Effectiveness of Diet Recommendations for Laryngopharyngeal Reflux Disease: A Systematic Review for Clinical Practice and Studies*

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SUMMARY: Objective. To review the current literature dedicated to the effectiveness of the diet recommendations for laryngopharyngeal reflux disease (LPRD).

Methods. Two independent investigators conducted a PubMED, Scopus, and Cochrane Library database search for studies investigating the effectiveness of anti-reflux diet in LPRD patients. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements and the Methodological Index for Non-Randomized Studies (MINORS) tool were considered for study analyses.

Results. Ten studies (868 patients) were included: two prospective controlled, four prospective uncontrolled, and four retrospective series. Diet recommendations primarily included low-fat (n = 7), alcohol-free (n = 7), low-caffeine (n = 6), and alkaline (n = 6) foods. Studies demonstrated that diet adherence led to significant symptom reduction (54%-83.3%) in untreated patients, comparable to medication effectiveness. In patients with recalcitrant symptoms despite proton pump inhibitor therapy, specific diets (alkaline, low-fat, high-protein, or gluten-free) provided significant symptom relief. All studies combining diet with medication demonstrated better outcomes than medication alone. The overall quality of studies was low with a mean MINORS of 9. 5 \pm 2.2. No randomized controlled study has been conducted to compare diet versus medication.

Conclusion. Low-fat, high-protein, low-high-released sugar, and alkaline diet may appear as an effective single or combined treatment to medical therapy for patients with LPRD. Future controlled studies are needed to compare diet versus medication in LPRD populations, while considering mid- to long-term effects of diet.

Key Words: Laryngopharyngeal–Reflux–Voice–Diet–Otolaryngology–Head Neck Surgery.

INTRODUCTION

Laryngopharyngeal reflux disease (LPRD) is defined by the Dubai consensus as a disease of the upper aerodigestive tract resulting from the direct and/or indirect effects of gastroduodenal content reflux, inducing morphological and/or neurological changes in the upper aerodigestive tract. Diet and autonomic nerve dysfunction have been identified as primary contributing factors of gastroesophageal and pharyngeal reflux events, leading to LPRD. From a physiological standpoint, foods and beverages may influence the gastroesophageal physiology, transient sphincter relaxation, and the related risk of pharyngeal reflux events according to their chemical composition, macronutrient profile, and physical properties. The current medical therapeutic approaches for LPRD may include diet and lifestyle

changes, proton pump inhibitors (PPIs), alginates, and antacids, with most medical treatment regimens being associated with diet recommendations. The anti-reflux diet recommendations are primarily based on gastroesophageal reflux disease (GERD) studies, and they are not sufficiently supported by LPR study findings. The consideration of LPRD studies rather than GERD ones is however important because both conditions substantially differ in pathophysiological and clinical findings, eg, the role of esophageal dysmotility in the disease development, the pH properties, and the nature of reflux events.

This systematic review aimed to investigate the effectiveness of diet in LPRD.

METHODS

The author of the review and a university librarian conducted a systematic review using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.⁸ The criteria for considering studies were based on population, intervention, comparison, outcome, timing, and setting (PICOTS) framework.⁹

Types of studies

The literature search included randomized controlled trials, prospective studies, or retrospective chart reviews exploring the therapeutic effectiveness of anti-reflux diet in patients with suspected or confirmed LPRD. Studies were published between January 1990 and April 2023 in English-language

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peer-reviewed journals. Case reports, letters to the editor, comments, and basic science studies were excluded.

Population

Populations included adult patients with suspected or confirmed LPRD. Consistent with European and International Federation of Otorhinolaryngological Societies consensus guidelines, the LPRD diagnosis was confirmed only for patients with more than one acid, weakly acid, or nonacid pharyngeal reflux events at the 24-hour hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH). Subjects with more than one pharyngeal reflux events identified at the 24-hour dual- or triple-probe pH testing with pharyngeal sensor but without impedance ring were considered as acid LPRD patients. The LPRD diagnosis was suspected but not confirmed in patients with laryngopharyngeal reflux symptoms and findings, positive reflux symptom index (RSI),¹⁰ reflux symptom score (RSS),¹¹ and validated sign instruments (eg, reflux finding score (RFS), 12 reflux sign assessment (RSA)¹³), or positive diagnosis at the 24-hour Dx-pH system (oropharyngeal pH monitoring, Restech).

