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Specificity of the Diagnostic Materials for Laryngopharyngeal Reflux

In fulfilment of the requirements for the degree
MA Speech Pathology
by research

Jeanneane Logan

0112716W

February, 2011

Declaration

I hereby declare that this dissertation is my own unaided independent work. It has not been submitted before for any degree or examination at this or any other academic institution, nor has it been published in any form.

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February, 2011
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Introduction and Rationale

Laryngopharyngeal reflux is defined by Sataloff, Hawkshaw and Gupta, (2010), as "an extraoesophageal variant of gastroesophageal reflux disease, (GORD), that affects the larynx and pharynx" (p 124). Hoarseness, chronic unexplained cough, frequent throat clearing, and a feeling of a lump in the throat are all common symptoms of laryngopharyngeal or "silent" reflux (Fouad & Rifaat, 2010). The general nature of these symptoms translates into difficulties with differential diagnosis and at present, the diagnosis and treatment of extraoesophageal reflux disease is still controversial (Lee, Kim, Ryu, Kim, Cheong, Lee & Song, 2010).

"There is no consensus on the diagnosis and treatment of laryngopharyngeal reflux and the majority of clinicians depend mainly on clinical findings and empirical therapeutic tests rather than more specific investigations." (Ali, 2008, p. 28).

In fact the mere existence of 'silent reflux' is currently controversial (Barry & Vaezi, 2010). Due to such controversy and lack of definitive diagnostic criteria laryngopharyngeal reflux remains challenging to diagnose and manage effectively.

The aim of this study is therefore to examine the specificity of, and relationship between diagnostic methods used in laryngopharyngeal reflux, (LPR), disease, specifically the Reflux Symptom Index, (RSI), and the Reflux Finding Score, (RFS). Through a retrospective chart review of 105 patients this research attempted to provide a degree of clarity regarding the controversial nature of LPR.

As mentioned, one of the main symptoms of LPR is a hoarse voice. A complex interplay of muscle contraction, inhalation, relaxation and exhalation in a sequenced and timed manner allows a vibratory movement that is audible as voice (Tanner, 2007). This vibration is unique to each person. Voice is essentially part of an individual's personality. For many it defines who they are. Consider for example how we recognise people on the phone, at the door or on the radio by their voice. Voice is used as a means for nonverbal communication (Tanner, 2007). We make judgments about people based on their voice, such as their age, gender, educational level and even in some instances socioeconomic

background. Voice is strongly linked to emotion and is used to convey primary emotions such as: anger, fear, joy, disgust and surprise (Titze, 1994). Personality traits of confidence, kindness, honesty and cheerfulness are associated with vocal characteristics. If an individual's voice is altered it may therefore affect emotion and personality.

For many, voice comprises a crucial and irrevocable part of their personal and professional lives. Modern technology has also come to rely on voice more and more with vocal recognition dialling, security systems and voice-to-text typing (Tanner, 2007). Consequently, fluctuations in voice quality may be insignificant or may be catastrophic and cause a large amount of suffering in individuals. For some it may lead to changes in vocation, lifestyle, hobbies, social patterns and ultimately quality of life (Tanner, 2007). Professionals who use their voice in order to work e.g. lawyers, ministers, teachers, singers, sales people and speech therapists - may be unable to work if their voice is affected even mildly (Titze, 1994).

Voice disorders may reduce job effectiveness and productivity and may even lead to job loss in many professions. Vocal disorders are evaluated and may be classified as disabilities which can be a huge cost to company. People who suffer from voice disorders may be candidates for vocational rehabilitation and they may require compensation for lost earnings and retraining for a new job (Tanner, 2007). In many instances people may need to be put on extended sick leave and often are unable to return to their previous profession due to their poor vocal quality.

A study by Roy, Merrill, Grey and Smith, (2005), of 1326 people randomly selected from the general population in the United States revealed that 29,9% of the sample had suffered from a vocal pathology during their lifetime. Of the sample, 4,3 % indicated that their job performance had been negatively impacted by their voice disorders and had hindered and obstructed their ability to perform certain job tasks. Attendance at work was also cited as being impeded by voice problems. Further 7,2% of participants reported they were absent from work for 1 or more days in the previous year and 2% reported more than 4 days of voice-related absence. (Roy et al., 2005).

Another study found similar results with teachers who have voice disorders. Results indicate that teachers with vocal disorders go into retirement earlier than those without

vocal disorders and are more likely to have to change professions compared to their non voice disordered counterparts (Chen, Chiang, Chung, Hsiao & Hsiao, 2010). Voice difficulties therefore have an impact on attendance at work and ultimately on productivity.

Vocal disorders are a disability and create a feeling of helplessness, grief, anguish and loss. Therefore disorders such as laryngopharyngeal reflux that create vocal symptoms needs to be diagnosed and treated effectively in order to reduce these and other effects on people.

Voice disorders are generally treated by a team of specialists, with the speech therapist making a significant contribution. The speech therapist's role is to provide behavioural treatment for the vocal pathology and aid the patient in managing the vocal symptoms with which they present, through a number of procedures and techniques (Colton & Casper, 1996). The speech therapist also aims to educate the patient regarding: the vocal mechanism, identification and reduction of phono-trauma and high-risk vocal situations, conservation of voice or vocal rest, controlling the amount of talking, monitoring vocal pitch and intensity, encouraging local lubrication and systemic hydration, and promoting optimal dietary considerations (Behlau & Oliveira, 2009). Many of these are intended to aid in reducing further damage to the vocal folds by modifying certain behaviours e.g. vigorous throat clearing.

LPR is found in a high percentage of patients who have laryngeal carcinoma (Galli, Cammarota, Volante, De Corso, Almadori, & Paludetti, 2006). This is thought to be due to inflammation and cellular mutation from direct chemical assault in the form of reflux. LPR therefore represents a potentially life threatening disorder and it is crucial to have precise and early diagnosis.

The findings outlined here indicate that the need for clarity in diagnosis and effective management of LPR has become a priority. "Evidence confirming the diagnostic significance of various complaints and findings is scarce and contradictory" (Sataloff, Castell, Katz & Sataloff, 2006 p. 58).

Sataloff, Hawkshaw and Gupta (2010) outline the need for additional multidisciplinary research into the diagnosis and treatment of LPR. If a more reliable method of diagnosis could be established then LPR would not be such an enigma and appropriate treatment could commence. Interdisciplinary studies should focus on trying to answer crucial questions regarding sensitivity and specificity of the numerous findings associated with LPR (Sataloff et al., 2006).

The Reflux Severity Index (RSI) (Belafsky, Postma & Koufman, 2002), is a useful tool in drawing attention to the symptoms associated with reflux. Additionally, the relationship between symptoms, signs and reflux severity needs to be characterised (Noordzij, Khidr, Desper, Meek, Reibel & Levine, 2002). The Reflux Finding Score (RFS) (Belafsky, Postma & Koufman, 2001b), and RSI scores are designed to grade severity and clinical findings in LPR. Therefore, research into the relationship between the RSI and the RFS is warranted and findings may have significant clinical relevance and impact.

Literature Review

The purpose of this literature review is to define core concepts and theories related to laryngopharyngeal reflux with particular emphasis on appropriate diagnosis. The rationale for the proposed research is also further developed.

Voice disorders account for a large proportion of the problems encountered by patients seen at otolaryngology practices. A team approach is used to treat voice disorders as they often require lifestyle, behavioural and medical intervention (Sataloff, 2005). The team members involved with voice disorders would typically include a speech therapist, an otolaryngologist and in cases of professional voice users a voice and/or singing coach (Tanner, 2007). Each member of the team brings a particular set of skills and knowledge to the diagnostic process. The otolaryngologist is highly skilled in the assessment of health and disease in the larynx, whereas the singing coach recognises problems in vocal technique that are specific to the singing voice (Colton & Casper, 1996). The speech therapist's role in vocal pathology is to diagnose the type of vocal disorder the patient presents with. This is done through assessment of perceptual characteristics, case history and patient interview where aspects such as respiration, prosody and tone are considered. Patients are diagnosed and provided with an in depth individualised treatment plan to aid in reducing vocal disorders and change damaging and pathological vocal behaviours. In general the goal of voice therapy is to restore the best voice possible to aid in functional communication and employment (Colton & Casper, 1996). The speech therapist is able to recognise the potential for serious disease and the need for medical intervention and refer appropriately. The speech therapist specialises in the phonatory function of the speech mechanism and the manner in which various conditions disturb this (Colton & Casper, 1996).

Voice disorders have an impact on the quality of life and often negatively influence an individual's functioning. Both leisure and professional aspects are affected. The Voice Handicap index (VHI), (Jacobson, Johnson, Grywalski, Silbergleit, Jacobson, Benninger & Newman, 1997), quantifies this impact. The voice handicap index examines three

areas: physical (perceived vocal functioning and laryngeal discomfort), emotional (emotional response to vocal problems) and functional (the impact of voice difficulties on daily activities). Each aspect is assessed by ten questions rated by the patient on an ordinal scale from 0 to 5 (Welham, Dailey, Ford & Bless, 2007).

A number of studies have examined patients' subjective experiences of voice disorders using the VHI (Maertens & de Jong, 2007; Rosen, Lee, Osborne, Zullo & Murry, 2004; Orlikoff & Baken, 1993). A study by Chen, Chiang, Chung, Hsiao & Hsiao (2010), on teachers with voice disorders indicated they had increased absenteeism, changes in teaching style, changes in job performance and pressure in the functional sphere of their lives. Further, they indicated a reduction of social activities overall and an avoidance of social situations. They stated that the voice problem brought on feelings of embarrassment, being upset and a negative effect on overall emotional state, with an adverse impact on their self image. Patients have reported an increase in anxiety, psychological distress and 77% of patients also reported reduced social activities compared to controls without a history of voice difficulties (Siupsinskiene, Adamonis & Toohill, 2007). The study further indicated that patients' quality of life is more impacted by symptoms of reflux than laryngoscopic findings would suggest (Siupsinkiene et al., 2007).

The present study is an investigation of the symptoms and signs of a particularly common condition, that both results in and compounds voice disorders namely laryngopharyngeal reflux.

2. 1 Definition and incidence/ prevalence

Laryngopharyngeal reflux (LPR), is also known as pharyngeal, supra-oesophageal, silent or extra-oesophageal reflux (EER), and refers to the backflow of stomach contents into the laryngopharynx (Koufman, Aviv, Casiano & Shaw, 2002; Musser, Kelchner, Neils-trunjas & Montrose, 2009; Belfasky, Rees, Rodriguez, Pryor & Katz, 2008). LPR is

closely associated with gastro-oesophageal reflux disease (GORD). The relationship between LPR and GORD is further elaborated on in section 2. 2.

LPR is described as being extremely common and a potentially debilitating chronic disease process (Aviv, Parides, Liu, Kaplan & Close, 2000). It has been reported that more than 50% of patients complaining of hoarseness have LPR (Ford, 2005), and further, that 4-10% of patients who, consult ENT's do so for gastro-oesophageal reflux disorder (GORD) complaints (Reimer & Bytzer, 2008). According to Ford (2005), 25% of patients with LPR experience spontaneous resolution of symptoms while 50% have a chronic course of intermittent remissions.

LPR can be found in all populations regardless of background. However, a trend has emerged with the primary occupation of patients diagnosed with LPR being professional voice users, especially singers (Sataloff, 2005a). This may assist the voice care team in predicting which patients coming into voice clinics will present with LPR. Further, health care workers may be able to treat such individuals prophylactically with lifestyle, dietary and relaxation methods as well as with vocal hygiene measures.

Sataloff et al. (2006), postulate a number of reasons for this high prevalence of LPR in professional voice users. Firstly, LPR may be due to the muscular mechanisms taking place during singing where the stomach is compressed by forceful contraction of the abdominal muscles. Secondly, singers often perform on an empty stomach and consequently eat large meals before retiring for the evening. Thirdly, psychological stress has been closely associated with gastroenterological conditions. Performance careers have a high incidence of stress, which can increase production of stomach acid. Fourth, many professional voice users consume a lot of caffeine and often make less healthy food choices (Sataloff et al., 2006). The current study thus included a group of professional voice users.

2. 2 LPR and GORD

LPR and GORD differ in symptomology, manifestations as well as in response to treatment (Koufman et al., 2002). Patients diagnosed with GORD suffer primarily from

heartburn and oesophagitis, which is not the case in LPR (Reimer & Bytzer, 2008; Schreiber, Garten & Sudhoff, 2009). GORD in general, tends to occur nocturnally in supine position, whereas, LPR is an intermittent daytime occurrence, when the patient is upright (Abaza, 2004). GORD is characterised by prolonged periods of oesophageal acid exposure and dysmotility (Koufman et al., 2002). GORD is postulated to occur from lower oesophageal sphincter dysfunction and dysmotility leading to prolonged periods of oesophageal acid exposure (Koufman, Aviv, Casiano & Shaw, 2002). The laryngopharynx is not exposed to acid for prolonged periods of time in LPR, (unlike the oesophagus is in GORD), and the primary defect anatomically in LPR is upper oesophageal sphincter dysfunction. (Koufman et al., 2002). It is likely that these differences in anatomical dysfunction lead to the differing presentations of GORD and LPR.

Another difference between LPR and GORD is that an increased body mass index (BMI) or obesity is not positively linked to pharyngeal reflux in LPR patients whereas GORD is strongly linked to increasing BMI and obesity (Halum, Postma, Johnston, Belafsky, & Koufman, 2005). It is clear that LPR and GORD are not the same entity. Their aetiology must be different considering the discrepancy between the symptoms and presentation of the two disorders.

LPR and GORD are however, both due to mucosal injury from acid and pepsin exposure (Remacle & Lawson, 2006). They differ in that the oesophagus has inherent structures and processes that assist in preventing mucosal injury. These include bicarbonate production, mucosal tissue resistance and oesophageal motor function with acid clearance. The laryngopharynx by contrast does not have such protective mechanisms (Remacle & Lawson, 2006). The laryngeal mucosa is fundamentally different to oesophageal mucosa and is more sensitive to acid and pepsin (Hammer, 2009). The larynx is more susceptible to reflux injury than the oesophagus, since it has fewer extrinsic and intrinsic epithelial cells than the oesophagus (Koufman et al., 2002). Even brief exposure to small amounts of reflux can cause damage to the laryngopharynx. Thus the oesophagus is well equipped to deal with reflux whereas the larynx and laryngopharynx is less so. The larynx is more delicate than the oesophagus with ciliated respiratory epithelium. This epithelial structure enables mucus to be cleared from the pharynx and trachea. Therefore when these structures are compromised through failure of

any of the protective mechanisms of the upper aerodigestive tract (upper and lower oesophageal sphincters, oesophageal motor function and cellular construction of oesophageal mucosal tissue), mucus stasis follows (Ford, 2005). The resultant accumulation of mucus leads to a post nasal drip and throat clearing (Ford, 2005). Choking and coughing can be caused by irritation of the airway due to a direct mechanism of contact with the refluxate material and the reflux of gases into the oesophagus (Hanson & Jiang, 2000; Mosca, Rossillo, & Leone, 2006). This combination of factors can lead to vocal fold oedema, contact ulcers and granulomas that lead to typical symptoms of hoarseness, globus pharyngeus (the sensation of a lump in the throat) and sore throat reported by patients suffering from LPR (Ford, 2005). Globus sensation is caused by cricopharyngeal muscle spasms and it is not necessary for the acidity to reach the pharynx in order to bring on this symptom (Mosca et al., 2006). Inflammation and irritation may in turn promote excess mucus production as a protective mechanism.

Four main mechanisms responsible for the presentation of LPR have been outlined by Maron and Jordaan (2010). These are: chemical, mechanical, hypersensitivity and immunologic.

The *chemical mechanism* is mainly due to the acid and non-acid components of the refluxate: bile and pepsin which cause microscopic inflammation of the mucosal lining. The refluxate dilates the intercellular spaces by breaking down cell membrane integrity and constructing a more permeable environment which allows the refluxate to penetrate the submucosa (Maron & Jordaan, 2010; Johnston, Knight, Dettman, Lively & Koufman, 2004).

Pain and heartburn are explained through the *mechanical processes* of oesophageal lumen distention and contraction of the musculature. Some of the symptoms that present clinically (coughing, lump in the throat etc.) are due to stimulation of the peripheral and central vagal nerve fibres caused by *hypersensitivity* of the gastrointestinal tract (Maron & Jordaan, 2010; Gupta & Sataloff, 2009). Bronchospasm, chest pain, cough and asthma may be the result of acidification of the distal part of the oesophagus which stimulates acid sensitive receptors (Maron & Jordaan, 2010). In addition, the refluxate may indirectly stimulate the vagal nerve fibres in the oesophagus (Reimer & Bytzer, 2008),

leading to an ongoing and persistent cough which damages the vocal chords due to continued contact.

The fourth mechanism is an *immunologic phenomenon* within the submucosa which leads to inflammation. Papilla elongation, basal cell hyperplasia and dilated intercellular spaces are all histological changes that take place in the presence of reflux (Maron & Jordaan, 2010).

LPR may also be associated with Paradoxical Vocal Fold Movement (PVFM), vocal nodules, postnasal drip, allergies, sinus inflammation, and various pulmonary diseases (such as asthma and chronic obstructive pulmonary disease) and polypoid degeneration (the membranous portion of the vocal fold becomes filled with thick gelatinous fluid) (Koufman et al., 2002; Barry & Vaezi, 2010). Lifestyle modifications such as cessation of smoking, weight loss, and decreased activities that cause stress on the voice are advised for these cases (Barry & Vaezi, 2010). According to Carrau, Khidr, Gold, Crawley, Hillson, Koufman and Pashos (2005), a number of studies indicate that acid reflux is present in 50-80% of patients with asthma, 10% to 20% of patients with chronic cough, and 25% -50% of patients with globus sensation. This is in all likelihood due to the inherent nature of LPR. Changes in the anatomy and physiology of the hypopharynx as a result of LPR can also lead to dysphagia as well as a number of other symptoms (Aviv, Liu, Parides, Kaplan & Close, 2000).

2. 3 Symptoms and complications of LPR

It is reported that the most common symptoms of LPR include throat clearing, persistent cough, voice-quality change and globus pharyngeus (Ford, 2005; Remacle & Lawson, 2006; Sataloff, Hawkshaw & Gupta, 2010). A study conducted by Pribuisiene, Uloza and Saferis (2005) analysed and quantified the voice characteristics of LPR patients to determine the most important voice tests and voice quality parameters in the functional diagnosis of LPR. Findings indicated that the mean values of hoarseness on a visual analogue scale and the total Voice Handicap Index were significantly higher in LPR patients as compared to asymptomatic patients. A significant increase in mean values of

jitter, shimmer and normalised noise energy (NNE) were seen in LPR patients' acoustic assessment. Jitter is defined as the variation of fundamental frequency present when sustaining a vowel, shimmer is the variance in amplitude of vocal folds during sustained phonation (Colton & Casper, 1996). A significant decrease in pitch range, maximum frequency, phonetogram area (S) and maximum phonation time (MPT) was seen in the same LPR patients (Pribuisiene, Uloza & Saferis 2005). Patients with LPR complain about various combinations of voice symptoms, such as intermittent or chronic dysphonia, vocal fatigue and voice breaks (Cohen, Bach & Postma, 2002). Generally, the voices of LPR patients are of poorer quality with restricted phonation abilities compared to those of healthy people (Jin, Lee, Jeong, Jeong, Lee & Tae, 2008).

Other symptoms frequently seen in LPR, delineated by Sataloff, Hawkshaw and Gupta (2010), include: morning hoarseness, prolonged voice warm-up time (greater than 20 to 30 minutes), halitosis, excessive phlegm, xerostomia (dry mouth), coated tongue, possibly geographic tongue, throat tickle, chronic sore throat, dysphagia, aspiration, regurgitation of gastric contents, nocturnal cough, difficulty breathing (especially at night), occasionally pneumonia, and laryngospasm. Reimer and Bytzer (2008), and Schreiber, Garten and Sudhoff, (2009), concur saying that dysphagia and odynophagia are frequently observed.

Hoarseness is a general term used for any change in the character of a patient's voice, and is described by a variety of terms such as breathiness, strain, tremor or roughness (Ulis & Yanagisawa, 2009). A study conducted by Pribuisiene, Uloza and Jonaitis (2002) suggested that in cases where LPR is suspected, idiopathic hoarseness as a symptom was identified in 90, 2% of patients. Other manifestations of the head and neck that have been reported include otitis media, asthma and sinusitis (Koufman et al., 2002).

Sataloff et al. (2006) also emphasise that LPR may lead to a number of other more serious maladies, including infant death syndrome, and carcinoma. Subglottic stenosis and laryngeal cancer have also been associated with LPR (Westcott, Hopkins, Bach, Postma, Belafsky & Koufman, 2004).

A recent case-control study found that patients with reflux were more likely to develop laryngeal cancer compared to controls (Rees, Pazmany, Gutowska-Owsiak, Inman, Phillips, Stokes, Johnston, Koufman, Postma, Bailey & Birchall, 2008). Studies suggest that between 68% and 87% of patients with laryngeal carcinoma have LPR, but caution that despite this high incidence, a causal relationship can be inferred only after due consideration of the multifactorial nature of cellular damage and transformation (Galli, Cammarota, Volante, De Corso, Almadori, & Paludetti, 2006). An important mechanism highlighted in the development of cancer is chronic inflammation. Alternating regular tissue damage and repair-phases trigger alteration at a cellular level and ultimately is a factor that leads to cellular mutation and many tumours. (Galli et al., 2006). LPR is characterised by the exposure of the larynx and hence laryngeal mucosa to reflux and may be the root of the chronic inflammation mechanism (Galli, Cammarota, Volante, De Corso, Almadori, & Paludetti, 2006).

Chronic inflammation is due to the contents of the secretions which are refluxed. These include hydrochloric acid and pepsin which combine to form chlorhydro-peptic complex. This complex causes damage at the intercellular junctions of the epithelium leading to increased permeability and as a result intercellular acidity, alteration of the osmotic balance and cellular death (Galli et al., 2006). The damage caused by reflux on laryngeal mucosa combined with additional inflammatory factors (voice abuse, chronic cough, vomit, recurring infections of the upper airway) would have an influence on the mutation action of well known cancer-causing extraneous factors such as smoking and alcohol consumption (Galli et al., 2006).

Laryngeal carcinoma seems to be highly related to the risk factors of tobacco and alcohol. Awareness is growing that LPR also seems to be an important co-factor, especially in non-smokers (Postma & Halum, 2006). Koufman (1991) reported that in 31 consecutive cases of laryngeal carcinoma LPR was evident in 84%, but only 58% were active smokers. The extent of the relationship between LPR and malignant cellular changes remains to be fully investigated, but the available data suggest that most patients who develop laryngeal carcinoma both smoke and have LPR (Koufman, 1991). Additionally, leukoplakia (a precancerous growth caused by chronic irritation that is visible as white

patches) and other premalignant lesions may resolve or significantly improve with antireflux therapy (Postma & Halum, 2006).

A recent study by Doustmohammadian, Naderpour, Khoshbaten and Doustmohammadian (2010) examined the association between acid-related inflammation of the upper digestive tract and laryngeal cancer. Their study involved 65 patients with diagnosed laryngeal cancer and 65 matched controls. Endoscopic results were collected on all the patients and results indicated a significant difference between groups. The laryngeal control group had erosive oesophagitis and gastritis at a statistically higher level than controls. The researchers concluded that increased acid secretion could account for the increased severe inflammation and erosion present in the patients with laryngeal cancer. Further, they concluded that their study supported the hypothesis that gastric acid and pepsin play a role in laryngeal cancer (Doustmohammadian et al., 2010).

2. 4 Diagnosis of LPR

Diagnosis of LPR is thus important because of its association with laryngeal and upper aerodigestive tract cancer (Ford, 2005). However, the diagnosis of LPR is controversial and a number of methods have been postulated to be effective, although, each presents with a number of shortcomings. The controversy related to diagnosis raises the question whether LPR may be misdiagnosed, over-diagnosed, or under-diagnosed.

There are 3 principal methods for diagnosis of LPR. Diagnosis can be made on the basis of ambulatory 24-hour double probe pH monitoring, impedance testing, as well as symptoms and laryngeal findings (Koufman, et al., 2002). However, lack of consensus on diagnosis of LPR has arisen from issues with all of these methods.

pH testing is considered the diagnostic gold standard for LPR by some (Habermann, Kiesler, Eherer, 2002; Barry & Vaezi, 2010). This is because reflux laryngitis is deemed to be caused by episodes of acid and peptic reflux into the laryngopharynx (Joniau et al., 2007). Dual pH probes are conducted over an 18 to 24 hour period in an outpatient setting. The lower probe is placed approximately 5 centimetres above the lower oesophageal sphincter. The upper probe is placed just above the upper oesophageal

sphincter. Placement is made with the assistance of manometry or endoscopy (Postma & Halum, 2006). The upper oesophageal sphincter is seen as the final barrier against LPR. Therefore placement of the probe at this point ensures that if measurements are made at the upper probe and indicate the presence of LPR, is in all likelihood taking place.

There is however, controversy regarding the efficacy pH testing in LPR diagnosis, (Vaezi, Hicks & Abelson, 2003) be it with single or dual probes (Abaza, 2004). False negatives may result from the intermittent nature of LPR or pH may be neutral possibly due to suggested changes in pepsin and non-acid content of the refluxate as suggested by Abaza (2004).

