favorable outcomes with regard to amplitude of left vocal cord

Left VC	**Group A**	**Group B**	**P value**
Rater 1	16/16 (100%)	13/13 (100%)	0.9
Rater 2	16/16 (100%)	12/13 (92%)	0.4

5.Symmetry

There was no significant difference between the two arms of the trial with regard to the preoperative and post-operative symmetry of vocal fold motion.

Table 13: Improvement in symmetry of vocal fold motion

Symmetry	**Group A**	**Group B**	**P value**
Rater 1	15/16	15/15	0.51
Rater 2	16/16	14/15	0.46

Discussion

The patients who undergo micro laryngeal surgeries are usually advised absolute or relative voice rest according to the decision of the surgeon. There is a lack of evidence as to the type and duration of voice rest and the modality of voice therapy after micro laryngeal surgeries. We attempted to study the optimal time of initiating voice therapy after micro laryngeal surgery. We decided to look at patients with benign laryngeal pathologies which presented to our department and underwent micro laryngeal surgery. The two arms of the study were 2 days voice rest followed by voice therapy and 5 days voice rest followed by voice therapy.

The age of the participants in our study ranged from 18 to 66 and the mean age was 41.4 years.

The majority of the benign lesions were vocal cord polyps which were similar to a previous study reported from our centre regarding the outcome analysis of benign vocal cord lesions (1).

The majority of our lesions were unilateral which was also comparable to the previous results from the same study.

Interpretation of our results:

We compared the differences among the two groups regarding the various outcome measures. We compared our results with the results obtained by Kaneko etal (1)in their study published in 2016.

GRBAS score

When followed up at 3 months the difference between the mean improvements in the two groups was 0.5. (p=0.525) The mean improvement in GRBAS score in the longer voice rest group was slightly better than that of the shorter voice rest group. This difference was not clinically significant as well. The rate of improvement also didn't show a significant difference between the two groups. Kaneko etal had found that, the shorter voice rest group had a significantly better improvement of GRBAS scores at 1 month postoperatively, but at 3 month and 6 month follow ups, the difference between the groups were not statistically significant.

VHI-10 score

We assessed the VHI-10 score at 6 weeks post operatively and 3 months post operatively. At the 6 weeks follow up the longer voice rest had a significantly better score than the shorter voice rest group (p=0.022). However, when we assessed the rate of improvement, the results were not statistically significant (p=0.143).

At three month post op visit, the VHI scores showed 91% improvement in the shorter voice rest group and 97% improvement in the longer voice rest group. This too was not statistically significant (p=0.262).

The results from the reference study favored the shorter voice rest group at 1 month follow up but at further follow ups at 3 months and 6 months, the difference was not statistically/ clinically significant.

Jitter

When acoustic analysis was done the mean improvement in jitter was 0.13 in shorter voice rest group and 0.34 in longer voice rest group (p=0.017). The rate of improvement was 37.2% in shorter voice rest group and 47% in the longer voice rest group (p=0.038).

The study published by Kaneko etal had shown a benefit in shorter voice rest group in the early post op visit, but at 3 months and 6 months follow ups there was no difference between the 2 groups.

Shimmer

The mean improvement in shimmer at 3 months in the shorter voice rest group (1.91) was not significantly different from that of the longer voice rest group (2.21). The rate of improvement in shorter voice rest group was 44%, whereas in the longer voice rest group it was 48%. This was not statistically significant (p=0.782).

These were comparable to the results of the study by Kaneko etal.

S/Z ratio

The mean improvement in s/z ratio was 0.49 in short voice rest group and 0.58 in long voice rest group. The rate of improvement too wasn't statistically significant (p=1.00).

Harmonics to Noise ratio

The mean improvement in the shorter voice rest group was 4.13 and in the longer voice rest group it was 7.64. The rate of improvement also wasn't statistically significant (p=0.14).

Stroboscopic Assessment

The improvement in stroboscopic parameters didn't show any significant variation when the two arms of the study were compared.

Compliance on voice rest

The compliance to the advice regarding absolute voice rest after surgery was 43%. The shorter voice rest group had a compliance of 50% and the longer voice rest group had 36%. A similar poor compliance for complete or absolute voice rest was also reported by Roussaeu etal (1) when they evaluated the self-reported compliance among their patients and found it to be 35%. In the socio cultural setting of our country, the poor compliance to absolute voice rest is understandable.

