

Treating and Managing Laryngopharyngeal Reflux Disease in the Over 65s: Evidence to Date

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Purpose: The clinical presentation and therapeutic outcomes of elderly patients may be different from those in younger populations, leading to additional diagnostic and therapeutic difficulties. The present study reviewed the findings on the epidemiology, and clinical, diagnostic, and therapeutic outcomes of elderly patients with laryngopharyngeal reflux (LPR).

Methods: A PubMed, Cochrane Library, and Scopus literature search was conducted on the epidemiological, clinical, diagnostic, and therapeutic findings of elderly LPR patients.

Findings: The prevalence of LPR in the elderly population remains unknown. From a clinical standpoint, older LPR patients report overall lower symptom scores and related quality-of-life outcomes at the time of the diagnosis. The required treatment time to obtain symptom relief appears to be longer in older compared with younger patients. Particular attention needs to be paid to prolonged medication use because the elderly population is characterized by polypharmacy and there is a higher risk of proton-pump inhibitor (PPI) interactions and adverse events. The plasma clearance of most PPIs is reduced with age, which must be considered by practitioners in the prescription of antireflux therapy.

Conclusion: The clinical presentation and treatment efficacy of elderly LPR patients differ from those in younger patients. Practitioners need to carefully consider the risk of drug interactions and adverse events in elderly patients.

Keywords: laryngitis, laryngopharyngeal reflux, reflux, otolaryngology, head neck surgery, gastroesophageal reflux, voice, elderly, aging, age

Introduction

Laryngopharyngeal reflux (LPR) is an inflammatory disease of the upper aerodigestive tract tissues related to the backflow of gastroduodenal content reflux, which induces morphological changes in the upper aerodigestive tract.¹ The diagnosis of LPR is based on non-specific symptoms and findings, the positive response to an empirical therapeutic trial, or the demonstration of pharyngeal reflux episodes upon hypopharyngeal–esophageal multichannel intraluminal impedance pH monitoring (HEMII-pH).^{1,2} The clinical diagnosis of LPR remains complicated owing to the non-specificity of symptoms and signs, and their overestimation by practitioners.^{3,4} Thus, elderly patients represent a challenging population because of their tendency to report atypical clinical presentations of many digestive diseases.^{5,6} In addition, this population is growing in Western countries, representing more than 16% of the US population in 2020.⁷

The aim of this state-of-the art review was to report the current knowledge on the epidemiology, and clinical, diagnostic, and therapeutic outcomes of elderly patients with LPR.

Methods

A PubMed, Cochrane Library, and Scopus database search was conducted for relevant peer-reviewed publications in English, Spanish, and French language related to epidemiology, clinical presentation, pathophysiology, diagnosis, and

treatment of LPR in elderly populations. The following keywords were used (and/or): “reflux”, “laryngopharyngeal”, “gastroesophageal”, “extra-esophageal”, “elderly”, “aging”, “old”, “symptoms”, “findings”, “treatment”, and “physiology”. We included clinical prospective/retrospective controlled/uncontrolled studies, systematic reviews, and meta-analyses. From this initial review, papers were selected for inclusion in the final review if they focused on the epidemiology, pathophysiology, clinical picture, diagnosis, and treatment of LPR in the aging population. The authors should report the inclusion and exclusion criteria, diagnostic method, therapeutic outcomes, and treatment regimen. Critical analysis of this literature was carried out focusing on incidence and prevalence, clinical presentation, diagnosis, and treatment of elderly patients with LPR. From this review, implications for practice were summarized. Ethics committee approval was not required for this review. Individuals agreed (by informal consent) to the use of the photographs (Figure 1) for publication.

Note that a systematic review or meta-analysis was not performed because of the low number of studies and the important heterogeneity in inclusion/exclusion criteria, use of ambulatory reflux monitoring, treatment and outcome measures.

Epidemiology

The first important epidemiological study on LPR was conducted in 1991 by Jamie Koufman.⁸ In this prospective study, Dr Koufman estimated that acid LPR was present in 10% of outpatients presenting to otolaryngology departments with laryngopharyngeal symptoms and findings.⁸ This study was the first report to differentiate LPR from gastroesophageal reflux disease (GERD), because 62% of patients had abnormal esophageal acid exposure but only 30% reported acid hypopharyngeal reflux events on dual-probe pH monitoring. Several studies estimated the prevalence of LPR symptoms to be 5–30% of outpatients consulting otolaryngological offices, but the authors based their evaluation of prevalence on the results of patient-reported outcome questionnaires without diagnostic confirmation.^{9–11} To date, the

