IJBPAS, April, 2026, 15(4): 1734-1746

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ETIOLOGY, PATHOPHYSIOLOGY AND MEDICAL MANAGEMENT OF GASTROESOPHAGEAL REFLUX DISEASE

CH. B. PRAVEENA DEVI*, B. KOUSHIK, M. RAJYALAXMI, R. SONY, K. GAYATRI, VSS GUPTA ATYAM AND B. MAHESHWARI

Department of Pharmacy, Joginpally B. R. Pharmacy College, Yenkapally, Moinabad, Hyderabad, Telangana- 500 075

***Corresponding Author: Dr. CH. B. Praveena Devi: E Mail: medicinalchemistonline123@gmail.com**

Received 20th Jan. 2025; Revised 19th March 2025; Accepted 5th May 2025; Available online 1st April 2026

https://doi.org/10.31032/IJBPAS/2026/15.4.10060

ABSTRACT

The symptoms of sub sternal burning and/or acid regurgitation brought on by the abnormal reflux of stomach contents into the esophagus are what define gastroesophageal reflux (GERD). Most patients with chronic heartburn will report having trouble falling asleep or staying asleep through the night due to reflux symptoms. Reflux symptoms are becoming more and more common in the developed world.

The effectiveness of both LNF and CNF over ten years was found to be similar regarding the alleviation of GERD symptoms, the use of proton pump inhibitors (PPIs), quality of life improvements, and objective reflux control as demonstrated by impedance studies. Consequently, the long-term findings from this trial provide level 1 evidence supporting LNF as the preferred surgical option for GERD

Keywords: gastroesophageal reflux (GERD), Reflux symptoms, developed world

INTRODUCTION

The symptoms of sub sternal burning and/or acid regurgitation brought on by the abnormal reflux of stomach contents into the esophagus are what define gastroesophageal reflux (GERD) **[1]**. Most patients with chronic heartburn will report having trouble

falling asleep or staying asleep through the night due to reflux symptoms **[2]**. Reflux symptoms are becoming more and more common in the developed world **[3]**. North America has a prevalence of GERD ranging from 18.1% to 27.8%, Europe from 8.8% to 25.9%, East Asia from 2.5% to 7.8%, the Middle East from 8.7% to 33.1%, Australia from 1.6%, and South America from 23.0 The overall incidence rate for the populations of the United States and the United Kingdom was approximately 5 cases per 1,000 person-years. In contrast, pediatric patients in the UK, specifically those aged 1 to 17, exhibited an incidence rate of 0.84. There is evidence that the prevalence of GERD has increased since 1995 ($p < 0.0001$), especially in East Asia and North America **[4]**. To guarantee proper diagnosis and treatment of the condition, GERD awareness and recognition must rise in tandem **[5]**. In certain people who have had a thorough objective evaluation for GERD, surgery may be effective when intense medication therapy has failed **[6]**.

Pathophysiology and Epidemiology

Research on the pathophysiology of GERD is still evolving, with new insights emerging thanks to technological advancements. Our current understanding is shaped by studies on reflux exposure and sensitivity. By considering anatomical and motor factors, we can gain a clearer picture of what causes reflux exposure. The type of reflux plays a significant role in how it contributes to symptoms, lesions, and other outcomes. This interaction is influenced by sensory mechanisms **[7]**.

Being older, having a higher body mass index (BMI), smoking, experiencing anxiety or depression, and having a lower level of physical activity at work are all risk factors for GERD **[8-10]**.

Variations in reflux exposure, visceral sensitivity, and epithelial resistance are all part of the complicated pathophysiology of gastroesophageal reflux disease (GERD). A toxic substance that damages the esophagus and causes symptoms is gastric refluxate. The main factor influencing the severity of the condition is esophageal exposure to stomach reflux. Reflux disease results from this exposure through a breakdown of the anti-reflux barrier and a decreased capacity of the esophagus to filter and buffer the refluxate. However, when there is either weak epithelial resistance or enhanced visceral sensitivity, problems and symptoms can also arise in the setting of a typical reflux burden. Therefore, changes in the ratio of defensive to aggressive forces are how reflux arises **[7]**.

