

Comparison of Endoscopic Findings with Gastroesophageal Reflux Disease Questionnaires (GerdQ) and Reflux Disease Questionnaire (RDQ) for Gastroesophageal Reflux Disease in Medan

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ABSTRACT

Background: There are many questionnaires that have been developed to diagnose gastroesophageal reflux disease (GERD), i.e. reflux disease questionnaire (RDQ), and the recently developed, gastroesophageal reflux disease questionnaires (GerdQ). In this study, we tried to compare GerdQ and RDQ in terms of sensitivity and specificity to diagnose GERD and its relationship with endoscopic findings.

Method: This study was a cross sectional analytical study. Subsequently, all the subjects were evaluated using the GerdQ and RDQ, then underwent esophagogastroduodenoscopy examination. The severity of endoscopically observed reflux esophagitis was graded with the Los Angeles classification. All endoscopy was performed by well-trained doctor.

Results: A total of 85 patients were examined, 34 (40%) patients had reflux esophagitis at endoscopy examination, including 15 (44.1%) cases of grade A, 11 (32.3%) cases of grade B, 4 (11.8%) cases of grade C, and 4 (11.8%) cases of grade D. Analysis study using sensitivity, specificity, and receiver operating characteristic (ROC) test showed that GerdQ had sensitivity (49%), specificity (91%), and an area under the ROC of 0.701 ($p = 0.002$). RDQ had sensitivity (24%), specificity (91%), and an area under the ROC of 0.574 ($p = 0.253$). Taking 11 as the cut off point for GerdQ, a maximal sensitivity of 73.5%, specificity of 82.4%, and an area under the ROC of 0.779 was achieved.

Conclusion: GerdQ and RDQ can be used to help diagnose GERD, but GerdQ is more superior than RDQ in diagnosing GERD. A multi-center study with larger samples is needed to determine the best GerdQ's cut off point in Indonesia.

Keywords: gastroesophageal reflux disease, gastroesophageal reflux disease questionnaires (GerdQ), reflux disease questionnaire (RDQ), reflux esophagitis, endoscopy

ABSTRAK

Latar belakang: Ada banyak kuesioner yang dikembangkan untuk mendiagnosis gastroesophageal reflux disease (GERD), sebagai contoh reflux disease questionnaire (RDQ), dan yang baru-baru ini dikembangkan, gastroesophageal reflux disease questionnaires (GerdQ). Dalam studi ini, kami mencoba untuk membandingkan

GerdQ dan RDQ dalam hal sensitivitas dan spesifisitas dalam diagnosis GERD dan hubungannya dengan hasil endoskopi.

Metode: Penelitian ini merupakan penelitian analitik potong lintang. Selanjutnya, semua subjek penelitian akan dievaluasi menggunakan GerdQ dan RDQ, kemudian menjalani pemeriksaan esophagogastroduodenoscopy. Tingkat keparahan refluks esofagitis yang diamati melalui endoskopi dinilai dengan klasifikasi Los Angeles. Pemeriksaan endoskopi dilakukan oleh dokter terlatih.

Hasil: Sebanyak 85 pasien diperiksa, 34 (40%) pasien menderita refluks esofagitis pada pemeriksaan endoskopi, termasuk 15 kasus dengan grade A (44,1%), 11 kasus dengan grade B (32,3%), 4 kasus dengan grade C (11,8%) dan 4 kasus dengan grade D (11,8%). Data dianalisis menggunakan sensitivitas, spesifisitas, dan uji receiver operating characteristic (ROC) menunjukkan bahwa GerdQ memiliki sensitivitas (49%), spesifisitas (91%), dan daerah di bawah ROC 0,701 ($p = 0,002$). RDQ memiliki sensitivitas (24%), spesifisitas (91%), dan daerah di bawah ROC 0,574 ($p = 0,253$). Dengan mengambil nilai 11 sebagai titik potong dari GerdQ, GerdQ dapat mencapai sensitivitas 73,5%, spesifisitas 82,4% dan daerah di bawah ROC dari 0,779.

Simpulan: GerdQ dan RDQ dapat digunakan untuk membantu mendiagnosis GERD, tetapi GerdQ lebih unggul dari RDQ dalam mendiagnosis GERD. Penelitian multi-center dengan jumlah sampel yang lebih besar diperlukan untuk menentukan nilai titik potong GerdQ di Indonesia.

