Eur Arch Otorhinolaryngol (2012) 269:2219–2225
DOI 10.1007/s00405-012-2028-1

LARYNGOLOGY

The prevalence of laryngopharyngeal reflux in the English population

Tawakir Kamani · Susannah Penney · Indu Mitra · Vijay Pothula

Received: 12 December 2011 / Accepted: 23 March 2012 / Published online: 11 May 2012

Abstract Although symptoms of laryngopharyngeal reflux (LPR) symptoms are commonly seen in the ENT clinic, their aetiology and prevalence in the population remain unknown. Lifestyle changes have been seen to be effective in symptom relief. We aimed to establish the prevalence of these symptoms and identify any associated factors. Pseudo-random sampling was performed on 2,000 adults that were sent a validated questionnaire containing the Reflux Symptom Index (RSI) and questions on their health and lifestyle. 45.8 % of the 378 responders were male. The mean RSI was 8.3. 30 % had an RSI of more than 10, of which 75 % had symptoms of gastro-oesophageal reflux disease ($r = 0.646$ at $p = 0.01$). Patients with depression and irritable bowel syndrome are more likely to have LPR symptoms. LPR symptoms are highly prevalent in the community and may be influenced significantly by the presence of gastro-oesophageal reflux, depression and irritable bowel syndrome.

T. Kamani (✉)
Department of Otolaryngology Head and Neck Surgery, Queen's Medical Centre, Nottingham, UK
e-mail: tawakirkamani@gmail.com

S. Penney
Department of Otolaryngology, Head and Neck Surgery, Manchester Royal Infirmary, Manchester, UK

I. Mitra
Department of Radiology, Southampton General Hospital, Southampton, UK

V. Pothula
Department of Otolaryngology Head and Neck Surgery, Royal Albert Edward Infirmary, Wigan, UK

Keywords Laryngopharyngeal reflux · Gastro-oesophageal reflux disease

Introduction

Laryngopharyngeal reflux (LPR) is defined as the retrograde movement of gastric contents into the larynx and pharynx leading to a diversity of upper aero digestive tract symptoms. LPR has also been termed as extra-esophageal or silent reflux. Patients most commonly present with the symptoms of hoarseness, foreign body sensation within the throat, sore throat, dysphagia, post-nasal drip, excessive throat mucous, chronic cough and repeated throat clearing [1, 2]. Other manifestations of LPR are sinusitis, otitis media with effusion [3] and risk of aspiration of acid into lungs [4]. About 4–10 % of all ENT outpatient clinics consultations involve LPR symptoms [5]. LPR is considered to be a separate entity from gastro-oesophageal reflux disease (GORD) as salient differences exist between these conditions. LPR tends to occur during the daytime, in the upright position and is not associated with obesity [6]; GORD occurs mainly in the supine position and is characterized by heartburn and regurgitation. However, there is consensus that symptoms of LPR are related to reflux of acid and pepsin from the stomach into the upper aero digestive tract [5]. LPR symptoms can lead to severe anxiety, fear of malignancy, social embarrassment, and have significant negative impact on patient's social functioning, vitality and generally a poor quality of life [7, 8]. The aetiology of GORD and LPR remains unclear. A number of potential risk factors and co-morbidities have been described for GORD [9], but those for LPR remain unknown. The mainstay of treatment of LPR remains prescription of a

proton pump inhibitor (PPI) and a liquid alginate [10] with concomitant lifestyle changes.

The prevalence of GORD in the UK population varies between 10.3 and 18 % [11, 12]. Maxmillian Groome et al. [13] demonstrated that patients with established GORD had a significantly higher LPR scores with severity of LPR being directly proportional to GORD. The actual prevalence and predisposing factors of symptoms of LPR in the community has not been established. The validated scoring system, the Reflux Symptom Index (RSI) was devised by Belafasky et al. [7] in an attempt to standardize patient symptoms. It uses a scale of 0–5 to quantify the severity of the nine most common LPR symptoms. A score of more than 10 out of 45 is regarded as diagnostic of LPR. This tool is now widely used clinically in the management of LPR. The aim of this study was to estimate the prevalence of LPR symptoms in the adult English population using the RSI. The secondary aim was to identify any predisposing, risk or associated factors responsible for this condition.

