HHS Public Access

Author manuscript

Dig Dis Sci. Author manuscript; available in PMC 2022 August 15.

Published in final edited form as:

Dig Dis Sci. 2022 July ; 67(7): 2730–2738. doi:10.1007/s10620-022-07496-7.

Factors that Impact the Variability of Day-to-Day Esophageal Acid Reflux Exposure and its Diagnostic Significance for Gastroesophageal Reflux Disease

Steven Ma, MD[1], **Vandan Patel, MD**[2], **Rena Yadlapati, MD**[3]

[1]Department of Medicine, University of California San Diego, La Jolla, CA, USA.

[2]Department of Medicine, University of California San Diego, La Jolla, CA, USA.

[3]Division of Gastroenterology, Department of Medicine, University of California San Diego, La Jolla, CA, USA.

Abstract

Gastroesophageal reflux disease (GERD) is a common disease affecting a significant number of adults both globally and in the United States. GERD is clinically diagnosed based on patient-reported symptoms and the gold standard for diagnosis is ambulatory reflux monitoring, a tool particularly utilized in the common scenario of non-response to therapy or atypical features. Over the past 20 years there has been a shift towards extending the duration of reflux monitoring, initially from 24-hours to 48 hours and more recently to 96 hours, primarily based on a demonstrated increase in diagnostic yield. Further, multiple studies demonstrate clinically relevant variability in day-to-day acid exposure levels in nearly 30% of ambulatory reflux monitoring studies. For these reasons an ongoing clinical dilemma relates to the optimal activities that patients should engage in during prolonged reflux monitoring. Thus, the aims of this review are to detail what is known about variability in daily acid exposure, discuss factors that are known to influence this day-to-day variability (i.e., sleep patterns, dietary/eating habits, stress, and exercise), and finally provide suggestions for patient education and general GERD management to reduce variation in esophageal acid exposure levels.

Keywords

ambulatory reflux monitoring; sleep; diet; stress; exercise

Corresponding Author: Rena Yadlapati MD MS, Associate Professor of Clinical Medicine, Medical Director, Esophageal Diseases & Motility, UCSD Center for Esophageal Diseases, Division of Gastroenterology, University of California San Diego, 9500 Gilman Drive MC 0956 La Jolla, CA 92093, ryadlapati@health.ucsd.edu.

Conflicts of Interests:
SM: None
VP: None
RY: Consultant for Medtronic, Phathom Pharmaceuticals, StatLinkMD; Research Support: Ironwood Pharmaceuticals; Advisory Board with Stock Options: RJS Mediagnostix

Writing Assistance: None

INTRODUCTION

Gastroesophageal reflux disease (GERD) is extremely common in the United States, affecting up to 30% of adults and accounting for over 7 million ambulatory visits annually[1, 2]. GERD is primarily a clinical diagnosis based on patient reports of typical symptoms such as heartburn or regurgitation, atypical symptoms such as non-cardiac chest pain, or extra-esophageal symptoms including chronic cough, dysphonia or globus sensation. First-line diagnosis and management typically involve an empiric trial of proton pump inhibitor (PPI) therapy[3]. Despite this, approximately 50% of patients on PPI therapy do not achieve symptomatic relief[1, 4].

Current guidelines recommend the use of ambulatory reflux monitoring off antisecretory therapy over patient-reported symptoms, GERD questionnaires, PPI trial, and endoscopy alone for definitive diagnosis of GERD[5]. Studies have shown that patient-reported symptoms or response to PPI therapy do not necessarily correlate with reflux burden on ambulatory reflux monitoring[6]. This is important to acknowledge as patients with pathologic reflux on ambulatory reflux monitoring (i.e. those with abnormal acid exposure time) tend to have improved rates of response to antireflux therapy[7].

A prominent question in the field relates to whether 24 hours of acid exposure monitoring is sufficient for a diagnosis of GERD. This stems from the fact that day-to-day variability of esophageal acid exposure is seen on ambulatory reflux monitoring[8–10], as well as multiple studies that highlight increased diagnostic yield of GERD with prolonged pH monitoring[11–13]. In this review, we will discuss the day-to-day variability seen with esophageal acid exposure time (AET) and explore factors such as sleep, diet and eating habits, stress, and exercise that may modulate acid exposure throughout the day to account for this variability.

