# ORIGINAL ARTICLE



# Correlation between reflux symptom index and reflux finding score in patients with laryngopharyngeal reflux: Our experience

Deepthi Satish<sup>1</sup>, H. C. Badari Datta<sup>1</sup>, B. V. Manjula<sup>2</sup>, Brinda A. Poojari<sup>1</sup>, Bhaskar Reddy Molluru<sup>1</sup>

<sup>1</sup>Department of ENT, Bangalore Baptist Hospital, Bengaluru, Karnataka, India, <sup>2</sup>Department of ENT & Head and Neck Surgical Oncology, Bangalore Baptist Hospital, Bengaluru, Karnataka, India

#### Keywords

Extraesophageal reflux disease, laryngopharyngeal reflux, reflux finding score, reflux symptom index

#### Correspondence

Dr. B. V. Manjula, Department of ENT & Head and Neck Surgery, Bangalore Baptist Hospital, Bellary Road, Hebbal, Bengaluru - 560 024, Karnataka, India. Phone: +91-9980166444. E-mail: drmanjubv@gmail.com

Received 25 May 2015; Accepted 22 January 2016

Doi: 10.15713/ins.jcri.96

#### Abstract

**Background:** Laryngopharyngeal reflux (LPR) also known as extraesophageal reflux disease refers to retrograde flow of gastric contents to the upper aero-digestive tract. Belafsky, Postma, and Koufman have developed the reflux symptom index (RSI) and the reflux finding score (RFS) to diagnose LPR. Although both have been widely used, there is some controversy about their sensitivity and specificity in LPR diagnosis.

**Materials and Methods:** Patients who presented with symptoms of LPR were prospectively evaluated to study the correlation between scoring systems of RSI and RFS and also to assess the change in scores of RSI and RFS following 1 month of treatment with proton pump inhibitors (PPIs). Wilcoxon signed rank test and Student's *t*-test (paired) have been used to find the significance of RSI and RFS components at baseline and follow-up. Pearson correlation of RSI and RFS scores are done at baseline and follow-up.

**Results:** In our study, we found no correlation between the RSI and RFS at baseline (P = 0.501) as well as on follow-up after treatment (P = 0.136). A significant improvement was noted in the RSI following treatment with PPIs for 1 month but no improvement was noted in the signs following treatment.

**Conclusion:** Based on our analysis, RSI scoring alone is fast and convenient to start treatment for patients with LPR medically along with lifestyle modifications.

#### Introduction

Laryngopharyngeal reflux (LPR) also known as extraesophageal reflux disease refers to retrograde flow of gastric contents to the upper aero-digestive tract. LPR is a relatively new entity, the interest for which has grown during the past 10-15 years. However, it was initially described at least four decades back and is now the most common condition seen in otolaryngological practice. It is diagnosed in approximately 10% of otolaryngological patients and at least 50% of patients with voice complaints. Due to the lack of agreement as to how to diagnose LPR and the different methodologies used by investigators, the true prevalence of LPR is not known. Connor *et al.* reported that symptoms of LPR were seen in 49% of the normal community.<sup>[1]</sup>

The symptoms of LPR are a result of exposure of the upper aero digestive tract to gastric juice; this causes a variety of symptoms such as hoarseness of voice, post-nasal drip, sore throat, dysphagia, chronic cough, chronic throat clearing, and excessive phlegm in the throat. The most frequent complaint is cervical dysphagia (33%) followed by globus 19%, sore throat 17%, and chronic throat clearing 14%. LPR is the reflux of gastric acid into the larynx and pharynx. There are various synonyms of LPR like reflux laryngitis, extraesophageal reflux, gastropharyngeal reflux, pharyngoesophageal reflux, supraesophageal reflux out of which extraesophageal reflux is the most accepted term.<sup>[2]</sup>

Gastroesophageal reflux disease (GERD) or gastro-esophagohypopharyngeal reflux occurs because of the pressure gradient between the positive intra-abdominal pressure and the negative pressure in the thorax/hypopharynx and also in combination with the transient relaxations of the loweresophageal sphincter (LES). The transient relaxation of LES is triggered by postprandial gastric distension and stretch receptors in the gastric wall.<sup>[3]</sup> These relaxations release swallowed air by belching and are followed by after contraction of the LES. The factors responsible for producing upper airway symptoms and laryngeal pathology are acid, pepsin, bile acids, and trypsin. Pepsin along with acid was found to be the most injurious agents with a strong association with laryngeal lesions.<sup>[4]</sup>

The esophagus acts as a passage for transfer of material from the pharynx to the stomach, and also allows for some retrograde flow of gasses and gastric contents. In LPR, the esophageal refluxate although normal in range causes damage to the sensitive laryngeal epithelium.

