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Observational Study

Causative factors of discomfort in esophagogastroduodenoscopy: A large-scale cross-sectional study

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Abstract

BACKGROUND

It is important to reduce patient discomfort in esophagogastroduodenoscopy. Remedial measures can be taken to alleviate discomfort if the causative factors are determined; however, all the factors have not been elucidated yet.

AIM

To clearly determine the factors influencing discomfort in transoral esophagogastroduodenoscopy using a large-size cross-sectional study with readily available data.

METHODS

Consecutive patients who underwent screening transoral esophagogastroduodenoscopy consecutively between August 2017 and October 2017 at a health check-up center were included. Discomfort was evaluated using a face scale between 0 and 10 with a 6-level questionnaire. Univariate and multiple regression analyses were performed to investigate the factors related to the discomfort in esophagogastroduodenoscopy. Univariate analysis was performed in both the unsedated and sedated study groups. Age, sex, height, body mass index, smoking status, alcohol intake, hiatal hernia, history of gastrectomy, biopsy during examination, Lugol's solution usage, administration of butylscopolamine with/without a sedative (pethidine, midazolam, or both), endoscope model, history of endoscopy, and endoscopists were considered as possible factors of discomfort.

RESULTS

Finally, 1715 patients were enrolled in this study. Overall, the median discomfort score was 2 and the interquartile range was 2-4. High discomfort (score ≥ 6) was recorded in 18% of the participants. According to univariate analysis, in the

checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

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unsedated group, young age ($P < 0.001$), female sex ($P < 0.001$), and no history of endoscopy ($P < 0.001$) were factors associated with increased discomfort. Significant differences were also noted for height ($P = 0.007$), smoking status ($P = 0.003$), and endoscopists ($P < 0.001$). In the sedation group, young age ($P < 0.001$), female sex ($P < 0.001$), and no history of endoscopy ($P = 0.004$) were associated with increased discomfort; additionally, significant differences were found in smoking status ($P < 0.001$), type of sedation ($P < 0.001$), and endoscopists ($P = 0.027$). There was also a marginal difference due to alcohol intake ($P = 0.055$). Based on multiple regression analysis, young age, female sex, less height, current smoking status, and presence of hiatal hernia [regression coefficients of 0.08, $P < 0.001$ (for -1 years); 0.45, $P = 0.013$; 0.02, $P = 0.024$ (for -1 cm); 0.35, $P = 0.036$; and 0.34, $P = 0.003$, respectively] were factors that significantly increased discomfort in esophagogastroduodenoscopy. Alternatively, sedation significantly reduced discomfort and pethidine (regression coefficient: -1.47, $P < 0.001$) and midazolam (regression coefficient: -1.63, $P = 0.001$) significantly reduced the discomfort both individually and in combination (regression coefficient: -2.92, $P < 0.001$). A difference in the endoscopist performing the procedure was also associated with discomfort.

CONCLUSION

Young age, female sex, and smoking are associated with esophagogastroduodenoscopy discomfort. Additionally, heavy alcohol consumption diminished the effects of sedation. These factors are easily obtained and are thus useful.

Key words: Esophagogastroduodenoscopy; Discomfort; Smoking; Alcohol; Pethidine; Endoscopy

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Core tip: It is essential to reduce discomfort in esophagogastroduodenoscopy. The present study clearly identified the factors associated with discomfort in esophagogastroduodenoscopy using a large-size cross-sectional study. Young age, female sex, and current smoking were identified as the contributive factors. Smoking status was a newly identified predictor of this study. Furthermore, heavy alcohol consumption was noted to diminish the effect of the sedative(s). These factors are useful because they can be easily obtained, and we can take remedial measures for reducing discomfort.

