[Environmental Health and Preventive Medicine 5, 90-96, October, 2000]

Original Article

Lifestyle-Related Risk Factors for Total and Cancer Mortality in Men and Women.

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Abstract

We conducted a 14-year follow-up study to analyze the hazard ratio (HR) of mortality regarding lifestyle-related factors in Saga Prefecture, Japan. The subjects included 2,170 people, who were randomly selected from men and women aged from 40 to 69 years old, and who also completed the standardized questionnaire on lifestyle in 1983. Information about death and corresponding data were obtained either by mail and/or through the city offices in 1997. We found that a lower body weight, a lower physical fitness level, not consuming a balanced diet, and cigarette smoking to be significantly elevated risks for all-causes of death in males after adjustment by age and health status. In addition, these results did not change even after excluding subjects for early death. The HR of the female subjects who quit smoking was significantly high, although it changed to insignificant after excluding subjects for early death. These results suggested that being underweight might be an index of a positive risk of death, while maintaining a higher physical fitness level, being careful to consume a more balanced diet, and non smoking all appear to be indexes of a negative risk of death. In addition, these results might also be considered good evidence for improving poor health habits in health promotion activities.

Key words: lifestyle, mortality, physical activity, body mass index, smoking, prospective cohort study

INTRODUCTION

Evidence-based public health, so called EBPH, has been regarded as increasingly important, and it is also necessary when we engage in health promotion. These days, the occurrence of cancer, cardiovascular diseases, and cerebrovascular disorders, which are the main causes of death in Japan [1], have been suggested to be related to environmental factors, genetic factors, and lifestyle [2-4]. However, the precise influence of environmental or genetic factors on diseases or deaths are extremely complex and thus have yet to be identified. Therefore, health promotion should focus on improving lifestyle-related risk factors when we engage in community health promotion activities.

Many studies have been conducted to identify the lifestyle-related risk factors for developing disease, since Belloc et al. indicated the existence of a relationship between several health practices and mortality [5,6]. A number of studies have shown that the curve representing the risk of total mortality in relation to obesity is U-shaped, J-shaped, positive, inverse, or absent [7-13]. Numerous studies have shown an inverse relationship between physical activity levels and total mortality [14-22], and a linear dose-response relationship between cigarette smoking and all causes of mortality [13,18,22-25]. Several investigators have suggested that heavy drinking also increases the risk of all causes of mortality, while light-to-moderate drinking decreases the risk [13,26].

It is meaningful to identify the risk factors for death in order to promote a community's overall health. The relationship between lifestyle and mortality might differ depending on the population because of biological and environmental differences. However, not enough studies have been performed among the general population. To carry out EBPH, it is necessary to explore the evidence based on the findings of the typical Japanese. In this follow-up study, we analyzed the relationship between some lifestyle-related factors and total mortality and cancer mortality among randomly selected inhabitants of Saga Prefecture in Japan to promote health by means of EBPH.

Received Jan. 6 2000/Accepted Mar. 30 2000
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MATERIALS AND METHODS

Baseline survey

The baseline survey was conducted from October through November of 1983. The study subjects consisted of 2,406 individuals (1,203 males and 1,203 females), aged from 40 to 69 who were randomly selected after stratification by age and residential area from all areas of Saga Prefecture in Japan. 2,170 subjects (1,126 males and 1,044 females) (90.2%) answered a self-administrated questionnaire completely, while 134 subjects (5.6%) who did not respond, and 102 subjects (4.2%), who answered incompletely, were excluded from the follow-up survey.