The larynx and pharynx are devoid of the normal acid clearance mechanism found in the esophagus. For the esophagus even up to 50 episodes of reflux per day is considered normal, whereas for the larynx even 3 episodes per week is seen to be associated with a significant disease.<sup>[5]</sup> The reflux can be either gas liquid or both. The majority of the pharyngeal reflux is gaseous without pH drop which is seen in normal patients while the mixed variety and liquid type is seen in LPR patients.<sup>[6]</sup>

The 4 main constituents which prevent reflux are the UES, LES, Esophageal acid clearance and epithelial resistance.<sup>[6]</sup> In LPR, the primary defect is the dysfunction of the upper esophageal sphincter, whereas in GERD it is the LES. Even though these two terms are used in conjunction, they are two different entities with different pathophysiology.

A meticulous history is crucial for the diagnosis and treatment of patients with LPR; various other factors such as habits, diet, occupation and drug intake have to be identified in each patient as these can predispose to LPR. Fraser, Morton, and Gillibrand in their study on patients with symptoms of LPR had positive pH probe studies and found that a cough and hoarseness of voice are the most common symptoms in these patients.<sup>[7]</sup> There are major controversies in the diagnosis of LPR; traditionally diagnosis of LPR was based on the resolution of symptoms after empirical treatment with proton pump inhibitors (PPIs).<sup>[8]</sup>

The common symptoms of patients with LPR are hoarseness of voice, the sensation of lump in the throat (globus), frequent throat clearing, dysphagia, excessive throat mucus, choking attacks breathing difficulty, chronic or night time cough, heartburn/indigestion.<sup>[9,10]</sup> Only 20-43% of patients with LPR had classical symptoms of GERD such as heartburn and regurgitation.<sup>[11]</sup> GERD is readily recognized by symptoms, but the symptomatology of LPR is more diverse and not easily recognized. LPR and GERD can occur simultaneously.

Belafsky *et al.* developed the reflux symptom index (RSI), which is a validated self-administered questionnaire with 9 questions being answered by patients on a 5 point scale.<sup>[12]</sup> They demonstrated that the instrument is reliable and that it provides reproducible and valid findings. An RSI of more than 13 is considered to indicate LPR.<sup>[12]</sup>

A good physical examination can help in diagnosis of LPR; the larynx can be examined by a videolaryngoscopy which helps in visualizing subtle changes in the larynx and also documenting the treatment effects. Belafsky *et al.* have developed an endoscopic grading scale for LPR. The reflux finding score (RFS) is an 8-item clinical severity rating scale based on fiberoptic laryngoscopic findings. It includes the most common laryngeal findings related to LPR and ranges from 0 to 26; it has been shown that any individual with an RFS of more than 7 has LPR.<sup>[13]</sup> Although both indices have been widely used, there is some controversy about their sensitivity and specificity in LPR diagnosis.

Our aim was to prospectively evaluate patients with LPR and study the correlation between scoring systems of RSI and RFS and also to assess the change in scores of RSI and RFS following 1 month of treatment with PPIs.

# **Materials and Methods**

All patients who presented with symptoms of LPR between 2011 and 2013 were prospectively evaluated in the Department of ENT, at Bangalore Baptist Hospital, a referral center in Bangalore, South India, after the approval of the hospital ethics committee to study the Correlation between scoring system of RSI and RFS. Patients with age less than 18 years, chronic rhinosinusitis, chronic voice misuse, chronic chest infections, malignancy, and smokers and alcoholics were excluded from the study as they may have symptoms and signs similar to LPR. About 77 patients who fulfilled our strict inclusion and exclusion criteria were explained about the study and informed consent was taken. All patients were then asked to grade their symptoms based on the RSI questionnaire [Table 1a]. As patients would have difficulties in grading their symptom on a 5 point scale of RSI, we modified symptoms into mild, moderate and severe, 0 - No problem 1, 2 - Mild problem and 3, 4 - Moderate, and 5 - Severe problem.

