Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 May 12; 10(B):1991-1995.
https://doi.org/10.3889/oamjms.2022.9817
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Gastroenterohepatology*

Relationship of Gastroesophageal Flap Valve with Gastroesophageal Reflux Disease Assessed Based on GerdQ Scores and Endoscopic Images

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Edited by: Ksenija Bogoeva-Kostovska
Citation: Neilufar AF, Akil F, Daud NAS, Bakri S, Rasyid H, Kasim H, Aman AM, Seweng A. Relationship of Gastroesophageal Flap Valve with Gastroesophageal Reflux Disease Assessed Based on GerdQ Scores and Endoscopic Images. Open-Access Maced J Med Sci. 2022 May 12; 10(B):1991-1995. https://doi.org/10.3889/oamjms.2022.9817
Keywords: Gastroesophageal reflux disease; Gastroesophageal reflux disease questionnaire; Reflux esophagitis; *Helicobacter pylori*; Body mass index
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Received: 15-Apr-2022
Revised: 26-Apr-2022
Accepted: 02-May-2022

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

BACKGROUND: Gastroesophageal reflux disease (GERD) is a condition where reflux of stomach contents causes troublesome symptoms or complications. The gastroesophageal flap valve (GEFV) is one of the protective structures against esophageal reflux.

AIM: This study aimed to determine the relationship between GEFV, measured by GERD questionnaire (GerdQ) scores, and the endoscopic features of GERD patients.

METHODS: This observational cross-sectional study was performed at Wahidin Sudirohusodo Hospital Makassar from August 2021 to October 2021. The participants were GERD patients who met the inclusion criteria. They were diagnosed using GerdQ scores and endoscopic features based on the Los Angeles criteria. The GEFV was assessed using retroflection endoscopy according to Hill's criteria. Data analysis using SPSS version 25. The Kolmogorov–Smirnov test was used to assess data normality, along with the Chi-square test and calculation of odds ratio (OR). The results of the statistical tests were significant if $p < 0.05$.

RESULTS: This study included 100 GERD patients: 49 men and 51 women. They had a mean age of 40.5 ± 12.8 years and a mean body mass index of 22.4 ± 3.8 kg/m^2. Abnormal GEFV was a risk for a GerdQ score of ≥8 compared to <8 (OR 4.56; 95% CI 1.53–13.52). Both normal and abnormal GEFVs in esophagitis reflux were higher than in non-erosive reflux disease ($p = 0.943$).

CONCLUSION: Abnormal GEFV was a risk factor for GERD based on a GerdQ score of 8, at 4.56 times higher than with normal GEFV. No statistically significant relationship existed between GEFV and endoscopic images.

Introduction

Gastroesophageal reflux disease (GERD), which is commonly found in Western countries, has recently been reported to have an increased incidence in Asian countries [1]. Although it rarely causes death, GERD is associated with considerable morbidity and complications such as peptic stricture and Barrett's esophagus in up to 20% of cases. GERD is also a condition that can significantly impair quality of life, especially since it is accompanied by irritative bowel syndrome and psychological stress in 36% and 41% of patients, respectively, due to failure to respond to acid antisecretory therapy [2], [3].

Many tests are available to evaluate patients with suspected GERD, including questionnaire tests, proton-pump inhibitor trials, radiology, endoscopy, and impedance manometry. Some tests are sometimes unnecessary because the classic symptoms of heartburn and acid regurgitation are specific enough to identify reflux disease and initiate medical therapy. The GERD questionnaire (GerdQ) is an easy-to-use 6-item objective clinical questionnaire developed as a diagnostic tool for GERD in patients in primary facilities [4], [5], [6].

The pathogenesis of GERD is complex and results from an imbalance between the defensive factors that protect the esophagus (antireflux protection, esophageal acid clearance, and tissue resistance) and the aggressive factors of gastric reflux (gastric acidity, duodenal volume, and contents). The gastroesophageal flap valve (GEFV) is one of the protective structures against reflux of the esophagus and plays a role in the development of hiatal hernia as a pathophysiological factor that triggers reflux in GERD. Since gastroesophageal reflux is primarily caused by gastroesophageal junction (GEJ) incompetence,

the estimated GEJ opening based on retroflexed endoscopic examination can provide useful information in the evaluation of cases with suspected GERD [7], [8].