Outcomes

The primary outcomes were the pretreatment to post treatment symptoms/findings changes in patients treated with only diet recommendations, and the composition and features of the related diet. Studies investigating diet effectiveness when combined with medication versus medication only were included as a separate study group. The secondary outcomes included demographics, gender ratio, mean/median age, and additional therapeutic outcomes (comparison with medication, duration, and follow-up). The inclusion and exclusion criteria were collected for the bias analysis.

Intervention and comparison

All types of diet were considered, including low-fat, high-protein, Mediterranean, low-high released sugar, and al-kaline diets. The features related to potential comparisons of therapeutic effectiveness with other conventional treatments (eg, PPIs, alginates, and antacids) were collected. Controlled studies were defined as studies comparing pre-treatment to post treatment findings of at least two groups of LPRD patients with one being treated with diet only or in combination with medication. Studies associating diet with voice therapy or alternative medicines, including Chinese herbs or acupuncture, were excluded.

Time and setting

There were no strict criteria for time and setting.

Search strategy

The two investigators independently searched the PubMED, Scopus, and Cochrane Library databases for relevant peer-reviewed publications related to the diet

therapeutic effectiveness in LPRD populations. The following keywords were used: Larynx; Laryngeal; Reflux; Laryngopharyngeal; Gastroesophageal; Diet; Food; Beverage; Change; and Outcomes. Studies reporting database abstracts, available full texts, or titles with the search terms were considered. The research findings were reviewed for relevance and the reference lists of state-of-the-art or systematic reviews were examined for additional references. The data from a 2019 systematic review were re-evaluated, included, and retrieved for the present updated review.

Bias analysis

The bias analysis was carried out with the Methodological Index for Non-Randomized Studies (MINORS) tool. 14 The MINORS tool consists of several items related to the analysis of methodological points of uncontrolled or controlled studies. Each item was rated as 0 if absent or not mentioned; 1 when reported but inadequate or unclear; and 2 when reported and adequate. Among MINORS outcomes, the aim of the study was not reported (0), unclear (1), or clearly stated (2). The prospective inclusion of consecutive patients was considered as optimal (2). The endpoints were considered as fully appropriate for studies evaluating the effectiveness of diet with both validated patient-reported outcome questionnaires and finding instruments (2), partially appropriate for unvalidated symptom and/or finding scores (1), and inappropriate for symptom or finding evaluation without metric scores. According to the subjectivity in the sign assessment, an unbiased assessment was defined as a blinded evaluation of laryngoscopic examination by two independent practitioners (2). A period of 6 weeks or more was considered as adequate to observe significant symptom and finding changes (2). A period ranging from 2 to 5 weeks was considered as partially adequate (1).

RESULTS

Of the 124 identified papers, 10 studies met the inclusion criteria (868 patients) (Figure 1). 15-24 There were two prospective controlled, 17,22 four prospective controlled, 15,19,20,23 and four retrospective case series (Table 1). 16,18,21,24 There were 458 (53.9%) females and 410 (46.1%) males. The mean age ranged from 30.2 to 64 years, with one study without age information.²² There was a myriad of LPRD diagnosis approaches (Table 2). The diagnosis was supported by objective approaches in five studies, 15,17,20,24 with only two 15,17 adhering to international consensus guidelines consisting of > 1 pharyngeal reflux events at the 24-hour HEMII-pH. The diagnosis was supported by dual-probe pH monitoring in one study,²⁰ single-probe pH monitoring in another, 22 and Dx-pH measurement in another one.²⁴ Other studies included suspected LPRD patients according to validated patientreported outcomes questionnaires and/or instruments 16,19,21 or not. 18,23 In two studies, the authors

Identification of studies via databases Records identified from PubMED - Scopus-Cochrane after duplicate removal: N=132 Records screened: N=124 Records excluded or not retrieved for inclusion criteria mismatch (N=109 Reports assessed for eligibility N=15 Records excluded for ineligible studies (N=5) Studies considered for the review (Diet effectiveness in patients with laryngopharyngeal reflux disease): N=10