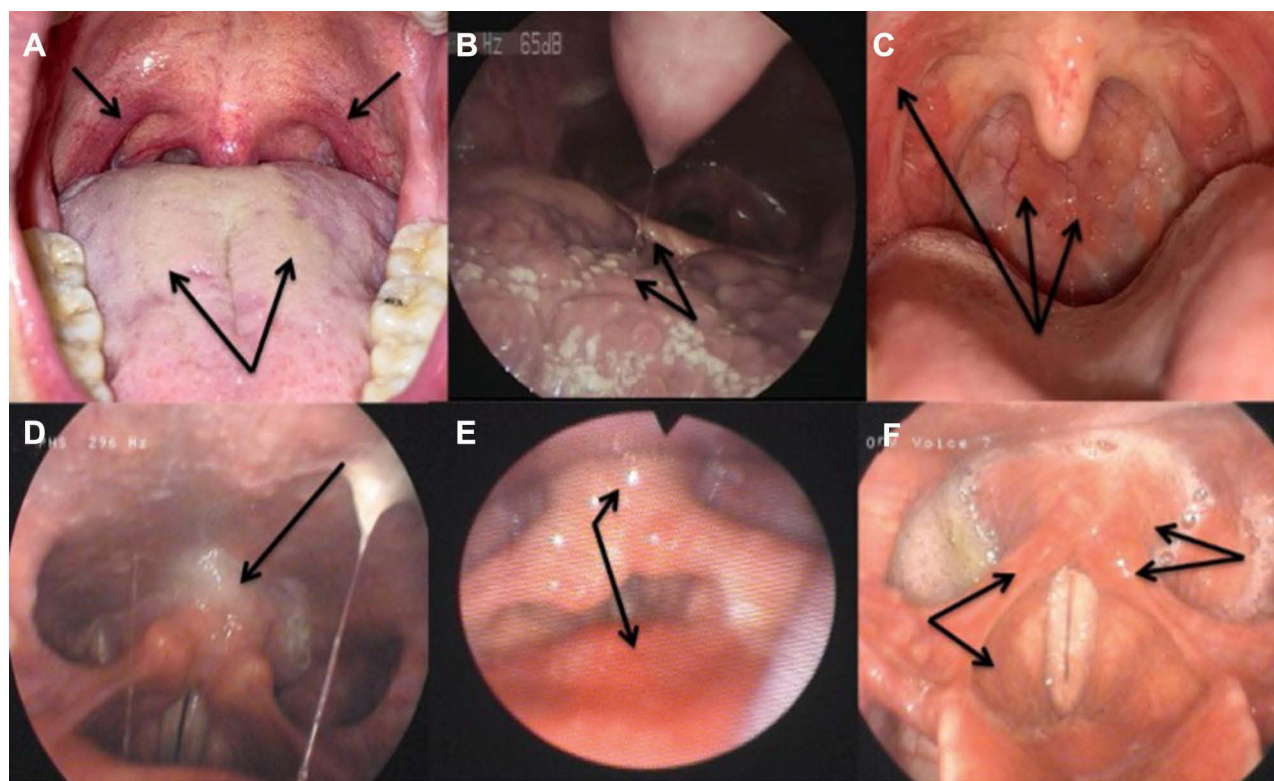


Figure 1 Findings in patients with laryngopharyngeal reflux.

Notes: Patients with laryngopharyngeal reflux often reported anterior pillar erythema (A), coated tongue (A), tongue tonsil hypertrophy and posterior coated tongue (B), granulations of the posterior wall of the oropharynx (C), sticky mucus in the throat and edema of the retrocricoid region (D), epiglottis erythema and posterior commissure hypertrophy (E), and laryngeal erythema (F).

prevalence of LPR in the general population is still unknown. According to the largest cohort studies, the mean age of LPR patients ranged from 37 to 53 years old.^{4,12–15} Thus, LPR seems to be a disease of the forties, but the first episodes may appear earlier in acute or recurrent forms.¹⁶ There have been no population-based surveys evaluating the prevalence of LPR-related symptoms in elderly populations, although the prevalence of GERD has been investigated in many elderly populations.¹⁷ According to large-cohort studies, the prevalence of GERD increases with aging,^{17,18} affecting 6–17% of the elderly US population^{17,19} and up to 31.5% of European individuals >60 years of age.¹⁸ However, the prevalence of GERD in the elderly population may be underestimated owing to the aging of esophageal nerve sensitivity and the related decrease in GERD alarm symptoms, such as heartburn or non-cardiac chest pain. The exact proportion of GERD patients with laryngopharyngeal symptoms and findings was not investigated in these studies, making any estimation of LPR in elderly populations difficult.

