The Role of Perceived Job Stress in the Relationship between Smoking and the Development of Peptic Ulcers

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Although smoking has been considered a risk factor in causing peptic ulcers, no study has examined the effects of job stress on the relationship between peptic ulcers and smoking. To establish a link between gastric or duodenal ulcers over two years and a state of perceived job stress, a questionnaire, including questions on demographics, smoking, history of peptic ulcer and perceived job stress was conducted. Follow-up surveys were carried out every six months to accumulate the data for this analysis and the time span of this follow up study was two years. To examine the role of perceived job stress on the relationship between smoking and peptic ulcers, stratified analyses were performed. Some specific causes of perceived job stress such as "Too much competition," "Schedule is too tight or pressed to work too hard" had high estimated relative risks: 2.13 with 95% confidence interval (CI) of 1.09 - 4.16 and 2.50 with 95% CI of 0.98 - 6.40, respectively. Stratified analyses suggested an effect-measure modification of perceived job stress in the relationship between peptic ulcers and smoking. Multiplicative and additive models suggest positive interaction between perceived job stress and smoking. These results suggest that specific perceived job stress is an effect modifier in the relationship between the history of the peptic ulcer and smoking. *J Epidemiol*, 1999 ; 9 : 320-326

perceived job stress, peptic ulcer, smoking habit, effect-measure modification, follow up study

Peptic ulcers are one of the prevalent diseases in the alimentary tract. It has been established that non-steroidal anti-inflammatory drug (NSAID) and smoking are major risk factors for this disease¹⁾. Recently, *Helicobacter pylori* has received attention as a representative causal factor of peptic ulcers.¹ In Japan, the life-time risk of active or inactive peptic ulcers in male workers was estimated at 23%,² and the incidence rate at 5% per year or more²⁾. Thus, peptic ulcers are a work-related disease because of an increased prevalence of peptic ulcers found among certain segments of working population³⁾. Accordingly, occupational factors such as job stress are suspected as risk factors for peptic ulcers. However, there are few studies⁴⁾ examining the relationship between job stress and peptic ulcers.

Many studies⁵⁻¹⁰⁾ have been performed to investigate the causal relationship between peptic ulcers and smoking. It is established that smoking is one of the risk factors for peptic

ulcers. There has been no study, however, investigating the effects of job stress on the relationship between smoking and peptic ulcers.

The purpose of our research was to investigate the relationship between perceived job stress, smoking and peptic ulcers, particularly to clarify the effect of perceived job stress on the relationship between smoking and peptic ulcers.

MATERIALS AND METHODS

The study subjects comprised of employees of a middle-sized company producing minute electric parts in Japan. We conducted a follow up study over two years, during which the questionnaire surveys were performed every six months to obtain information about gastric or duodenal ulcers. In the surveys, a self-administered questionnaire posed questions about smoking habits, perceived job stress¹¹⁾, previous or current gas-

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tric or duodenal ulcers, and additional questions about the workers demographics.

Among 782 workers, 763 workers (97.6%) answered the questionnaire satisfactorily in the baseline survey. During the follow up, 140 workers dropped out, and prevalent cases of peptic ulcers numbered 39. In the follow up study, we eliminated the prevalent cases mentioned above in the baseline survey. Consequently, 584 workers were eligible for this study and there were 32 incidences of peptic ulcers over the two years. Response rate of eligible workers was 76.5% and not high value. To examine workers gastric or duodenal ulcer history, each respondent was asked the question: "Have you ever had medical treatment for a gastric or duodenal ulcer?" Based on the answer that workers gave to this question, they were divided into two groups; the men newly treated for peptic ulcers during the follow up period and the rest. We regarded, the former as newly detected cases of peptic ulcers and the latter as non-ulcer subjects.

Because peptic ulcers were defined as work-related disease⁹, we used the job stress questionnaire as recognition of job stress. However, this questionnaire has not been validated. On the other hand, this questionnaire has been already used in the relationship between peptic ulcer and work-related factors¹⁰. In addition to this contents, as we considered that this questionnaire covered various types of perceived job stress, this questionnaire was selected. The job stress questionnaire¹² consisted of the 13 items which are described in Table 2. For each item, we defined those who answered "yes, frequently" or "yes, sometimes" as positive and those who answered "almost never" as negative for each item. In our previous study²⁶, we calculated a reliable measure. In this result, Cronbach's alpha coefficient was 0.80, which is thought to be a high value of reliable measure in this questionnaire.