The number and timing of meals, especially in relation to sleep, as well as the acidity of

food can all have an impact on GERD. Recreational exercise seems to provide protective effects, with the exception of post-prandially **[8, 11]**.

Although the lower esophageal sphincter (LES) is the primary cause of gastroesophageal reflux, a number of factors may also play a role in its development. GERD is influenced by both pathologic and physiological variables. Transient lower esophageal sphincter relaxations (TLESRs) are the most frequent cause. Short-lived, non-swallowing episodes of lower esophageal sphincter tone inhibition are known as TLESRs **[12]**. While these are physiologic in nature, there is an increase in frequency in the postprandial phase and they contribute greatly to acid reflux in patients with GERD. Other factors include reduced lower esophageal sphincter (LES) pressure, hiatal hernias, impaired esophageal clearance, and delayed gastric emptying **[10, 13]**.

Symptoms

Heartburn is the classic and most prevalent GERD symptom. Acid reflux into the esophagus causes heartburn, which is a burning feeling in the chest that travels to the mouth. Only a tiny portion of reflux episodes, meanwhile, are accompanied by symptoms. A sour taste in the back of the mouth, with or without refluxate regurgitation, is another common symptom of heartburn. Notably, non-cardiac chest pain is frequently caused by GERD **[14-15]**.

Given the potentially dangerous consequences of cardiac chest pain and the variety of etiology based diagnostic and therapy algorithms, it is critical to differentiate between the underlying causes of the chest pain **[15]**.

It is important to distinguish GERD symptoms from dyspepsia. Epigastric discomfort that lasts more than a month and is not accompanied by heartburn or acid regurgitation is known as dyspepsia. It may be linked to nausea, vomiting, belching, and bloating or epigastric fullness. Dyspepsia is a condition that may require endoscopic evaluation and

H. pylori tests and it may be treated differently than GERD **[16]**.

Diagnosis

The diagnosis of GERD is usually established through a blend of clinical symptoms, response to acid suppression therapy, and objective assessments such as upper endoscopy and esophageal pH monitoring. For instance, the presence of moderate to severe typical symptoms along with endoscopic findings (like erosive esophagitis or Barrett's esophagus) shows a high specificity (97%) for GERD, as verified by

pH testing **[17]**.

But even with heartburn and acid regurgitation, which have very high specificity (89% and 95%, respectively) but low sensitivity (38% and 6%) for GERD, a well-taken history can be very helpful in the diagnosis **[18]**.

Instead of doing a thorough and expensive evaluation on every patient who presents with simple symptoms, this can enable one to make a tentative diagnosis and start empiric medication **[19]**.

However, those who do not respond to acid suppression, those who exhibit alarm symptoms (such as dysphagia, odynophagia, iron deficiency anemia, weight loss, etc.), and those who have had Barrett's esophagus for a long time may require further testing **[20]**.

GERD is usually diagnosed clinically by typical symptoms and a depressed acid response. Heartburn with or without reflux is usually enough to suspect GERD, especially if symptoms are worse after eating or lying down **[16]**.

Initiation of treatment with a histamine type 2 (H2) receptor blocker or proton pump inhibitor (PPI) and subsequent discontinuation of symptoms is considered diagnostic. Patients who respond to empirical therapy do not require further testing unless there are alarming signs or symptoms **[21]**.

Even after using high-dose PPIs, some individuals will continue to experience reflux symptoms. To check for potential GERD problems and to assess for alternative reasons of their symptoms, more testing might be necessary. It is crucial to remember that the degree of mucosal injury is not always correlated with the intensity of reflux symptoms.

The upper gastrointestinal endoscopy, also known as an esophagogastroduodenoscopy (EGD), is the most commonly used diagnostic procedure for assessing GERD and its potential consequences. Direct esophagus mucosal vision is the main advantage of endoscopy. This aids in the diagnosis of GERD problems such Barrett's esophagus, strictures, and esophagitis. The Los Angeles classification is one endoscopic GERD severity rating system; it ranges from A to D, with D representing the most severe **[22]**.