FIGURE 1. Chart flow.

included patients with recalcitrant LPRD symptoms and findings after PPI therapy. ^{16,20} The treatment regimens are reported in Table 1. The findings of patients treated with only a diet were available in 6 studies, providing comparison with a medication group or not. ^{15–20} In other studies, the diet effectiveness data were extracted from patient groups treated with medication only versus medication and diet. ^{21–24}

Diet features and results

The specific diet and lifestyle recommendations are summarized in Tables 3 and 4. The most common diet recommendations included the consumption of low-fat (n = 7), alcohol-free (n = 7), low-fat dairy products (n = 6),

low-caffeine (n = 6), low-theine/mint (n = 6), alkaline (n = 6), and high-protein (n = 5) foods and beverages (Table 3). Among lifestyle recommendations, most authors recommended avoiding both late meals (n = 6) and postmeal lying down (n = 6), and elevation of the head of the bed (n = 5). Discrepancies across diet recommendations were found for eggs, small dish portion, and elevation of bed head (Table 4).

The effectiveness of diet and lifestyle recommendations was evaluated in several patient profiles with LPRD (Table 1). Three studies have investigated the diet effectiveness in untreated patients with primary LPRD symptoms and findings. ^{17–19} Hamdan et al observed that fasting may lead to worsening of some LPRD symptoms,

TABLE 1. Demographic, Clinical, and Therapeutic Outcomes	al, and Therapeu	tic Outcomes							
References	Design	Populations	F/M	Age	Diagnosis	Treatments	Outcomes	Results	Duration
Hránková et al, 2024 ¹⁵	Uncontrolled	36 mild CC	21/15	49	неміі-рн	Diet	RSI reduction	Pre > post diet	3 months
	Prospective	LPRD			CC > 3 months	Diet + alginate/PPIs	Reflux episodes (<i>n</i>)	Pre > post diet	
Balouch et al, 2023 ¹⁶	Retrospective	81 gluten-free sLPRD	29/52	49.7	Recalcitrant sLPRD Gluten SE	Gluten-free diet	RSA-10-RSS-12 RFS/reduction in gluten-free	Pre = post diet Pre > post diet 77.1% vs 43.9%	145 days
Lechien et al, 2021 ¹⁷	Prospective Controlled	50 LPRD	31/19	52.3	HEMII-pH	Diet	RSI reduction RSS and RSA No-trt vs diet	55.4% vs 25.8% Pre > post diet Diet > nothing	6 we
Zalvan et al, 2017 ¹⁸	Retrospective	85 PPI sLPRD	47/38	60	Symptoms/signs	Diet Diet + PPIs	RSI % reduction	PPI = diet 57 1 vs 62 6	6 we
Hamdan et al, 2012 ¹⁹	Prospective	22 fasting	0/22	30.2	RSI > 9/RFS > 7	Fasting	RSI-RFS	Fasting = non	1 mo
Koufman, 2011 ²⁰	Prospective	20 acid LPRD	8/12	54.3	Dual-probe pH	Diet	RSI	Pre > post diet	2 we
Uncontro Combined Diet and Medication Studies	Uncontrolled <i>Medication</i>				Recalcitrant symptoms	SU			
Lechien et al, 2019 ²¹	Retrospective	26 diet + PPIs 39 PPIs sLPRD	16/10 18/21	50.3 52.4	RSI > 13/RFS > 7	Diet + PPIs PPIs	RSI reduction Jitt%, Shim% reduction	Diet > PPI Diet > PPI	3 mo
Giacchi et al, 2000 ²³	Prospective	24 diet + PPIs/	0/24	64	Symptoms/signs	Diet + PPIs/H2	Diet adherence and		4 mo
	Uncontrolled	H2 blockers sLPRD				blockers	symptom reduction	+ correlation	
Nanda, 2016 ²²	Prospective	100 diet + PPIs	88/112	A P	Symptoms/signs	Diet + PPIs	Symptom reduction	Diet > PPI	3 mo
Yang et al, 2018 ²⁴	Controlled Retrospective	100 PPIs sLPRD 105 sLPRD	77/28	NP 60	pH monitoring Symptoms/signs	PPIs Diet + PPIs	Symptom	Diet > PPI	Diet: 2 we
		81 sLPRD	62/19	59	Dx-pH testing	red PPIs/PPIs + H2 blockers	reduction ers		6 we

