

Physical Activity and Physical Fitness as Predictors of All-Cause Mortality in Korean Men

We examined the associations between physical activity (PA), fitness and all-cause mortality and compared their contributions, taking smoking status into consideration. A retrospective cohort study of 18,775 men was carried out between May 1995 and December 2003. Fitness was measured by maximum oxygen uptake and regular PA was defined as at least three times a week, for more than 30 min of leisure time PA. During the mean 6.4 yr of follow-up, 547 deaths were recorded. The hazard ratio (HR) (95% confidence interval [CI]) of regular PA for all-cause mortality was 0.63 (0.52-0.76). The HRs (95% CIs) for men with middle and highest tertile levels of fitness were decreased by 0.58 (0.47-0.70) and 0.58 (0.45-0.75) in comparison to men with lowest one. The inverse association between fitness and mortality was significant among the men who did not engage in regular PA, but not among those who did (p for interaction=0.031). Smoking status did not influence on the associations between regular PA, fitness and mortality. Our result suggested that regular PA and fitness predicted mortality in men. The influence of fitness on mortality was pronounced in the men who did not engage in regular PA.

Key Words : Motor Activity; Exercise; Physical Fitness; Mortality, Smoking

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INTRODUCTION

Physical inactivity is an important risk factor for all-cause, cardiovascular (CV) and cancer mortality in both men and women (1, 2). Epidemiologic evidences have shown strong associations between physical fitness (fitness), measured by maximal exercise testing, and survival from CV and non-CV causes (1-4).

Fitness, a physiologic attribute, quantifies the ability of the body to transport and use oxygen and is determined principally by training status and, to some extent, by genetic predisposition (5). Physical activity (PA) is a behavioral attribute and comprises the energy expenditure from volitional or non-volitional activity throughout the day (5). Whereas fitness can be directly and accurately quantified with graded exercise tests, the measure of PA pattern has relied on cruder methods, such as self-reports, motion detectors (i.e., Caltrac) (6), or structured interviews (7). Although fitness is often used as an indicator of PA, there has been recent debate as to whether daily PA patterns largely determine one's fitness and therefore its inverse association with mortality, or whether fitness level predicts mortality, independent of PA patterns (8). Most of these issues have been evaluated in asymptomatic Caucasians and other ethnic population (9-11) or patients with existing cardiovascular disease (5). It has not been well studied as to whether PA and fitness are independent deter-

minants of all-cause mortality in Korean subjects.

Chronic smoking usually induces elevated myocardial work and reduces exercise capacity and thus impairs overall cardiopulmonary fitness (12). In addition, it is a well established risk factor for mortality. Accordingly, chronic smoking reduces one's fitness level and therefore might influence on the association between physical fitness and mortality. Furthermore, there has been debate as to whether the beneficial effects of physical activity are modified by the smoking status (13, 14). Therefore, the aim of this study was to examine the association between fitness (measured by maximum oxygen uptake [VO_2 max]) and all-cause mortality, independent of regular PA or smoking status in Korean men.

MATERIALS AND METHODS

Subjects

We collected data for 19,410 men who had undergone medical check-ups and graded exercise tests for obtaining VO_2 max at the Health Promotion Center at Seoul National University Hospital from May 1995 to December 2003. Of those, we excluded 148 subjects who had prior histories of cancer (N=78), stroke (N=44) or myocardial infarction (N=26), and 487 subjects who had missing information on reg-

ular PA. A total of 18,775 men were included in the final analysis. The institution review board of Seoul National University Hospital reviewed and approved the protocol, retrospectively.

Baseline measurements

Information on age, education level, occupation, income, smoking status, alcohol consumption, regular leisure time PA (light moderate, or vigorous activities for more than 30 min at least three times a week) by a structured self-reported questionnaire, supervised by trained nurse. Smoking status were classified into 3 categories; current, former, or never smokers. Subjects who reported smoking at least one cigarette per day at present time were classified as current smokers. Non-smokers were defined as those who had never smoked. Subjects who reported as not smoking currently but had smoked ever were classified as former smokers. History for alcohol drinking was evaluated by the subject's reported average frequency (times per week) during the month before the screening examination. Regular drinker was defined as drinking alcoholic beverages at least once a week.