Materials and methods

Ethical approval was obtained from Oldham Local Research Ethics Committee, REC reference number 07/Q1405/52. An anonymous survey questionnaire containing the validated RSI (Table 1) was posted to our study population with additional questions concerning demographics (age, gender, weight, and height), behavioural characteristics (smoking status, coffee, and alcohol consumption), co-morbidities (irritable bowel syndrome IBS), asthma/chronic obstructive pulmonary disease (COPD), presence of a psychosomatic disorder, peptic ulcer disease (PUD) social and lifestyle history was designed. The total RSI scores were evaluated to discern the presence (scores >10) or absence (score ≤ 10) of LPR.

Sampling was done on the basis of single-item data from a similar population. Our study population was recruited from four Wigan general practices with between 1 and 5 doctors. These practices were chosen based on the Townsend Deprivation Index (TDI) of their practice (based on postcode) to maximise external validity representative of deprivation index of England. Pseudo-random sampling was performed within participating practices based on all patients on their practice register aged between 18 and 64 years (inclusive). Taking every *n*th eligible person on the register to give approximately 500 from each practice will do this. 2,000 patients from 4 practices chosen to participate were sent an anonymous questionnaire with a prepaid envelope for reply. To maintain patient confidentiality and anonymity, GP practices were given the resources to send out the questionnaires to their patients. To maximize response rate, a second copy of the questionnaire was sent out approximately 3 weeks after the first.

All pseudo-randomly selected patients between the ages of 18–64 years (inclusive) were included in the study. Exclusion criteria were those patients outside this age range.

Statistical analysis

A point and interval (99 % confidence interval) estimate of the prevalence of LPR was obtained. A sample size of at least 340 completed questionnaires was required to detect, with 99 % confidence, a true prevalence of LPR of 150 per 1,000 (15 %) within 50 per 1,000 (±5 %). Based on a 15–20 % response rate, we distributed 2,000 questionnaires. Low response rates can be common in postal questionnaires and with this in a mind, a second mailing was sent out and an overall low response rate allowed for in the power calculation. This sample size was calculated to lead to approximately 50 patients with LPR (if the prevalence is around 15 %). This would give an "events per

Table 1 Please answer the following questions by circling your chosen answer

Within the last month, how have the following problems affected you?	0 = no problem 5 = severe problem					
Hoarseness or a problem with your voice	0	1	2	3	4	5
Clearing your throat	0	1	2	3	4	5
Excess throat mucus or feeling of postnasal drip	0	1	2	3	4	5
Difficulty swallowing food, liquids or tablets	0	1	2	3	4	5
Coughing after eating or lying down	0	1	2	3	4	5
Breathing difficulties or choking episodes	0	1	2	3	4	5
Troublesome or annoying cough	0	1	2	3	4	5
Sensation of something sticking in your throat or of a lump in your throat	0	1	2	3	4	5
Heartburn, indigestion or stomach acid coming up (dyspepsia component mentioned in text)	0	1	2	3	4	5

Please choose just one answer unless instructed otherwise

variable" of at least 5, as we investigated no more than 10 factors: whilst this is a little low, it enabled us to detect factors strongly related to LPR with sufficiently high power.

The large sample approximation method was used for the interval estimate. The relationship between the chosen factors (age, sex, weight, height and various lifestyle/social factors) was investigated using multiple logistic regressions. A forward stepwise selection strategy was used to choose the significant factors, using a 5 % significance level for inclusion (and a 10 % level for subsequent exclusion).

