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Research Paper

The statistical investigation between stress factors and GERD symptoms

Noboru Saito[1]*, Hiroshi Saito[2] and Kaoru Nomura[2,3]

[1]Department of General Medicine, Dokkyo Medical University Saitama Medical Center, Saitama, 343-8555, Japan.
[2]Department of General Medicine, Tokyo Women's Medical University School of Medicine, Tokyo, 162-8666, Japan.
[3]Department of General Medicine, Otsuki Municipal Central Hospital,Yamanashi, 401-0015, Japan.

*Corresponding author. E -mail: no-saito@dokkyomed.ac.jp

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ABSTRACT

This study was a statistical investigation to elucidate the correlation between stress factors and the symptoms of acid reflux-related diseases, represented by gastroesophageal reflux disease (GERD). We used the frequency scale for the symptoms of GERD (FSSG) for the assessment of reflux esophagitis (RE) and the Public Health Research Foundation (PHRF) stress check list for the assessment of stress. The FSSG is a questionnaire with 12 questions, with 7 related to symptoms of gastroesophageal reflux (reflux), and 5 to symptoms of dysmotility-like dyspepsia (dysmotility). The PHRF Stress Check List rates 4 stress factors, anxiety/uncertainty, tiredness/physical responses, autonomic symptoms and depression/feelings of inadequacy. We obtained the consent of potential subjects with an FSSG total score ≥ 8, treated their acid-related disease symptoms and evaluated the relationship between stress factors and GERD symptoms using the FSSG and PHRF Stress Check List. A correlation was suggested between dysmotility symptoms and both tiredness/physical responses and autonomic symptoms. A correlation was seen in males between the FSSG reflux score and tiredness/physical responses. In particular, a consistent correlation was seen between autonomic symptoms and the dysmotility score. A correlation was also seen between the FSSG dysmotility score, the PHRF Stress Check List and age, and a negative correlation between the dysmotility score and depression/feelings of inadequacy. We found a correlation between the PHRF Stress Check List and the FSSG scale. Our results suggest the possibility that age and the PHRF Stress Check List may be used to perform risk classification of gastroesophageal reflux disease, in particular, the symptoms of dysmotility-like dyspepsia (FSSG dysmotility score).

Keywords: Stress factors, gastroesophageal reflux disease (GERD), stress check list, FSSG scale, dysmotility.

INTRODUCTION

The reported prevalence of acid reflux-related disease, as represented by gastroesophageal reflux disease (GERD) and reflux esophagitis (RE), has increased in recent years. The cause of this increase may be increased acid secretion in the Japanese population, related to lifestyle changes and diet Westernization (Fujimoto, 2004). Reflux of gastric acid into the esophagus gives rise to upper abdominal and chest pain and discomfort (GERD symptoms) and is reported to cause marked impairment of the patient's quality of life (QOL) (Shimazu et al., 2005).

At present, the treatment of acid reflux-related diseases, such as RE and GERD, mainly comprises of proton pump inhibitors (PPIs) and inhibitors of gastric acid secretion. PPIs are reported to improve the symptoms of RE and GERD, as well as the endoscopic findings (Ponce et al., 2004).

In the Japanese clinical setting, outpatients presented with symptoms affecting multiple regions, such as heartburn, upper abdominal and chest pain and discomfort, back pain, or cough, are dealt with by the

Department of General Medicine. In the past, the majority of patients experienced reflux of gastric acid associated with age-related laxity of the diaphragm in the vicinity of the lower esophageal sphincter (LES).

In recent years, however, GERD symptoms are reported by a variety of age groups, including young people in their twenties and hard working men and women in their thirties and forties, suggesting the involvement of stress factors. Many people in our modern society are under stress in one form or another and this may cause increased acid secretion, including during sleep. This makes it important to identify and ameliorate any psychological etiological factors and reduce any stress factors.

In practice, in many cases it is possible to control symptoms to avoid any interference with daily activities through the amelioration of psychological factors in addition to pharmacotherapy, typically with PPIs.

There have been few studies that have elucidated the relationship between stress factors and the onset or prolongation of GERD symptoms. In this study, we aim to statistically demonstrate a correlation between stress factors and the symptoms of GERD, including RE.

MATERIALS AND METHODS

Patients attending the Department of General Medicine were administered the frequency scale for the symptoms of GERD (FSSG) and developed for the detection of acid reflux-related diseases. Informed consent to participate in this study was obtained from patients with a total FSSG score ≥ 8. After treatment for their acid-related symptoms, they were reassessed using the FSSG (Kusano et al., 2004) and the Public Health Research Foundation (PHRF) Stress Check List (Imazu et al., 2006).