Kata kunci: penyakit refluks gastroesophageal, gastroesophageal reflux disease questionnaires (GerdQ), reflux disease questionnaire (RDQ), refluks esofagitis, endoskopi

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a disorder marked by reflux of gastric contents to the esophagus that cause troublesome symptoms (esophageal and extra-esophageal) and complications (i.e. Barrett esophagus).^{1,2,3} The prevalence of reflux esophagitis in Western Countries show a mean value ranging between 10-20%, while in Asia, the prevalence ranges between 3-5%. However, Indonesia has no complete epidemiological data. The study conducted by Syam et al showed there is an increased prevalence of esophagitis from 5.7% in 1997 to 25.18% in 2002. Upper gastrointestinal endoscopy (UGIE) is considered the gold standard for establishing the diagnosis GERD with erosive esophagitis.⁴

There are many questionnaires that have been developed to diagnose GERD, i.e. questionnaire for the diagnosis of reflux esophagitis (QUEST), frequency scale for the symptoms of GERD (FSSG), reflux questionnaire (ReQuest), reflux disease questionnaire (RDQ), and the recently developed, gastroesophageal reflux disease questionnaires (GerdQ).⁵

GerdQ is an instrument that was developed by Jones et al, to assist in establishing the diagnosis of GERD. GerdQ consists of 6 questions including reflux symptoms, dyspepsia, and drugs to alleviate symptoms. GerdQ had been validated in Indonesia language.^{1,4,6,7} Yu Bai et al reported that GerdQ may be used for diagnosis of GERD, but a low GerdQ score

can't exclude the possibility of reflux esophagitis.⁸ RDQ is a questionnaire that was developed by Shaw et al, to assess the frequency and severity of heartburn, regurgitation, and dyspeptic complaints and to facilitate the diagnosis of GERD in primary care.⁹ The RDQ is useful in primary care for screening and diagnosis of GERD.^{10,11,12} In this study, we try to compare GerdQ and RDQ in terms of sensitivity and specificity in diagnosing GERD and its relationship with endoscopic findings.

METHOD

This study was a cross sectional analytical study on eighty five consecutive patients with dyspepsia-related symptoms with or without heartburn and/or regurgitation that were admitted to endoscopy units at Adam Malik General Hospital and Permata Bunda Hospital, Medan, Indonesia from October-December 2015. Inclusion criteria are stated as followings: male or female aged ≥ 18 years old, patients with dyspepsia related symptoms with or without heartburn or regurgitations, willing to be recruited in the study, and signed the informed consent. While the exclusion criteria were defined as subjects with liver and kidney disorders, upper gastrointestinal (GI) bleeding, severe hematologic malignancies (e.g. aplastic anemia), severe heart disease (e.g. myocardial infarction and other heart disease), malignancy, pregnancy, surgical history of upper GI, postoperative reflux esophagitis,

and patients in NSAIDs therapy. All patients gave informed consent and the study was approved by the local ethics committee.

On admission, each patient gave and asked to sign informed consent paper. The baseline information of patients' demographics, history taking, physical examination, and laboratory tests (i.e. routine hematology, liver and kidney function tests, blood glucose level, and abdominal ultrasonography) were recorded. Subsequently, all the subjects were evaluated using the GerdQ and RDQ, then underwent esophagogastroduodenoscopy examination. The severity of endoscopically observed reflux esophagitis is graded with the Los Angeles classification. All endoscopy was performed by well-trained doctor.

GerdQ contain 6 questions, including reflux symptoms, dyspepsia, and medications used to alleviate the symptoms. GerdQ evaluated using the symptoms' frequency score, recorded in days (0 day, 1 day, 2-3 days, 4-7 days). The cut-off point was defined as 8. GerdQ had been validated in the Indonesian language.^{6,7} RDQ contains 12 questions, including heartburn, regurgitation, and dyspeptic symptoms. RDQ evaluated using the symptoms' frequency (did not have, less than 1 day a week, 1 day a week, 2-3 days a week, 4-6 days a week, daily) and severity (did not have, very mild, mild, moderate, moderately severe, severe) score.^{3,6,9} The cut off point was defined as 12.¹¹ For the purpose of the study, the authors translated the RDQ into the Indonesian language.

All data were analyzed with SPSS for windows version 22. Categorical data were described as number and continuous data as mean \pm SD. Sensitivity and specificity were counted. Data was analyzed using receiver operating characteristic (ROC) curve and Youden index, $p < 0.05$ was considered as statistically significant.