LPR signs can occur in patients with weakly acid or non-acid reflux. Reflux is classified as either being acidic or non-acidic based on the pH of the refluxate measured by the probes during monitoring (Mainie, Tutuian, Shay, Vela, Zhang, Sifrim & Castell, 2006). Gastric refluxate typically contains both pepsin and acid. Pepsin is an enzyme produced in the stomach as pepsinogen. However, when pepsinogen is exposed to acid it is converted to pepsin and is able to digest protein (Printza, Speletas, Triaridis & Wilson 2007). Therefore when pepsin is absorbed by laryngeal cells and reactivated by a drop in pH as seen in LPR, this causes further damage to the larynx (Gupta & Sataloff, 2009). This mechanism provides one possible explanation for the finding of LPR symptoms and signs in patients with weak or non-acid reflux (Gupta & Sataloff, 2009).

Patients with nonerosive reflux disease (NERD) have less lower oesophageal acid exposure than patients with Erosive Oesophagitis (EE). A study by (Savarino, Tutuian, Zentilin, et al., 2010) as cited by Lee, Kim, Ryu, Kim, Cheong, Lee and Song, (2010) compared reflux episodes and symptoms associated in NERD and EE patients using combined Multichannel Intraluminal Impedence (MII)/pH-metry. They reported that acid reflux episodes, volume, and acid clearance were crucial factors in the cause of reflux induced lesions (Lee, Kim, Ryu, Kim, Cheong, Lee & Song, 2010).

Joniau et al. (2007) reviewed 13 double pH probe studies on patients diagnosed with LPR and 11 studies on normal controls. The findings reveal a low number of reflux events in diagnosed LPR patients and only a marginally higher incidence than normal controls. No

statistical differences were found between the prevalence of pharyngeal reflux events in normal controls or diagnosed patients (Joniau et al., 2007).

Disagreement abounds regarding the normative data and values related to reflux in pH studies (Ford, 2005). Normal pH values for the hypropharynx are not well established (Printza, Speletas, Triaridis & Wilson, 2007). However, the aim of a recent study was to use a new probe measure in order to try to establish the pH thresholds in normal subjects in order to be able to identify abnormality in pH (Ayazi, Lipham, Hagen, Tang, Zehetner, Leers, Oezcelik, Abate, Banki, & DeMeester, 2010).Results from this study indicate that even normal subjects have distinctly different pH thresholds in upright, (pH of 5.5), compared to supine ,(pH of 5.0), positions (Ayazi et al., 2010).

Smaller changes in pH are necessary to damage laryngopharyngeal tissue, than for oesophageal tissue (Ford, 2005), although lower oesophageal standards for GORD are often applied to LPR diagnosis. Ford (2005) suggests that a drop in pH to less than 5 may better indicate LPR as neutralising factors such as saliva and airway secretions can raise pH values. In addition, the potential harm from non-acid or gaseous refluxate is not accounted for in pH tests (Ford, 2005). This system may be susceptible to damage by non-acid reflux due to mucosal differences of the oesophagus and the upper aerodigestive tract.

Furthermore, a study by Johnston et al. (2004) suggests that exposure to pepsin during LPR causes a decrease in carbonic anhydrase III in the laryngeal epithelium which results in reflux related inflammatory laryngeal injury. Carbonic anhydrase III is responsible for producing bicarbonate ions that neutralise refluxed gastric acid by entering the extracellular spaces. Therefore a reduction in carbonic anhydrase would translate into less protection of mucosa due to decreased bicarbonates, enabling the pepsin to remain active and cause cellular damage.

Smaller pH changes in gaseous refluxate, a decrease of more than 1 (>1), have been found increasingly in patients with LPR compared to those with GORD or healthy controls (Ford, 2005). Joniau et al. (2007) postulate that unreliability in pH tests leads to significant over-diagnosis of this disease.

A study by Muderris, Gokcan and Yorulmaz (2009) indicates that placement of the pH probes during measurement is crucial to accurate identification of true hypopharyngeal reflux episodes. They suggest that a bifurcated, triple-sensor pH probe allows for monitoring of the oesophagus and hypopharynx simultaneously. Ideal placement of the probes is above the upper oesphogeal sphincter, one below the upper oesophageal sphincter and one in the distal oesophagus. Single probe, double sensor pH monitoring is more commonly utilised in LPR diagnosis and Muderris et al. (2009) suggest that greater accuracy is achieved if the proximal probe is placed in the pharynx as opposed to the upper oesophagus. Clearly placement of the probe will have an impact on whether occurrences of refluxate are accurately monitored and recorded. This in itself poses a problem with diagnostic accuracy as probes may shift or reflux may occur at instances when the patient is not being tested (Gupta & Sataloff, 2009).

Further evidence against pH monitoring is found in a study where patients with pharyngeal reflux documented by pH monitoring were no more likely to respond to acid-suppressive therapy than patients with no documented reflux (Ulualp, Toohill & Shaker, 2001). These findings along with the lack of consensus regarding placement of the pH probe, decreased consistency in the pH being measured and the intermittent nature of LPR reduces the enthusiasm for pharyngeal pH monitoring in the diagnosis of LPR.

Impedance testing is a more recent form of diagnosis and relies on a catheter that measures electrical resistance (impedance) between different points along the oesophagus. It is superior to pH monitoring in that it is able to detect the reflux of acid and non-acid liquid or gaseous material. (Barry & Vaezi, 2010). Liquid boluses decrease impedance while gaseous boluses increase the impedance between electrodes (Maron & Jordaan, 2010).

Another method that seems to have had some success in diagnosing LPR is the ambulatory multichannel intraluminal impedance (MCII) (Srinivasan, Vela, Katz, Tutuian & Castell, 2001). MCII functions by measuring changes in the resistance of intraluminal gases, liquid, or bolus to alternating current between a series of metal electrodes, placed in the oesophagus (Srinivasan et al., 2001). MCII is able to detect the direction of the flow of small amounts of material in the oesophagus (Abaza, 2004). This

is important in those patients who, experience non-acid or weak acid reflux as refluxate can still be detected regardless of the pH (Abaza, 2004).

Other patients who may not be suitable candidates for regular dual probe pH monitoring can also be successfully identified using this method. Another advantage is that the pH level, as well as the normative standards for the oesophagus and the larynx become less important, provided that it is was clear that refluxate is reaching the laryngopharynx and therefore causing damage. This method of diagnosis is often reserved for those whom, do not respond to empirical treatment regimes, thus warranting alternative diagnostic investigation (Bove & Rosen, 2006). Because non-acid reflux events in symptomatic patients who have had negative pH probe studies may therefore be detected (Postma & Halum, 2006), Musser et al. (2009) have suggested that impedance testing may provide greater agreement amongst diagnostic methods and ultimately diagnosis of LPR may become less elusive.

Due to the absence of definitive diagnostic criteria laryngopharyngeal reflux remains a subjective entity according to, Bove and Rosen (2006). Attempts to increase the reliability of clinical investigation for identifying patients with LPR led to the establishment of the Reflux Severity Index (RSI) and the Reflux Finding Score (RFS) (Joniau et al., 2007). The development of such scales has begun to remedy the diagnostic void (Bove & Rosen, 2006). pH testing and impedance measures of assessment are then only recommended for those patients who do not respond to treatment (Bove & Rosen, 2006).

The Reflux Finding Scale (RFS) (Appendix C) is a well known multipoint scale designed by Belafsky, Postma and Koufman (2001b) that rates clinical signs and appearance of the larynx and pharynx in order to determine the presence and severity of LPR. The scale investigates eight laryngoscopic signs: subglottic oedema, (swelling below the glottic region), ventricular obliteration, (refers to oedema of the true and false vocal folds appearing to obliterate or obscure visualisation of the laryngeal ventricle), erythemia or hypermia (erythemia of the arytenoid cartilages), vocal cord oedema (oedema of the false

and true vocal folds), diffuse laryngeal oedema, posterior commissure hypertrophy (mucosa of the posterior commisure is hyperatrophied and becomes swollen to varying degrees), granuloma or granulation tissue (most commonly in the region of the vocal process) and the presence of thickened endolaryngeal mucus (Abaza, 2004; Barry & Vaezi, 2010; Sataloff, Hawkshaw & Gupta, 2010; Postma & Halum, 2006; Belafsky, Postma et al., 2002).

The total reflux finding score can range from 0 (best) to 26 (worst) (Barry & Vaezi, 2010). The authors of the scale determined that an individual with a score higher than 7 can with 95% certainty be diagnosed as having LPR (Belafsky et al., 2001b).

There have been conflicting reports on the validity and reliability of the RFS. Koufman et al. (2004) indicate that the RFS has been shown to be a valid scale with good inter- and intra -rater reliability. Joniau et al. (2007) contradict this in their paper highlighting that only laryngeal granulations have been associated with reflux and claim that validation of the RFS has been weak. In contrast, a study by Aviv, Liu, Parides, Kaplan and Close (2000) indicated that posterior laryngeal oedema is the hallmark of LPR. Joniau et al. (2007) noted that laryngeal findings commonly ascribed to LPR can be identified in as many as 64%- 86% of normal controls. This indicates that laryngoscopic findings have decreased specificity or sensitivity to LPR diagnosis. A study by Branski, Bhattacharyya and Shapiro (2002) cited by Barry and Vaezi (2010) indicate the diagnosis of LPR tends to be subjective as laryngeal findings are often nonspecific. Barry and Vaezi (2010) feel that the RFS as a diagnostic method has not been validated in a large-scale randomised trial and consequently has yet to be incorporated into routine otolaryngology practice. Despite this, laryngeal clinical findings as a means of diagnosis are widely utilised.

Patient report and rating of symptoms is another method commonly used in clinical practice. The Reflux Severity Index (RSI) (Appendix B) was developed by Belafsky, Postma & Koufman (2002). They advocate the use of this scale in conjunction with the RFS. The RSI is a 9 item self-rating system scaled from 0-5, in which the patient rates reflux symptom frequency (Koufman et al., 2002). This subjective scale is utilised in measuring changes beyond clinical laryngeal findings (Abaza, 2004). The maximal score

is 45 points and a score of greater than 5 strongly suggests LPR (Belafsky, Postma, Amin & Koufman, 2002). The symptoms outlined in the RSI include: hoarseness, throat clearing, excessive mucus or postnasal drip, difficulty swallowing, coughing, breathing difficulties, a sensation of a lump in the throat, heartburn, chest pain or indigestion (Belafsky, 2008).

The symptoms described above are not however, exclusive to reflux related damage, and may be associated with smoking, voice abuse, allergies, viral infections, inhaled environmental irritants and alcohol abuse (Ford, 2005; Reimer & Bytzer, 2008). Diseases that have similar symptoms may thus be mistakenly labelled as LPR. Belafsky, Rees, Rodriguez, Pryor and Katz (2008) suggest that some signs and symptoms of LPR may be attributed to oesophopharyngeal reflux (EPR) and LPR may therefore be over diagnosed. A combination of three symptoms, hoarseness, throat itching, and globus pharyngeus were found to separate LPR patients from healthy individuals significantly (Pribuisiene et al., 2002). However, a recent study on the RSI questionnaire indicated that it did not adequately capture the full range of potential reflux symptoms regularly encountered in otolaryngology patients. This study may in fact contribute to the ongoing uncertainty about the role of acid or pepsin suppression (Papakonstantinou, Leslie, Gray, Chadwick, Hudson, & Wilson, 2009). If this is indeed the case then a more comprehensive scale may be needed, although independent Israeli and Italian studies both found good reliability and clinical validity of the RSI in identifying patients with LPR when it was translated into Hebrew and Italian (Schindler, Mozzanica, Ginocchio, Peri, Bottero & Ottaviani, 2010; Cohen, Gil & Fliss, 2005)

The presentation of Paradoxical Vocal Fold Movement (PVFM) disorder may mimic a multitude of laryngeal and pulmonary entities such as asthma, LPR disease and polyps amongst others as well as dystonia and laryngospasm (Murry, Tabaee & Aviv, 2004). Rosen et al., (2004) claim that patients with LPR and noncompliant cough in the absence of pulmonary disease should be evaluated for PVFM disorder. This is due to the symptoms of PVFM disorder being both laryngeal and respiratory in nature including: wheeze, cough, dyspnea, choking sensation, chest pain, stridor, reflux, dysphonia, dysphagia (Murry et al., 2004). A number of these symptoms are used for differential

diagnosis of LPR, and therefore PVFM disorder may be co-occurring with LPR or LPR indeed may be mistaken for PVFM disorder.

Various other methods of diagnosis have been suggested. One such method is a trial treatment regime (Pribuisiene, Uloza & Jonaitis, 2002). Diagnosis in this method is usually based on the response of LPR symptoms to empirical treatment (Bove & Rosen, 2006) with proton pump inhibitors (PPI's). The success of this method will be discussed later under management of LPR. The success of the diagnosis then seems to depend on the success of the treatment. Therefore if treatment fails was the patient incorrectly diagnosed or is treatment not sufficient for other reasons?

This lack of specificity in all of the prevalent methods of diagnosis, may lead to a degree of over-diagnosis of LPR disease (Joniau et al., 2007, Randhawa, Mansuri & Rubin, 2010), or alternatively under-diagnosis, leading to prolonged symptoms, delayed healing and decreased quality of life (Ford, 1999). Both can lead to unnecessary costs (Ford, 1999).

Furthermore, a distinct correlation between symptoms and laryngitis is unclear (Reimer & Bytzer, 2008) A recent study by Musser, Kelchner, Neils-Strunjas and Montrose (2009) found that LPR symptoms and physical findings of LPR were not significantly associated on the RSI and the RFS. In cases of LPR the laryngeal findings are not always associated with symptom severity (Khan, Hashmi, Elahi, Tariq & Ingrams, 2006). A study by Qadeer, Swoger, Milstein, Hicks, Ponsky, Richter, Abelson and Vaezi (2005) found that the most common symptoms in LPR were sore throat (40%), hoarseness (30%), and cough (20%), whereas the most common signs were medial arytenoid wall erythemia/oedema (60%), interarytenoid erythemia (50%), and arytenoid complex erythemia/oedema (50%). The study involved 72 patients with symptoms of LPR and laryngoscopic findings suggestive of LPR despite aggressive acid suppression therapy. Each patient underwent fundoplication, a surgical treatment for reflux, and was monitored post operatively for a year using a daily record of symptoms and laryngeal signs. Patients were assessed at 6 and 12 months post-fundoplication via laryngoscopy. Interestingly laryngeal signs resolved in 80% of patients by the 12 month laryngoscopy indicating successful surgery. However, only 10% of patients had symptomatic improvement. Therefore neither signs nor symptoms may be used as a substitute for the

other. The study concluded that there appears to be poor correlation between signs and symptoms of LPR.

This study confirmed earlier findings by Belafsky, Postma and Koufman (2001a) in which laryngeal signs of LPR continued to improve while symptoms of LPR only showed limited improvement following a 6 month treatment with twice-daily PPI's.

A survey of approximately 2,000 gastroenterologists and ENT physicians indicated that oedema and erythemia of the larynx were the most common signs used for LPR diagnosis (Ahmed, Khandwala, Abelson, Hicks, Richter, Milstein, & Vaezi, 2006). This however, should be done with caution as studies have found that 86% of healthy volunteers had at least one sign attributed to LPR (Hicks, Ours, Abelson, Vaezi, & Richter, 2002; Milstein, Charbel, Hicks, Abelson, Reicheter, & Vaezi, 2005). Specifically 70% of the normal controls had interarytenoid bar, 29% had erythemia on the medial edge of the arytenoids and 21% had posterior pharyngeal wall cobble stoning (Hicks et al., 2002). Alarmingly they also found that different instruments used for endoscopic evaluation lead to different laryngoscopic findings. Flexible endoscopy was able to detect abnormalities in 93% of the population compared with 83% through the rigid endoscope (Milstein, Charbel, Hicks, et al., 2005).The study by Qadeer et al. (2005) suggests a multifactorial aetiology for LPR, since most of the authors patients' symptoms improved only after adjunctive therapy for other conditions.

2. 5 Management of LPR

Difficulties experienced with effectively treating LPR raise questions regarding accuracy of diagnosis. Three conventional methods of treatment are outlined in the literature (Ford, 2005). These include; *lifestyle* and *dietary* changes; *medication* and *surgery*.

Koufman et al. (2002), suggest that mild and/or intermittent cases of LPR should be treated with *dietary and lifestyle* modifications, as well as with an H2 antagonist. Lifestyle and dietary changes recommended are limiting fat intake, cessation of smoking, avoidance of caffeine, carbonated drinks, alcohol and acidic fruit juices. Further, not eating within 3 hours of bedtime; and limiting wearing tightly fitted clothing around the waist (Sataloff, 2005). Some research indicates that lifestyle and dietary changes are less

effective in patients with LPR than those with GORD (Abaza, 2004). Bove and Rosen (2006) state that LPR is seldom managed with behaviour modification alone.

Medical management is the most commonly utilised treatment method (Abaza, 2004). Proton Pump Inhibitors (PPI's) are the mainstay of therapy in LPR, although they are not without controversy regarding their efficacy (Reimer & Bytzer, 2008). PPI's are the drug of choice in GORD and are highly effective in resolution of long-term acid-related symptoms (Reimer & Bytzer, 2008). However, management of LPR using PPI's are successful in as few as 60% of patients (Belfasky et al., 2008). This has caused some clinicians to question the role of gastric refluxate in these patients (Belfasky et al., 2008). Difficulties with PPI management may be attributed in some instances to contents of the proximal oesophagus being refluxed into the laryngopharynx, and so it has not had time to mingle with gastric juices. The American Academy's Speech and Swallowing Committee recommended a 6 month empiric treatment with bid PPI for LPR as initial treatment (Abaza, 2004). More prolonged and aggressive treatment for LPR compared to GORD is needed according to, Koufman et al. (2002). However, a resistance to PPI's in those who, initially respond to treatment may develop (Sataloff et al., 2006). A study by Karkos and Wilson (2006) could not establish a significant effect of this medication over placebo on the symptoms and signs of reflux laryngitis (Joniau et al., 2007).

The failure of a percentage of patients to successfully respond to PPI therapy may be due to the fact that the laryngeal and pharyngeal symptoms associated with reflux are very common and can also be due to a number of other aetiologies such as -: allergy, smoking, asthma, infections, voice abuse or alcohol abuse (Printza, Speletas, Triaridis & Wilson, 2007). Specifically a number of patients with allergic laryngitis are misdiagnosed with LPR and therefore fail treatment with proton pump inhibitors (Randhawa, Mansuri & Rubin, 2010). The diagnosis of such cases may be called into question. PPI therapy as a means of management seems to be inaccurate and erratic as symptoms (as measured by the RSI), laryngoscopic findings (as measured by the RFS), or abnormal findings on pH monitoring will not predict response to PPI therapy (Reimer & Bytzer, 2008). In juxtaposition to this Hammer (2009) indicates that a reflux symptom index and a reflux finding score may be beneficial in assisting with selection of the minority of patients who, may profit from acid-suppressive therapy.

Voice problems are associated with LPR and require a team approach (Sataloff, 2005b). Care is provided by the otolaryngologist, speech therapist and voice and singing coach, when applicable. The otoloaryngologist plays a key role in diagnosis and medical management of LPR. The voice and singing coach teach the patient to use various vocal and body movement techniques to optimise physical function and break down tension (Sataloff, 2005b). The singing coach promotes relaxation, abdominal and thoratic muscle strength as well as breath control (Sataloff, 2005b). Chronic throat clearing and a feeling of a lump in the throat, symptoms of LPR according to, Belafsky et al. (2008), may lead to vocal abuse and consequently may cause vocal chord oedema, contact ulcers and polyps (Martin, 1987). The speech therapist will attempt to improve the vocal symptoms related to these physiological and anatomical changes through various techniques. However, it is likely that a combination of treatment options is able to give the best and most sustainable results in treating LPR.

For those who do not experience any relief with the individual or combined approaches to treatment there is *surgical* management. Surgical intervention is reserved for severe cases of LPR, non-acid reflux and those who have not found success with alternative management (Bove & Rosen, 2006). Laprascopic Nissen fundoplication surgery is found to be useful in certain patients (Abaza, 2004; Lindstrom, Wallace, Loehrl, Merati & Toohill, 2002). Restoration of lower oesophageal competence is the goal of surgery (Ford, 2005). Positive feedback has been reported in a study by Oeschlager, Eubanks, Oleynikov, Pope and Pellegrini (2002) where a significant decrease in pharyngeal reflux was reported in patients who, underwent surgical intervention.

It must however, be noted that one study of surgical fundoplication indicated that surgery is not recommended for patients whose symptoms do not respond to aggressive PPI therapy (So, Zeitels & Rattner, 1998). Alternatively Remacle and Lawson (2006) suggest that surgical intervention is a good option for patients with observable high volume reflux and abnormal lower sphincter competence when medical management fails. Despite these conflicting reports, surgical intervention must be considered as a last resort for those patients with severe LPR, and it may not be successful in resolving or even reducing LPR. However, for some, nissen fundoplication's role in LPR has yet to be defined (Westcott, Hopkins, Bach, Postma, Belafsky & Koufman, 2004).

Treatment of LPR is difficult and not consistent across all patients. What works in some cases has no impact on others. Treatment is thus arduous and controversial due to diagnosis being vague and challenging (Joniau et al., 2008).

> 'Because of a paucity of convincing evidence regarding techniques for establishing definitive diagnosis and causation in individual patients, and because of a plethora of imperfect studies that have produced conflicting conclusions, LPR diagnosis and management remain controversial'
>
> (Sataloff, Hawkshaw & Gupa, 2010 p.214).

This research therefore aimed to establish the relationship between the Reflux Severity Index (RSI) and the Reflux Finding Score (RFS) in participants that have attended the Wits University Donald Gordon Voice and Swallowing clinic. The aims were:

- to establish if there is a correlation between the total RFS and RSI scores
- to ascertain if certain test items of the RSI and RFS are elevated in said patients
- to describe trends related to RFS and RSI sub-scores and
- to verify if extraneous factors such as age, gender, professional voice use and smoking impact on the sub scores of the RFS and RSI and to describe trends based on these variables.

Method

3.1 Aims

The primary aim of this research was to establish the relationship between ratings on the RSI and RFS in participants who attended the WITS University Donald Gordon Voice and Swallowing clinic. The subordinate aims were:

(1) to establish if there was a correlation between the total RFS and RSI scores

(2) to ascertain which test items of the RSI and the RFS were elevated in the participants

(3) to describe trends in RFS and RSI sub scores and

(4) to determine if extraneous factors such as age, gender, professional voice use and smoking impact on the sub-scores of the RFS and RSI and to describe the trends based on these variables.

3.2 Research Design

The research study employed a retrospective descriptive quantitative design with a correlational within-subject component and a comparative between-subject component (Schiavetti & Metz, 2002).

Retrospective research enables investigation of a large amount of data that has been collected prior to the formulation of the research question (Schiavetti & Metz, 2002). This is particularly relevant to this study as 105 patient's charts were reviewed. The charts contained information that had been previously collected between 2005 and 2008 at the clinic where the records are stored. This aspect of the design is crucial as it allows the data which may not have been collected with the formulated research question to be used for research purposes.

A descriptive design is used to observe differences in a group, developmental trends, or interaction among variables that can be measured by the researcher (Schiavetti & Metz, 2002). In this study the RSI and the RFS results were evaluated. Trends and interactions among the different subscores were described.

Quantitative data is also known as measurement data and refers to one of the two kinds of numerical data. Quantitative data is obtained by measuring objects or events (Howell, 1999). In this study the scores on the RSI and the RFS were measured as well as the scores on the individual items for a given sample of participants.

Correlational research is an example of a within-subject design in descriptive research as a number of measures are applied to a group of participants (Schiavetti & Metz, 2002). An advantage of a within-subject design is that the problem of extraneous variables impacting on one group of participants and not the other is eliminated (Shiavetti & Metz, 2002). Within the current research all the participants were assessed on the RFS and the RSI, and the relationship between the two measures was evaluated. A correlational research design is employed to study the relationship among two or more variables by evaluating the degree to which changes in one variable affects change in the other variable (Schiavetti & Metz, 2002). One of the major components of the current research project aimed at identifying the relationship between variables on the RFS and RSI and gaining insight into the impact that change in one variable has on another variable.
The comparative component involved comparing groups of participants in terms of age, gender, smoking status and professional voice use to evaluate the effects of these variables on the RFS and RSI ratings.

3.3 Participants

Inclusion Criteria
The participants were selected based on the following criteria.

Firstly, they had to have attended the Donald Gordon Voice and Swallowing Clinic (DGVS). All of the patients attending this clinic will have a voice or swallowing disorder that may be reflux related, as discussed in the literature review. In the initial stages of data collection, patients files from the DGVS clinic were utilised. During the data collection phase the files were moved to the Netcare Parklane Clinic, where the remainder of the data was collected. This did not impinge on the study as all of the patients RFS and RSI scores had been completed whilst they were attending the DGVS clinic. Therefore, no interference from the new site was evident due to the retrospective

nature of the research. A clinic similar to that held at DGVS clinic is conducted at Netcare Parklane Clinic. The Netcare Parklane clinic is serviced by the same team of specialists that scored and evaluated the scales for each patient in this study.

Secondly, each participant must have completed the Reflux Symptom Index questionnaire themselves prior to consultation with the multidisciplinary team. Only patients with a total RSI score of greater than 5 (>5) were included in the study as according to, Belafsky, Postma, Koufman (2001b).

