Use of the Montreal Global Definition as an Assessment of Quality of Life in Reflux Disease

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Abstract

Background—According to the Montreal Group's Classification, GERD develops when the reflux of stomach contents causes *troublesome* symptoms and/or complications such as esophagitis. The characteristic GERD symptoms included in this statement are retrosternal burning and regurgitation. *Troublesome* is meant to imply that these symptoms impact on the well-being of affected individuals; in essence, quality of life. We sought to determine whether heartburn and regurgitation symptoms would be characterized as more *troublesome* in those with confirmed pathologic acid reflux. A second purpose was to assess how well *troublesome* scores correlated with the results of a validated, disease-specific quality of life instrument.

Methods—We interviewed subjects who underwent EGD with 48 hour wireless esophageal pH testing off PPI therapy. Esophagitis on EGD or pH < 4.0 for 4.5% of time over the two day period was considered positive for acid reflux. We assessed how *troublesome* their symptoms of heartburn and regurgitation were using separate 0–100 visual analog scales. We then asked them to complete the Quality of Life in Reflux and Dyspepsia (QOLRAD) 25- item questionnaire.

Results—We identified 67 patients (21M, 46 F); mean age 47.8 ± 15.6 years. Forty (59.7%) had an EGD or pH study positive for acid reflux. Overall 35/40 (87.5%) complained of either heartburn or regurgitation. There was no difference (P=0.80) in heartburn VAS *troublesome* ratings for those with (54.0 ± 43.9) and without (56.7 ± 37.6) confirmed acid reflux. The same was true for regurgitation VAS *troublesome* ratings (P=0.62). Likewise, mean QOLRAD scores did not differ between those with and without confirmed acid reflux by pH or EGD (4.5 ± 1.7 vs. 4.3 ± 1.7; p =0.61). There was a moderately strong inverse correlation between patient self-rated VAS *troublesome* scores for both heartburn and regurgitation with each dimension (Emotional Distress, Sleep Disturbance, Eating Problems, Physical/Social Functioning, and Vitality) of the QOLRAD (p < 0.05 for all comparisons). In regression analysis, both heartburn and regurgitation *troublesome* ratings were associated with the overall QOLRAD score independent of pH data, frequency of reflux episodes, age, and gender.

Conclusions—Use of the term *troublesome* in the Montreal Classification is supported by our findings. It correlates well with the results of a validated disease-specific quality of life instrument. Use of heartburn and regurgitation VAS may serve as accurate measures of the burden of reflux disease on patients. It is likely that these scales will not have sufficient discriminate value to identify individuals with pathologic acid reflux from those with negative studies.

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Introduction

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders in the western world with a reported prevalence ranging between 10–20%. [1] The symptoms associated with GERD, mainly heartburn and regurgitation, are among the most common complaints encountered by general physicians and specialists. [2] Several surveys have suggested that 20–44% of the adult population experience heartburn at least once a month, and 7–10% may report this symptom as often as daily. [3,4] In the United States, GERD symptoms have placed a significant strain on the health care system evidenced by a three-fold increase in primary care visits and almost five-fold increase in specialist visits between 1990 and 2001.[5] Overall this has represented an annual direct and indirect cost calculated to be more than US $14 billion. [6] The impact of GERD extends beyond its economic burden. Studies indicate that these patients experience significantly impaired health-related quality of life compared with the general United States population. [7,8] GERD-related symptoms have considerable impact on measures of pain, emotional well being, and social function. When compared to other chronic diseases such as moderate angina and mild congestive heart failure, patients with GERD score lower in quality of life (QOL) assessments. [9]

A number of guidelines for the evaluation and management of GERD have been published despite the absence of a universally accepted definition for this disorder.[10–14] To overcome this, the Montreal Consensus Group consisting of 44 experts from 18 countries, used a modified Delphi process to develop a globally acceptable definition and classification of GERD.[15] The primary objective of the Group was to simplify disease management in order to promote collaborative research across cultures and languages. [15] The group defined GERD (the "Montreal Global Definition of GERD") as a condition which develops when the reflux of stomach content causes *troublesome* symptoms, characteristically retrosternal burning (often labeled as heartburn) and regurgitation. The panel also specified that symptoms become *troublesome* when they adversely affect an individual's well-being. The Group had hoped to achieve a patient-centered endpoint which was easily understood and readily measured in clinical practice. The word *troublesome* was carefully chosen by the Group because it is a term that is inferred to correlate with quality of life (QOL) and depicts the negative impact of these symptoms on a patient's well-being.