Chi square analyses were carried out to identify factors significantly associated with LPR. Those identified would be included in subsequent logistic regression analysis. Owing to their low incidence in the sample, three factors were excluded: cerebrovascular accident (CVA—1 case), ulcerative colitis (UC—5 cases) and Crohn's disease (1 case). Factors included were medication, asthma, hiatus hernia (HH), hypertension (HT), peptic ulcer disease (PUD), diabetes mellitus (DM), depression, ischemic heart disease (IHD), irritable bowel syndrome (IBS), exercise, lifestyle, smoking status, alcohol and caffeine intake.

Tests for differences between non-LPR and LPR group means for the continuous variables [age group, weight, height, body mass index (BMI), presence of dyspepsia, timing of mealtime before bed and number of pillows used] were conducted using MANOVA. Those variables for which significant LPR group differences found were entered into subsequent logistic regression analysis.

Results

A total of 378 responses, 173 men and 205 women, were obtained and analyzed. Demographics of gender and age group distribution are given in Table 2.

Descriptive statistics showed that participants had a mean age of 44.34 years (SD 13.03) with a mean BMI of 26.41 (SD 5.44) and 19 % (71/378) were smokers and 71 % (299/378) consumed alcohol. The mean RSI was 8.31 (SD 8.77) with the highest total being 43. One hundred and thirty patients had a significant RSI score giving an LPR symptom prevalence of 34.4 %.

There was no significant difference in LPR incidence between men and women (OD = 0.98, 95 % CI, 0.64–1.50).

Age distribution to LPR incidence was calculated and found to be higher in certain age groups ($p < 0.001$, two-tailed). This was significant at the age ranges of 41–50 and 51–60 years when compared with the age ranges of 18–30 years, 31–40 years and over 60 years. This is illustrated in Table 3.

Similar differences were noted when the dyspepsia (GORD) component of the RSI was considered and both 41–50 and 51–60 years age groups were found to have statistically greater frequency of symptoms of dyspepsia when compared with the 18–30 years age group ($p = 0.004$, 95 % CI for difference, 0.19–1.66 and $p = 0.026$, 95 % CI for difference, 0.06–1.58).

Table 2 Demographics of gender and age group of the study population

Age groups	Sex		
	Male (%)	Female (%)	Total (%)
18–30	25 (6.6)	42 (11.1)	67 (17.1)
31–40	34 (9.0)	35 (9.3)	69 (18.3)
41–50	46 (12.2)	60 (15.9)	106 (28.0)
51–60	38 (10.1)	52 (13.8)	90 (23.8)
>60	30 (7.9)	16 (4.2)	46 (12.2)
Total	173 (45.8)	205 (54.2)	378 (100)

Table 3 Incidence of LPR in the different age groups

Age_group	LPR_status		
	No LPR	LPR	Total
18–30			
N	51	16	67
% of 18–30 s	76.1 %	23.9 %	100.0 %
% within LPR_status	20.6 %	12.3 %	17.7 %
31–40			
N	52	17	69
% of 31–40 s	75.4 %	24.6 %	100.0 %
% within LPR_status	21.0 %	13.1 %	18.3 %
41–50			
N	62	44	106
% of 41–50 s	58.5 %	41.5 %	100.0 %
% within LPR_status	25.0 %	33.8 %	28.0 %
51–60			
N	50	40	90
% of 51–60 s	55.6 %	44.4 %	100.0 %
% within LPR_status	20.2 %	30.8 %	23.8 %
Over 60			
N	33	13	46
% of over 60 s	71.7 %	28.3 %	100.0 %
% within LPR_status	13.3 %	10.0 %	12.2 %
Total			
N	248	130	378
% within Age_group	65.6 %	34.4 %	100.0 %
% within LPR_status	100.0 %	100.0 %	100.0 %

LPR_status: no LPR = score <10, LPR = score 10+

A significant difference in the prevalence of LPR was found depending on dyspepsia (GORD) scores (low scores 0–2, high scores 3+) within the RSI tool itself. One hundred and nineteen patients (31.5 %) had a high (>3) score. There was a greater prevalence (62.3 %) evident for patients with high dyspepsia scores. 74.3 % of those with high dyspepsia scores had LPR compared with 25.7 % of those with low dyspepsia scores, $p < 0.001$ (2-tailed) (Table 4).