Pathophysiology

Physiology of Laryngopharyngeal Reflux

The development of LPR symptoms and findings is related to the backflow of gastroduodenal content (eg pepsin, bile salts, and other gastrointestinal proteins) into the upper aerodigestive tract mucosa. The deposition of enzymes, especially pepsin, leads to mucosal injury, inflammatory reaction, mucus dryness, epithelial thickening, and microtrauma.²⁰ The mucosal irritation leads to mucus production and dehydration through a down-regulation of mucin and carbonic anhydrase gene expression.²¹ The accumulation of sticky mucus induces postnasal drip, globus sensation, throat clearing, dysphagia, and cough. Depending on patients' mucosa sensitivity, as well as unknown factors,²² patients with acute, recurrent, or chronic LPR may develop mild, moderate, or severe symptoms.

The recent use of HEMII-pH monitoring in otolaryngology has improved the understanding of LPR physiology and the differences between LPR and GERD. The profile of LPR at the HEMII-pH is characterized by daytime and upright gaseous weakly or non-acid hypopharyngeal reflux events in most patients.^{23,24} In more than 50% of cases, patients do not report GERD.²⁵ The gaseous nature of events and the lack of GERD have led to a clinical picture characterized by otolaryngological symptoms without heartburn or abdominal findings.

Influence of Aging on Physiology

The main mechanisms of defense against reflux (eg esophageal motility, bicarbonate secretion, and lower [LES] and upper esophageal sphincter [UES] tonicity) appear to be impaired with aging.^{26,27} Older patients have decreased salivary flow and bicarbonate secretion, which is associated with a reduction in the neutralization of refluxed acid²⁸ and an increase in pepsin activity.²⁹ Others have reported that esophageal motility and the LES and UES pressure are weakened in elderly patients, leading to a theoretical increase in esophagopharyngeal reflux events.^{30,31} Mei et al observed that UES pressure and esophageal body motility responses to reflux and post-reflux residue were decreased in elderly populations, which may be associated with a higher proportion of hypopharyngeal reflux events and impaired airway protection.³¹ Moreover, it was suggested that elderly patients were found to have a higher proportion of hiatal hernia, present in 60% of >60-year-old patients, compared with young people.³² The presence of hiatal hernia is an additional predisposing factor for GERD but is also associated with recalcitrant LPR.³³ All of these physiological aging changes were associated with more intense patterns of abdominal acid contact time and advanced erosive diseases on gastrointestinal endoscopy compared with younger patients.^{34,35}

Elderly Diseases and Reflux

LPR is suspected to be associated with many prevalent conditions in the elderly population. Parkinson's disease,³⁶ pulmonary fibrosis,³⁷ chronic obstructive pulmonary disease,³⁸ systemic sclerosis,³⁹ and other conditions increase in prevalence with aging, and their related impairments in respiratory, digestive, or swallowing physiology may be associated with an increased risk of reflux. In the same vein, the consumption of some medications (eg benzodiazepines, antidepressants, anticholinergics, theophylline, nitrates, calcium antagonists, lidocaine, and prostaglandins) increases the

risk of GERD,⁴⁰ although these associations have not been formally investigated in LPR patients. Note that, irrespective of their age, LPR patients are commonly not obese.^{41,42}

Clinical Picture

Symptom Presentation

The most prevalent symptoms of LPR include dysphonia, globus sensation, throat pain, odynophagia, accumulation of sticky mucus, throat clearing, and cough.^{1,4} These are summarized in the reflux symptom score (RSS), which is a validated patient-reported outcome questionnaire assessing symptom frequency, severity, and quality of life.⁴³ The clinical presentation of elderly patients with LPR has been investigated in a few studies.^{44–47} In 2013, Lee et al investigated the influence of age on the clinical presentation and treatment of patients with suspected LPR.⁴⁴ The authors reported that the oldest group (60–79 years old) had higher baseline clinical (reflux symptom index [RSI]) and quality of life (LPR health-related quality of life) scores than the 18–39-year-old group. The findings of Lee et al were not confirmed in a European multicenter study in which elderly patients (>60 years old) with suspected LPR showed lower RSI scores than younger individuals.⁴⁵ Moreover, the impact of LPR on quality of life was lower in the elderly group compared with the younger group, which supported that aging reduces the subjective perception of LPR symptoms.⁴⁵ The differences between the study of Lee et al and others may be related to their inclusion criteria. Lee et al based the LPR diagnosis on the presence of at least one laryngopharyngeal symptom and finding in all age groups, whereas they did not exclude some confounding conditions associated with laryngopharyngeal symptoms and findings, eg tobacco- or alcohol-related laryngopharyngitis, chronic rhinosinusitis, or radiation or trauma history. The use of such inclusion criteria in all patients irrespective of age may constitute a selection bias because elderly patients were selected with the same clinical criteria as the younger ones. In that way, the analysis of symptom presentation (at baseline) may be biased because these symptoms were similarly considered in the inclusion criteria. In other studies, diagnosis was based on pH/impedance findings or on criteria associated with validated thresholds in sign and symptom instruments. The lower symptom scores of elderly LPR populations were confirmed in a study of 237 patients with LPR at the HEMII-pH.⁴⁶ In this study, individuals in the oldest group (>60 years) had lower RSS and lower quality-of-life scores than younger patients. Interestingly, the lower clinical scores concerned otolaryngological and digestive symptom scores. There were no difference in gastrointestinal endoscopy findings between age groups, while older patients exhibited significantly lower numbers of supine hypopharyngeal reflux events than younger individuals.⁴⁶ The decrease in symptom scores with aging was supported by Cervera-Paz and Jordano-Cabrera, who reported a mean RSI of 9.8 in elderly patients, with only 28% of cases having an abnormal threshold score (RSI >12).⁴⁷ Although this study did not compare clinical and pH monitoring findings between several age groups, the mean RSI was lower than those of large clinical studies.^{44,45}