Thirdly, patients must have undergone both a trans-nasal and trans-oral fibreoptic video - stroboscopy so that their laryngeal status had been observed and recorded. This allowed the researcher to obtain the Reflux Finding Score.

Rigid and flexible endoscopy was conducted with each patient for a number of reasons including:

> "Videostroboscopy is performed with a rigid endoscope placed in the mouth up to the tongue base or a flexible fibre-optic trans-nasal endoscope with a xenon light source passed through the hypo-pharynx for an unimpaired view of the larynx. Flexible fibre-optic trans-nasal endoscopy is preferred for evaluation of neurolaryngeal disorders (including hypokinetic dysarthria, spasmodic dysphonia, essential tremor, and paradoxical vocal fold motion) for best visualisation of vocal fold mobility, differentiation of vocal fold paralysis from paresis, hypo- and hyper-functional vocal fold behaviours, and laryngeal muscle tone and agility. The latter is also used when examination with a rigid endoscope does not allow adequate visualisation due to structural interference or patient discomfort."
>
> (Thibeault & Zelazny, 2010, paragraph 45)

The two approaches are thus used for different purposes and are important in differential diagnosis. Previous research has shown that flexible endoscopes significantly underrepresented reflux signs and a rigid laryngeal endoscope should be utilised as an ideal when examining the larynx for signs of LPR (Eller, Ginsberg, Lourie, Heman-Ackah, Lyons & Sataloff, 2009). However, contradictory findings indicate that signs such as interarytenoid bar, erythemia of the medial wall of the arytenoids, considered to be signs in LPR, were more often detected with flexible than with rigid laryngoscopes, suggesting that flexible laryngoscopy is more sensitive in identification of laryngeal tissue irritation (Milstein, Charbel, Hicks, Abelson, Reicheter, & Vaezi, 2005). Sataloff, Hawkshaw & Gupta (2010), also indicate that flexible laryngoscopy may be useful in patients with a hyperactive gag reflex which is common in patients with severe LPR. Therefore there are pros and cons for each of these endoscopes and both were utilised as they provide the most holistic picture of the larynx.

The majority of patients included in the study were adults who are more reliable in terms of their completion of the RSI which is a subjective rating scale. Children may have difficulty understanding what the questionnaire is asking them, and parents may not be able to adequately record the child's experience of a symptom as they do not experience the symptom themselves.

Further, children are assessed using a number of different rating scales compared to those utilised with adult patients. This is because many of the symptoms for LPR must in fact be visible or noticeable to an external person (such as a parent) in order for them to be scored on a scale. Adult's symptoms of LPR may be subjective and only noticed by the patient for example lump in the throat. The children's scales were developed to account for these factors and have been tested for reliability and validity. Three well known surveys of voice for adults have been adapted to the paediatric population. Firstly, the Voice Outcome Survey has been adapted to create the Paediatric Voice Outcome Survey which is a four-item parental proxy.
Secondly, the well utilised voice related Quality of Life questionnaire adapted to a 10 item parental substitute, the Paediatric Voice Related Quality of life questionnaire. Thirdly, the voice Handicap index which was adapted to a 23 item parent replacement – Paediatric Voice Handicap Index (Verduyckt, Remacle, Jamart, Benderitter, & Morsomme, 2009). The youngest participant included in the study was 12 years old.

Although this participant is legally not an adult, the literacy abilities and understanding of a 12 year old was considered adequate. This implies that the participant would be able to read the RSI independently or have it read to him, answer the scale questions accurately and therefore be included in the study.

Sampling

A retrospective chart review of 250 patients seen at the DGVS Clinic from 2005 to 2008 was conducted. Of these files, 105 records were considered viable and were included in the research, based on the selection criteria described above.

Sample Recruitment

Participants were recruited through the use of written informed consent during their first consultation at the DGVS clinic. Each patient attending the clinic, decided prior to consultation if their files and data may be used for research purposes (Appendix A). If patients met the inclusion criteria and had provided written consent for the use of their records they were included in the study. The flow diagram in figure 3.1 represents the process of sample recruitment.

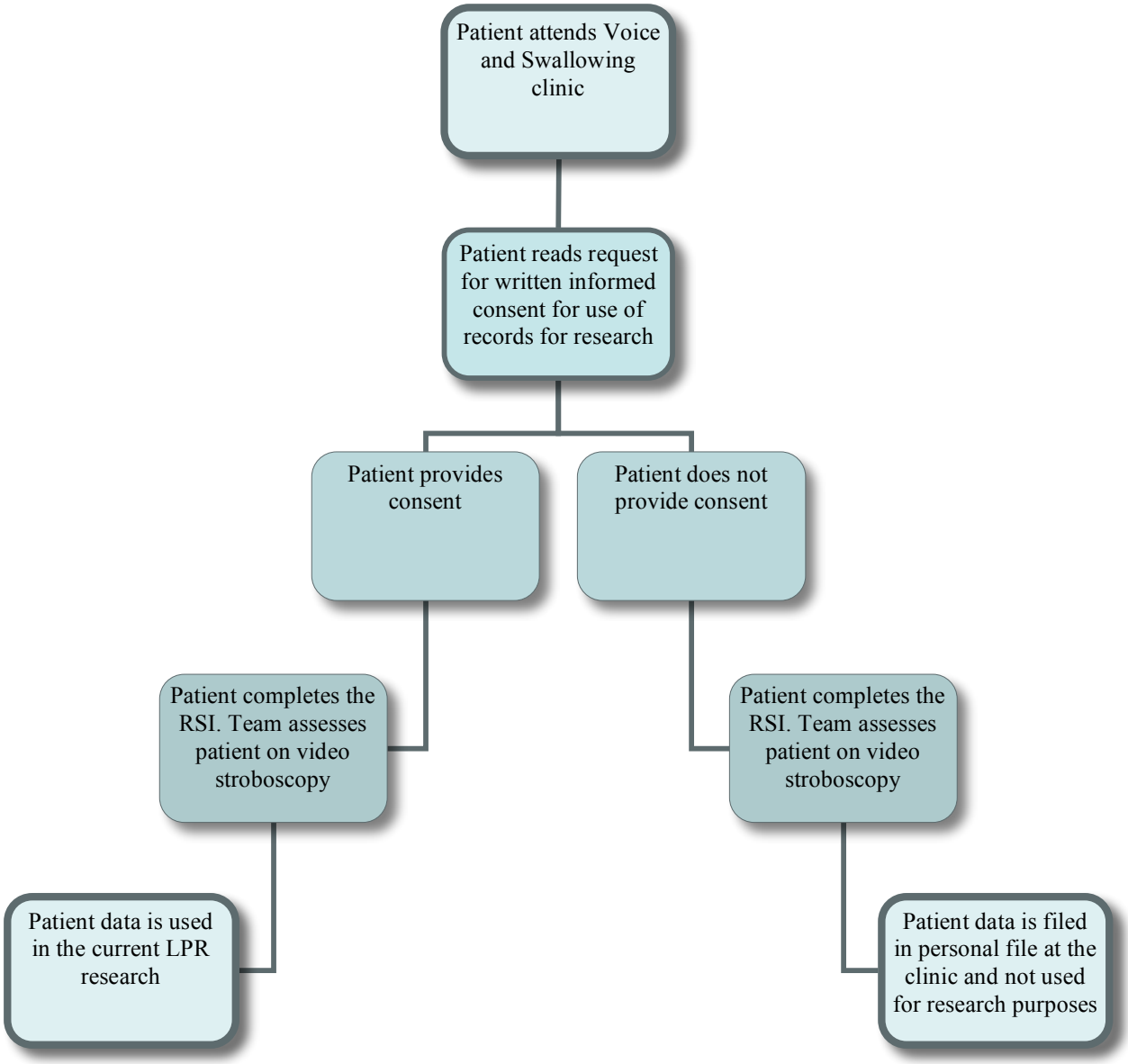

Diagram 3.1 Flow Diagram representing the procedure for Data collection

Description of Patients

One hundred and five (n=105) patients' records were included in the study. The participants are described in Table 3.1.

Table 3. 1. Description of patients

Total patients	Male	Female	Smoker	Non-smoker	Prof. voice user	Non-prof. voice user
105	43	62	21	84	50	55

Of the sample 43 participants (40,95%) were men and 62 participants (59,05%) were women. This does not necessarily translate into females being more prone to LPR than males. This difference in gender within the sample is due to the fact that the sample was not age and gender matched. Rather participants were incorporated into the study based solely on the inclusion criteria and not extraneous variables. It may in fact be that women attend to health related queries before men do, or that females feel that a vocal problem is more of an issue than men do based on their background and propensity for communication and speaking. Alternatively there may be more LPR in females than males based on minute structural differences in enzymes, histology and general levels of sensitivity. We cannot make these assumptions based on the information that we have on this topic. This may be a topic for further research.

The age range of the sample was from 12 years to 89 years with highest proportion of patients (n=21 or 20%) , (n=19 or 18%) for patients in the age range from 20–to-29 years and 30-to-39 years of age respectively. The 50-59 year old age range comprised 17 (16%) participants while the 40-49 year decade comprised 16 (15%) participants and the 60-69 year old category (13%; n=14) of the sample. The lowest age range from 12 years to 19 years comprised (8%; n=9) while the upper end of the age spectrum, 70-79 years reflected (5%; n=6) of the sample. The smallest number of participants were in the 80-89 year old population with only 3 (2%) of the sample in this range. This distribution may be affected by a number of factors and again a relationship between age and LPR prevalence can not be inferred on this data alone. However, age and its relationship with the signs of LPR as evaluated on the RFS and symptoms as evaluated by the RSI were explored statistically and descriptively as part of this research report.

The mean age of participants was 43,4 years. The median age was 41 years. (The median refers to the number in the range that is in the centre or middle of the data set.) The sample demonstrated a bimodal distribution with 27 and 61 years of age representing the modes. (Mode refers to the highest or most commonly occurring number within the data set). The wide age range contributes to the external validity of the study, as these results have applicability to a greater age range of the general population. Table 3.2 shows the mean, mode and median of the ages of patients included in the study.

Table 3. 2. Measures of central tendency of patients' age

Mean age	**Median**	**Mode**
43,4 years	41 years	27 & 61 years

Within the sample, 21 (20%) of the participants were smokers and 84 (80%) were non-smokers. This represents an unexpectedly large difference between the number of smokers and non-smokers in the research group. This difference may be attributed to social factors, such as socio economic background, or perhaps fewer people smoke due to widespread knowledge regarding the health risks of smoking. This may also be linked to the higher proportion of females in the sample compared to males. Young males are more likely to be smokers than middle aged females. The mode of the sample was 61 years and this population may have reduced smoking tendencies due to other health issues they may experience e.g. diabetes etc. However, perhaps the most obvious explanation is that patients who, suffer from LPR had noticed a reduction in respiratory difficulties and cough if they reduce or cease smoking. Smoking status as a variable impacting on the RSI and RFS ratings was also examined.

Of the sample 50 (47,6%) were professional voice users. This is marginally lower than non professional voice users. Despite this small difference it confirms the notion that this group does constitute a significant proportion of the case load at a voice clinic. This population does seem to have a propensity for developing reflux. Professional voice users

are justifiably even more anxious about their voices than the rest of the population because a voice problem is a threat to their livelihood.

These two subgroups have a small amount of overlap as can be seen from diagram 3.2 below. Of the 105 participants,46,7% (n=49), were non-smokers and non-professional voice users. Non-smoking professional voice users made up 33,4% (n=35) of the sample. Professional voice users who, smoked made up 14,2% (n=15), of the sample and smokers who, were non-professional voice users constituted only 5,7% (n= 6) of the sample. Therefore 30% of the professional voice users in the sample were smokers compared to 11% of non-professional voice users being smokers. More than a quarter of the professional voice users are smokers. This is surprising as one would expect professional voice users to be aware of the effects that smoking may have on respiration, voice and damage to the oral and laryngeal structures. It is commonly recommended that professional voice users should take these risks more seriously as their careers depend on the optimal functioning of their voice. It is clear that the majority of patients in the sample are non-professional voice users who, do not smoke.

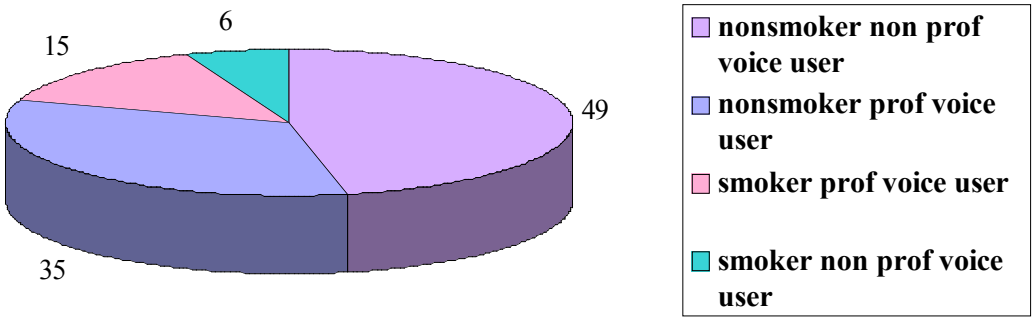

Diagram 3. 2 Pie chart illustrating the relationship between smoking status and professional voice status in the sample (n=105).

The sample size was large enough to allow for results to be generalised with more confidence and leads to better external validity of the study (Schiavetti & Metz, 2002). The large sample size also allowed for a representative sample of each category of participants in terms of gender, age and professional vs non-professional voice users.

3 4 Ethical considerations

This research hinged on patients records. Patients are deemed to be at risk populations and research using their records necessitates ethical clearance from the University of the Witwatersrand Medical Ethics Committee. Ethical clearance was obtained in April 2009 Protocol number: M090467 (Appendix E).

Ethical considerations necessitated obtaining written informed consent from patients of the WITS University Donald Gordon Voice and Swallowing Clinic to have their records and results utilised for research purposes. On the initial visit to the WITS University Donald Gordon Voice and Swallowing Clinic each patient was given a written consent form (Appendix A). The form was explained and each patient asked if they would consent to have their files and data utilised for research purposes. The patient is not under any obligation to agree and there are no negative consequences to indicating they would not like their results to be used for research purposes. This was explained to each patient and they were also told that they were entitled to withdraw their consent at any point without any implications. The patient is requested to complete the informed consent form marking either that they do consent to their details being utilised for research or they do not consent. This written informed consent form is filed in their patient files at the Donald Gordon Voice and Swallowing clinic.

Patients were reassured that personal information will not be utilised or documented in the research. In this study, a coding system, assigning a number to differentiate patients' ratings, assured that the research was anonymous and confidential. The retrospective methodology also protected the patient, taking into account their rights as well as enabling the researcher to extract and examine information in a way least intrusive to the

patient. The researcher has accounted for reliability and validity threats that may interfere with data collection and analysis.

3.5 Measures

Patient Rating Scale:

Symptoms of laryngopharyngeal reflux were measured using the Reflux Symptom Index, a scale developed by Belafsky et al. (2002). The self-rating scale allows 9 items to be rated from 0-5 by the patient. This scale is typically used in otolaryngology practices to establish the subjective perception of possible reflux (Appendix B). Patients are required to fill in the RSI prior to seeing the team of specialists at the clinic. Patients are instructed to fill in the scale as best as they can, rating each symptom on the scale from 0 = no problem to 5 = severe problem. The patient is requested to rate each of the items on the scale according to, how the symptoms affected them in the last month. Patients are given time before their consultation with the team to complete the form, some may even complete the scale prior to their arrival for the evaluation. Any areas that are unclear to the patient can be explained by a nurse or a staff member at the clinic familiar with the scale. Once the patient has completed the RSI scale they take it with them into the team consultation and the specialists review their symptoms before physical examination.

Clinical Rating Scale:

The presence and signs of reflux laryngitis are rated using the Reflux Finding Score (Appendix C). This scale was developed by Belafsky et al. (2001b). The scale is utilised during fiberoptic and stroboscopic laryngoscopic evaluation to gauge the presence or absence of reflux based on clinical observation of typical signs. Observation is made possible through the use of videostroboscopy. The team view structures within the larynx and pharynx and rate them on the basis of presence or absence and severity of pathology. This scale is independent of the patient and only the medical team conduct the rating. The RFS is a consensus rating by three independent experts in voice, and was developed to standardise laryngeal findings enabling clinicians to better diagnose and assess therapeutic efficacy in patients with LPR (Belafsky et al., 2002).

Instrumentation:

The laryngoscopic evaluation for each patient was conducted using the Kay Elemetrics 9100B rhino-laryngeal stroboscope. This allowed the anatomical structure of the larynx and pharynx to be observed while functioning, therefore, sanctioning the clinician to make judgements related to any possible pathological structures seen and their impact on functioning of the vocal folds. The stroboscopy is a crucial part of the measurement procedure, as it enables the clinician to complete the RFS.

This form of evaluation allows detection of vibratory asymmetries, structural abnormalities, small masses, submucousal scars, laryngeal neoplasims and other conditions that are not visible under ordinary light (Sataloff, 2005a). The strobe illuminates different points on consecutive vocal fold waves and the lighted portions are fused together visually to create a cycle. The perception of the stroboscopy being in slow motion is created by the strobe light and the frequency of vocal fold vibration desynchronised by approximately 2 Hertz (Sataloff, 2005a). By combining the strobe light with a camera these patients evaluations can be recorded and re-evaluated at a later date or by other professionals. Sataloff (2005a) indicates that on initial examination his practice routinely evaluates patients with both flexible and rigid endoscopes. The flexible laryngoscope allows evaluation and documentation of the natural laryngeal motion without obstruction from the tongue, as well as being useful in patients with a sensitive gag reflex who, cannot tolerate rigid trans-oral endoscopic usage (Sataloff, 2005a).

Both flexible trans-nasal and rigid trans-oral endoscopic video-stroboscopy was conducted. The trans-nasal flexible fiberscope allowed for observation of the upper vocal tract and full evaluation of connected speech, laryngeal and supraglottal postures (Morrison, Nichol & Rammage, 2001). The rigid fiberoptic scope was used orally to view the same structures. Both trans-oral rigid fiberoptic endoscopes and trans-nasal flexible fiberoptic endoscopes are used as they provide different information. The flexible trans-nasal endoscope provides visualisation of the vocal folds with normal laryngeal posture and provides a more accurate assessment of the posterior glottic opening, than during rigid endoscope usage (Sataloff, 2005b). A rigid fiberoptic endoscope used trans-orally provides a better more detailed picture which allows more intricate findings, as well as a better 3 dimensional perspective of the vocal fold edge (Sataloff, 2005b).All patients

were examined using the same equipment, ensuring no differences or discrepancies in the overall RFS rating between participants.

3.6 Procedure

A letter requesting permission to use the DGVS clinic as a site for research into laryngopharyngeal reflux was submitted to the ENT's who, work in the clinic. The proposed area of research, rationale and implications for the study were presented in the letter. A letter of approval from the site allowing access to their records was granted (Appendix D).

The patients were previously evaluated at the clinic by an interdisciplinary team composed of: two Otolaryngologists, a Speech Therapist and a Voice Coach. The members of the team are experienced with voice patients and professional voice users. The team members consult from the Donald Gordon Voice and Swallowing Clinic. At each consultation with said team the participant completed a RSI form and the team completed a RFS evaluation based on stroboscopy findings. Both the RFS and the RSI scores were filed in the patient files at the clinic.

The researcher reviewed the files of patients seen at the clinic. The files of each patient were dissected and the relevant information necessary for this study extracted. The RFS and RSI totals for each patient's first visit were examined and evaluated. An RSI score of more than five (>5) indicates the possibility of Laryngopharyngeal Reflux, (Belafsky et al., 2001b). Therefore, patients whom had a score of greater than 5 on the RSI scale were included in the study. The totals for the RFS and the RSI and the score for each item on the scales were captured on a spreadsheet thus constructing a database. Further, information required to fulfil the sub-aims of the study including age, gender, profession and smoking status were also included in the database. With respect to age, participants were divided into subgroups of a 10 year age span producing 8 subgroups numbered 1 to 8. Patients were classed as either professional voice users (speech therapist, actor, singer, performer, rabbi, teacher/lecturer) or non professional voice users.

Therefore each patient on the Microsoft Excel database had a set of RFS and RSI sub-scores as well as total RFS and RSI scores. Gender, age, profession and smoking status were also captured. Each patient's information and data was allocated a file number within a coding system instead of being correlated to a name. Therefore anonymity and confidentiality of patient records was maintained.

From this data a summarised Microsoft Excel spreadsheet was constructed. The summary was more concise and was formatted so that it could be used in the SAS program for statistical analysis. The patients were coded as 's' if they were smokers and 'ns' if non-smokers. They were labelled as 'm' for male and 'f' for female, 'y' if they were professional voice users and 'n' if they were non-professional voice users. Patients were separated into age subgroups (1-8) as described above. Items on the RFS and the RSI were abbreviated to an acronym in order to make the spreadsheet more succinct than the original spreadsheet. An abbreviated example of an entry on the Excel spreadsheet is provided below in figure 3.3.

#	smoke	Age	gender	Prof voice	SO	VO	ER	VCO	DLO	PCH	GRAN	OT	Tot
2.	ns	35	m	n	0	0	4	3	3	3	2	2	17

Figure 3.3. An example of the coding system utilised in the excel spreadsheet.

Patient files were examined and analysed in sets of 20-30. The researcher made a list of files that were being utilised and left this at the clinic, should it be required for follow up visits by the patients or for reports.

The database was held by the researcher as it was a working document and was updated as more patient files and scores were added to the database. Once the spreadsheet was completed and all aspects had been coded, statistical analysis was conducted using the SAS 9.2 analysis programme.

3.7 Data Analysis

The scores on the RFS and RSI scales are categorical variables that can only take on a small set of values (Howell, 1999). Therefore, the scores are discrete points (0,1,2,3,4,5) and are ordinal, providing no information regarding differences between points of the scale (Howell, 1999). Ordinal data requires a nonparametric methods of analysis. (Shiavetti & Metz, 2002). The total RSI and RFS scores could however, be treated as continuous variables and analysed using parametric statistics. Specifically the Pearson Correlation coefficient was used to establish the relationship between the RFS and the RSI scores, the primary aim of the research.

The non-parametric Cohen's Kappa co-efficient was used to correlate the sub-scores within and between the RSI and RFS. However, this proved difficult as the RFS and the RSI use varying methods of measuring the data i.e. some aspects on the RFS are scored as absent or present using scores of 0 or 2 whereas others are rated in severity from 0 to 4. The RSI uses a 5 point rating scale for all items. Where possible therefore, the correlation was done automatically by the SAS 9.2 programme.

The second aim to ascertain which aspects of the RSI and the RFS are raised in the patients was achieved using descriptive statistics.

The third aim was to describe trends related to the RFS and the RSI. This aim was also achieved through descriptive statistics.

The fourth aim to verify if extraneous factors such as age, gender, professional voice use and smoking impact on the totals of the RFS and RSI was achieved using t-tests for gender, smoking status and professional voice use and an analysis of variance to assess whether the age groups were significantly different from each other on the total RSI and RFS scores.

The differences between groups on the sub-scores of the RSI and RFS were assessed using the non parametric Chi–square statistic.

3.8 Reliability & Validity

Reliability:

The Rosenthal effect, specifically the interactional effect (i.e. the observer affects the recording of the participant's behaviour), observer effects, interpreter effects and intentional effects (Shiavetti & Metz, 2002) are reduced in the current research through the following methods. Observer and interpreter effects are reduced as the researcher and the team conducting the assessments are not the same. The researcher is not present during the rating of the RFS nor is the researcher present with the patient while completing the RSI. As the team assessing the patient have no vested interest in the outcome it is unlikely they will influence the RFS score either to indicate or not to indicate reflux laryngitis. The fact that the researcher does not have any interaction with the participants at any stage in the research further reduces observer and interpreter effects. Intentional effects are accounted for by having more than one team member assessing the participant's clinical characteristics on the RFS. By doing so any discrepancies between scores are discussed and a consensus regarding the score is achieved and thus inter-rater reliability is achieved (Schiavetti & Metz, 2002). Essentially three raters (2 otolaryngologists and 1 speech therapist) score each item on the RFS together as a group, and a consensus between raters must be reached on each item of the RFS before the result is recorded. Therefore the RFS's reliability is realized.

Validity

The RFS is a nonreactive measure, it does not change what is being measured, and does not impact on the internal validity of the study (Schiavetti & Metz, 2002). The Reflux Severity Index is a reliable and validated measure of reflux signs. It is highly reproducible and exhibits excellent construct-based and criterion-based validity (Belafsky et al., 2002). Both the RFS and the RSI are well utilised scales in research (Joniau, Bradshaw et al., 2007). The external validity and the ability to generalise the results of this study is improved by increasing the sample size (Schiavetti & Metz, 2002).

Results

The results will be presented according, to the aims set out in the methodology. Descriptive statistics will supplement the statistical results. The level of significance chosen for the various statistical analyses was p=0,05 (5%), as the larger the sample the smaller the level of significance selected (Dallal, 2003).

4. 1 Description of Results on the RFS and the RSI

The mean, mode, median, maximum and minimum for the RSI and RFS totals are indicated in table 4.1 below.

