#### LARYNGOLOGY



# Patients with acid, high-fat and low-protein diet have higher laryngopharyngeal reflux episodes at the impedance-pH monitoring

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#### Abstract

**Objective** To assess the impact of diet on the occurrence of proximal reflux episodes at the multichannel intraluminal impedance-pH monitoring (MII-pH) in patients with laryngopharyngeal reflux (LPR).

**Methods** Patients with LPR symptoms and findings were recruited from three European hospitals. The LPR diagnostic was confirmed through MII-pH and patients were benefited from gastrointestinal (GI) endoscopy. Regarding the types of reflux at the MII-pH (acid, nonacid, mixed), patients received a 3 month-therapy based on the association of alkaline, low-fat and high-protein diet, proton pump inhibitors, alginate or magaldrate. Reflux symptom score (RSS) and reflux sign assessment (RSA) were used to evaluate laryngeal and extra-laryngeal symptoms and findings from pretreatment to posttreatment. The Global Refluxogenic Score (GRES) was used to assess the refluxogenic potential of the diet of the patients at baseline and posttreatment. The relationship between GRES severity; the MII-pH findings; GI endoscopy; and the therapeutic response was explored through multiple linear regression.

**Results** Eighty-five LPR patients were included. The mean GRES significantly improved from pretreatment  $(50.7 \pm 23.8)$  to posttreatment  $(27.3 \pm 23.2; P = 0.001)$ . Similarly, RSS and RSA significantly improved from baseline to posttreatment. The baseline GRES was significantly associated with the occurrence of proximal reflux episodes at the MII-pH (P = 0.001). Trends were found regarding the association between GRES and the occurrence of esophagitis (P = 0.06) and between hiatal hernia and DeMeester score (P = 0.06). There was a significant and strong association between the concomitant respect of diet and medication and the improvement of RSS (P = 0.001).

**Conclusion** The consumption of high-fat, low-protein, high-sugar, acid foods, and beverages is associated with a higher number of proximal reflux episodes at the MII-pH, according to the global refluxogenic score of LPR patients.

Keywords Reflux · Laryngitis · Impedance · pH monitoring · Laryngopharyngeal · Diet · Foods · Beverages

Alexandra Rodriguez and Sven Saussez have equally contributed to this work and should be regarded asjoint last authors.

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#### Introduction

Laryngopharyngeal reflux (LPR) is an inflammatory condition of the upper aerodigestive tract tissues related to direct and indirect effects of gastroduodenal content reflux, which induces morphological changes in the upper aerodigestive tract [1]. Many etiopathological mechanisms of reflux have been identified, including diet [2-4]; anxiety [5]; and autonomic nerve dysfunction [6, 7]. A diet composed of acid, high-fat, low-protein foods, and acid, alcoholic or high-sugar beverages leads to gastroesophageal dysfunction, including transient relaxations of lower (LES) and upper (UES) esophageal sphincters, which increase both acid esophageal and laryngopharyngeal exposure [8, 9]. The authors interested in diet and behavioral changes have mainly studied the impact of an alkaline, low-fat and high-protein diet in patients with LPR symptoms, but not demonstrated LPR [3] or with recalcitrant symptoms to proton pump inhibitors (PPIs), corresponding to potential resistant patients [4, 10]. The realization of researches investigating the involvement of diet in the development of LPR was limited by the lack of clinical tool providing rigorous rating to the refluxogenic potential of diet. Recently, experts of the LPR Study Group of Young Otolaryngologists of the International Federation of Otorhino-laryngological societies (YO-IFOS) developed an European diet score assessing the refluxogenic potential of foods and beverages [11]. Based on the pH and the composition of foods and beverages, the Refluxogenic Diet Score (REDS) provides a classification of foods and beverages, allowing secondarily, the rating of the refluxogenic potential of dishes and the overall diet of patients [11].

The aim of this study is to investigate the relationship between the diet of LPR patients, the clinical findings, and the results of the multichannel intraluminal impedance-pH monitoring (MII-pH).

# **Material and methods**

The local ethics committee approved the study (n°BE076201837630). Patients were invited to participate and the informed consent was obtained.