Physicians and health-services researchers have increasingly recognized the importance of QOL measures in understanding the burden of illness and the outcomes of medical treatments for many diseases including GERD. [16] Therefore the Montreal Consensus Group's recommendations have important implications. Unfortunately, to date, validation of the use of the term *troublesome* as a reliable measure of QOL in GERD has not been published. In addition, there exists no data on the correlation between the term *troublesome* and objective measures of acid reflux using endoscopy and pH testing.

Therefore this study had two specific aims. The primary aim was to assess how well *troublesome* reflux and regurgitation scores correlated with the results of a validated, GERD-specific QOL instrument. A secondary aim was to provide endoscopic and pH data for patients complaining of *troublesome* symptoms of heartburn and/or regurgitation.

Methods

Study population

The setting for this study was the endoscopy unit at our hospital. Between June 2010 and September 2011, all patients undergoing upper endoscopy along with 48-hour catheter-free esophageal pH testing (BRAVO pH Monitoring System, Given Imaging, Duluth, GA) for the evaluation of upper gastrointestinal symptoms were eligible for study inclusion. In order to be included, patients had to be older than 18 years and off therapy with proton pump inhibitors (PPI) for at least 7 days prior to the pH study. Sedated upper endoscopy was performed using an Evis Exera II Olympus GIF-Q180 high definition gastroscope (Olympus America, Inc, Center Valley, PA). During the exam the distance from the incisors to the squamocolumnar junction was measured three times with the stomach fully deflated. BRAVO pH capsules were placed 6 cm above the squamocolumnar junction. Patients were considered to have acid reflux disease if either of the following conditions were met: (1) Upper endoscopy demonstrated one or more mucosal breaks in the esophageal mucosa consistent with reflux esophagitis or; (2) 48 hour wireless esophageal pH monitoring yielded a $pH < 4.0$ for 4.5% of time on either study day. Results for pH data were further stratified into supine and upright reflux. For either day, in our lab, a $pH \ 4$ for 8.0 % of time is considered abnormal in the upright position and a value 3.0 % of time is abnormal in the supine position. "Reflux Episodes" were defined as discrete episodes of esophageal acidification to a $pH \ 4$ lasting for 5 minutes. All qualifying patients were requested to complete two questionnaires within 6 months after the completion of their endoscopy/pH study.

Questionnaire 1 – Troublesome assessment

This questionnaire addressed the presence of symptoms and how *troublesome* they were for subjects. Using the exact terminology proposed by the Montreal Consensus Group, "Heartburn" was defined as a burning sensation in the chest behind the breastbone, and "Regurgitation" as the presence of food or liquid coming back into the subject's food pipe after eating or lying down. Quantification of *troublesome* was performed by using separate 0–100 visual analog scales (VAS) for each symptom. Definitions for symptoms were provided immediately above their respective scales. The scales were exactly 10 cm in length and patients were asked to mark along the scale how *troublesome* their symptoms were over the prior two weeks. A score of "100" (i.e. 10 cm) indicated most *troublesome*. Patients also reported how many days per week they experienced symptoms.

Questionnaire 2 - Quality of Life assessment

One of the most extensively used instruments to assess QOL in patients presenting with upper gastrointestinal symptoms is the Quality of Life in Reflux and Dyspepsia (QOLRAD) scale.[17] This validated instrument has 25 items with five dimensions including physical/ social functioning, emotional distress, sleep disturbance, food and drink problems and vitality. Responses are based on a 7-point Likert scale (1–7) which is used to assess how often and how much the item reflected the feelings of the patient with respect to the degree of distress. Total QOLRAD score is calculated as the mean of each dimension. There is no threshold or specific value to consider a poor quality of life but rather lower scores indicate more severe impact on daily functioning or degree of distress. A mean score is calculated using the overall items in each dimension, which helps determine the functional effect of GERD on the patient and any clinically relevant change after an intervention. [18,19] Previous validation studies showed baseline QOLRAD scores for adults in the range of 5.3 for mild cases and scores of 3.6 for severe symptoms. [18,19] The study was approved by the Institutional Review Board at Temple University Hospital.

Statistical analysis

Descriptive data included frequency distributions and the assessment of mean values along with standard deviation. Patient data was assessed for normality prior to the performance of inferential statistics. Comparison of mean values between independent categorical variables was performed using Student's t-tests. Stratified bivariate correlations were performed for the comparison of rank variables using Spearman methodology and the data was expressed with the correlation coefficient and corresponding p value. Linear regression with backward elimination methodology was performed to identify factors associated with the total QOLRAD score. We used IBM SPSS Statistics 19 (IBM, Somers, NY) for all statistical calculations. A 2-tailed P value 0.05 was considered statistically significant.