Treatment

GERD is a non-communicable disease that usually requires long-term treatment in the form of lifestyle changes medical therapy and surgical therapy for a subset of patients.

1. Life style changes

In the management of GERD, a crucial approach is making lifestyle changes, which are often overlooked by doctors and not

followed by patients. It is advised to steer clear of foods that can relax the lower esophageal sphincter, including chocolate, spicy dishes, caffeine, tobacco, and alcohol **[23]**. Research has been conducted on the connection between diet and GERD to offer patients a more effective strategy **[24]**. Avoiding certain drinks is important for managing GERD, particularly acidic beverages, as they are known to aggravate the condition and trigger its symptoms **[25]**. The sole effective lifestyle change for managing GERD is to elevate the head of the bed **[26]**.

Along with steering clear of specific drinks, adjustments in macronutrient composition, eating behaviors, and timing also play a role in both the onset and worsening of GERD symptoms. It is strongly advised to have dinner at a regular time, as this helps ensure a consistent pH level during the night, reducing the chances of reflux occurrences while lying down during sleep **[24]**.

Weight loss is advised for individuals with GERD who are either overweight or have experienced recent weight gain. To alleviate night time reflux symptoms, it is recommended that patients elevate the head of their bed and refrain from lying down for at least three hours after eating. A recent study sought to compare the recurrence rates of erosive reflux disease (ERD) and non-erosive reflux disease (NERD), as well as to identify the risk factors associated with recurrence. Recurrence was identified when patients reported GERD symptoms that necessitated additional medication following an initial recovery period of 4 to 8 weeks of proton pump inhibitor (PPI) treatment. The study concluded that a shorter interval between dinner and bedtime was the most significant factor affecting GERD recurrence, with patients who typically went to sleep within three hours of eating exhibiting higher rates of recurrence **[27]**.

2. Medical Theraphy

GERD treatment is mainly acidic inhibitory effect. Studies have shown that corrosive esophageal and stomach burning relief PPIs and H2RA reduced complete healing, and the rate of this effect is almost twice the speed (healing speed and gastric burning 11.7%/week, 11.5 %/week against 5, 9 %5.9 %/week and 6.4 %/week and 6.4 %/week and 6.4 %/week in PPI and H2RA groups) **[28]**. In addition, studies show that it is more difficult to treat with H2RA compared to PPIS **[29]**. As compared to their NERD counterparts, patients with ERD typically respond more strongly to PPIs in terms of symptoms **[30]**. Because most patients with erosive reflux disease may return after stopping treatment, it is advised to treat the

condition with maintenance PPI therapy at the lowest therapeutic dose **[31]**.

With the exception of dexlansoprazole, which can be taken regardless of food intake, PPIs are generally seen to be similarly effective and patients should be advised to take those 30 to 60 minutes before meals. On the other hand, on-demand PPIs or, alternatively, less expensive treatments like H2RAs may be able to effectively treat NERD patients. The goal of a 2001 study was to ascertain whether step-down therapy was feasible for GERD patients who wre no longer experiencing symptoms after using PPIs. 58% of patients in the step-down group were asymptomatic after a year of follow-up, either on nonPPI therapy or no therapy at all. 59% of people who didn't take PPIs needed H2RAs **[32]**.

Attempts should be made to treat patients with the least expensive yet effective drug, especially in patients with NERD who may be able to be kept on H2RAs with control of symptoms, given the high cost associated with long-term PPI use. Maintenance PPI therapy should be reevaluated if symptoms return in **Figure 1**.

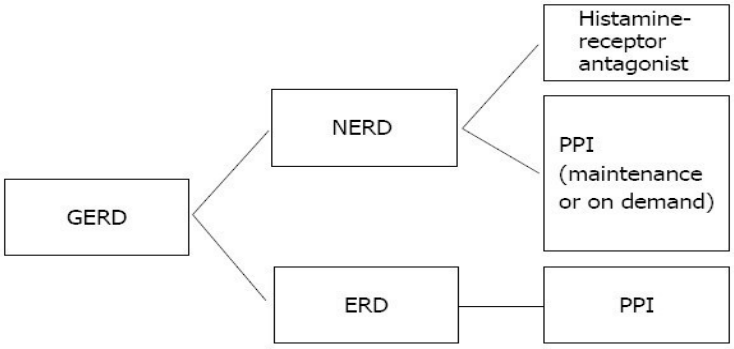

Figure 1: https://pubmed.ncbi.nlm.nih.gov/25133039/#&gid=article-figures&pid=figure-1-uid-0