DAY-TO-DAY ACID REFLUX EXPOSURE VARIABILITY

Esophageal pH monitoring measures multiple metrics related to acidic gastro-esophageal reflux. One of the most reliable and reproducible parameters in diagnosing GERD is measuring the acid exposure time (AET)[14], which is defined as the percent time esophageal pH is less than 4.0[15]. According to the Lyon Consensus, patients with AET less than 4.0% is considered normal/physiologic, AET greater than 6.0% is considered definitively abnormal, and AET between 4.0–6.0% being inconclusive[16]. Various studies have shown that the 95th percentile of normal AET ranged from 4.4% to 5.3%[17, 18].

Although the thresholds for AET are defined, day-to-day variability in AET over multiple days of recording poses a diagnostic dilemma. Prior studies have shown that symptomatic patients undergoing 48 hours wireless pH monitoring may have normal esophageal acid exposure values on either day 1 or day 2 of recordings[17]. In fact, Ayazi et al. demonstrated a 27% discordance between the first and second day of recording in patients with suspected GERD[18]. Another study also showed that sensitivity and detection accuracy can increase up to 22% if at least two days of testing were completed compared to just a single 24-hour

period[19]. For these reasons, the duration of monitoring was extended from 24 hours to 48 hours in the early 2000s.

In more recent years, investigators demonstrate the added utility of extending monitoring to 96 hours. A study performed by Patel et al. highlights the suboptimal diagnostic accuracy of acid exposure over the first 24 hours of monitoring. This group of investigators demonstrated that extending recording times to 96 hours allowed for the confident diagnosis of GERD in an additional 22% of patients[20]. Another study by Hasak et al. also highlights the advantage of prolonged pH monitoring up to 96 hours being beneficial, particularly in the 35.9% of their patients with discordant/borderline acid exposure metrics during the first 48 hours of monitoring[21]. A unique study examined trajectory modeling to examine patterns of acid exposure burden over 96 hours, highlighting that an assessment of acid exposure trajectory (low, mid, or high) may better categorize severity of acid burden and improve the diagnostic yield of GERD[22]. As such, current guidelines recommend prolonged, ranging anywhere from 48 to 96 hours, recording times as it increases diagnostic yield for identification of abnormal/pathologic reflux burden[23].

In order to further improve our framework in GERD diagnosis, the underlying factors that can modulate and affect day-to-day variability must also be explored.

FACTORS ASSOCIATED WITH DAY-TO-DAY ACID REFLUX VARIABILITY

Factor 1: Sleep

Sleep is a quintessential part of survival in which humans devote approximately one third of their lifetime. However, approximately 1 in 3 American adults sleep less than 7 hours each night; this timeframe of sleep deprivation is where physiologic and neurobehavioral deficits begin to manifest and worsen with further deprivation[24], including GERD. Sleep and GERD share a bidirectional relationship with one another. First, GERD may be promoted during sleep as a result of slowed gastric emptying[25], reduced swallowing and salivary secretion[26, 27], and reduced occurrence of esophageal peristalsis[28]. Nocturnal reflux in itself is clinically significant as it has been associated with more severe GERD symptoms and complications such as strictures, Barrett’s esophagus, and esophageal adenocarcinoma[29]. At the same time, GERD can lead to impaired sleep through two mechanisms: 1) nocturnal heartburn symptoms awakening patients leading to reports of sleep deprivation, and 2) through multiple short, amnestic arousals causing sleep fragmentation[30]. Sleep deprivation in turn can lead to somatic hyperalgesia[31, 32].

In a first of its kind study, Schey et al. assessed 10 patients with erosive GERD and 10 healthy controls who were randomized into sleep deprivation or sufficient sleep with crossover to the other arm after a washout period. Stimulus-response function testing to esophageal acid perfusion was conducted after their respective sleep protocol where a nasoesophageal catheter was placed with infusion of hydrochloric acid to the mid-esophagus to stimulate acid reflux. Amongst GERD patients, 9 of 10 experienced statistically significant worsening of all stimulus-response functions after sleep deprivation characterized by shortened lag time to symptom report, increased sensory intensity rating, and increased acid perfusion sensitivity; healthy controls did not have significant results regardless of

sleep deprivation[33]. GERD patients with sufficient sleep tended to have reduced values in stimulus-response testing, thus highlighting the vicious cycle of GERD during sleep resulting in progressive sleep deprivation and subsequently worsening GERD[34–36].