Abbreviations: CC, chronic cough; F/M, female/male; GS, globus sensation; Jitt%, percent jitter; HEMII-pH, hypopharyngeal-esophageal multichannel intraluminal impedance-pH testing; HR, high-released; mo, month(s); NP, not provided; NS, not specified; PND, postnasal drip; PPIs, proton pump inhibitors; RFS, reflux finding score; RSI, reflux symptom index; SE, sensitivity; Shim%, percent shimmer; sLPRD, suspected laryngopharyngeal reflux disease; TC, throat clearing; we, week(s).

TABLE 2. Demographics and Clinical Summary	
Outcomes	n (%)
Total number of patients	868
Gender	
Females	458 (53.9)
Males	410 (46.1)
Mean age (range, years)	30.2-64
Diagnosis methods	
HEMII-pH (> 1 pharyngeal reflux events)	2
Dual-probe pH monitoring	1
Single-probe pH monitoring	1
Dx-pH measurement	1
RSI > 9 and RFS > 7	1
RSI < 13 and RFS > 7	1
Symptoms and findings	3
LPRD patients with primary symptoms/	8
findings	
LPRD patients with recalcitrant symptoms/ findings	2
Alternative treatments (control group)	
Proton pump inhibitors	5
Proton pump inhibitors and alginates/ antacids	1
Proton pump inhibitors and H2 blockers	2
Therapeutic outcomes	
RSI	5
RSS	1
RSS-12	1

Abbreviations: HEMII-pH, hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring; LPRD, laryngopharyngeal reflux disease; N, number; RFS, reflux finding score; RSA, reflux sign assessment; RSI, reflux symptom index; RSS, reflux symptom score.

2

1

3

RFS

RSA

RSA-10

shimmer)

Symptom/sign reduction

Acoustic voice parameters (%jitter, %

including throat clearing, postnasal drip, and globus sensation, while they did not find significant differences across fasting and nonfasting patients for the RSI total score. ¹⁹ In a crossover observational study, our group evaluated the effectiveness of a 6-week diet on 50 patients with a demonstrated LPRD at the HEMII-pH and compared their findings to those of a control period where patients did not receive any treatment or diet. In this study, diet adherence led to a 54% symptom relief without using any medication. ¹⁷

Zalvan et al retrospectively compared the findings of patients with suspected LPRD treated with PPI and reflux diet and precautions prohibiting coffee, tea, chocolate, soda, greasy, fried, fatty and spicy foods, and alcohol versus those treated with alkaline water (pH > 8.0), plant-based Mediterranean-style diet, and standard reflux precautions. The authors recommended that patients replace all beverages with alkaline water and eat a 90%-95% plant-

	Overall	Overall diet features	res	Detaile	od foor	Detailed food and beyerages recommendations	verages	recomi	nendatio	Suc					
		400.000	2		5	2	2062101			2					
References	Fat H	RS Prote	in Diet pH	Spicy	CB	Alcohol	RM B	utter L	P Egg	s Caffeir	ne Onions	Tomato	MT	BD GI	Fat HRS Protein Diet pH Spicy CB Alcohol RM Butter DP Eggs Caffeine Onions Tomato TM PBD Gluten Lactose
Hránková et al, 2024 ¹⁵ Low Low High	Low Lo	ow High	Alkaline	1		1	- Lo	Low L	Low -	ı	ı	ı		ı	
Balouch et al, 2023 ¹⁶	1	1	ı		1	1	1	•	•	1	ı	ı		. Free	ا ق
Lechien et al, 2021 ¹⁷	Low L	Low Low High	Alkaline Low	Low	Low Low	Low	د	Low	Low NR	Low	Low	Low	Low	High NR	N.
Zalvan et al, 2017 ¹⁸	Low L	Low Low High	Alkaline Low	Low	Low Low	Low	Low Lo	Low	Low -	Low	ı	1	Low	High -	ı
Hamdan et al, 2012 ¹⁹	Fasting														
Koufman, 2011 ²⁰	Low -	High	Alkaline Low	Low	Low Low	Low	Low Low		Low Low	/ Low	Low	Low	Low .	1	ı
Lechien et al, 2019 ²¹	Low L	Low Low High	Alkaline Low	Low	Low	Low	۔ ۔	Low L	Low NR	Low	Low	Low	Low High	High NR	N.
Giacchi et al, 2000 ²³	Low		ı		Low	Low		_	Low -	Low	ı		Low	•	ı
Nanda, 2016 ²²	Low -		ı	Low	1	Low	1	•	1	Low	ı	,	Low .	1	ı
Yang et al, 2018 ²⁴	'		Alkaline -			Low	1	•		•		,		•	ı