#### Subjects and setting

From January 2018 to June 2019, patients with LPR symptoms and findings were enrolled from three European hospitals (CHU Saint-Pierre and Cesar De Pape Hospital, Brussels, Belgium; Polyclinique Elsan de Poitiers,

Poitiers, France). The recruitment of patients was prospectively made through similar inclusion and exclusion criteria by one otolaryngologist in Poitiers (FB) and several otolaryngologists in Brussels (JRL, MPT, MH, AR, DD).

The diagnostic was confirmed through positive MII-pH. Gastrointestinal (GI) endoscopy was performed in patients with gastroesophageal reflux disease (GERD) symptoms and in patients of age  $\geq 60$  years, regarding the reduced esophageal sensitivity [12]. To be included, patients had to have positive LPR diagnosis at the MII-pH. Patients were excluded if they presented with one of the following conditions: smoking, alcohol dependence, pregnancy, neurological or psychiatric illness, upper respiratory tract infection within the last month, current use of anti-reflux treatment (i.e., PPIs, antihistamine, alginate, and magaldrate), previous history of neck surgery or trauma, benign vocal fold lesions, malignancy, history of ear, nose, and throat radiotherapy, and active seasonal allergies or asthma.

# Multichannel intraluminal impedance-pH monitoring

The characteristics of MII-pH device, placement, and analyses have been described in previous publications [13]. In summary, the MII-pH was composed of eight impedance segments and two pH electrodes (Versaflex Z®, Digitrapper pH-Z testing System, Medtronic, Europe). Six impedance segments were placed along the esophageal zones (Z1-Z6)and they were centered at 19, 17, 11, 9, 7, and 5 cm above the LES. Two additional impedance segments were placed 1 and 2 cm above the UES in the hypopharyngeal cavity. The pH electrodes were placed 2 cm above LES and 1-2 cm below UES, respectively. Proximal reflux event was defined as an episode that reached two impedance sensors in the hypopharynx. Acid reflux episode consisted of an episode with pH  $\leq$  4.0. Non-acid reflux episode consisted of an episode with pH > 4.0. The LPR diagnostic consisted of the occurrence of  $\geq 1$  proximal episode [14].

#### Treatment and clinical outcomes

The therapeutic algorithm was based on recent recommendations of the LPR Study Group of YO-IFOS [1]. Based on the characteristics of LPR at the MII-pH (acid, non-acid, or mixed LPR), patients were treated with a personalized treatment scheme, including diet, behavioral changes, and the use of PPIs (pantoprazole)  $\pm$  alginate  $\pm$  magaldrate for 3 months. The respect of medication intake was carefully assessed posttreatment through a structured anamnesis.

Symptoms and findings were assessed from pretreatment to posttreatment with Reflux Symptom Score and Reflux [13] Sign Assessment [15], respectively.

#### **Diet evaluation**

Global Refluxogenic Score (GRES) was used to assess the diet habits of the patients. GRES consists of a score which rates the refluxogenic potential of foods and beverages (REDS) [11] that are usually consumed by patients; western European foods and beverages being classified into five categories from very low refluxogenic food/beverage (cat.1) to very high refluxogenic food/beverage (cat.5) (Tables 1, 2). In practice, based on Tables 1 and 2, the patient selects the foods and beverages that she/he have consumed over the previous 3 weeks and the physician may add the categories of the foods and beverages to get a score. In case of daily consumption of a food, the physician has to multiply the category of the food by the number of day on which it was consumed. Thus, at most the patient eats high refluxogenic foods/beverages, at the most the GRES will be high. At the end of the initial consultation, patient received a personalized diet grid identifying the foods and beverages to avoid.

The respect of the anti-reflux diet has been assessed posttreatment for evaluating the potential impact of diet on the clinical improvement.

#### **Statistical methods**

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS version 22.0; IBM Corp, Armonk, NY, USA). The relationship between GRES and the MII-pH data and the impact of the respect of diet and medication on the clinical evolution were investigated through multiple linear regression. Changes in RSS, RSA, and GRES from pretreatment to posttreatment were evaluated using the Wilcoxon signed-rank test. A level of significance of P < 0.05 was used.