Recognizing the influence of sleep on GERD, variation in daily sleep quantity and quality likely contributes to day-to-day variability seen on prolonged pH monitoring. Thus, in an ideal standardized scenario, patients should optimize sleep habits during pH monitoring and in management of their GERD. Outside of invasive devices such as pH-impedance or wireless pH monitoring placement, there are limited validated and noninvasive biodevices for use of measuring GERD parameters overnight. There is certainly potential in future investigation of wearable biodevices such as wrist actigraphy, which has been shown as a reliable, noninvasive, and wearable biodevice to monitor sleep parameters[37–40]. These sleep parameters can be coupled with reflux monitoring to examine the relationships between sleep quality and quantity and esophageal acid exposure on a day-to-day basis.

Factor 2: Diet and Eating Habits

Diet and eating habits have been long postulated to play a significant role in the pathogenesis, course, and day-to-day variability observed with GERD and esophageal acid reflux exposure. In terms of eating habits, certain practices such as eating too quickly, having an irregular eating schedule, eating a larger meal, and/or eating before bed are recognized as exacerbating factors for esophageal acid reflux and GERD symptoms. Unfortunately, there is conflicting data to support particular lifestyle regimens[41–46]; the American Gastroenterology Association (AGA) and American College of Gastroenterology (ACG) generally recommend empiric lifestyle/behavioral interventions such as avoiding late night meals and recumbency 2–3 hours after eating, particularly for patients with nocturnal symptoms[3, 47].

Similar to eating habits, the relationship between diet and GERD in various studies have generally been inconsistent with conflicting findings regarding specific diets and their influence on exacerbating esophageal acid exposure/GERD-related symptoms[48]. Theoretically, food products such as carbonated/caffeinated beverages, citric/acidic products, spicy foods, and chocolate have been cited to cause transient lower esophageal sphincter relaxations (TLESRs) or reduce lower esophageal sphincter (LES) pressures[49–54]. Likewise, patients are generally advised to avoid fatty meals due to observational studies citing how it can lower LES pressure and exacerbate esophageal acid reflux[55, 56]. A study conducted by Fox et al. attempts to further elucidate the relationship between dietary fat, calorie density, and esophageal acid exposure. Through this study, they found how dietary fat can increase visceral sensitivity to reflux events and how high-calorie diets can significantly increase duration of GERD episodes, thus suggesting a potential relationship between high-caloric meals, delayed gastric emptying, and increased acid reflux[57]. However, other studies on fat intake and GERD-symptoms have shown conflicting results[58].

Despite multiple studies supporting food avoidance to reduce esophageal reflux exposure, the data to support this in a clinically meaningful context is not available and patients should generally only be advised to limit certain types of food that are known to specifically trigger

their symptoms. Diet and eating habits can vary drastically from person-to-person due to a wide-range of factors such as culture, ethnicity, finances, and personal views. As such, diet and eating habits can also significantly vary day-by-day and modulate the variability seen on esophageal pH monitoring as patients change their daily dietary/eating habits based on current events and preferences.

Factor 3: Stress

Stress is a universal condition, both physical and/or psychological, that affects individuals in different ways. Recent studies have improved our understanding about the ways stress affect the pathogenesis of gastrointestinal diseases, including its effect on gastric secretion, gut motility, mucosal permeability, visceral sensitivity, gut microbiota, and mucosal blood flow[59]. The communication between the brain and gut as well as the gut response to said stress is termed the brain-gut axis (BGA)[60].

In regards to esophageal acid reflux, stress can exacerbate GERD-related symptoms by lowering LES pressure and increasing hypersensitivity of esophageal mucosa to acid exposure[59]. Acute stress and induction of anxiety seem to be associated with decreased gastric compliance, inhibition of meal-induced accommodation, and increased symptoms[61]. An animal model study completed by Farre et al. shows how acute stress can increase mucosal permeability and dilation of intercellular space in esophageal mucosa which could account for the above findings[62]. Although there are conflicting studies that show an increase in GERD symptoms without a change in number of acid reflux events[59, 63], other studies highlight the ways that amplified psychosocial stress increases severity of reported reflux symptoms[63], amplifies gastric acid output[64], and correlates with worsened severity of reflux esophagitis[65].

A study conducted by McDonald-Haile et al. provides further insight into the effect of psychosocial stress/anxiety on esophageal acid reflux and efficacy of relaxation techniques to combat exacerbation of symptoms. Their study not only showed that relaxation techniques helped reduce GERD-related symptoms, but also significantly decreased esophageal acid exposure secondary to a decrease in number of reflux episodes on esophageal pH-monitoring[66]. Thus, psychosocial factors can play an important role to account for variability seen on prolonged pH monitoring.