Table 4.1 Summary statistics for the RFS and the RSI

Description	RFS (max score = 26)	RSI (max score = 45)
Mean	16,95	19,24
Mode	19	12
Median	18	19
Max	26	45
Min	1	6
Standard Deviation	4,73	8,08

The mean total rating of 16,95 on the RFS is indicative of LPR according, to Belafsky et al. (2001b). The mean total rating of 19,23 on the RSI indicates LPR (Belafsky et al., 2002).

Of the 105 participants, three were rated as presenting with signs reflecting the highest score (26) on the RFS, while only one participant's laryngeal signs were rated as a 1 which according, to Belafsky et al. (2001b) is not indicative of LPR. Only two participants attained the lowest score considered to be indicative of LPR (=7) on the RFS. The mode, which is the most frequent rating attained, on the RFS is 19, suggestive of mild to moderate LPR. The median, the rating that is most central in the distribution is 18, also indicative of mild-to-moderate LPR. After the mode of 19, the next most frequent rating was 17 in 9 participants. More detailed analysis of the number of participants who attained total ratings in various categories on the RFS is shown in figure 4.1.

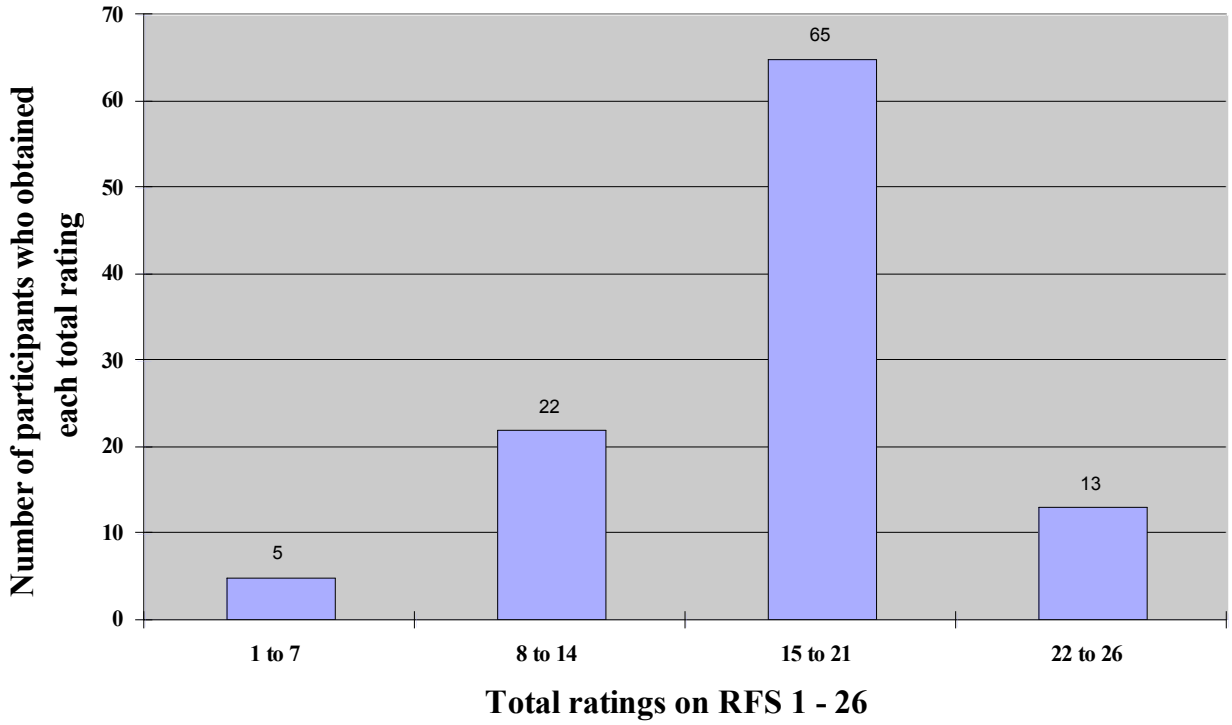

Figure 4.1 Number of participants who attained various total RFS scores.

The totals' ratings on the RFS indicate that the majority of participants were rated between 15 and 21 (65 participants) followed by a rating of between 8 and 14 (22 participants). The upper end of the RFS ratings was from 22 to 26 and only applied to 13 participants, while the lowest ratings between 1 and 7 applied to 5 participants. The exact counts for each rating on the RFS are located below in table 4.2

Table 4.2 Exact ratings on the RFS and number of participants to whom each rating applied.

RFS Rating	Number of participants
1	1
6	1
7	3
8	2
9	1
10	4
11	1
12	3
13	4
14	7
15	6

RFS Rating	Number of participants
16	8
17	9
18	12
19	14
20	9
21	7
22	1
23	6
24	3
26	3

Further descriptions of the number of participants obtaining different totals on the RSI are found in figure 4.2 below. The mode on the RSI is 12 while the median is 19. The maximum rating on the RSI was 45 obtained by 1 person, while the minimum rating was 6.

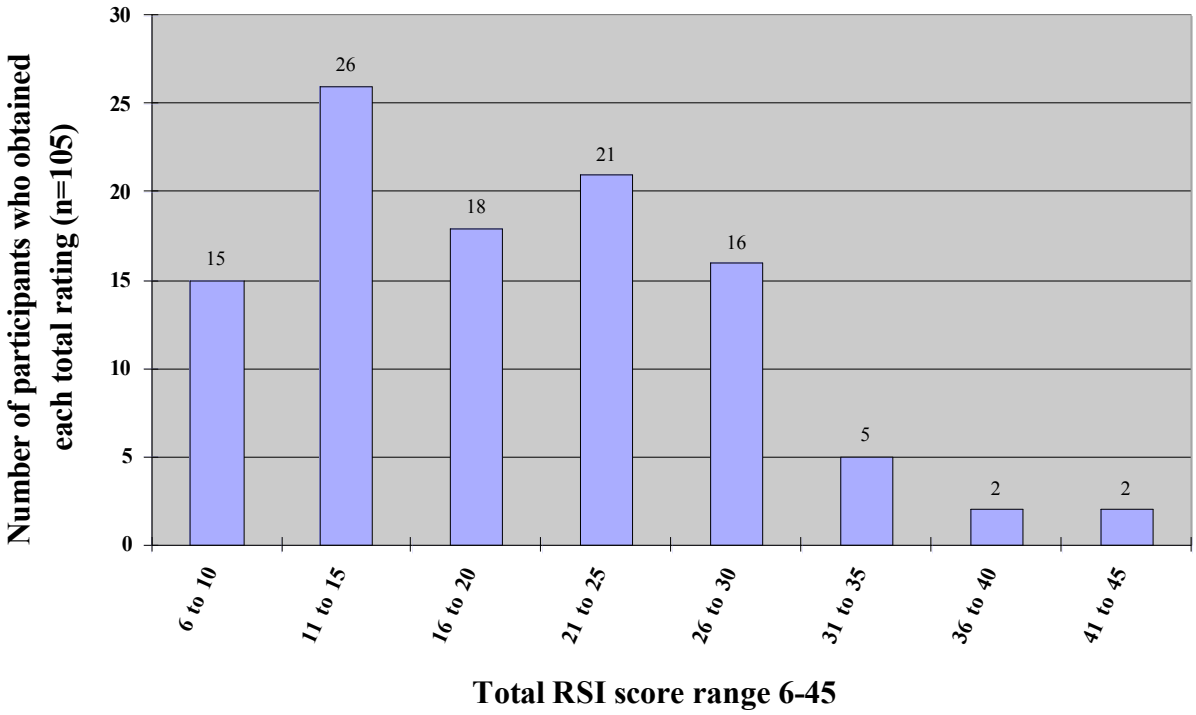

Figure 4.2 Number of participants who rated the total RSI as various severity scores.

Figure 4.2 depicts in which self-rating category most participants placed their symptoms on the RSI. The higher ratings only applied to 4 participants whereas the range from 11 to 15 yielded the most participant ratings (26), closely followed by the 26 to 30 range (21), then 16 to 20 (18), 26 to 30 (16), the lowest range between 6 and 10 applied to 15 participants and the 31 to 35 range applied to 5 participants.

Table 4.3 Number of participants to whom each rating on the RSI applied.

RSI Rating	Number of participants
6	6
7	3
8	3
9	2
10	1
11	4
12	10
13	6
14	4
15	2
16	2
17	5
18	3
19	3
20	5
21	6

RSI Rating	Number of participants
22	5
23	2
24	3
25	5
26	4
27	6
28	1
29	2
30	3
33	1
34	2
35	2
37	1
38	1
43	1
45	1

Table 4.3 indicates the number of participants to whom each exact rating on the RSI applied. The number of ratings over 30 steadily decline and only a handful of participants had total RSI ratings over 35.

4. 2 Trends on RFS and RSI ratings

To establish which test items of the RSI and the RFS were most elevated in patients. The cumulative total rating on each item for the 105 participants was divided by the total possible maximum score yielding a percentage rating for each item.

The motivation for using a percentage as the best way to establish the most frequently rated signs or symptoms in the sample is twofold. Firstly, the number of participants that attained a rating on that item could not be used as each participant is rated on every item.

This means there would be 105 for each item (the total number of participants). Secondly, the RFS is not a uniform scale of measurement unlike the RSI. The RFS has some items that are quandary (have a point rating system) and others that are binary. The total rating for each sign could not be used as a measure for highest rated sign as certain signs would yield a higher total score based on the fundamental nature of the scoring utilised on the RFS. By using percentage to establish which signs and symptoms were most elevated provides a uniform measurement regardless of rating system.

The RFS sub-score trends were examined first. These are provided in table 4.4 below which clearly indicates which laryngeal sign was rated the highest and was therefore the most common laryngeal sign seen in the participants.

Table 4.4 Totals for each sign on the RFS and percentage of the total score

	SO	**VO**	**ER**	**VCO**	**DLO**	**PCH**	**Gran**	**OT**
Total cumulative recorded score	46	190	378	299	317	342	67	148
Possible max total score	210	420	420	420	420	420	210	210
Percent	21,9%	45,2%	90%	71,1%	75,4%	81, 4%	31,9%	70,4%

The most common laryngeal sign was erythemia (90%), followed by posterior commisure hypertrophy (81,4%) and then by diffuse laryngeal oedema (75,4%). Erythemia is rated on a three point scale. Of the 105 participants erythemia was rated as diffuse in 86 (81,90%) participants and 17 (16,19%) participants were rated as having partial erythemia, while only 2 (1,9%) participants were rated as having no erythemia present. The vast majority of patients were rated as having diffuse erythemia.

Posterior commisure hypertrophy was rated as absent (0) in 3 (2,86%) participants, mild (1) in 4 (3,81%) participants, moderate (2) in 14 (13,33%), severe (3) in 26 (24,76%) and

obstructing (4) in 58 (55,24%) participants. The majority of patients were thus rated as having obstructing posterior commisure hypertrophy.

Diffuse laryngeal oedema (DLO) was the third most common laryngeal sign seen in the participants' laryngeal examination. DLO was rated as absent in one participant (0, 95%) and mild (1) in one participant (0, 95%). A moderate rating (2) was assigned to 18 (17, 14%) participants while 60 (57, 14%) received a rating of 3, which is severe. Only 25 (23, 81%) participants were rated as having obstructing diffuse laryngeal oedema. Severe was the most often assigned description to laryngeal oedema in the 105 participants.

Vocal Cord Oedema at any severity was seen in 103 participants and was the fourth highest score (71, 1%) compared to other subtests on the RFS. This was closely followed by "Other" (which indicates thick endolaryngeal mucous) 70,4%. Vocal cord oedema is rated as absent to polypoid. The participants' ratings revealed that 2 (1, 9%) were rated as having no vocal cord oedema (VCO), 5 (4,7%) with mild VCO, 23 (21,9%) with moderate, 52 (49,52%) with severe and 23 (21,9%) participants with polypoid VCO. Therefore the same number of participants who had moderate VCO had polypoid VCO. The majority of participants had severe VCO.
Laryngeal mucus ("other") was deemed to be absent in 31 (29,52%) participants and present in 74 (70,48%) of them.

Ventricular oedema and granuloma were the next most common laryngeal signs seen and lastly subglottic oedema was identified in only 21, 9% of participants. Of the total participants 57 (54,29%) had partial ventricular oedema (VO), 18 (17,14%) had complete VO and 28 had no VO. Granuloma was absent in the majority of participants (71) and present in 33 of the sample. Subglottic oedema (SO) was present in 23 (21,9%) of the records reviewed and absent in most, 82 (78,1%) of the sample.

The description of RSI sub-score trends was conducted in the same way as for the RFS and are set out in table 4.5 located below.

Table 4.5 Totals for each sub-rating on the RSI and percentage of the total

	HRS	TC	Muc	SWD	CLD	BRD	AC	Lum	HB
Total score for category	365	328	349	111	144	108	195	226	199
Possible total	525	525	525	525	525	525	525	525	525
Percent	69,5%	62,4%	66,4%	21,1%	27,4%	20,5%	37,1%	43,04%	37,9%

The total summary indicates that hoarseness was the most commonly self-rated symptom by 69,5% of all participants, followed by mucous in 66,4% of participants and throat clearing in 62,4%. The next most frequently rated symptom was globus sensation (43,04%). Heartburn (37,9%) and annoying cough (37,1%) were very similarly rated in terms of frequency of occurrence by participants. Coughing when lying down was rated as less frequent by 27,4% of participants. Swallowing difficulties (21,1%) and breathing difficulties (20,5%) were both rated as occurring less frequently than the other symptoms.

Below is a more in-depth look at each symptom and the number of participants for each rating on that symptom.

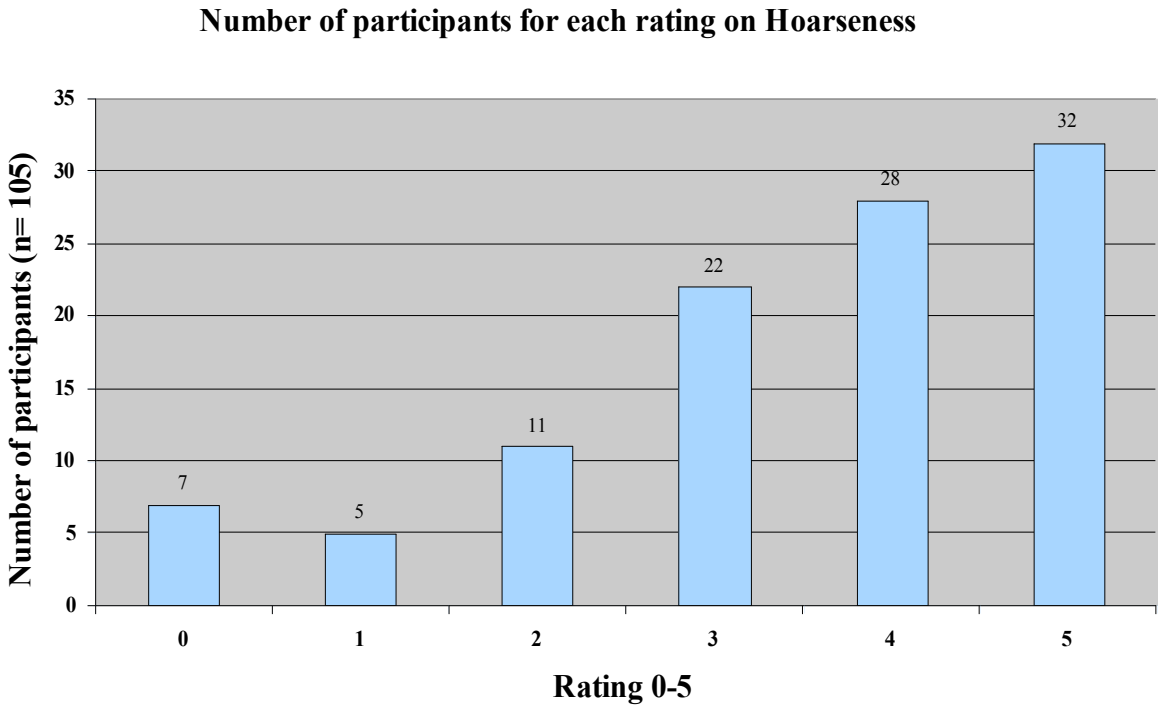

Figure 4.3 Number of participants for each rating of hoarseness

It is clear that hoarseness is most commonly rated by 32 (30,48%) participants as severe (5), 28 (26,67%) rated hoarseness as 4, 22 (20,95%) rated hoarseness as (3), 11 (10,48%) rated this symptom as (2) and 5 (4,76%) rated hoarseness as (1) and 7 (6,67%) rated it as no problem (0).

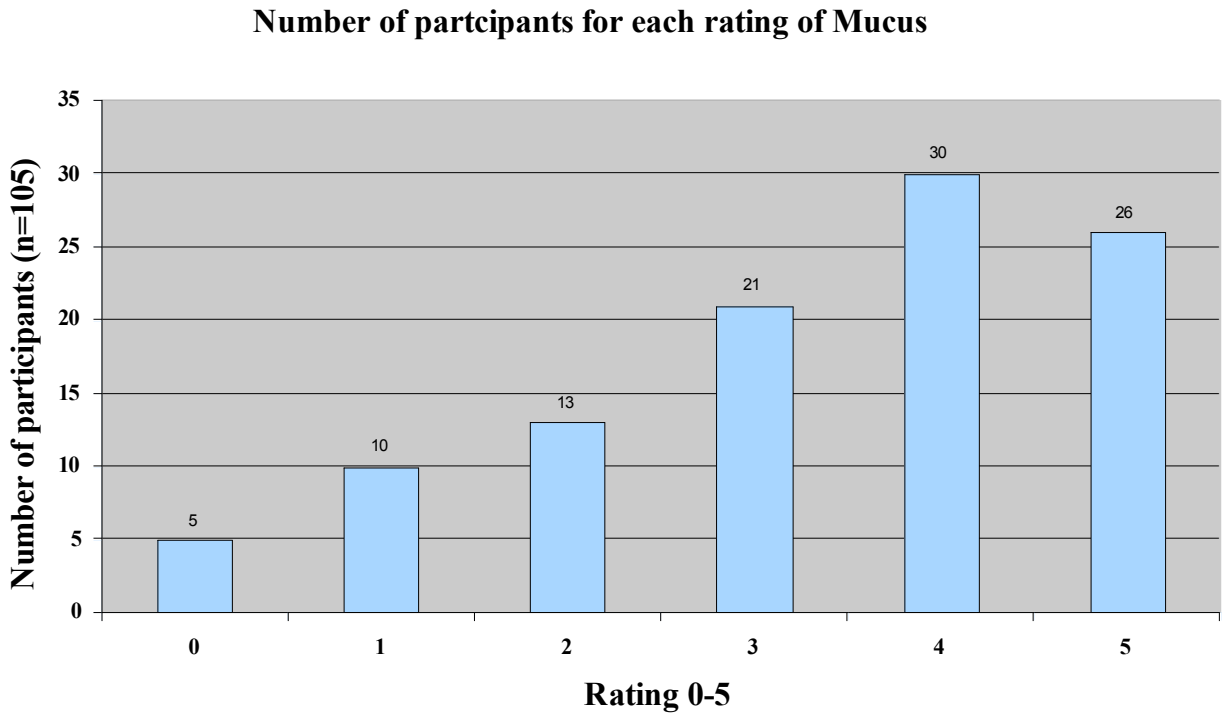

Figure 4.4 Number of participants for each rating of Mucus

Excess mucous was the second highest rated symptom on the RSI with 66, 4% of participants 26 (24, 76%) rating it a (5), and 30 (28, 57%) rating this symptom as a (4). The majority of participants felt this symptom was a (4) as opposed to severe (5). Of the participants 21 (20%) rated mucous as (3), 13 (12, 38%) as (2), 10 (9, 52%) as (1) and 5 (4, 76%) as no problem. Therefore most patients feel that their mucous is not severe enough to warrant being on the highest end of the rating scale.

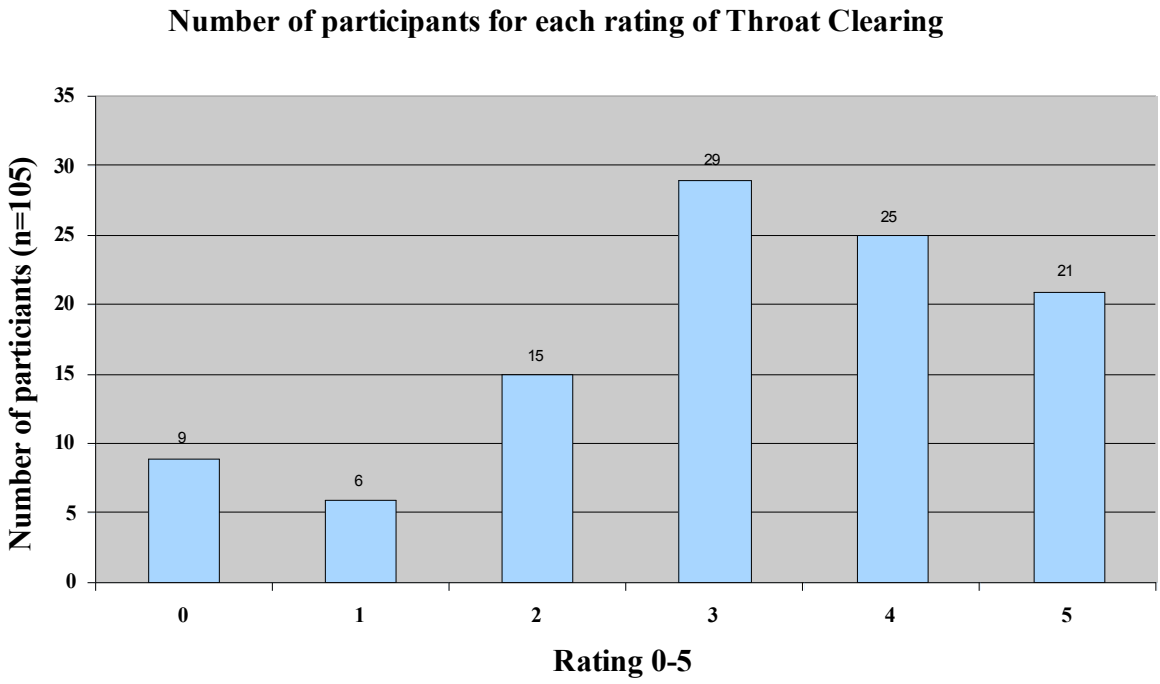

Figure 4.5 Number of participants for each rating of Throat Clearing

Throat clearing was rated as third most common symptom by participants with a score of 62,4%. Of the sample 21 (20%) rated throat clearing as severe (5), and 25 (23,8%) rated throat clearing as relatively severe (4). The majority of participants 29 (27,62%) rated this symptom as moderate (3), and 15 (14, 29%) assigned a rating of (2). The smallest group of participants (6 i.e 5,71%) rated this as (1) while 9 (8,57%) of the sample rated throat clearing as no problem.

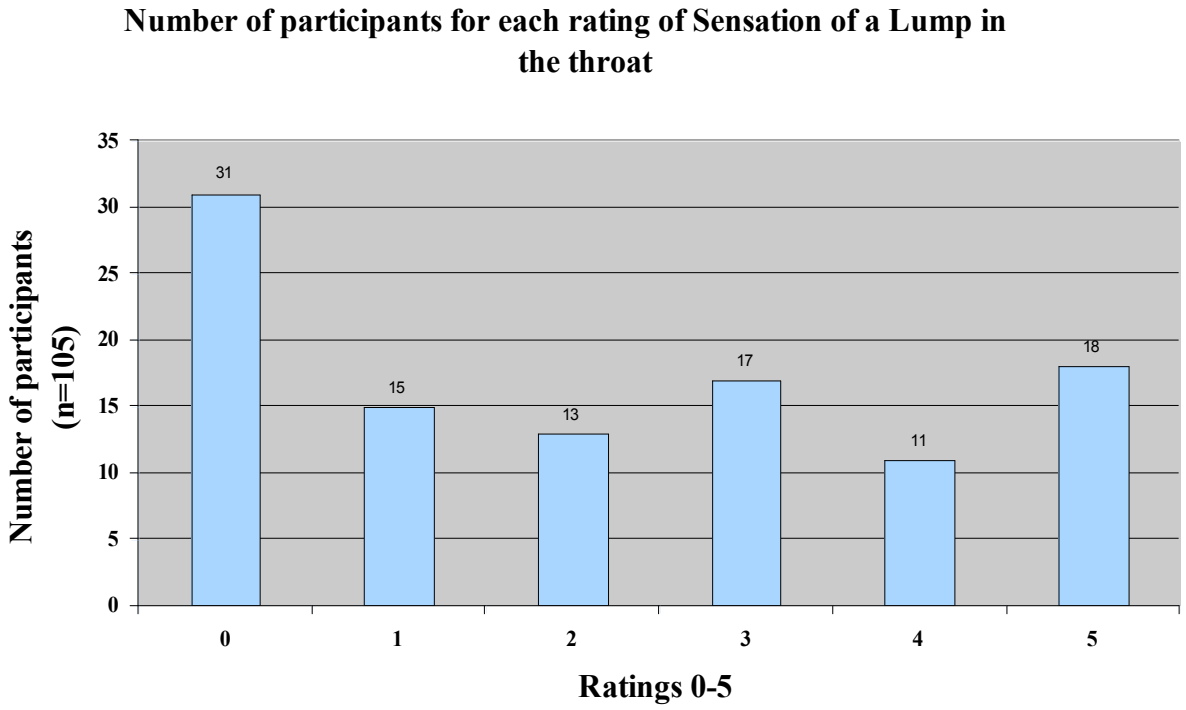

Figure 4.6 Number of participants for each rating of Sensation of a Lump in the Throat

Lump in the throat (43,04 %,) was rated as having less impact on the participants. Lump in the throat was rated by 31 of the participants (29,52%) as never occurring (0). Juxtaposing this, was the next largest group of participants 18 (17,14%) who, rated lump in the throat as severe (5). This symptom was rated by 17 (16,19%) participants as (3), 11 (10,48%) rated this as (4) and 13 (12,38%) rated globus sensation as (2) while only 15 (14,29%) rated this symptom as a (1).