TABLE 4.	
Lifestyle Recommendation	ıs

	Lifestyle I	Recommendat	tions					
	DiP	Smok.	TC	PMS	PL	BE	LM	Hot
Hránková et al, 2024 ¹⁵	Small	-	-	-	Low	-	-	-
Balouch et al, 2023 ¹⁶	-	-	-	-	-	-	-	-
Lechien et al, 2021 ¹⁷	NR	Low	NR	Low	Low	NR	Low	-
Zalvan et al, 2017 ¹⁸	-	-	-	-	-	-	-	-
Hamdan et al, 2012 ¹⁹				-				-
Koufman, 2011 ²⁰		Low	Low	Low	Low	+	Low	-
Lechien et al, 2019 ²¹	Small	Low	Low	Low	Low	+	Low	-
Giacchi et al, 2000 ²³	-	-	-	-	Low	+	Low	-
Nanda, 2016 ²²	-	Low	-	-	Low	+	Low	Low
Yang et al, 2018 ²⁴	-	Low	Low	-	-	-	Low	-

Abbreviations: BE, bed head elevation; DiP, dish portion; LM, late meals; NR, no restriction; PL, postmeal lying down; PMS, postmeal sport; Smok., smoking; TC, tight clothing.

based diet consisting of vegetables, fruits, whole grains, and nuts with less than 5%-10% animal-based products. The adherence to this Mediterranean diet led to a significant reduction of RSI in 62.6% of cases, which was comparable to the intake of PPIs (57.1%). 18

The comparable effectiveness of diet with medication was similarly supported by Hrankova et al in a prospective study comparing LPRD patients with mild chronic cough treated with diet only versus those with severe chronic cough treated with PPIs and alginates. ¹⁵ In the group of patients with mild cough, the authors observed 30/36 (83.3%) patients with substantial symptom improvement after 12 weeks of diet and lifestyle modifications, which was comparable to the group of patients with severe LPRD-induced chronic cough treated with medications.

Patients with recalcitrant symptoms and findings despite PPI therapy were invited to adhere to a strict diet in two studies. ^{16,20} In the first study, Koufman observed a significant RSI reduction after 2 weeks of alkaline, low-fat, and high-protein diet in 20 patients with recalcitrant LPRD-related symptoms. ²⁰ Balouch et al investigated gluten-free diet in patients with recalcitrant symptoms and findings despite intensive medical therapy, including high-dose PPI, bedtime H2 blocker, low-acid diet, alginate, and alkaline water. In a subgroup of patients with positive gluten sensitivity on blood tests, the adherence to a gluten-free diet for 3 months led to significant reduction of laryngeal findings (RFS). ¹⁶

Of the four studies investigating the effectiveness of diet and lifestyle recommendations in patients treated with LPRD medication, all authors demonstrated that adherence to diet and lifestyle changes was positively associated with a better reduction of symptoms than medication intake only (Table 1).^{21–24}