All patients underwent videolaryngoscopic examination using rigid 70° endoscope (Karl Storz) by the same clinician and the findings were documented based on the RFS [Table 1b]. This score documents treatment efficacy and also helps in monitoring treatment improvement.<sup>[13]</sup>

Tab	le	1a:	Reflux	symp	tom	index	questionnaire
				· / I			1

Symptoms	No	Mild	Moderate	Severe
Hoarseness of voice	0	1.2	3.4	5
Clearing your throat	0	1.2	3.4	5
Excess throat mucus or PND	0	1.2	3.4	5
Cough after eating or lying down	0	1.2	3.4	5
Difficulty in swallowing food or liquids	0	1.2	3.4	5
Breathing difficulty or choking	0	1.2	3.4	5
Troublesome cough	0	1.2	3.4	5
Sticking sensation in throat or lump in the throat	0	1.2	3.4	5
Heartburn, chest pain, indigestion	0	1.2	3.4	5
DUD D ( 11)				

PND: Post-nasal drip

#### Table 1b: Reflux finding score

Table 10. Reliux linuing score					
Pseudosulcus	0-Absent		2-Present		
Ventricular obliteration	0-None		2-Partial		4-Complete
Erythema hyperemia	0-None		2-Arytenoid		4-Diffuse
Vocal fold edema	0-None	1-Mild	2-Moderate	3-Severe	4-Polypoidal
Diffuse laryngeal edema	0-None	1-Mild	2-Moderate	3-Severe	4-Obstructing
Posterior commissure hypertrophy	0-None	1-Mild	2-Moderate	3-Severe	4-Obstructing
Granuloma, granulation	0-Absent		2-Present		
Thick endolaryngeal mucus	0-Absent		2-Present		

Table 2: Comparison of symp	ptoms (RSI) at basel	ine and RSI at follo	ow-up after treatment

		Baseline ( <i>n</i> =77) (%)			Follow-up ( <i>n</i> =77) (%)			
	No problem	Mild problem	Moderate problem	Severe problem	No problem	Mild problem	Moderate problem	Severe problem
Hoarseness	47 (61)	16 (20.8)	14 (18.2)	0 (0)	57 (74)	18 (23.4)	2 (2.6)	0 (0)
Throat dealing	21 (27.3)	27 (35.1)	28 (36.4)	1 (1.3)	42 (54.5)	24 (31.2)	11 (14.3)	0 (0)
Throat mucus	33 (42.9)	20 (26)	22 (28.6)	2 (2.6)	49 (63.6)	19 (24.7)	7 (9.1)	2 (2.6)
Dysphagia	50 (64.9)	16 (20.8)	9 (11.7)	2 (2.6)	55 (71.4)	20 (26)	2 (2.6)	0 (0)
Coughing oil lying down	55 (71 4)	7 (9.1)	13 (16.9)	2 (2.6)	57 (74)	12 (15.6)	8 (10.4)	0 (0)
Breathing difficulty	56 (72.7)	13 (16.9)	6 (7.8)	2 (2.6)	62 (80.5)	11 (14.3)	3 (3.9)	1 (1.3)
Troublesome cough	55 (71.4)	6 (7.8)	11 (14.3)	5 (6.5)	57 (74)	9 (11.7)	10 (13)	1 (1.3)
Sticky sensation throat, lump in throat	22 (28.6)	11 (14.3)	35 (45.5)	9 (11.7)	28 (36.4)	34 (44.2)	12 (15.6)	3 (3.9)
Heart burn, chest pain, indigestion	16 (20.8)	22 (28.6)	28 (36.4)	11 (14.3)	26 (33.8)	30 (39)	18 (23.4)	3 (3.9)

0 - No Problem, 1 And 2 - Mild Problem, 3 And 4 - Moderate Problem, 5 - Severe Problem. RSI: Reflux symptom index

These patients were empirically started on PPIs (omeprazole) after ruling out all other causes, they were also explained about the antireflux measures they have to follow and a leaflet was given to them. These patients were followed up after 1 month, and their symptoms were again graded, and a repeat videolaryngoscopy was done and findings documented.