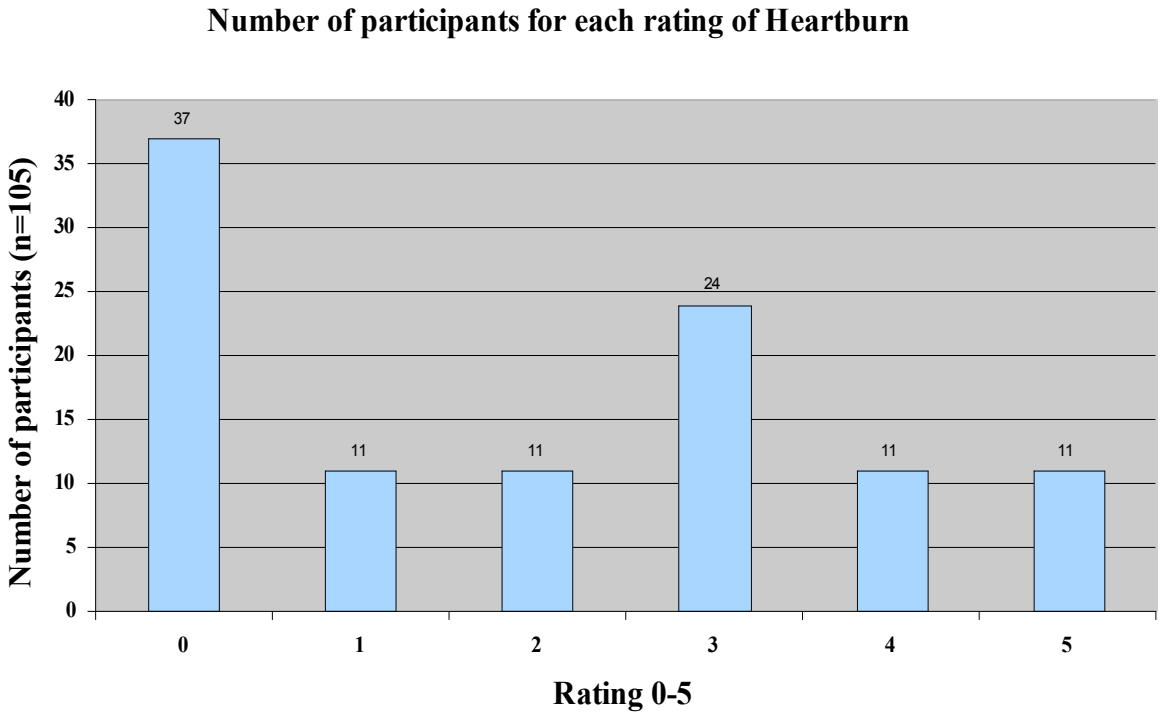

Figure 4.7 Number of participants for each rating of Heartburn

Heartburn was rated as having less impact on the total number of participants (37,9%). Heartburn was rated as not a problem (0) by 37 (35,24%) participants, 11 (10,48%) of the sample rated it as (1), (2), (4) and severe (5). Of the charts reviewed, 24 (22,86%) indicated that heartburn was moderate (3).

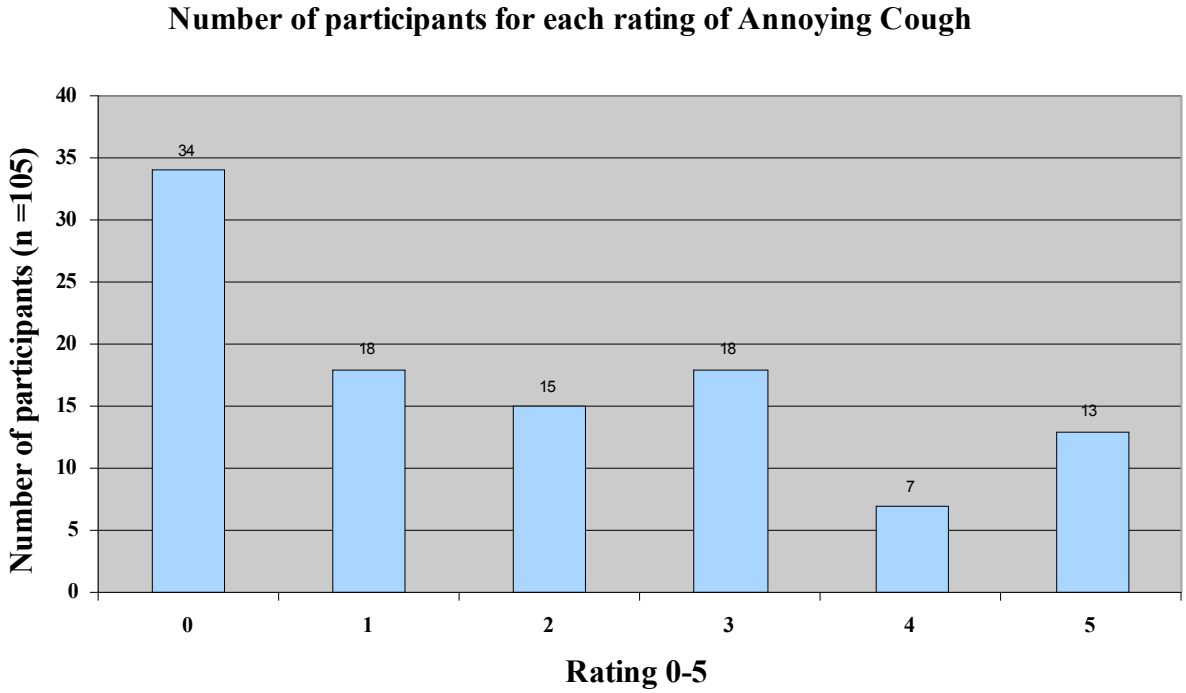

Figure 4.8 Number of Participants for each rating of Annoying cough

Annoying cough (37,1%) which according, to participants occurred less frequently than other symptoms was rated by 34 (32,28%) as no problem (0), 18 (17,14%) rated it as (1), 15 (14,29%) of the sample experienced this symptom as a (2), 18 (17,14%) rated it as (3), 7 (6,67%) rated this symptom as relatively severe (4) and only 13 (12,38%) rated this as severe (5).

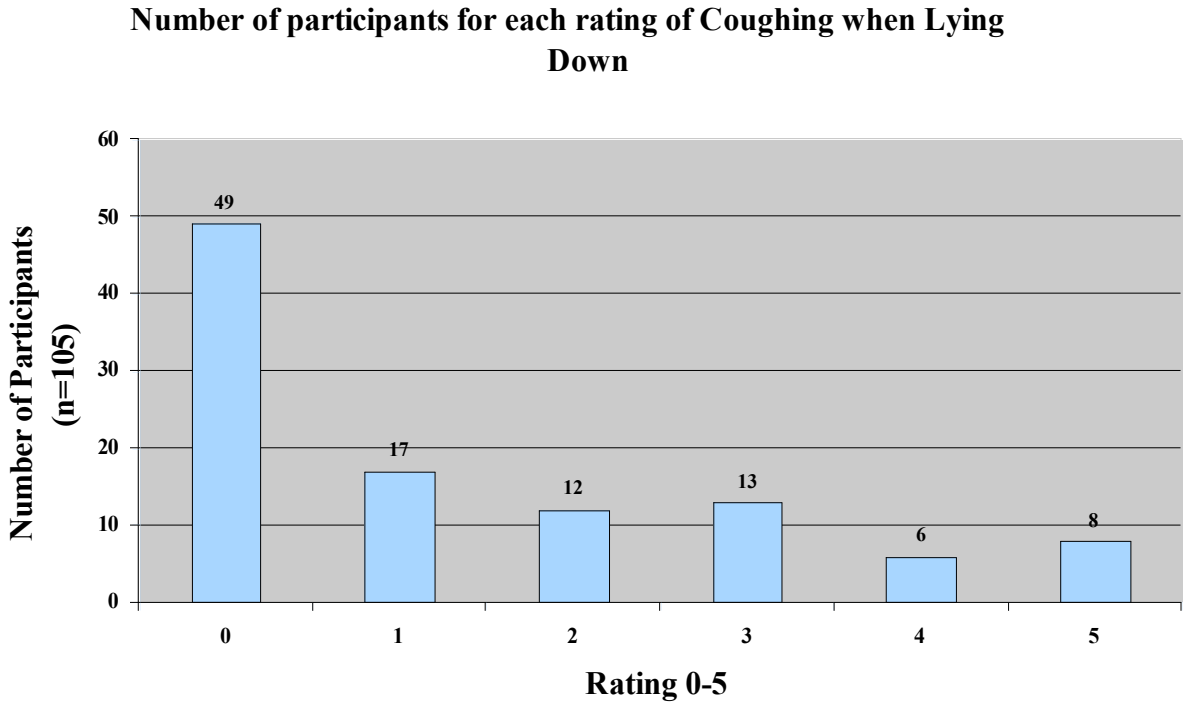

Figure 4.9 Number of participants for each rating of Cough when Lying down

Coughing while lying down was noted as occurring less often (27, 1%) than other symptoms on the scale. The majority of participants 49 (46,67%) said coughing while lying down never occurred, 17 (16,19%) rated this as mild (1), 12 (11,43%) as (2), 13 (12,38%) rated this as occurring sometimes (3), 6 (5,71%) rated it as a (4) and only 8 (7,62%) rated this as severe (5).

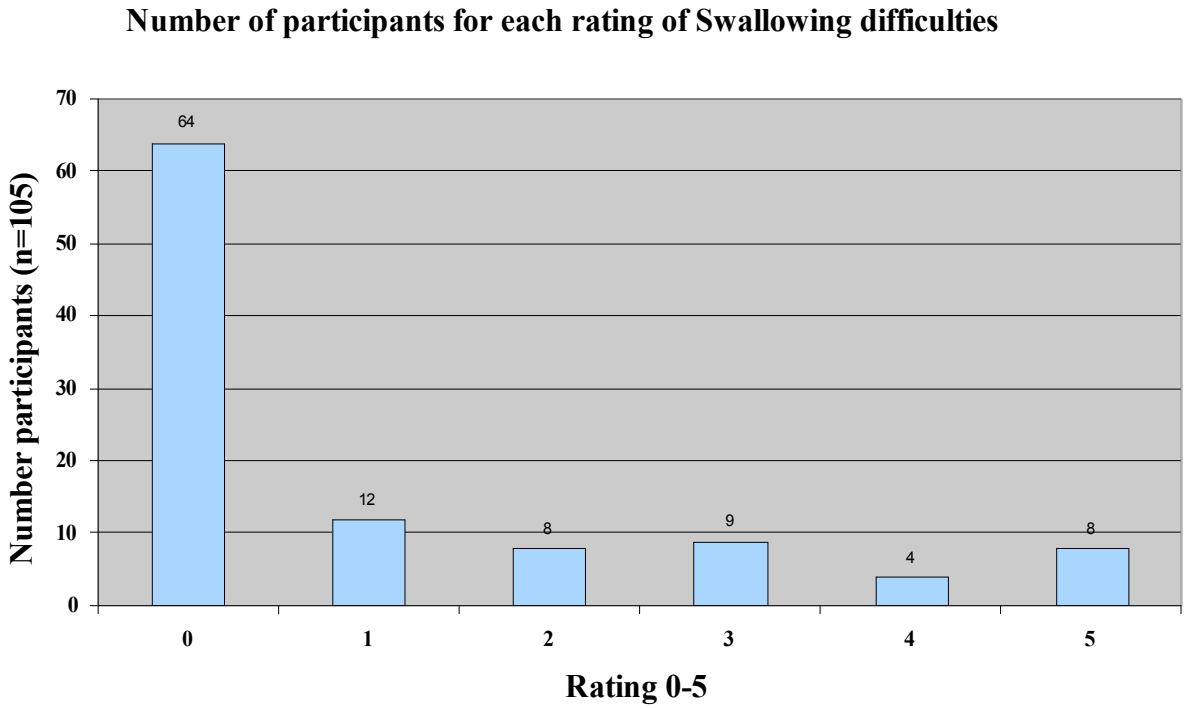

Figure 4.10 Number of participants for each rating of Swallowing Difficulties

Swallowing difficulty occurred less frequently only 21,1% compared to other items on the RSI. Swallowing difficulties were rated by most participants as never occurring (0). Swallowing difficulty was rated as severe (5) by only 8 (7,62%) people, 4 (3,81%) rated the symptom as relatively severe (4), 9 (8,57%) rated it as a (3), 8 (7,62%) rated this as a (2), 12 (11,43%) rated this symptom as (1) and the majority 64 (60,95%) more than half, rated this as never occurring (0).

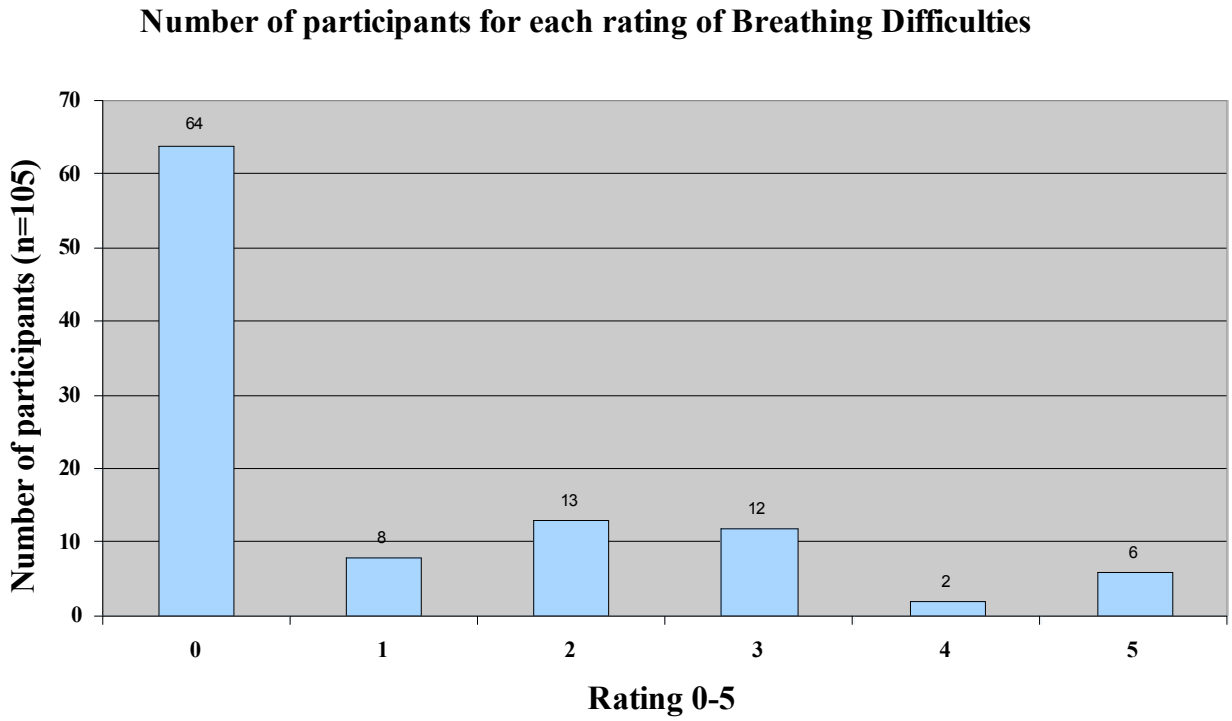

Figure 4.11 Number of participants for each rating of Breathing Difficulties

Breathing difficulties were rated according, to the charts reviewed as being the least common symptom for LPR (20,5%). Breathing difficulty was rated as severe (5) in only 6 (5,71%) participants, 2 (1,90%) rated themselves as a (4), 12 (11,43%) rated this as a (3), 13 (12,38%) rated this a (2) and 8 (7,62%) rated this as a (1), while the overwhelming majority 64 (60,95%) of 105 participants rated this symptom as never occurring (0).

4. 3 Correlation of the total RFS and RSI ratings, and inter-item and intra-scale correlations:

A comparison of each of the total scores on the RSI and the RFS for each participant was conducted. The comparison revealed that the participants (18) who, were rated as demonstrating mild LPR on the RFS, had total RSI ratings of 22 and 11 respectively. The three participants whose LPR signs warranted a total rating of 26 (severe LPR) on the RFS, subjectively rated their symptoms on the RSI as 12, 19 and 23. Only one participant rated her symptoms as 45 on the RSI, which is the highest total rating, yet her RFS rating

was only 10, which is indicative of mild LPR on the RFS. The minimum score on the RSI (6) was only seen in six participants, and these participants were considered to have moderately severe signs on the RFS (18, 6, 18, 12, 19, and 23)

Thus in general, there appears to be a lack of agreement between the subjective RSI rating scale and the more objective RFS rating scale, and the subjective perception of symptoms on the RSI are often more or less severe than the signs observed by the team of specialists.

Statistically this relationship was analysed using a Pearson correlation coefficient in order to determine if a significant relationship exists between the two measures of LPR. The results are set out in table 4.6.

Table 4.6 Correlation matrix for the total RFS and total RSI

	RFS total	**RSI total**
RFS	1.00000	-0.20125 p=0.0395
RSI	-0.20125 p=0.0395	1.00000

A statistically significant weak negative correlation emerged from the analysis (r = - 0, 20 & p= 0,0395). Therefore there is an inverse relationship between the total RFS and RSI ratings. This implies that while one rating increases the other decreases. The mean RFS and RSI ratings (seen in table 4.1) may offer a degree of confirmation of this finding in that the RSI total mean (19,24%) is higher than RFS total mean (16,95%).

Cohen's Kappa Correlation co-efficient was used to statistically evaluate the intra-correlation of items on the RFS and the RSI as well as the inter-item correlation across the two scales. However, it was not always possible to use this method due to the differences in scoring individual items on the RFS and the differences between the RFS and the RSI as described in the methodology section. However, sub-scores that could be correlated were done automatically in the SAS 9,2 programme

4. 4 RSI intra-item correlation

Table 4.7 Intra-item correlations on the RSI between hoarseness and other items

Variable	Cohen's Kappa	One-sided p	Two-sided p	Significant Correlation
Throat clearing	0, 2206	<0, 0001	<0, 0001	Yes
Mucous	0, 1367	0, 0004	0, 0008	Yes
Annoying cough	0, 0739	0, 0217	0, 0434	Yes
Globus sensation	0, 1561	<0, 0001	<0, 0001	Yes
Heartburn	0, 0396	0, 1505	0, 3006	No
Swallowing difficulty	0, 0099	0, 3648	0, 7296	No
Coughing when lying down	-0, 0333	0, 1504	0, 3007	No
Breathing difficulties	0, 0225	0, 2144	0, 4289	No

The intra- item–correlations on the RSI revealed the following relationships:

Hoarseness had a significant positive correlation with throat clearing, excess mucus, annoying cough and lump in the throat. The relationship between hoarseness and heartburn was not significant as was the case for swallowing difficulties, coughing when lying down and breathing difficulties.

Values in table 4.8 show the intra-item correlation of throat clearing with other items on the RSI.

Table 4.8 Intra-item correlations on the RSI between throat clearing and other items

Variable	Cohen's Kappa	One-sided p	Two-sided p	Significant Correlation
Hoarseness	0, 2206	<0, 0001	<0, 0001	Yes
Mucous	0, 2381	<0, 0001	<0, 0001	Yes
Annoying cough	0, 0633	0, 0503	-	Yes (one-sided)
Globus sensation	0, 1546	<0, 0001	<0, 0001	Yes
Heartburn	0, 0588	0, 0731	0, 3916	No
Swallowing difficulty	0, 0038	0, 4505	0, 9010	No
Coughing when lying down	0, 0189	0, 0088	0, 0176	Yes
Breathing difficulties	0, 0086	0, 3916	0, 7832	No

Throat clearing was found to have a significant positive correlation with excess mucus, coughing when lying down, feeling of lump in the throat and annoying cough (one-sided p only). Non-significant correlations were found between throat clearing and swallowing problems, heartburn and breathing difficulties.

It was established statistically that excess mucous had a significant positive relationship with coughing while lying down (kappa = 0,0994; one-sided p = 0,0010 and two-sided p = 0,0020), annoying cough (kappa = 0,1208; one-sided p = 0,0005 and two-sided p = 0, 00010) and the sensation of a lump in the throat (kappa = 0,0948; one-sided p = 0,0076 and two-sided p = 0,0153) Non-significant correlation was noted between mucous and breathing difficulties (kappa = -0,0092; one-sided p = 0,3693 and two-sided p = 0, 7386) as well as swallowing difficulties (kappa = 0,0094; one-sided p = 0, 3685 and two-sided p

= 0,7371) and heartburn (kappa = 0,0573; one-sided p = 0,0637 and two-sided p = 0,1274). The relationship between swallowing difficulties and coughing while lying down was a strong positive correlation (kappa = 0,2321; one-sided p = < 0,0001 and two-sided p = < 0, 0001). This strong positive correlation was also seen between swallowing difficulties and breathing difficulties (kappa = 0,3123; one-sided p = < 0,0001 and two-sided p = < 0,0001), annoying cough (kappa = 0,1185; one-sided p = 0,00047 and two-sided p = 0, 0093), feeling of lump in the throat (kappa = 0,1267; one-sided p = 0,0018 and two-sided p = 0,0037) and heartburn (kappa =0,1303; one-sided p = 0,0022 and two-sided p = 0,0044). A non-significant relationship was found between swallowing difficulties and mucous (kappa = 0,0094; one-sided p = 0,3685 and two-sided p = 0,07371).

Coughing when lying down had strong positive correlation with breathing difficulties (kappa = 0,3172; one-sided p = < 0,0001 and two-sided p = < 0,0001), annoying cough (kappa = 0,3695; one-sided p = 0,0001 and two-side p = 0,0001), feeling of lump in the throat (kappa = 0,1880; one-sided p = 0,0001 and two-sided p = 0,001) and heartburn (kappa = 0,1527; one-sided p = 0,0006 and two-sided p = 0,0012).

Breathing difficulties had a strong positive correlation with annoying cough (kappa = 0,2319; one-sided p = < 0,0001 and two-sided p = < 0,0001), a feeling of lump in the throat (kappa = 0,1019; one-sided p = 0,0096 and two-sided p = 0,0196) and heart burn (kappa = 0,1391; one-sided p = 0,0014 and two-sided p = 0,0028). Furthermore a positive significant correlation was found between annoying cough and feeling of lump in the throat (kappa = 0,1849; one-sided p = < 0,0001 and two-sided p = < 0,0001), annoying cough and heartburn (kappa = 0,1482; one-sided p = 0,0007 and two-sided p = 0,0014) and heartburn and the sensation of a lump in the throat (kappa = 0,1213; one-sided p = 0,0040 and two-sided p = 0,0080).

Thus there were a number of significant intra-item correlations on the RSI, suggesting that it is a reliable measure of LPR symptoms, as perceived by the patient, as this indicates good content validity of this scale (Schiavetti & Metz, 2002).

An analysis of the co-occurrence of symptoms in terms of severity revealed interesting results. The severity of many of the RSI items was closely associated. Severe hoarseness (rated as 5) has a high association with severe throat clearing in 14 (13,33%) participants,

severe excess mucus (rated as 5) in 14 (13,33%) participants and severe sensation of a lump in the throat (rated as 5) in 14 (13,33%) participants. Severe throat clearing has the highest association to severe excess mucous in 15 (14,29%) of all participants. Severe excess mucous is highly associated with severe throat clearing in 15 (14,29%) of participants. Swallowing difficulties (rated as 3 which denotes that a symptom is moderate) are associated with mild mucous (1) by 5 (4,76%) of participants and mild swallowing difficulties (rated as 1); with mild coughing while lying down (rated as 1) by 5 (4,76%) of participants. Mild coughing when lying down (rated as 1) is associated with infrequent throat clearing (2) in 7 (6,67%) of participants. Infrequent coughing while lying down (2) was associated with infrequent annoying cough (2) by 7 (6,67%) of participants.

Breathing difficulties that are moderate (3) are associated with severe hoarseness (rated a 5) in 9 (8,57%) participants. Severe annoying cough (5) is associated with severe mucous (5) by 10 (9,52%) of participants. Moderate heartburn (3) is associated with severe mucous (5) by 11 (10,48%) of participants. A severe sensation of a lump in the throat (5) is associated with severe hoarseness (5) by 14 (13,33%) of participants.

4. 5 Intra-item RFS correlation

Within the RFS intra-item correlation revealed the following:
Posterior commisure hypertrophy had a positive significant correlation with diffuse laryngeal oedema (kappa = 0,2825; one –sided p = < 0,0001 and two-sided p = < 0,0001) and ventricular obliteration (kappa = 0, 0622; one-sided p = 0,0391). A non-significant relationship was seen between posterior commisure hypertrophy and vocal cord oedema (kappa = 0,04008; one-sided p = 0,2215 and two-sided p= 0,4430).