Standard questionnaire

The questionnaire included inquiries regarding health status, previous diseases, management of health, and lifestyle habits. The health status was divided into 5 categories as follows: 1) I don't feel fatigue, or I have no symptoms, 2) I sometimes feel fatigue 3) I sometimes get sick, but I recover from it easily, 4) I have minor ailments, but I do not have any limitations in daily living, 5) I have some kind of limitations in daily living, because I have disease. The lifestyle-related factors adopted were as follows: body mass index (body weight (kg)/body height $(m)^2$, BMI), scores on physical fitness tests based on daily living, frequency of physical activity, eating a balanced diet, alcohol consumption, and smoking. The physical fitness scores were determined based on 10 items, and the subjects were requested to answer after they had done each by themselves. They were as follows: 1) Can you dance or exercise easily? 2) Can you dodge quickly, when you are going to be hit? 3) Can you go up steps without shortness of breath? 4) How long can you stand on one leg with eyes closed? 5) How high can you jump? 6) After sitting on the floor with your legs outstretched, are you able to touch your toes with your fingers? 7) How long can you lift your legs when lying down? 8) Can you stand up without holding on to something? 9) How many times can you squat and stand repeatedly? 10) How heavy a box can you lift up to your chest height? Each item was estimated on a grade from 0 to 2 points. The total score for the physical fitness test was calculated.

Follow-up survey

From May through July of 1997, we conducted a follow-up study by mail on 2,170 subjects who answered our questionnaire completely in 1983. We received 1,543 (71.1%) returns from either individuals or the families of 762 males and 781 females, including 109 who had died. We ascertained whether 588 subjects among the residual 627 subjects were alive, dead, or lost to the follow-up (moved away) with the help of the city office, but 39 subjects could not be ascertained. Finally, we could ascertain 2,131 subjects (98.2% out of 2,170 subjects) regarding whether they were alive, dead, or lost to the follow-up (moved away). However, we could not ascertain the date of death of 5 dead subjects, or the date of moving away of 5 subjects lost to the follow-up. Therefore, we excluded 49 subjects in total, and we conducted an analysis on 2,121 subjects (1,099 males, 1,022 females) to clarify the relationship between lifestyle-related factors and death. The cause of death, if dead, was confirmed by a death certificate with the help of the city offices in Saga Prefecture.

Statistical analysis

To assess the relative risks of each category according to lifestyle-related risk factors, we calculated the hazard ratios (HRs) and their 95% confidence intervals (95%CIs) of the independent association of health status and each health-related habit in total and cancer mortality by using Cox's proportional hazard regression model[27]. The regression model tested for trend by treating a continuous or numerically-discrete variable as an ordinal one. We applied different models having different sets of factors both separately and in common for males and females. We divided the subjects into four classes according to the BMI, which consisted of less than 20 (the lowest category), equal to or above 20 but less than 22, equal to or above 22 but less than 24, and equal to or above 24 (the highest category). The BMI was included in the model based on three dummy variables for the last three groups, using the least quartile group (BMI<20) as the reference category. The subjects were divided into four classes according to the physical fitness score; below 6 (the lowest category), equal to or above 7 to below 9, equal to or above 10 to below 11, and equal to or above 12 (the highest category). The physical fitness score was also included in the model by means of three dummy variables for the last three groups. We calculated the HRs based on no physical activity, not having a balanced diet, never drinking alcohol, and never smoking cigarettes as the reference categories. The diagnostic plots of log S(t) versus log(t) showed that the assumptions of the proportional-hazard model were acceptable. We used the Statistical Analysis System (SAS) [28] to analyze the data. The SAS program PROC PHREG procedure provides the values for hazard ratio in Cox's proportional hazard regression analysis. Statistical significance was assumed when a two-tailed P value of less than 0.05 was observed based on the Wald test. Ninety-five confidence intervals were calculated around the point estimates of the risk.

RESULTS

After a 14-year follow-up, 309 subjects (230 males and 79 females) had died and 57 subjects (27 males and 30 females) had moved away. The proportions of death were significantly larger in males (20.9%) than in females (7.7%) (P<0.001). One hundred and thirty-eight deaths (107 males and 31 females) from cancer, 29 deaths (24 males and 5 females) from cardiovascular disease, 24 deaths (16 males and 8 females) from cerebrovascular disease, 118 deaths (83 males and 35 females) from other causes had occurred during the follow-up period.

