DEVELOPMENT OF BAHASA MALAYSIA REFLUX SYMPTOM INDEX (M-RSI)

BY

DR NIK MOHD YUNUS MOHAMMAD

Dissertation Submitted in Partial Fullfillment Of The Degree of Master of Medicine

(Otorhinolaryngology –Head and Neck Surgery)

UNIVERSITI SAINS MALAYSIA

2015

Title page

DEVELOPMENT OF BAHASA MALAYSIA REFLUX SYMPTOM INDEX (M-RSI)

Corresponding author

Nik Mohd Yunus**,**

Senior Medical Officer,

Department of Otorhinolaryngology–Head & Neck Surgery,

School of Medical Sciences, Universiti Sains Malaysia,

16150 Kota Bharu, Kelantan,

Malaysia.

Email: m_kodro@yahoo.com

Author 2

Baharudin Abdullah

Lecturer,

Department of Otorhinolaryngology–Head & Neck Surgery,

School of Medical Sciences, Universiti Sains Malaysia,

16150 Kota Bharu, Kelantan,

Malaysia.

Postal address: Department of Otorhinolaryngology–Head & Neck Surgery,

School of Medical Sciences, Universiti Sains Malaysia,

16150 Kota Bharu, Kelantan,

Malaysia.

Author 3

Nik Fariza Husna

Lecturer,

Department of Otorhinolaryngology–Head & Neck Surgery,

School of Medical Sciences, Universiti Sains Malaysia,

16150 Kota Bharu, Kelantan,

Author 4

Lee Yeong Yeh

Lecturer,

Department of Medicine,

School of Medical Sciences, Universiti Sains Malaysia,

16150 Kota Bharu, Kelantan

TABLE OF CONTENTS

LIST OF TABLES Page

LIST OF FIGURES Page

LIST OF ABBREVIATION

M-RSI - Bahasa Malaysia Reflux Symptoms Index

RSI - Reflux Symptoms Index

LPR - Laryngopharyngeal Reflux

ORL-HNS - Otorhinolaryngology Head and Neck

HUSM - Hospital Universiti Sains Malaysia

RFS - Reflux Finding Score

ICC - Intraclass Correlation

GERD - Gastroesophageal Reflux Disease

LES - Lower Esophageal Sphincter

UES - Upper Esophageal Sphincter

GORD - Gastrooesophageal Reflux Disease Score

GSAS - Gastrooesophageal Assessemnt Scale

SERQ - Supraesophageal Reflux Questionnaire

MCII - Multichannel Intraluminal Impedence

EORTC - European Organization for Research and Treatment

EFA - Explatory Factor Analysis

ABSTRACT

Introduction : Reflux Symptom Index (RSI), is a nine-item self-administer questionnaire, functioned to help clinician to assess the relative degree of Laryngopharyngeal Reflux (LPR) symptoms during initial evaluation and outcome after treatment.

Objective : The purpose of this study was to develop a Malay version of the RSI (M-RSI) and to evaluate its validity, concistency and reliability in normal Malaysia population with suspected LPR.

Materials and methods : This is a prospective study involving a total of 84 patients presenting to otorhinology and head and neck (ORL-HNS) clinic. It was carried out at Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan. The developed Malaysian RSI (M-RSI) was administered to 50 patients with suspected LPR. Internal consistency and test-retest reliability were evaluated. Then, two group which consists of 17 patients with LPR and other 17 participants from control group were recruited to undergo the M-RSI questionnaire answering session, laryngeal examination and insertion of the 24 hours ambulatory pH monitoring. This is to test the validity of the M-RSI questionnaire by comparing with other tools for diagnosis of LPR including reflux finding score (RFS) by laryngeal examination and oropharnygeal pH monitoring.

Results : The Malaysian M-RSI showed satisfactory internal consistency (Cronbach's α = 0.60). Test-retest reliability was assessed using intraclass correlation coefficient (ICC). Intraclass Correlation Coefficient is 0.727 which is a good correlation between pre and post assessment. Spearman Rank correlation coefficient is applied to determine the correlation between the total M-RSI with total RFS, Ryan score upright and Ryan score supine. Significant correlation is demonstrated between total M-RSI and total RFS ($r = 0.80$, $p<0.001$).

Conclusion: This study shows that Malaysian M-RSI is easily administered, highly reproducible and demonstrates good clinical validity. It is a valid tool for self-assessment of LPR that can be used by Malaysian population.

ABSTRAK

Pengenalan: Reflux Gejala Index (RSI), adalah sembilan item diri pentadbir-selidik, berfungsi untuk membantu doktor menilai tahap relatif Laryngopharyngeal Reflux (LPR) gejala semasa penilaian awal dan hasil selepas rawatan.

Objektif: Tujuan kajian ini adalah untuk menghasilkan satu versi Bahasa Malaysia RSI

(M-RSI) dan untuk menilai kesahihannya, konsistensi dan kebolehpercayaan di kalangan penduduk Malaysia yang mengidapi masalah penyakit LPR.