There was a significant difference in the percentage of patients with LPR depending on BMI grouping. 44.6 % (58/130) of all patients with LPR were found in the 'Overweight' category (BMI 25–29.99), representing 38.9 % of patients in this category. However, a greater percentage again of patients in the 'Obese' category (51.4 %: 38/74) had LPR, Fisher's exact, $p < 0.001$, two-tailed (Table 5).

On Chi square analysis, medication, asthma, hiatus hernia, depression, IBS, and lack of exercise statistically showed an association with increased LPR incidence. These then were further analysed using logistic regression.

In addition, the presence of PUD, DM, lifestyle (sedentary or active), history of smoking or alcohol (solely or in combination) intake and caffeine intake showed no statistical significant association to the incidence of LPR ($p > 0.05$).

Tests for differences between non-LPR and LPR group using MANOVA showed significant differences in mean scores of LPR status for: age group ($p = 0.038$), weight ($p = 0.002$), BMI ($p < 0.001$) and dyspepsia (GORD) score on RSI ($p < 0.001$). These were then analysed further using logistic regression.

Mealtime before bed and number of pillows used showed no association with LPR incidence.

Table 4 Correlation of LPR with GORD score within RSI

LPR_status	Low	High	Total
No LPR			
N	220	28	248
% within LPR_status	88.7 %	11.3 %	100.0 %
% within GORD group	81.8 %	25.7 %	65.6 %
LPR			
N	49	81	130
% within LPR_status	37.7 %	62.3 %	100.0 %
% within GORD group	18.2 %	74.3 %	34.4 %
Total			
N	269	109	378
% within LPR_status	71.2 %	28.8 %	100.0 %
% within GORD group	100.0 %	100.0 %	100.0 %

[a] GORD group: low = score 0–2, high = score 3+

Table 5 Correlation of BMI with LPR status

BMI group[a]	LPR_status[b]		
	No LPR	LPR	Total
Underweight			
N	4	1	5
% of underweight	80.0 %	20.0 %	100.0 %
% within LPR_status	1.6 %	0.8 %	1.3 %
Normal			
N	116	33	149
% of normal	77.9 %	22.1 %	100.0 %
% within LPR_status	47.0 %	25.4 %	39.5 %
Overweight			
N	91	58	149
% of overweight	61.1 %	38.9 %	100.0 %
% within LPR_status	36.8 %	44.6 %	39.5 %
Obese			
N	36	38	74
% of obese	48.6 %	51.4 %	100.0 %
% within LPR_status	14.6 %	29.2 %	19.6 %
Total			
N	247	130	377
% within BMI group	65.5 %	34.5 %	100.0 %
% within LPR_status	100.0 %	100.0 %	100.0 %

[a] BMI group: underweight = BMI 0–18.49, normal = BMI 18.5–24.99, overweight = BMI 25–29.99, obese = BMI 30+

[b] LPR status: no LPR = score <10, LPR = score 10+

On the basis of the above analyses, the following independent variables were selected for inclusion in a logistic regression analysis to identify those independent variables that significantly predict LPR after controlling for any associations between them. Independent variables: age group, weight, BMI, dyspepsia, medication, asthma, HH, depression, IBS, exercise, and lifestyle.

Significant predictors of LPR status are depression, dyspepsia, medication, and IBS ($p < 0.05$). An increased BMI and lack of exercise are approaching significance ($p = 0.077$ and $p = 0.092$). Associations between predictors and LPR status are in the expected direction for BMI, depression and IBS and exercise, i.e. those with these conditions or are more likely to have LPR symptoms and people who do not exercise are more likely to have LPR.

Regarding medication, the odds of those who take GORD medication in addition to other medication are 8.68 times more likely to have LPR than in those who take medication for GORD/LPR (4.16 times).

After GORD, LPR and other medication, the next most important predictor of LPR symptoms is depression (OR = 7.21, 95 % confidence interval) followed by IBS (OR = 3.54, 95 % confidence interval). With those

reporting depression are 7.21 times more likely and those with IBS are 3.54 times more likely to have LPR than those without depression and IBS.