Generalizability of our results:

The results of our study pointed that there was duration of post-operative voice rest was not causing a significant difference in the voice outcome after micro laryngeal surgery for benign vocal cord pathologies. The study was done with a sample population including benign vocal cord lesions with a predominance of vocal cord polyp which underwent excision using micro flap techniques which avoid the loss of cover of the vocal fold. Thus the results may be extrapolated to similar lesions undergoing micro laryngeal surgeries.

Limitations:

The study time period was a period of 1 year and 6 months which accounted for a smaller sample size. The follow up period was up to 3 months due to the short study period. Since the participants of the study were from different parts of the country, serial follow ups were not practically feasible. A serial follow up would have helped in identifying differences between the groups with regard to the various parameters assessed; during the early post op period. This same reason has attributed to roughly 20% loss of follow up. There was homogeneity in the study population with regard to the diagnoses and hence the generalizability of these interpretations to other laryngeal lesions is poor.

The technical limitations we identified during our study were

1. Lack of a voice handicap assessment questioned tailored to our population. The VHI-10 questionnaire we used in our study was on many an occasion irrelevant to participants.

2. Lack of an objective assessment of stroboscopy. We lacked a stroboscopy evaluation software and because of this we did a subjective assessment of the stroboscopy videos.

CONCLUSION

- The improvement of voice after micro laryngeal surgery for benign laryngeal lesions is independent of the duration of the post-operative voice rest advised.
- 2 day voice rest before initiating voice therapy produces the same clinical outcome in terms of improvement of voice as compared to a longer duration of voice rest.

Prolonged voice rest after micro laryngeal surgery is difficult to be complied upon. As there was no significant difference between the two groups studied, clinicians might as well prescribe a shorter duration of voice rest and facilitate an earlier initiation of voice therapy after micro laryngeal surgery.

ANNEXURE

Annexure 1: Bibliography

Annexure 2: Proforma

Annexure 3: Consent Form

Annexure 4: Data Sheet

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PROFORMA FOR DATA COLLECTION

IRB NO: 10328/19-10-2016

Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial.

STUDY NO:

UNIQUE ID

RANDOMISATION CODE:

NAME: OCCUPATION:

AGE: | | | Level of voice use: 1/2/3/4

SEX: 1. MALE 2.FEMALE

HOSPITAL NUMBER: | | | | | | | |

PHONE NUMBER: | | | | | | | | | | |

EMAIL ID:

DIAGNOSIS

SIDE:

1. RIGHT
2. LEFT
3. BILATERAL

Clinical Lesion:

1. VOCAL POLYP
2. VOCAL NODULE
3. VOCAL CYST
4. REINKES EDEMA
5. VOCAL CORD GRANULOMA
6. OTHERS

If Others:

PREOPERATIVE EVALUATION: date: | | | | | | | | |

GRBAS	NORMAL	MILDLY ABNORMAL	MODERATELY ABNORMAL	SEVERELY ABNORMAL
GRADE	0	1	2	3
ROUGHNESS	0	1	2	3
BREATHINESS	0	1	2	3
ASTHENIA	0	1	2	3
STRAIN	0	1	2	3
TOTAL				

VOICE HANDICAP INDEX ASSESSED ON: **DATE:** | | | | | | | | |

Question	0	1	2	3	4
My voice makes it difficult for people to hear me.					
People have difficulty understanding me in a noisy room.					
My voice difficulties restrict personal and social life.					
I feel left out of conversations because of my voice					
My voice problem causes me to lose income					
I feel as though I have to strain to produce voice.					
The clarity of my voice is unpredictable.					
My voice problem upsets me.					
My voice makes me feel handicapped.					
People ask, “What’s wrong with your voice?”					