# Results

From the 89 patients who were recruited, 85 completed the study. The characteristics of patients are described in Table 3. Globus sensation, chronic cough, throat pain, and sticky mucus were the main reasons for consultation. There were 36 acid, 31 mixed, and 18 non-acid LPRs. Forty (47%) patients had both LPR and GERD. The most common findings reported by the GI endoscopy were LES insufficiency (58.7%); esophagitis (42.9%); gastritis (42.9%); and hiatal hernia (33.3%). GI endoscopy was normal in 14.4% of cases. The mean value of GRES significantly decreased throughout the treatment (Table 3).

#### **Clinical evolution**

The RSS significantly decreased from pretreatment to posttreatment (Table 4). Precisely, the pretreatment to posttreatment improvements of RSS subscores were significant for ear, nose, and throat and digestive symptoms. The quality of life scores of RSS significantly decreased throughout treatment.

The RSA total score significantly decreased from pretreatment to posttreatment. Similar evolution was found for the RSA subscores (Table 5).

#### Association between GRES and clinical findings

Irrespective to the types of reflux (acid, non-acid, mixed), there was a significant positive association between GRES and the occurrence of proximal reflux episodes at the MII-pH (P=0.001). This significant association was maintained considering the position of patient during the occurrence of reflux episodes [upright/daytime (P=0.001) and recumbent/ nighttime (P=0.04)].

Trends were found regarding the association between GRES and the occurrence of esophagitis (P = 0.06); and hiatal hernia and DeMeester score (P = 0.06). Posttreatment, patients with higher GRES had higher score of indigestion (P = 0.003).

The respect of diet was not associated with better clinical improvement, when the variable (diet respect) was considered individually. Similar result was found for medication respect. However, there was a significant and strong association between the concomitant respect of diet and medication, and the improvement of RSS (P=0.001). At most the patient respected the diet advices and the medication intake, at most the improvement of RSS was high.

## Discussion

The role of diet in the development of reflux has long been recognized and well-studied in patients with GERD. In LPR, there are only a few conducted studies; all of them investigating the impact of low-fat, high-protein, and alkaline diet on the clinical evolution of LPR patients treated by PPIs or with recalcitrant symptoms [2, 3, 10, 16–20]. Nowadays, there is no study that specifically investigates the refluxogenic potential of foods and beverages on the development of LPR, regarding MII-pH. The main finding of this study is the strong association between the severity of the global refluxogenic diet score of the patient (GRES) and the occurrence of proximal reflux episodes at the MII-pH. In other words, at most the patients have high refluxogenic diet score, at most they have a high number of proximal reflux episodes; the refluxogenic diet, including acidic, high-fat and low-protein