Bahan dan kaedah: Ini adalah kajian prospektif yang melibatkan sejumlah 84 pesakit yang datang ke otorhinology dan kepala dan leher klinik (ORL-HNS). Ia dilakukan di Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan. RSI Malaysia (M-RSI) yang terhasil telah diberikan kepada 50 pesakit yang disyaki LPR. Ketekalan dalaman dan kebolehpercayaan ujian-ujian semula telah dinilai. Kemudian, dua kumpulan yang terdiri daripada 17 pesakit dengan LPR dan lain-lain 17 peserta dari kumpulan kawalan telah diambil untuk menjalani soal selidik M-RSI sesi, pemeriksaan laring dan penyisipan 24 jam ambulatori pemantauan pH menjawab. Ini adalah untuk menguji kesahihan soal selidik M-RSI dengan membandingkan dengan alat-alat lain untuk diagnosis LPR termasuk ‘Reflux Finding Score’ (RFS) dengan pemeriksaan laring dan pemantauan pH oropharnygeal

Hasil: Malaysia M-RSI menunjukkan ketekalan dalaman yang memuaskan (α Cronbach = 0.60). Kebolehpercayaan ujian-ujian semula dinilai dengan menggunakan pekali 'Intraclass correlation' (ICC). 'Intraclass correlation'(ICC) adalah 0.727 iaitu korelasi yang baik antara penilaian sebelum dan selepas soal selidik. 'Spearman Rank correlation' digunakan untuk menentukan hubungan di antara jumlah M-RSI dengan jumlah RFS, 'Ryan score upright' dan 'Ryan score supine'. Hubungan yang signifikan ditunjukkan antara jumlah M-RSI dan jumlah RFS ($r = 0.80$, $p < 0.001$)

Kesimpulan: Kajian ini menunjukkan bahawa Malaysia M-RSI mudah diberikan, sangat direproduksi dan menunjukkan kesahihan klinikal yang baik. Ini adalah alat yang sah untuk penilaian diri dari LPR yang boleh digunakan oleh penduduk Malaysia.

ACKNOWLEDGEMENT

First and foremost, i would like to thank my supervisors, Assoc. Prof. Baharudin Abdullah, Dr Nik Fariza Husna, Dr Lee Yeong Yeh for their continous support, motivation and guidance to make my study become reality.

My sincere thanks to Dr Wan Nor Arifin from the Biostatistics Unit, HUSM for his help and guidance along the course of my study.

Not to forget Puan Zuraihan Zakaria and Siti Aishah Meor from the Language department HUSM for their participation in the translation procedure.

For the staff in ORL-HNS clinic, Ms Ong and other staffs in Endoscopy Unit HUSM, thank you very much for your support.

Finally i would like to take this opportunity to thank my beloved family who had always supported and encouraged me in all my undertakings.

Last but not least, my deepest gratitude to Allah S.W.T for helping me complete this study.

Thank you.

1.0 INTRODUCTION

1.1 INTRODUCTION TO LARYNGOPHARYNGEAL REFLUX

Laryngopharyngeal reflux(LPR) is a common condition seen by otolaryngologist. This disorder account for almost 10% of patient who present to otolaryngologist office (Koufman, 1991). LPR is considered the most common extraesophageal manifestation of gastro esophageal reflux disease (GERD). It is a gastrointestinal and otolaryngological condition related but distinct from GERD, thus it appears as a different clinical variant of GERD.

LPR is defined as a retrograde flow of gastric contents into laryngopharynx where it comes in contact with tissue of upper aerodigestrive tract (Ford, 2005). This reflux of gastric content will cause damage to laryngeal mucosal tissues. The reflux may consist of liquid, gas or both and its pH may cover a wide range from highly acidic to neutral. Inflammation of laryngeal tissue will cause localized symptom. These localized symptoms such as chronic cough, hoarseness, throat clearing was previously considered as atypical manifestation of GERD until further studies done showed that it is a diagnosis of its own (Karkos, Thomas, Temple, & Issing, 2005). Previously other synonyms which have been used are supraesophageal GERD, atypical GERD, and extraesophageal complications of GERD. However, currently LPR appears to be the most appropriate term (Handa, 2005).

Many laryngeal disorders such as subglottic stenosis, laryngeal carcinoma, contact ulcer, granuloma, vocal nodules and arytenoids fixation has been associated with LPR (Little, Koufman & Kohut, 1985), (Morrison 1988). Inflammed laryngeal

tissues are more easily damaged from intubation, have a greater risk of progressing to formation of contact granuloma or subglottic stenosis (Maronian et al,2001). LPR symptoms were found to be more prevalent in patients with esophageal adenocarcinoma (Reavis et al, 2004). It has been reported that 50% of patients with hoarseness have been found to be reflux related disease (Koufman, 1991). In a prospective study carried out in 2000 on 113 patients with voice disorder, Koufman et al (2001) estimated that 50% of these patient had LPR, documented by pH-metry. Symptoms of reflux are common with 25-40% of British population having heartburn and indigestion on a weekly basis (Issing and Karkos, 2003). Failure to recognize LPR would lead to prolong symptoms and delayed healing. It is claimed that the expenditure of proton pump inhibitors accounts for 10% of United Kingdom(UK) annual £4.5 billion drug costs which results in the single biggest item of UK National Health Service expenditure (Choudhry, Soran & Ziglam, 2008). Paul et al (2006) reported that 20% of the Asian population have LPR.

There are many studies conducted in relation to LPR. Basically the studies done involves many aspect which either covers the aspect of diagnosing LPR as a different entity from GERD, tools or instrument in diagnosing LPR, correlation between LPR and other condition such as asthma, obstructive sleep apnoea and many more. There is one study done in Malaysia and from the study, they were able to suggest that intensive empirical therapy with proton pump inhibitor is effective in diagnosing Laryngopharyngeal Reflux (Masaany , 2011). This study had applied the validated assessment instrument, the Reflux Symptoms Index (RSI) and Reflux Finding Score (RFS) as a choice of diagnostic tool for LPR. Although there are many issues and

controversies surrounding both subjective tools of measurement but to date it is still the recognized and accepted method for clinical diagnosis of LPR.