Table 3 shows the FSSG is used in the diagnosis of RE. The FSSG is a questionnaire comprising 12 questions, for each question, subjects rate the symptom frequency on a 5 point scale from 0 to 4 (never=0; occasionally=1; sometimes=2; often=3; or always=4). A score of ≥ 8 is diagnostic for GERD. The lowest possible score is 0 points, and the highest possible score 48.

Of the 12 questions in the FSSG, 7 were related to symptoms of gastroesophageal reflux (reflux) and 5 to symptoms of dysmotility-like dyspepsia (dysmotility). Calculation of the separate subtotals yields a more symptom-specific diagnosis. The maximum reflux score is 28 points, while that for dysmotility is 20 points.

The PHRF Stress Check List is used in the diagnosis of stress (Table 4). The Check List is a questionnaire comprising 24 questions, with 6 questions pertaining to each of 4 factors. Each question is rated on a 3 point scale from 0 to 2, with a maximum possible score of 12 points for each factor and a maximum possible total score of 48. The 4 stress factors are anxiety/uncertainty, tiredness/physical responses, autonomic symptoms and depression/feelings of inadequacy.

Statistical analyses

The statistical analyses were:

1) Analysis parameters;
a) FSSG scores;
b) Upper gastrointestinal symptom questionnaire score;
c) PHRF Stress Check List score;
d) Subject demographics.

Statistical analyses were performed using SAS 9.3 (SAS Institute, Cary NC) software.

Analytical methods

Statistical analyses of continuous variables were performed using Wilcoxon's signed rank test and intergroup comparisons were made using the Mann-Whitney U test. Comparisons of non-continuous variables were made using Fisher's exact test (χ^2 test). A p value < 0.05 was considered statistically significant.

Informed consent was obtained from all subjects in accordance with the Helsinki Declaration of the World Medical Association, and the study protocol was approved by the Ethics Committee of Tokyo Women's Medical University.

RESULTS

Before performing analyses of each assessment parameter, a basic analysis of each variable was conducted. We then collated the data for males and females. Comparison of differences between males and females in each variable, using the two sample t-test and 95% confidence limits between mean values (both using the Satterthwaite approximation), revealed no significant differences between groups except for greater age in females.

Thereafter, the Pearson correlation coefficient was calculated and the non-parametric Spearman correlation coefficient for the FSSG scores and PHRF Stress Check List scores (Table 1). The results show correlation coefficients ≥ 0.4 for the tiredness/physical responses and autonomic symptoms vs. the dysmotility score and total FSSG score. Then, we made the same calculations for males and females. In males, a correlation was seen between the reflux score and tiredness/physical responses.

Subsequently, we assigned age, gender and the PHRF Stress Check List scores as explanatory variables and performed analysis of variance (ANOVA) with the FSSG total score as the objective variable. Statistically significant results were seen for age and gender and a near statistically significant result was also seen for the PHRF total score. In other words, the FSSG total score decreased on average 2 points for every 10 year increase in age, the mean score for females was 4.4 points higher than that for

Table 1: Pearson correlation coefficientfor the FSSG scores and PHRF Stress Check List scores.

Age	Age	Reflux	Dysmotility	FSSG total score
	1.000	**-0.121**	**-0.362**	**-0.256**
Anxiety/uncertainty	-0.255	-0.015	0.161	0.070
Tiredness/physical responses	-0.138	0.268	0.353	0.345
Autonomic symptoms	-0.175	0.293	**0.486**	**0.427**
Depression/feelings of inadequacy	-0.316	0.063	0.161	0.120
PHRF total score	-0.285	0.188	0.364	0.300

FSSG: frequency scale for the symptoms of GERD; **PHRF:** Public Health Research Foundation.

Table 2: Analysis of variance of the FSSG total score as the object variable.

Parameter	Estimate	SE	t-value	p-value	LCL	UCL
Intercept	17.3	4.0	4.37	<0.0001	9.4	25.3
Age	-0.2	0.1	-2.92	0.0048	-0.3	-0.1
Female	3.9	1.9	2.07	0.0426	0.1	7.7
Anxiety/uncertainty	0.0	0.4	0.05	0.9597	-0.7	0.8
Tiredness/physical responses	0.5	0.4	1.54	0.1288	-0.2	1.3
Autonomic symptoms	1.2	0.4	2.92	0.0047	0.4	2.0
Depression/feelings of inadequacy	-0.8	0.4	-1.88	0.0648	-1.6	0.1

SE: Standard error of the mean, **LCL:** Lower confidence limit, **UCL:** Upper confidence limit.