STROBOSCOPY DATED:

Investigator 1

	Right vocal cord	Left vocal cord
Mucosal wave		
Adynamic segments		
Amplitude of vibration		
Glottic closure		
Symmetry		

0= Not assessable, 1= Absent, 2= Reduced, 3=Present (MW, Amplitude)

0=Not assessable, 1= absent, 2= present (adynamic segments, glottic closure, symmetry)

Investigator 2

	Right vocal cord	Left vocal cord
Mucosal wave		
Adynamic segments		
Amplitude of vibration		
Glottic closure		
Symmetry		

0= Not assessable, 1= Absent, 2= Reduced, 3=Present (MW, Amplitude)

0=Not assessable, 1= absent, 2= present (adynamic segments, glottic closure, symmetry)

Acoustic Analysis

Jitter: MAXIMUM PHONATION TIME (s/z ratio):

Shimmer: Harmonics to noise ratio (HNR):

SURGERY:

HISTOPATHOLOGY No:

FINAL DIAGNOSIS:

SIDE:

1. RIGHT
2. LEFT
3. BILATERAL

Lesion:

4. VOCAL POLYP
5. VOCAL NODULE
6. VOCAL CYST
7. REINKES EDEMA
8. VOCAL CORD GRANULOMA
9. OTHERS

If Others:

VOICE REST COMPLIANCE:

DID YOU USE YOUR VOICE DURING YOUR PRESCRIBED PERIOD OF VOICE REST?

0. NEVER [ ]
1. ALMOST NEVER [ ]
2. I USED MY VOICE [ ]

VOICE THERAPY INITIATED ON:

VOICE HANDICAP INDEX-10 at 6 weeks after surgery (mailed over post by the participant)

Question	0	1	2	3	4
My voice makes it difficult for people to hear me.					
People have difficulty understanding me in a noisy room.					
My voice difficulties restrict personal and social life.					
I feel left out of conversations because of my voice					
My voice problem causes me to lose income					
I feel as though I have to strain to produce voice.					

The clarity of my voice is unpredictable.					
My voice problem upsets me.					
My voice makes me feel handicapped.					
People ask, “What’s wrong with your voice?”					

POST OPERATIVE VISIT **DATE**: | | | | | | | | |

GRBAS SCORE

DATE:	NORMAL	MILDLY ABNORMAL	MODERATELY ABNORMAL	SEVERELY ABNORMAL
GRADE	0	1	2	3
ROUGHNESS	0	1	2	3
BREATHINESS	0	1	2	3
ASTHENIA	0	1	2	3
STRAIN	0	1	2	3
TOTAL				

VOICE HANDICAP INDEX-10

Question	0	1	2	3	4
My voice makes it difficult for people to hear me.					
People have difficulty understanding me in a noisy room.					
My voice difficulties restrict personal and social life.					
I feel left out of conversations because of my voice					
My voice problem causes me to lose income					
I feel as though I have to strain to produce voice.					
The clarity of my voice is unpredictable.					
My voice problem upsets me.					
My voice makes me feel handicapped.					
People ask, “What’s wrong with your voice?”					

STROBOSCOPY:

Investigator 1

	Right vocal cord	Left vocal cord
Mucosal wave		
Adynamic segments		
Amplitude of vibration		
Glottic closure		
Symmetry		

0= Not assessable, 1= Absent, 2= Reduced, 3=Present (MW, Amplitude)

0=Not assessable, 1= absent, 2= present (adynamic segments, glottic closure, symmetry)

Investigator 2

	Right vocal cord	Left vocal cord
Mucosal wave		
Adynamic segments		
Amplitude of vibration		
Glottic closure		
Symmetry		

0= Not assessable, 1= Absent, 2= Reduced, 3=Present (MW, Amplitude)

0=Not assessable, 1= absent, 2= present (adynamic segments, glottic closure, symmetry)

Acoustic Analysis

Jitter: MAXIMUM PHONATION TIME (s/z ratio):

Shimmer: Harmonics to noise ratio (HNR):

Informed Consent form to participate in a research study

Study Title: ***Is early initiation of voice therapy after micro laryngeal surgery beneficial? A randomized control trial.***

Study Number: _____

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.[ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

(vi) I am aware of the Audio-visual recording of the Informed Consent. [ ]

(vii) I agree to carry out the instructions told to me regarding voice rest and voice therapy. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/_____