1.2 ANATOMY OF PHARYNX, LARYNX AND ESOPHAGUS

Regarding the anatomy, the structures related to this condition would be pharynx, larynx and esophagus. Pharynx is a conical fibromuscular tube forming one part of upper aerodigestrive tract. It is 12-14 cm long extending from base of skull to the lower border of cricoids cartilage where it becomes continous with the esophagus. It has wide communication with the nose, mouth and larynx thus it is descriptively divided into three parts, nasopharynx, oropharynx and laryngopharynx (Sinnatamby, 2006). However the one area that we are concerned of is the laryngopharynx. The laryngopharynx extends from the upper border of the epiglottis to the level of cricoids cartilage (C6 vertebra) where it becomes continous with the esophagus. In the upper part of the anterior aspect is the opening into the laryngeal inlet. Below the inlet, the lower part of pharynx is clinically referred as hypopharynx, which possesses an anterior wall, comprising of arytenoids and lamina of cricoids cartilage. The posterior wall of laryngopharynx is formed by the three overlapping constrictors down to the level of the vocal folds (upper border of cricoids lamina). Below this, behind the cricoids lamina, there is only inferior constrictor muscle and finally cricopharyngeal sphincter (upper esophageal sphincter) (Sinnatamby, 2006)

The larynx is situated in between the pharynx and the upper end of the trachea. It lays opposite the third to sixth cervical vertebrae. There are many functions of the larynx. It is involved in phonation, respiration and also to provide a protective sphincter against food passages during swallowing. The skeletal framework of the larynx is formed by cartilages, which are connected by ligaments and membranes and are moved in relation to one another by both intrinsic and extrinsic muscles. It is lined with mucous membrane which is continuous with the pharynx and trachea. It is closely attached over the posterior surface of the epiglottis, over the corniculate and cuneiform cartilages and over vocal ligament. Elsewhere it is loosely attached and therefore liable to become swollen. Epithelium of the mucous membrane is ciliated columnar except over the vocal folds, upper part of aryepiglottic folds, posterior commisure and upper half of the posterior surface of the epiglottis which are covered by squamous epithelium. Laryngeal inlet is an oblique opening bounded anteriorly by free margin of epiglottis, on the sides by aryepiglottic folds and posteriorly by interarytenoid folds. Ventricle is a deep elliptical space between vestibular and vocal folds whereas the vestibule extends from the laryngeal inlet to vestibular fold. Larynx can also be subdivided into supraglottis, glottis and subglottis area. These are important structures and landmarks that will be affected by the reflux and the mucosal changes can be viewed through endoscopic examination.

The esophagus is a fibromuscular tube, about 25cm long and it extends from the lower end of pharynx (C6 vertebrae) to the cardiac end of stomach (T11 vertebrae). There are three constrictions site along the esophagus which are at the pharyngo-esophageal junction(C6 vertebra), crossing of arch of aorta and left main bronchus (T4 vertebra) and where it pierces the diaphragm (T10 vertebra). The wall of esophagus

consists of four layers, the mucosa, submucosa, muscular and fibrous layer. The mucosal layer is lined by stratified squamous epithelium. The submucosa layer connects the mucosa to muscular layer. Muscular layer have inner circular and outer longitudinal fibers. The fibrous layer will form the loose covering of esophagus. Manometric studies have shown two high pressure zones in esophagus and they form the physiological sphincters, the upper esophageal sphincter and lower esophageal sphincter. The upper esophageal sphincter starts at the upper border of esophagus and is about 3-5 cm in length. It is anatomically made up of cricopharyngeus, thyropharyngeus, proximal cervical esophagus. The lower esophageal sphincter is situated at lower portion of esophagus and it is also 3-5cm in length. It is anatomically surrounded by diaphragmatic crura and it contributes to nearly 25% of LES competence. This portion is formed by the collar sling musculature and clasp fibers of the distal esophagus and gastric cardia, which normally remain tonically contracted except when signaled to relax during swallowing.

1.3 PATHOPHYSIOLOGY OF LPR

The term ‘reflux’ literally means backflow (Latin, ‘re’ back, ‘fluere’ to flow). The term ‘gastroesophageal reflux’ (GER) means the backflow of gastric content into esophagus while ‘laryngopharyngeal reflux’ refers to backflow of stomach content into laryngopharynx, where it comes into contact with tissue of the upper aerodigestrive tract. There are four physiological barriers protecting the upper aerodigestive tract from reflux injury, the lower esophageal sphincter (LES), esophageal motor function with acid clearance, esophageal mucosal tissue resistance and the upper esophageal sphincter

(UES) (Koufman, 1991). UES is the final gatekeeper of antireflux barrier. Dysfunction in the sphincter mechanism can be either due to hypotonia or decrease pressure and this will lead to backflow of refluxate to the laryngopharynx. LES has an intraluminal pressure of 15-25mmhg. Normally, the tonically contracted state of the lower esophageal sphincter provides an effective barrier to reflux of acid from the stomach back into the esophagus. This is reinforced by secondary esophageal peristaltic waves in response to transient lower esophageal sphincter relaxation. Effectiveness of that barrier can be altered by loss of lower esophageal sphincter tone, increase frequency of transient relaxation, increased stomach volume or pressure, or increase production of acid, all of which can damage the mucosa, resulting in inflammation. Recurrent reflux itself can predispose to further reflux because the scarring that occurs with healing of the inflammed epithelium renders the lower esophageal sphincter progressively less competent as a barrier (Vishwanath, 1997).