Height and weight were measured after an overnight fast while the subject wore a lightweight gown. Blood pressure was measured using an automated blood pressure device (Jawon, Busan, Korea) after the subject had rested for at least 20 min in a sitting position. Blood samples were obtained after an overnight fast of at least 12 hr for chemical analysis. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg at baseline examination, a reported history of previous hypertension, or current uses of antihypertensive medication (15). Diabetes was defined as fasting plasma glucose ≥ 126 mg/dL at enrollment, a reported history of previous diabetes mellitus, or current use of anti-diabetic agents.

Physical activity and physical fitness assessment

Leisure time PA was determined by assessing the results of a self-administered questionnaire that included questions regarding the subjects' participation in any kind of regular physical exercise or walking, the duration and the frequency of each activity per week over a month prior to the examination. This process was supervised by a trained nurse, and the subjects were encouraged to ask questions if they needed further clarification on any question. The PA of each subject was confirmed by a doctor, face-to-face, just after the completion of the self-administered questionnaire. Those who reported engaging in leisure time PA once a week or more were asked about the average duration and intensity (light, moderate or vigorous) (16) of the activity. In this study, PA was classified into two categories: regular PA, defined as leisure time PA engaged in any intensity of PA for 30 min at least three times a week, and no regular PA group.

Graded exercise tests were performed on a cycle ergometer (Cateye Ergociser, EC 1600, Osaka, Japan), and VO_2 max was estimated by a skilled examiner in order to evaluate the subject's physical fitness level. The subjects exercised to a cardiac frequency of 85% of their predicted maximum until stopping due to dyspnea, fatigue, chest pain or systolic blood pressure greater than or equal to 250 mmHg (17).

Mortality ascertainment

Participants were followed for mortality from baseline examination until death for decedents or until December 31, 2005 for survivors. Death was ascertained through record linkage with the national death certificate files in Korea. Follow-up for deaths was more than 98% complete (18). For all deaths, a computerized search of death certificate data from the National Statistical Office in Korea was performed using personal identification numbers assigned at birth. International Classification of Diseases (ICD) 10th Revision was used for coding the cause of death. Cardiovascular death was defined with codes I00-99 and cancer death was defined with codes C00-C97 (19) at the hospitals.

Table 1. Baseline characteristics of the study subjects according to the regularity of physical activity

	Regular PA (N=7,157)	No regular PA (N=11,618)	<i>p</i> value
Age (yr)	58.3 (10.8)	54.0 (11.00)	<0.001
BMI (kg/m ²)	24.3 (2.63)	24.0 (2.98)	<0.001
Smoking*			<0.001
Never	1,560 (22.0)	1,968 (17.1)	
Former	2,963 (41.8)	2,997 (26.0)	
Current	2,569 (36.2)	6,572 (57.0)	
Regular drinker*	5,155 (72.7)	8,129 (70.8)	0.004
Total cholesterol (mg/dL)	200.3 (34.29)	199.4 (36.66)	0.102
Glucose (mg/dL)	103.2 (27.75)	101.0 (28.22)	<0.001
Triglyceride (mg/dL)	145.6 (110.4)	162.6 (115.7)	<0.001
Diagnosis of hypertension*	3,004 (42.0)	4,042 (34.8)	<0.001
Diagnosis of diabetes*	957 (13.5)	1,162 (10.1)	<0.001
VO_2 max (mL/kg/min)*	26.0 (15.46)	23.8 (10.34)	<0.001
Low	2,541 (35.5)	4,246 (38.7)	
Moderate	2,114 (29.5)	3,085 (28.1)	
High	2,502 (35.0)	3,639 (33.2)	

Data are mean (SD), *frequency (%).

Chi-square test or Student's t-tests were used (missing information for smoking status=144).

VO_2 max was categorized as low (VO_2 max ≤ 22 mL/kg/min), moderate (23 mL/kg/min $\leq VO_2$ max ≤ 29 mL/kg/min) and high (VO_2 max ≥ 30 mL/kg/min).

Regular drinker means the men drinking alcoholic beverages at least once a week.

VO_2 max, maximum O_2 uptake measured by graded exercise test with bicycle ergometer. Regular physical activity (PA) means 'engaging in light, moderate or vigorous activities for at least 30 min more than three times a week.'