Table 3: The FSSG questionnaire [frequency scale for the symptoms of gastroesophageal reflux disease (GERD)]

Question	Frequency				
	Never	Occasionally	**Sometines**	Often	Always
Do you get heartburn?		1	2	3	4
Does your stomach get bloated?		1	2	3	4
Does your stomach ever feel heavy after meals?		1	2	3	4
Do you sometimes subconsciously rub your chest with your hands?		1	2	3	4
Do you ever feel sick after meals?		1	2	3	4
Do you get heartburn after meals?		1	2	3	4
Do you have an unusual (for example, burnibg sensation in your throat?		1	2	3	4
Do you feel full while eating meals?		1	2	3	4
Do some things get stuck when you swallow?		1	2	3	4
Do you get bitter liquid (acid) coming up into your throat?		1	2	3	4
Do you burp alot?		1	2	3	4
Do you get heartburn if you bend over?		1	2	3	4

males, and the FSSG total score increased on average 2 points for every 10 point increase in the PHRF total score.

Furthermore, a similar analysis including the separate factors of the PHRF Stress Check List in the model as explanatory variables (Table 2) was conducted. The results showed a strong correlation between autonomic symptoms and the FSSG total score. A negative correlation was suggested between depression/feelings of inadequacy and the FSSG total score.

Similar analyses with the FSSG reflux score as the objective variable was then conducted. Although the results were not statistically significant, a tendency was seen towards a correlation between autonomic symptoms and the FSSG reflux score.

Finally, similar analyses with the FSSG dysmotility score as the objective variable was conducted. The results showed a non-significant tendency towards a correlation between age, gender and the PHRF total score with the dysmotility score. The dysmotility score decreased as age increased, scores were higher in females, and the higher the PHRF total score the higher was the dysmotility score. Analysis of individual stress factors revealed that the dysmotility score increased as the autonomic symptom scorenn increased, nwhereas ndysmotility symptoms were

Table 4:. Public Health Research Foundation (PHRF) Stress Check List.

Question	Never	Sometimes	Frequent
My eyes get tired easily	0	1	2
I feel dizzy	0	1	2
It suddenly becomes hard to breathe	0	1	2
I am aware of my heartbeat	0	1	2
I experience chest pain	0	1	2
My head is fuzzy (heavy)	0	1	2
I do not feel like eating even my favourite foods	0	1	2
I experience back pains	0	1	2
I get tired easily	0	1	2
I have trouble getting to sleep	0	1	2
I am irritable	0	1	2
I grt pain and stiffness in my neck and shoulders	0	1	2
I am always fatigue, no matter how much rest I get	0	1	2
I get angry over little things	0	1	2
I have no confidence in my work	0	1	2
When I do something, I worry it will not go well	0	1	2
I cannot believe in other people	0	1	2
I have no hope for the future	0	1	2
I have trouble making decisions	0	1	2
I cannot put my full effort into things	0	1	2
I feel overwhelmed by the weight of work	0	1	2
Everywhere there are people I do not get along with	0	1	2
Whether I survive an environmental change I am afraid	0	1	2
I want you to evaluate my effort fairly	0	1	2

reduced as the depression/feelings of inadequacy score increased. The correlations between the remaining two stress factors and the dysmotility score were relatively weak.

DISCUSSION

Many medical conditions have common ages of onset, but the onset of GERD can occur at any age from the young and the elderly (Kleinman et al., 2006; Murray et al., 2007; Amano et al., 2001). In females, symptom severity tends to agree with the endoscopic findings more than in males (Lin et al., 2004). An epidemiological study of reflux diseases identified an increased prevalence in Japan and other East Asian countries (Hongo and Shoji, 2003). Established diagnostic modalities for GERD include endoscopic assessment (Lundell et al., 1999). X-ray examinations and pH monitoring (Ohno and Kogure, 2005; Wong et al., 2005).

The depth and complexity of acid reflux-related diseases can be seen from reports of non-erosive reflux disease (NERD), with strong symptoms but minor or absent endoscopic findings (Joh et al., 2007; Miwa et al., 2004; Xiong et al., 2008). One study identified the duration and severity of heartburn symptoms and obesity, as risk factors for the severity of erosive esophagitis in *Helicobacter pylori* negative patients with GERD (EI-Seragand, 2002). A meta-analysis also identified obesity as a risk factor for GERD and its complications (Hampel et al., 2005).