Table 1 Categories of Refluxogenic potential of foods	Refluxc	genic	potential of loods											
Very low reflux. foods	REDS	Cat	Low reflux. foods	REDS	Cat	Moderate reflux. foods	REDS	Cat	High reflux. foods	REDS	Cat	Very high reflux. foods	REDS	Cat
Artichoke	0.086	1	Aubergine	0.166	2	Apricot	0.391	3	Apple	0.534	4	Avocado	5.610	5
Asparagus <sup>a</sup>	0.072	1	Banana	0.227	7	Blueberry	0.472	3	Blackberries	0.640	4	Bacon	25.40	5
Baked spinach	0.025	-	Carrots	0.132	7	Boiled egg	0.348	3	Brie, Blue, bread cheeses	1.001	4	Butter	I	S
Beetroot	0.082	1	Cherry	0.243	7	Camembert	0.495	33	Cake	1.850	4	Candy or sweets	5.216	5
Broccoli	0.077	1	Chicken fillet	0.148	7	Cereals (corn flacks)	0.470	3	Cauliflower	0.596	4	Chocolate (dark)	4.171	5
Brussels sprout	0.030	-	Chilli	0.171	0	Courgettes	0.289	33	Cheddar	1.068	4	Chocolate (Milk)	3.787	5
Celery	0.101	-	Corn	0.244	7	Cucumber	0.274	ю	Chocolate cookies	1.920	4	Chocolate (white)	4.543	5
Cooked mushrooms	0.103	-	Fat chicken	0.236	0	Dried plum	0.252	Э	Cookies	1.695	4	Chocolate croissant	2.911	5
Crabs	0.088	1	Fennel	0.131	7	Duck (without skin and fat)	0.350	б	Cracker	0.952	4	Chocolate eclairs	2.079	S
Egg white	0.006	1	Ketchup <sup>b</sup>	0.166	0	Fat fish	0.368	Э	Egg yolk	1.334	4	Croissant	2.860	5
Endive	0.014	-	Kidneys	0.192	7	Fig	0.267	3	Feta	1.501	4	Curry	2.985	5
Fresh and thin fish	0.058	-	Lamb	0.232	7	Fish oil (sardines, cods)	I	ю	Fontina	0.946	4	French fries and frying	2.836	5
Garlic	0.035	-	Lamb chops or shoul- der	0.201	7	Fish oil (herrings)	I	б	Goat cheese	1.061	4	Ice cream	3.364	S
Green beans	0.054	-	Leek	0.139	0	Fish sauce	0.428	б	Gouda	1.193	4	Macadamia nut	7.074	5
Green peas	0.095	1	Melon	0.189	0	Ginger	0.362	3	Ground meat	0.704	4	Mayonnaise	56.80	5
Green salad <sup>a</sup>	0.074	-	Oat	0.243	7	Grapefruit	0.392	3	Gruyere	0.992	4	Meat sauce (Bearnaise)	45.04	5
Honey	0.000	-	Onion <sup>a</sup>	0.129	7	Guava	0.376	3	Hard cheese, full-fat cheese	1.093	4	Meat sauce (Pepper)	3.839	S
Horse (meat)	0.076	-	Parsley	0.139	0	Lamb cutlets	0.462	3	Kiwi	0.540	4	Meat sauce (Roquefort)	3.060	5
Lentil	0.064	1	Pepper	0.186	7	Mandarin	0.478	3	Lychee	0.512	4	Milk (coco)	6.521	5
Low-fat cheese	0.003	1	Pork tenderloin	0.208	7	Milk (goat, semi- skimmed)	0.272	Э	Mango	0.536	4	Nut, cashew, hazelnut	3.585	S
Milk (Skimmed)	0.030	1	Rib steak	0.153	7	Milk (soja)	0.298	ю	Meat sauce (Mush- room)	1.116	4	Olive (black)	7.478	5
Mollusk	0.060	-	Ribs	0.246	7	Milk (Semi-skimmed)	0.363	ю	Milk (whole)	0.690	4	Oliver (green)	12.92	5
Pork roast	0.110	1	Rice (Brown)	0.188	0	Mint	0.302	Э	Mozzarella	1.025	4	Pasta sauce (carbonara)	2.071	5
Pumpkin	0.085	1	Rindless, fatless,	0.131	0	Nectarine	0.292	3	Munster	1.223	4	Pasta sauce (pesto)	8.331	5
Red cabbage	0.046	1	Cooked ham	0.131	0	Olive oil	I	Э	Mustard	1.839	4	Pesto	8.331	5
Rice (Red)	0.121	1	Rye bread	0.166	0	Orange	0.381	3	Noodles	0.565	4	Potato chips	2.830	5
Rice (White)	0.089	1	Shallot <sup>a</sup>	0.201	7	Peach	0.361	3	Orange jam	0.623	4	Sauerkraut	5.696	5
Roast veal	0.090	-	Steak, fillet, striploin	0.208	0	Pear	0.364	3	Parmesan	0.836	4	Spicy <sup>d</sup>	0.000	5
Shrimps or lobster	0.033	-	Tofu	0.248	0	Pickle	0.270	3	Pasta sauce (bolognese)	1.134	4			
Spaghettis (cooked)	0.060	-	Turnip	0.186	7	Plum	0.471	3	Pâté	1.612	4			
Sweet potato	0.073	-	Veal chop	0.181	7	Pork chops and shoul- der	0.316	Э	Peanut	1.618	4			
Tuna (low-fat)	0.043	-	Watermelon	0.175	7	Potato	0.357	ю	Pomegranate	0.725	4			