#### Statistics

Descriptive and inferential statistical analyses have been performed in this study. Wilcoxon Signed rank test and Student's *t*-test (paired) have been used to find the significance of RSI and RFS components at baseline and follow-up. Pearson correlation of RSI and RFS scores are done at baseline and follow-up.

# Results

In our study on 77 patients, 30 were male (39%) and 47 were female (61%). Age of the patients ranged from 20 to 65 years with the majority of patients in the age range of 31-45 years, 35 patients (45%) and 2 patients (2.6%) above 60 years. We have included all patients who presented with symptoms of LPR some of them even below the significant score of RSI 13.

Heart burn was the most common symptom seen in 79.2% of patients followed by throat clearing seen in 72.7% and sensation of a lump in the throat seen in 71.6%. The least common

symptom seen was breathing difficulty [Table 2]. The most common finding on the RFS was arytenoid congestion (70.1%), followed by vocal fold edema (15.6%), and pseudosulcus (13.6%) [Table 3].

We found that correlation between RSI and RFS was not statistically significant at baseline as well as after 1 month of treatment with PPIs [Table 4]. Significant improvement was noted in the RSI following treatment with PPIs for 1 month (P < 0.001) but no improvement was noted in the signs (RFS) following treatment (P = 0.241) [Table 5].

Each symptom in the RSI score showed a statistically significant improvement on follow-up after treatment [Table 6]. RFS did not show any significant difference in findings on follow-up [Table 6], except for erythema which showed just a borderline significance (P = 0.059).

#### Discussion

Diagnosis of LPR is based on a back ground of symptoms and signs. A 24 h ambulatory dual probe ph-metry is the current gold standard in diagnosing LPR; however, it is not without its limitations.<sup>[14]</sup> It is an invasive test, and its sensitivity is not more than 75-80%. Hence, diagnosis of LPR in the outpatient setting is usually made based on the symptoms and laryngeal signs. The mainstay of managing a diagnosed case of LPR is a mix of

RFS	Num	ber (%)
	Baseline (n=77)	Follow-up (n=77)
Pseudosulcus		
Absent	65 (84.4)	63 (81.8)
Present	12 (13.6)	14 (18.2)
Ventricular obliteration		
None	71 (92.2)	72 (93.5)
Partial	5 (6.5)	4 (5.2)
Complete	1 (1.3)	1 (1.3)
Erythema		
None	20 (26.0)	24 (31.2)
Arytenoid congestion	54 (70.1)	50 (64.9)
Diffuse	3 (3.9)	3 (3.9)
Vocal fold edema		
None	62 (80.5)	62 (80.5)
Mild	12 (15.6)	12 (15.6)
Moderate	3 (3.9)	3 (3.9)
Severe	-	-
Polypoidal	-	-
Diffuse laryngeal edema		
None	65 (84.4)	64 (83.1)
Mild	6 (7.8)	7 (9.1)
Moderate	6 (7.8)	6 (7.8)
Severe	-	-
Obstructing	-	-
Post commissure hypertrophy		
None	70 (90.9)	74 (96.1)
Mild	3 (3.9)	1 (1.3)
Moderate	4 (5.2)	2 (2.6)
Severe	-	-
Obstructing	-	-
Granuloma/granulation		
Absent	73 (92.2)	72 (93.5)
Present	4 (7.8)	5 (6.5)
Thick endolaryngeal mucus		
Absent	75 (97.4)	75 (97.4)
Present	2 (1.3)	1 (1.3)

 Table 3: Comparison of findings (RFS) at baseline and follow-up

RFS: Reflux finding score

PPIs and lifestyle modifications. Antireflux pharmacotherapy classically consists of administration of twice daily PPIs for a minimum of 1 month extending up to 3 months.