Results

Patients

We identified 67 patients who met the inclusion criteria during the study period. There were 46 (68.7%) females and 21 (31.3%) males. The mean age of the study group was 47.8 ± 15.6 (range 19–84) years. Additional characteristics of the study group are shown in Table 1.

Endoscopic and pH Findings

Forty subjects (59.7%) had a positive study for acid reflux. This included 15 patients with an endoscopy demonstrating esophagitis. Five of the fifteen (33%) had a demonstrable hiatal hernia. There were 32 patients with an abnormal pH study on either day 1 or day 2. Nine were abnormal for day 1, eleven for day 2, and the remainder abnormal for both days. There were 7 patients with both a positive endoscopy and pH study. For those patients with an abnormal pH study, the mean % time pH 4 on day 1, day 2, and overall was, 12.6 ± 19.3, 9.6 ± 4.8 and 10.0 ± 6.1 respectively. For the subgroup with an abnormal pH study, the % upright reflux time on days 1 and 2 were 11.9 ± 7.5 and 11.5 ± 8.4 respectively. Supine reflux % time was 6.3 ± 8.8 and 4.5 ± 5.6 respectively. The mean number of Reflux Episodes lasting longer than 5 minutes was 5.8 ± 4.5 and 4.4 ± 4.0 for days 1 and 2.

Heartburn and Regurgitation Symptoms

Of the 67 patients included, 10 (14.9%) complained of heartburn alone and denied other symptoms. They complained of heartburn a mean of 4.8 ± 1.4 days per week. There were 13 (19.4%) patients who complained of regurgitation solely and denied heartburn. They experienced regurgitation a mean of 4.9 ± 2.5 days per week. There were 37 (55.2%) patients who stated they had both heartburn and regurgitation according to the definitions of the Montreal Group. There were 7 (10.4%) patients who underwent upper endoscopy and pH testing who did not complain of heartburn or regurgitation but rather other symptoms including bloating (n=2), early satiety (n=1), and dysphagia (n=4). Five (71.4%) had either a positive endoscopy or pH study.

Relationship between Troublesome Scores and Endoscopic/pH Data

The mean heartburn *troublesome* score for the entire group was 56.1 ± 40.5. Eighteen (26.9%) patients selected a heartburn *troublesome* score of 0 and thirteen (19.4%) selected 100 (maximal score). The mean regurgitation *troublesome* score for the entire group was 49.6 ± 39.1. Fifteen (22.4%) had a regurgitation *troublesome* score of 0 and eleven (16.4%) selected a score of 100. Visual analog *troublesome* scores for both heartburn and regurgitation were not associated with endoscopic findings. For those with normal endoscopic findings (n=52) the mean *troublesome* score was actually higher than for those with an endoscopy demonstrating reflux changes although this did not meet statistical significance (59.8 ± 38.8 vs. 43.7 ± 45.0; p= 0.18). Likewise, *troublesome* scores for

regurgitation also did not differ for those with a normal vs. abnormal endoscopy (45.0 ± 38.8 vs. 65.6 ± 37.2; p = 0.07) although the trend was in the expected direction. Table 2 shows the correlation between *troublesome* scores for heartburn and regurgitation and their relationship to pH findings. As shown in the table, the only variable to correlate with both heartburn and regurgitation *troublesome* scores was the number of reflux episodes patients experienced on day 1 of the pH study.

Relationship between Troublesome Scores and QOLRAD

The mean values for each of the QOLRAD dimensions were as follows: physical/social functioning = 4.9 ± 1.8, emotional distress = 4.4 ± 1.9, sleep disturbance = 4.7 ± 1.9, food and drink problems = 4.1 ± 1.8 and vitality = 4.3 ± 1.9. The mean overall QOLRAD score for the entire group was 4.4 ± 1.7 demonstrating a moderate impact on QOL due to symptoms. Mean QOLRAD scores did not differ between those with and without confirmed acid reflux by pH or EGD (4.5 ± 1.7 vs. 4.3 ± 1.7; p =0.61). Table 3 summarizes the relationship between VAS *troublesome* scores for heartburn and regurgitation and each domain of the QOLRAD instrument. As can be seen, there was a stronger relationship between these two questionnaires than was seen with the pH/endoscopy results. In fact, *troublesome* scores for both heartburn and regurgitation correlated significantly with each domain of the QOLRAD. Because increased *troublesome* scores usually lead to a lower quality of life, the relationship between these two scales is inversed.