In general, patients with gastroesophageal reflux disease who are found to have evidence of erosive esophagitis on endoscopy should be placed on maintenance proton pump inhibitor due to the high risk of relapse off proton pump inhibitor. However, patients with NERD may achieve symptom control on H2RAs or, alternatively, with on- demand PPI. If symptoms persist, maintenance PPI should be considered. GERD: Gastro-esophageal reflux disease; PPI: Proton pump inhibitor; ERD: Erosive reflux disease; NERD: Non-erosive reflux disease **(Figure 1)**.

Non-steroidal anti-inflammatory medicines (NSAIDs) should also be avoided by all GERD patients due to their ability to interfere with the body's natural defenses against mucosal inflammation. The goals of GERD

medication therapy are to minimize acid reflux-related mucosal damage and to lessen symptoms. With the exception of Zollinger-Ellison syndrome, there does not seem to be a direct correlation between the severity of GERD and elevated gastric acid levels, even if acid suppression is effective in treating the condition **[33]**.

3. Surgical Therapy

GERD can be treated using a variety of surgical techniques. But according to a survey, the use of surgical fund oplications has recently decreased in the US, particularly between 2009 and 2013 **[34]**. Patients whose symptoms are uncontrollable with PPI medication may benefit from surgical fundoplication, which is the gold standard in these situations; however, most patients have reported satisfaction after the procedure. But minor dysphagia, bloating, and the return of PPI treatment after surgery are also typical **[35]**. The esophagogastric junction (EGJ) was found to be more distensible after Dor fundoplication, while there was no discernible difference in distensibility between Nissen and Toupet fundoplication. This was the result of another study that compared the mechanical efficiency of the three types of fundoplications: Dor and Toupet, which are partial fundoplications, and the full Nissen fundoplication. Failure point measurements, however, showed that Toupet was more effective than Dor and Nissen was more effective than Toupet **[36]**.

Laparoscopic another extremely successful treatment option is Nissen's fundoplication, which has the benefits of being minimally invasive and capable of fixing any hiatal defect. Additionally, the need for long-term medicine ends. Modern equipment and a highly skilled and experienced surgeon are necessary for Nissen's fundoplication since it is minimally invasive and requires a great deal of precision **[37]**. Additionally, compared to Nissen's complete fundoplication (NF), anterior partial fundoplication (AF) has been found to have fewer mechanical adverse effects. A comparison of the long-term outcomes of the two forms of fundoplication was done using a randomized control experiment. The study included about 100 patients who had laparoscopic AF and NF, and postoperative problems such as dyspepsia and flatulence were considered. Following surgery, patients' reflux-related symptoms were reasonably controlled by both NF and AF. But following the procedure, a noticeably smaller percentage of patients in the AF group reported having flatulence **[38]**.

A laparoscopic, transabdominal method is typically favored for most patients receiving

anti-reflux surgery. On rare occasions, transthoracic and open abdominal techniques might be necessary and could be considered for individuals undergoing revision of their previous anti-reflux procedures **[39]**. Nonetheless, reoperation surgery is generally possible through laparoscopic techniques. A significant reduction in perioperative morbidity (65%) was observed following laparoscopic fundoplication in comparison to open fundoplication **[40]**. Laparoscopic fundoplication entails extended surgical durations but results in reduced hospital admissions. As a result, the rates of conversion to open surgery were under 5%. Laparoscopic fundoplication is favored compared to open surgery due to its correlation with a shorter duration of hospital stay, reduced pain levels, lower rates of postoperative wound infections, and a decreased occurrence of abdominal wall hernias **[41]**. Surgeons utilizing the laparoscopic technique benefit from a magnified view of all hiatal structures. A decade-long randomized trial comparing laparoscopic Nissen fundoplication (LNF) to conventional Nissen fundoplication (CNF or open technique) revealed that patients undergoing CNF were twice as likely to require reoperation, with a significantly higher incidence of incisional hernia repairs. The effectiveness of both LNF and CNF over ten years was found to be similar regarding the alleviation of GERD symptoms, the use of proton pump inhibitors (PPIs), quality of life improvements, and objective reflux control as demonstrated by impedance studies. Consequently, the long-term findings from this trial provide level 1 evidence supporting LNF as the preferred surgical option for GERD. **[42]**