To check on smoking habits, we asked a dichotomous question to workers, "smoking" or "non smoking".

We hypothesized that perceived job stress contributes to developing peptic ulcers. In particular, that specific items of perceived job stress effect the relationship between smoking and developing peptic ulcers as a confounder, or as an effect modifier. Stratified analysis of perceived job stress about the relationship between smoking and peptic ulcers was carried out. To examine multiplicative interaction between job stress and smoking habit, we carried out a multiple logistic regression analysis. As Aldoori et al¹³, reported little association between caffeine and risk of duodenal ulcers and Brenner et al¹⁴, suggested the protective effect of alcohol consumption against active infection with *Helicobacter pylori* and the opposite effect with coffee consumption, we adjusted for the effects of alcohol and coffee consumption in the analysis of the multiple logistic regression model. Since age was significantly related to smoking proportion by chi-square test, we considered age a confounding factor. In addition to the multiplicative

interaction model, we used an additive model and we calculated the interaction constant ratio (ICR) in accordance with Rothman and Greenland's textbook¹⁵ because, epidemiologically, the additive interactive model is an important idea, especially in the area of public health. We did these analyses using the computer programs SPSS-Windows¹⁶ and Epi-Info¹⁷.

RESULTS

The demographics of workers who responded to our study in the eligible population are shown in Table 1. The smoking percentages were 57.8% of males, 5.6% of females. The distribution of job type in the incident cases of peptic ulcer was 17/298 in the department of production, 6/98 in the department of technology and development, 3/45 in the department of investigation and inspection, and 6/129 in the department of management. Table 2 shows crude relative risks in the relationship between perceived job stress and peptic ulcers in the follow up study. The item "Too much competition" had a significant relationship with peptic ulcer incidence. Although the chi-square test was not significant, partly because of a small number of cases, the item of perceived job stress: "Schedule is too tight or

Table 1.

Demographics of eligible workers who participated in our survey.

Sex	Male	296	(50.6%)	
	Female	289	(49.4%)	
	Total	585		
Age	-29yr	235	(40.2%)	
	30-39yr	160	(27.4%)	
	40-49yr	175	(30.0%)	
	50+ yr	14	(2.4%)	
	Total	584	(100%)	
Departments				
	Business	8	(1.4%)	
	Production	298	(50.9%)	
	Technology and Development	98	(16.8%)	
	Investigation and Inspection	45	(7.6%)	
	Personnel	7	(1.2%)	
	Management	129	(22.1%)	
	Total	585	(100%)	
Smoking Percentages				
Sex	Male	171/296	(57.8%)	p<0.001
	Female	16/289	(5.6%)	
Age	-29yr	57/235	(24.3%)	p<0.001
	30-39yr	75/160	(46.9%)	
	40-49yr	43/175	(24.7%)	
	50+ yr	9/ 14	(64.3%)	

pressed to work too hard" showed a relative risk (95% confidence interval) of 2.5 (0.98-6.40). Results of multiple logistic regression analysis controlling gender, age, smoking and other potential confounders were shown in table 3. In this results, the item "Schedule is too tight or pressed to work too hard" showed 2.00 of point estimated odds ratio. However, this measure was not significant partly because of small sample size.

The results of stratified analysis on perceived job stress are shown in Table 4. In several items of perceived job stress, smoking status, and peptic ulcer, relative risks of smoking for peptic ulcer were larger in the stress group than in the non-stress group, with significant relative risks observed in the

stress group, and non-perceived job stress groups showing no significant relationship. These risks were linked to the items such as "Too much trouble at work," "Too much responsibility," "Work hours too long," "Feel pressed for time," and "Shortage of workers". This discrepancy between the job stress group and the non stress group in the stratified analyses suggests effect-measure modification of specific perceived job stress.

The results of the multiple logistic regression models with interaction between perceived job stress and smoking are shown in Table 5. There were five items of job stress which suspected multiplicative positive interaction because of more

Table 2. Relative risks (RR) between perceived job stress and peptic ulcers by crude analysis.