In the analysis setting, dysmotility-like dyspepsia symptoms as the objective variable, a significant tendency to correlation was seen with age, gender and the PHRF total score. As age increased, the dysmotility score decreased, the mean score was higher in females and the higher the PHRF total score, the higher the dysmotility score. Looking at individual stress factors, the higher the autonomic symptoms score, the higher was the dysmotility score, whereas the higher the depression/feelings of inadequacy score, the lower the dysmotility score. Possible interactions between factors were also examined.

We found an interaction between age and gender, but none between autonomic symptoms and depression/feelings of inadequacy, suggesting a need for caution in the interpretation of age and gender as explanatory variables. For example, the reason that a significant correlation was seen with gender may be different ages for the males and females, and the reason a

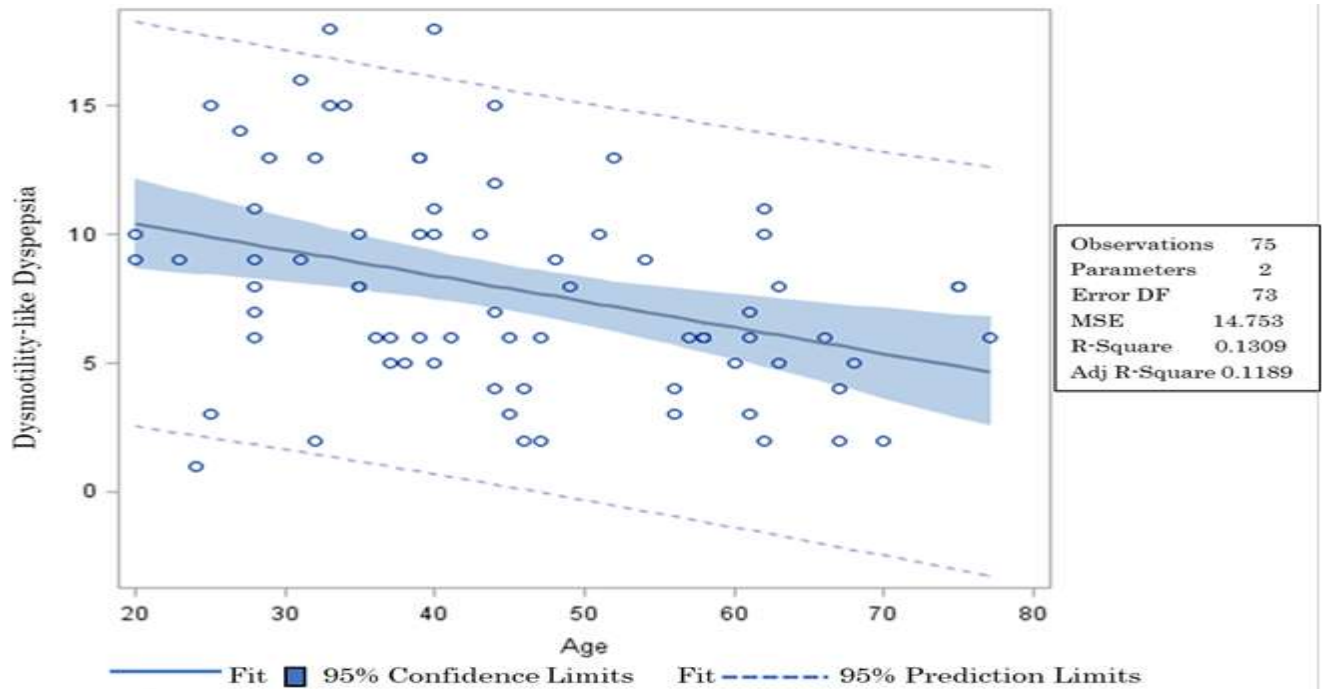

Figure 1: Correlation between age and dysmotility.