Basically GERD and LPR shared almost the same pathophysiology where weakening of the sphincter mechanism leads to the backflow of the gastric content. However the clinical dichotomy between LPR and GERD is based on differences in symptoms, manifestations, patterns, mechanism and responses to therapy (Wong et al, 2000, Koufman, 1991, Little et al, 1985, Belafsky et al, 2001, Olson ,1991). The larynx is exquisitely sensitive to peptic injury (Johnston et al, 2006, Koufman, 1991). According to normative pH-monitoring data, the upper limit of normal (mean plus two standard deviations) for the total number of esophageal reflux episodes per 24 hours is approximately 50 (Koufman, 1991, Veizi, 2003). In contrast, it has been shown experimentally that as few as three reflux episodes per week can result in significant laryngeal damage (Olson, 1983). It takes much less acid/pepsin exposure to cause tissue

damage in the pharynx and larynx. Therefore patients might not develop symptoms of esophagitis or GERD but they can still have LPR due to the increase vulnerability of laryngeal tissue damage.

Recent investigation suggests that vulnerable laryngeal tissues are protected from reflux damage by the pH-regulating effect of carbonic anhydrase in the mucosa of the posterior larynx (Axford et al, 2001). However this protective enzyme mechanism is absent in 64% of biopsy specimen taken from laryngeal tissues of LPR patient (Johnston et al, 2003). In comparison with esophagus, there is an active production of bicarbonate by the catalization of carbonic anhydrase, thus the esophagus has more effective protective mechanism than the larynx and pharynx. Patient with LPR are usually upright (daytime) refluxes with normally intact esophageal motor function. They uncommonly have esophagitis and heartburn. Anatomic abnormality of LPR is believed to be at the UES. Esophageal motility and acid clearance are usually normal. The refluxate in LPR spends very little time in esophagus and does most of the damage above UES. As oppose to GERD, patients are supine (nocturnal) refluxes with heartburn, esophagitis and esophageal dysmotility.

Initially, before the introduction of the term LPR, the atypical symptoms such as hoarseness, cough, sore throat and globus (sensation of feeling lump in the throat) was classified as extraesophageal syndromes (Karkos et al., 2005). However the association between GERD and extraesophageal symptoms is poorly understood and difficult to document. The traditional pH monitoring is not sensitive in detecting the association between GERD and the extraesophageal symptoms and even the therapeutic studies of proton pump inhibitors (PPI) in extraesophageal GERD have shown mixed results.

Koufman (1991) was the first to clearly distinguish LPR from GERD. He studied 899 patients and reported that throat clearing was a complaint of 87% LPR patients vs 3% of those with GERD, while only 20% of LPR patients complained of heartburn vs 83% in the GERD group. Ossakow at el (1987) compared the symptoms and findings of reflux disease in two discrete groups of reflux patients; otolaryngology (ORL) patient (n=63) and gastroenterology (GI) patients (n=36). They reported that hoarseness was present in 100% of the ORL patients and 0% of the GI patients, but heartburn was present in 89% of the GI patients and only 6% of the ORL patients.

Therefore it is important to note that the difference between LPR and GERD would require different clinical outcome and measurement. However although most patients with LPR do not have GERD, some patients do have both. In a study done by Martyn et al. in 2009, 26.5% of patients with GERD had positive reflux symptom index (RSI) scores. Tawakir et al.(2012) also found that 130 patients in his study had a significant RSI score giving an LPR symptoms prevalence of 34.4%. In a another study done by Rukiye et al. in 2012, he recorded an even higher prevalence rate of LPR in which 484 patients (70%) with GERD had positive reflux finding score (RFS) score.

1.4 CLINICAL DIAGNOSIS OF LPR

Common symptoms and signs of reflux include morning hoarseness, halithosis, excessive phlegm, recurrent throat clearing, xerostomia (dry mouth), coated tongue, sensation of lump in the throat (globus sensation), throat trickle, dysphagia, regurgitation of gastric content, chronic sore throat, nocturnal cough, chronic or

recurrent cough, difficulty breathing especially at night, aspiration, occasional pneumonia, laryngospasm, worsening of asthma, recurrent airway problem in infant, dyspepsia and heartburn (Belafsky, 2002; Book, 2002). An international survey of American Bronchoesophagological Association members revealed that the most common LPR symptoms were throat clearing (98%), persistent cough (97%), globus pharyngeus (95%) and hoarseness (95%) (Book, 2002). However these laryngeal symptoms are nonspecific (Book, 2002).

The typical LPR symptoms such as hoarseness, clearing throat and globus pharyngeus can also be caused by infections, vocal abuse, allergy, smoking, inhaled environmental irritants and alcohol abuse (Ylitalo, Lindestad & Ramel, 2001). The laryngeal tissue inflammation often known as laryngitis and it is often mild and resolves spontaneously. When persistent, laryngitis must be further defined based on probable etiologic factors such as viral or bacterial, allergy, trauma or LPR. Persistent or progressive hoarseness lasting beyond 2 to 3 weeks requires examination of laryngopharynx to rule out esophageal or gastric carcinoma, or other serious condition such as erosive esophagitis, hiatal hernia and Barrett's esophagus.