Table 1 shows age adjusted HRs and their 95% CIs based on the health status according to sex. The HR was significantly higher in the subjects who suffered from any type of disease and also had limitations in daily living (HR=2.36, 95%CI: 1.50 ~ 3.70, P<0.01) than that in the subjects who did not feel fatigue, or had no symptoms after adjusting for age. Also, a linear positive correlation was observed in total mortality in males with a worse health status (linear trend: P<0.01). Therefore, we explored the association individually between each lifestyle-related factor and total mortality while adjusting for age and health status.

Tables 2 and 3 show univariately and multivariately analyzed HRs and their 95%CIs based on categories regarding the lifestyle-related factors on total mortality according to sex. The HR adjusted age and health-status (or adj1-HR) was significantly lower in the subjects whose BMI was equal to or above 24 (adj1-HR=0.50, 95%CI: 0.33 ~ 0.75, P<0.01) than that in the male subjects whose BMI was less than 20. We thus found a negative linear trend in total mortality in males with a low BMI (linear

Table 1 Hazard ratios and their 95% confidence intervals for total mortality according to health status after adjusting for age.

	males (n=1,099)				females (n=1,022)			
Health status	No. of subjects	No. of deaths	HR	95%CI	No. of subjects	No. of deaths	HR	95%CI
1. not feeling any fatigue, no symptoms	177	36	1.00		130	15	1.00	
2. sometimes feeling fatigue	538	90	0.95	0.65 ~ 1.40	492	30	0.64	0.34 ~ 1.19
3. getting sick sometimes, recovering from it easily	157	29	1.19	0.73 ~ 1.94	218	11	0.49	0.22 ~ 1.06
4. having minor ailments, no limitations in daily living	134	35	1.32	0.83 ~ 2.11	108	9	0.68	0.30 ~ 1.56
5. having some limitations in daily living	93	40	2.36 **	1.50 ~ 3.70	74	14	1.42	0.69 ~ 2.95
	linear trend: P<0.01				linear trend: P=0.38			

HR: Hazrd ratio (HR was determined by Cox's proportional hazard regression model after adjusting for age).
95%CI: 95% confidence interval of HR.
**: P<0.01(P value was tested based on the Wald test).

trend: P<0.01).

The adj1-HR of each physical fitness test was not statistically significant. The adj1-HR was significantly lower in male subjects whose physical fitness scores in 1983 were in the highest category (adj1-HR=0.58, 95%CI: 0.40 ~ 0.84, P<0.01) than that of the subjects whose physical fitness scores were in the lowest category. We found a negative trend in total mortality in males with a low physical fitness score (linear trend: P<0.01). However, we did not find a negative trend between total mortality and physical fitness scores in females, although the adj1-HR was significantly lower in the subjects whose physical fitness scores was the second lowest category in 1983 (adj1-HR=0.50, 95%CI: 0.27 ~ 0.92, P<0.05).

The adj1-HR was significantly lower in the male subjects who ate a balanced diet than in the subjects who did not (adj1-HR=0.70, 95%CI: 0.54 ~ 0.91, P<0.01).

The adj1-HR was significantly higher in the male subjects who were current cigarette smokers in 1983 (adj1-HR=1.57, 95%CI: 1.03 ~ 2.41, P<0.05) than in the subjects who had never smoked in 1983. The adj1-HR was significantly higher in the female subjects who quit smoking in 1983 (adj1-HR=2.69, 95%CI: 1.08 ~ 6.66, P<0.05) than in the subjects who had never smoked in 1983. When allocating the values as follows: never smoking=1, quitting=2 and current smoking=3, the smoking status trend was significant for males (linear trend: P<0.01), but it was not significant for females.