The GEFV in GERD has not been widely studied. In Indonesia, GEFV as a predictor of reflux and its relationship with GERD scores and endoscopic features have not been studied to date. This study aimed to investigate the distribution of GEFV in patients with suspected GERD and any relationship between GEFV and GERD incidence based on GerdQ score and GERD endoscopic appearance.

Methods

Research design

This was an observational cross-sectional study based on medical record data. The research was carried out at Dr. Wahidin Sudirohusodo Hospital Makassar, Indonesia, following a protocol approved by our institution's ethics committee (number: 546/UN4.6.4.5.31/PP36/2021). The study was carried out from August 2021 to October 2021. Our work is reported following the criteria of Strengthening the Reporting of Cohort Studies [9], [10].

The population of this study included all patients with a diagnosis of GERD who were outpatients or inpatients and underwent endoscopy at our institution. The research sample was taken from the population meeting the research inclusion criteria: Patients aged >18 years, with typical symptoms of GERD, who underwent esophagogastroduodenoscopy (EGD) examination, were not pregnant, and had no history of gastric surgery. In purposive sampling, the data were already available and taken according to the inclusion criteria.

A total of 100 patients were selected using purposive sampling. From the calculations obtained, a minimum sample size of 100 patients was identified. Clinical diagnosis of GERD can be made using the GerdQ questionnaire, according to the Diamond study [4]. A low chance of GERD is reflected by scores <8, and GERD is suggested by scores ≥8. Endoscopic examination of GERD patients evaluated the presence of complications in the esophageal mucosa distal to the lower esophageal sphincter (LES) in the form of mucosal damage, strictures, or Barrett's esophagus. Assessment of the severity of mucosal damage used the Los Angeles classification of Grades A, B, C, and D [8], [11].

The GEFV is a morphological component of the GEJ in the form of a musculomucosal fold created by the angle of entry of the esophagus into the stomach, extending 3–4 cm along the curve of the curvature minor [12]. The degree of GEFV and its significance on endoscopic retroflection were assessed according to Hill's classification [6], [13], [14]. We classified age according to the World Health Organization (WHO). The body mass index (BMI) was calculated using the following formula: Weight (kg)/[height (m)]^2 [15]. We classified BMI according to the WHO [8].

Data analysis

Data analysis was performed using SPSS version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA: IBM Corp.). The statistical analysis performed was descriptive statistical calculation and frequency distribution, using the Kolmogorov–Smirnov test to assess the normality of the data as well as the Chi-square test. The results of the statistical tests were significant if $p < 0.05$ was considered.

Results

Participant characteristics

Data analysis was performed on 100 GERD patients (Table 1) aged 19–77 years, with a mean age of 40.5 ± 12.8 years. The majority were aged <35 years (42; 42%). Based on BMI, with a mean of 22.4 ± 3.8 kg/m^2, 43% of participants had a normal weight, and 42% were overweight.

Table 1: Participant characteristics

Variable	n	%
Gender		
Female	51	51
Male	49	49
Age (years)		
35	42	42
35–50	37	37
>50	21	21
BMI (kg/m^2)		
<18.5	15	15
18.5–24.9	43	43
>25	42	42
H. pylori		
Positive	5	5
Negative	95	95
GerdQ score		
<8	17	17
≥8	83	83
GERD on endoscopy		
NERD	31	31
eGERD A	54	54
eGERD B	10	10
eGERD C	3	3
eGERD D	2	2
GEFV		
1	13	13
2	23	23
3	52	52
4	12	12

BMI: Body mass index, GerdQ: GERD questionnaire, GERD: Gastroesophageal reflux disease, GEFV: Gastroesophageal flap valve.

Helicobacter pylori were found in 5 participants (5%), and 95 (95%) had GERD without *H. pylori* infection. The majority of participants had a GerdQ score of ≥8 (83; 83%), and 17 (17%) had a GerdQ score of <8. The results of the EGD examinations showed that the most common GERD grade was GERD A (54;

54%), followed by non-erosive reflux disease (NERD; 31; 31%), GERD B (10; 10%), GERD C (3; 3%), and GERD D (2; 2%). Based on the distribution of GERD grades, 69 participants (69%) had erosive GERD.

The results of the retrograde EGD examinations showed that the most common GEFV degree was Grade 3 (52; 52%), followed by Grade 1 (13; 13%), Grade 2 (23; 23%), and Grade 4 (12; 12%). Therefore, 64 participants (64%) belonged to the abnormal GEFV group.