We performed a linear regression using the total QOLRAD score as the dependent variable and imputed the following independent variables; age, % time pH < 4 (overall, supine, and upright), total reflux episodes > 5 minutes, Heartburn *troublesome* score, and Regurgitation *troublesome* score. As shown in Table 4, after sequential backward elimination of variables with a p> 0.10 at each model run, those variables associated with total QOLRAD score included age, % time pH <4, Heartburn *troublesome* score, and Regurgitation *troublesome* score. This suggests that both *troublesome* scales are associated with overall QOLRAD scores independent of pH data, frequency of reflux episodes, and age of the patient. We repeated the analysis imputing gender as a potential effect modifier. There was a < 5% change in the standardized β for each parameter suggesting that these findings were not modified by the gender of the patient.

Discussion

This study shows that the proposed term *troublesome* is a useful descriptor to evaluate the symptoms experienced by patients with GERD. Our results show a moderate correlation between the self-rated *troublesome* scores for heartburn and regurgitation symptoms with each of the dimensions of the QOLRAD, a quality of life instrument specific for GERD. This finding supports the Montreal Group's decision to use this term. The term *troublesome* can be easily translated into a number of languages and describes the negative impact of these symptoms from a patient's standpoint. It highlights the importance of a patient-centered evaluation of symptoms and the use of clear and simple wording while addressing this condition.

Despite not being the primary objective of the Montreal Group, correlation of simple VAS measurements with a validated disease-specific QOL instrument might have an important impact in the management of patients with GERD. Beyond severity, how symptoms affect the lives of patients enables clinicians to make more suitable and tailored decisions regarding further diagnostic work up and treatment decisions.[20] Our rationale for examining the term *troublesome* is that it assesses the impact of a symptom on several domains including psychological well-being, energy level, interpersonal relationships, and others. This concept overlaps significantly with QOL. Generally, health-related QOL instruments

are perceived by clinicians as too complicated, time-consuming, and impractical to use on a frequent basis. Additionally it has been suggested that the terms "heartburn" and "regurgitation" are confusing for many patients. [4,21] Our questionnaire, which provided a description of each symptom and a visual analog scale adapted from the Montreal Global Definition of GERD, may quantify symptoms in substantially more patients. Use of our questionnaire provides a simplified tool, easy to use at the bedside. It may also provide a guide to therapeutic decisions or the evaluation of treatment response.

It is not surprising that *troublesome* scores for heartburn and regurgitation correlated poorly with the results of endoscopy and pH studies. Our findings indicate that heartburn and regurgitation *troublesome* scores are highly sensitive but not specific symptoms for acid reflux. Additionally, and similarly to the QOLRAD scores, *troublesome* scores failed to show sufficient discriminate value to identify those individuals with and without acid reflux. This agrees with previous reports that have suggested that the impact of reflux symptoms on health-related QOL does not depend on the presence of mucosal damage because symptom severity in patients with non-erosive GERD is similar to those patients with erosions. [2] Moayyedi, using likelihood analysis showed that patients with dominant heartburn have a little over 50% chance of having GERD as defined by 24-hour esophageal pH study.[22] There is also a poor correlation between the occurrence of symptoms and the timing of reflux episodes, suggesting for many cases a temporal dissociation. [23] Additionally, there is a considerable fraction of patients with typical reflux symptoms and normal pH test results that respond to antisecretory medication. [24] Our results may have been influenced by prior treatment with PPI therapy which may have healed esophageal erosions prior to endoscopy. An additional limitation in our ability to correlate pH and endoscopic findings with symptoms is the modest sample size of our study. A type II error for these comparisons cannot be excluded.

Our results contrast with previous reports, where the symptoms of heartburn and regurgitation have been characterized as highly specific but insensitive[25]; providing positive and negative predictive values in the ranges 20–60% and 90–95% respectively. [26,27] Our study differed because we included results from not only high definition upper endoscopy but also from 48 hour esophageal pH monitoring. Of note, the Montreal Group identified 40 studies reporting the prevalence of heartburn in GERD but none of them had correlated the findings with both endoscopy and pH monitoring. [15] Use of impedance technology and the identification of weakly acidic reflux may have improved the correlation between symptoms and objective measures of reflux.