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INTRODUCTION

Esophagogastroduodenoscopy often causes discomfort in patients. Discomfort due to the endoscope contributes to a negative experience and reduces the patient's satisfaction^[1,2]. Therefore, it is important to reduce discomfort as much as possible. Sedation is mainly considered as a method to reduce such discomfort; however, due to the cost and risk of complications, the consensus is to perform endoscopy without sedation in appropriately selected patients^[3]. To identify the patients who are likely to have marked discomfort, so that they can be considered for sedation, the predictive factors of discomfort must be ascertained. In previous studies, young age^[4-7], female sex^[4,5,8,9], anxiety before the examination^[4,5,6,9], and pharyngeal sensitivity^[6,7] were identified as factors that increased the discomfort of transoral esophagogastroduodenoscopy; however, all factors have not yet been elucidated. Most previous studies have conducted investigations only in several hundred subjects, which is a relatively small sample. The aim of this study was to elucidate the

contributing factors of discomfort in transoral esophagogastroduodenoscopy by a large-scale cross-sectional study, using easily available information from a regular endoscopy examination practice.

MATERIALS AND METHODS

Ethical considerations

This study was reviewed and approved by the Institutional Review Board of Kameda Medical Center. Since this was a retrospective observational study, using already existing data, and did not include invasive interventions, the requirement for informed consent from the study participants was waived by the Institutional Review Board. However, written informed consent for endoscopy was obtained at the time of the procedure. The study protocol was published on the hospital's website. This study's methods are in accordance with the Japanese "Ethical Guidelines for Medical and Health Research Involving Human Subjects".

Study population and methods

All consecutive patients who had undergone screening transoral esophagogastroduodenoscopy at a health check-up center associated with a general hospital between August 2017 and October 2017 were included. The discomfort experienced by the patients during examination was evaluated using a questionnaire subsequent to either completion of the examination or recovery from sedation. Originally, the questionnaires were intended for the improvement of hospital services to the patients; the questionnaire results and medical records of the patients were utilized for this study. Accordingly, participants with inadequate responses in the questionnaire were excluded. In order to increase the statistical accuracy of this study, the data was collected from the largest sample size possible.

In preparation for endoscopy, dimethicone (Barugin antifoam solution; Kaigen Pharmaceutical Co., Ltd.; Osaka, Japan) containing pronase (PronaseMS; Kaken Pharmaceutical Co., Ltd.; Tokyo, Japan) and sodium bicarbonate (Yoshida Pharmaceutical Co., Ltd.; Tokyo, Japan) were administered orally. For topical pharyngeal anesthesia, 8% lidocaine spray (Xylocaine Pump Spray 8%; Aspen Japan Co., Ltd.; Tokyo, Japan) was administered. The decision to administer an antispasmodic agent depended on the endoscopist; when administered, intravenous injection of 10 mg butylscopolamine (Scopolamine butylbromide; Nichi-Iko Pharmaceutical Co., Ltd.; Tokyo, Japan) was used. Sedatives were administered upon the request of the patients and with the permission of the doctor; accordingly, an intravenous injection of pethidine (Takeda Pharmaceutical Company Ltd.; Tokyo, Japan) was predominantly used, sometimes in combination with midazolam (Sandoz Co., Ltd.; Tokyo, Japan); however, midazolam was rarely used alone. Sedation was induced prior to scope insertion. Patients expected to drive were not administered any sedatives, even upon request. The endoscope used either the GIF-PQ260, GIF-Q260, or GIF-H290 (Olympus Corporation, Tokyo, Japan). The number of endoscopists who conducted the examination was 27. The esophagus, stomach, and partial duodenum were endoscopically observed. The mouthpiece for endoscopic examination had a tube capable of aspirating saliva continuously.

The questionnaire was distributed to the patients at a different location from the endoscopy unit, by staff other than the ones who performed the endoscopy. Discomfort was evaluated on a face scale of 0 to 10 on a 6-level questionnaire (Figure 1).