Because the various risk factors may influence each other, we next investigated the multivariate analysis for all items. The HRs that were analyzed multivariately were named adj2-HRs. They were all still statistically significant, except for those of the subjects whose BMI was equal to or above 24 and current cigarette smokers for males. Because the subjects who died within 2 years after the baseline survey might have had prior disease, we excluded early death subjects (death within 2 years after the baseline survey), and thus we found that the adj2-HR of the female subjects who quit smoking decreased and became insignificant (adj2-HR=2.27, 95%CI: 0.81 ~ 6.37, P=0.12). Although the adj2-HRs of the other factors slightly decreased, the main results did not change (data not shown).

We examined the HRs according to the lifestyle-related categories for cancer mortality after adjusting for all items and excluding the subjects with early death (within 2 years after the baseline survey) to reduce the influence of either pre-existing cancer or a delay in diagnosis in males. It was significantly lower in the male subjects who ate a balanced diet (HR=0.66, 95%CI: 0.44 ~ 0.99, P<0.05) than in the subjects who did not. It was significantly higher in the subjects who were current cigarette smokers in 1983 (HR=2.09, 95%CI: 1.07 ~ 4.10, P<0.05) than in the subjects who never smoked in 1983, and the smoking trend was statistically significant (linear tend: P<0.01). In contrast, no significant lifestyle-related risk factors for cancer mortality were observed in females (data not shown).

Figure 1 illustrates the survival curves for two typical male groups having good or poor health habits related to total mortality such as physical fitness scores, BMI, smoking after adjusting for age, and health status, eating a balanced diet, according to the age group. The subjects who were in the highest category on the physical fitness score and whose BMI was in the highest category, and who were not current cigarette smokers were assigned to the "good habit group", while the subjects who were in the lowest category on the physical fitness score and whose BMI was in the lowest category, and who were current cigarette smokers were assigned to the "poor habit group". The good habit groups show a higher survival rate than the poor habit groups among all age groups. The survival curves of the good habit group aged 60 to 69 and the poor habit group aged 40 to 49 were quite similar. The degree of difference in the survival probability between the good habit group and the poor habit group increased more in the 60 to 69 age group than in the groups aged 40 to 49 or 50 to 59 after 13 years.

DISCUSSION

The present study showed that such factors as being underweight, having a low physical fitness level, not eating a balanced diet, and cigarette smoking, should be considered separately in the index of risk factors for total mortality in Japanese men.

In this study, we found a negative trend between BMI and total mortality in men. The relationship between BMI and mortality has been shown as J- or U-shaped [8, 10, 29] in other populations than Japanese. In Japan, Nakayama [13] and Tsukamoto [30] have reported that the relationship between BMI and mortality has been shown to be U-shaped, while Ishii et al. [9] have reported a relationship between the BMI and mortality which resulted in an L-shaped relationship in males, and a U-shaped one in females. Lean subjects have been reported to have a high mortality due to the effects of smoking, alcohol use and disease-related weight loss [8, 11, 13, 23, 31-33]. Manson [34] reviewed the prospective studies regarding body weight and mortality, and pointed out the failure to control cigarette smoking, the biologic effects of obesity, and weight loss due to subclinical disease. The HR of the highest category of BMI changed insignificantly after adjusting for age, health status, smoking, physical activity, and

Table 2 Hazard ratios and their 95% confidence intervals for total mortality according to lifestle-related factors in males.