Discussion

LPR-related symptoms are a common presentation to the Otolaryngologist. Koufman et al. [1] found that 10 % of patients presenting to the ENT clinic had LPR. This is from a pre-selected cohort of the population. A number of studies have been carried out worldwide in different populations to identify the prevalence of GORD. In the UK, a study by Lowden et al. [14] demonstrated that 26.5 % of the patients attending a general practice in the UK had an RSI of more than 10.

Our study postulates that the prevalence of LPR symptoms in the UK population is 34.4 %. This figure of every one in three adults in the UK suffering from LPR-related symptoms suggests that the prevalence of LPR may be higher than previously thought. This has significant implications for both primary and secondary care resources—GP and clinic visits, treatment costs and investigations. LPR-related symptoms of hoarseness and foreign body sensation in the throat cause much anxiety among patients who fear they may have a malignancy. These patients are therefore often referred to the Otolaryngologist for further investigation and management as well as reassurance, more often than not. Treatment of LPR may also require a multidisciplinary team approach with the need for a speech and language therapist as well as the otolaryngologist. In addition, these patients often require treatment with PPI and liquid alginates. All these use a significant share of the already limited funds available to the NHS. The cost of treatment can be quite high. The US spends 1 billion dollars a year in medical treatment of GORD alone [15].

Thompson et al. [12] demonstrated that symptoms of heartburn (dyspepsia) and globus pharyngeus (LPR) in the normal population are not uncommon. In their study, they found that the elderly and the middle aged groups of patients had statistically significantly higher symptoms of dyspepsia than the younger groups. This was further noted in a systematic analysis on prevalence of GORD [16]. Our study found findings along a similar theme with the heartburn component of the RSI being more prevalent in the middle age groups (41–60 years), but not so in the over 60-year olds. We also found that the age group between 41 and 60 years of age had a higher overall incidence of LPR symptoms with a score of >10 in comparison to those in the 18–40 years age group. Again, only 10 % of the 60+ years old group were found to have LPR-related symptoms, comparable to the 18–40 age groups. In addition, we found that patients with a severe heartburn score (>3) were more likely to have LPR ($p < 0.001$).

The positive association of BMI has been identified in GORD a number of times [17]. Similarly increased BMI in our study showed a significant difference when compared between the LPR and non-LPR groups ($p < 0.001$). Although on logistic regression analysis, it was not found to be statistically significant as an independent variable, it was approaching significance ($p = 0.077$). Our study is limited to LPR-related symptoms and it may be that this would be apparent in a study of subjects with a confirmed clinical diagnosis of LPR. Given that BMI is an important variable in GORD and may be so in LPR, it is important that this is addressed in the treatment of patients with GORD or LPR.

It was noted that participants with a history of depression were 7.21 times more likely to have LPR-related symptoms than those without (OR = 7.21). A study by Pacini et al. [18] on GORD patients suggested that depression may be a causal effect of the impact of GORD affecting the individual. It is not clear whether depression is a linked causative feature of LPR-related symptoms through a psychosomatic pathway or that it is a direct result of the LPR-related symptoms on the quality of life (QoL) of the affected individual. However, if the latter is indeed valid, the impact of LPR is understated and active treatment with diagnosis in such patient groups should be considered. This area requires further study to provide the clarity of the relationship between depression and LPR as well as GORD.

A UK-based study on GORD epidemiology found that a history of IBS was associated with an increased risk of GORD diagnosis (ORD = 1.6) [19]. A similar association was noted in our study with patients with IBS having a 3.54-fold risk of having LPR-related symptoms.

GORD has been associated with use of prescription medication. The use of anti-cholinergic drug therapy was associated with a significant increase in LPR (OR 1.52) as well as use of nitrates (OR 1.5), oral steroids (OR 1.3) and current use of NSAIDs (OR 1.5) [16]. No association was found with aspirin and an inverse relationship was noted with use of HRT [19].