Signatory's Name: _____

Or

Representative: _____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

Serialnumber	studyno	Randomcode	Age	Sex	Occup	Level_voiceuse	Diagnosis	Diag_oth	Side_of_Lesion	Preop_evaluation_date	Pre_GRBAS	Pre_VHI	pre_Jitter
1	1	1	19	2	SINGER	1	1		2	03-03-17	3	29	0.784
2	2	2	36	1	CLERK	3	1		3	25-02-17	5	13	1.985
3	3	2	33	2	HOUSEWIFE	4	1		2	28-02-17	5	14	0.468
4	4	2	44	1	SINGER	1	2		1	25-03-17	6	16	1.829
5	5	1	60	1	FARMER	4	2		2	25-03-17	5	18	0.511
6	6	1	45	1	TEACHER	3	1		2	24-03-17	5	26	1.158
7	7	2	47	1	MANAGER	3	1		2	28-03-17	5	13	0.89
8	8	1	36	1	BUSINESSMAN	3	1		2	28-03-17	5	6	0.755
9	9	2	54	1	CARPENTER	4	1		1	28-03-17	5	21	2.617
10	10	1	31	2	HOUSEWIFE	4	2		2	25-03-17	5	20	0.54
11	11	1	49	1	SUPERVISOR	3	1		1	31-03-17	5	21	0.336
12	12	1	21	1	UNSKILLED LABOUR	4	1		1	31-03-17	5	19	3.456
13	13	2	39	1	TEACHER	2	2		1	31-03-17	3	3	0.733
14	14	2	38	1	LAB ASSISTANT	3	1		2	01-04-17	5	16	0.61
15	15	1	30	1	CIVIL WORK	3	1		1	07-04-17	2	6	0.372
16	16	2	47	1	SKILLEDLABOUR	4	1		1	07-04-17	8	17	0.59
17	17	1	35	1	TEAM LEADER-SALES	3	1		2	04-04-17	3	4	0.338
18	18	2	33	1	BEAUTY PARLOUR	4	1		2	13-04-17	6	20	2.614
19	19	1	48	1	COAL MMMINE WORKER	4	1		2	25-04-17	3	3	0.526
20	20	2	49	1	FARMER	4	1		1	09-05-17	5	17	1.467
21	21	1	49	1	PHARMACY SHOP OWNER	3	1		3	12-05-17	6	12	0.789
22	22	1	32	1	LOTTERY SHOP	3	1		2	06-05-17	5	3	0.72
23	23	2	56	1	ADMINISTRATIVE OFFIC	3	2	RT VC POLY	2	19-05-17	8	11	0.812
24	24	2	50	1	AUTO DRIVER	4	2	RT VC POLY	2	20-05-17	6	19	0.88
25	25	1	44	1	VILLAGE DOCTOR	3	1		2	30-05-17	3	2	0.263
26	26	2	43	1	SALESMAN	3	1		2	03-06-17	7	20	0.915
27	27	1	66	1	NOT WORKINGF	4	1		2	13-06-17	10	15	4.005
28	28	1	36	1	LABOUR CONTRACTOR	3	1		1	09-06-17	7	12	0.639
29	29	1	37	1	COOLIE	4	1		1	02-06-17	7	15	2.084
30	30	2	34	2	ANGANWADI WORKER	2	1		1	20-06-17	3	12	0.559
31	31	2	42	1	DRIVER	4	1		1	27-06-17	6	14	0.852
32	32	2	36	1	COMPUTER OPERATOR	4	1		1	27-10-17	3	22	0.365
33	33	2	44	1	PASTOR	2	1		1	07-07-17	8	16	1.173
34	34	2	47	1	SONG TEACHER	1	1		2	11-07-17	4	14	0.34
35	35	1	55	1	FARMER`	4	1		1	27-06-17	4	11	1.036
36	36	1	33	1	LABOUR	4	1		1	14-07-17	5	9	0.246
37	37	1	57	1	SUPERVISOR	3	1		2	04-07-17	6	15	0.844
38	38	2	44	1	LEATHERBAG MAKER	3	1		3	07-07-17	5	19	1.432
39	39	2	36	2	HOUSEWIFE	4	1		1	21-07-17	5	19	1.678
40	40	1	40	1	WORSHIP LEADER	2	1		1	25-07-17		13	
41	41	2	45	1	OFFICE JOB	3	4	CA GLOTTIS	2	27-06-17	7	7	0.307
42	42	1	27	1	DRIVER	3	1		1	04-08-17	5	14	0.645
43	43	2	41	1	CRUSHER OWNER	4	1		2	04-08-17	5	26	0.909
44	44	1	44	1	GOLDSMITH	3	1		2	24-10-17	5	16	0.502
45	46	1	37	1	TAILOR	3	1		1	12-09-17	3	8	0.333
46	47	2	52	2	HOUSEWIFE	4	2		2	22-09-17	6	10	1.975
47	48	2	36	1	PANCHAYAT OFFICER	3	1		2	29-09-17	6	8	0.513
48	49	1	41	1	CHEF	3	1		1	19-09-17	5	13	0.988
49	50	2	29	1	BANK STAFF	3	1		3	03-11-17	9	14	6.728
50	51	1	42	1	BUS CONDUCTOR	3	1		3	03-11-17	6	15	3.124
51	52	1	43	1	STEEL DUST COLLECTOR	4	1		1	31-10-17	3	5	0.231