REFERENCES

[1] Princeton, N. A. (1988). Gallup survey on heartburn across America. Washington, DC: The Gallup Organization.

[2] Johnson LF, Demeester TR, Haggitt RC. (1978). Esophageal epithelial response to gastroesophageal reflux. A quantitative study. *Am J Dig Dis*, 23(6), 498-509. https://doi.org/10.1007/BF01072693.

[3] El-Serag HB. (2007). Time trends of gastroesophageal reflux disease: a systematic review. *Clin Gastroenterol Hepatol*, 5(1), 17-26. https://doi.org/10.1016/j.cgh.2006.09.016.

[4] El-Serag HB, Sweet S, Winchester CC, Dent J. (2014). Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review.

Gut, 63(6), 871-880. https://doi.org/10.1136/gutjnl-2012-304269.

[5] Wong BC, Kinoshita Y. (2006). Systematic review on epidemiology of gastroesophageal reflux disease in Asia. *Clin Gastroenterol Hepatol*, 4(4), 398-407. https://doi.org/10.1016/j.cgh.2005.10.011.

[6] Irwin RS. (2006). Chronic cough due to gastroesophageal reflux disease: ACCP evidence-based clinical practice guidelines. *Chest*, 129(1 Suppl), 80S-94S. https://doi.org/10.1378/chest.129.1_suppl.80S.

[7] Tack J, Pandolfino JE. (2018). Pathophysiology of gastroesophageal reflux disease. *Gastroenterology*, 154(2), 277-288. https://doi.org/10.1053/j.gastro.2017.09.047.

[8] Zheng Z, Nordenstedt H, Pedersen NL, Lagergren J, Ye W. (2007). Lifestyle factors and risk for symptomatic gastroesophageal reflux in monozygotic twins. *Gastroenterology*, 132(1), 87-95. https://doi.org/10.1053/j.gastro.2006.11.019.

[9] Jarosz M, Taraszewska A. (2014). Risk factors for gastroesophageal reflux disease: the role of diet. *Prz Gastroenterol*, 9(5), 297-301. https://doi.org/10.5114/pg.2014.46166.

[10] Ferriolli E, Oliveira RB, Matsuda NM, Braga FJ, Dantas RO. (1998). Aging, esophageal motility, and gastroesophageal reflux. *J Am Geriatr Soc*, 46(12), 1534-1537. https://doi.org/10.1111/j.1532-5415.1998.tb01538.x

[11] Emerenziani S, Zhang X, Blondeau K, Silny J, Tack J, Janssens J, Sifrim D. (2005). Gastric fullness, physical activity, and proximal extent of gastroesophageal reflux. *Am J Gastroenterol*, 100(6), 1251-1256. https://doi.org/10.1111/j.1572-0241.2005.41695.x.

[12] Herregods TV, Bredenoord AJ, Smout AJ. (2015). Pathophysiology of gastroesophageal reflux disease: new understanding in a new era. *Neurogastroenterol Motil*, 27(9), 1202-1213. https://doi.org/10.1111/nmo.12611.

[13] Richter JE. (2000). Gastroesophageal reflux disease in the older patient: presentation,

treatment, and complications. *Am J Gastroenterol*, 95(2), 368-373. https://doi.org/10.1111/j.1572-0241.2000.t01-101791.x.

[14] Bredenoord AJ, Weusten BL, Curvers WL, Timmer R, Smout AJ. (2006). Determinants of perception of heartburn and regurgitation. *Gut*, 55(3), 313-318. https://doi.org/10.1136/gut.2005.074690.

