

REVIEW

Body weight, lifestyle, dietary habits and gastroesophageal reflux disease

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Abstract

While lifestyle modifications are currently used as first-line treatment for subjects with gastroesophageal reflux disease (GERD), the pathogenetic role of lifestyle factors and consequently, the efficacy of lifestyle measures is controversial. Our aim was to systematically review the pathogenetic link between overweight/obesity, dietary habits, physical activity and GERD, and the beneficial effect of specific recommended changes, by means of the available literature from the 1999 to the present. Obesity, in particular, abdominal obesity, plays a key role in determining GERD symptoms and complications through mechanical and metabolic effects. Controlled weight loss (by diet or surgery) is effective in improving GERD symptoms. No definitive data exist regarding the role of diet and, in particular, of specific foods or drinks, in influencing GERD clinical manifestations. Moderate physical activity seems to be beneficial for GERD, while vigorous activity may be dangerous in predisposed individuals. In conclusion, being obese/overweight and GERD-specific symptoms and endoscopic features are related, and weight loss significantly improves GERD clinical-endoscopic manifestations. The role of dietary behavior, mainly in terms of specific dietary components, remains controversial. Mild routine physical activity in association with diet modifications, i.e. a diet rich in fiber and low in fat, is advisable in preventing reflux symptoms.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is defined as an abnormal reflux of the gastric contents into the esophagus at least once a week, leading to symptoms, such as heartburn and/or acid regurgitation, and/or esophageal mucosal damage, which may also provoke long-term complications, such as Barrett's esophagus^[1,2]. GERD represents a common disorder, particularly in the Western world (about 10%-20% in Western countries and under 5% in Asia) and its prevalence appears to be increasing^[3,4]. The incidence rate, reported by two longitudinal studies^[5,6], was 4.5 and 5.4/1000 people per year, respectively.

GERD is a multifactorial disease in which anatomical and functional factors both play a pathogenetic role. The main pathogenetic mechanism of GERD is considered to be transient lower esophageal sphincter relaxation (TLESR)^[7] which may account for the majority of reflux episodes, in patients with esophagitis and in those with non-erosive reflux disease (NERD). An increased number of TLESR episodes, combined or not with an impaired LES basal tone or with gastric or esophageal motor dysfunction, may lead to GERD, but the underlying causes of these functional disorders are still partially unknown^[2].

However, the role of genetic factors was suggested by twin studies^[8,9] wherein heritability accounted for 31%-43% of the likelihood of reflux disease, which suggests that genetic and environmental factors both

play an important role. Among the environmental factors, lifestyle factors, in particular being overweight/obese, incorrect dietary habits, the lack of regular physical activity and smoking have frequently been suggested to be possible GERD risk factors. However, the exact pathogenetic role of these factors is still under debate and the beneficial effect of specific recommended changes in lifestyle habits is also controversial^[10].

A comprehensive search of the literature (Medline/PubMed databases 1999-June 2008, using the following keywords singly and in different combinations: GERD, food intake, food questionnaire, energy intake, motor activity, exercise, obesity, abdominal obesity) was carried out and the evidence available was critically reviewed.

RELATIONSHIP BETWEEN OVERWEIGHT/OBESITY AND GERD

The observation of a consensual increase in the frequency of obesity and GERD^[7,11,12] in Western countries has suggested a possible pathogenetic link between these two diseases, and it has generated great interest in elucidating the mechanisms demonstrating this association. However, although the relationship between GERD and obesity has been the subject of several studies, conflicting results have been obtained.

In a meta-analysis of epidemiological studies regarding the association between obesity and GERD-related disorders, it was found^[13] that being overweight (BMI, 25-30 kg/m²) and being obese (BMI, > 30 kg/m²) were associated with GERD symptoms (OR, 1.43; 95% CI, 1.158-1.774 and OR, 1.94; 95% CI, 1.468-2.566, respectively), erosive esophagitis (OR, 1.76; 95% CI, 1.156-2.677 in overweight subjects) and esophageal adenocarcinoma (OR, 1.52; 95% CI, 1.147-2.009 and OR, 2.78; 95% CI, 1.850-4.164, respectively). A cross-sectional study on 206 consecutive patients not on acid-suppressing medications who underwent 24-h pH measurement showed^[3] a significant ($P < 0.005$) association between a BMI > 30, a high waist circumference and acid reflux episodes. An additional meta-analysis of clinical studies on the relationship between obesity and reflux symptoms, esophagitis or GERD-related hospitalization documented a positive association between BMI (OR, 1.57; 95% CI, 1.36-1.80 in overweight and OR, 2.15; 95% CI, 1.89-2.45 in obese subjects) and GERD in studies carried out in the USA, but the results were heterogeneous in those carried out in Europe^[14].

Different explanations have been proposed in order to interpret these geographical differences. In fact, the relationship between BMI and the percentage of body fat differs between ethnic groups^[15].