There is no pathognomonic symptoms or findings that gives a clear cut diagnosis of LPR. Nonetheless the characteristic symptoms and laryngoscopic findings could provide the basis for validated assessment instruments; the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) which is useful for initial diagnosis(Ford, 2005). At first, since many patients responded well to behavioral modification and initial medical management, an acid suppression trial by proton pump inhibitor (PPI) is frequently used approach to initial diagnosis (Vaezi, 2003). The purpose of RSI and

RFS initially were to assess the severity, outcome or response towards the initial empirical treatment. Currently, there are three approaches to confirm the diagnosis of LPR; response of symptoms to behavioral and empirical medical treatment, endoscopic observation of mucosal injury; demonstration of reflux event by multichannel impedence and pH monitoring studies(Ford, 2005). Response of symptoms improvement after medical treatment is based on the score of the reflux symptom index (RSI). Endoscopic observation of mucosal injury is recorded by applying the reflux finding score (RFS).

Normally the general practitioner(GP) would adopt the first approach as it is practical and patient normally would respond towards the initial treatment. If the symptoms persist only then they would refer to otolaryngologist for endoscopic examination to rule out other sinister cause. The third approach is normally reserved for patients who are not responding towards treatment. Although many studies have been done during this recent years, regarding the establishment of LPR as a diagnosis of its own, controversies remains, in terms of confirming the diagnosis and what comprises the appropriate medical management. In mild LPR cases, symptoms and physical findings lack sufficient specificity and laryngoscopic findings can be misleading. Lund et al (1999) found posterior erythema in 73% of asymptomatic singing students and Hicks et al (2002) found tissue changes associated with LPR in a group of more than 100 asymptomatic volunteers. Albeit all those setbacks, the main aim of this study is to validate a malay version of RSI and to establish a correlation between the translated questionnaire with RFS and the pH monitoring device which remains the gold standard tools of confirmatory diagnosis. It is not to confirm the validity of the RSI and RFS

methods for diagnosing LPR since there are already medical literatures on the subject that supports these instruments.

1.5 REFLUX SYMPTOM INDEX (RSI)

It has become increasingly apparent that LPR differs in many ways from classic GERD. The already established GERD has many questionnaire scale such as the Gastro-Oesophageal Activity Index (Wiliford, Krol & Speechler, 1994), Gastro-oesophageal Reflux Disease Score (GORD) (Allen et al, 2000) and Gastro-oesophageal Symptom Assessment Scale (GSAS) (Rothman et al, 2001). All of them are gastro-oesophageal reflux disease specific. Lock at el (1994), Colwell et al (1999) and Shaw at el (2001) have developed and validated a GERD questionnaire to assess severity and response to treatment. However these outcome instruments are lengthy and rely heavily on typical GERD symptoms. At that point of time there was no validated instrument used by otolaryngologist to assess outcome in LPR patients.

Based on careful study of pH probe-confirmed LPR cases, Belafsky et al (2001) had developed a self administered tool, nine-item Reflux Symptoms Index (RSI) questionnaire that can help clinician to assess the relative degree of LPR symptoms during initial evaluation and after treatment, (Table 1.5). The questionnaire comprises of LPR symptoms such as hoarseness or voice problem; throat clearing; excess throat mucus or postnasal drip; difficulty in swallowing; coughing after lying down; breathing difficulties or choking spells; troublesome or annoying cough; sensation of something sticking or a lump in the throat and lastly heart burn, chest pain or indigestion. Patients are asked to scale for each individual item which ranges from 0 (no problem) to 5 (severe problem). From the study, Belafskey (2001) was able to prove that the RSI

questionnaire is easily administered, highly reproducible and exhibits excellent construct-based and criterion based validity. They also conclude that a RSI score of 13 and above would be abnormal.

RSI can be easily included in the daily clinical care of patient suspected of having LPR. It can be completed in less than one minute. It is not a time-consuming and cost-intensive tool of examination as compared to pH-metry studies. The RSI is an excellent instrument used not just as a first-line assessment of patients having LPR, but also to measure the outcome or response towards post PPI treatment. The application of this reliable RSI may help to prevent unjustified and unselected prescription with an impact on health insurance system.

Table 1.5 Reflux Symptom Index (RSI)

Within the past month, how did the following problems affect you?	0 = No problem 5=Severe problem					
1. Hoarseness or a problem with your voice?	0	1	2	3	4	5
2. Clearing your throat	0	1	2	3	4	5
3. Excess throat mucous or postnasal drip	0	1	2	3	4	5
4. Difficulty swallowing food, liquids or pills	0	1	2	3	4	5
5. Cough after you eating and after lying down	0	1	2	3	4	5
6. Breathing difficulties and choking episodes	0	1	2	3	4	5
7. Troublesome and annoying cough	0	1	2	3	4	5
8. Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5
	Total					

Adapted from Belafsky et al. (2002)

Since symptoms of LPR are varied, some labeled it as supraesophageal reflux and they developed a more comprehensive and detailed Supraesophageal Reflux

Questionnaire (SERQ). Although it proved to be more dynamic in terms of superior clinical and research purposes but it lacks practicality. It is said that patients took at least 10 minutes or longer to complete the SERQas compared to RSI which only takes 1 minute of completion. Therefore RSI has been recognized worldwide and is being currently used extensively as an instrument to assess severity for initial diagnosis and post treatment response. To date the RSI has been translated and adapted into Hebrew language, Italian, Arabic and Chinese version.