[15] Gastal OL, Castell JA, Castell DO. (1994). Frequency and site of gastroesophageal reflux in patients with chest symptoms. Studies using proximal and distal pH monitoring. *Chest*, 106(6), 1793-1796. https://doi.org/10.1378/chest.106.6.1793.

[16] Dent J, Armstrong D, Delaney B, Moayyedi P, Talley NJ, Vakil N. (2004). Symptom evaluation in reflux disease: workshop background, processes, terminology, recommendations, and discussion outputs. *Gut*, 53 Suppl 4, iv1-iv24. https://doi.org/10.1136/gut.2003.034272.

[17] Tefera L, Fein M, Ritter MP, Bremner CG, Crookes PF, Peters JH, Hagen JA, DeMeester TR. (1997). Can the combination of symptoms and endoscopy confirm the presence of gastroesophageal reflux disease? *Am Surg*, 63(10), 933-936.

[18] Klauser AG, Schindlbeck NE, Müller-Lissner SA. (1990). Symptoms in gastro-oesophageal reflux disease. *Lancet*, 335(8683), 205-208. https://doi.org/10.1016/0140-6736(90)90287-f.

[19] Giannini EG, Zentilin P, Dulbecco P, Vigneri S, Scarlata P, Savarino V. (2008). Management strategy for patients with gastroesophageal reflux disease: a comparison between empirical treatment with esomeprazole and endoscopy-oriented treatment. *Am J Gastroenterol*, 103(2), 267-275. https://doi.org/10.1111/j.1572-0241.2007.01659.x.

[20] DeVault KR, Castell DO; American College of Gastroenterology. (2005). Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Am J Gastroenterol*, 100(1), 190-200. https://doi.org/10.1111/j.1572-0241.2005.41217.x.

[21] Wang WH, Huang JQ, Zheng GF, Wong WM, Lam SK, Karlberg J, Xia HH, Fass R, Wong BC. (2005). Is proton pump inhibitor testing an effective approach to diagnose gastroesophageal reflux disease in patients with noncardiac chest pain?: a meta-analysis. *Arch Intern Med*, 165(11), 1222-1228. https://doi.org/10.1001/archinte.165.11.1222.

[22] Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, Johnson F, Hongo M, Richter JE, Spechler SJ, Tytgat GN, Wallin L. (1999). Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut*, 45(2), 172-180. https://doi.org/10.1136/gut.45.2.172.

[23] Sandhu DS, Fass R. (2018). Current trends in the management of gastroesophageal reflux disease. *Gut Liver*, 12(1), 7-16. https://doi.org/10.5009/gnl16615.

[24] Newberry C, Lynch K. (2019). The role of diet in the development and management of gastroesophageal reflux disease: why we feel the burn. *J Thorac Dis*, 11(Suppl 12), S1594-S1601. https://doi.org/10.21037/jtd.2019.06.42.

[25] Gomes DC, Dantas RO. (2014). Acidic and neutral liquid ingestion in patients with gastroesophageal reflux disease. *Arq Gastroenterol*, 51(3), 217-220. https://doi.org/10.1590/s0004-28032014000300010.

[26] Khan BA, Sodhi JS, Zargar SA, Javid G, Yattoo GN, Shah A, Gulzar GM, Khan MA. (2012). Effect of bed head elevation during sleep in symptomatic patients of nocturnal gastroesophageal reflux. *J Gastroenterol Hepatol*, 27(6), 1078-1082. https://doi.org/10.1111/j.1440-1746.2011.06968.x.

[27] Yang JH, Kang HS, Lee SY, Kim JH, Sung IK, Park HS, Shim CS, Jin CJ. (2014). Recurrence of gastroesophageal reflux disease correlated with a short dinner-to-bedtime interval. *J Gastroenterol Hepatol*, 29(4), 730-735. https://doi.org/10.1111/jgh.12455.

[28] Chiba N, De Gara CJ, Wilkinson JM, Hunt RH. (1997). Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a

meta-analysis. *Gastroenterology*, 112(6), 1798-1810. https://doi.org/10.1053/gast.1997.v112.pm9178669.