Relationship of GEFV with GerdQ score

Based on the degree of normal and abnormal GEFV, in normal GEFV, more subjects had a GerdQ score of ≥8 than <8 (66.7% vs. 33.2%). In abnormal GEFV, more subjects had a GerdQ score of ≥8 than <8 (92.2% vs. 7.8%). This difference was statistically significant (p = 0.001). Abnormal GEFV had a 4.56 times greater risk of a GerdQ score of ≥8 compared to <8. Abnormal GEFV was a risk for a GerdQ score of ≥8 compared to <8 odds ratio (OR) 4.56; 95% CI 1.53–13.52; Table 2.

Table 2: Relationship of GEFV with GerdQ score

GEFV	GerdQ score	
	<8	≥8
Normal		
n	12	24
%	33.3	66.7
Abnormal		
n	5	59
%	7.8	92.2

Chi-square test (p = 0.001); OR 4.56; 95% CI (1.53–13.52).

Relationship of GEFV with the endoscopic appearance

In both normal and abnormal GEFVs, the incidence of esophagitis reflux (ER) was greater than NERD (69.4% vs. 30.4% and 68.8% vs. 31.3%, respectively). This difference was not statistically significant (p > 0.05; Table 3).

Table 3: Relationship of GEFV with endoscopic features of GERD

GEFV	GERD end endoscopic picture	
	NERD	Esophagitis reflux
Normal		
n	11	25
%	30.6	69.4
Abnormal		
n	20	44
%	31.3	68.8

Chi-square test (p = 0.943).

Discussion

GERD is defined as a symptom or complication resulting from reflux of gastric contents into the esophagus or further. GERD can be further classified as the presence of symptoms without erosions on endoscopic examination (NERD) or symptoms of GERD in the presence of erosion ER [16]. The GEFV is a musculomucosal fold at the lower part of the GEJ, which is seen in the lowest curvature through retrograde endoscopy [12]. Reflux can be caused by disruption of the esophageal reflux protection system, including the GEFV. The GerdQ is one of the objective clinical questionnaires developed as an easy-to-use GERD diagnostic tool in primary care [5].

The GerdQ score indicates the severity of reflux complaints experienced by the patient. The GEFV is one of the protective anti-esophageal reflux structures and plays a role in the development of hiatal hernia as a pathophysiological factor that triggers reflux in GERD, so the GerdQ score increases along with the severity of the GEFV disorder.

This study found that the GerdQ score was significantly higher than the severity of GEFV (p = 0.001; OR 4.56; 95% CI 1.53–13.52). This is in line with Quach *et al*. (2018) [11] who found a higher percentage of a GerdQ of ≥8 in abnormal GEFV.

A previous study by Kaplan *et al*. [17] found a relationship between the Reflux Symptom Index Score, a questionnaire that can be used for laryngopharyngeal reflux, with GEFV. In the present study, a highly significant relationship existed between GEFV and GerdQ scores. Abnormalities of the GEFV are associated with reduced LES length and pressure, which can increase mechanical damage to the esophageal sphincter, in turn, increasing exposure to reflux, including acid, which causes heartburn [18], [19].

The first level of esophageal defense against acid damage, the antireflux barrier, is a complex anatomical region including the intrinsic LES, crural diaphragm, intra-abdominal location of the LES, pharyngoesophageal ligament, and GEFV [20]. The sphincter and valve work together and prevent strong reflux in normal situations. If the valve that normally feeds the sphincter gives way, in hernias, smooth muscle abnormalities may lead to loss of the GEFV and sphincter, then a hiatal hernia occurs [12], [20]. Acid is considered the main ingredient that refluxes into the esophagus and causes damage to the esophageal mucosa or symptoms of GERD. The acidic component of reflux is responsible for ER development and heartburn complaints [19].

Analyzing the relationship between GEFV and endoscopic images of GERD patients found that both normal and abnormal GEFVs had more ER than NERD (p = 0.943). In normal GEFV, the proportion of NERD was 30.6%, and ER was 69.4%. In abnormal GEFV, the proportion of NERD was 31.3%, and ER 68.8%. This result is not in line with the study by Quach *et al*. (2018), where the prevalence of abnormal GEFV also increased gradually among patients with dyspepsia and NERD [11]. Lin *et al*. (2006) [21] demonstrated a significantly higher proportion of abnormal GEFV in patients with ER than in those with NERD. A study by Pelechas *et al*. (2013) [22] showed a significant

relationship between the prevalence of mucosal damage and the degree of GEFV in 406 patients. Wu *et al*. (2019) [23] also found that abnormal GEFV was more common in patients with esophagitis.