Statistical analysis

Since the discomfort scores had a non-normal distribution, the median and interquartile ranges were calculated for all cases. In addition, the proportion of high discomfort (score ≥ 6) was calculated. Age, sex, height, body mass index, smoking status, alcohol intake, hiatal hernia, history of gastrectomy, biopsy performed during examination, administration of Lugol's solution, administration of butylscopolamine with/without a sedative (pethidine, midazolam, or both), endoscope model, history of endoscopy, and endoscopists were considered as probable factors of discomfort. Based on the smoking status the participants were classified as current-smoker, past-smoker and non-smoker. Classification based on alcohol consumption included non-drinker, never to rare drinking; heavy drinker, ≥ 40 mg/d of alcohol for ≥ 3 d/wk; and the rest as normal drinker. GIF-Q260 and GIF-H290 with a diameter of 9.2 mm and 8.9 mm, respectively, defined as a normal diameter, and GIF-PQ260 with 7.9 mm, defined as a small diameter, were the endoscope models used. The participants were divided into subgroups: Sedated and non-sedated, which was expected to be

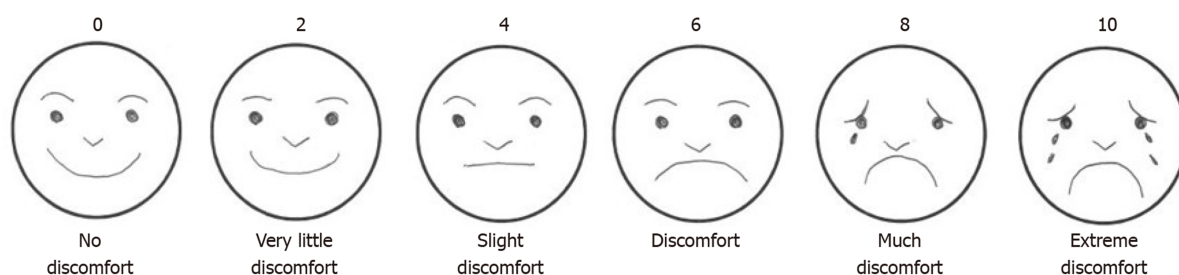


Figure 1 Discomfort rating scale.

strongly related to discomfort. The median discomfort score and the proportion of high discomfort (score ≥ 6) were calculated for each factor, and a univariate analysis was performed.

Furthermore, as an adjustment for bias, we implemented multiple regression analysis to clarify the factors associated with discomfort for the primary outcome. In this analysis, the objective variable was the discomfort score, and the explanatory variables were the probable factors relating to the discomfort.

In order to investigate the effect of heavy alcohol consumption on sedation, multiple regression analysis adjusted for the factors of discomfort was performed in the subgroups with and without sedation as an additional analysis. All statistical analyses were performed using EZR (ver1.37; Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). *P* value < 0.05 was considered as statistically significant.

RESULTS

The number of participants were 1792. Seventy-seven patients were excluded due to inadequate questionnaire responses; finally, 1715 patients were enrolled in this study. **Table 1** includes the demographics of all participants by possible factors relating to discomfort. We were able to obtain all the data for the factors without any gaps. Overall, the median discomfort score and the interquartile range were 2 and 2-4, respectively, and 18% of the participants had high discomfort levels (score ≥ 6).

According to the univariate analysis in the non-sedated group, the factors associated with increased discomfort were young age ($P < 0.001$), female sex ($P < 0.001$), and no history of endoscopy ($P < 0.001$); additionally, significant differences were also found for height ($P = 0.007$), smoking status ($P = 0.003$), and endoscopist ($P < 0.001$) (**Table 2**). With reference to the proportion of high discomfort (score ≥ 6) in the non-sedated group, young age ($P < 0.001$), female sex ($P = 0.03$), and no history of endoscopy ($P < 0.001$) were the factors related to increased discomfort; significant differences were also found for smoking status ($P = 0.033$) and endoscopists ($P = 0.011$) (**Table 2**). For the sedated group, young age ($P < 0.001$), female sex ($P < 0.001$), and no history of endoscopy ($P = 0.004$) were the factors associated with increased discomfort; significant differences were also found for smoking status ($P < 0.001$), type of sedation ($P < 0.001$), and endoscopist ($P = 0.027$). There was a marginal difference based on alcohol consumption ($P = 0.055$) (**Table 3**). Additionally, for the proportion of high discomfort in this group, young age ($P < 0.001$) and no history of endoscopy ($P = 0.018$) were the factors associated with increased discomfort. Significant differences were also found based on alcohol intake ($P = 0.001$). However, there was only a marginal difference based on the smoking status ($P = 0.055$) (**Table 3**).