No significant difference was noted between men and women in the prevalence of LPR related symptoms (OR = 0.98). The study on prevalence of LPR in the general practice population by Lowden et al. [14] also found no significant difference on RSI scores between male and females. This was also noted in a systematic analysis of 15 studies on prevalence and epidemiology of GORD [16].

Although the impact of smoking on GORD is well described, our study shows no association of smoking on LPR-related symptoms. It is interesting to note that smoking is associated with symptoms of dyspepsia, which is noted to be significantly high in patients with LPR-related symptoms. Smit et al. [20] performed a 24 h PH

monitoring study of 15 smokers and found that smoking altered the defence mechanism of the oesophagus against acid reflux with objective evidence of acid at the upper and lower oesophageal sphincters. They found that the percentage time the PH was <4 during smoking were significantly higher than the non-smoking period in the same patient. In view of this, the current practice of recommended smoking cessation (as part of lifestyle changes advice) in the treatment of LPR should continue and further studies to assess the direct effect of smoking on LPR need to be undertaken.

Our study found that alcohol was not a risk factor for LPR-related symptoms. Controversy exists as to the effect of alcohol consumption on GORD as results of different studies are diverse and contradictory. Two systematic reviews have suggested further well-designed prospective studies are needed to clarify the effect of alcohol on GORD. Due to controversial evidence, it is important to identify patients that consume more than the average acceptable amount of alcohol and advice them on reduction in alcohol as a lifestyle change in the management of LPR or GORD [11, 21, 22].

The above study has certain limitations. The main one being that it is subjective and relies only on information that a patient may be aware of from their GP. The second limiting factor is the poor response rate to the postal questionnaires. Although this was allowed for in the power calculation prior to mailing such a low rate will inevitably call into to question the accuracy of the results. Nevertheless, a number of responses analysed should have sufficient power to give a reliable indication of the true incidence of LPR in a typical GP population in the UK.

The study gives an indication of possible LPR, but this would require pH monitoring and endoscopy for Reflux Finding Score to give a true indication of the exact prevalence of LPR in the community. This would be a very difficult study to conduct if at all due to the many ethical underlying dilemmas.

Conclusion

Our study suggests that LPR related symptoms are highly prevalent within the UK population with every one in three adults suffering from its symptoms. As discussed, this has significant implications on not just the QoL of the patients, but also on the financial impact this has on the health service. The impact would include attendances at the primary care centre with the symptoms as well as necessitated referrals to secondary care due to symptoms mimicking symptoms of upper aerodigestive tract malignancies. The treatment would also have a financial impact.

Treatment of LPR should therefore also entail the reduction of risk factors identified in our study. For example, weight reduction in patients with high BMI, treatment of depression, encouraging exercise and advising on lifestyle changes in patients with GORD.

Health prevention strategy is another aspect that should be considered. Although the study did not identify BMI as a significant risk factor for LPR, a number of studies discussed above have shown it to be a risk factor in GORD; it may therefore be beneficial to consider it as one given their positive association in this study. The above study also highlights potential avoidable risk factors, such as depression, poly-pharmacy, high BMI and lack of exercise, amongst others. Educating patients on these would potentially reduce the prevalence of LPR and this would positively have an impact on improving the overall health of the population, but also on the financial implications that treatment of a very common condition brings.

Conflict of interest This study and its authors have no financial disclosures.