Table 1 (continued)													
Very low reflux. foods REDS Cat Low reflux. foods	REDS C	Cat L	low reflux. foods	REDS	Cat	REDS Cat Moderate reflux. foods REDS Cat High reflux. foods	REDS	Cat	High reflux. foods	REDS	Cat Very hig	REDS Cat Very high reflux. foods REDS Cat	EDS Cat
Turkey fillet	0.026 1	1	0.026 1 White bread	0.187 1		Raspberry	0.307 3	3	Raisin	0.758	4		
Veal cutlet	0.059 1		Whole ham	0.236 2		Rhubarb	0.362	ю	Raspberry jam	0.566	4		
Wheat	0.079 1	1				Salmon	0.375	б	Redcurrant	0.922	4		
						Sardines	0.290	б	Ricotta	1.030	4		
						Strawberry	0.340	ю	Roquefort	1.288	4		
						Sugar <sup>c</sup>	0.000	б	Salami	1.177	4		
						Tomato (raw)	0.297	ю	Sausages	0.722	4		
						Tripes	0.255	ю	Sorbet	1.942	4		
						Wholemeal/brown bread	0.264	ŝ	Strawberry jam	0.618	4		
									Tomato sauce	1.538	4		
									Vinaigrette	T	4		
									Yoghurt and Ice cream	0.674	4		

Several foods may be upgraded or downgraded regarding to characteristics

<sup>a</sup>Raw vegetables are less digestible and may be associated with low gastric emptying time: in case of raw consumption, the food has to be upgraded for 1 category. Not for green salad, the addition of vinegar or vinaigrette upgrades the category

<sup>b</sup>In case of addition of spicy (for example, spicy ketchup), these foods have to be upgraded

 $^{\circ}$ For sugar, only the pH and the glycemic index have been considered regarding the lack of fat

<sup>d</sup>Because spices have no lipid and no pH, the authors based the classification of this food on the literature. If the patients only eat industrial foods (ready-made food), the foods may be upgraded regarding the acidifying potential of industrial conservative

Table 2 Categories of Refluxogenic potential of beverages

Juice, water and alcohols	pН	GI>40	Cat	UCat
Alcohol (strong and licor) <sup>ac</sup>	4	+	3	5
Aloe vera	6.1	0	2	2
Apple juice	3.65	+	4	5
Beer <sup>b</sup> (°)	4	+	3	5
Cacao (hot chocolate)	6.3	+	2	3
Chamomile	6.5	0	2	2
Chicory	5.95	0	3	3
Coffee <sup>d</sup>	5	0	3	4
Grapefruit juice	3.05	+	4	5
Lemon juice	2.3	+	4	5
Multi-fruit juice	3.8	+	4	5
Orange juice	3.5	+	4	5
Soda (sugar-free) <sup>b</sup>	2.5	0	4	5
Soda (with sugar) <sup>b</sup>	2.5	+	4	5
Syrup (Mint, lemon, grenadine)	2.15	+	4	5
Tea <sup>d</sup>	5	0	3	4
Tea (blackberry) <sup>d</sup>	2.5	0	4	5
Tea (black) <sup>d</sup>	5.3	0	3	4
Tea (green) <sup>d</sup>	7	0	2	3
Tea (lemon) <sup>d</sup>	2.9	0	4	5
Tomato juice	4.35	0	3	3
Water (sparkling) <sup>b</sup>	7	0	2	3
Water (still)	7	0	2	2
Water (alkaline)	8	0	1	1
Wine (red) <sup>c</sup>	4	0	4	5
Wine (rose) <sup>c</sup>	4	0	4	5
Wine (white) <sup>c</sup>	4	0	4	5

For hot chocolate, the category is upgraded in case of additional sugar

*GI* glycemic index, *cat.* category at baseline, *ucat.* upgraded category The classification of beverages depends on pH <sup>a</sup>glycemic index (GI; high sugar-related osmolarity), <sup>b</sup>sparkling (upgrade), <sup>c</sup>the alcohol degree (>3%=upgrade), and the <sup>d</sup>presence or lack of caffeine or theine (<sup>d</sup>upgrade or downgrade)

foods, spicy, high-fiber raw vegetables, and acidic, sparkling or alcoholic beverages. Many pathophysiological explanations may explain our results.