Theoretically, more ER should occur in abnormal GEFV, but in this study, it was also found in normal GEFV. This may be since, in the normal GEFV group, many risk factors play a role, but unfortunately, these factors were not analyzed.

The relatively large sample size and different methods of data collection add to the strength of the study and allow the generalizability of its findings. However, recall bias, which is common in such studies, and the use of the GerdQ, which has not yet been validated in the studied population, are important limitations. Nonetheless, our findings highlight the high prevalence of GERD without *H. pylori* infection and its association with sociodemographic and lifestyle characteristics, which need to be validated by further research.

Our research suggestions are: (a) The GerdQ score is used to diagnose GERD by assessing the clinical course of reflux patients, but it cannot be used to diagnose GEFV, because many other factors cause a high GerdQ score. (b) Abnormal GEFV should be further treated to overcome GERD problems, especially in patients with a GerdQ score of ≥8.

Conclusion

Abnormal GEFV was a risk factor for GERD based on a GerdQ score of ≥8, at 4.56 times higher than normal GEFV. Although abnormal GEFV ER incidence was higher than in normal GEFV, ER incidence was also higher in normal GEFV. This was probably because other factors also played a role. No statistically significant relationship existed between GEFV and endoscopic images.

Acknowledgments

The authors would like to thank Muhammad Faruk, MD for his assistance in language polishing and formatting of this manuscript.

References

1. Shiota S, Singh S, Anshasi A, El-Serag HB. Prevalence of barrett's esophagus in Asian countries: A systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2015;13(11):1907-18. https://doi.org/10.1016/j.cgh.2015.07.050
PMid:26260107
2. Richter JE, Vaezi MF. Gastroesophageal reflux disease. In: Feldman M, Friedman LS, Brandt LJ, editors. Sleisenger Fordtran's Gastrointest, Liver Dis. 11th ed. Netherlands: Elsevier; 2020. p. 670-90.
3. Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. Gastroenterology. 2018;154(2):267-76. https://doi.org/10.1053/j.gastro.2017.07.045
PMid:28780072
4. Suzuki H, Matsuzaki J, Okada S, Hirata K, Fukuhara S, Hibi T. Validation of the GerdQ questionnaire for the management of gastro-oesophageal reflux disease in Japan. United Eur Gastroenterol J. 2013;1(3):175-83. https://doi.org/10.1177/2050640613485238
PMid:24917957
5. Jones R, Junghard O, Dent J, Vakil N, Halling K, Wernersson B, *et al*. Development of the GerdQ, a tool for the diagnosis and management of gastro-oesophageal reflux disease in primary care. Aliment Pharmacol Ther. 2009;30(10):1030-8. https://doi.org/10.1111/j.1365-2036.2009.04142.x
PMid:19737151
6. Jonasson C, Wernersson B, Hoff DA, Hatlebakk JG. Validation of the GerdQ questionnaire for the diagnosis of gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2013;37(5):564-72. https://doi.org/10.1111/apt.12204
PMid:23289763
7. Xirouchakis E, Kamberoglou D, Kalos D, Zambeli E, Doulgeroglou V, Tzias V. The effect of gastroesophageal flap valve appearance on the management of patients with symptoms of gastroesophageal reflux disease. Dig Dis Sci. 2009;54(2):328-32. https://doi.org/10.1007/s10620-008-0347-2
PMid:18600453
8. Kang MS, Il Park D, Oh SY, Yoo TW, Ryu SH, Park JH, *et al*. Abdominal obesity is an independent risk factor for erosive esophagitis in a Korean population. J. Gastroenterol Hepatol. 2007;22(10):1656-61. https://doi.org/10.1111/j.1440-1746.2006.04518.x
PMid:17845694
9. Darmadi S, Mappincara J, Hendarto I, Labeda RE, Lusikooy S, Sampetoding MI, *et al*. Profile of collagen prolines level of anterior rectus sheath tissue in indirect inguinal hernia: A cross-sectional study. Ann Med Surg. 2021;68:102546. https://doi.org/10.1016/j.amsu.2021.102546
PMid:34367633
10. Mathew G, Agha R, Albrecht J, Goel P, Mukherjee I, Pai P, *et al*. STROCSS 2021: Strengthening the reporting of cohort, cross-sectional and case-control studies in surgery, Ann Med Surg. 2021;72:103026. https://doi.org/10.1016/j.amsu.2021.103026
11. Quach DT, Nguyen TT, Hiyama T. Abnormal gastroesophageal flap valve is associated with high gastresophageal reflux disease questionnaire score and the severity of gastroesophageal reflux disease in vietnamese patients with upper gastrointestinal symptoms. J Neurogastroenterol Motil. 2018;24(2):226-32. https://doi.org/10.5056/jnm17088
PMid:29605978
12. Hill LD, Kozarek RA. The Gastroesophageal Flap Valve. J Clin Gastroenterol. 1999;28(3):194-7. https://doi.org/10.1097/00004836-199904000-00002
PMid:10192602
13. Muthusamy VR, Lightdale JR, Acosta RD, Chandrasekhara V, Chathadi KV, Eloubeidi MA, *et al*. The role of endoscopy in the management of GERD. Gastrointest Endosc.