Based on multiple regression analysis (**Table 4**), young age (regression coefficient for -1 years: 0.08, $P < 0.001$), female sex (regression coefficient: 0.45, $P = 0.013$), shorter height (regression coefficient for -1 cm: 0.02, $P = 0.024$), current smoking status (regression coefficient: 0.35, $P = 0.036$), and presence of hiatal hernia (regression coefficient: 0.34, $P = 0.003$) were the factors that significantly increased the discomfort in esophagogastroduodenoscopy. The use of sedation significantly reduced discomfort. Pethidine (regression coefficient: -1.47, $P < 0.001$), midazolam (regression coefficient: -1.63, $P = 0.001$), and their combination (regression coefficient: -2.92, $P < 0.001$) were found to significantly reduce the discomfort. The individual endoscopist performing the procedure was also associated with the discomfort (regression coefficient estimates: Maximum 2.78 differences). According to the multiple regression analysis performed in both groups, the regression coefficient of heavy

Table 1 Participants' demographics (*n* = 1715)

Possible factors relating to discomfort	Mean (SD)
Age	59 (11)
BMI	23.5 (3.6)
Height	163.1 (8.8)
Possible factors relating to discomfort number (%)	
Age	
≤ 39	80 (4.7)
40-49	308 (18.0)
50-59	431 (25.1)
60-69	610 (35.6)
≥ 70	286 (16.7)
Male sex	950 (55%)
BMI ≥ 25	503 (29.3)
Height	
< 150 cm	114 (6.7)
150-160 cm	546 (31.8)
160-170 cm	644 (37.6)
≥ 170 cm	411 (24.0)
Smoking status	
Non-smoker	988 (57.6)
Past-smoker	487 (28.4)
Current-smoker	240 (14.0)
Alcohol consumption	
Non-drinker	761 (44.4)
Normal drinker	812 (47.4)
Heavy-drinker	142 (8.3)
History of endoscopy	1602 (93.4)
History of gastrectomy	30 (1.8)
Butylscopolamine administration	511 (29.8)
Biopsy performed	49 (2.9)
Lugol's solution use	7 (0.4)
Small diameter endoscope	1657 (96.6)
Hiatal hernia	775 (45.2)
Sedative	
None	774 (45.1)
Pethidine	797 (46.5)
Midazolam	19 (1.1)
Pethidine and midazolam	125 (7.3)

BMI: Body mass index.

alcohol consumption was 0.90 ($P = 0.001$) in the sedation group and 0.008 ($P = 0.78$) in the non-sedation group. Therefore, under sedation, the discomfort experienced by a heavy drinker was greater than that experienced by a non-heavy drinker.

DISCUSSION

Based on the multiple regression analysis, the factors associated with increased discomfort in esophagogastroduodenoscopy were young age, female sex, short height, current smoking status, and hiatal hernia. Individual endoscopists were also related to the discomfort. Additionally, heavy alcohol consumption diminished sedation. This is consistent with the previous report that revealed young^[4-7] and female patients^[4,5,8,9] have higher levels of discomfort. The high discomfort in younger patients is considered to be mainly due to gag reflex^[10]. The high discomfort in women

Table 2 Discomfort for each factor in the group without sedation (*n* = 774) and univariate analysis results