Since there are probably multiple pathogenetic mechanisms of GERD (TLESR, esophageal and gastric motor function, and gastric secretion), it is possible that not all of them are related to, or influenced by, the presence of obesity^[16]. Furthermore, different definitions of GERD (endoscopic, symptom reports by self-administered or validated questionnaires) have

been utilized in the different studies, as well as different measures of obesity (BMI, central adiposity).

RELATIONSHIP BETWEEN BEING OVERWEIGHT/OBESITY AND GERD: SUGGESTED PATHOGENETIC MECHANISMS

The exact pathophysiological mechanisms that demonstrate the association/relationship between being overweight/obese and GERD have not been fully identified, but some hypotheses have been suggested.

It has long been hypothesized^[17-20] that visceral adiposity, expressed by an increased abdominal waist circumference, could be associated with increased intra-abdominal pressure which would, in turn, promote GERD by increasing intragastric pressure (IGP).

Using high-resolution manometry, it was found^[17] that IGP as well as the gastroesophageal pressure gradient (GEPG), during expiration and inspiration, was significantly higher ($P < 0.0001$) in obese and overweight patients, as compared to those with a normal BMI. This showed an IGP increase of 0.3 mmHg per unit of increase in BMI and the association was stronger in men than in women. Similar results were obtained in a recent retrospective analysis^[18] in patients with typical GERD symptoms who underwent pH-monitoring and esophageal manometry. By means of multiple regression analysis, an increase of BMI was independently associated with IGP and with an increase of GEPG during inspiration; furthermore, BMI, IGP and GEPG were strong independent predictors of hiatal hernia, and IGP and GEPG were not independently associated with abnormal acid exposure or esophagitis.

A further pathogenetic mechanism has been suggested by Pandolfino *et al*^[17] who observed that obesity was associated with a separation between LES and the extrinsic crural diaphragm, a disruption which could predispose obese subjects to hiatal hernia. It is known that hiatal hernia is commonly associated with symptomatic GERD, and patients with abnormal esophageal acid exposure have a significantly higher prevalence of hiatal hernia^[21,22]. Furthermore, in patients with hiatal hernia, esophagitis or abdominal low distal esophageal pH are more common than in those without hiatal hernia^[23]. In a retrospective case-control study on 1389 patients, obesity was found to represent an independent risk factor for hiatal hernia^[24]. Therefore, it is possible that obesity, through alteration of normal IGP and separation between LES and the extrinsic crural diaphragm, predisposes to hiatal hernia and consequently, to GERD.

Another plausible mechanism for the association between obesity and GERD is represented by slower esophageal acid clearance, as shown by Quiroga *et al*^[25] in a case-control study using esophageal manometry in normal weight and obese patients with GERD and in healthy subjects. All subjects with GERD showed altered

Table 1 Association between being overweight/obese and GERD-related symptoms

Author	Year	Country	Study design	Population size	Obesity index	Method of data collection	Association
Nilsson <i>et al</i> ^[42]	2003	Norway	Population-based	65 363	BMI	Questionnaire	Yes
Nandurkar <i>et al</i> ^[41]	2004	USA	Population-based	211	BMI	Validated questionnaire	Yes
Hampel <i>et al</i> ^[13]	2005	USA	Meta-analysis		BMI	Validated symptoms score	Yes
Corley <i>et al</i> ^[14]	2006	USA	Meta-analysis		BMI	Questionnaire	Yes
Jacobson <i>et al</i> ^[38]	2006	USA	Cross-sectional, women	10 545	BMI	Questionnaire	Yes
Nocon <i>et al</i> ^[39]	2006	Germany	Population-based	7 124	BMI	Interview	Yes
Corley <i>et al</i> ^[37]	2007	USA	Cross-sectional	80 110	BMI and abdominal diameter	Questionnaire	Yes
Nocon <i>et al</i> ^[40]	2007	Germany	Population-based	6 215	BMI	Validated questionnaire	Yes
Zheng <i>et al</i> ^[43]	2007	Sweden	Swedish twin registry	27 717	BMI	Questionnaire, telephone interview	Yes
Andersen <i>et al</i> ^[44]	1991	Denmark	Population-based	1 321	BMI	Validated questionnaire	No
Lagergren <i>et al</i> ^[46]	2000	Sweden	Cross-sectional	820	BMI	Interview	No
Talley <i>et al</i> ^[45]	2004	Australia	Cross-sectional	777	BMI	Questionnaire	No
Zagari <i>et al</i> ^[47]	2008	Italy	Population-based	10 330	BMI	Questionnaire	No

esophageal motility and obese patients also had impaired esophageal acid clearance.

In obese patients, other esophageal motor abnormalities, such as hypotensive LES pressure, nutcracker esophagus and non-specific motility disorders^[26-29] have been observed.