PA, physical activity; BMI, body mass index.

Statistical analysis

SPSS for Windows 12.0 was used for statistical analysis. All analyses were performed after excluding the subjects who died during the first two years of follow-up. The chi-square-tests or Student's t-tests were used to analyze the statistical differences between the characteristics of the study participants according to PA. Cox proportional hazard models were used to calculate the adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) in model for all-cause mortality. Physical fitness level was first classified into tertile in total subjects: low ($VO_2 \text{ max} \leq 22 \text{ mL/kg/min}$), moderate ($23 \text{ mL/kg/min} \leq VO_2 \text{ max} \leq 29 \text{ mL/kg/min}$) and high ($VO_2 \text{ max} \geq 30 \text{ mL/kg/min}$). Then, fitness was divided into tertile separately according to the regular or no regular PA groups: low ($VO_2 \text{ max} \leq 23 \text{ mL/kg/min}$), moderate ($24 \text{ mL/kg/min} \leq VO_2 \text{ max} \leq 29 \text{ mL/kg/min}$) and high ($VO_2 \text{ max} \geq 30 \text{ mL/kg/min}$) in the regular PA group; low ($VO_2 \text{ max} \leq 22 \text{ mL/kg/min}$), moderate ($23 \text{ mL/kg/min} \leq VO_2 \text{ max} \leq 28 \text{ mL/kg/min}$) and high ($VO_2 \text{ max} \geq 29 \text{ mL/kg/min}$) in the no regular PA group. Stratified by the regularity of PA, all-cause, CV and cancer mortality at the different levels of fit-

ness (by each tertile increase) were estimated after adjusting for age, study year, body mass index (BMI), total cholesterol, alcohol consumption, smoking status (never, former, or current) and diagnosis of hypertension or diabetes.

We also examined stratified analyses according to the categories of smoking status in the multivariate analyses to examine whether the associations between regular PA, fitness and mortality were modified by smoking status. *p* values are 2-sided, and *p*<0.05 was considered to be statistically significant.

RESULTS

During the mean follow-up period of 6.4 yr, 547 deaths were recorded, of which 262 (47.9%) were due to cancer and 101 (18.5%) were due to CV disease. The characteristics of the study subjects according to PA status at baseline were compared (Table 1). The mean (SD) age of the study participants was 55.7 (11.1) yr, and the mean (SD) $VO_2 \text{ max}$ of the subjects in the regular PA group was 26.0 (15.5) mL/kg/min and that of the subjects in the no regular PA group was

Table 2. Multivariate hazard ratios (HRs) (95% CI) of all-cause, CV and cancer mortality among men

Variables	All-cause mortality HR (95% CI)	CV mortality HR (95% CI)	Cancer Mortality HR (95% CI)
Age	1.08 (1.07-1.09)	1.11 (1.09-1.13)	1.08 (1.06-1.09)
BMI (per 1- unit increment)	0.96 (0.93-1.00)	0.97 (0.93-1.01)	0.94 (0.89-0.99)
Cholesterol (per 1 mg/dL increment)	1.00 (0.99-1.00)	1.01 (1.00-1.01)	1.00 (0.99-1.00)
Regular physical activity			
No	1	1	1
Yes	0.63 (0.52-0.76)	0.42 (0.27-0.68)	0.72 (0.55-0.94)
Regular drinking			
No	1	1	1
Yes	0.75 (0.63-0.90)	0.78 (0.52-1.18)	0.73 (0.57-0.94)
Smoking			
No	1	1	1
Former	1.25 (0.96-1.64)	0.92 (0.47-1.98)	2.08 (1.34-3.25)
Current	1.97 (1.52-2.55)	1.44 (0.85-2.43)	3.00 (1.94-4.63)
Diagnosis of hypertension			
No	1	1	1
Yes	1.44 (1.20-1.72)	2.27 (1.48-3.48)	1.26 (0.97-1.63)
Diagnosis of diabetes			
No	1	1	1
Yes	1.30 (1.04-1.61)	1.16 (0.70-1.93)	1.48 (1.09-2.02)
$VO_2 \text{ max}$			
Low	1	1	1
Moderate	0.58 (0.47-0.70)	0.47 (0.29-0.77)	0.60 (0.45-0.80)
High	0.58 (0.45-0.75)	0.64 (0.35-1.19)	0.52 (0.36-0.76)

Regular physical activity (PA) means 'engaging in light, moderate or vigorous activities for at least 30 min more than three times a week.'