Currently, there is no RSI in Malay version (M-RSI). It has not been used in its present forms in Malaysia due to specific language constraints of terminology used. RSI in Malay version is important as such an instrument would be of value for Malaysian population. This is because it would provide an insight to the occurrence of throat problem on the individual's quality of life. The information gathered from m-RSI can be used for evaluation, intervention planning and provide outcome measurements after treatment. Therefore translating and validating RSI in use in Malay version is very crucial for otorhinolaryngologist clinicians in concern regarding LPR patients. Hence the purpose of the this study is to culturally adapt the RSI to Malay version, and to obtain measures of reliability, reproducibility and responsiveness of this translation in a group of individuals with LPR problem and control subjects

1.6 REFLUX FINDING SCORE (RFS)

RFS is designed to characterize morphologic lesions presumably associated with LPR. It is developed to standardize the laryngeal findings of LPR so that clinicians may better diagnose, evaluate clinical improvement and assess therapeutic efficacy of patients with LPR. Laryngeal irritation and inflammation will demonstrate tissue changes such as thickening, redness and edema especially concentrated at the posterior larynx (Ylitalo, Lindestad & Ramel, 2001). Although they are nonspecific, these findings are highly suggestive of LPR. Contact granuloma was found to be associated with pH monitoring-confirmed case of LPR in 64%-74% of patiens (Ohman et al, 1983; Ylitalo & Ramel, 2002).

Pathological condition called pseudosulcus has been reported in as much as 90% of LPR cases (Hickson et al, 2001). Since there is no pathognomonic LPR finding, Belafsky et al (2001) developed an 8-item clinical severity scale for judging laryngoscopic findings, the Reflux Finding Score (RFS) (Table 1.6). They rated 8 LPR-associated findings on a weighted scale from 0 to 4: subglottic edema; ventricular obliteration; erythema/hyperemia; vocal fold edema; diffuse laryngeal edema; posterior commisure hypertrophy; granuloma and thick endolaryngeal edema. The results could range from 0 (normal) to 26 (worst possible score). Based on their analysis, one can be 95% certain that a patient with a reflux finding score of 7 or more will have LPR.

Table 1.6 : Reflux Finding Score (RFS)

1. Infraglottic edema (pseudosulcus vocalis) 0 (absent) 2 (present)
2. Ventricular obliteration 0 (none) 2 (partial) 4 (complete)
3. Erythema/ Hyperemia 0 (absent) 2 (arytenoids only) 4 (diffuse)
4. Vocal fold edema 0 (none) 1 (mild) 2 (moderate) 3 (severe) 4 (polypoid)
5. Diffuse laryngeal edema 0 (none) 1 (mild) 2 (moderate) 3 (severe) 4 (obstructing)
6. Posterior commisure hypertrophy 0 (none) 1 (mild) 2 (moderate) 3 (severe) 4 (obstructing)
7. Granuloma / Granulation 0 (absent) 2 (present)
8. Thick endolaryngeal mucus 0 (absent) 2 (present)

Adapted from Belafsky et al. (2001)

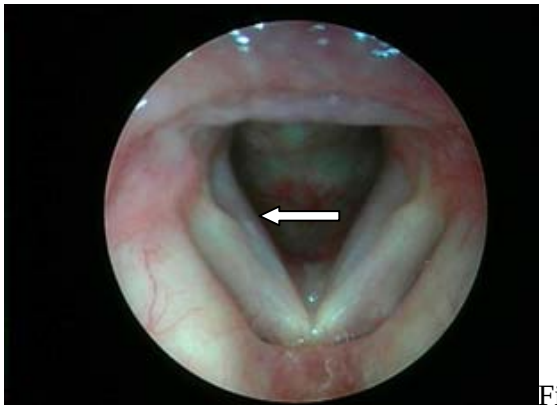


Figure 1.6(a): Pseudosulcus vocalis(white arrow)

Pseudosulcus vocalis; Figure 1.6 (a), is one of the most common laryngeal findings of LPR. It refers to edema of the undersurface of the vocal fold that extends from the anterior commisure to the posterior larynx and creates the appearance of a groove or sulcus. This finding is also referred to as subglottic edema, even though the edema is not really subglottic. However pseudosulcus as the only finding is rare in LPR. In other words, LPR patients usually have several LPR findings at the same time.

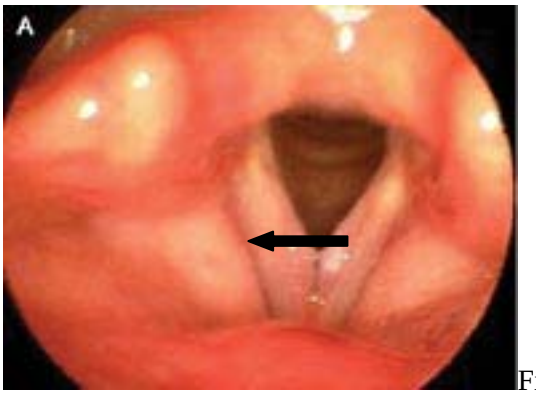
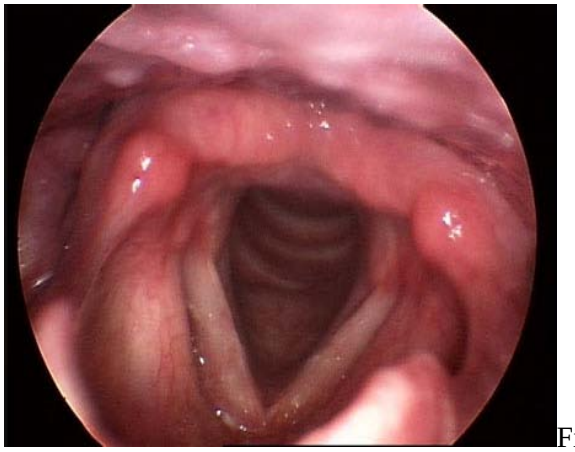


Figure 1.6 (b) : Ventricle obliteration(black arrow)

The laryngeal ventricle; Figure 1.6(b), is the space between the true and false vocal folds. When both sets of vocal folds become swollen, this space can become diminished or completely obliterated. With ventricular obliteration, the medial edge of the ventricular bands usually becomes broad and swollen. With the RFS scale, ventricular oliteration is graded as partial or complete. Ventricular obliteration is an important LPR finding. This finding can be treated with effective antireflux treatment.