Pre_Shimmer	S	Z	pre_sz_ratio	Pre_HNR	surgerydate	Compliance_voicerest	sixweek_followup	6weeks_VHI	Postopvisit_date	Post_GRBAS	post_VHI
3.802	12	5	2.4	17.021	04-03-17	0	20-04-17	4	27-06-17	0	0
10.981	10	3	3.333333333	11.626	06-03-17	1	20-04-17	0	20-06-17	3	0
3.67	11	4	2.75	15.578	07-03-17	0					
7.169	14	7	2	12.245	27-03-17	0	08-05-17	0	05-07-17	3	0
8.506	7	3	2.333333333	12.786	27-03-17	0	20-05-17	0	04-07-17	0	0
10.311	9	9	1	15.851	27-03-17	2					
4.31	11	7	1.571428571	18.413	29-03-17	1	15-05-17	1	04-07-17	0	0
2.893	15	8	1.875	15.076	29-03-17	1					
14.433	15	3	5	7.151	29-03-17	1	15-05-17	0	22-08-17	0	0
6.009	9	6	1.5	17.694	03-04-17	0	15-05-17	8	29-12-17	3	7
11.593	10	2	5	11.248	03-04-17	1	15-05-17	1	30-06-17	0	0
18.765	7	5	1.4	7.287	03-04-17	0					
4.769	12	10	1.2	17.457	03-04-17	0	15-05-17	0	07-07-17	0	0
3.82	14	14	1	14.739	03-04-17	0	15-05-17	0	07-07-17	3	0
4.139	12	11	1.090909091	19.162	07-04-17	0	25-05-17	1	28-07-17	0	0
11.659	7	2	3.5	9.498	10-04-17	0	25-05-17	2	28-07-17	0	0
2.172	18	12	1.5	23.804	10-04-17	1	25-05-17	0	08-08-17	0	0
8.579	12	5	2.4	8.597	17-04-17	1	01-06-17	1	18-07-17	3	0
5.529	10	4	2.5	21.008	26-04-17	0	15-06-17	2	24-11-17	3	2
8.138	8	2	4	11.903	10-05-17	1					
14.581	9	7	1.285714286	6.644	15-05-17	0	10-07-17	0	06-01-18	0	0
3.178	13	10	1.3	18.056	17-05-17	1	01-07-17	0	22-08-17	0	0
6.288	9	4	2.25	15.157	20-05-17	1					
10.395	4	4	1	7.912	22-05-17	2	01-07-17	0			
0.992	8	5	1.6	27.23	31-05-17	1	15-07-17	0	05-09-17	0	0
4.423	8	4	2	10.681	05-06-17	1	20-07-17	0	05-09-17	0	0
18.981	7	2	3.5	2.131	14-06-17	1	10-08-17	0	01-12-17	3	0
5.575	10	1	10	11.1	14-06-17	1	15-08-17	0	29-11-17	0	0
9.642	9	2	4.5	13.544	14-06-17	1	01-08-17	0			
4.072	12	2	6	23.039	26-06-17	1	15-08-17	0	23-09-17	0	0
6.189	11	7	1.571428571	15.522	28-06-17	2	20-08-17	4	30-01-18	0	3
3.192	8	8	1	26.408	02-11-17	1	20-12-17	0	20-02-18	3	0
6.437	11	7	1.571428571	9.193	10-07-17	1	20-08-17	2	20-02-18	3	2
1.659	11	9	1.222222222	24.8	12-07-17	0	20-08-17	0	24-10-17	0	0
3.136	15	11	1.363636364	13.861	17-07-17	2	01-09-17	2	17-10-17	3	1
1.861	15	10	1.5	21.07	17-07-17	1	10-09-17	0	27-10-17	0	0
6.714	20	17	1.176470588	16.023	19-07-17	0	10-09-17	2	14-11-17	3	0
9.766	10	8	1.25	13.936	19-07-17	1	10-09-17	0	14-11-17	2	0
6.494	7	3	2.333333333	16.413	26-07-17	0	10-09-17	0			
					26-07-17	0	15-09-17	0	29-12-17		0
9.212	11	3	3.666666667	13.613	07-08-17	1					
3.178	9	6	1.5	17.469	07-08-17	0					
7.636	14	7	2	9.227	09-08-17	2	25-09-17	0			
4.666	7	2	3.5	10.941	01-11-17	0					
1.484	1	1	1	21.458	19-09-17	1	02-12-17	0	12-01-18	0	0
14.625	8	1	8	8.862	27-09-17	0	02-12-17	0	20-03-18	4	0
2.661	10	9	1.111111111	20.556	05-10-17	0	20-11-17	0	09-01-18	0	0
5.919	19	7	2.714285714	18.591	09-10-17	1					
3.172	7	2	3.5	14.648	06-11-17	1	20-12-17	2	13-02-18	3	2
5.814	15	7	2.142857143	11.321	06-11-17	0	20-12-17	4	13-02-18	5	4
1.92	10	10	1	22.546	06-11-17	0					