Items	Units	No. of subjects	No. of deaths	adj1-HR	95%CI	adj2-HR	95%CI
BMI	BMI<20	199	63	1.00		1.00	
	20≦BMI<22	329	71	0.82	0.58 ~ 1.15	0.82	0.51 ~ 1.32
	22≦BMI<24	282	59	0.80	0.56 ~ 1.14	0.80	0.41 ~ 1.59
	24≦BMI	289	37	0.50 **	0.33 ~ 0.75	0.54	0.19 ~ 1.54
				linear trend: P<0.01		linear trend: P<0.01	
Physical fitness score	~ 6	157	55	1.00		1.00	
	7 ~ 9	223	53	0.78	0.53 ~ 1.14	0.78	0.53 ~ 1.14
	10 ~ 11	205	50	0.93	0.63 ~ 1.38	0.91	0.62 ~ 1.36
	12 ~	514	72	0.58 **	0.40 ~ 0.84	0.60 **	0.41 ~ 0.87
				linear trend: P<0.01		linear trend: P<0.05	
Physical activity	nothing	490	105	1.00		1.00	
	vigorous or light intensity	609	125	0.78	0.60 ~ 1.01	0.86	0.65 ~ 1.14
Ate a balanced diet	no	520	119	1.00		1.00	
	yes	579	111	0.70 **	0.54 ~ 0.91	0.76 *	0.58 ~ 0.99
Current alcohol drinker	no	267	68	1.00		1.00	
	yes	832	162	0.89	0.67 ~ 1.18	0.94	0.70 ~ 1.26
Current smoker	never	180	25	1.00		1.00	
	quit	300	61	1.14	0.71 ~ 1.83	1.26	0.70 ~ 1.81
	current	619	144	1.57 *	1.03 ~ 2.41	1.50	0.97 ~ 2.31
				linear trend: P<0.01		linear trend: P<0.05	

BMI: Body mass index.
HR: Hazrd ratio (HR was determined by Cox's proportional hazard regression model).
adj1-HRs were calculated after adjusting for age and health status.
adj2-HRs were calculated after adjusting for age, health status, smoking, physical activity, and balance of daily food intake.
95%CI: 95% confidence interval of HR.
*: P<0.05, **: P<0.01(P value was tested based on the Wald test).

Table 3 Hazard ratios and their 95% confidence intervals for total mortality according to lifestle-related factors in females.

Items	Units	No. of subjects	No. of deaths	adj1-HR	95%CI	adj2-HR	95%CI
BMI	BMI<20	198	21	1.00		1.00	
	20≦BMI<22	278	14	0.53	0.27 ~ 1.04	0.56	0.25 ~ 1.25
	22≦BMI<24	267	23	0.78	0.43 ~ 1.41	0.86	0.32 ~ 2.32
	24≦BMI	279	21	0.65	0.36 ~ 1.20	0.73	0.16 ~ 3.24
				linear trend: P=0.37		linear trend: P=0.48	
Physical fitness score	~ 6	345	42	1.00		1.00	
	7 ~ 9	289	14	0.50 *	0.27 ~ 0.92	0.51 *	0.27 ~ 0.96
	10 ~ 11	184	13	0.78	0.41 ~ 1.48	0.81	0.42 ~ 1.55
	12 ~	204	10	0.66	0.32 ~ 1.37	0.70	0.33 ~ 1.48
				linear trend: P=0.23		linear trend: P=0.33	
Physical activity	nothing	583	46	1.00		1.00	
	vigorous or light intensity	439	33	0.82	0.53 ~ 1.29	1.00	0.62 ~ 1.61
Ate a balanced diet	no	435	37	1.00		1.00	
	yes	587	42	0.81	0.52 ~ 1.26	0.88	0.57 ~ 1.39
Current alcohol drinker	no	871	72	1.00		1.00	
	yes	151	7	0.74	0.34 ~ 1.63	0.76	0.35 ~ 1.68
Current smoker	never	952	71	1.00		1.00	
	quit	24	5	2.69 *	1.08 ~ 6.66	2.77 *	1.09 ~ 7.03
	current	46	3	0.90	0.28 ~ 2.86	0.94	0.29 ~ 3.02
				linear trend: P=0.57		linear trend: P=0.52	

BMI: Body mass index.
HR: Hazrd ratio (HR was determined by Cox's proportional hazard regression model).
adj1-HRs were calculated after adjusting for age and health status.
adj2-HRs were calculated after adjusting for age, health status, smoking, physical activity, and balance of daily food intake.
95%CI: 95% confidence interval of HR.
*: P<0.05, **: P<0.01(P value was tested based on the Wald test).