Belafsky *et al.* in their study stated that RFS is a highly reproducible score with the high correlation coefficient for each individual item without much inter or intra-observer

# Table 4: Pearson correlation of RSI and RFS score showing no correlation between RSI and RFS

Pearson	Bas	eline	Follow-up		
correlation	r value	P value	r value	P value	
RSI versus RFS	0.078	0.501	0.172	0.136	

RSI: Reflux symptom index, RFS: Reflux finding score

#### Table 5: Comparison of RSI and RFS of patients studied

	Baseline	Follow-up	Difference	Significance
RSI	12.56±3.00	7.90±3.65	4.662	t=14.426; P<0.001**
RFS	2.79±1.96	2.69±1.85	0.104	<i>t</i> =1.183; <i>P</i> =0.241

\*: Significant value 13, \*\*: Significant value 13, RSI: Reflux symptom index, RFS: Reflux finding score

**Table 6:** Comparison of RSI scores at baseline versus RSI at follow-up for each symptom and comparison of RFS at baseline versus RFS at follow-up for each finding

	Baseline	Follow-up	P value
RSI			
Hoarseness	$1.01 \pm 1.37$	$0.49 \pm 0.88$	< 0.001**
Throat clearing	$1.92 \pm 1.37$	$1.00 \pm 1.18$	< 0.001**
Throat mucus	$1.49 \pm 1.51$	0.83±1.3	< 0.001**
Dysphagia	0.88±1.36	$0.55 \pm 0.94$	0.002**
Coughing on lying down	$0.87 \pm 1.51$	$0.64 \pm 1.17$	0.010*
Breathing difficulty	0.68±1.23	$0.43 \pm 0.98$	0.017*
Troublesome cough	$0.97 \pm 1.68$	0.71±1.33	0.031*
Sticky sensation throat, lump in throat	$2.35 \pm 1.71$	$1.45 \pm 1.37$	< 0.001**
Heart burn, chest pain, indigestion	$2.43 \pm 1.64$	$1.69 \pm 1.45$	< 0.001**
RFS			
Pseudo sulcus	$0.32 \pm 0.77$	$0.38 \pm 0.81$	0.157
Ventricular obliteration	$0.18 \pm 0.66$	$0.16 \pm 0.63$	0.317
Erythema	$1.55 \pm 1.01$	$1.45 \pm 1.06$	0.059*
Vocal fold edema	$0.23 \pm 0.51$	$0.23 \pm 0.51$	1.000
Diffuse laryngeal edema	$0.23 \pm 0.58$	$0.25 \pm 0.59$	0.317
Post commissure hypertrophy	$0.13 \pm 0.47$	$0.06 \pm 0.34$	0.102
Granuloma granulation	$0.13 \pm 0.47$	$0.12 \pm 0.46$	0.785
Thick endolaryngeal mucus	$0.04 \pm 0.25$	$0.04 \pm 0.25$	1.000

\*: Significant value 13, \*\*: Significant value 13, RSI: Reflux symptom index, RFS: Reflux finding score

variability.<sup>[13]</sup> Mesallam and stemple in their study demonstrated a highly significant correlation between the RFS and RSI.<sup>[15]</sup> All their study patients had an RSI of more than 13. RFS ranged from 0 to 20 with 29 patients having LPR positive scores and 11 patients having LPR negative scores, and they had a strong correlation between the two scores (r = 0.86; P < 0.0001).

In another study by Vázquez de la Iglesia *et al.*, on 34 patients a statistically significant correlation was found between the RSI and RFS and also observed that the correlation is greater when the RFS score is more than 7 (r = 0.3, P = 0.007).<sup>[16]</sup>

In contrast to the above studies, in our study we observed no statistically significant correlation between RSI and RFS (r = 0.078; P = 0.501) at baseline, as well as on follow-up after treatment (r = 0.172, P = 0.136). We have also observed that patients with a high symptom score (RSI > 13) had no corresponding signs or high RFS. In patients with low symptom score (RSI < 13), we diagnosed as "probable LPR" and started them on empirical treatment with a twice daily dose of Omeprazole along with antireflux measures and found significant improvement in RSI in this group also at follow-up.

Branski *et al.* did a prospective randomized blinded study to assess the reliability of the laryngoscopic findings in LPR patients and found that both inter and intra-observer reliability was poor. The authors concluded that using laryngoscopic findings as the only diagnostic tool for LPR was highly subjective.<sup>[17]</sup> Our observations were in accordance to the above study and our results suggest that laryngoscopic findings are not important in the diagnosis of LPR.