However, the most important reflux mechanism in obese subjects seems to be TLESR^[7]. The main stimulus for generating TLESR episodes is gastric distension, which leads to intense stimulation of both stretch and tension mechanoreceptors in the proximal stomach^[30,31]. In fact, in a recent study^[32], three groups of subjects without GERD (28 obese, 28 overweight and 28 normal) underwent BMI measurements, upper endoscopy, manometry and pH recordings for both the fasting and the postprandial period and were given a symptom questionnaire. During the 2-h postprandial period, both overweight and obese individuals showed a significantly ($P < 0.001$) higher rate of TLESR episodes, and a higher proportion of TLESR episodes accompanied by acid reflux and total acid exposure than normal weight subjects. A direct correlation between increasing BMI, an increased number of TLESR episodes, and an increased number of TLESR episodes associated with acid reflux was identified. Therefore, it seems that obese subjects have a higher postprandial IGP, which provokes more postprandial TLESR episodes.

Another mechanism by which obesity can cause GERD is related to the visceral component of abdominal obesity. In fact, visceral fat is metabolically active^[33] and it has been associated with low serum levels of protective cytokines, such as adiponectin, and high levels of inflammatory cytokines, such as tumor necrosis factor (TNF)- α , interleukin (IL)-1 β and IL-6. An increase in these inflammatory cytokines in patients with erosive esophagitis and Barrett's esophagus has also been observed^[34].

In conclusion, although conflicting and non-definitive results exist, it is likely that GERD and obesity are in some way linked; in particular, abdominal obesity seems to play a key role in determining GERD symptoms and complications through mechanical and metabolic effects. Consistent with this evidence, it is

possible to hypothesize that GERD may be a curable condition through the control of body weight and, in particular, by reducing abdominal obesity.

OBESITY AND GERD-RELATED SYMPTOMS

Different studies have analyzed the possible relationship between obesity and GERD by evaluating the clinical manifestation of the disease since reflux symptoms (mainly, heartburn and acid regurgitation) represent the main target for diagnostic evaluation and treatment in GERD patients. However, the factors responsible for the generation of symptoms, in normal or overweight subjects, have not been clearly identified.

Sensitization of esophageal chemoreceptors, either directly by intermittent exposure to refluxed acid or indirectly through esophagitis-associated inflammatory mediators, is thought to be one of the most important mechanisms responsible for symptom generation in GERD^[35,36].

Several authors have evaluated the relationship between obesity and the symptoms of GERD, both to confirm the association between obesity and GERD and to find potential risk factors for symptom generation (Table 1). In all the studies available, only typical GERD symptoms (i.e. heartburn and regurgitation) have been taken into account, with the use of interviews or structured questionnaires.

In a large cross-sectional study^[37] on abdominal obesity, GERD symptoms and ethnicity performed on 80 110 members of a health organization, it was found that increased abdominal diameter, adjusted for BMI, was an independent risk factor for reflux symptoms (OR, 1.85; 95% CI, 1.55-2.21) in the white population but not among blacks and Asians, and this aspect was not influenced by gender.

A recent large cohort study in 10 545 women reported a significant ($P < 0.001$) dose-dependent relationship between increasing BMI and frequent reflux symptoms; this relationship was present even in the normal range of BMI^[38].

Table 2 Association between overweight/obesity and reflux esophagitis

Author	Year	Country	Study design	Population size	Obesity index	Method of data collection	Association
Ruhl <i>et al</i> ^[49]	1999	USA	Cohort	12349	BMI	Upper endoscopy	Yes
Hampel <i>et al</i> ^[13]	2005	USA	Meta-analysis		BMI	Upper endoscopy	Yes
Nocon <i>et al</i> ^[40]	2007	Germany	Population-based	6215	BMI	Upper endoscopy	Yes
Kim <i>et al</i> ^[48]	2007	South Korea	Population-based	27319	BMI	Upper endoscopy	Yes
Kang <i>et al</i> ^[51]	2007	South Korea	Population-based	2457	BMI, waist circumference	Upper endoscopy	Yes
Lee <i>et al</i> ^[50]	2008	South Korea	Population-based	3363	BMI, waist-to-hip ratio	Upper endoscopy	Yes
Chung <i>et al</i> ^[52]	2008	South Korea	Cross-sectional	7078	BMI, waist circumference, visceral adipose tissue	Upper endoscopy	Yes
Furukawa <i>et al</i> ^[58]	1999	Japan	Cross-sectional	6010	BMI	Upper endoscopy	No
Baldi <i>et al</i> ^[59]	2008	Italy	Cohort	1542	BMI	Upper endoscopy	No
Zagari <i>et al</i> ^[47]	2008	Italy	Population-based	1033	BMI	Upper endoscopy	No

Two large population studies^[39,40] and a case-control study^[41] have found a positive association between BMI and reflux symptoms. The same results were previously obtained in a large population-based study carried out in Norway^[42]; the authors found a stronger association among women, especially premenopausally, and that the use of hormone therapy strengthened the association, which suggested that estrogens may play an important role in the etiology of reflux disease. Another recent study^[43] performed in Sweden on a large number of twins, confirmed that BMI seems to be a risk factor for GERD symptoms in monozygotic twins.