A significant positive correlation was found between vocal cord oedema and diffuse laryngeal oedema (kappa =0,1489; one-sided p = 0,0106 and two-sided p = 0,0212). Vocal cord oedema and ventricular obliteration (kappa = - 0,0058; one-sided p = 0,4331 and two-sided p = 0,8661) displays a non-significant negative correlation. Diffuse laryngeal oedema and ventricular obliteration have a significant positive relationship (kappa = 0,0788; one-sided p = 0,0057 and two-sided p = 0,0115). “Other” and subglottic oedema (kappa = 0,0554; one-sided p = 0,1772 and two-sided p = 0,3554) as well as granuloma

and erythemia (kappa = 0,0321; one-sided p = 0,1286 and two-sided p = 0,2571) displayed a non significant correlation.

Table 4. 9 The intra-item association on the RFS: Severity levels at which the majority of participants have co-occurrence between items.

	VO (2)	**SO (2)**	**ER (4)**	**VCO (3)**	**DLO (3)**	**PCH (4)**	**GRAN (2)**	**OT (2)**
VO (2)		14 = 13,33%	51 = 48,57%	34 = 32,38%	37 = 35,24%	33 = 31,45%	19 = 18,10%	44 = 41,90%
SO (2)	14 = 13,33%		23 = 21,90%	10 = 9,52%	12 = 11,43%	17= 16,19%	8 = 7,62%	18 = 17,14%
ER (4)	51 = 48,47%	23 = 21,90%		47 = 44,76%	53 = 50,48%	55 = 52,38%	29 = 27,62%	67 = 63,81%
VCO (3)	34 = 32,38%	10 = 9,52%	47 = 44,76%		31 = 29,52%	34 = 32,38%	15 = 14,29%	41 = 39,05%
DLO (3)	37 = 35,24%	12 = 11,43%	53 = 50,48%	31 = 29,52%		32 = 30,48%	22 = 20,95%	40 = 43,81%
PCH (4)	33 = 31,43%	17 = 16,19%	55 = 52,38%	34 = 32,38%	32 = 30,48%		17 = 16,19%	48 = 45,71%
GRAN (2)	19 = 18,10%	8 = 7,62%	29 = 27,62%	15 = 14,29%	22 = 20,95%	17 = 16,19%		29 = 27,62%
OT (2)	44 = 41,90%	18 = 17,14%	67 = 63,81%	41 = 39,05%	46 = 43,81%	48 = 45,71%	29 = 27,62%	

The above table highlights the severity levels at which the majority of participants have co-occurrence between signs and symptoms. Ventricular obliteration (2) has the highest co-occurrence with diffuse erythemia (ER), as 51 (48,47%) of all participants with this sign, also had ER.

Diffuse erythemia was also found to have the highest association with subglottic oedema in 23 (21,90%) participants, vocal cord oedema in 47 (44,76%) participants, severe diffuse laryngeal oedema in 53 (50,48%) participants, obstructing posterior commisure hypertrophy in 55 (52,37%) participants, granuloma in 29 (27,62%) participants and "other" in 67 (63,81%) participants.

4. 6 RFS and RSI inter-item correlation

The between item analysis on the RSI and RFS was not possible using a Cohen's' Kappa coefficient. However, the between item co-occurrence/association of the two scales was evaluated. This was done by identifying the percentage and severity level at which the majority of participants had rated themselves (RSI) and had been rated (RFS). Results of this evaluation are found below in table 4.10

Table 4.10 Inter-item association of the RFS and the RSI: Severity levels at which the majority of participants have an association between items.

	HRS	**TC**	**MUC**	**SW**	**CL**	**BR**	**AC**	**HB**	**LUM**
VO (2)	19 = 18,10 % (4)	22 = 20,95 % (3)	17 = 16,19 % (4)	7 = 6,67% (1)	8 = 7,62% (3)	6 = 5,71% (2)	12 = 11,43 % (3)	15 = 14,29 % (3)	12 = 11,43 % (3)
SO (2)	7 = 6,67% (4)	5 = 4,76% (3)	7 = 6,67% (4)	2 = 1,90% (5)	5 = 4,76% (3)	4 = 3,81% (3)	5 = 4,76% (3)	6 = 5,71% (3)	4 = 3,81% (5)
ER (4)	25 = 23,81 % (4)	27 = 25,71 % (3)	23 = 21,90 % (4)	12 = 11,43 % (1)	15 = 14,29 % (1)	11 = 10,48 % (2)	15 = 14,29 % (1)	19 = 18,10 % (3)	15 = 14,29 % (3)
VCO (3)	16 = 15,24 % (4)	18 = 17,14 % (3)	14 = 13,33 % (4)	9 = 8,57% (1)	10 = 9,52% (1)	7 = 6,67% (2+3)	10 = 9,52% (3)	14 = 13,33 % (3)	12 = 11,43 % (3)
DLO (3)	18 = 17,14 % (5)	20 = 19,05 % (3)	17 = 16,19 % (5)	10 = 9,52% (1)	8 = 7,62% (1)	9 = 8,57% (2)	10 = 9,52% (1)	11 = 10,48 % (3)	11 = 10,48 % (5)
PCH (4)	17 = 16,19 % (5)	17 = 16,19 % (3)	16 = 15,24 % (4)	10 = 9,52% (1)	13 = 12,38 % (1)	7 = 6,67% (2)	11 = 10,48 % (1+2)	10 = 9,52% (3)	10 = 9,52% (3+5)
GRAN (2)	10 = 9,52% (3)	13 = 12,38 % (3)	9 = 8,57% (4)	6 = 5,71% (1)	6 = 5,71% (1)	6 = 5,71% (2)	9 = 8,57% (3)	9 = 8,57% (3)	7 = 6,67% (1)
OT (2)	22= 20,95 % (4)	22 = 20,95 % (3)	19= 18,10 % (3+4)	9 = 8,57% (1)	12 = 11,43 % (1+3)	9 = 8,57% (2)	12 = 11,43 % (1+3)	18 = 17,14 % (3)	11 = 10,48 % (1+3)

This table indicates that laryngeal symptoms of the RFS clearly have a propensity to be associated with certain RSI symptoms more than others. Partial ventricular obliteration has the highest association with a moderate amount of throat clearing (3), in that 22 (20,95%) participants had VO and TC (3). Subglottic oedema was associated the most with hoarseness in 7 participants (6,67%) and excess mucous in 7 participants or (6,67%). Diffuse erythemia had the highest association with throat clearing (3) with 27 (25, 71%) participants, the majority, displaying both the symptom and the laryngeal sign. Severe vocal cord oedema (5) was also highly associated with throat clearing (3) with 17, 14% or 18 participants out of the sample experiencing this configuration of signs and symptoms. Diffuse laryngeal oedema (5) was associated most with throat clearing (3) by 20 (19, 05%) of participants. Obstructing posterior commisure hypertrophy had the highest association with both severe hoarseness (5) in 17 (16, 19%) participants and moderate throat clearing (3) in 17 (16, 19%) participants. Granuloma was highly associated with moderate throat clearing (3) by 13 (12, 38%) participants. “Other” was associated most with relatively severe hoarseness (4) in 22 (20, 95%) participants and moderate hoarseness (3) in 22 (20, 95%) participants.

The symptoms of the RSI are easily seen to be associated with certain laryngeal signs of the RFS. Hoarseness (4) has the highest association with diffuse erythemia by 25 (23,81%) of participants. Throat clearing (3) has the highest association with diffuse erythemia as 27 (25,71%) participants presented with this combination. Mucus (4) and diffuse erythemia had a distinct association in 23 (21,90%) of the participants. Swallowing difficulties (1) was associated with diffuse erythemia by 12 (11,43%) of participants; infrequent coughing while lying down (1) in 15 (14,29%) participants, breathing difficulties (2) in 11 (10,48%) and infrequent annoying cough (1) in 15 (14,29%). A moderate amount of heartburn (3) in 19 (18,10%) as well as a moderate feeling of a lump in the throat (3) in 15 (14,29%) displayed a higher association to diffuse erythemia.

Tables 4.9 and 4.10 expose the co-occurrence and associations between the items on the RFS and the RSI and the inter-item associations of the RSI scale and RFS measures. These associations allow insight into how symptoms and signs are related but do not and should not lead to inferences on causation.

4. 7 Effects of gender, age, smoking and professional voice use on the RFS and RSI totals

Table 4.11 Summary statistics for the total RFS and RSI by gender, smoking status and professional voice use.

	Gender		**Smoker**		**Prof voice user**	
	Male	**Female**	**Yes**	**No**	**Yes**	**No**
N	43	62	21	84	50	55
Mean RFS	18,40	16,05	18,43	16,63	17,68	16,36
Mean RSI	17,26	20,60	19,33	19,20	19,62	18,87

Summary statistics for the total RFS (table 4. 11) indicate insubstantial differences between the means for males and females, as well as for smokers and non-smokers and also professional and non-professional voice users.

Summary statistics for the total RSI (table 4. 11) reveal that the mean for males is approximately 17 and 20 for females. Smokers and non-smokers have very similar mean ratings on the RSI, as do professional and non-professional voice users. However, non-professional voice users have a lower total RSI rating than professional voice users.

Table 4.12 Mean ratings for each age group on the RFS and the RSI

RFS	N	Mean	Age Range	Mean	N	RSI
	9	6,01	**12-19**	7,03	9	
	20	17,80	**20-29**	18,71	20	
	20	19,16	**30-39**	21,19	20	
	15	16,97	**40-49**	14,95	15	
	17	17,25	**50-59**	15,54	17	
	15	13,76	**60-69**	13,76	15	
	6	6,91	**70-79**	18,66	6	
	3	15,33	**80-89**	22	3	

The mean totals for the RFS and the RSI for each age range are indicated in table 4.12 below. The highest mean for the RFS was seen in the 30-to-39 and the RSI the 80-to-89 (RFS= 19,16; RSI= 22) year old age range .This was followed by the 20-29 year olds (RFS= 17,80) and 30-39 (RSI= 21,19) year olds. Then the 50-59 year olds (RFS= 17,25; and 20-to-29 year olds RSI= 18,71. The lowest means for the RSI were seen in the lower and upper end of the spectrum as was fewer participants for the age ranges. Interestingly the 80-89 year olds had the highest RSI rating indicating they perceive their symptoms as more severe.

ANOVA was used to assess the effects of age on the RFS and RSI totals. Participants were divided into 8 age groups. There were no significant differences between age groups on the total rating of the RFS ($F = 1,48$ and $p = 0,1850$) or the RSI ($F = 0,45$ and $p = 0,867$).

Using t-tests, the mean total ratings on the RSI and the RFS were compared to establish if there are any significant differences between genders, and whether smoking status and professional voice use affected these ratings significantly.

Smoking status did not have any significance on the total RFS assuming both equal (t= -1,57; p= 0,1197) and unequal variance (t= -1,76; p= 0,0870) nor did it have an impact on the total score of the RSI at the 5% level for equal (t= -0,06; p= 0, 9512) and unequal (t= -0,08; p= 0,9403) tests of variance.

The gender comparison revealed interesting results. There were significant differences between males and females on the RFS and RSI total ratings. Both tests for variance, equal an unequal, were examined. Both the unequal tests of variance (t = -2,57, p = 0,0119) and equal tests of variance (t = -2,61, p = 0,0105) yielded a significant difference on the RFS. Gender showed a significant effect on the RSI total in the unequal test of variance only (t= 2,06 and p = 0,0414). Therefore gender does have an impact on the total RFS and RSI ratings.

Professional voice use does not have any impact on the total of the RFS for both tests of variance: equal (t = -1,43 and p = 0,1552) and unequal (t= -1,44 and p= 0,1520). The total of the RSI is also not impacted by professional voice use for equal (t=-0,44; p= 0,6627) and unequal (t= -0,44; p= 0,6609) tests of variance.

The Chi-squared statistic was used as a nonparametric measure to analyse the difference between these variables on individual items of the RSI and the RFS. The only significant differences were between age groups on throat clearing (Chi value = 64,469 and p = 0,0018) and coughing when lying down (chi value = 51,7848 and p = 0,0336); and between males and females on subglottic oedema (chi value = 4,8315 and p = 0,0279) and thick endolaryngeal mucous (chi value = 4,1728 and p = 0,0411).

4. 8 Trends related to variables of smoking, gender, age and professional voice use:

Despite the fact that there were very few statistically significant differences related to age, gender, smoking status and professional voice on the individual items of the RSI and RFS, specific trends were noted.

RFS trends related to smoking, gender, age and professional voice use:

The severity rating on each item of the RFS in each sample group is described. Subglottic oedema (SO) was rated as present in smokers more frequently than it was in non-smokers (28,57% vs. 24%). Participants in the age range of 70-79 (50%), 80-89 (33,3%) and 30-39 (26,32%) were more inclined to have SO. Males tended to be rated with SO more than females (32,56% vs. 14,52%). Professional voice users were marginally more inclined to be rated as having SO than non-professional voice users (24% vs. 20%).

Ventricular obliteration was rated as complete more often in smokers (28,57%) than in non-smokers (14,29%). The age ranges from 70-79 (33,3%) and 80-89 (33,3%) as well as 50-59 (29,45%) were rated as having complete VO more commonly than the other age ranges. Females and males had similar ratings for ventricular obliteration (16,13% vs. 18 6%). Professional voice users were rated as having VO in 18% of cases compared to 16% of non-professional voice users. This is not a major difference between groups and represents only a small proportion of both groups.

Erythemia (ER) was rated as diffuse in more smokers (90%) than non-smokers (79,9%). Participants from 70-79 years (100%), 50-59 years (94, 12%) and 40-49 years (93,75%) were rated as having erythemia more than the other age ranges. Males were rated with erythemia in 90% of cases and females in only 75% of cases. ER was diffuse in 78,18% of non-professional voice users and 86% of professional voice users. Therefore erythemia is more prevalent in professional voice users within this sample.

Vocal cord oedema was rated as being severe in 61% of smokers and 46% of non smokers, while 80-89 year olds' (33,3%), 50-59 year olds (29,41%) and 20-29 years olds (28,57%) were rated as having severe VCO more than the other age ranges. More men (60,46%) were rated as having severe vocal cord oedema than women (41,94%). This symptom was rated as polypoid in 28% of professional voice users and in 16, 36% of non-professional voice users.

Diffuse laryngeal oedema was rated as obstructing in 38,10% of smokers and 20,24% of non smokers. DLO was also seen in participants in the age ranges of 70-79 (66,6%), 60-69 (42,86%) and 50-59 (29,41%) more than the other ages. Obstructing DLO was rated substantially more frequent in men (32,56%) than in women (17,74%), while 20% of professional voice users and 27.27% of non-professional voice users were rated as having obstructing oedema.

Post commisure hypertrophy was substantially more severe in smokers (71,3%) than non-smokers (51,19%). Patients in ages 80-89 (66,67%), 70-79 (66,67%) ad 50-59 (64,71%) had higher rating of PCH than the other ages. Of all the men 60% were rated as having obstructing PCH compared to 51% of the female participants. Non-professional voice users were rated with obstructing PCH in 50,91% of cases and 60% in professional voice users.

Granuloma was rated as present more in non-smokers (34,52%) than smokers (19,05%). The ages of 70-79 (50%), 40-49 (43,75%) and 50-to-59 (35,29%) were rated as having granuloma more than other participant ages. This sign was rated as present in 41% of men and only 24% of women. Granuloma was rated as present in 29,09% of non-professionals and 34% of professional voice users.

Thick endolaryngeal mucous was rated as present almost equally in smokers (71%) and non smokers (70%). The age ranges of 70-79 year olds (100%), 50-59 (76,46%) and 60-69 years olds (71,43%) were rated as having this symptom more often than the other age ranges. Thick endolaryngeal mucus was rated as present in 81,40% of men and 62,90% of females. Professional voice users were rated as having thick endolaryngeal mucus in 76% of cases and non-professional voice users in 65,45% of cases.

Summary of RFS trends

Smokers were rated more frequently with the laryngeal signs of subglottic oedema, erythemia, diffuse laryngeal oedema, posterior commisure hypertrophy and vocal cord oedema, while non-smokers were more likely to present with granuloma. Thick

endolaryngeal mucus was rated as present in both smokers and non-smokers who, participated in the study.

Male patients' laryngeal signs were rated as more severe compared to females with respect to subglottic oedema, erythemia, vocal cord oedema, diffuse laryngeal oedema, post commisure hypertrophy, granuloma and thick endolaryngeal mucous. Males and females had similar severity ratings for ventricular obliteration. Males on the whole appeared to have more severe ratings than females on the RFS items.

Age trends related to the RFS reveal that the age group from 70-79 years were rated as having the most severe laryngeal signs on six of the eight items on the RFS. These were subglottic oedema, ventricular obliteration, erythemia, diffuse laryngeal oedema, granuloma and thick endolaryngeal mucous. The age group from 80-89 was the group with the next highest number of severe ratings. They were rated as most severe in one of the eight laryngeal signs (vocal cord oedema). The 70-79 and 80-89 year old age groups ranked the same on severity ratings for posterior commisure hypertrophy. On these eight items, the 50-59 year old age group also had the most severe ratings on seven of the eight items. Therefore age groups that seem to have a higher incidence of severe LPR ratings on the RFS are: 70-79 year olds, 80-89 year olds and 50-59 year olds.

Professional voice users were rated as more severe than non-professional voice users on selected items of the RFS, namely posterior commisure hypertrophy, thick endolaryngeal mucus, granuloma, vocal cord oedema, erythemia, subglottic oedema. Professional and non professional voice users had very similar ratings for ventricular oedema. Non professional voice users were rated higher on diffuse laryngeal oedema.

RSI trends related to smoking, gender, age and professional voice use:

The highest rating on each RSI symptom was investigated and the percentage of occurrence in the different populations noted.

Hoarseness was rated as severe (5) by 47,62% of smokers compared to 26,19% of non smokers. Ages ranges of 40-49 (50%), 80-89 (33,3%) and 30-39 (31,58%) rated this symptom as severe (5). Significantly more females than males rated themselves as a (5) for this symptom (37,10% vs. 20,93%).

Throat clearing (TC) was rated as severe (5) by 21,43% of non-smokers and 14,29% of smokers. Age ranges of 30-39 years (36,84%), 12-19 years (33,3%) and 80-89 years (33,3%) rated the symptom of TC as (5). TC was rated as severe by more females (25,81%) than males (11,63%). Professional voice users and non-professional voice users displayed similar self ratings for severity of throat clearing (22% vs. 18,18%).

Similar numbers of non smokers (25%) rated excess mucous as severe (5) compared to smokers (23%), however, more smokers (38%) rated mucous as a (4) compared to non smokers (26%). Smokers may have different standards for excess mucous. Since smoking is related to excess mucous production smokers may therefore not see this symptom as a specific problem. The ages from 80-89 years (66,6%), 20-29 years (33,3%) and 30-39 years (31,58%) rated excess mucous as more frequent than the other age groups. Excess mucus was rated as severe (5) by more females (29,03%) than males (18,60%). Excess mucus was rated as severe by 18,18 % of non-professional voice users and 32% of professional voice users.

Severe swallowing difficulties were rated very similarly by smokers (9,52%) and non-smokers (7,14%). The ages of 80-89 years (33,3%), 70-79 years (33,3%) and 50-59 years (11,76%) rated swallowing difficulties as severe (5). Gender comparison indicates that males and females are fairly similar in their rating of this symptom as severe (9,30% and 6,45%). Swallowing difficulties were rated by 12,73% of non-professional voice users and 2% of professional voice users as severe (5).

Coughing while lying down was rated by most smokers (47,62%) and non-smokers (46%) as never occurring (0). Participants from 80-89 years (33,3%), 40-49 years (18,75%) and 30-39 years (15,79%) rated this symptom as more severe (5) than other age groups. Females (9,57%) rated this symptom as severe (5) whereas only (4,65%) of men rated it as such (5). This is not a substantial difference but more females rated this symptom as

severe. Professional (6%) and non professional voice (9,09%) users were similar in their rating of this symptom as severe.

Breathing difficulties or choking episodes were rated as severe (5) by more non-smokers (7,14%) than smokers (0%). This may again be attributed to smokers having a higher tolerance for coughing and choking due to the effects of smoking on the respiratory system. Participants from 80-89 years (33,3%), 70-79 years (16,67%) and 60-69 years (14,29%) rated this symptom as more severe (5) than other age groups. Breathing difficulties were rated as severe (5) by (8,06%) of females and (2,33%) of males. A small number (2%) of professional voice users rated this symptom as severe (5), while (9,09 %) of non-professional voice users rated it as severe. Non-professionals therefore experienced this symptom more frequently than professional voice users.

Annoying cough was rated by more non-smokers (20,24%) as severe (5) than by smokers (4,76%). AC was rated by participants 80-89 (33 3%), 60-69 (21 43%) and 50-59 (17,65%) years of age as more severe than the other age ranges. Females (19,35%) rated this symptom as a (5) substantially more than males (2, 33%). Annoying cough was rated as severe by more professional voice users (18%) compared to non professional voice users (7,27%).

Sensation of a lump in the throat was rated as severe by more non-smokers (17,86%) than smokers (9,52%). Ages from 30-39 years (26,32%), 60-69 years (21,43%) and 40-49 years (18,75%) rated this as severe (5) more than the other age ranges. Of females (22%) rated this symptom as severe (5) whereas only (9,3%) of males did so. There was not much of a difference between non-professional (16, 36%) and professional voice users' (18,00%) ratings of severe (5) for this symptom.

Heartburn is rated as severe by fewer smokers (14,29%) than non-smokers (25%). Participants aged 80-89 (33,3%), 50-59 (23,53%) and 60-69 (21,43%) rated heartburn as severe more than the other age groups. 16 (13%) of females and only (2.33%) of males rated heartburn as severe. Heartburn was rated by (14,55%) of non-professional voice users and only (6%) of professional voice users severe (5).

Summary of RSI trends

Smokers perceived their symptoms of excess mucus and hoarseness as more severe than non-smokers. Non-smokers perceived their symptoms of lump in the throat, heartburn, breathing difficulties, throat clearing and annoying cough as more severe than smokers do. Smokers and non-smokers experience a similar severity of swallowing difficulties and coughing while lying down.

Gender trends indicate that females rated symptoms of hoarseness, throat clearing, excess mucus, coughing when lying down, annoying cough, breathing difficulties, a sensation of a lump in the throat and heartburn as more severe than the male participants did. Females and males seem to have similar severity ratings for swallowing difficulties. Females seemed to perceive their symptoms as more severe than male participants did.

Age and RSI symptom related trends reveal that the age group from 40-49 years rated their symptoms the most severe (5) in one out of the 9 items on the RSI. The age group 30-39 years rated their symptoms the most severe (5) in 2 out of the 9 RSI items and 80-89 year old people rated their symptoms as the most severe (5) in 6 out of the nine RSI items. Ages 70-79 years, 60-69 years, 50-59 years and 20-29 year olds also featured as the top three ages to have the highest ratings on RSI symptoms.

Professional voice users rated their symptoms of hoarseness, throat clearing, excess mucus and annoying cough as more severe than non-professional voice users. Sensation of a lump in the throat was rated similarly by professional and non-professional voice users, although professionals rated this symptom as slightly more severe. Non-professional voice users rated swallowing difficulties, breathing difficulties and heartburn as more severe. Coughing while lying down was rated similarly by professional and non-professional voice users, although non-professionals rated it as marginally more severe.

Discussion and Conclusion

The literature review conducted at the beginning of this study showed that the diagnosis of LPR has been hotly debated. Consequently in some studies current methods of diagnosis have been reviewed, re-examined and compared, while in others new diagnostic methods have been proposed and their validity and reliability investigated. The investigation undertaken here is representative of the former group and was aimed at validating the specificity of diagnostic materials used for LPR.

The larynx is rendered more susceptible to acid and non acid reflux damage, than the oesophagus, due to its histology and so the importance of a consistent and reliable method for LPR diagnosis is crucial, especially when the long term medical repercussions (e.g. cancer of the larynx) of LPR are taken into account.

The results from this study reveal a statistically significant but weak negative correlation between the total RFS and RSI rating scales. As one variable changes it does in fact effect change in the other. The negative correlation indicates that as the ratings on one scale decreased, the ratings on the other increased. The findings also delineate trends related to individual items on the RFS and RSI, as well as intra-item and between item correlations and associations. The impact of other variables such as age, gender, smoking status and professional voice use on the total RFS and RSI ratings also emerged.

Interpretation of Results

The significant weak negative correlation (r =- 0,20 & p= 0,0395) between the RFS and RSI total ratings is confirmed by the means on the RFS and the RSI totals. As the RFS ratings decrease the RSI ratings increase. This may be due to a number of factors and impacting variables that will be discussed later.

Previous Studies

The results of this study are both confirmed and contradicted by similar studies such as one by Mesallam, Stemple, Sobeih, and Elluru (2007). Messallam et al. (2007)

conducted a retrospective chart review of the RFS and RSI scores of 40 patients. They found a significant strong positive correlation between the total RFS and RSI score ($r = 0,86$; $p < 0001$).