Item of perceived job stress	stress		non-stress		RR	95% confidence interval
	case	group non-case	case	group non-case		
1. Too much competition	16	169	6	388	2.13	(1.09-4.16)
2. Too much work	24	371	8	182	1.44	(0.66-3.15)
3. Schedule is too tight or pressed to work too hard	27	372	5	180	2.50	(0.98-6.40)
4. Too much trouble at work	25	360	7	190	1.83	(0.80-4.15)
5. Too much responsibility	23	316	9	232	1.82	(0.86-3.86)
6. Work hours too long	18	234	13	313	1.79	(0.89-3.59)
7. Poor relationship with superiors	12	173	20	374	1.28	(0.64-2.56)
8. Feel pressed for time	25	395	7	157	1.39	(0.62-3.16)
9. Are not allowed to make mistakes	28	454	4	97	1.47	(0.53-4.09)
10. Shortage of workers	22	284	10	265	1.98	(0.95-4.10)
11. Must entertain guests at night and weekends too much	1	21	31	523	0.78	(0.11-5.45)
12. Labor too strenuous	14	175	18	375	1.62	(0.82-2.18)
13. Cannot keep up with new technology	17	217	15	330	1.67	(0.85-3.28)

Table 3. The results of multiple logistic regression analysis of the relationship between perceived job stress and peptic ulcers adjusted for gender, age, satisfaction with family life, physical health, smoking habits, alcohol and coffee consumption.

Perceived job stress item	adjusted risk odds ratio	95% confidence interval
1. Too much competition	1.55	0.70-3.43
2. Too much work	1.04	0.41-2.61
3. Schedule is too tight or pressed work too hard	2.00	0.66-6.06
4. Too much trouble at work	1.08	0.42-2.85
5. Too much responsibility	1.37	0.58-3.22
6. Work hours too long	1.37	0.62-3.07
7. Poor relationship with superiors	1.14	0.52-2.50
8. Feel pressed for time	0.68	0.25-1.86
9. Are not allowed to make mistakes	1.62	0.53-5.01
10. Shortage of workers	1.70	0.72-4.00
11. Must entertain guests at night and weekends too much	0.79	0.08-6.13
12. Labor too strenuous	1.28	0.58-2.82
13. Cannot keep up with new technology	1.14	0.49-2.62

Table 4. Stratified analysis between smoking and peptic ulcers by perceived job stress.

item of perceived job stress	risk of smoking group	risk of non-smoking group	RR	95% CI	MHPR	95% CI
1. Too much competition overall					3.85	(1.81-8.18)
non-stress	8/104	8/290	2.79	(1.07-7.24)		
stress	13/81	3/104	5.66	(1.64-18.87)		
2. Too much work overall					3.89	(1.92-7.87)
non-stress	5/41	3/149	6.06	(1.51-24.29)		
stress	16/146	8/249	3.41	(1.50-7.77)		
3. Schedule is too tight or pressed to work too hard overall					4.05	(1.80-9.10)
non-stress	0/28	5/157	-			
stress	21/158	6/241	5.34	(2.20-12.93)		
4. Too much trouble at work overall					4.34	(1.90-9.89)
non-stress	1/30	6/167	0.93	(0.12-7.43)		
stress	20/156	5/229	5.87	(2.25-15.31)		
5. Too much responsibility overall					4.08	(1.91-8.72)
non-stress	3/57	6/184	1.61	(0.42-6.25)		
stress	18/128	5/211	5.93	(2.26-15.60)		
6. Work hours too long overall					2.81	(1.80-8.05)
non-stress	6/86	7/239	2.38	(0.82-3.89)		
stress	14/98	4/154	5.50	(1.86-16.23)		
7. Poor relationship with superiors overall					4.01	(1.98-8.35)
non-stress	13/125	7/268	3.58	(1.63-11.69)		
stress	8/61	4/124	4.07	(1.27-12.97)		
8. Feel pressed for time overall					4.11	(1.98-8.56)
non-stress	3/35	4/128	2.74	(0.64-11.69)		
stress	18/151	7/269	4.58	(1.96-10.72)		
9. Are not allowed to make mistakes overall					4.15	(2.04-8.43)
non-stress	3/37	1/64	5.19	(0.56-48.10)		
stress	18/149	10/333	4.02	(1.90-8.50)		
10. Shortage of workers overall					3.99	(1.83-7.87)
non-stress	5/65	5/209	3.22	(0.96-10.76)		
stress	16/121	6/185	4.08	(1.64-10.13)		
11. Must entertain guests at night and weekends too much overall					4.09	(2.01-8.32)
non-stress	20/176	11/378	3.90	(1.91-7.97)		
stress	1/8	0/15	-			
12. Labor too strenuous overall					3.95	(1.95-7.98)
non-stress	13/123	5/269	5.69	(2.07-15.60)		
stress	8/64	6/125	2.60	(0.94-7.18)		
13. Cannot keep up with new technology overall					4.05	(1.87-8.78)
non-stress	7/81	8/264	2.85	(1.07-7.62)		
stress	14/105	3/129	5.73	(1.69-19.42)		