[29] Bate CM, Keeling PW, O'Morain C, Wilkinson SP, Foster DN, Mountford RA, Temperley JM, Harvey RF, Thompson DG, Davis M, et al. (1990). Comparison of omeprazole and cimetidine in reflux oesophagitis: symptomatic, endoscopic, and histological evaluations. *Gut*, 31(9), 968-972. https://doi.org/10.1136/gut.31.9.968.

[30] Dean BB, Gano AD Jr, Knight K, Ofman JJ, Fass R. (2004). Effectiveness of proton pump inhibitors in nonerosive reflux disease. *Clin Gastroenterol Hepatol*, 2(8), 656-664. https://doi.org/10.1016/s1542-3565(04)00288-5.

[31] Vigneri S, Termini R, Leandro G, Badalamenti S, Pantalena M, Savarino V, Di Mario F, Battaglia G, Mela GS, Pilotto A, et al. (1995). A comparison of five maintenance therapies for reflux esophagitis. *N Engl J Med*, 333(17), 1106-1110. https://doi.org/10.1056/NEJM199510263331703.

[32] Inadomi JM, Jamal R, Murata GH, Hoffman RM, Lavezo LA, Vigil JM, Swanson KM, Sonnenberg A. (2001). Step-down management of gastroesophageal reflux disease. *Gastroenterology*, 121(5), 1095-1100. https://doi.org/10.1053/gast.2001.28649.

[33] Hirschowitz BI. (1991). A critical analysis, with appropriate controls, of gastric acid and pepsin secretion in clinical esophagitis. *Gastroenterology*, 101(5), 1149-1158. https://doi.org/10.1016/0016-5085(91)90062-p.

[34] Khan F, Maradey-Romero C, Ganocy S, Frazier R, Fass R. (2016). Utilisation of surgical fundoplication for patients with gastro-oesophageal reflux disease in the USA has declined rapidly between 2009 and 2013. *Aliment Pharmacol Ther*, 43(11), 1124-1131. https://doi.org/10.1111/apt.13611.

[35] Zimmermann CJ, Lidor A. (2021). Endoscopic and surgical management of gastroesophageal reflux disease. *Gastroenterol Clin North Am*, 50(4), 809-823.

https://doi.org/10.1016/j.gtc.2021.07.005.

[36] Gefen R, Marom G, Brodie R, Elazary R, Mintz Y. (2022). Complete vs partial fundoplication: a laboratory measurement of functionality and effectiveness. *Minim Invasive Ther Allied Technol*, 31(4), 635-641. https://doi.org/10.1080/13645706.2021.1878538.

[37] Pavlidis TE. (2001). Laparoscopic Nissen fundoplication. *Minerva Chir*, 56(4), 421-426.

[38] Cao Z, Cai W, Qin M, Zhao H, Yue P, Li Y. (2012). Randomized clinical trial of laparoscopic anterior 180° partial versus 360° Nissen fundoplication: 5-year results. *Dis Esophagus*, 25(2), 114-120. https://doi.org/10.1111/j.1442-2050.2011.01235.x.

[39] Iqbal A, Awad Z, Simkins J, Shah R, Haider M, Salinas V, Turaga K, Karu A, Mittal SK, Filipi CJ. (2006). Repair of 104 failed anti-reflux operations. *Ann Surg*, 244(1), 42-51. https://doi.org/10.1097/01.sla.0000217627.59289.eb.

[40] Peters MJ, Mukhtar A, Yunus RM, Khan S, Pappalardo J, Memon B, Memon MA. (2009). Meta-analysis of randomized clinical trials comparing open and laparoscopic anti-reflux surgery. *Am J Gastroenterol*, 104(6), 1548-1561. https://doi.org/10.1038/ajg.2009.176.

[41] Qu H, Liu Y, He QS. (2014). Short- and long-term results of laparoscopic versus open anti-reflux surgery: a systematic review and meta-analysis of randomized controlled trials. *J Gastrointest Surg*, 18(6), 1077-1086. https://doi.org/10.1007/s11605-014-2492-6.

[42] Broeders JA, Rijnhart-de Jong HG, Draaisma WA, Bredenoord AJ, Smout AJ, Gooszen HG. (2009