References

1. Koufman JA, Aviv JE, Casiano RR, Shaw GY (2002) Laryngopharyngeal reflux: position statement of the committee on speech, voice, and swallowing disorders of the American Academy of Otolaryngology-Head and Neck Surgery. Am J Otolaryngol Head Neck Med Surg 127:32–35
2. Rouev P, Chakarski I, Doskov D, Dimov G, Staykova E (2005) Laryngopharyngeal symptoms and gastroesophageal reflux disease. J Voice 19:476–480
3. Al-Saab F, Manoukian JJ, Al-Sabah B et al (2008) Linking laryngopharyngeal reflux to otitis media with effusion: pepsinogen study of adenoid tissue and middle ear fluid. J Otolaryngol Head Neck Surg 37:565–571
4. Phua SY, McGarvey LP, Ngu MC et al (2005) Patients with gastro-oesophageal reflux disease and cough have impaired laryngopharyngeal mechanosensitivity. Thorax 60:488–491
5. Koufman JA (1991) The otolaryngologic manifestations of gastroesophageal (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 101 (4pt 2 Suppl 53):1–78
6. Halum SL, Postma GN, Johnston C, Belafsky PC, Koufman JA (2005) Patients with isolated laryngopharyngeal reflux are not obese. Laryngoscope 115:1042–1045
7. Belafasky PC, Postma GN, Koufman JA (2002) The validity and reliability of the reflux symptom index (RSI). J Voice 16:274–277
8. Cheung TK, Lam PK, Wei WI et al (2009) Quality of life in patients with laryngopharyngeal reflux. Digestion 79:52–57
9. Festi D, Scaioli E, Baldi F, Vestito A, Pasqui F, Di Biase AR, Colecchia A (2009) Body weight, lifestyle, dietary habits and gastroesophageal reflux disease. World J Gastroenterol 15:1690–1701
10. McGlashan JA, Johnstone LM, Sykes J (2009) The value of a liquid alginate suspension (Gaviscon Advance) in the management of laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 266:243–251

11. Mohammed I, Cherkas LF, Riley SA, Spector TD, Trudgill NJ (2003) Genetic influences in gastro-oesophageal reflux disease: a twin study. Gut 52:1085–1089
12. Thompson WG, Heaton KW (1982) Heart burn and globus in apparently healthy people. Can Med Assoc J 126:46–48
13. Groome M, Cotton JP, Borland M, McLeod S, Johnston D, Dillon JF (2007) Prevalence of laryngopharyngeal reflux in a population with gastroesophageal reflux. Laryngoscope 117:1424–1428
14. Lowden M, McGlashan JA, Steel A, Strugala V, Dettmar P (2009) Prevalence of symptoms suggestive of extra-oesophageal reflux in a general practice population in the UK. Logoped Phoniatr Vocol 34:32–35
15. Ruigomez A, Rodriguez LA, Wallander MA, Johansson S, Graffner H, Dent J (2004) Natural history of gastro-oesophageal reflux disease diagnosed in general practice. Aliment Pharmacol Ther 20:751–760
16. Shaheen NJ, Hansen RA, Morgan DR et al (2006) The burden of gastrointestinal and liver diseases. Am J Gastroenterol 101:2128–2138
17. Dent J, El-Serag HB, Wallander M-A, Johansson S (2005) Epidemiology of gastroesophageal reflux disease: a systematic review. Gut 54:710–717
18. Locke GR III, Talley NJ, Fett SL et al (1999) Risk factors associated with symptoms of gastroesophageal reflux. Am J Med 106:642–649
19. Pacini F, Calabrese C, Cipolletta L, Valva MD, Russo A, Savarino V, Vigneri S (2005) Burden of illness in Italian patients with gastro-oesophageal reflux disease. Curr Med Res Opin 21:495–502
20. Mohammed I, Nightingale P, Trudgill N (2005) Risk factors for gastro-oesophageal reflux disease symptoms: a community study. J Aliment Pharmacol Ther 21:821–827
21. Smit CF, Copper MP, van Leeuwen JA, Schoots IG, Stanojcic LD (2001) Effect of cigarette smoking on gastropharyngeal and gastroesophageal reflux. Ann Otol Rhinol Laryngol 110:190–193
22. Chen SH, Wang JW, Li YM (2010) Is alcohol consumption associated with gastroesophageal reflux disease? J Zhejiang Univ Sci B 11:423–428
23. Ruigomez A, Rodriguez LA, Wallander MA, Johansson S, Graffner H, Dent J (2004) Natural history of gastro-oesophageal reflux disease diagnosed in general practice. Aliment Pharmacol Ther 20:751–760