$VO_2 \text{ max}$ was categorized as low ($VO_2 \text{ max} \leq 23 \text{ mL/kg/min}$), moderate ($24 \text{ mL/kg/min} \leq VO_2 \text{ max} \leq 29 \text{ mL/kg/min}$) and high ($VO_2 \text{ max} \geq 30 \text{ mL/kg/min}$) in the regular PA group and low ($VO_2 \text{ max} \leq 22 \text{ mL/kg/min}$), moderate ($23 \text{ mL/kg/min} \leq VO_2 \text{ max} \leq 28 \text{ mL/kg/min}$) and high ($VO_2 \text{ max} \geq 29 \text{ mL/kg/min}$) in the no regular PA group.

Regular drinking means drinking alcoholic beverages at least once a week.

$VO_2 \text{ max}$, -: maximum O_2 uptake measured by graded exercise test with bicycle ergometer; CI, confidence interval; CV, cardiovascular; BMI, body mass index.

23.8 (10.3) mL/kg/min. The subjects who engaged in regular PA were older and had higher fasting glucose levels and a lower prevalence of current smoker in comparison to those who did not.

The effects of regular PA and physical fitness on mortality

The adjusted HR (95% CI) of regular PA for all-cause mortality was 0.63 (0.52-0.76). The HRs (95% CI) of all-cause mortality for the men with moderate and high levels of fitness decreased to 0.58 (0.47-0.70) and 0.58 (0.45-0.75), respectively, in comparison to the men with a low level of fitness. Engaging in regular PA and higher level of fitness also reduced CV and cancer mortality. The HRs (95% CI) of men who engaged in regular PA was 0.42 (0.27-0.68) for CV mortality and 0.72 (0.55-0.94) for cancer mortality. The adjusted HRs (95% CI) in men with moderate and high levels of fitness, using men with a low level of fitness as reference, were 0.47 (0.29-0.77) and 0.64 (0.35-1.19) for CV mortality and 0.60 (0.45-0.80) and 0.52 (0.36-0.76) for cancer mortality, respectively. Diagnosis of hypertension or Diabetes, BMI, smoking status and alcohol consumption were also significantly related to mortality (Table 2).

Combined effect of regular PA and fitness on mortality

The association between fitness and mortality was significantly stronger among the men who did not engage in regular PA than those who did (p for interaction=0.031 for all-cause mortality, table not shown). When stratified by regu-

larity of PA, the men in higher level of fitness did not show significant reduction of the HRs for total mortality and CV mortality (p for trend=0.15 for total mortality, p for trend=0.63 for CV mortality) compared to men in the lowest level of fitness. Cancer mortality decreased significantly in men with higher level of fitness in the regular PA group (p for trend=0.037) On the other hand, in the no regular PA group, all-cause, CV and cancer mortality decreased significantly with increased fitness level. The adjusted HRs in men with moderate and high levels of fitness, using men with a low level of fitness as reference, were 0.49 and 0.49 (p for trend <0.001) for total mortality, 0.41 and 0.46 (p for trend=0.007) for CV mortality, and 0.57 and 0.42 (p for trend<0.001) for cancer mortality, respectively, after full adjustment for age, study year, total cholesterol, BMI smoking status, alcohol consumption and diagnosis of hypertension or diabetes (Table 3).

The effect of regular PA and fitness on mortality according to smoking status

In the analysis stratified by smoking status, there was statistically significant decrease in all-cause mortality with increased fitness level in all smoking categories in the no regular PA group. In the group of subjects who did not engage in regular PA, the HRs of men with moderate and high levels of fitness in never smokers for all-cause mortality were 0.21 and 0.53 (p for trend=0.007), those of former smokers were 0.58 and 0.45 (p for trend=0.018) and those of current smokers were 0.52 and 0.50 (p for trend<0.001), respectively, in comparison to the men with a low level of fitness in

Table 3. Hazard ratios for all-cause, cardiovascular and cancer mortality according to level of physical fitness and regularity of physical activity