However, the association between obesity and GERD symptoms was not confirmed in subjects with benign esophageal disease^[44]. Furthermore, a cohort study from New Zealand found no association between BMI and reflux symptoms^[45] but, as its authors noted, the cohort consisted of young adults, and GERD symptoms do not usually appear until middle age. The same results were produced by a nationwide case-control study in Sweden^[46] and by a recent population-based epidemiological study in Italy^[47].

No data are available yet about the possible correlation between obesity and atypical GERD symptoms.

In conclusion, although further studies are probably needed, most of the available evidence suggests a relationship between obesity, mainly abdominal obesity, and GERD-related typical symptoms.

OBESITY AND REFLUX ESOPHAGITIS

Endoscopic investigation, alone or combined with information regarding specific symptoms obtained by means of structured questionnaires, has been carried out in order to evaluate the possible correlation between GERD-related disorders, such as esophagitis, and obesity (Table 2).

The above mentioned meta-analysis by Hampel *et al*^[13] has documented the association between a BMI ≥ 25 kg/m² and erosive esophagitis. This association was confirmed by Nocon *et al*^[40] using a symptomatic questionnaire and upper endoscopy in 6215 patients and by Kim *et al*^[48] who observed, in 27319 subjects, an association between an increasing BMI and abnormal endoscopic findings, such as erosive gastritis, gastric

ulcer, duodenal ulcer (OR, 1.31; 95% CI, 1.22-1.40; $P < 0.0001$ for overweight subjects; OR, 1.40; 95% CI, 1.14-1.72; $P < 0.001$ for obese patients) and reflux esophagitis (OR, 1.61; 95% CI, 1.42-1.83; $P < 0.001$ for overweight subjects, OR, 2.23; 95% CI, 1.59-3.11; $P < 0.001$ for obese patients). In a long-term follow-up study (median 18.5 years) on 12349 subjects^[49], increased hospitalization rates for esophagitis and hiatal hernia were documented in patients with a BMI > 25 kg/m². Other population-based studies^[50,51] have also confirmed the correlation between obesity, mainly abdominal obesity, and erosive esophagitis.

Furthermore, an association between the metabolic syndrome and reflux esophagitis has recently been documented^[52] in a cross-sectional case-control study on 7078 subjects. In particular, it was observed that, among the single components of the metabolic syndrome, abdominal obesity (in particular visceral fat) and elevated serum triglycerides represented independent risk factors for reflux esophagitis (OR, 1.60; 95% CI, 1.03-2.48). Furthermore, it has been demonstrated that only visceral adipose tissue, evaluated by cross-sectional computed tomography, was an independent risk factor for reflux esophagitis. This tissue, in fact, is recognized to be metabolically active and it has been associated with elevated serum levels of pro-inflammatory adipokines (IL-6, TNF- α and adiponectin), compounds which may play a role in GERD development^[53,54]. It seems that visceral adipose tissue plays a key role in increasing lipolysis and free fatty acid, leading to insulin resistance, which is considered the major pathophysiological factor for the development of the metabolic syndrome^[55-57]. It has been suggested that these substances might alter the LES pressure or affect the esophageal clearance of refluxate^[52].

However, the association between BMI and esophagitis has not been confirmed in a recent Japanese prospective study^[58], as well as in an epidemiological survey^[47] and a multicenter Italian observational study^[59]. The different percentages of body fat in different ethnic groups may represent a possible explanation for these different results^[15].

In conclusion, as occurs for specific GERD symptoms, most of the evidence available also suggests a positive correlation for the association between being

overweight/obese and GERD-related morphological lesions.

WEIGHT CHANGES AND GERD-RELATED SYMPTOMS

The observed relationship between weight gain and an increase in GERD-related symptoms^[60,61], as well as that between weight reduction and a decrease in GERD-related symptoms^[62-64], represents additional evidence of the close relationship between obesity and GERD. However, results from studies of weight loss for the control of GERD-related symptoms in obese subjects are not conclusive^[65].

In an uncontrolled study on selected patients with a BMI > 25 kg/m², Fraser-Moodie *et al*^[64] found that weight loss, induced by general dietary advice, had a beneficial effect on GERD symptoms, as evaluated by a structured questionnaire. Different results were obtained^[66,67] in obese patients with reflux disease who were on a very-low-calorie diet, in which no reduction in reflux symptoms or changes in reflux episodes measured by 24 h pH-monitoring were documented. However, these studies have presented important limitations since they included patients with hiatal hernia, which represents an irreversible condition that contributes to the occurrence of GERD despite the weight loss, and they were carried out on very small numbers of patients, 20 and 15, respectively.