In sum, most studies reporting age features in LPR populations supported the occurrence of less symptom sensation and related quality-of-life impact in elderly patients. This observation may support the existence of neurological deterioration of the terminal sensitive laryngopharyngeal nerve endings, and strengthens the findings of gastrointestinal studies that reported less severe heartburn and related digestive complaints in older patients with esophageal lesions.^{34,48}

Finding Presentation

The most common signs associated with LPR in aging individuals include posterior commissure hypertrophy, laryngeal erythema, anterior pillar erythema, laryngopharyngeal erythema, tongue tonsil hypertrophy, and retro-cricoid edema (Figure 1).^{45–47} Irrespective of the clinical instrument used in the study (reflux finding score versus reflux sign assessment), the authors did not find any significant influence of age, smoking, drinking, or diet on the presentation of laryngeal, oral, or pharyngeal signs in LPR patients.^{44–46} Hence, the observations for LPR do not corroborate those for GERD, according to studies highlighting more advanced erosive disease in elderly patients with GERD.^{35,48,49}

In gastroenterology, the body mass index is an important factor contributing to GERD and other digestive diseases. A high body weight in elderly patients increases the risk of GERD and hiatal hernia.³⁴ In the study by Cervera-Paz and Jordano-Cabrera, 50 patients (59%) with suspected LPR had a high body mass index, which was associated with abnormal single-probe esophageal pH monitoring.⁴⁷ The lack of comparison with younger groups, as well as the lack of HEMII-pH use, limit the drawing of clear conclusions on the influence of both age and weight on LPR findings. The above-mentioned studies did not report a significant influence of age on the body weight of LPR patients.^{44,46} The main symptoms and features found in elderly patients with LPR versus those with GERD are described in Table 1.

Therapeutic Outcomes

The treatment of LPR was long term, based on proton pump inhibitors (PPIs). However, meta-analyses suggested that the superiority of PPIs over placebo has still not been demonstrated.^{50,51} In practice, 60% of LPR patients reported a decrease in symptoms or relief of symptoms with once- or twice-daily PPIs.⁵² The low efficacy of PPIs is related to the high prevalence of weakly acid and non-acid (alkaline) LPR, which require treatment with alginate or magaldrate.^{53,54}

According to data in the literature, elderly LPR patients report different therapeutic responses from younger patients.^{44–46} Lee et al reported significantly more responders to PPI therapy, defined as those whose RSI score improved by more than 50%, in both the 18–39-year-old group (86%) and the 40–59-year-old group (75%), compared with the >60-year-old group (57%).⁴⁴ These findings were corroborated in our 2017 study, in which elderly LPR patients at the HEMII-pH needed more time (6 months versus 3 months) to achieve cure than younger patients.⁴⁵ Note that there were substantial therapeutic differences between these two studies. Indeed, Lee et al used PPIs only, whereas we used a combination of diet, PPIs, and alginate.^{46,53}

In practice, many elderly patients take long-term PPI therapy for LPR, GERD, or other gastrointestinal conditions. According to a large population-based cross-sectional study, the percentages of 18–39, 40–59, and ≥60-year-old people

Table 1 Laryngopharyngeal and Gastroesophageal Reflux Features of Elderly Patients