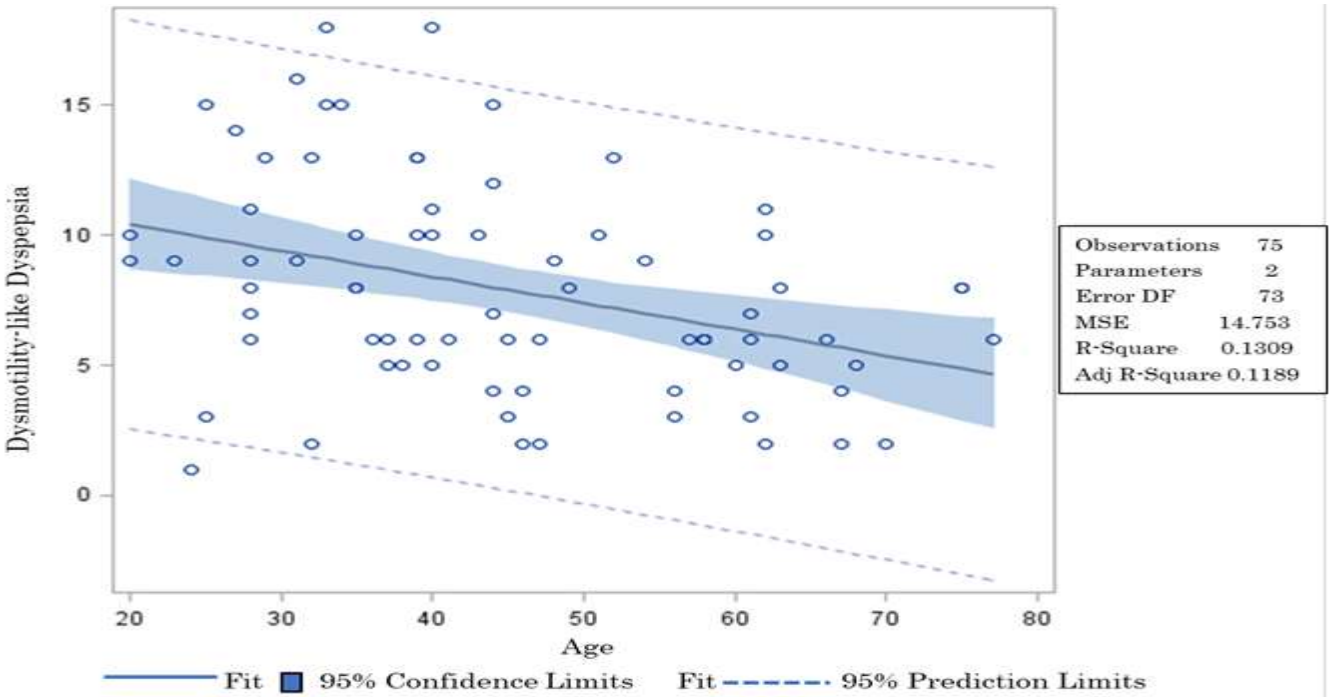

Figure 2: Correlation between age and depression/feelings of inadequacy.

significant correlation was seen with age may be different genders in the different age groups.

Interestingly, ANOVA of the dysmotility score with depression/feelings of inadequacy as the sole explanatory variable yielded an inverse relationship that did not reach statistical significance. This was thought to be due to a complex interaction between age and depression/feelings of inadequacy, where a high depression/feelings of inadequacy score ⇔lower age⇔high depression/feelings of inadequacy score (Figures 1 and 2). Furthermore, in view of the correlation between autonomic symptoms and each of the other factors, each of the aforementionrd

factors were considered as a set when we talk about their correlations with dysmotility-like dyspepsia symptoms.

The results of this study indicate a correlation between the PHRF Stress Check List and the FSSG, in particular, a consistent correlation was observed between autonomic symptoms and dysmotility-like dyspepsia symptoms. Of the FSSG subscales, the correlation between the reflux scale and the PHRF total score was generally weak, whereas a correlation was seen between the dysmotility scale, both age and the PHRF total score. The inverse relationship between depression/feelings of inadequacy and the dysmotility score is worthy of note in making clinical assessments.

Our results suggest the possibility that, in particular for dysmotility-like dyspepsia symptoms, age and the PHRF Stress Check List can be used to conduct risk classification. If in future studies factors with a strong correlation to reflux symptoms can be identified, the clinical applications of questionnaires will broaden further. We anticipate with pleasure the results of further studies in this field.

Conclusions

Possible correlations between GERD and stress factors using the FSSG and the PHRF Stress Check List was investigated. The results suggest a correlation between tiredness/physical responses and autonomic symptoms and dysmotility-like symptoms. In males, a correlation was seen between the FSSG reflux score and tiredness/physical responses.

A correlation between the PHRF Stress Check List and the FSSG was demonstrated in particular a consistent correlation between autonomic symptoms and dysmotility-like dyspepsia symptoms. A correlation was seen between the FSSG dysmotility score and age and the PHRF total score, whereas a negative correlation was seen with depression/feelings of inadequacy. Accordingly, it is possible that age and the PHRF total score may be used for risk classification for patients presenting with symptoms of GERD.

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