Vazquez, Fernandez and Gomez (2007) completed a study to evaluate the correlation between the RFS and the RSI. They recruited a sample of 34 volunteers, all of whom had no prior history of voice disorders. Each member of the sample was required to complete a self-administered laryngeal symptom questionnaire (an amended RSI). Following this all the participants underwent a comprehensive transnasal laryngoscopy in order to document the reflux finding score. The results of their study concluded that there was a statistically positive significant correlation between the RFS and the RSI. Furthermore their study indicated that the correlation is greater when the total RFS is above 7.

Further, investigations into correlation of the total RFS and the total RSI was conducted in a study of fifty–six laryngitis patients who were divided into two sub-groups, reflux laryngitis and chronic laryngitis as well as 15 healthy subjects (Wang, Liu, Liu, Zeng, Wu, Yang, Shen & Li, 2010). An oral and hypopharyngeal secretion was collected from said patients and an assay was used to measure the pepsin concentration. This study found that the total RFS and the total RSI were rated more severely (higher scores) in the laryngitis patients who were part of the pepsin-positive group.

In contrast to this, a German study by Gugatschka, Schoekler, Kiesler & Friedrich (2008) evaluated signs of the laryngeal tissue irritation through laryngoscopy (using the RFS) and reflux associated complaints (using the RSI) in a cohort of 64 “healthy” male volunteers. The researchers further wanted to describe if and to which grade subjective symptoms correlate with clinical signs. Results of the study were that one third of the patients presented with symptomology that was pathological on the RSI. Laryngoscopy found laryngeal signs that could be attributed to LPR in only 6 of the participants. They revealed further that symptoms and laryngoscopic findings did not correlate.

Musser et al. (2010) were also unable to find a statistically significant correlation between the abnormal findings of the RFS (>7) and abnormal findings on the RSI (>13).

Current Study

The weak negative correlation in this study implies that as the RSI increases the RFS decreases. This can be explained in a number of ways:

This suggests that laryngeal symptoms of LPR are experienced as more severe than reflected by the actual examination of signs. This is not unusual as patients often experience their symptoms of illness as more severe than they actually are, and given the significance of voice for overall wellbeing, it is possible that this phenomenon is applies to laryngeal pathology more than other pathologies. It is also possible that the laryngeal signs of LPR develop more slowly than the symptoms do. This may be particularly true of participants that have already undergone some degree of medical management from other medical doctors. This information was not factored into the current study, and it is unknown whether these participants had already had a trial medical management from their general practioners.

Further issues such as professional voice users' increased awareness of symptoms may impact on their subjective ratings on the RSI, resulting in higher ratings than reflected on the RFS. In addition, gender differences in ratings on the RSI may be due to fundamentally different psychological ideologies of disease and the disease process. These factors will be evaluated in more detail.

The way the RFS and the RSI were developed may also be a factor influencing the correlation. The RFS and the RSI were created in tandem. The symptoms are a reflection of the underlying laryngeal signs commonly seen in LPR. The 8 items on the RFS were derived from a pool of the most common laryngeal findings of patients with LPR seen at a voice clinic. That is, the creators (Belafasky et al., 2001b & Belafasky et al., 2002) based the symptom ratings on the laryngeal findings and proposed that these findings should result in specific symptoms. Therefore it is reasonable to assume that certain symptoms would be more common with certain laryngeal signs.

Results from within and between-item correlations do indicate that there more within-item correlations on the RSI than on the RFS.

For example, the perceived severity of a sensation of a lump in the throat was correlated significantly with the perceived severity of all the other 8 items on the RSI. Globus pharyngeus, or sensation of a lump in the throat, is according, to Mosca, Rossillo, & Leone (2006) caused by cricopharyngeal muscle spasm. It is logical to conclude that if one had a sensation of a lump in the throat one may experience increased symptoms of throat clearing, annoying cough and coughing while lying down all in an effort to dislodge the lump or ease the sensation. Perceived swallowing difficulties, breathing difficulties and hoarseness may be increased by the ongoing feeling of a lump in the throat. This is not to say that globus pharyngeus has a causative relationship with the other symptoms, but an increased frequency in one will lead to an increased frequency in the other.

Again, the symptom of annoying cough correlated significantly with: sensation of a lump in the throat, heartburn, breathing difficulties, coughing while lying down, swallowing difficulties, mucus, throat clearing and hoarseness. Cough in LPR is caused by airway irritation due to the direct mechanism of contact with the refluxate and also gaseous refluxate (Mosca, Rosillo & Leone, 2006). It is reasonable to think that with an increase in annoying cough a patient will have a perceived increase in the symptoms of breathing difficulties, swallowing difficulties, throat clearing, hoarseness and coughing while lying down. The more a patient coughs to try to clear mucus and the globus sensation the more damage is done to the larynx in terms of oedema and erythemia therefore causing the symptom of hoarseness to worsen.

Interestingly, hoarseness which had correlations at significant levels with only four items on the scale: throat clearing; mucus; annoying cough and a sensation of a lump in the throat, has very significant correlation with two symptoms – throat clearing and sensation of a lump in the throat. Hoarseness is directly related to local irritation of the vocal cords caused by refluxate returning to the hypopharynx (Mosca, Rosillo & Leone, 2006). Reflux into the larynx stimulates increased mucus production as a defence mechanism by the larynx. The excess thick endolaryngeal mucus provokes an increase in throat clearing, which is considered vocal abuse (Sataloff, 2005b), because increased throat clearing creates oedema and inflammations of the vocal cords as they are traumatically forced together. Hoarseness is the consequence of this chain of events.

Coughing while lying down was correlated with all items except hoarseness. This is because the increased mucus in the larynx creates a globus sensation and encourages throat clearing and an annoying cough. This is especially true when reclining as the mucus drains posteriorly. Excess mucus and oedema mean that the symptoms of throat clearing, globus sensation, difficulty breathing, annoying cough and swallowing difficulties become apparent. The diffuse laryngeal oedema and subglottic oedema may shift posteriorly when the patient reclines thereby causing partial constriction of the trachea and oesophagus leading to breathing and swallowing difficulties. Coughing when lying down is not correlated with hoarseness as oedema in the vocal folds may have a chance to dissipate slightly in the supine position allowing the folds to meet anteriorly. It also seems unlikely that patients would be aware of the impact of hoarseness when lying down as it is generally assumed that they would be retiring for the night.

Although mucus only correlates significantly with 4 items on the RSI (throat clearing, annoying cough, hoarseness and globus sensation) it is one of the most commonly rated symptoms and is one of the initiating factors in other symptom development. Mucus may correlate less with the other symptoms (swallowing difficulties, breathing difficulties and heartburn) as patients have already cleared the majority of mucus with throat clearing and coughing before it has a chance to drain into the trachea and oesophagus in the upright position. Therefore the mucus does not have the opportunity to be a causative agent of these uncorrelated symptoms.

Swallowing problems correlated with 5 items on the RSI other than mucus, throat clearing and hoarseness. Swallowing problems are generally directly related to diffuse laryngeal oedema, erythemia and posterior commisure hypertrophy which will also cause the manifestations of breathing difficulties, annoying cough, coughing while lying down, and globus sensation.

Breathing difficulties are significant in LPR patients and are due to subglottal and laryngeal oedema. The larynx is not able to perform one of its basic protection functions of the airway when it is inflamed and swollen and consequently difficulties in breathing may result.

Throat clearing correlated significantly with hoarseness, mucus, annoying cough and globus sensation. This is important because of the relationship between these symptoms and the complex interplay of one upon the other. Mucus goads throat clearing and annoying cough which produce erythemia and oedema of the vocal cords and trigger hoarseness.

A study mentioned previously by Wang et al. (2010) found similarly that the symptoms of throat clearing, annoying coughing, and sensing a lump in the throat ($P<0.006$), were more severe in the study group that had pepsin-positive assay than those who did not. They therefore found that these symptoms were more prevalent in those patients who had LPR. With the exception of the symptom of throat clearing, the current study had similar findings. However, as discussed above these items are interlinked with each other due to the patho-physiology of LPR. The symptoms are manifestations of the laryngeal signs.

The correlation between laryngeal signs on the RFS was not as abundant as the correlations between symptoms on the RSI. Results of the Cohen's kappa correlation analysis indicate that only four laryngeal signs were significantly related. These were diffuse laryngeal oedema, posterior commisure hypertrophy, vocal cord oedema and ventricular obliteration. Posterior commisure hypertrophy appeared to correlate significantly with only diffuse laryngeal oedema and ventricular obliteration. Diffuse laryngeal oedema indicates that the entire larynx is swollen and therefore posterior commisure hypertrophy is expected to correlate with this sign as posterior commisure hypertrophy is caused by oedema. This is also the case with ventricular obliteration as swelling in the larynx means that the ventricles are not easily distinguishable. Diffuse laryngeal oedema correlated with only 2 other laryngeal signs – vocal cord oedema and ventricular obliteration. Vocal cord oedema had significant correlations with ventricular obliteration only, as swelling in the vocal folds leads to the ventricles being difficult to differentiate. Ventricular obliteration appeared to correlate with the most number of signs on the RFS, namely posterior commisure hypertrophy, vocal cord oedema and diffuse laryngeal oedema. This is because posterior commisure hypertrophy (swelling posterior to the commisure), vocal cord oedema (swelling of the vocal cords) and diffuse laryngeal oedema (generalised swelling in the larynx) all obscure the visualisation of the ventricles leading to their obliteration. The positive correlations seen in these laryngeal signs

essentially mean we can use one sign to predict the severity of another. If a patient is rated highly on ventricular obliteration the rater can expect to see a more severe rating on posterior commisure hypertrophy, vocal cord oedema and diffuse laryngeal oedema. As with the symptoms of LPR the signs are highly interlinked.

The individual items on the RFS and the RSI could not be correlated statistically due to reasons already discussed. The most common symptoms and signs in the cohort were examined.

The total percentage for each symptom was calculated and the most common symptom was hoarseness (69,5%) followed by excess mucus (66,4%) and then throat clearing (62,4%). It is hardly surprising then that these are among the most commonly co-occurring symptoms. These co-occurring items on the RSI were evaluated by examining which sets of symptoms at all frequencies were self-rated by the highest proportion of participants.

Remacle and Lawson (2006) suggest that the symptoms most related to LPR were throat clearing, annoying cough, globus sensation and heartburn. In this study globus sensation and heartburn were only the fourth and fifth most common symptoms. In a study by Pribuisiene et al. (2002) a combination of three symptoms, hoarseness, throat itching, and globus pharyngeus were found to separate LPR patients from healthy individuals, while sore throat (40%), hoarseness (30%), and cough (20%) were the most common laryngeal symptoms reported in a study by Qadeer et al. (2005). Another study found the most important laryngopharyngeal symptoms were hoarseness in approximately 90% of the sample, and globus sensation as well as chronic cough or difficulty swallowing (Rouev, Chakarski, Doskov, Dimov, & Staykova, 2004). Thus, although there is some variation in the symptoms listed as the most common in these studies, the current study has hoarseness and annoying cough in congruence with these studies.

Hoarseness appears to be consistently seen as the most common symptom of LPR across studies. Hoarseness may therefore be viewed as a consistent warning sign that clinicians may use to alert them to the possible presence of LPR. However, hoarseness is a general symptom that is the hallmark of many vocal pathologies e.g. PVFM and muscle tension dysphonia. This idea was explored by Cohen & Garrett (2008) who found that patients

with persistent hoarseness may be over referred for trial PPI therapy (a trial PPI therapy intervention is one method of diagnosis utilised in LPR), and that this may impact on their treatment outcome. In other words hoarseness may be used as a means of compartmentalising patients into LPR and non-LPR patients. By doing so patients may fail to respond to PPI therapy as the patient does not have LPR. Therefore hoarseness may be a red herring, a double edged sword. It may be that it is a strong indicator of LPR whereas at the same time it may indicate other vocal pathologies. Thus, hoarseness should be taken as only one possible symptom and should not be used to diagnose LPR without further investigation.

Of all of the laryngeal signs, erythemia (90%) was rated the most severe in the total sample of patients. This was followed by posterior commisure hypertrophy (81,4%) and then vocal cord oedema (71,1%). This is not in agreement with Koufman, Amin & Panetti (2000) who suggest that oedema is the most common sign used to diagnose LPR. However, Remacle and Lawson (2006) indicated that physical examination mostly revealed arytenoid erythemia and oedema, vocal cord erythemia and oedema, and posterior commisure hypertrophy to be most related to LPR. Their findings are equivalent to the findings from the current study. Another study reported that the most common laryngeal signs in LPR were medial arytenoid wall erythemia/oedema (60%), interarytenoid erythema (50%), and arytenoid complex erythemia/oedema (50%) (Qadeer et al., 2005). These essentially mean erythemia and oedema are the most common laryngeal findings in their study. This is the case in the current research project as well. This is because reflux promotes inflammation and swelling of the larynx, which extends to the vocal cords and the posterior commisure.

Commonly co-occurring laryngeal signs were examined by reviewing the severity of the total set of signs. The set with the highest proportion of participants presenting with those signs was considered to be the most commonly co-occurring set of signs. The severity of each of these signs from the set was noted. The commonly co-occurring signs on the RFS were not unexpected based on the highest/most rated laryngeal signs described in the studies above. All laryngeal signs co-occurred with erythemia. This is the first sign of tissue damage to develop from exposure to reflux and other signs develop from this one. Therefore all the signs on the RFS will co-occur with erythemia.

Between-item correlation of the RFS and the RSI was not possible to due statistical constraints. The scales are not equal types of measurement. The RSI is a 5 point scale whereas the RFS has aspects that are binary and other aspects that are quandary (rated from 1-4).

Musser, Kelchner, Neils-Strunjas, & Montrose, (2010) propose that the RFS where '0' always represents 'absent' but all other scores represent something different between scores makes rating difficult and not homogenous across raters. The RSI although having a uniform rating of all items was criticised by Ali (2008) for not including throat pain, which was found in up to 40% of LPR patients and for the inclusion of heartburn which is a commonly reported symptom in esophageal reflux, not in LPR, and is known to respond well to proton-pump inhibitors (PPIs). The researcher also questions the motives for evaluating "cough" in two items (Ali, 2008). However, one rationale for the inclusion of heartburn is perhaps to aid in differential diagnosis. Those who do have heartburn may therefore be better able to be excluded from having LPR despite the RSI score.

A retrospective chart review of 40 randomly selected patients from a voice clinic in the United States comprised the sample of a similar study. The charts were reviewed and potential patients with signs of LPR included. All participants completed and RSI and the RFS was completed post videostroboscopy. Between-item correlation of the RSI and the RFS were calculated statistically and they report highly significant correlations between signs and symptoms. Hoarseness correlated highly with vocal fold oedema ($p < .01$) diffuse laryngeal oedema ($p < .01$) thick endolaryngeal mucus ($p < .01$) and erythemia ($p < .05$). Throat clearing correlated with thick endolaryngeal mucus ($p < .01$) and vocal fold oedema ($p < .01$). Globus sensation correlated with erythemia ($p < .001$) and posterior commisure hypertrophy ($p < .05$) (Mesallam, Stemple, Sobeih & Elluru, 2007). The statistical tests utilised in obtaining these results are unknown. However, it may be that the researchers grouped or paired the data on the scales. The effects of this on the reliability and validity of the scales is unclear, and it may detract from the significance of the score when paired with another score.

A recent literature review of 383 articles related to LPR over the last thirty years was undertaken by Kotby, Hassan, El-Makhzangy, Farahat, Shadi, and Milad (2010). This review revealed that in 140 articles, 18 had used the incorrect statistical analysis

procedure. It is unclear if the study mentioned above by Mesallam et al. (2007) was included in this review but it is likely, based on the date of publication.

Due to the differences in measurement of the RFS and the RSI inter-item correlation was not possible statistically. Therefore links were made through examining the most commonly co-occurring symptoms and signs on the two scales in a similar manner described for inter-item co-occurrence. Co-occurrence between the scores indicates that all the items on the RSI (symptoms) are seen the most often with the sign of erythemia. Erythemia is inflammation and in this region it is the precursor to many of the signs that follow, for example oedema. Therefore the symptoms of the RSI are seen with erythemia as it is usually diffuse by the time patients' experience symptoms related to laryngeal oedema.

The laryngeal signs on the RFS were highly co-occurring with three core symptoms: throat clearing, hoarseness, and excess mucus. This clearly defines the link between laryngeal signs and symptoms. Reflux increases the amounts of mucus produced which increases throat clearing which causes laryngeal irritation and oedema and ultimately hoarseness.

Signs of ventricular obliteration, erythemia, vocal cord oedema and diffuse laryngeal oedema were seen most often with an increased frequency of throat clearing. These laryngeal signs and symptoms are interlinked. Erythemia and oedema are a result of throat clearing as the patient tries to clear the excess mucus caused by refluxate.

Posterior commisure hypertrophy and thick endolaryngeal mucus occurred most commonly with the symptoms of hoarseness and throat clearing. This is not surprising as mucus and oedema, including posterior commisure hypertrophy, is the cause of throat clearing and ultimately hoarseness. Participants who suffer from subglottic oedema were found to have the symptoms of hoarseness and mucus as the highest symptoms compared to others on the RSI. Those participants who had granuloma were found to have hoarseness as the highest co-occurring symptom. This is because granuloma are growths on the vocal cords and as a result this, incites hoarseness as the vocal folds are not able to adduct completely. Therefore we can deduce that patients who present with laryngeal signs of ventricular obliteration, erythemia, vocal cord oedema and diffuse laryngeal

oedema will in all likelihood present with an increased throat clearing rating. Those with laryngeal signs of posterior commisure hypertrophy and thick endolaryngeal mucus may have increased symptoms of hoarseness and throat clearing. The thick endolaryngeal mucus goads throat clearing which is traumatic to the vocal cords and hoarseness is the symptom that is experienced. Posterior commisure hypertrophy results from the reflux, eryhthemia, and consequent oedema. Patients with raised ratings of granuloma may have higher scores for symptoms of hoarseness as discussed above.

Clinically these connections may provide clinicians with some insight into what patients may present with. Despite not being statistically relevant, we may have a better idea of which symptoms and signs are more likely to be seen in combination.

In Table 4.10 the frequency with which each symptom is most commonly seen with laryngeal signs and the severity level of that sign and symptom is highlighted. A direct link can be drawn from the laryngeal sign to the symptom and the progression of LPR and the frequency with which most patients experience particular combinations of signs and symptoms. The same is true of table 4.4 and table 4.5 located in the results section. In fact the most commonly seen signs and symptoms may be initial indicators of the presence of LPR.

Trends

Other factors such as gender, age, smoking status and professional voice use were examined to establish if they have any impact on the RFS and the RSI total scores as well as on individual items. Very few studies that take into account, or at least discuss, the impact of these variables on the RSI and the RFS, could be found.

Gender differences on the RSI indicate that females have higher self-ratings on the RSI than males, since the mean total rating for females on the RS was 20,59% and for males it was 17,25%. Females experienced all of the symptoms on the RSI as more severe than males did. The symptom of swallowing difficulty was the only instance where males and females had a very similar rating, not considered to be relevant.

These gender differences may indicate increased sensitivity and awareness of symptoms in females or alternatively that males are reluctant to admit the actual severity of their symptoms. Banks (2001) outlined in his article that men attend doctors less often than females. Further men may view attending the general practitioner as a sign of weakness and consequently look down on those who innconvenience the doctor with “minor” symptoms (Banks, 2001). Males may in fact view their symptoms as minor and therefore not weight them as heavily as they perhaps should. Females on the other hand may not be hypersensitive to the symptoms, but may actually be reporting the severity of symptoms more accurately than males do.

Smoking status in RSI symptoms revealed that smokers perceive the symptoms of excess mucus and hoarseness as more severe than non-smokers. However, non-smokers perceived their symptoms of breathing difficulties, throat clearing, annoying cough, heartburn and sensation on a lump in the throat as more severe than non-smokers. Both non-smokers and smokers had similar perceptions of the frequency of coughing while lying down and swallowing difficulties. Non-smokers therefore perceive more of their symptoms as worse than smokers. This may be due to the fact that smokers already have many of the symptoms associated with LPR from smoking. Smoking is an irritant of both respitory and laryngeal structures and has been linked to thinning of the mucosal lining of these areas (Awan & Morrow, 2005). Due to this decrease in mucosal lining, some smokers may present with an abusive cough as a result of increased sensitivity of the structures. The study by Awan and Morrow (2005) elucidated further that smoking is known to have effects on voice characteristics, such as fundamental frequency changes and limitations in pitch range and is often connected to chronic laryngitis. Therefore some of the symptoms listed on the RSI may in fact already be suffered by smokers and hence they rate them as less severe than non-smokers who do not suffer from these symptoms on a regular basis.

Age related RSI symptoms indicate that older participants in the age range 80-89 years rated their symptoms the most severe on 6 of the 9 items. Participants in the age range from 30-39 years rated their symptoms as the most severe on 2 of the 9 items and 40-49 years olds only rated one symptom as the most severe. However, participants in their 70’s, 60’s, 50’s and 20’s also featured in the top 3 age groups rating various symptoms as

severe. Clearly, participants in their 80th decade perceived their symptoms as more severe than any other age group. This may be due to a number of reasons. Firstly, there were only 3 participants in their 80's. Therefore if any of the sample have a high score on an item it skews the data upwards (or downwards if it is a low score) as one participant is equivalent to 33,33% of the group. For this reason the researcher circumvented this small sample dilemma by noting the top three age groups for each symptom, to provide a clearer understanding of which age groups scored highest on each symptom. Secondly, the participants in the 80-89 year old age group may have perceived their symptoms as more severe due to other illnesses that have similar symptoms. It is well documented that the symptoms used to diagnose LPR are not exclusive (Ford, 2005; Reimer & Bytzer, 2008). Elderly patients may also be on medication for concomitant disorders that have similar symptoms or may make worse the symptoms the participant may already be experiencing as a side effect. There are also a number of voice changes such as hoarseness and changes in fundamental frequency that are related to age (Honjo, Isshiki, 1980). Patients should be counselled on these changes to ensure that the RSI is measuring LPR and not age related symptoms.

Professional voice users rated their symptoms of hoarseness, throat clearing, mucus and annoying cough as worse than non-professional voice users. Professional voice users rated globus sensation as marginally more severe than non-professional voice users. Non-professional voice users rated swallowing difficulties, breathing difficulties and heartburn as more severe than professional voice users. While they had similar ratings for coughing while lying down the non-professional voice users rated this as marginally more severe. Overall the professional voice users rated more symptoms as severe than the non-professionals did. In a study of 20 volunteer singing teachers, only 2 of the 20 complained of heartburn (linked to GERD). However, after completion of a questionnaire it was found that 13 of the 20 had symptoms consistent with LPR (Heman-Ackah, Dean & Sataloff, 2002), indicating that the singing teachers themselves may not be aware what their symptoms suggest.

Another published study found that self-reported voice problems were twice as likely in singing teachers as in controls (64% versus 33%) (Miller & Verdolini, 1995). When singers and non-singers were asked to report on the history of any previously diagnosed

voice problems and if they had experienced any vocal disability within the last year, it was found that singers were 1.7 times more likely to have had a history of vocal disability in the preceding year (69% singers versus 41% non-singers) and singers were twice as likely to have had a previously diagnosed voice problem when compared to the non-singers(44% versus 21%,) (Phyland, Oates & Greenland, 1999).

Singers are more aware of vocal fluctuations and changes (Heman-Ackah, Dean, Sataloff & 2002). They are also more aware of what changes in their voices may do to their careers. For this reason, some professional voice users may rate their symptoms more severely as a result of anxiety related to the voice changes that may impact their careers.

The impact of gender on the signs of LPR on the RFS indicate that males have higher ratings for subglottic oedema, erythemia, vocal cord oedema, diffuse laryngeal oedema, posterior commisure hypertrophy, granuloma and thick endolaryngeal mucus. Females were not rated higher than males on any of the RFS items. Females and males had very similar scores for one item on the scale, ventricular obliteration. Males are therefore rated as having more severe signs of LPR than females do. This is confirmed when comparing the total means on the RFS for males (18,39) and females (16,01). It is possible that males only seek treatment later than females do, resulting in more severe laryngeal signs later in the disease progression. An article on men and illness indicated that men with health problems are less likely than women to have had recent contact with a doctor regardless of income or ethnicity (Banks, 2001). This reluctance to seek medical attention means that by the time they do seek attention the disease may have progressed significantly. Late presentation can have serious consequences (Banks, 2001). Therefore the males in this study in all likelihood fit the profile of males in general and probably waited until the LPR symptoms had progressed further than the females did before consulting a medical practioner. This would explain why males have higher RFS ratings on all signs of LPR.

Sataloff (2005b) indicates that adult females tend to be more prone to vocal nodules and Reinke's Oedema. Reinke's oedema is a mucoid gelatinous fluid in the superficial layer of the lamina propria creating a polypoid appearance of the vocal fold (Sataloff, 2005a). This increase in Reinke's oedema in said population may be due to hormonal fluctuations for example in peri-menopausal women (Sataloff, 2005b). Therefore, there is a chance

that hormonal differences and changes may impact other physiological sites to create some of the signs assessed on the RFS. This is an area that should be studied further to examine the effects of hormones on the laryngeal structures. This is also relevant in considering the interaction between age and gender.

Smoking status is an important consideration when evaluating signs of laryngopharyngeal reflux. After all, the oropharynx and laryngopharynx are the direct tissue sites for contact with smoke. Results indicate that smokers were rated more severely on stroboscopic examination than non-smokers on the following items: subglottic oedema, erythemia, diffuse laryngeal oedema, posterior commisure hypertrophy and vocal cord oedema. Interestingly non-smokers were only rated as more severe than smokers on granuloma. Thick endolaryngeal mucus was rated almost equally severe in smokers and non-smokers. The mean rating on the total RFS for smokers is 18,42 and for non-smokers is 16,63. This difference indicates as the descriptive findings did, that smokers were rated with more severe signs on the RFS than non-smokers.