The effect of weight loss induced by endoscopic or surgical procedures has been evaluated. A significant reduction in esophageal acid exposure was documented during weight loss induced by an intragastric balloon^[62,63] in a randomized, double-blind, sham-controlled study. An improvement in GERD symptoms was also found after weight loss induced by bariatric surgery^[68]. In particular, the Roux-en-Y gastric bypass seems to represent the surgical procedure that is most effective in improving GERD symptoms in obese subjects^[68-72]. Roux-en-Y gastric bypass may be successful at reducing GERD symptoms by diverting bile away from the esophagus^[68,73], eliminating acid production in the gastric pouch^[73], and reducing the volume of acid refluxate^[70]. This hypothesis is supported by the observation of rapid symptom improvement after the surgical procedure; long-term symptom improvement is likely to be the result of weight loss^[68].

Studies evaluating other types of bariatric surgery, such as laparoscopic gastric banding or vertical banded gastroplasty, have produced conflicting results^[26,74-78]. In particular, laparoscopic adjustable gastric banding has no, or minimal, effect on GERD-related symptoms but, over time, symptoms increase toward baseline or beyond. This effect is likely caused by slippage of the band distally, which results in more stomach above the band. Therefore, the impact of laparoscopic adjustable gastric banding on GERD is independent of weight loss; instead, it is the direct anatomical alteration of the band that impacts on GERD symptoms^[65].

However, these studies are still limited by small sample sizes, lack of randomization, failure to use control groups, use of retrospective data and inconsistent timing of postoperative re-evaluation. Furthermore, it has yet to be clarified whether the surgical technique itself, and/or weight loss, represents the mechanism of action for symptom improvement.

In obese subjects undergoing weight loss, the effect of changes in meal composition on reflux symptoms has also been investigated^[79,80], although in small studies. In a study on eight obese volunteers, a lower carbohydrate diet reduced reflux symptoms and reflux episodes, which was evaluated by means of 24-h pH monitoring^[79]. A higher frequency of reflux symptoms with a high-fat diet as compared to a low-fat diet has also been demonstrated^[80], using four different calorie/fat composition diets, in 15 patients with GERD. Furthermore, esophageal acid exposure was higher with the high-calorie diet as compared to the low-calorie diet.

Together, these data indicate an effective role for weight loss in improving GERD symptoms as well as the effect of differing meal compositions on reflux disease.

DIET AND GERD

It is a common belief that some foods may induce or worsen GERD symptoms; in fact, in daily clinical practice, this belief leads to advising patients to avoid the suspect foods^[81]. Furthermore, since GERD symptoms are most commonly reported postprandially, the role of diet components in inducing symptoms has been suggested. However, different and conflicting results exist in the literature for identifying the most "refluxogenic" foods (Table 3).

Old experimental and clinical studies have shown a decrease in LES pressure and an increase in esophageal acid exposure in response to the ingestion of food rich in fats, chocolate and carminatives^[82-85]. Nebel *et al*^[86] have demonstrated that fried foods, spicy foods and alcohol are the most common precipitating factors of heartburn; however, this study had no control group and did not quantify the intake of dietary items.

In order to elucidate the association of different nutrients with the risk for GERD, El-Serag *et al*^[87] carried out a cross-sectional study on 915 employees, using a dietary questionnaire to estimate the average food consumption over the previous year, and a GERD questionnaire together with an upper endoscopy for assessing GERD severity. A positive association between high fat intake, and GERD symptoms and erosive esophagitis was observed, while a high-fiber diet seemed to reduce reflux symptoms. However, the effects of fat on GERD symptoms and erosive esophagitis were dependent on BMI since this is statistically significant only in overweight individuals. Furthermore, a higher daily intake of fats and proteins was observed in those participants with erosive esophagitis.

More recently, Shapiro *et al*^[88] observed in 58 subjects with typical heartburn symptoms that increased consumption of cholesterol, saturated fatty acids and an