First, the digestion of fat or fried foods is longer than the digestion of low-fat foods. The increased emptying gastric time is associated with a high number of transient relaxations of LES, related increase of the esophageal acid exposure [21–23] and should be associated with UES relaxations regarding our results. Thus, there would be a positive association between the consumption of fat foods and development of esophagitis [24, 25]. Second, the LES pressure may also be decreased by high-osmolality beverages, coffee (caffeine), and some teas [26]; the latter being associated with an increase of erosive esophagitis [27]. Similar findings were partly reported for alcoholic beverages, including wine, beer, and liquor [27–31]. Alcoholic beverages would be associated

 Table 3 Characteristics of patients

Characteristics		
Age	$N/m \pm SD$	Range
Mean $\pm$ standard deviation (SD)	$49.6 \pm 17.0$	18–90
Gender		
Male	35	41.2%
Female	50	58.8%
Gastrointestinal endoscopy ( $N=63$ )	Ν	Prevalence
Normal	9	14.4%
Esophagitis (LA grading system)	27	42.9%
Los Angeles Grade A	24	38.1%
Los Angeles Grade B	2	3.2%
Los Angeles Grade C	1	1.6%
Los Angeles Grade D	1	1.6%
Hiatal hernia	21	33.3%
LES insufficiency	37	58.7%
Gastritis	27	42.9%
Duodenitis	3	4.8%
Helicobacter pilori infection	4	6.3%
MII-pH ( $m \pm SD$ )		
Proximal reflux episodes	$34.1 \pm 24.2$	
Upright reflux episodes	$27.0 \pm 21.2$	
Recumbent reflux episodes	$6.2 \pm 9.8$	
DeMeester Score	$23.8 \pm 41.6$	
GRES (pretreatment posttreatment)	$101.4 \pm 23.8$	$54.6 \pm 23.2$

*GRES* global refluxogenic score, *LA* Los Angeles, *LES* lower esophageal sphincter, *MII-pH* multichannel intraluminal impedance-pH monitoring, *SD* standard deviation

with a decrease of the gastric pH (through gastrin stimulation) and a reduction of the perception of the esophageal acid reflux events [25, 32]. A moderate consumption of alcohol is even associated with a decrease of esophageal pH in asymptomatic individuals, regarding pH measurements [33-36]. A third class of foods reporting increased risk of reflux is the raw high-fiber vegetables and acidic fruits. The raw high-fiber vegetables are little digestible, which is associated with an increased gastric emptying time, whereas the fiber concentration is partly reduced once the vegetables are cooked [37]. Another factor is the acid content of some fruits and vegetables. In that respect, the tomato-derived products are high-refluxogenic foods, because they contain two prominent organic acids (citric and malic acids), which are the most potent triggers of acid reflux in prone individuals and higher tomato consumers [30, 38, 39]. Other mechanisms of the refluxogenic potential of fruits and vegetables are still unknown according to studies exhibiting that some fruits are associated with the increase of heartburn [40, 41] and GERD [42], irrespective of the fiber concentration or the pH [43]. Finally, as found in some studies [44–46], chilli and spicy foods are important factors negatively impacting the

Table 4         Evolution of Reflux
symptom score throughout
treatment

Reflux symptom score	<b>Pre-treatment</b>	Post-treatment	P value
Ear, nose, and throat symptoms			
1. Voice disorder	$5.32 \pm 6.91$	$2.89 \pm 5.22$	0.002
2. Throat pain	$6.24 \pm 7.67$	$2.61 \pm 4.72$	0.001
3. Pain during swallowing time	$3.27 \pm 5.37$	1.61 ± 3.99	0.011
4. Dysphagia	$4.08 \pm 6.49$	$1.33 \pm 2.98$	0.001
5. Throat clearing	$11.92 \pm 9.66$	$7.74 \pm 8.74$	0.001
6. Globus sensation	$10.56 \pm 9.58$	$8.37 \pm 10.07$	0.069
7. Excess throat mucus	$13.42 \pm 10.16$	$7.79 \pm 9.08$	0.001
8. Ear pressure/pain	$4.35 \pm 6.70$	$2.21 \pm 4.65$	0.001
9. Tongue burning	$2.68 \pm 6.07$	$1.64 \pm 4.82$	0.344
Ear, nose, and throat total score	$61.41 \pm 39.13$	$35.79 \pm 31.29$	0.001
Digestive symptoms			
1. Heartburn	$8.73 \pm 8.84$	$3.46 \pm 5.97$	0.001
2. Regurgitations or burps	$5.77 \pm 7.52$	$1.76 \pm 3.86$	0.001
3. Abdominal pain	$4.36 \pm 6.92$	$2.71 \pm 5.70$	0.144
4. Diarrheas	$2.74 \pm 75.75$	$0.99 \pm 3.59$	0.007
5. Constipation	$3.68 \pm 7.20$	$2.43 \pm 5.39$	0.108
6. Indigestion	$2.12 \pm 5.21$	$0.83 \pm 2.65$	0.068
7. Abdominal distension/flatus	$6.52 \pm 8.24$	$4.44 \pm 6.97$	0.004
8. Halitosis	$7.12 \pm 9.47$	$4.16 \pm 7.29$	0.033
9. Nausea	$2.81 \pm 5.87$	$1.53 \pm 4.84$	0.017
Digestive total score	$43.38 \pm 33.92$	$22.07 \pm 25.93$	0.001
Respiratory symptoms			
1. Cough after eating/lying down	$6.45 \pm 8.38$	$3.33 \pm 6.29$	0.001
2. Cough	$6.23 \pm 8.06$	$3.50 \pm 7.03$	0.003
3. Breathing difficulties	$3.18 \pm 6.49$	$2.21 \pm 5.18$	0.242
4. Chest pain	$4.89 \pm 7.60$	$3.04 \pm 5.88$	0.071
Respiratory total score	$20.51 \pm 20.54$	$11.92 \pm 17.62$	0.152
RSS - score total	$125.18 \pm 74.22$	$69.77 \pm 58.63$	0.001
Quality of life score	$33.71 \pm 19.01$	$21.32 \pm 13.49$	0.001
Ear, nose, and throat QoL	$15.35 \pm 9.20$	$10.10 \pm 6.66$	0.001
Digestive QoL	$12.59 \pm 8.98$	$7.39 \pm 6.39$	0.001
Respiratory QoL	$5.76 \pm 4.98$	$3.86 \pm 4.49$	0.001