Finally it is worth noting that this study has several limitations other than those previously listed. First, included patients were asked to recall their symptoms during the time of their diagnostic procedures which was months prior to completing the questionnaires. This could introduce recall bias for the obtained data. However, we would expect the bias to be non-differential. Additionally, as mentioned, the sample size of this study was relatively modest and our findings need to be replicated by other groups with larger samples. Finally, patients included in this study represent a unique group and their results may not be applicable to the entire GERD population. Specifically, patients included where those referred for pH testing at a tertiary care facility, many of whom had an unsatisfactory response to PPI therapy in the past. The potential for sample selection bias needs to be avoided in future studies.

In summary, the results of this study indicate that the term *troublesome* satisfactorily describes the impact of heartburn and regurgitation on the QOL of patients diagnosed with GERD. This supports the terminology chosen by the Montreal Consensus Group. However the *troublesome* scale for the mentioned symptoms, as well as the QOLRAD score has insufficient discriminate value to identify individuals with evidence of acid reflux from

those without this finding. Further research is required on GERD patients in other settings such as from the community or those presenting to primary care physicians. If validated, a simple questionnaire has been developed which correlates with the QOL of patients with GERD. This may assist in the diagnostic evaluation and treatment of these patients.

Acknowledgments

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Table 1

Characteristics of the 67 patients included in study.

Age, y (SD) (range)	47.8 (15.6) (19–84)
Female (%)	46 (68.7)
Body mass index (SD) (range)	27.8 (8.2) (15.8–57.1)
Current smoking (%)	11 (16.4)
Disturbed sleep by GERD (%)	43 (64.2)
At least daily PPI Use (%)	57 (85.1)
Use rescue antacids (%)	27 (40.3)
Supplemental H2 blocker	30 (44.8)
Referring Physician (%)	
Primary Care	10 (14.9)
Gastroenterologist	57 (85.1)

Table 2

Bivariate Correlations between Troublesome Scores and pH Findings

Variable	Heartburn Troublesome* Score		Regurgitation Troublesome* Score	
	Correlation (r)**	P	Correlation (r)	P
Total: % Time pH < 4.0				
Day 1	0.19	0.14	0.24	0.07
Day 2	−0.11	0.39	0.21	0.11
Supine: % time pH < 4.0				
Day 1	0.14	0.28	0.09	0.50
Day 2	0.14	0.28	0.15	0.25
Upright: % time pH < 4.0				
Day 1	0.16	0.22	0.29	0.03
Day 2	0.12	0.36	0.18	0.16
Total Reflux Episodes				
Day 1	0.26	0.05	0.29	0.03
Day 2	0.03	0.85	0.14	0.28

*
Troublesome scores range from 0–100.

**
Bivariate correlations adjusted for age and gender.

Table 3

Bivariate Correlations between Troublesome Scores and QOLRAD Scores

QOLRAD Domain [*]	Heartburn Troublesome[†] Score		Regurgitation Troublesome Score	
	Correlation (r) [**]	P	Correlation (r)	P
Emotional Distress	−0.282	0.030	−0.328	0.010
Sleep Disturbance	−0.331	0.011	−0.417	0.001
Food and Drink Limits	−0.396	0.002	−0.332	0.010
Physical	−0.363	0.005	−0.350	0.006
Vitality	−0.320	0.013	−0.327	0.011
Total QOLRAD	−0.359	0.005	−0.373	0.003

QOLRAD = Quality of Life in Reflux and Dyspepsia

[*] Responses use a 7-point Likert scale to assess how often and how much the item reflected the feelings of the patient with respect to the degree of distress. Lower scores indicate more severe impact on daily functioning or degree of distress.

[**] Bivariate correlations adjusted for age and gender.

[†] Troublesome scores range from 0–100. Higher scores means symptom more troublesome.

Table 4

Linear regression output using total QOLRAD score as dependent variable.

| Variable* | Unstandardized Coefficients | | | 95% Confidence Interval for Slope | |
	Slope	Std. Error	p	Lower Bound	Upper Bound
Constant	6.816	.819	.000	5.173	8.459
Heartburn Troublesome Score	−.012	.005	.031	−.022	−.001
Regurgitation Troublesome Score	−.014	.006	.019	−.026	−.002
Age	−.032	.014	.026	−.060	−.004
% Time pH < 4.0**	.092	.045	.047	.001	.183

*
Output from second model after elimination of total reflux episodes for Day 1 and Day 2 (p > 0.1 in first regression model).

**
For both days of pH study.