Factor 4: Exercise

Regular exercise has long been regarded as an important lifestyle activity with significant health benefits, including but not limited to reducing risks for the development of cardiovascular diseases[67], combating components of metabolic syndrome[68], and improving psychiatric disorders such as anxiety and depression[69]. The benefits of exercise on the gastrointestinal system is less defined. Although there is evidence that exercise provides benefits for patients with inflammatory bowel disease and lowers relative risk of colon cancer[70], it has been associated with increased GERD-related symptoms such as heartburn, chest pain, or abdominal fullness in up to 45% to 90% of athletes[71].

There appears to be a relationship between type of exercise, body movement, and fasting/post-prandial state in exacerbation of esophageal acid reflux and GERD-related symptoms.

A study conducted by Clark et al. enrolled 12 asymptomatic patients and revealed that runners had the most amount of reflux frequency/duration (both fasting and worse post-prandial) on 24-hour esophageal pH-monitoring; they were followed by weight trainers and lastly cyclists, who have lower degree of body movement/agitation with their physical activity[72]. This finding was subsequently supported by a study by Yazaki et al. where healthy adults experienced increased esophageal acid reflux on esophageal pH-monitoring with running and rowing, more so after a meal[73].

The main mechanism in which exercise is thought to exacerbate esophageal acid reflux is through TLESRs as seen in 82% of episodes in a study by Schoeman et al. where LES pressures were measured in ambulatory healthy subjects during a standardized exercise program involving cycling and moderate/fast walking[73]. A more recent study by Herregods et al. further supports this finding where the effects of running was studied in 10 healthy participants via a combination of both pH-impedance monitoring and prolonged high-resolution manometry. Not only did this novel study show that exercise led to a significantly higher esophageal AET and frequency/duration of acid reflux episodes, but also revealed all but one reflux episode was associated with TLESRs[74]. In fact, exercise resulted in significantly increased frequency of TLESRs, in conjuncture with increased abdominal pressure and decreased duration/contractility of peristaltic contractions[74].

The majority of the studies exploring the effects of exercise and acid reflux were completed with healthy, asymptomatic volunteers or athletes, so concerns on whether the above data can be extrapolated to patients with symptoms exist. Regardless, it is important to acknowledge that exercise in numerous forms can increase both TLESRs and esophageal acid exposure even in healthy patients, which can subsequently modulate day-to-day esophageal acid reflux and contribute to the variability seen on esophageal pH-monitoring testing.

SUMMARY OF SUGGESTIONS TO REDUCE VARIABILITY IN ACID EXPOSURE

In summary, GERD is an incredibly common gastrointestinal disorder for which the gold standard for diagnosis is ambulatory reflux monitoring, with a preference towards prolonged wireless pH monitoring when available. However, day-to-day variability with pH-monitoring has been observed and established in prior studies[17–19]. A multitude of environmental, psychosocial, and physical factors can modulate day-to-day esophageal acid exposure, with significant impacts on diagnostic interpretation. Thus, optimal acid exposure management should be recommended during reflux monitoring, which includes optimizing long-term sleep hygiene, dietary/eating habits, exercise (type and frequency), and stress reduction. Future areas of interest include methods to improve biowearable devices to measure these components of stress, sleep, exercise, and their relationship to an individual patient’s esophageal acid burden and symptoms. Incorporating these measured parameters into mobile apps for easy monitoring could also be developed. Doing this would allow patients suffering from GERD to better target and monitor specific factors affecting their GERD so that they can improve their overall health and wellness.

In the meantime, patients can be recommended to avoid exercise after eating. Performing relaxation techniques have also been shown to reduce stress, esophageal acid exposure, and number of acid reflux events[66] which could subsequently influence day-to-day variability in acid reflux patterns. Likewise, diet restriction, inspiratory muscle training, and abdominal/diaphragmatic breathing exercises have been shown to reduce day-to-day variability in pH composite score[75], improve esophagogastric junction pressure[76], and subsequently reduce the number of postprandial acid reflux events[77, 78]. These lifestyle modifications can not only improve diagnostic yield by reducing variable/confounding factors that affect interpretation of prolonged esophageal pH monitoring, but also assist in long-term symptom management.

Funding Support:

RY is supported by NIH K23 DK125266 (PI: Yadlapati).