Table 3 Dietary intake and GERD-related clinical manifestations

Author	Year	Country	Study design	Population size	Method of data collection	Effects
Fatty foods, chocolate, carminatives						
Nebel <i>et al</i> ^[84]	1972	USA	Case series	10	Infused open-tipped system	Lowered LESP
Becker <i>et al</i> ^[82]	1989	USA	Case-control	20	24-h pH-metry	Increased esophageal acid exposure
Nebel <i>et al</i> ^[86]	1976	USA	Population-based	1004	Symptom questionnaire	Worsened reflux symptoms
Iwakiri <i>et al</i> ^[89]	1996	Japan	Population-based	20	pH-monitoring	
Holloway <i>et al</i> ^[90]	1997	Australia	Case-control	23	Esophageal manometry and pH-monitoring	
Meyer <i>et al</i> ^[91]	2001	USA	Population-based	11	Esophageal perfusion with HCl and duodenal perfusion with fat and saline, symptoms interview and scales	
El-Serag <i>et al</i> ^[87]	2005	USA	Cross-sectional	371	Dietary and symptom questionnaire and upper endoscopy	
Shapiro <i>et al</i> ^[88]	2007	USA	Case series	50	GERD symptoms checklist, upper endoscopy, 24-h pH-metry, dietary intake records	
Ruhl ^[49]	1999	USA	Epidemiological	12349	Upper endoscopy, symptoms interview, total dietary servings of high fat foods	No association with GERD symptoms,
Phel ^[92]	1999	Germany	Case series	12	Esophageal manometry, pH-metry	reflux episodes
Colombo ^[93]	2002	Italy	Case series	13	pH-metry in three solid/liquid meals	or lower esophageal sphincter pressure
Nandurkar ^[41]	2004	USA	Population-based, nested case-control	211	GERD, energy expenditure, dietary intake questionnaires	
Zheng ^[43]	2007	Sweden	Swedish Twin Registry	27717	Questionnaire, telephone interview	
High caloric load						
Colombo ^[93]	2002	Italy	Case series	13	pH-metry in three solid/liquid meals	
Fox ^[80]	2007	UK	Case series	15	pH-monitoring in four dietary conditions	
Fruits, vegetable, high fiber intake						
El-Serag <i>et al</i> ^[87]	2005	USA	Cross-sectional	371	Dietary and symptom questionnaire and upper endoscopy	Improved symptoms
Zheng <i>et al</i> ^[43]	2007	Sweden	Monozygotic co-twin study based on Swedish Twin Registry	27717	Questionnaire, telephone interview	No association
Alcohol						
O'Leary <i>et al</i> ^[97]	2003	Ireland	Randomized, double-blind, placebo-controlled trial	56	Symptom questionnaires and drug-diet-alcohol records	Worsened reflux symptoms
Rosaida <i>et al</i> ^[98]	2004	Malaysia	Cross-sectional	1000	Upper endoscopy and symptom and risk factor questionnaire	
Wang <i>et al</i> ^[96]	2004	China	Epidemiological	2789	Symptom and risk factor questionnaire	
Mohammed <i>et al</i> ^[95]	2005	UK	Population-based	1533	Symptom and lifestyle questionnaire	
Talley <i>et al</i> ^[102]	1994	USA	Cross-sectional	1644	Symptom and lifestyle questionnaire	No association
Stanghellini <i>et al</i> ^[101]	1999	Multinational	Cross-sectional	5581	Symptom and lifestyle questionnaire	
Nilsson <i>et al</i> ^[99]	2004	Norway	Case-control	> 40000	Symptom and lifestyle questionnaire	
Zheng <i>et al</i> ^[43]	2007	Sweden	Swedish Twin Registry	27717	Questionnaire, telephone interview	
Shapiro <i>et al</i> ^[88]	2007	USA	Case series	50	GERD symptoms checklist, upper endoscopy, 24-h pH-metry, dietary intake records	Reduced perception of acid reflux
Coffee						
Price <i>et al</i> ^[103]	1978	USA	Population-based	66	Intraesophageal infusion of coffee, orange juice, spicy tomato drink and HCl	Worsened reflux symptoms
Stanghellini <i>et al</i> ^[101]	1999	Multinational	Cross-sectional	5581	Symptom and lifestyle questionnaire	No association
Boekema <i>et al</i> ^[104]	1999	Netherlands	Randomized controlled crossover study	15	24-h pH-monitoring and coffee and water drinking	
Wang <i>et al</i> ^[96]	2004	China	Epidemiological	2789	Symptoms and risk factor questionnaire	
Zheng <i>et al</i> ^[43]	2007	Sweden	Swedish Twin Registry	27717	Questionnaire, telephone interview	Protective factor

higher percentage of calories from fats was significantly associated with an increased likelihood of having reflux events. The role of fats in symptom generation has been confirmed by some^[89-91], but not by others^[41,49,92,93]. Ruhl *et al*^[49] failed to document an association between dietary fat intake and erosive esophagitis and reflux symptoms,

although higher reflux disease hospitalization rates were associated with an increased BMI. These results are consistent with those produced by Nandurkar *et al*^[41], who analyzed potential risk factors for reflux among 211 community subjects and concluded that only BMI, and not diet, may influence symptomatic GERD.

Also Pehl *et al*^[92] did not find differences in reflux parameters comparing a high-fat meal with a low-fat meal; similar results were obtained by Colombo *et al*^[93], although they found that a caloric load increased esophageal acid exposure.

Furthermore, none of the dietary items evaluated (i.e. vegetables, fruits, fish, meat, rice, milk, grilled and fried food), including alcohol, was associated with the risk of GERD symptoms in the above-mentioned monozygotic co-twin study based on the Swedish Twin Registry^[43], which investigated lifestyle factors that potentially cause GERD.

Considering the recommended advice of controlling alcohol drinking and reducing, or avoiding, coffee to prevent GERD symptoms^[81,94], several studies investigated the role of alcohol and coffee in GERD. While some authors have suggested that alcohol is an independent risk factor for GERD-related symptoms^[95-98], others have not found such a relationship^[99-102]. In their study about the lifestyle habits and GERD symptoms of the participants in two consecutive public health surveys in Norway (> 40000 people), Nilsson *et al*^[99] did not find that alcohol, coffee or tea were risk factors for reflux-related symptoms. Shapiro *et al*^[88] not only confirmed these results, but also documented that alcohol was associated with a reduced perception of intra-esophageal acid reflux events.