Bias analysis

The mean MINORS was 9.5 ± 2.2 (Table 5). Most studies prospectively collected clinical data, but only one included consecutive patients.¹⁷ The endpoints were fully

appropriate, associating both symptom and finding evaluations in six studies, ^{15–17,19–21} while therapeutic outcomes were limited to symptoms or signs only, or were collected without using clinical instruments in others. ^{18,22–24} The duration of diet is reported in Table 1. The assessment of the effectiveness of diet and lifestyle adherence was evaluated after 6 weeks in seven studies, ^{15–18,21–23} which was considered as optimal regarding the literature. ^{7,25} While most authors reported > 5% loss to follow-up of patients, the sample size was calculated prior to the conduction of the study in only one study. ¹⁶

DISCUSSION

The cost burden associated with the diagnostic and therapeutic management of LPRD has significantly increased in the past decades. The national cost burden of diagnosing and treating LPRD in the United States of America could be 5.6 times the cost of treating GERD, with a total expenditure estimated at > \$50 billion annually. ²⁶ In Europe, the lack of knowledge related to the etiological factors, clinical presentations, and therapeutic findings led to similar expenditure for public healthcare systems.²⁷ Regarding treatment, LPRD medication use increased 233%, particularly among PPIs,²⁶ while there are few studies evaluating the cost related to the management of long-term PPI and other medication use.²⁸ The investigation of the effectiveness of diet and lifestyle changes as a primary treatment of LPRD or as prevention factors is therefore mandatory to reduce both cost burden and adverse events in LPRD patients.

The findings of this review suggest that diet and lifestyle recommendations are effective as single or combined therapy with medication in patients with suspected or confirmed LPRD. Despite positive overall trends across studies, many points limit the drawing of valid conclusions.

From a methodological standpoint, most studies are retrospective chart reviews or uncontrolled prospective studies with none conducting a randomized controlled trial

Clearly Inclusion of Prospective Stated Consecutive Data Aim Patients Collection 15 2 0 2								
Hránková et al, 2024 ¹⁵ 2 0 2 2 Balouch et al, 2023 ¹⁶ 2 0 0 2 Lechien et al, 2021 ¹⁷ 2 2 2 Zalvan et al, 2017 ¹⁸ 2 0 0 1 Hamdan et al, 2012 ¹⁹ 2 0 2 Koufman et al, 2011 ²⁰ 2 0 2 Lechien et al, 2011 ²⁰ 2 0 2 Lechien et al, 2011 ²⁰ 2 0 2 2 Lechien et al, 2011 ²⁰ 2 0 2 2		Pro Dat Col	Endpoints Appropriate to Study	Unbiased Endpoint Assessment	Follow-Up Adequate Period	< 5% of Lost to Follow-Up	Sample Size Calculation	Total MINORS Score
Balouch et al, 2023 ¹⁶ 2 0 0 0 2 Lechien et al, 2021 ¹⁷ 2 2 2 Zalvan et al, 2017 ¹⁸ 2 0 0 1 Hamdan et al, 2017 ¹⁹ 2 0 2 2 Koufman et al, 2011 ²⁰ 2 0 2 Lechien et al, 2019 ²¹ 2 0 2	1 ¹⁵ 2 0	2	2	2	2	0	0	10
Lechien et al, 2021 ¹⁷ 2 2 2 2 Zalvan et al, 2017 ¹⁸ 2 0 0 1 Hamdan et al, 2012 ¹⁹ 2 0 2 2 Koufman et al, 2011 ²⁰ 2 0 2 2 Lechien et al, 2019 ²¹ 2 0 2 2	6 2 0	0	2	2	2	0	2	10
Zalvan et al, 2017 ¹⁸ 2 0 0 1 Hamdan et al, 2012 ¹⁹ 2 0 2 2 Koufman et al, 2011 ²⁰ 2 0 2 2 Lechien et al, 2019 ²¹ 2 0 2 2 Ciochi et al, 2002 ³¹ 2 2 2	7 2 2	2	2	2	2	2	0	14
Hamdan et al, 2012 ¹⁹ 2 0 2 2 2 Koufman et al, 2011 ²⁰ 2 0 2 2 2 Lechien et al, 2019 ²¹ 2 0 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	2 0	0	_	_	2	0	0	9
Koufman et al, 2011 ²⁰ 2 0 2 2 Lechien et al, 2019 ²¹ 2 0 2 2 Ciscoli et al, 2000 ²³ 3 3 4	19 2 0	2	2	_	_	2	0	10
Lechien et al, 2019 ²¹ 2 0 2 2 2 Circle of all 2019 ²¹ 2 0 2 2	²⁰ 2 0	2	2	_	_	2	0	10
Ciccobi c+ c1 200023 2	2 0	2	2	2	2	0	0	10
Glaccill et al, 2000 2 0 2	2 0	2	_	_	2	0	0	œ
Nanda, 2016 ²² 2 0 2 1	2 0	2	_	_	2	2	0	10
Yang et al, 2018^{24} 2 0 2 1	2 0	2	_	_	_	0	0	7