Discomfort score value median (quartile ranges)			Proportion of high discomfort (score ≥ 6)	
Age				
≤ 39	6 (4-8)	<i>P</i> < 0.001	60.5% (23/38)	<i>P</i> < 0.001
40-49	4 (4-6)	Kruskal-Wallis test	45.1% (51/113)	χ^2 test
50-59	4 (2-6)		34.7% (66/190)	
60-69	4 (2-4)		18.3% (48/262)	
≥ 70	2 (0-4)		9.9% (17/171)	
Male sex	4 (2-4)	<i>P</i> < 0.001	23.5% (130/554)	<i>P</i> = 0.003
Female sex	4 (2-6)	Mann-Whitney <i>U</i> test	34.1% (75/220)	χ^2 test
BMI				
≥ 25	4 (2-6)	<i>P</i> = 0.796	27.2% (62/228)	<i>P</i> = 0.773
< 25	4 (2-6)	Mann-Whitney <i>U</i> test	26.2% (143/546)	χ^2 test
Height				
< 150 cm	4 (2-5)	<i>P</i> = 0.007	25.7% (9/35)	<i>P</i> = 0.219
150-160 cm	4 (2-6)	Kruskal-Wallis test	29.4% (53/180)	χ^2 test
160-170 cm	4 (2-4)		22.7% (75/330)	
≥ 170 cm	4 (2-6)		29.7% (68/229)	
Non-smoker	4 (2-6)	<i>P</i> = 0.003	26.5% (104/393)	<i>P</i> = 0.033
Past smoker	4 (2-4)	Kruskal-Wallis test	22.4% (57/255)	χ^2 test
Current smoker	4 (2-6)		34.9% (44/126)	
Non-drinker	4 (2-6)	<i>P</i> = 0.098	29.4% (91/309)	<i>P</i> = 0.291
Normal drinker	4 (2-4)	Kruskal-Wallis test	24.9% (96/386)	χ^2 test
Heavy drinker	4 (2-4)		22.8% (18/79)	
History of endoscopy (+)	4 (2-4)	<i>P</i> < 0.001	24.8% (180/727)	<i>P</i> < 0.001
History of endoscopy (-)	6 (4-7)	Mann-Whitney <i>U</i> test	53.2% (25/47)	χ^2 test
History of gastrectomy (+)	2 (2-4)	<i>P</i> = 0.202	16.7% (3/18)	<i>P</i> = 0.428
History of gastrectomy (-)	4 (2-6)	Mann-Whitney <i>U</i> test	26.7% (202/756)	Fisher's exact test
Butylscopolamine (+)	2 (2-4)	<i>P</i> = 0.115	20.6% (14/68)	<i>P</i> = 0.249
Butylscopolamine (-)	4 (2-6)	(Mann-Whitney <i>U</i> test	27.1% (191/706)	χ^2 test
Biopsy performed (+)	4 (2-6)	<i>P</i> = 0.461	39.1% (9/23)	<i>P</i> = 0.163
Biopsy performed (-)	4 (2-6)	Mann-Whitney <i>U</i> test	26.1% (196/751)	χ^2 test
Lugol's solution (+)	4 (2-6)	<i>P</i> = 0.950	40.0% (2/5)	<i>P</i> = 0.612
Lugol's solution (-)	4 (2-6)	(Mann-Whitney <i>U</i> test	26.4% (203/769)	Fisher's exact test
Endoscope				
Normal diameter	4 (2-6)	<i>P</i> = 0.737	28.6% (6/21)	<i>P</i> = 0.826
Small diameter	4 (2-6)	Mann-Whitney <i>U</i> test	26.4% (199/753)	χ^2 test
Hiatal hernia (+)	4 (2-6)	<i>P</i> = 0.257	27.6% (113/410)	<i>P</i> = 0.472
Hiatal hernia (-)	4 (2-6)	Mann-Whitney <i>U</i> test	25.3% (92/364)	χ^2 test
Sedation agent				
No use	4 (2-6)	-	26.5% (205/774)	-
Pethidine alone	-	-	-	-
Midazolam alone	-	-	-	-
Pethidine and Midazolam	-	-	-	-

Number of endoscopists: 27. Range of median score: 0 to 6. Proportion of high discomfort responses: 0 to 60% (details are omitted). Kruskal-Wallis test result for median score: *P* < 0.001. χ^2 test result for proportion of high discomfort: *P* = 0.011. BMI: Body mass index.

is considered due to a low pain threshold^[11]. Additionally, it is reported that vomiting, belching, or retching increases significantly in patients with hiatal hernia^[10], which can be the cause of the high levels of discomfort in such cases.