Abbreviations:

AET	Acid exposure time
ACG	American College of Gastroenterology
AGA	American Gastroenterology Association
BGA	brain-gut axis
GERD	gastroesophageal reflux disease
LES	loweresophageal sphincter
PPI	proton pump inhibitor
TLESR	transient lower esophageal sphincter relaxation

REFERENCES

1. Delshad SD, et al. , Prevalence of Gastroesophageal Reflux Disease and Proton Pump Inhibitor-Refractory Symptoms. Gastroenterology, 2020. 158(5): p. 1250–1261.e2. [PubMed: 31866243]
2. Peery AF, et al. , Burden of Gastrointestinal, Liver, and Pancreatic Diseases in the United States. Gastroenterology, 2015. 149(7): p. 1731–1741.e3. [PubMed: 26327134]
3. Katz PO, Gerson LB, and Vela MF, Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol, 2013. 108(3): p. 308–28; quiz 329. [PubMed: 23419381]
4. Abdallah J, et al. , Most Patients With Gastroesophageal Reflux Disease Who Failed Proton Pump Inhibitor Therapy Also Have Functional Esophageal Disorders. Clin Gastroenterol Hepatol, 2019. 17(6): p. 1073–1080.e1. [PubMed: 29913281]
5. Katz PO, et al., ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. Official journal of the American College of Gastroenterology| ACG, 2021: p. 10.14309.
6. Bello B, et al. , Gastroesophageal reflux disease and antireflux surgery-what is the proper preoperative work-up? J Gastrointest Surg, 2013. 17(1): p. 14–20; discussion p. 20. [PubMed: 23090280]

7. Patel A, Sayuk GS, and Gyawali CP, Parameters on esophageal pH-impedance monitoring that predict outcomes of patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol, 2015. 13(5): p. 884–91. [PubMed: 25158924]
8. Carlson DA, et al. , The relationship between esophageal acid exposure and the esophageal response to volumetric distention. Neurogastroenterol Motil, 2018. 30(3).
9. Fass R, et al. , Effect of ambulatory 24-hour esophageal pH monitoring on reflux-provoking activities. Dig Dis Sci, 1999. 44(11): p. 2263–9. [PubMed: 10573372]
10. Zerbib F, et al. , Normal values and day-to-day variability of 24-h ambulatory oesophageal impedance-pH monitoring in a Belgian-French cohort of healthy subjects. Aliment Pharmacol Ther, 2005. 22(10): p. 1011–21. [PubMed: 16268977]
11. Penagini R, et al. , Inconsistency in the diagnosis of functional heartburn: usefulness of prolonged wireless pH monitoring in patients with proton pump inhibitor refractory gastroesophageal reflux disease. Journal of neurogastroenterology and motility, 2015. 21(2): p. 265. [PubMed: 25843078]
12. Prakash C and Clouse RE, Value of extended recording time with wireless pH monitoring in evaluating gastroesophageal reflux disease. Clinical Gastroenterology and Hepatology, 2005. 3(4): p. 329–334. [PubMed: 15822037]
13. Sweis R, et al. , Prolonged, wireless pH-studies have a high diagnostic yield in patients with reflux symptoms and negative 24-h catheter-based pH-studies. Neurogastroenterology & Motility, 2011. 23(5): p. 419–426. [PubMed: 21235685]
14. Wiener GJ, et al. , Ambulatory 24-hour esophageal pH monitoring. Reproducibility and variability of pH parameters. Dig Dis Sci, 1988. 33(9): p. 1127–33. [PubMed: 3044715]
15. Yadlapati R, et al. , Ambulatory reflux monitoring guides proton pump inhibitor discontinuation in patients with gastroesophageal reflux symptoms: a clinical trial. Gastroenterology, 2021. 160(1): p. 174–182. e1. [PubMed: 32949568]
16. Gyawali CP, et al. , Modern diagnosis of GERD: the Lyon Consensus. Gut, 2018. 67(7): p. 1351–1362. [PubMed: 29437910]
17. Pandolfino JE, et al. , Ambulatory esophageal pH monitoring using a wireless system. Am J Gastroenterol, 2003. 98(4): p. 740–9. [PubMed: 12738450]
18. Ayazi S, et al. , Bravo catheter-free pH monitoring: normal values, concordance, optimal diagnostic thresholds, and accuracy. Clinical gastroenterology and Hepatology, 2009. 7(1): p. 60–67. [PubMed: 18976965]
19. Tseng D, et al. , Forty-eight-hour pH monitoring increases sensitivity in detecting abnormal esophageal acid exposure. Journal of gastrointestinal surgery, 2005. 9(8): p. 1043–1052. [PubMed: 16269374]
20. Patel R, et al. , Su1096–96-Hour Esophageal PH Monitoring: The Tiebreaker for Abnormal Demeester Score and Symptom Index. Gastroenterology, 2018. 154(6): p. S-486–S-487.
21. Hasak S, et al. , Prolonged wireless pH monitoring in patients with persistent reflux symptoms despite proton pump inhibitor therapy. Clinical Gastroenterology and Hepatology, 2020. 18(13): p. 2912–2919. [PubMed: 32007543]
22. Yadlapati R, et al. , Trajectory assessment is useful when day-to-day esophageal acid exposure varies in prolonged wireless pH monitoring. Diseases of the Esophagus, 2019. 32(3): p. doy077. [PubMed: 30124795]
23. Gyawali CP, et al. , ACG Clinical Guidelines: Clinical Use of Esophageal Physiologic Testing. Am J Gastroenterol, 2020. 115(9): p. 1412–1428. [PubMed: 32769426]
24. Luyster FS, et al. , Sleep: a health imperative. Sleep, 2012. 35(6): p. 727–734. [PubMed: 22654183]
25. Goo R, et al. , Circadian variation in gastric emptying of meals in humans. Gastroenterology, 1987. 93(3): p. 515–518. [PubMed: 3609660]
26. Lear CS, Flanagan J Jr, and Moorrees C, The frequency of deglutition in man. Archives of oral biology, 1965. 10(1): p. 83–IN15. [PubMed: 14262163]
27. Schneyer LH, et al. , Rate of flow of human parotid, sublingual, and submaxillary secretions during sleep. Journal of dental research, 1956. 35(1): p. 109–114. [PubMed: 13286394]
28. Orr WC, Gastrointestinal functioning during sleep: a new horizon in sleep medicine. Sleep medicine reviews, 2001. 5(2): p. 91–101. [PubMed: 12531048]