 Figure 1.6 (c) : Laryngeal erythema

Laryngeal erythema; Figure 1.6(c) or hyperemia is defined as localized to arytenoids only or diffuse when it affects the entire larynx.

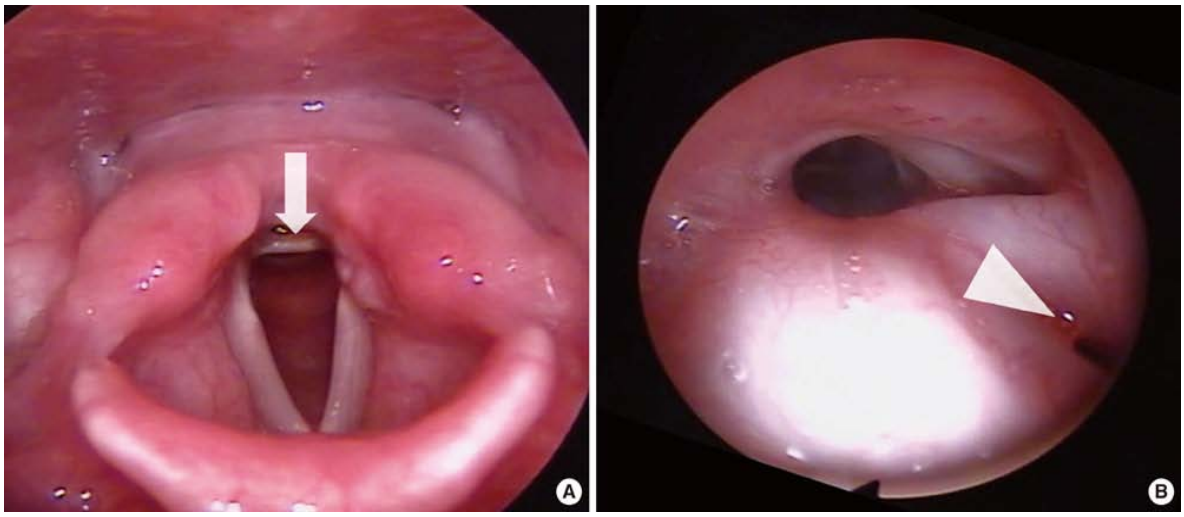


Figure 1.6 (d) : Posterior commisure hypertrophy(white arrow)

Mucosal hypertrophy of the posterior commmisure epithelium; Figure 1.6 (d), is graded as mild when there is a moustache-like appearance of the posterior commisure mucosa, moderate when the posterior commisure is swollen, severe when there is bulging of the posterior larynx into the airway and obstruction when significant portion of the airway is obliterated.

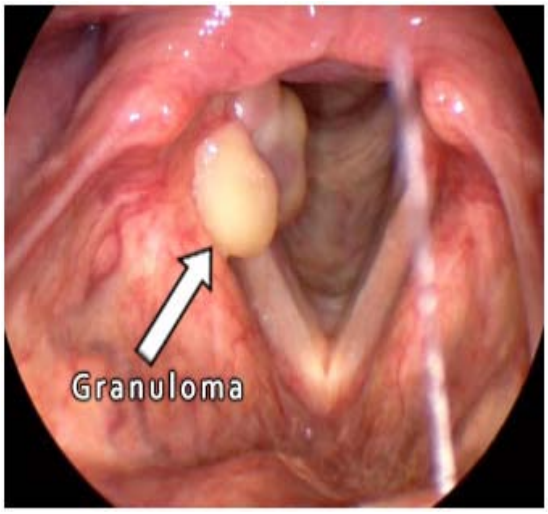


Figure 1.6 (e) : Granuloma

Granuloma; Figure 1.6(e), or granulation tissue anywhere in the larynx is graded as a positive LPR finding. Otherwise, presence of white, thick endolaryngeal mucus;

Figure 1.6(f) on vocal folds or elsewhere in the endolarynx is graded as positive physical finding.

Figure 1.6 (f) : Endolaryngeal mucus

Figure 1.6 (g) : Diffuse laryngeal edema

The presence of diffuse laryngeal edema; Figure1.6(g), refers to the relative ratio of the endolaryngeal airway to the whole larynx. It can be graded as grade 1 with diffuse laryngeal edema to grade 4 which denotes some degree of clinical airway obstruction.

Figure 1.6 (h) : Vocal fold edema(black arrow)

In discussing vocal fold edema in LPR, it can range from mild to end stage polypoid degeneration; Figure 1.6(h).

The RSI and RFS have been proven to be useful and practical parameters in the management of LPR patients and they mutually complement each other. By implementation of RFS and RSI in daily use, we are able to reserve the usage of pH monitoring device for the non-respond patients towards medical treatment.