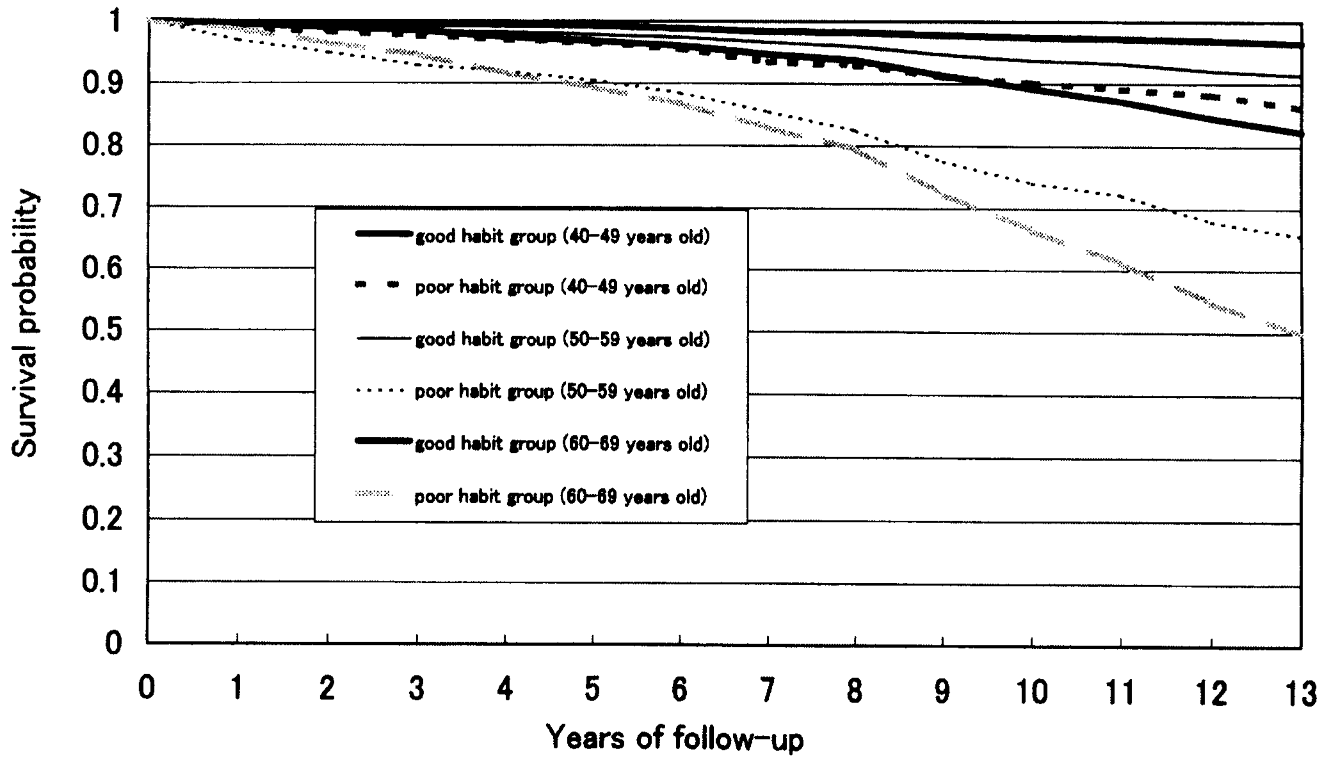

Figure 1 Survival Curve determined by Cox's proportional hazard model after adjusting for age, BMI, physical fitness score, daily food intake, smoking status and health status according to age group. The good habit group (solid line) consisted of subjects whose lifestyle was as follows; Physical fitness score was equal to or above 12, BMI was equal to or above 24, and were not current cigarette smokers. The poor habit group (dotted line) consisted of the subjects whose lifestyle was as follows; Physical fitness score was equal to or less 6, BMI was less than 20, and they were current cigarette smokers.