* RR : relative risk

* MHRR : Mantel-Haenszel weighted relative risk

* CI : confidence interval

than 2.0 of exp(coefficient); "Too much trouble at work," "Too much responsibility," "Work hours too long," and "Cannot keep up with new technology." The specific items of perceived job stress, which found to be the effect-measure modifiers in the stratified analyses, showed positive multiplicative interactive effects. However, statistical tests were not significant, partly due to the same reason of small case samples.

Table 6 shows the results of additive interactive models for

the five items of perceived job stress. ICR¹⁵ is the "interaction constant ratio" and has previously been labeled the "relative excess risk of interaction". If we take this as positive for additivity hypothesis, ICR shows the value of more than 0. The same items of perceived job stress as the multiplicative interactive models indicate positive interaction; in other words "superadditivity"¹⁵ in the relationship with smoking, because all of the ICR were more than 0 with the range of 1.78 to 3.03.

Table 5. The multiplicative coefficient : exp (interactive coefficient : smoking $\times$ perceived job stress) using a multiple logistic regression model.

perceived job stress item	exp (coefficient)	95% confidence interval
1. Too much competition	2.36	0.43-12.8
4. Too much trouble at work	9.19	0.81-104
5. Too much responsibility	4.44	0.72-27.2
6. Work hours too long	2.64	0.49-14.2
13. Cannot keep up with new technology	2.30	0.42-12.7

Table 6. The results from the additive interactive model between perceived job stress and smoking.

Notation for risks with two binary exposure indicators such as perceived job stress and smoking			
	smoking	Z=1	Z=0
perceived job stress	X=1	R ₁₁	R ₁₀
	X=0	R ₀₁	R ₀₀
Perceived job stress item	Risk ratio (RR)		95% confidence interval
1. Too much competition	RR ₁₁	5.82	2.50-13.55
	RR ₁₀	1.05	0.28-3.87
	RR ₀₁	2.79	1.07-7.24
	RR ₀₀	1.00	
	ICR = RR ₁₁ - RR ₁₀ - RR ₀₁ + 1 = 2.98 > 0		
4. Too much trouble at work	RR ₁₁	3.57	1.47-8.65
	RR ₁₀	0.61	0.19-1.96
	RR ₀₁	0.93	0.12-7.43
	RR ₀₀	1.00	
	ICR = 3.03 > 0		
5. Too much responsibility	RR ₁₁	4.31	1.76-10.56
	RR ₁₀	0.73	0.23-3.34
	RR ₀₁	1.61	0.42-6.25
	RR ₀₀	1.00	
	ICR = 2.97 > 0		
6. Work hours too long	RR ₁₁	4.08	2.03-11.72
	RR ₁₀	0.89	0.26-2.98
	RR ₀₁	2.28	0.79-6.59
	RR ₀₀	1.00	
	ICR = 1.91 > 0		
13. Cannot keep up with new technology	RR ₁₁	4.40	1.90-10.18
	RR ₁₀	0.77	0.21-2.84
	RR ₀₁	2.85	1.07-7.62
	RR ₀₀	1.00	
	ICR = 1.78 > 0		

* ICR : Interaction constant ratio

Consistently, these results indicate effect-measure modification or positive interaction of specific perceived job stress in the causal relationship between smoking and developing peptic ulcers.

DISCUSSION

Araki² reported that the life-time risk of active and inactive peptic ulcers was 23% in male workers aged 31-60 and that the incidence of active and inactive peptic ulcers over one year was 5% or more. In our follow up study over two years, 584 workers were eligible and 32 cases had a history of peptic ulcers over the two years, which indicate a 5.5% risk of peptic ulcer over two years.

In Japan, Araki¹⁸ failed to find an association between medically diagnosed peptic ulcers and frustration at work in his case-control study. On the other hand, Sugisawa and Uehata¹⁰ claimed that there was a relationship between perceived job stress and peptic ulcers in their follow up study. In other countries, several researchers^{19, 20} suggested the relationship between self-perceived stress and peptic ulcers. The findings in this study were consistent with those of the latter three studies. In Araki's study¹⁸, he asked only about job stress frustration, so he might fail to find the relationship between job stress and peptic ulcers.