Despite the observation that the intraesophageal infusion of coffee in patients with acid sensitivity may induce heartburn^[103], two large epidemiological studies have found no association between coffee drinking and GERD^[96,101]. Boekema *et al*^[104] have found that coffee does not alter postprandial acid reflux time or the number of acid reflux episodes, and others^[41] have noted that coffee consumption is lower in subjects with reflux symptoms. However, the latter result might reflect avoidance of coffee by those who suffer from reflux because the beverage aggravates symptoms.

Furthermore, in their recent study of twins, Zheng *et al*^[43] have found that coffee intake might be a protective factor for GERD symptoms in men, but not in women. The authors have suggested that the differences observed might be caused by sex differences regarding caffeine metabolism. In fact, it has been demonstrated that the conversion of caffeine to paraxanthine, which accounts for 84% of the primary degradation of caffeine in humans^[105], is markedly inhibited by exogenous estrogen in women taking oral contraceptives^[106] or in postmenopausal women on hormone replacement therapy^[107]. Given the conflicting data reported, the relationship between coffee and GERD remains unclear; as a consequence, there is insufficient evidence to support the routine recommendation of avoiding such beverages for patients with GERD.

In conclusion, no definitive data exist regarding the role of diet and, in particular, of specific foods or drinks, in GERD clinical manifestations. Despite the insufficient evidence to support an association between dietary behavior and GERD, some dietary interventions continue to be recommended as first-line therapy^[81]. Larger prospective controlled trials are required to

conclusively recommend dietary modifications in the treatment of GERD.

SMOKING AND GERD

Population-based and epidemiological studies have suggested that tobacco smoking may represent a risk factor for GERD^[9,39,108-113]. Studies using specific questionnaires have reported that smoking is significantly associated with GERD-related symptoms (OR, 1.35; 95% CI, 1.01-1.82)^[114-116]. Furthermore, a recent monozygotic co-twin study^[43] has provided compelling evidence that tobacco smoking increases the risk for the occurrence of frequent GERD symptoms, and a case-control study^[99] on 3153 patients with severe GERD-related symptoms has shown that the duration of smoking was associated with increasing reflux symptoms (OR, 1.7; 95% CI, 1.5-1.9 in subjects who had smoked for > 20 years). Different mechanisms have been suggested to justify the association between smoking and GERD. Cigarette smoking can reduce the LES pressure^[117-119] and decrease salivary bicarbonate secretion, thus reducing the physiological neutralizing effect of saliva on intraesophageal acid and prolonging acid clearance^[120,121]. Furthermore, abrupt increases in intra-abdominal pressure, as occur during coughing or deep inspiration, have been associated with reflux symptoms in smokers^[122]. However, studies that have examined acid perfusion using the Bernstein test or esophageal pH^[123-125] have reported that smokers compared to non-smokers do not show an increased esophageal acid exposure time, despite having more "reflux episodes"^[126]. Furthermore, two old case-control studies evaluating, on very small samples, the effect of smoke cessation on GERD outcomes^[126,127] were unable to document an improvement in GERD symptoms after the cessation of tobacco use.

PHYSICAL ACTIVITY AND GERD

Since previous investigations have demonstrated that strenuous exercise may induce GERD^[128-130] and that GERD symptoms are common among athletes^[131], it has been suggested that physical activity represents another risk factor for GERD. However, available evidence indicates that a positive association between exercise and GERD is present in vigorous, but not in moderate, exercise^[41,132,133]. In fact, Clark *et al*^[134] have reported that running, cycling and weight lifting increase GERD in asymptomatic volunteers. Furthermore, these authors have found that specific types of exercise are more likely to induce reflux symptoms, with running and resistance exercises being more refluxogenic than cycling.

Similar results have been obtained by Peters^[135], in addition, this author has found increased reflux using high-carbohydrate sport drinks with respect to water, which demonstrates a possible role of sport drinks in facilitating reflux symptoms. Therefore, it seems that a hierarchy of exercises in inducing reflux symptoms exists^[134]. However, there is no general agreement with respect to the mechanism by which vigorous exercise