RESULTS

During the study, a total of 85 patients were examined, consisted of 50 males (58.8%) and 35 females (41.2%). The basic characteristics of these patients are shown in Table 1. The mean age of these subjects was 45.09 ± 13.44 years old. The highest number of age group was from the age group of 31-49. The majority of subject's employment status was housewife (37.7%) and self-employed (31.8%). The majority of the subjects' nutritional status was overweight and obese (51 patients, 60%). Overall, 34 (40%) patients had reflux esophagitis at endoscopy

examination, including 15 cases of grade A (44.1%), 11 cases of grade B (32.3%), 4 cases of grade C (11.8%), and 4 cases of grade D (11.8%). The GerdQ and RDQ scores in cases with positive endoscopic findings were higher than those with negative findings. The more severe the Los Angeles classification, the higher were the GerdQ and RDQ scores (Table 2).

Table 1. Basic characteristics of the study population

Characteristics	Endoscopy		Total
	Non-reflux esophagitis	Reflux esophagitis	
Sex			
Male	29 (56.9%)	21 (61.8%)	50 (58.8%)
Female	22 (43.1%)	13 (38.2%)	35 (41.2%)
Age (years)			
< 30	8 (15.7%)	8 (23.5%)	16 (18.8%)
31-49	23 (45.1%)	12 (35.3%)	35 (41.2%)
50-69	19 (37.2%)	13 (38.2%)	32 (37.6%)
> 70	1 (2%)	1 (3%)	2 (2.4%)
Educational Status			
Primary school	14 (27.5%)	12 (35.3%)	26 (30.6%)
Secondary school	27 (52.9%)	18 (52.9%)	45 (52.9%)
College	10 (19.6%)	4 (11.8%)	14 (16.5%)
Occupation			
Self employed	12 (23.5%)	15 (44.1%)	27 (31.8%)
Farmer	4 (7.8%)	3 (8.8%)	7 (8.2%)
Housewife	20 (39.2%)	12 (35.3%)	32 (37.7%)
Civil servant	9 (17.7%)	2 (5.9%)	11 (12.9%)
Others	6 (11.8%)	2 (5.9%)	8 (9.4%)
Nutritional status			
Underweight	3 (5.8%)	1 (2.9%)	4 (4.7%)
Normal	16 (31.4%)	14 (41.2%)	30 (35.3%)
Overweight	13 (25.5%)	13 (38.2%)	26 (30.6%)
Obese	19 (37.3%)	6 (17.7%)	25 (29.4%)
Total	51 (60%)	34 (40%)	85 (100%)

Table 2. Relationship between endoscopic classification with GerdQ and RDQ score

Los Angeles classification	n	Gastroesophageal reflux disease questionnaires (GerdQ)		Reflux disease questionnaire (RDQ)	
		Mean	Standard deviation	Mean	Standard deviation
Non-reflux Esophagitis	51	7.86	2.96	18.65	9.56
Grade A	15	10.73	2.76	24.40	11.84
Grade B	11	12.36	4.25	30.55	11.83
Grade C	4	16.25	0.50	34.25	5.62
Grade D	4	16.75	1.89	43.25	6.24

Among 85 patients with reflux esophagitis, 57 (67%) patients' GerdQ score was higher than 8, while it was below 8 in the other 28 (33%) patients. In 57 patients with GerdQ ≥ 8 , 31 (54.4%) patients were found to have reflux esophagitis during upper endoscopy, but the remaining 45.6% patients (26/57) were negative at endoscopy. Among 85 patients with reflux esophagitis, 70 (82.4%) patients' RDQ score was higher than 12, while it was below 12 in the other 15 (17.6%) patients. For 70 patients with RDQ ≥ 12 , 31 (44.3%) patients were found to have reflux

esophagitis during upper endoscopy, but the remaining 55.7% patients (39/70) were negative at endoscopy. The diagnostic accuracy of GerdQ and RDQ for reflux esophagitis was listed in Table 3.

Table 3. Diagnostic accuracy of GERDQ and RDQ

	Sensitivity	Specificity	PPV	NPV	PLR	NLR
GERDQ	49%	91%	89%	54%	5.56	0.56
RDQ	24%	91%	80%	44%	2.67	0.84

NLR: negative likelihood ratio; NPV: negative predictive value; PLR: positive likelihood ratio; PPV: positive predictive value.

Analysis study using ROC test showed that GerdQ had an area under the ROC of 0.701 ($p = 0.002$) and RDQ had an area under the ROC of 0.574 ($p = 0.253$). Based on the ROC results (Figure 1), we concluded that GerdQ is more superior than RDQ in diagnosing reflux esophagitis ($p = 0.002$ vs. 0.253).