Many studies⁵⁻¹⁰ have concluded that smoking is a risk factor for peptic ulcers. Therefore, we conducted the stratified analysis using perceived job stress in order to evaluate the effects of job stress on the relationship between smoking and peptic ulcers. Our results suggest that specific perceived job stress is an effect-measure modifier¹⁵ rather than a confounder.

In addition to stratified analysis, we analyzed the statistical interaction between smoking habits and perceived job stress. Statistical interaction is considered to be equivalent to effect-measure modification in an epidemiology textbook¹⁵. However, Rothman and Greenland explain in their textbook¹⁵ that the term "effect modification" is also ambiguous, and they advise more precise terms such as "risk-difference modification" or "risk-ratio modification," as appropriate. In this case, we used the term "risk-ratio modification" in the stratified analysis.

Initially, we analyzed multiplicative interaction with multiple logistic regression analysis because most epidemiological statistics are based on multiplicative models. Although statistical tests were not significant, partly because of the small sample size, they suggest a multiplicative positive interaction between smoking and perceived job stress.

However, Rothman and Greenland¹⁵ point out that statistical interaction is a phenomenon whose presence or absence, as well as magnitude, is entirely determined by the scale chosen for measuring additivity of the effects. Accordingly, we calcu-

lated the additive interaction between smoking and perceived job stress. In the pointed estimated risk ratio, these results showed positive interaction between smoking and specific perceived job stress such as "Too much competition," "Too much trouble at work," "Too much responsibility," "Work hours too long", and "Cannot keep up with new technology" in the relationship with peptic ulcers.

In the stratified analysis, the item of perceived job stress "Labor too strenuous" showed the opposite result compared to the items "Too much trouble at work," "Too much responsibility," and "Work hours too long". Using cross-table analysis, many workers who answered negatively for perceived job stress, had specific perceived job stress which included the latter items. For this reason, the item "Labor too strenuous" may generate the opposite result.

In these analyses, the proportions of perceived job stress were higher in smoking group than in non smoking group. These results are suspected that the stress was enhanced because of smoking. About the relationship between perceived job stress and withdrawal symptoms of nicotine, the cases who stopped smoking in our follow up study were only about 20. Adding this content, duration of withdrawal symptoms of nicotine was generally within two weeks at the longest. For these reasons, it is difficult that withdrawing nicotine affects to perceived job stress in our study.

Lastly, we discuss the limitations of this study. Firstly, our sample size were relatively small. Consequently, some statistical tests may not yield significant results. Further study is required with a larger sample to investigate the relationship between perceived job stress and peptic ulcer and to confirm the effect-measure modification of job stress in the relationship between smoking and peptic ulcers.

Secondly, the response rate of eligible workers was 76.5%. These results suggested that we should pay attention to selection bias. However, because there were no significant differences among demographic variables between eligible workers and workers lost in follow-up, a possibility of selection bias might be small.

In addition, we collected information on peptic ulcers using a self-administered questionnaire with no clinically diagnostic confirmation. Therefore, there could be a bias in the information collecting process. However, major bias is thought to be a non-differential misclassification in our study, so the magnitude of the effects may be underestimated¹⁵.

We did not get information on *Helicobacter pylori* infection as a potential confounder of the relationship²¹⁻²⁵. Since the purpose of this study was to investigate the causal relationship between perceived job stress and peptic ulcers, it is unlikely that *Helicobacter pylori* infection is related to the perceived job stress of the workers. Therefore, an infection with *Helicobacter pylori* does not satisfy sufficient criteria¹⁵ as a confounding factor.

As stated, we used a self-administered questionnaire consisting of 13 items to evaluate perceived job stress. The validity of this questionnaire was not evaluated prior to the study. It is doubtful whether all the perceived job stresses items in the Japanese workers could be generally or accurately covered by this questionnaire. However, this questionnaire has already been used in the study of occupational stress-related cardiovascular disease and of mental health in Japanese workers^{12,26-27}.

In conclusion, the results of this study suggest that perceived job stress items such as "Too much competition" could be risk factor for developing peptic ulcers. Specific perceived job stress could have an effect-measure modification on the relationship between smoking habits and developing peptic ulcers. Both the multiplicative and the additive interaction models suggest positive interaction between specific items of perceived job stress and smoking.

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