comparing medication versus diet only. The lack of consideration of objective LPRD diagnosis at the 24-hour HEMII-pH is an additional limitation, which may bias the evaluation of diet effectiveness. Indeed, many prevalent conditions are associated with LPRD-like symptoms and findings, including allergy, chronic rhinosinusitis, inhaled corticosteroid-induced laryngitis, or tobacco laryngopharyngitis.^{29–32} Among studies using symptoms and signs as inclusion criteria, confounding conditions were not excluded,²² or only partially considered.^{18,23} The duration of diet is an important point in the study finding interpretation. In practice, the diet and lifestyle changes may take time for patients, leading to potential mid- to long-term benefits that are not immediately perceived by both patients and practitioners. 18,33 This finding was strengthened in a recent study evaluating the weaning of LPRD patients with chronic PPI use.³³ Among 53 LPRD patients with a mean duration of PPI therapy of 142.3 months, Geoffroy et al observed that PPIs were successfully discontinued in 66.0% of patients who adhered to a standardized anti-reflux diet and lifestyle recommendations for at least 3 months.

From a physiopathological point of view, most diet and lifestyle recommendations were based on GERD studies, which aimed to reduce acid production and backflow of gastric content into the esophagus.³⁴ However, GERD and LPRD share distinct pathophysiological mechanisms. Contrary to GERD, LPRD is primarily an upright, daytime, gaseous and alkaline reflux disease, with less than 50% of patients having both GERD and LPRD.^{1,35–37} According to these differences, some recommendations may need revision, especially those recommending avoiding low-pH foods and beverages, and the elevation of head during nighttime.

The studies investigating the reflux event profiles of LPRD patients demonstrated that most patients with LPRD and without GERD have no nighttime pharyngeal reflux events, 35,36 which can be attributed to the upright and gaseous pattern of reflux events. In the same vein, the pH of pharyngeal reflux events is commonly weakly acid (4.0 to 7.0) or alkaline (> 7.0), 35,36 and LPRD patients have a more alkaline saliva than controls, which calls into question the need for considering alkaline foods and beverages and avoiding low-pH ones.

Pathophysiologically, the enzyme-induced inflammation of upper aerodigestive tract mucosa requires the backflow of gastroduodenal enzymes, which is related to the relaxation of both lower and upper esophageal sphincters. The consideration of foods and beverages associated with esophageal dysmotility and sphincter transient relaxations makes sense for establishing valid anti-reflux diet and lifestyle recommendations. A mathematical model of refluxogenic potentials of foods and beverages has been developed by our European group (Table 6), considering the available literature about the impact of foods and beverages on esophageal function. Despite encouraging findings, demonstrating a significant

TABLE 6.		
Recommendation (Grid (Diet and Lifestyle I	Modifications)