post_jitter	post_shimmer	S2	z2	post_sz_ratio	post_hnr	one_pre_ mucosalw averight	two_pre_ mucosalw averight	one_Pre_ adynamic _right	two_Pre_ adynamic _right	one_pre_ glotticclos	two_pre_ glotticclos ure	one_pre_ ampRt	two_pre_ ampRt	one_pre_ symmetry	two_pre_ symmetry	one_pre_ mucosalw aveLt
0.355	1.885	16	11	1.454545455	22.688	2	3	2	1	1	1	3	3	2	2	3
0.375	1.781	14	12	1.166666667	21.958	3	3	2	2	1	1	3	3	1	2	1
0.33	2.037	21	16	1.3125	21.847	3	3	2	2	1	1	3	0	1	2	3
0.409	3.041	13	13	1	21.205	3	3	2	2	1	1	3	3	1	1	3
0.61	4.003	14	10	1.4	22.012	3	3	2	1	1	1	3	3	1	1	1
0.817	7.461	15	12	1.25	12.248	0	0	0	0	0	0	0	0	0	0	0
0.6	5.819	9	6	1.5	18.841	3	3	1	1	1	1	3	3	2	2	3
0.311	8.593	11	8	1.375	13.348	3	3	2	2	1	1	3	3	1	2	3
0.512	3.814	14	12	1.166666667	18.214	3	3	1	1	1	1	3	3	2	2	3
0.352	1.976	12	12	1	23.082	3	3	2	1	1	1	3	3	2	2	3
0.419	1.744	12	12	1	22.583	3	3	2	1	1	1	3	3	2	2	3
0.226	1.729	20	18	1.111111111	28.672	3	3	1	1	1	1	3	3	2	2	3
0.212	2.11	18	18	1	27.8	3	3	2	1	1	1	3	1	2	2	3
0.305	1.636	22	18	1.222222222	28.879	3	3	1	1	1	1	3	3	1	2	3
0.224	1.11	8	11	0.727272727	27.365	3	3	1	1	1	1	3	3	2	2	3
0.282	3.814	10	9	1.111111111	15.84	3	3	1	1	1	1	3	3	2	2	3
0.247	1.479	12	12	1	24.369	3	3	2	1	1	1	3	3	2	2	3
0.218	0.549	10	9	1.111111111	29.43	3	3	1	1	1	1	3	3	2	2	3
0.721	2.121	10	10	1	18.241	3	3	0	0	1	1	0	0	2	2	3
1.209	4.576	10	7	1.428571429	14.933	0	0	0	0	1	0	0	0	0	0	0
0.401	1.518	22	15	1.466666667	20.376	2	2	1	1	1	1	3	2	2	2	3
0.319	3.238	13	11	1.181818182	23.538	2	3	1	1	1	1	3	3	2	2	3
0.722	4.144	10	8	1.25	23.242	2	2	1	1	1	1	3	3	2	2	3
0.207	1.084	10	9	1.111111111	28.986	2	2	2	2	1	1	3	3	2	2	3
0.576	2.157	12	11	1.090909091	19.008	0	0	0	0	0	0	0	0	0	0	0
0.274	1.354	17	12	1.416666667	26.023	3	3	1	1	1	1	3	3	2	2	2
0.552	2.07	7	5	1.4	17.998	1	1	0	2	1	1	0	0	2	2	3
0.186	1.135	15	14	1.071428571	28.072	3	3	1	1	1	1	3	3	2	2	3
0.5	3.8	10	13	0.769230769	14.668	3	1	1	2	1	1	3	0	2	2	2
0.352	5.647	12	12	1	20.453	2	3	1	1	1	1	3	3	2	2	2
0.375	1.675	14	14	1	25.488	3	3	1	1	1	1	3	3	2	1	3
1.452	8.865	15	12	1.25	15.544	3	3	1	1	1	1	3	3	2	2	3
0.184	1.281	12	12	1	28.321	0	0	0	0	0	0	0	0	0	0	0
0.232	3.052	14	8	1.75	24.351	2	2	1	2	1	1	3	3	2	2	2
3.214	4.62	15	10	1.5	13.384	3	3	1	2	1	1	3	3	2	2	2