29. Fujiwara Y, Arakawa T, and Fass R, Gastroesophageal reflux disease and sleep disturbances. Journal of gastroenterology, 2012. 47(7): p. 760–769. [PubMed: 22592763]
30. Green C, et al. , The effect of sleep duration on symptoms perception of patients with gastroesophageal reflux disease (GERD). Gastroenterology, 2003. 4(124): p. A255–A256.
31. Onen SH, et al. , The effects of total sleep deprivation, selective sleep interruption and sleep recovery on pain tolerance thresholds in healthy subjects. Journal of sleep research, 2001. 10(1): p. 35–42. [PubMed: 11285053]
32. Roehrs T, et al. , Sleep loss and REM sleep loss are hyperalgesic. Sleep, 2006. 29(2): p. 145–151. [PubMed: 16494081]
33. Schey R, et al. , Sleep deprivation is hyperalgesic in patients with gastroesophageal reflux disease. Gastroenterology, 2007. 133(6): p. 1787–1795. [PubMed: 18054551]
34. Fass R, The relationship between gastroesophageal reflux disease and sleep. Current gastroenterology reports, 2009. 11(3): p. 202–208. [PubMed: 19463220]
35. Maneerattanaporn M and Chey WD, Sleep disorders and gastrointestinal symptoms: chicken, egg or vicious cycle? 2009.
36. Shibli F, et al. , Nocturnal gastroesophageal reflux disease (GERD) and sleep: an important relationship that is commonly overlooked. Journal of Clinical Gastroenterology, 2020. 54(8): p. 663–674. [PubMed: 32657961]
37. Marino M, et al. , Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep, 2013. 36(11): p. 1747–1755. [PubMed: 24179309]
38. Morgenthaler T, et al. , Practice parameters for the use of actigraphy in the assessment of sleep and sleep disorders: an update for 2007. Sleep, 2007. 30(4): p. 519–529. [PubMed: 17520797]
39. Sadeh A, The role and validity of actigraphy in sleep medicine: an update. Sleep medicine reviews, 2011. 15(4): p. 259–267. [PubMed: 21237680]
40. Smith MT, et al. , Use of actigraphy for the evaluation of sleep disorders and circadian rhythm sleep-wake disorders: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. Journal of Clinical Sleep Medicine, 2018. 14(7): p. 1209–1230. [PubMed: 29991438]
41. Fujiwara Y, et al. , Association between dinner-to-bed time and gastro-esophageal reflux disease. Am J Gastroenterol, 2005. 100(12): p. 2633–6. [PubMed: 16393212]
42. Iwakiri K, et al. , Relationship between postprandial esophageal acid exposure and meal volume and fat content. Digestive diseases and sciences, 1996. 41(5): p. 926–930. [PubMed: 8625764]
43. Jarosz M and Taraszewska A, Risk factors for gastroesophageal reflux disease: the role of diet. Przeglad gastroenterologiczny, 2014. 9(5): p. 297. [PubMed: 25396005]
44. Orr W and Harnish M, Sleep-related gastro-oesophageal reflux: provocation with a late evening meal and treatment with acid suppression. Alimentary pharmacology & therapeutics, 1998. 12(10): p. 1033–1038. [PubMed: 9798810]
45. Song JH, et al. , Relationship between gastroesophageal reflux symptoms and dietary factors in Korea. Journal of neurogastroenterology and motility, 2011. 17(1): p. 54. [PubMed: 21369492]
46. Wildi SM, Tutuian R, and Castell DO, The influence of rapid food intake on postprandial reflux: studies in healthy volunteers. Official journal of the American College of Gastroenterology| ACG, 2004. 99(9): p. 1645–1651.
47. Kahrilas PJ, Shaheen NJ, and Vaezi MF, American Gastroenterological Association Medical Position Statement on the management of gastroesophageal reflux disease. Gastroenterology, 2008. 135(4): p. 1383–1391. e5. [PubMed: 18789939]
48. Meining A and Classen M, The role of diet and lifestyle measures in the pathogenesis and treatment of gastroesophageal reflux disease. The American journal of gastroenterology, 2000. 95(10): p. 2692–2697. [PubMed: 11051337]
49. Choe JW, et al. , Foods inducing typical gastroesophageal reflux disease symptoms in Korea. Journal of neurogastroenterology and motility, 2017. 23(3): p. 363. [PubMed: 28147346]
50. Crookes P, et al. Response of lower esophageal sphincter to ingestion of carbonated beverages. in Gastroenterology. 1999. WB SAUNDERS CO-ELSEVIER INC 1600 JOHN F KENNEDY BOULEVARD, STE 1800 ….