QoL quality of life, RSS reflux symptom score

esophageal sphincter pressure, even if they do not change the esophageal motility [47–49].

However, these explanations could be balanced by some studies, which did not find significant impact of fat foods [50, 51], coffee (caffeine) or tea [52, 53], and alcohol [54–56] on LES tonicity, esophageal motility, or GERD development. In fact, the majority of these researches studied very specific food/beverage components and did not consider the global diet of patients. The focus on one specific food/beverage component may easily lead to controversial results, because there are many inter-individual factors involving in the digestive response to a food/beverage component. The inter-individual variability includes the component metabolism; the various trigger threshold of symptoms (mucosa perception); heredity; and many unknown environmental

factors [11]. Thus, it has been demonstrated that the sensitivity of esophageal mucosa to acidic foods varies from one patient to another and would depend on the composition of food [25]. In that respect, the reduction of the perception of esophageal acid reflux events could be an important factor, leading to heterogeneity in the studies investigating the impact of a component of food/beverage in a cohort of patients considered as homogeneous. The metabolism of some refluxogenic molecules would be different from one patient to another [57, 58], leading to similar biases. For these reasons, the assessment of the global refluxogenic score of the patient needs to remain global, considering all refluxogenic diet factors.

Additionally to the composition, the pH of foods and beverages would be an important etiological factor of LPR with