two_pre_mucosalwaveLt	one_pre_adynamicleft	two_pre_adynamicleft	one_pre_ampLt	two_pre_ampLt	one_post_mucosal_wave_right	two_post_mucosal_wave_right	one_post_adynamic_right	two_post_adynamic_right	one_post_glottticclosure	two_post_glottticclosure	one_post_amplitude_right	two_post_amplitude_right	one_post_symmetry	two_post_symmetry	one_post_mucosalwave_left	two_post_mucosalwave_left	one_post_adynamic_left	two_post_adynamic_left	one_post_amplitude_left	two_post_amplitude_left
1	1	1	3	3	3	3	2	1	2	2	3	3	2	2	3	3	1	1	3	3
3	2	2	1	3	3	1	2	2	1	1	3	3	2	2	3	3	2	1	3	3
3	2	2	3	3	0	0	0	0	1	1	0	0	2	2	0	0	0	0	0	0
3	1	1	3	3	3	3	2	2	2	2	1	3	1	2	3	3	1	1	3	3
1	2	2	1	1	3	3	1	2	1	1	3	3	2	2	3	3	1	1	3	3
0	0	0	0	0	3	3	1	1	1	1	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	1	1	3	2	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	2	3	3	3	3	1	1	2	2	3	3	2	2	3	3	2	1	3	3
3	2	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	2	1	3	3
3	1	1	3	3	3	3	2	1	1	1	3	3	2	2	3	3	2	2	3	3
3	1	2	3	3	3	3	1	2	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	1	3	3	3	1	1	2	2	3	3	2	1	3	3	1	1	3	2
3	1	1	3	3	3	3	1	1	1	2	3	3	2	2	3	3	2	1	3	3
3	1	1	3	2	3	3	1	1	2	2	3	3	2	2	3	3	2	1	3	3
3	1	1	1	2	3	3	1	1	2	2	3	3	2	2	3	3	2	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	0	1	0	0	3	3	1	1	2	2	3	3	2	2	3	3	0	1	0	0
0	0	0	0	0	3	3	2	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	2	1	1	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	2	1	1	3	3	2	2	3	3	1	1	3	3
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	1	3	2	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	2	1	1	1	1	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
3	1	1	3	3	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
0	0	0	0	0	3	3	1	1	2	2	3	3	2	2	3	3	1	1	3	3
2	1	2	3	3	2	3	1	2	1	1	3	3	2	2	2	2	1	2	3	3
3	1	2	3	3	2	2	1	2	1	1	3	3	2	2	3	3	1	1	3	3