balance of daily food intake with a multivariate analysis, while we found a negative trend between total mortality and BMI in men. It has been reported that mortality increased significantly in the subjects whose BMI was above 28[23]. In the present study, the mean of BMI of the males was 22.4 ± 2.7 (Mean ± 1SD), and there were no extremely obese subjects. Therefore, we might find a negative linear trend between mortality and BMI instead of a J- or U-shaped BMI-mortality relation due to a lack of extreme obesity. On the other hand, it has been reported that a low BMI increased mortality more than that observed for extremely overweight subjects, which does not appear to be due to smoking or existing disease[9, 29, 35]. Shirasaki[35] et. al. suggested that a low body-weight person has decreased protection against disease. Our results suggest that a lower body weight might possibly be a disadvantage to longevity, although we could not identify any relationships between obesity and mortality.

Current smokers have reported that they tend to have a lower physical fitness level than either subjects who have never smoked or those who quit smoking[36-38]. Smoking has also been demonstrated to be one of the strongest risk factors for total mortality and mortality from cardiovascular disease, cerebrovascular disease, and cancer[22-25, 33]. However, we found that the risk of death was significantly lower in the subjects who kept a higher physical fitness score, after adjusting for several factors including smoking by a multivariately analysis. Sawada[39] et. al. examined the relationship between physical fitness and all causes of mortality in 9,986 Japanese men who had their maximal oxygen uptake estimated, and reported that the risk of death was significantly lower in the subjects who kept a higher physical fitness level after adjusting for age, BMI, hypertension, urinary protein, alcohol consumption, and cigarette smoking. Smoking was a risk factor of total and cancer mortality, and the risk for cancer mortality was higher than the risk for total mortality in males of this study. There were also no significant differences between the ex-smoker and never smoker, while current smokers showed a significantly high risk of death. Our findings may suggest that non smoking has a positive effect on longevity, and it is also effective in reducing cancer in males.

Individuals who include moderate to high levels of physical activity are reported to experience even greater longevity[14-22]. It has been reported that physical activity promotes physical fitness, and reduces obesity, and also reduces blood pressure, lipids and the glucose level in blood[40, 41]. To have a physically active lifestyle, and to keep a high level of physical fitness thus appears to have a positive influence on overall health through the above mechanism. We did not evaluate the levels of physical activity in terms of intensity, duration, and frequency, although we estimated the physical fitness level as reflected in the total score of a physical fitness test. Physical fitness assessed either subjectively or objectively, is considered to be an integral level of the functional status of many organ systems, and it can be frequently perceived as the degree of effort required to perform daily actions. Good physical fitness suggests the presence of a normal cardiorespiratory function, efficient oxygen transport and uptake, muscular and skeletal function, and psychological fitness. Our observations may also support the importance of physical activity in health maintenance, since the self-assessed fitness score was closely related to a decreased risk of death.

In this study, the risk of total mortality was reduced due to decreased cancer mortality in those subjects with a balanced diet. These results support the fact that improvements in dietary habits or having knowledge of a healthier dietary pattern may contribute to a primary prevention of total and cancer mortality.

The BMI, physical fitness score, having a balanced diet, and smoking were respectively significant risk factors for death in males, but they were not significant in females. Other studies have also reported a lack of association in females[7, 8, 12]. In this study, females tended to have a healthier lifestyle than males since the percentage of individuals consuming a balanced diet was higher while the number of females who smoked, and drank alcohol was far less than in males. Furthermore, there was a lower mortality in females than males. These facts might therefore provide us with important information regarding health promotion in men.

In conclusion, it is worth mentioning that being underweight might also be an index of a positive risk of death, while having a balanced diet, keeping a high physical fitness level, and non smoking might be indexes of a negative risk of death at least in our male study population. In addition, these results might also be considered good evidence for improving poor health habits when we engage in health promotion activities.

ACKNOWLEDGMENTS

We thanked the staff members of the various city and town offices of Saga Prefecture for their valuable assistance. This study was supported mainly by public school (Saga Medical School) expenses and in part by the Daiwa Health Foundation, Japan.

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