#### Conclusion

LPR is a common problem seen in otolaryngological practice. Based on our analysis and results, we found no correlation between the RSI and reflux findings score at baseline (P = 0.501) as well as on follow-up (P = 0.136). Significant improvement was noted in RSI following 1-month treatment with PPIs, but no improvement was noted in the signs following treatment. RFS has shown no added advantage in our study. Hence, our observations suggest that RSI scoring tool alone is fast and convenient to treat patients with LPR medically along with lifestyle modifications.

# **Limitations of Our Study**

- We have followed up patients for 1 month due to time constraints and suggest a longer period of follow-up to note improvement in the signs on a larger sample size
- Subjectivity in recording the RFS by the examiner.

# Recommendations

The RSI can be used as a good prognostic marker to assess improvement after treatment but its diagnostic value cannot be assessed as it is not the gold standard investigation. The RFS cannot be used as a diagnostic or prognostic marker.

#### References

- Connor NP, Palazzi-Churas KL, Cohen SB, Leverson GE, Bless DM. Symptoms of extraesophageal reflux in a communitydwelling sample. J Voice 2007;21:189-202.
- 2. Collins S. Upper airway manifestations of gastroesophageal reflux disease. Cummings Otolaryngology Head and Neck

Surgery. 4<sup>th</sup> ed. Vol. 3. Philadelphia: Elsevier Health Sciences; 2010. p. 2498-510.

- Holloway RH, Penagini R, Ireland AC. Criteria for objective definition of transient lower esophageal sphincter relaxation. Am J Physiol 1995;268:G128-33.
- 4. Adhami T, Goldblum JR, Richter JE, Vaezi MF. The role of gastric and duodenal agents in laryngeal injury: An experimental canine model. Am J Gastroenterol 2004;99:2098-106.
- Koufman JA. The otolaryngologic manifestation of gastroesophageal reflux disease. (GERD): A clinical investigation of 225 patients using ambulatory 24 hr pH monitoring and an experimental investigation of role of acid and pepsin in development of laryngeal injury. Laryngoscope 1991;101:1-78.
- Kawamura O, Aslam M, Rittmann T, Hofmann C, Shaker R. Physical and pH properties of gastroesophagopharyngeal refluxate: A 24-hour simultaneous ambulatory impedance and pH monitoring study. Am J Gastroenterol 2004;99:1000-10.
- 7. Fraser AG, Morton RP, Gillibrand J. Presumed laryngopharyngeal reflux: Investigate or treat? J Laryngol Otol 2000;114:441-7.
- Gupta R, Sataloff RT. Laryngopharyngeal reflux: Current concepts and questions. Curr Opin Otolaryngol Head Neck Surg 2009;17:143-8.
- 9. Belafsky PC, Postma GN, Koufman JA. Laryngopharyngeal reflux symptoms improve before changes in physical findings. Laryngoscope 2001;111:979-81.
- Cohen JT, Bach KK, Postma GN, Koufman JA. Clinical manifestations of laryngopharyngeal reflux. Ear Nose Throat J 2002;81:19-23.
- 11. Toohill RJ, Kuhn JC. Role of refluxed acid in pathogenesis of laryngeal disorders. Am J Med 1997;103:100S-106.
- 12. Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). J Voice 2002;16:274-7.
- Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope 2001;111:1313-7.
- 14. Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: A global evidence-based consensus. Am J Gastroenterol 2006;101:1900-20.
- Mesallam TA, Stemple JC, Sobeih TM, Elluru RG. Reflux symptom index versus reflux finding score. Ann Otol Rhinol Laryngol 2007;116:436-40.
- 16. Vázquez de la Iglesia F, Fernández González S, Gómez Mde L. Laryngopharyngeal reflux: Correlation between symptoms and signs by means of clinical assessment questionnaires and fibroendoscopy. Is this sufficient for diagnosis?. Acta Otorrinolaringol Esp 2007;58:421-5.
- Branski RC, Bhattacharyya N, Shapiro J. The reliability of the assessment of endoscopic laryngeal findings associated with laryngopharyngeal reflux disease. Laryngoscope 2002;112:1019-24.

How to cite this article: Satish D, Datta HC, Manjula BV, Poojari BA, Molluru BR. Correlation between reflux symptom index and reflux finding score in patients with laryngopharyngeal reflux: Our experience. J Adv Clin Res Insights 2016;3:13-17.