The results of the present study suggest that current smokers have increased discomfort due to esophagogastrroduodenoscopy. Although smoking is considered a

Table 3 Discomfort for each factor in the sedation group (*n* = 941) and univariate analysis results

Discomfort score value median (quartile ranges)			Proportion of high discomfort (score 6 or higher)	
Age				
≤ 39	4 (2.5-6)	<i>P</i> < 0.001	40.5% (17/42)	<i>P</i> < 0.001
40-49	2 (2-4)	Kruskal-Wallis test	17.9% (35/195)	χ^2 test
50-59	2 (0-4)		10.8% (26/241)	
60-69	2 (0-4)		6.0% (21/348)	
≥ 70	2 (0-2)		3.5% (4/115)	
Male sex	2 (0-4)	<i>P</i> < 0.001	10.9% (43/396)	<i>P</i> = 0.942
Female sex	2 (2-4)	Mann-Whitney <i>U</i> test	11.0% (60/545)	χ^2 test
BMI				
≥ 25	2 (0-4)	<i>P</i> = 0.155	11.3% (31/275)	<i>P</i> = 0.837
< 25	2 (0-4)	Mann-Whitney <i>U</i> test	10.8% (72/666)	χ^2 test
Height				
< 150 cm	2 (1-4)	<i>P</i> = 0.185	13.9% (11/79)	<i>P</i> = 0.109
150-160 cm	2 (0-4)	Kruskal-Wallis test	9.6% (35/366)	χ^2 test
160-170 cm	2 (0-4)		9.2% (29/314)	
≥ 170 cm	2 (0-4)		15.4% (28/182)	
Non-smoker	2 (0-4)	<i>P</i> < 0.001	10.1% (60/595)	<i>P</i> = 0.055
Past smoker	2 (0-4)	Kruskal-Wallis test	9.9% (23/232)	χ^2 test
Current smoker	2 (2-4)		17.5% (20/114)	
Non-drinker	2 (0-4)	<i>P</i> = 0.055	9.5% (43/452)	<i>P</i> = 0.001
Normal drinker	2 (0-4)	Kruskal-Wallis test	10.3% (44/426)	χ^2 test
Heavy drinker	2 (1-5)		25.4% (16/63)	
History of endoscopy (+)	2 (0-4)	<i>P</i> = 0.004	10.3% (90/875)	<i>P</i> = 0.018
History of endoscopy (-)	2 (2-4)	Mann-Whitney <i>U</i> test	19.7% (13/66)	χ^2 test
History of gastrectomy (+)	2 (0-2.5)	<i>P</i> = 0.477	16.7% (2/12)	<i>P</i> = 0.631
History of gastrectomy (-)	2 (0-4)	Mann-Whitney <i>U</i> test	10.9% (101/929)	Fisher's exact test
Butylscopolamine (+)	2 (0-4)	<i>P</i> = 0.187	10.6% (47/443)	<i>P</i> = 0.755
Butylscopolamine (-)	2 (0-4)	Mann-Whitney <i>U</i> test	11.2% (56/498)	χ^2 test
Biopsy performed (+)	2 (0-3.5)	<i>P</i> = 0.287	11.5% (3/26)	<i>P</i> = 0.757
Biopsy performed (-)	2 (0-4)	Mann-Whitney <i>U</i> test	10.9% (100/915)	Fisher's exact test
Lugol's solution (+)	1 (0.5-1.5)	<i>P</i> = 0.35	0.0% (0/2)	<i>P</i> = 1.00
Lugol's solution (-)	2 (0-4)	Mann-Whitney <i>U</i> test	11.0% (103/939)	Fisher's exact test
Endoscope				
Normal diameter	2 (2-4)	<i>P</i> = 0.197	10.8% (4/37)	<i>P</i> = 1.00
Small diameter	2 (0-4)	Mann-Whitney <i>U</i> test	11.0% (99/904)	Fisher's exact test
Hiatal hernia (+)	2 (0-4)	<i>P</i> = 0.891	12.3% (45/365)	<i>P</i> = 0.279
Hiatal hernia (-)	2 (0-4)	Mann-Whitney <i>U</i> test	10.1% (58/576)	χ^2 test
Sedation agent				
No use	-		-	
Pethidine alone	2 (0-4)	<i>P</i> < 0.001	11.7% (93/797)	<i>P</i> = 0.186
Midazolam alone	2 (0-4)	Kruskal-Wallis test	10.5% (2/19)	Fisher's exact test
Pethidine and Midazolam	0 (0-2)		6.4% (8/125)	