Table 4 Physical activity and GERD-related clinical manifestations

Author	Year	Country	Study design	Population size	Method of data collection	Association/Effect
Vigorous/agonistic exercise						
Clark <i>et al</i> ^[134]	1989	USA	Crossover	12 asymptomatic volunteers	pH-monitoring, 1 h exercise period (bicycling, running and weight routine)	Yes
Schoeman <i>et al</i> ^[132]	1995	Australia	Randomized controlled crossover	10 healthy subjects	Perfused sleeve sensor for 24 h during moderate physical activity, rest and sleep, standardized meals, and standardized exercise	Yes
Peters <i>et al</i> ^[135]	2000	Netherlands	Randomized controlled crossover	7 males triathletes	pH-monitoring, 50 min of running, cycling and supplementation of conventional sport drinks and tap water	Yes
Collings <i>et al</i> ^[128]	2003	USA	Case series	30 athletes	pH-monitoring, evaluation of clinical symptoms during standardized exercise	Yes
Pandolfino <i>et al</i> ^[129]	2004	USA	Case-control	20	pH-monitoring, 60 min of exercise (running and resistance exercise), upper endoscopy and manometry	Yes
Nandurkar <i>et al</i> ^[41]	2004	USA	Population-based, nested case-control	211	GERD, energy expenditure, dietary intake questionnaires	Yes
Ravi <i>et al</i> ^[130]	2005	Ireland	Randomized controlled crossover	135	Esophageal manometry and pH-monitoring before, during and immediately after moderate exercise	Yes
Physical activity at work/postprandial exercise						
Zheng <i>et al</i> ^[43]	2007	Sweden	Swedish Twin Registry	27717	Questionnaire, telephone interview	Yes
Emerenziani <i>et al</i> ^[140]	2005	Belgium-Germany	Clinical trial	37 GERD pz	pH-impedance-monitoring, upper endoscopy, scintigraphic gastric emptying	Yes

induces reflux. Exercise may alter esophageal motility and worsen symptoms of the upper gastrointestinal tract^[136]. Clark *et al*^[134] have speculated that “body agitation” may be important in inducing reflux. Soffer *et al*^[137] have focused on a decreased duration, amplitude and frequency of esophageal contractions with increasing exercise intensity. This suggestion has not been confirmed by Choi *et al*^[138] who reported increased frequency, but not duration or amplitude, of peristaltic contractions. Furthermore, Pandolfino *et al*^[129] have suggested that the anatomical compromise of the esophagogastric junction, as a consequence of frequent abdominal straining associated with strenuous exercise, may predispose to exercise-induced reflux. Other studies have suggested that GERD may be increased in athletes because of a decreased gastrointestinal blood flow, alterations of hormone secretion, changes in the motor function of the esophagus and the ventricle, and constrained body position during exercise^[139].

All these studies suggest that a specific physical activity, i.e. an agonistic activity, plays a possible pathogenetic role in inducing GERD symptoms. However, these results should not be extended to normal physical activity, which has been demonstrated to have a protective effect against GERD^[99] (Table 4). In particular, in a large population-based study^[99], a protective effect of physical activity was observed, documenting a correlation between the number of exercise sessions lasting at least 30 min and a decreased risk of GERD symptoms (OR, 0.5; 95% CI, 0.4-0.7). Therefore, a mechanism of an exercise-strengthened antireflux barrier, possibly constituted by striated muscle was suggested. The same results were produced by Nocon *et al*^[39], who have also found that subjects with typical GERD symptoms are physically less active than those without symptoms.

Furthermore, in their monozygotic co-twin study, Zheng *et al*^[43] have provided evidence that physical activity at work increases the risk of GERD symptoms, whereas physical activity at leisure time decreases this risk. The authors have suggested that physical activity at work might be linked with postprandial exercise, which has been found to be a risk factor for the development of GERD symptoms^[140]. Indeed, physical exercise at leisure time is predominantly performed at times without a feeling of stomach fullness and is, therefore, most unlikely to be a reflux-provoking postprandial exercise^[140].

In conclusion, the relationship between exercise and GERD is also controversial. It may be a consequence of differences in the populations studied (age, race), evaluation of exercise (short-term, long-term), assessment of physical activity (different questionnaires) and diagnosis of the disease (symptom scale or pH-metry). However, mild routine physical activity in association with diet modifications, i.e. a diet rich in fiber and poor in fat, seems to be advisable to prevent reflux symptoms.

CONCLUSION

There is sufficient evidence to support the relationship between being obese/overweight and GERD, expressed as specific symptoms and endoscopic features. Furthermore, available evidence suggests that controlled weight loss (by diet or surgery) is able to induce a significant improvement in GERD symptoms and/or in GERD clinical-endoscopic manifestations. Definitive data still do not exist regarding the association between dietary behavior, mainly in terms of specific dietary components and GERD manifestations. Moderate

physical activity seems beneficial, while vigorous activity may be dangerous in predisposed individuals. However, owing to the evidence that incorrect dietary habits and the absence of regular physical activity represent important risk factors for the development of the so-called “non-communicable diseases”^[141], lifestyle changes are recommended in patients with or at high risk for GERD. According to the recent proposal by a panel of international experts of a new algorithm for GERD management^[142], life-style factors (i.e. meal size and timing, not lying down after a meal or lying down where the head is in a non-elevated position, not smoking, not consuming alcohol, not eating heavily spiced or fatty food and having a physically active life) are important instruments for the overall management of GERD. Additional clinical studies are required.

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