Table 5	Evolution	of reflux	sign	assessment	throughout	treatment

Reflux sign assessment	Pretreatment	Posttreatment	P value
Oral cavity findings			
1. Anterior pillar erythema	$3.23 \pm 1.50$	$2.97 \pm 1.68$	0.192
2. Uvula erythema $\pm$ edema	$1.52 \pm 1.41$	$1.38 \pm 1.34$	0.505
3. Coated tongue	$1.23 \pm 0.84$	$1.37 \pm 0.83$	0.117
Oral cavity subscore	$5.88 \pm 2.55$	$4.85 \pm 2.52$	0.004
Pharyngeal findings			
1. Nasopharyngeal wall erythema ± inflammatory granulations	$0.67 \pm 0.90$	$0.24 \pm 0.58$	0.047
2. Posterior oro- or hypopharyngeal wall erythema	$2.46 \pm 1.71$	$1.47 \pm 1.68$	0.003
3. Posterior oro- or hypopharyngeal wall inflammatory granulations	$1.03 \pm 1.31$	$0.73 \pm 1.10$	0.038
4. Tongue tonsil hypertrophy	$2.48 \pm 1.27$	$2.10 \pm 1.23$	0.140
5. Contact between epiglotitis and tongue tonsils	$2.93 \pm 1.66$	$2.52 \pm 1.80$	0.359
6. Pharyngeal sticky mucus	$2.27 \pm 1.75$	$1.78 \pm 1.78$	0.117
Pharyngeal cavity subscore	$10.90 \pm 4.18$	$7.08 \pm 3.70$	0.001
Laryngeal findings			
Sub- and supraglottic areas			
1. Subglottic edema $\pm$ erythema	$0.03 \pm 0.17$	$0.03 \pm 0.18$	0.180
2. Ventricular band erythema $\pm$ edema	$1.37 \pm 0.79$	$1.03 \pm 0.89$	0.055
3. Epiglottis redness $\pm$ edema	$1.19 \pm 1.33$	$0.60 \pm 1.00$	0.001
Posterior commissure			
1. Commissure posterior/arytenoid erythema	$3.34 \pm 1.63$	$2.00 \pm 1.98$	0.001
2. Inter-arytenoid granulatory tissue	$0.44 \pm 0.77$	$0.12 \pm 0.44$	0.022
3. Posterior commissure hypertrophy	$3.50 \pm 1.94$	$2.21 \pm 2.12$	0.001
4. Retro-cricoid erythema	$0.96 \pm 1.36$	$1.39 \pm 1.76$	0.008
5. Retro-cricoid edema	$1.89 \pm 1.81$	$0.54 \pm 1.01$	0.090
Vocal folds			
1. Endolaryngeal sticky mucus deposit	$1.36 \pm 1.25$	$1.08 \pm 1.24$	0.129
2. Vocal fold erythema	$0.07 \pm 0.22$	$0.03 \pm 0.14$	0.033
3. Edema of the free-edge or the entire vocal folds	$0.07 \pm 0.16$	$0.08 \pm 0.16$	0.782
4. Vocal fold lesions	$0.06 \pm 0.33$	$0.03 \pm 0.25$	0.180
Laryngeal subscore	$13.05 \pm 6.30$	$7.95 \pm 5.27$	0.001
RSA total	$27.57 \pm 9.14$	$19.91 \pm 7.43$	0.001

RSA reflux sign assessment

regard to studies reporting a significant clinical impact of alkaline water [2–4]. As expected, at most the food is acidic, at most the gastric content is acid, and the related gaseous droplets of reflux episodes that contain pepsin. Together, all high refluxogenic foods and beverages (the majority being classified in the category 5 regarding REDS) lead to a higher score of GRES and an obvious higher number of proximal reflux episodes. Because the MII-pH proximal sensors are placed in the hypopharynx, we may suspect that the consumption of the refluxogenic foods and beverages leads to UES relaxations.

The literature investigating the impact of diet in the development of UES abnormalities and the related-LPR symptoms remain lacking; limiting the comparison of our results with the literature. In fact, the lack of study assessing the impact of foods and beverages on LPR through MII-pH is related to two main points: the low use of MIIpH by otolaryngologists and the lack of development of score(s) that objectively rate(s) the refluxogenic potential of diet.

However, LPR is characterized by different mechanisms from GERD, i.e. daytime and upright gaseous reflux episodes (LPR) *versus* recumbent and liquid episodes (GERD), and the low prevalence of obese patients in LPR cohorts; involving different mechanisms of action of refluxogenic components of diet. These potential differences between GERD and LPR need to be explored in future studies, which should include a control group. The lack of control group is the main weakness of the present study, but it is difficult to realize MII-pH, especially in healthy individuals, regarding the cost of the technique and the inconveniences associated with the probe and device.

### Conclusion

The diet of the LPR patients has a significant impact on the occurrence of proximal reflux episodes, which define the LPR diagnosis. The consumption of acid, high-fat and low-protein foods and acid, high-sugar or alcoholic beverages may also lead to higher risk of esophagitis, but this trend needs to be confirmed in larger cohorts. Future controlled studies are needed to better understand the pathophysiological mechanisms underlying the impact of diet in the development of LPR. These studies should consider the use of diet scores, MII-pH, and esophageal manometry to provide objective information for the study of the relationship between LPR and diet. Meanwhile, the food and beverage tables related to the Refluxogenic Diet Score and the Global Refluxogenic Score may be used for the management of LPR.

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#### **Compliance with ethical standards**

Conflict of interest The authors have no conflicts of interest.

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