Number of endoscopists: 27. Range of median score: 0 to 4. Range of proportion of high discomfort responses: 0 to 27.8% (details are omitted). Kruskal-Wallis test result for median score: *P* = 0.027. χ^2 test result for proportion of high discomfort: *P* = 0.216. BMI: Body mass index.

cause of gag reflex^[12], smoking was not identified as a significant factor of discomfort in the previous studies^[7,9,10]. Thus, current smoking status associated with increased discomfort has been newly identified in the present study, which may be due to the larger sample size of the present study. It is reported that smokers have chronic laryngitis^[13]; hence, chronic irritation to the throat may be the cause of gag reflex in

Table 4 Multiple regression analysis and impact of each factor for discomfort

	Regression coefficient	Upper limit of 95%CI	Lower limit of 95%CI	P value
Age (+ 1)	-0.08	-0.09	-0.07	< 0.001
Sex (male)	-0.45	-0.79	-0.10	0.013
BMI (+ 1)	-0.002	-0.03	0.03	0.903
Height (+ 1)	-0.02	-0.04	-0.003	0.024
Smoking status				
Past smoker	-0.06	-0.32	0.20	0.638
Current smoker	0.35	0.02	0.67	0.036
Alcohol consumption				
Normal drinker	-0.05	-0.27	0.18	0.680
Heavy drinker	0.20	-0.21	0.61	0.337
Has no endoscopic experience	0.22	-0.20	0.65	0.300
History of gastrectomy	0.36	-0.41	1.14	0.362
Butylscopolamine use	-0.04	-0.35	0.27	0.802
Biopsy performed	0.11	-0.51	0.72	0.729
Lugol's solution use	1.02	-0.61	2.64	0.221
Normal diameter endoscope	0.48	-0.09	1.05	0.101
Hiatal hernia	0.34	0.11	0.57	0.003
Sedation agent				
Pethidine alone	-1.47	-1.71	-1.22	< 0.001
Midazolam alone	-1.63	-2.61	-0.66	0.001
Pethidine and midazolam	-2.92	-3.36	-2.49	< 0.001

Maximum difference in discomfort among endoscopists (regression coefficient): 2.78 (details of each endoscopist were omitted). BMI: Body mass index.

smokers. Additionally, since there was no difference in the discomfort experienced between past-smokers and non-smokers, smoking cessation could help eliminate the increasing discomfort. Although previous studies only investigated the discomfort or gag reflex based on body mass index as a body-type factor in^[5,9,10]; short height may be related to high discomfort levels because the scope diameter is relatively large. Therefore, in this study, height was also included as a factor and was found to be significantly related to discomfort. Although this is a new finding of interest, univariate analysis for high discomfort was not significantly different, and the regression coefficient in multiple regression analysis is relatively small and, therefore, has less clinical relevance.

Sedation was useful as it significantly reduced discomfort, and the use of either pethidine, midazolam, or their combination was effective. However, heavy alcohol consumption reduced the effect of sedation. Sedation is reported to be less effective in heavy drinkers^[14]. Previous studies have shown that the requisite doses of benzodiazepines and the combination of benzodiazepine and opioid are higher for heavy drinkers than for others^[15,16]. Unlike previous reports, in the majority of the cases in the present study, pethidine was used and was found to be less effective in heavy drinkers. Therefore, we believe that discomfort can be predicted from age, sex, smoking status, and alcohol consumption, which can be easily obtained before examination.