Lifestyle Habits	Foods to Favor	Foods to Avoid
Stress control Tobacco and other addiction(s)	1. Meat, fish, chicken, and eggs Fresh and thin fish	1. Meat, fish, chicken, and eggs Fat fish, fish oil (sardines, cods,
reduction		and herrings)
3. Reduction of size of meals (GERD)	Shrimps, lobster, and shellfishes	Fat chicken
4. Do not talk while eating	Chicken fillet (without skin)	High-fat meat*
5. Eat slowly	Turkey (without skin and fat)	-kidneys, bacon, and ground meat,
6. Avoid tight clothing (GERD only)	Duck (without skin and fat)	-Pâté, tripes, and lamb
7. Avoid postmeal sport (GERD only)	Low-fat meat*	-Lamb chops, shoulder, or legs of lamb
	-Veal cutlet, pork tenderloin,	-Ribs, rib steak
	-Rindless, fatless, cooked ham	-Pork chops, roast, and shoulder
	-Steak, fillet, and striploin	-Foie gras
	-Roast veal, veal chop, and horse	Delis, sausage, and salami
	*Remove fat from meat	
	Egg white	
	Other:	Other:
If heartburn/acid brash (GERD only)	2. Dairy products	2. Dairy products
1. Reduction of overweight	Low-fat cheese	Chocolate, ice cream, and whole milk
2. Elevating the head of the bed	Skim milk	Hard cheese, full-fat cheese
	Other:	-Goat cheese, cheddar, and Roquefort, -Fontina, gruyere, parmesan,
		munster, etc Other:
Laryngopharyngeal reflux treatment	3. Cereals and Starches	3. Cereals and Starches
Drug:	Oat, wheat, cracker, dark/whole	Chocolate cookies, peanut, and white
Drug	pasta,	bread,
	Whole-meal bread, brown bread,	French fries and frying
To take: before-during-after	Boiled potatoes, rice, brown rice,	Nut, cashew, and hazelnut
ro tanor poroto aariing ario.	and sourdough bread	Other:
	4. Fruit and vegetables	4. Fruit and vegetables
Meals (circle the adequate response):	Agave, asparagus,	Shallot
	Banana, melon	Spicy
-Breakfast	Broccoli, celery, and fennel	Onion
	Cooked mushrooms	Chilli
-Lunch	Cauliflower, green beans, and ginger	
	Turnip, parsley, and tofu	Raw vegetable
-Diner	Other:	
D	Vegetable preparation:	
Drug:	Cooked by steaming or boiling in	
	water 5. Beverage	5. Beverage
To take: before-during-after	Chamomile	Strong alcohol, red, and rosé wines
To take. Before during after	Water, alkaline water	Sparkling beverage (water, soda,
	vator, alkamic water	beer, etc)
	Apple/pear juices (no sugar added)	Coffee, tea
Meals (circle the adequate response):	Melon/banana juices (no sugar	Citrus juices (orange, grapefruit) and
	added)	apple
	Other:	Other:
-Breakfast	6. Greasy substances	6. Greasy substances
	Olive oil	Butter, spicy oils
-Lunch	Other:	Sauces (mayonnaise, mustard,
		ketchup, etc)
		Other:
-Diner	7. Sugar	7. Sugar
	Honey	Sweets, viennoiseries

association between the refluxogenic diet score of patients and the occurrence of pharyngeal reflux events at the 24-hour HEMII-pH, 41 this model is based on GERD literature, which reports conflicting data for many foods and beverages. 40 The lack of human studies evaluating the impact of commonly consumed food and beverages on esophageal and sphincter motility is therefore the primary limitation in drawing valid diet and lifestyle recommendations.

Despite substantial heterogeneity across studies, conflicting results in mechanistic studies, and the lack of LPRD-dedicated controlled studies, the findings of this review support the effectiveness of diet and lifestyle recommendations. The growing literature dedicated to the gut-laryngopharyngeal-brain axis, 42 highlighting the importance of microbiome in human health, 43,44 strengthens the importance of conducting future clinical and mechanistic studies investigating the short- to long-term benefit of diet in the management of LPRD. These studies should carefully consider potential confounding factors, especially autonomic nerve dysfunction, which was identified as a primary factor of resistance to anti-reflux treatments in LPRD patients.⁴⁵ Similar to some foods and beverages, autonomic nerve dysfunction has long been known to be associated with esophageal sphincter dysmotility.

CONCLUSION

Low-fat, high-protein, low-high-released sugar, and alkaline diet may appear as an effective single or combined treatment to medical therapy for patients with LPRD. The heterogeneity across studies and the lack of consideration of LPRD pathophysiology limit the drawing of valid conclusion. Future controlled studies are needed to compare diet versus medication in LPRD populations, while considering mid- to long-term effects of diet.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

Author Contributions

Jérôme R. Lechien: design, acquisition of data, data analysis and interpretation, drafting, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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