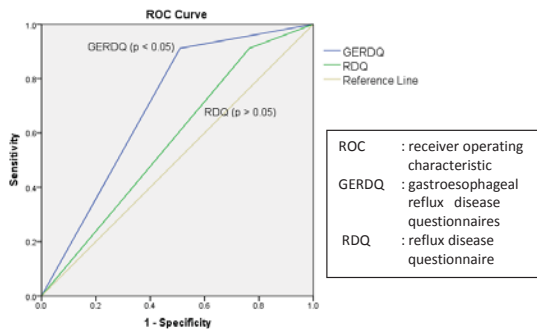


Figure 1. Comparison of ROC curve between GerdQ and RDQ

We calculated the Youden index (Figure 2) to determine the best GerdQ's cut off point to get better sensitivity and specificity also a larger area under the ROC. There were two cut off points (11 and 12) that had similar Youden index (0.558) and an area under the ROC of 0.779. We took 11 as the cut off for GerdQ because we got a better sensitivity of 73.5% and a specificity of 82.4%.

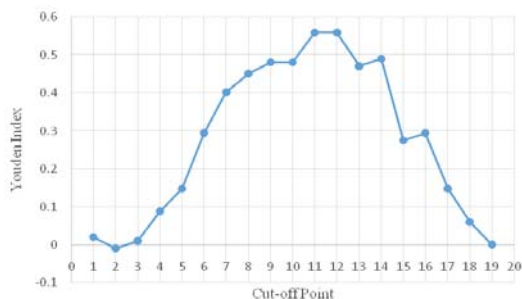


Figure 2. Youden index for GerdQ's cut-off point

DISCUSSION

The subjects' mean age in this study was 45.09 ± 13.44 years old, which is considered a productive age group. In addition, the 31-49 and 50-69 age groups were the majority group age that was diagnosed with reflux esophagitis. Our results were comparable to those reported by Jia et al (42.5 ± 15.2) and Zou et al (49.5 ± 12.3).^{13,14} Most patients with reflux esophagitis had nutrition status above normal (55.88%). These results are in line with the reports of many studies, one of them is the study by Sijabat et al that reported the increased body mass index was a risk factor for GERD.^{4,15}

The prevalence of reflux esophagitis increases with age, which is in accordance with Yu bai et al and Ma XQ et al.^{8,16} But, the prevalence of reflux esophagitis in this study (40%) was higher than those of previous studies. Rosaida et al reported that the prevalence of reflux esophagitis among Malaysian was 9.0%. In Indonesia, Syam et al showed that there is an increase prevalence of esophagitis from 5.7% in 1997 to 25.18% in 2002.¹⁸ This difference might be because this study was not population based study and there is an increasing prevalence of GERD in Indonesia.¹⁹

For patients with refluxesophagitis, the majority of them (76.4%) were suffering from grade A or grade B lesion. This result is in accordance with the Sijabat et al's study, which reported that grade A lesion was the most frequent lesion of reflux esophagitis.¹⁵ The mean GerdQ and RDQ score in patients without reflux esophagitis was 7.86 and 18.65 respectively, whereas in patients with reflux esophagitis, the GerdQ and RDQ scores were higher than those of without reflux esophagitis. Moreover, the more severe there flux esophagitis, the higher the GerdQ and RDQ scores. All of the data showed that there was a difference of GerdQ and RDQ scores between patients with GERD and without GERD. Therefore, the GerdQ and RDQ can be used as screening tools for GERD.

In sensitivity and specificity test, GERDQ (49%) has the higher sensitivity compared to RDQ (24%). Also on the receiver operator curve (ROC) test, GerdQ (0.701; $p = 0.002$) has the better area of under the ROC than RDQ (0.574; $p = 0.253$). Therefore, we concluded that GerdQ is more superior than RDQ in diagnosing GERD. This result was in line with Jones et al GerdQ's superiority is because GerdQ was a combination of validated questionnaires used in the Diamond study, so that improved the sensitivity and specificity of diagnosis.^{4,6}

Because GerdQ was more superior than RDQ, we

want to maximize the sensitivity, specificity, and the area under ROC. Therefore, we calculated the Youden index to determine the best cut off point of GerdQ. With an increase in the cut off point of GerdQ, the sensitivity increased but the specificity was reduced. Taking 11 as the cut off point of GerdQ for GERD, we got a maximal Youden index of 0.588, which implied a maximal sensitivity of 73.5%, specificity of 82.4% and area under ROC of 0.779. However, we need more studies with larger samples and a multi-center study to determine the best cut off point for GerdQ in Indonesia.

CONCLUSION

GerdQ and RDQ can be used to help diagnose GERD, but GerdQ is more superior than RDQ in diagnosing GERD. A multi-center study with larger sample is needed to determine the best GerdQ's cut-off point.

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