The limitation of this study is the possibility of a selection bias since it is a retrospective cross-sectional study from a single facility. However, various information was analyzed in connection with the health check-up data in many participants. Additionally, anxiety and pharyngeal sensitivity, which were identified as factors of discomfort in the previous studies, could not be analyzed before the examination^[4-7,9]. However, anxiety and pharyngeal sensitivity are rarely evaluated in general practice; therefore, it is meaningful to investigate the factor of discomfort by the information obtained ordinarily in daily practice. The strengths of the present study are that it is a large-size study, and smoking status was identified for the first time as a contributing factor to discomfort in esophagogastroduodenoscopy.

In conclusion, young and female patients experience more discomfort in esophagogastroduodenoscopy. Furthermore, the discomfort in current smokers may increase. Additionally, heavy alcohol consumption reduces the effect of sedatives. These factors are useful because they can be easily obtained, and we can take remedial

measures for reducing discomfort.

ARTICLE HIGHLIGHTS

Research background

Discomfort due to esophagogastroduodenoscopy contributes to a negative experience and reduces the patients' satisfaction. Therefore, it is important to reduce discomfort as much as possible. By identifying the factors that cause discomfort, we can take remedial measures such as using sedation.

Research motivation

However, not all factors of discomfort have been elucidated yet. Most previous studies have conducted investigations only in several hundred subjects, which is a relatively small sample.

Research objectives

The aim of this study was to elucidate the contributing factors of discomfort in transoral esophagogastroduodenoscopy by a large-scale cross-sectional study.

Research methods

This study was a retrospective observational study using a questionnaire for the improvement of hospital services. Discomfort was evaluated using a face scale between 0 and 10 with a 6-level questionnaire. Univariate and multiple regression analyses were performed to investigate the factors related to the discomfort in esophagogastroduodenoscopy. The primary outcome was the result of a multiple regression. In this analysis, the objective variable was the discomfort score and the explanatory variables were age, sex, height, body mass index, smoking status, alcohol intake, hiatal hernia, history of gastrectomy, biopsy during examination, Lugol's solution usage, administration of butylscopolamine with/without a sedative (pethidine, midazolam, or both), endoscope model, history of endoscopy, and endoscopists.

Research results

Finally, 1715 patients were enrolled in this study. Based on multiple regression analysis, young age, female sex, shorter height, current smoking status, and presence of hiatal hernia [regression coefficients of 0.08, $P < 0.001$ (for -1 years); 0.45, $P = 0.013$; 0.02, $P = 0.024$ (for -1 cm); 0.35, $P = 0.036$; and 0.34, $P = 0.003$, respectively] were factors that significantly increased the discomfort in esophagogastroduodenoscopy. Alternatively, sedation significantly reduced discomfort; pethidine (regression coefficient: -1.47, $P < 0.001$) and midazolam (regression coefficient: -1.63, $P = 0.001$) both individually and in combination (regression coefficient: -2.92, $P < 0.001$) significantly reduced the discomfort. A difference in the endoscopist performing the procedure was also associated with discomfort. Additionally, for the proportion of a high discomfort level (score ≥ 6) in the sedated group, significant differences were also found based on alcohol intake in univariate analyses ($P = 0.001$).

Research conclusions

The present study clearly identified the factors associated with discomfort in esophagogastroduodenoscopy using a large-size cross-sectional study. Young age, female sex, and current smoking were identified as the contributive factors. Smoking status was a newly identified predictor of this study. Furthermore, heavy alcohol consumption was noted to diminish the effect of the sedative(s). These factors are useful because they can be easily obtained, and we can take remedial measures for reducing discomfort.

Research perspectives

Prospective research is needed to clarify whether predicting discomfort and taking measures to alleviate it can effectively increase patient satisfaction.

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