A study that compared the videostoboscopic findings of smokers versus non-smokers revealed that smokers have more observable signs of laryngeal irritation than non-smokers (Awan & Morrow, 2005). Two key laryngeal characteristics related to smoking have been identified as erythemia and oedema. The study stated that habitual smoking is likely to promote thickening and possible oedema of the vocal folds. Further they explained that erythemia may be restricted to the vocal folds or may be diffuse in the surrounding laryngeal tissue. Awan and Morrow (2005) indicate that laryngeal exposure to noxious agents such as cigarette smoke has been associated with chronic laryngitis and erythemia. Fritzell and Hertegard (1986) as cited in Awan and Morrow (2005) reported that 98% (123 out of 126) of patients who were found to have chronic vocal fold oedema were smokers. The study found that even only relatively brief smoking habits can be responsible to some degree of the laryngeal signs mentioned above.

The signs that were indicated to be directly impacted by smoking in the article by Awan and Morrow (2005) were rated as more severe in this study for the smokers in the sample. Furthermore many of these signs are also used as diagnostic criteria on the RFS for LPR. It must be taken into account that smokers may therefore have another variable impacting on the severity of their laryngeal scores and this should be taken into account when

evaluating patients who smoke for LPR on the RFS. This information on smoking ultimately confirms that other airway irritation sources could be associated with larynx/pharynx signs often attributed to reflux (Hicks et al., 2002).

Professional voice users had more severe ratings of posterior commisure hypertrophy, thick endolaryngeal mucus, granuloma, vocal cord oedema, erythemia and subglottic oedema. Non professional voice users had more severe ratings for diffuse laryngeal oedema. Non professional and professional voice users had similar ratings for ventricular obliteration. Overall professional voice users are rated as more severe in the majority of items on the RFS than non professional voice users. The difference between the RFS total means for professional (17,68) and non professional (16,36) voice users is small but is skewed towards professional voice users.

A study into the laryngoscopic findings of singing teachers suggested that singers are more likely to experience and be aware of subtle voice changes and suffer disability from them. They may, as a result of this hyperawareness of their voice and how it fluctuates, be more likely to seek treatment earlier than the non-professional voice user (Heman-Ackah, Dean & Sataloff, 2002). Of the 20 singing teachers who volunteered for the study 7 complained of vocal issues while 13 were assigned to the 'normal' group based on no vocal complaints. Despite the lack of symptoms, all of the volunteers had signs of reflux laryngitis on examination. The signs included arytenoid oedema, arytenoid erythemia, postcricoid oedema, interarytenoid pachyderma laryngis, and/or posterior cobblestoning. Professional singers are widely known to have a higher incidence of vocal fold lesions including nodules cysts and varices as well as an increased incidence of asymmetries in vocal fold mobility (Heman-Ackah, Dean & Sataloff, 2002). In the study just mentioned signs of LPR were found in all of the patients. According, to the authors these results support the commonly held notion that laryngopharyngeal reflux may play an important role in the development of laryngeal pathology in singers (Heman-Ackah, Dean & Sataloff, 2002).

However, it is difficult to differentiate between the cause and the symptom. Are professional voice users at increased risk for LPR or does LPR cause many of the signs and symptoms seen in a population that may be susceptible to voice changes? Sataloff (2005b) points out "the impact of laryngopharyngeal reflux disease in laryngology… is

most likely presently over-recognised and, therefore, over diagnosed and overtreated" p. 33. This is especially true in professional voice users.

Other research has demonstrated that a degree of LPR clinical signs have been found in a large proportion of 'normal' healthy participants (e.g. Hicks et al., 2002). Their findings on 105 normal volunteers whose inclusion in the study meant they did not have any signs or symptoms related to reflux and no history of voice complaints, were revealing regarding prevalence of LPR signs. Furthermore, their smoking status and history was well documented with in-depth questions related to this. Their findings were that 86% of the sample presented with at least one hypopharyngeal symptom (Hicks et al., 2002). The fact that some normal people present with signs of LPR may lead one to conclude that even 'healthy' voice users may have some symptoms of LPR.

The effect of age on the RFS indicated that the group from 70-79 years of age is one of the top three age groups on ratings of subglottic oedema, ventricular obliteration, eryhtemia, diffuse laryngeal oedema, granuloma and thick endolarygeal mucus. Those from 50-59 years of age (50's) were also one of the top three age groups. This group was prevalent in six of the eight laryngeal signs, these were: erythemia, vocal cord oedema, diffuse laryngeal oedema, posterior commisure hypertrophy, granuloma, thick endolaryngeal mucus and ventricular obliteration.

Those in the age range from 80-89 (80's) years were the other member of the triad for age groups that scored the highest on laryngeal reflux signs. This age group featured in only four categories: subglottic oedema, ventricular obliteration, posterior commisure hypertrophy, and vocal cord oedema. The number of participants in the 50's age group was 17,6 in the 70's and 3 in the 80's age groups.

Sataloff (2005b) states that changes in true vocal folds related to age include oedema of the mucosa. Age related physical changes may impact the RFS scores of the said population. Also, older patients may be taking more medication for concomitant conditions that may have similar signs to LPR.

Conclusion

The results of this research add to the ongoing dispute regarding the diagnosis of laryngopharyngeal reflux. The results as a whole contribute to the school of thought that the RSI and the RFS are good predictors of LPR. The significant correlation of the results although negative, still allows for better predictions on which patients may have LPR, based on the results of the RSI. The findings essentially afford the team of professionals the comfort of knowing that the scales do identify LPR signs and symptoms. The total scores indicate that by examining the RSI a team can with accuracy predict if a patient will have LPR and also which patients will require further investigation. Clinically the knowledge derived from this research has impact on the management of patients presenting at voice clinics and may change the outcome for patients particularly for males and those with confounding variables.

The results related to associations on intra- and inter-item correlations on the RFS and the RSI provide further insight into specific symptoms and signs. Intra-item correlation of the RSI was substantially greater than the intra-item correlation on the RFS. Despite this both correlations allow us to make inferences of one symptom based on another and therefore have a better understanding of the various presentations of LPR. It is unfortunate that between-item correlation of the RSI and the RFS was not possible as this would have yielded valuable information regarding which symptoms and signs we would expect to see together. Despite this, the associations of symptoms and signs between the scales reveal beneficial information on commonly co-occurring factors. Although not statistically correlated they give clinicians some information on what to expect particularly at specific severity levels.

Furthermore, issues such as gender and prevalence and severity of LPR were raised. Men have more severe ratings on the RFS (signs) than females although they typically report their symptoms as occurring less frequently. This may be due to later disease progression. Male patients diagnosed with LPR may therefore be at greater risk for laryngeal carcinoma, oesophageal carcinoma and Barrett's Disease which are all associated with prolonged reflux (Sataloff, 2005a). Clinicians should therefore be aware that males may be at greater risk as they have only decided to seek medical advice and intervention once the signs are more severe. Therefore although more females may present at a clinic and

they may perceive their symptoms as more severe they may be at less risk for carcinoma than their male counterparts based on the progression of the LPR. One may consider also that if symptoms resolve more quickly than laryngeal signs (Belafsky et al. 2001a) that the laryngeal signs may also develop more slowly than the symptoms. If this was the case, females may have symptoms rated as occurring more frequently or severely despite their depressed laryngeal findings and this may be an accurate reflection of LPR.

Patients who smoke should also be evaluated with caution as a number of items used to rate severity of laryngeal signs on the RFS are related to smoking, as is the case with the RSI symptoms. Smoker's signs and symptoms may therefore complicate results leading to an over diagnosis of LPR, especially in heavy smokers who have done so for a number of years. This group should have full disclosure with their team of specialists regarding smoking status, time since cessation and classification as a light versus heavy smoker. This information will have an impact on how the signs are interpreted by the voice team. One study reported that smoking even only briefly within 5 years prior to assessment can impact laryngeal signs (Awan & Morrow, 2005).

Professional voice users represent a large proportion of the LPR populations as is confirmed in this study (non-professional=55 and professional=50). It reinforces the notion that LPR is prevalent in professional voice users for a number of reasons, but also raises a few questions. Specifically, questions regarding the nature of a normal professional voice users' larynx. Do professional voice users through the nature of their profession have more frequent symptoms or are they more aware of changes with their voices as their livelihood depends on it? The fact that a high percentage of healthy 'normal' subjects will have at least one sign related to LPR prompts the researcher to wonder if voice clinics don't see more professional voice users than non-professional voice users due to the sensitivity that professional voice users have to subtle changes in their voice. If this is the case then surely some of these professional voice users may be similar to the normal healthy non-professional voice users and present with laryngeal signs of LPR despite being healthy. This should be researched further.

The increased subjective ratings on the RSI by the older population groups indicate the need for counselling in that population regarding age related voice changes. There are a number of changes that have been documented in the larynx particularly after the 6th

decade (Mortelliti, Malmgren & Gacek, 1990; Kersing & Jennekens, 2004). These changes may be alarming to this population and misunderstood as to the aetiology. For this reason counselling that explains the basis for these changes and whether or not concern is warranted would be beneficial within the clinical setting.

Variables that can impact on the reliability of the RFS and the RSI must be considered. This is not to say that the RFS and the RSI are not measuring what they purport to do as this study confirms. However, the scales may not always be able to rule out other disorders, diseases and factors that may present as LPR. The concern is not whether the RFS and the RSI diagnose LPR, but rather does the RFS and the RSI over-diagnose LPR. There is a distinct possibility that this may be true due to the symptoms and signs which are not exclusive to LPR. Therefore diagnosis of LPR is possible using the scales evaluated in this research, and there is specificity in the materials utilised to diagnose LPR. However, the ability to differentially diagnose using these scales is another very important research project altogether.

The research allows professionals who work with patients who may suffer from LPR to draw conclusions on laryngeal findings based on reported symptomology. The findings related to the most prevalent signs and symptoms tie in well with what previous researchers have found and serve to show that these signs and symptoms should not be viewed lightly as they indicate a disease for more sinister than its individual signs and symptoms suggest. It is important to consider that both the subjective RSI and the objective RFS provide valuable information regarding LPR diagnosis, and further, that the subjective nature of the RSI cannot be overlooked in LPR diagnosis. Despite the subjectivity it does in fact provide clinicians with valuable data that is used to diagnose LPR.

One should also remember that the nature of LPR, with its multitude of symptoms and signs, does not always fit into a neat package. Although this research provides some demarcations for where LPR should fit into the picture it does not provide absolutes for diagnosis based on symptom and laryngeal sign presentation. Instead the current research should be utilised as a framework that can give some insight into the signs and symptoms that patients present with and provide a starting point for diagnosis and consequently correct management. Management is still primarily focused on PPI therapy, diet

modification and counselling. One interesting adjunct to symptom management is the use of chewing gum to alleviate symptoms of reflux. Chewing gum has been found to raise the pH of the oesophagus and the larynx therefore reducing the symptoms of LPR (Smoak & Koufman, 2001). The findings also indicated that the buffering effects of the gum last twice as long as the actual gum chewing itself (Smoak & Koufman, 2001)

Within the literature related to LPR there seems to be a movement away from diagnosis and more towards management. If a patient responds to the management strategies employed then diagnosis is confirmed, if not then the hunt for accurate diagnosis continues. This is the case with trail PPI therapy. This is also the case with a new product that is in the midst of being patented by Koufman, Ramsey and Battle (patent application number: 111953,029). The product is a method for treating existing LPR or preventing further damage to the oesophagus, larynx and hypopharynx from pepsin. A cellulose powder is inhaled either orally or intranasally. This cellulose powder adheres to the lining of the areodigestive tracts and becomes a gel on contact with the lining membranes. The gel prevents pepsin from binding and penetrating the mucosal cells of the areodigestive tract. They report the cellulose powder used is commonly found in food and cosmetic products and is non-toxic and indigestible. They state there are no side effects or overdose complications and that it may be used multiple times a day preventatively or as symptoms necessitate. They report that preliminary findings suggest that symptoms of LPR are reduced in over 70% of patients treated. If this method is successful then many of the issues related to diagnosis will be circumvented and so too will the more severe complications and consequences of LPR.

Until this time, however, we are bound to try and diagnose LPR effectively using the methods and materials that are best able to do this accurately and affordably, with the least patient discomfort. The RFS and the RSI scales are two such methods that this study has demonstrated show specificity in their diagnosis and can be utilised for such a purpose.

Limitations of the study

Although the relatively large sample size increases the external validity of the study and the generalisability (leading to a wider application) of results, no provision was made for socioeconomic status. The clinic that was utilised for the study is a private clinic and therefore by nature has patients who are of a certain socio-economic status. The results may thus be difficult to generalise to populations with lower socio-economic status.

In addition, further trends may have been easier to establish if sample sizes were matched in terms of smoking status, gender and age.
Small sample size for certain age groups may also have skewed the results. The small sample size for age group 80-89 years (n=3) caused outliers making it appear that many more participants from that age range had severe symptoms and laryngeal signs, when, in fact a smaller sample implied larger statistical differences in that age group. Alternatively these smaller age groups could have been eliminated from the study thereby only including larger age groups which would have more statistical impact. This however, would mean little information on the smaller age groups and would only therefore provide insight into the larger age groups. Further, the older age groups may have scored higher in their symptom severity based on other extraneous causative variables such as asthma, diabetes, and cardiac and blood pressure difficulties. Instead this was managed by including the top three age groups that rated a symptom or laryngeal sign as severe. A broader group is included in what we consider relevant and the smaller age groups taken with a measure of caution in interpretation of those results.

Further age related changes in the voice have been documented and changes in the superior laryngeal nerve showed up to 67% demyelination of these nerve fibres in patients over 60 years (Mortelliti, Malmgren & Gacek, 1990). These researchers suggest that these histomorphologic observations may be a direct correlate to the age-related sensorimotor dysfunction seen in the upper areodigestive tracts of many of the elderly. Further there have been documented changes in the muscle fibres of the larynx. Specifically one study found that mitochondrial abnormalities begin to develop from the 6th decade of life in the thyrovocalis muscle and may play a role in the functional deficit of the larynx in old age (Kersing & Jennekens, 2004). This may have impacted on the

results for this age group and therefore it may have been better only to include patients up to 60 years old in the study.

Patient's previous medical history, such as previous treatment for GERD, or reflux was not documented in the study. Therefore of the 105 participants that qualified for the study it is very possible that a percentage had already undergone some degree of medical management. It may be that some participants had previously been prescribed a trial regime of proton pump inhibitors from their general practioner or over the counter reflux medication. Further, alternative medication may have on effect on the signs and symptoms that we are measuring with the RFS and the RSI.

Smokers present with a number of the signs related to LPR and used diagnostically on the RFS. Smokers may therefore have abnormally raised RFS scores on these items specifically and one should consider excluding patients with even a brief history of smoking from the sample for a study of this nature. In the study cited in this research report a smoker was defined as any subject who, at the time of their study, had smoked at least two cigarettes per day for at least 1 year. Non-smokers were those who, at the time of their study, did not smoke and who had not smoked for at least 5 years (Awan & Morrow, 2005). More stringent inclusion criteria and in-depth information into smoking status of participants should therefore be included and considered in future research.

Implications of the research

The findings of this study will assist with diagnosis and therefore aid in reducing the number of missed diagnoses of LPR. This has important implications for a patient's health. Missed diagnosis translates into increased costs, mental anguish on the patient's side, frustration on the clinician's side and potentially disastrous health implications.

The first step in managing a disease is diagnosis. However, the difficulties that have been experienced with the diagnosis of LPR have led to a bottleneck when it comes to management. Poor and imprecise diagnosis has meant that knock-on diseases have greater impact on the patient. Therefore precise and early detection of LPR is optimal. Understanding the role that the RFS and the RSI play in diagnosis is crucial. With this

greater understanding of how they interact and the knowledge that they have specificity in diagnosis of LPR, we may in fact be able to streamline the diagnostic process.

Earlier and more accurate diagnosis means that patients may find resolution from their health queries and quandaries sooner. In a study of the perceived stress, anxiety and depression in patients with common vocal pathologies it was found that more females than males had increased levels of anxiety, stress and depression. The population with vocal pathologies had 25% more stress, 36,9% more anxiety and 31,2% more depression than healthy controls (Dietrich, Verdolini Abbott, Jackie Gartner-Schmidt, & Rosen, 2006). In the same study anxiety and stress have been described as causal triggers, which may in fact exacerbate, and maintain factors that cause voice related difficulties. This may be true of LPR. The more anxious a patient is about their symptoms the more severe they perceive their symptoms and perhaps this makes the physical laryngeal signs worse through depressed immune system functioning and increased gastrointestinal issues. If LPR is diagnosed timeously the stress on a patient can be reduced. This in turn will assist at least in part the patients' recovery as their reduced anxiety means they can have better recovery outcomes.

Other diseases that are highly associated with LPR, and the presence of which may be directly caused by LPR can be managed correctly if LPR is accurately diagnosed. Diseases such as asthma, otitis media, and sinusitis may therefore be better managed and their effects reduced once LPR is under control. In terms of laryngeal oesophageal carcinoma and Barrett's disease, accurate and early diagnosis of LPR will play an important role in the reduction of such life-threatening offshoots from LPR. Early detection of such diseases has better prognosis for the patient. Therefore any way in which it is possible to reduce their effects and increase the patients' chances of survival are positive.

By utilising the scales (RFS and RSI) as a mainstay of diagnosis for patients the number of costly referrals can be reduced. The use of pH - monitoring- which is very expensive and causes a fair amount of discomfort for the patient can be reserved for the truly ambiguous case or those with conflicting results. Trial PPI treatment to establish a diagnosis can be reduced as there is more clarity on those patients who will show more benefit than others.

This study has also thrown light on a population that may be at greater risk for serious consequences of LPR. Males as discussed only seek intervention later in disease progression. Therefore with an awareness of this trend clinicians can be more aware of the pressure for accurate disease diagnosis and correct management of this population. Further females that present with more severe symptom occurrence on the RSI, yet reduced laryngeal signs should be viewed in a serious light as these may be the best cases for early diagnosis if laryngeal signs develop more slowly than symptoms.

In light of the patent pending by Koufman, Ramsey and Battle, the scales as materials used in LPR diagnosis can be very beneficial. Patients who present with laryngeal signs and symptoms may be eligible for such treatment which may be a cost effective way of ruling out those who would benefit and those who would not.

Directions for future research

The discussion and implications for this research has brought to light a few areas that can be future research questions. The specificity of the RFS and the RSI in diagnosis of LPR has been established. However, the possibility of over diagnosis still exists. Therefore one avenue of research should look into the ability of the RFS and the RSI to differentially diagnose other diseases which have similar laryngeal signs and/or symptoms. If the scales could be utilised reliably to differentially diagnose other similarly presenting disorders then they would carry more weight clinically. Factors such as smoking and professional voice use need to be elaborated on as aspects of what may impact on the accuracy of the LPR diagnosis. Trends related to professional voice use and smoking status were briefly examined in this report, but there is scope especially in professional voice use which seems to comprise such a large sample of voice clinic patients.

It may however, be necessary to redefine the RFS scoring system. Although the RFS does have clinical significance the awkward scoring means that its items cannot accurately be correlated against the symptoms on the RSI. A more uniform scoring system for the RFS should be developed to allow for better intra- and inter-scale validation. Refining the RFS may aid in differential diagnosis of other similar diseases too.

As a follow up research project one could establish what percentage of males compared to females diagnosed with LPR develop carcinoma. By doing so the effects of the reported delay in which men seek intervention can be established. Obviously previous occupational history would have to be eliminated from the study, so that those who worked with metals, paints, asbestos and in many other construction occupations are not included in the study. Even if these patients had co-occurring LPR their history would serve to create confusion on the causative factor of their carcinoma.

An important issue that warrants some investigation is whether or not laryngeal signs develop more slowly than the symptoms of LPR. This would provide insight into why certain patients seem to present with many symptoms of LPR yet do not clinically have a definitive diagnosis of LPR on the RFS. In the defined absence of other similarly presenting disorders it may be the case that laryngeal signs do develop at a slower pace than symptoms.

Although the age group from 80-89 years old in this study only comprised a small part of the sample, they tended to skew data on the RSI specifically towards more severe occurrences. It may be that these patients are overly cautious regarding their symptoms or other confounding variables impacted on their scores as well as age related changes of the larynx. Either way it may be beneficial to include a sample that has specific age ranges, for example 20-60 years old. Participants within this range had higher means on both the RFS and the RSI and further, in all likelihood have better health than the older participants. This would therefore decrease the confounding variables. The chances of having a larger sample within the age range mentioned is higher as there are fewer older patients available to participate in research. Further as discussed in the limitations of the study, it is in patients in their 6th decade of life that start to have laryngeal nerve and muscular fibre changes and therefore it would be more conducive to eliminate patients from this age upward in further studies.

There is also at present research into the ability of a pepsin assay to be utilised for LPR diagnosis. This seems promising and another research option would be to correlate these findings with the RFS and the RSI results. Assay cultivation is also a fairly non-invasive

procedure and may be able to be utilised in unison with the scales instead of pH monitoring.

The role that hormone changes play on voice particularly in middle aged female patients is another area that begs examination

> "Whereas trends are observed and many clinical practices are accepted widely on the basis of experience, we need definitive, prospective, evidence-based studies. Until these studies are produced, critical questions will remain unanswered, and consistent, optimal patient care will remain elusive"
>
> (Gupta & Sataloff, 2009, p. 147).

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Appendix A

CONSENT FOR THE USE OF CLINICAL INFORMATION

This document must be explained to the patient by a member of the clinical staff

You are presently a patient or are scheduled to be seen for problems you are currently experiencing at the Wits University Donald Gordon Voice and Swallowing Centre. The centre not only renders treatment but is also actively involved in conducting research aimed at improving the quality of the care we deliver. From time to time such research involves the use of patient records from which information is extracted. The use of such information is subject to

- **Approval from the Committee for Research on Human Subjects (University of the Witwatersrand).**
- **Anonymity: in other words the identity of the patient from whose file information is extracted is never revealed to anyone but the researcher unless specific consent is obtained from the patient to do so.**

We would like to obtain your consent to use information from you / the patient's file for the purpose of our research, subject to the above mentioned conditions.

If you choose not to give your consent, then doing so will not compromise your or the patient's current or future treatment in any way. If at any time in the future, you choose to withdraw this consent, you are free to do so and this again will not prejudice your or the patient's current or future treatment in any way.

Should you wish to contact us at any stage regarding this consent, please contact the voice and swallowing centre on (011) 482 5524

_____ _____

Print patient's full name and surname VSC File Number (for office use)

DELETE WHICHEVER IS NOT APPLICABLE

YES I the undersigned, hereby give consent for my / the patient's records to be used as per the above mentioned conditions for the purpose of research.

NO I do not give consent for the use of my / the patient's records for the purpose of research

_____ _____

Full name of person **giving/declining** consent Write 'SELF' or give relationship to patient

Signed at _____ on _____

_____ _____

Patient Person Giving Consent

Witness #1 _____ Signature: _____

Appendix B

RSI

Within the last 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 mucous or postnasal drip.	0	1	2	3	4	5
4. Difficulty swallowing food, liquids or pills.	0	1	2	3	4	5
5. Coughing after you ate or after lying down.	0	1	2	3	4	5
6. Breathing difficulties or choking episodes.	0	1	2	3	4	5
7. Troublesome or annoying cough.	0	1	2	3	4	5
8. Sensation of something sticking 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

Appendix C

Reflux Finding Score

Finding	***Possible Score***				***Actual score***
Subglottic Oedema	0 = absent		2 = Present		
Ventricular Obliteration	2= Partial		4 = Complete		
Erythemia/ hyperemia	2 = Arytenoids only		4 = Diffuse		
Vocal Cord Oedema	1 = Mild	2=Moderate	3= Severe	4 =Polypoid	
Diffuse Laryngeal Oedema	1= Mild	2= Moderate	3= Severe	4=Obstructing	
Posterior commissure hypertrophy	1=Mild	2=Moderate	3=Severe	4= Obstructing	
Granuloma/ granulation	0 = absent		2=Present		
Thick endolarngeal mucus /Other	0 = absent		2=Present		
Total Reflux Finding Score					

Appendix D

Letter from the site providing permission to conduct research

THE VOICE AND SWALLOWING CLINIC

Dr. Lance Maron FCS. (SA)
Heila Jordaan MA (Speech Pathology)

Appointments: (011) 6438047 **Fax:** (011) 6438065 **Address:** Suite 12 Parklane Clinic, Parktown

31 March 2009

To whom it may concern

This is to confirm that Jennifer Logan has been granted permission to conduct research in the form of a record review at the Voice and Swallowing clinic, Parklane Clinic.

Dr Lance Maron

Heila Jordaan

Appendix E

Ethical Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Jeanneane Logan

CLEARANCE CERTIFICATE	**M090467**
PROJECT	Specificity of the Diagnostic Materials for Laryngopharyngeal Reflux
INVESTIGATORS	Ms Jeanneane Logan.
DEPARTMENT	Speech Pathology & Audiology
DATE CONSIDERED	09.04.29
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 09.04.29 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : H Jordaan

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**