Outcome Comparison with Younger Patients	Elderly Patients with	
	LPR	GERD
Symptom presentation		
Otolaryngological	Young>Elderly	–
Digestive	Young>Elderly	Young>Elderly
Quality-of-life scores	Young>Elderly	Young>Elderly
Finding presentation		
Laryngeal	Young=Elderly	–
Pharyngeal	Young=Elderly	–
Oral	Young=Elderly	–
Gastrointestinal endoscopy		
Erosive lesions	Young=Elderly	Elderly>Young
Hiatal hernia	Young=Elderly	Elderly>Young
Hypopharyngeal pH monitoring		
Upright pharyngeal reflux events (N)	Young=Elderly	Young=Elderly
Supine pharyngeal reflux events (N)	Elderly>Young	Young=Elderly
Prevalence of high BMI	Young=Elderly	Elderly>Young
Treatment effectiveness		
Time to cure	Elderly>Young	Controversial

Abbreviations: GERD, gastroesophageal reflux disease; LPR, laryngopharyngeal reflux.

taking PPIs in the UK were 23.1%, 35.1%, and 39.8%, respectively.⁵⁵ The overprescription of long-term PPIs in elderly patients is an important issue for many reasons.⁵⁶

First, most elderly individuals take several medications and there are some drug interaction risks between PPIs and many common medications, including antiretroviral (HIV) drugs, cytostatics (eg methotrexate, dasatinib, erlotinib, and nilotinib), anti-HCV, itraconazole, immunosuppressants, and clopidogrel (Table 2).⁵⁷

There are potential harms of PPI treatment, and the related potential drug interactions in elderly individuals who are characterized by polypharmacy are associated with a higher risk of long-term adverse effects.⁵⁸

Second, the long-term use of PPIs has for a long time been suspected to be associated with adverse events, eg altered mineral and vitamin absorption, fractures, orthopedic injury, acute coronary syndromes, colitis, infectious risks, and increased risk of mortality.^{59–63} Most patients on long-term PPIs and practitioners may be unaware about these interactions and adverse events.^{59,60,63} However, as stated by Kanno and Moayyedi,⁵⁸ “association is not causation”, and many confounding factors have biased some PPI–adverse event studies, leading to overinterpretation of modest increases in odds ratios. For example, the association between PPIs and pneumonia may be related to the prescription of PPIs for a presumed reflux cough, which was, however, due to lung infection.⁵⁸ The indication of long-term prescription of PPIs or other antireflux medication must be carefully assessed by the practitioner, who has to keep in mind that, irrespective of the patient’s age, more than 50% of LPR events are acute or recurrent,¹⁶ and, therefore, do not require long-term medication. According to studies, the weaning rates of antireflux therapy in LPR patients ranged from 64% to 75% of cases.^{59,64,65}

Third, the overprescription of PPIs, particularly in elderly patients, has a dramatic impact on the costs of healthcare systems. In the USA, the annual costs for treating LPR and GERD are estimated at between US\$9.3 and US\$50 billion, making reflux one of the costliest diseases to manage.^{66,67} Thus, cost-effective therapeutic approaches (including an antireflux diet) should be prioritized over medication therapy in mild and moderate LPR.⁶⁸

The usefulness of H₂-histamine blockers was not assessed in the present review because they are less potent than PPIs⁶ and these drugs have proven to be less effective in terms of healing rates and symptom relief for GERD, esophagitis, or LPR.⁶⁹ Finally, PPIs appear to have different clearance properties, which is an important issue to consider in older patients. Esomeprazole has a more rapid onset of action and less variation in clearance rates than omeprazole. The drug clearance decreases with age, exaggerating some of the differences between the PPIs. The reduction of PPI clearance may increase the risk of drug interactions. The reduction of PPI plasma clearance particularly concerns pantoprazole, rabeprazole, and lansoprazole, and was found to increase by up to 50–100%.^{70,71} However, clearance of esomeprazole is not significantly affected by age, supporting its usefulness in elderly populations.

Table 2 Drug Interactions of Proton Pump Inhibitors

Interactions	Impact of PPIs
HIV medications Tyrosine kinase inhibitors Itraconazole Iron and magnesium	PPI-induced Reduction of absorption
Digoxin	PPI-induced Increase of absorption
Warfarin Diazepam Citalopram Methotrexate	PPI-induced Inhibition of elimination
Clopidogrel	PPI-induced Reduction of liver activation

Abbreviation: PPI, proton pump inhibitor.

Conclusion

The clinical presentation and treatment efficacy of elderly patients with reflux differ from those in younger patients. Adverse events, clearance outcomes of PPIs, and drug interactions should be considered in future therapeutic approaches to guide more effective personalized treatment plans for elderly patients with LPR.

Ethics Committee Approval and Informed Consent

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