1.7 PHARYNGEAL PROBE pH-MONITORING

There are many instruments for objective measurement in the evaluation of GERD and these have been adapted towards diagnosing LPR. Demonstration of reflux events by ambulatory multichannel intraluminal impedence (MCII) manometry and pH-monitoring studies remains the gold standard in diagnosing GERD (Kawamura et al, 2004). Other diagnostic modality would be barium esophagoscopy, radionucleotide scanning, the Bernstein acid perfusion test and esophagoscopy with biopsy, however these results were often found negative in LPR patients (Koufman, 1991; Postma, 2000). Hydrogen ion concentration monitoring is considered the gold standard in detecting GERD but it is less reliable in confirming LPR. Studies have shown that traditional pH monitoring is not sensitive in detecting the association between GERD and the extraesophageal symptoms or LPR (Maldonado et al, 2003). These devices suggest that LPR symptoms manifest themselves as rapid pH drops (>10%) which are likely not to be identified using standard criteria of pH < 4 due to the gradient of increasing pH from lower esophagus to oropharynx. Variability in testing methods and lack of agreement on normative values have raised questions about the sensitivity of pH-monitoring (Nostrant, 2000; Baldi, 2002, Noordzij et al, 2002). Furthermore due to its invasive nature, time and cost consuming factors, this method is performed as a second step after therapeutic trial has failed.

Recently, a minimally invasive and easily tolerated probe has been created. It is called the Restech Dx-pH Measurement System, developed by the Respiratory Technology Corporation from the U.S.A. It is an accurate airway pH measurement that places the probe at the oropharynx. This objective measurement test provides a

graphical representation of the pH activity over 24-48-hour study. This data relays information about the reflux patterns in a clear fashion. Compared to conventional probe catheter that is normally placed above the upper esophageal sphincter (UES), this probe has the capability to measure the pH at the oropharynx area where the refluxate is normally aerosolized. When the reflux is aerosolized, conventional pH sensors are incapable of reliably measuring the pH. It contains a miniature sensor that rests in the tip of a teardrop shaped catheter. The unique shape keeps the sensor pointed down, where it reads the aerosolized reflux. Due to the unique configuration and positioning of the pH sensor, this device has virtually eliminate the problem of false negatives results. This new device is well tolerated by patients because of the small probe that rest well above the epiglottis thus the swallowing mechanism is not interrupted. It can be easily inserted and this system is equipped with wireless transmission therefore the monitoring can be done even at home. These additional features that gives the device an extra edge remains true as proven by studies done by George et al (2009) and S Ayazi et al (2009). In his study,George et al (2009) found that the most important advantage of the Restech pH is the ease of oropharyngeal placement in which it provided less discomfort yet maintaining the consistency of the result by being able to detect the aerosolized reflux. During their study to measure the normal values of pharyngeal pH and establish pH threshold, S Ayazi et al (2009) have compared between esophageal manometry, dual probe pH monitoring and Restech pharyngeal pH sensor. They concluded that Restech pharyngeal pH sensor was able to detect aerosolized and liquid acid and overcome the artifacts that occur while using the other catheter.

There are many studies that have been conducted to prove the clinical application of this device. A study done by Lauren C Anderson (2008) suggested that the Restech pH

probe is a useful diagnostic tool for LPR as the result showed that patients with high RSI and RFS will have positive Restech studies. There is a study done comparing the Restech pH system with esophageal manometry and ambulatory pH monitoring using dual pH sensor. The result showed that this pharyngeal probe was able to detect aerosolized and liquid acid reflux and thus overcomes the artifact that occurs using existing catheters (Ayazi et al,2008). By using Restech, studies showed that treatment of LPR based on pH monitoring gives greater compliance and improvement responds compared to empirical therapy alone (Friedman et al, 2011). This pharyngeal probe pH monitoring proved to be more sensitive than 24 hour ambulatory esophageal multichannel intraluminal impedence in detecting LPR because of its ability to differentiate GERD related respiratory symptoms which are closely related to LPR (Wilshire et al, 2009). Airway reflux is a frequent condition in asthma patients. The Restech pharyngeal probe pH monitor can be utilized to evaluate the presence of gaseous airway reflux especially in patients with asthma (Jackson, Burke, & Morice, 2011). There is also a study done that compare between Restech pH monitor and histologic diagnosis and it proved that the pH monitor is more superior in determining LPR (Andrew, 2011). Banaszkiewicz A, Dembinski L et al (2011) also revealed that the Restech pH probe can be used in assessing the prevalence of LPR in children with difficult to treat asthma. Nevertheless, all of these studies are clearly a preliminary pilot study with minimal statistical power and will need further validation and clinical testing. Although there is a study done using this device to establish the normal values and discriminating pH threshold, (Ayazi S. et al, 2009) it still needs to be validated by patients with LPR symptoms who respond to acid suppression therapy or antireflux surgery.

2.0 OBJECTIVE OF THE STUDY

2.1 GENERAL OBJECTIVE

To translate, validate the Bahasa Malaysia version of Reflux Symptoms Index (M-RSI) and correlate it with reflux finding score(RFS) and oropharyngeal pH score, (Ryan score upright and Ryan score supine) in laryngopharyngeal reflux disease.

2.2 SPECIFIC OBJECTIVES

1. To translate the original English version of RSI and culturally adapt it into the Bahasa Malaysia version (M-RSI).
2. To determine the validity and reliability of the M-RSI in diagnosis of LPR disease.
3. To validate and correlates the M-RSI with RFS and oropharyngeal pH scores(Ryan score upright and Ryan score supine) in participants with and without LPR disease.

2.3 RESEARCH HYPOTHESIS

NULL HYPOTHESIS

The RSI-BM is not a valid and reliable instrument to determine the presence of LPR in our population

ALTERNATE HYPOTHESIS

The RSI-BM is a valid and reliable instrument to determine the presence of LPR in our population