2015;81(6):1305-10. https://doi.org/10.1016/j.gie.2015.02.021
PMid:25863867

14. Dai JY, Tapsoba J, Buas MF, Onstad LE, Levine DM, Risch HA, *et al*. A newly identified susceptibility locus near FOXP1 modifies the association of gastroesophageal reflux with Barrett's esophagus. Cancer Epidemiol Biomarkers Prev. 2015;24(11):1739-47. https://doi.org/10.1158/1055-9965.EPI-15-0507
PMid:26377193
15. Kariri AM, Darraj MA, Wassly A, Arishi HA, Lughbi M, Kariri A, *et al*. Prevalence and risk factors of gastroesophageal reflux disease in Southwestern Saudi Arabia. Cureus. 2020;12(1):e6626. https://doi.org/10.7759/cureus.6626
PMid:31966942
16. Hsu PI, Kim N, Goh KL, Wu DC. Diagnosis and management of gastroesophageal reflux disease. Gastroenterol Res Pract. 2013;2013:709620. https://doi.org/10.1155/2013/709620
PMid:24307894
17. Kaplan M, Tanoglu A, Erkul E, Kara M, Yazgan Y. Association of reflux symptom index scores with gastroesophageal flap valve status. Auris Nasus Larynx. 2014;41(6):543-7. https://doi.org/10.1016/j.anl.2014.05.006
PMid:24889495
18. Öberg S, Peters JH, DeMeester TR, Lord RV, Johansson J, Crookes PF, *et al*. Endoscopic grading of the gastroesophageal valve in patients with symptoms of gastroesophageal reflux disease (GERD). Surg Endosc. 1999;13(12):1184-8. https://doi.org/10.1007/PL00009617
PMid:10594262
19. Xiong LS, Chen MH, Lin JK, Hu PJ. Stratification and symptom characteristics of non-erosive reflux disease based on acid and duodenogastroesophageal reflux. J Gastroenterol Hepatol. 2008;23:290-5. https://doi.org/10.1111/j.1440-1746.2007.05152.x
20. Bui E, Harken AH. Gastroesophageal reflux disease. In: Feldman M, Friedman LS, Brandt LJ, editors. Abernathy's Surg. 7th, 11th ed. Philadelphia, PA: Elsevier; 2018. p. 200-4. https://doi.org/10.1016/B978-0-323-47873-1.00045-0
21. Lin BR, Wong JM, Chang MC, Liao CC, Yang PM, Jeng JH, *et al*. Abnormal gastroesophageal flap valve is highly associated with gastroesophageal reflux disease among subjects undergoing routine endoscopy in Taiwan. J Gastroenterol Hepatol. 2006;21:556-62. https://doi.org/10.1111/j.1440-1746.2005.04003.x
PMid:16638098
22. Pelechas E, Azoicăi D. Gastroesophageal reflux disease: Epidemiological data, symptomatology and risk factors. Rev Medico Chir Soc Med Nat Iaşi. 2013;117(1):183-8.
PMid:24505912
23. Wu W, Li L, Qu C, Wang M, Liang S, Gao X, *et al*. Reflux finding score is associated with gastroesophageal flap valve status in patients with laryngopharyngeal reflux disease: A retrospective study. Sci Rep. 2019;9:15744. https://doi.org/10.1038/s41598-019-52349-5
PMid:31673091