51. Eslami O, et al. , Dietary habits and obesity indices in patients with gastro-esophageal reflux disease: a comparative cross-sectional study. BMC gastroenterology, 2017. 17(1): p. 1–9. [PubMed: 28049442]
52. Feldman M and Barnett C, Relationships between the acidity and osmolality of popular beverages and reported postprandial heartburn. Gastroenterology, 1995. 108(1): p. 125–131. [PubMed: 7806034]
53. Murphy DW and Castell DO, Chocolate and heartburn: evidence of increased esophageal acid exposure after chocolate ingestion. American Journal of Gastroenterology (Springer Nature), 1988. 83(6).
54. Wright LE and Castell DO, The adverse effect of chocolate on lower esophageal sphincter pressure. The American journal of digestive diseases, 1975. 20(8): p. 703–707. [PubMed: 239592]
55. Becker DJ, et al. , A comparison of high and low fat meals on postprandial esophageal acid exposure. American Journal of Gastroenterology (Springer Nature), 1989. 84(7).
56. Nebel OT and Castell DO, Inhibition of the lower oesophageal sphincter by fat—a mechanism for fatty food intolerance. Gut, 1973. 14(4): p. 270–274. [PubMed: 4706907]
57. Fox M, et al. , The effects of dietary fat and calorie density on esophageal acid exposure and reflux symptoms. Clinical Gastroenterology and Hepatology, 2007. 5(4): p. 439–444. e1. [PubMed: 17363334]
58. Penagini R, Mangano M, and Bianchi P, Effect of increasing the fat content but not the energy load of a meal on gastro-oesophageal reflux and lower oesophageal sphincter motor function. Gut, 1998. 42(3): p. 330–333. [PubMed: 9577336]
59. Konturek PC, Brzozowski T, and Konturek S, Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options. J Physiol Pharmacol, 2011. 62(6): p. 591–599. [PubMed: 22314561]
60. Konturek S, et al. , Brain-gut axis and its role in the control of food intake. Journal of physiology and pharmacology, 2004. 55(2): p. 137–154. [PubMed: 15082874]
61. Geeraerts B, et al. , Influence of experimentally induced anxiety on gastric sensorimotor function in humans. Gastroenterology, 2005. 129(5): p. 1437–1444. [PubMed: 16285945]
62. Farré R, et al. , Critical role of stress in increased oesophageal mucosa permeability and dilated intercellular spaces. Gut, 2007. 56(9): p. 1191–1197. [PubMed: 17272649]
63. Bradley LA, et al. , The relationship between stress and symptoms of gastroesophageal reflux: the influence of psychological factors. American Journal of Gastroenterology (Springer Nature), 1993. 88(1).
64. Holtmann G, Kriebel R, and Singer MV, Mental stress and gastric acid secretion. Digestive diseases and sciences, 1990. 35(8): p. 998–1007. [PubMed: 2384046]
65. Song EM, Jung H-K, and Jung JM, The association between reflux esophagitis and psychosocial stress. Digestive diseases and sciences, 2013. 58(2): p. 471–477. [PubMed: 23001402]
66. McDonald-Haile J, et al. , Relaxation training reduces symptom reports and acid exposure in patients with gastroesophageal reflux disease. Gastroenterology, 1994. 107(1): p. 61–69. [PubMed: 8020690]
67. Braith RW and Stewart KJ, Resistance exercise training: its role in the prevention of cardiovascular disease. Circulation, 2006. 113(22): p. 2642–2650. [PubMed: 16754812]
68. Katzmarzyk PT, et al. , Targeting the metabolic syndrome with exercise: evidence from the HERITAGE Family Study. Medicine and science in sports and exercise, 2003. 35(10): p. 1703–1709. [PubMed: 14523308]
69. Craft LL and Perna FM, The benefits of exercise for the clinically depressed. Primary care companion to the Journal of clinical psychiatry, 2004. 6(3): p. 104.
70. Bi L and Triadafilopoulos G, Exercise and gastrointestinal function and disease: an evidence-based review of risks and benefits. Clinical Gastroenterology and Hepatology, 2003. 1(5): p. 345–355. [PubMed: 15017652]
71. Yazaki E, et al. , The effect of different types of exercise on gastro-oesophageal reflux. Australian journal of science and medicine in sport, 1996. 28(4): p. 93–96. [PubMed: 9040897]
72. Clark CS, et al. , Gastroesophageal reflux induced by exercise in healthy volunteers. Jama, 1989. 261(24): p. 3599–3601. [PubMed: 2724505]

73. Schoeman MN, et al. , Mechanisms of gastroesophageal reflux in ambulant healthy human subjects. Gastroenterology, 1995. 108(1): p. 83–91. [PubMed: 7806066]

74. Herregods TV, et al. , Effect of running on gastroesophageal reflux and reflux mechanisms. Official journal of the American College of Gastroenterology| ACG, 2016. 111(7): p. 940–946.

75. Ahlawat SK, et al. , Day-to-day variability in acid reflux patterns using the BRAVO pH monitoring system. Journal of clinical gastroenterology, 2006. 40(1): p. 20–24. [PubMed: 16340628]

76. Nobre e Souza MA, et al. , Inspiratory muscle training improves antireflux barrier in GERD patients. American Journal of Physiology-Gastrointestinal and Liver Physiology, 2013. 305(11): p. G862–G867. [PubMed: 24113771]

77. Eherer A, et al. , Positive effect of abdominal breathing exercise on gastroesophageal reflux disease: a randomized, controlled study. Official journal of the American College of Gastroenterology| ACG, 2012. 107(3): p. 372–378.

78. Halland M, et al. , Effects of diaphragmatic breathing on the pathophysiology and treatment of upright gastroesophageal reflux: a randomized controlled trial. Official journal of the American College of Gastroenterology| ACG, 2021. 116(1): p. 86–94.

Figure 1.

: Educational infographic for GERD patients and/or those undergoing ambulatory pH monitoring with recommendations for optimization of GERD-related symptoms and esophageal acid reflux levels

Table 1:

Factors associated with day-to-day esophageal acid reflux variability

Factor	Mechanism	Intervention/Management
Sleep	Sleep deprivation → sleep fragmentation → nocturnal reflux → slowed gastric emptying, reduced swallowing/salivary secretions, reduced esophageal peristalsis, heightened hyperalgesia/ hypersensitivity	• Optimize long-term sleep hygiene • Cognitive Behavioral Therapy for Insomnia (CBT-I)
Dietary and Eating Habits	Certain food triggers/eating habits → increased transient lower esophageal sphincter relaxations (TLESRs) and/or reduced LES pressures	• Avoiding known food or eating habit triggers (patient-dependent)
Stress	Acute/chronic stress → reduced LES pressure, heightened hypersensitivity, increased gastric acid output, decreased gastric compliance	• Relaxation techniques such as meditation • Exercise/yoga
Exercise	High intensity exercise → increased abdominal pressure, decreased duration/contractility of peristaltic contractions, increased TLESRs	• Inspiratory muscle training • Abdominal/diaphragmatic breathing exercises • Avoiding exercise immediately after eating