	Physical activity						
	Regular		ID	aHR (95% CI)	No regular		aHR (95% CI)
	case/person-years				case/person-years	ID	
All cause mortality	1st tertile	81/16,735	484.02	1.00	240/28,123	853.39	1.00
	2nd tertile	58/14,252	406.96	0.71 (0.49-1.02)	50/20,608	242.62	0.49 (0.37-0.65)
	3rd tertile	35/14,482	241.68	0.77 (0.52-1.12)	43/22,027	195.22	0.49 (0.36-0.67)
				p for trend=0.148			p for trend <0.001
Cardiovascular mortality	1st tertile	13/16,735	77.68	1.00	53/28,123	188.46	1.00
	2nd tertile	8/14,252	56.13	0.62 (0.22-1.73)	14/20,608	67.93	0.41 (0.21-0.79)
	3rd tertile	5/14,482	34.53	1.01 (0.35-2.95)	8/22,027	36.31	0.46 (0.22-0.95)
				p for trend=0.625			p for trend=0.007
Cancer mortality	1st tertile	44/16,735	262.92	1.00	107/28,123	380.47	1.00
	2nd tertile	26/14,252	182.43	0.49 (0.27-0.85)	49/20,608	237.77	0.57 (0.39-0.85)
	3rd tertile	19/14,482	131.20	0.71 (0.41-1.24)	17/22,027	77.18	0.42 (0.26-0.68)
				p for trend=0.036			p for trend<0.001

Adjusting for age, study year, total cholesterol, body mass index, smoking status (never, former, current), regular drinking (drinking alcoholic beverages at least once a week) and diagnosis of hypertension or diabetes

Regular physical activity (PA) means 'engaging in light, moderate to vigorous activities for at least 30 min more than three times a week.'

VO₂ max was categorized as low (VO₂ max ≤23 mL/kg/min), moderate (24 mL/kg/min ≤VO₂ max ≤29 mL/kg/min) and high (VO₂ max ≥30 mL/kg/min) in the regular PA group and low (VO₂ max ≤22 mL/kg/min), moderate (23 mL/kg/min ≤VO₂ max ≤28 mL/kg/min) and high (VO₂ max ≥29 mL/kg/min) in the no regular PA group.

ID, incidence density (per 100,000 person-years); aHR, adjusted hazard ratio; CI, confidence interval.

Table 4. Hazard ratios for all-cause mortality according to level of physical fitness (VO₂ max) and regular physical activity and smoking status among men

Physical activity	aHR (95% CI)		
	Never smoker	Former smoker	Current smoker
Regular			
Low	1	1	1
Moderate	1.08 (0.43-2.75)	0.85 (0.50-1.82)	0.50 (0.27-0.91)
High	1.47 (0.54-3.96)	0.61 (0.30-1.24)	0.75 (0.41-1.36)
<i>p</i> for trend	0.744	0.379	0.076
No regular			
Low	1	1	1
Moderate	0.21 (0.07-0.59)	0.58 (0.34-0.97)	0.52 (0.36-0.74)
High	0.53 (0.23-1.21)	0.45 (0.23-0.89)	0.50 (0.34-0.73)
<i>p</i> for trend	0.007	0.018	<0.001

Adjusting for age, study year, total cholesterol, fasting glucose, body mass index, regular drinking (drinking alcoholic beverages at least once a week) and diagnosis of hypertension or diabetes.

Regular physical activity (PA) means 'engaging in light, moderate or vigorous activities for at least 30 min more than three times a week.'

VO₂ max was categorized as low (VO₂ max ≤ 23 mL/kg/min), moderate (24 mL/kg/min ≤ VO₂ max ≤ 29 mL/kg/min) and high (VO₂ max ≥ 30 mL/kg/min) in the regular PA group and low (VO₂ max ≤ 22 mL/kg/min), moderate (23 mL/kg/min ≤ VO₂ max ≤ 28 mL/kg/min) and high (VO₂ max ≥ 29 mL/kg/min) in the no regular PA group.

aHR, adjusted hazard ratio; CI, confidence interval.

each smoking category (Table 4). The HRs (95% CIs) in men who engaged in regular PA and who were current smokers with moderate and high levels of fitness decreased to 0.50 (0.27-0.91) and 0.75 (0.41-1.36), in comparison to those with a low level of fitness.

DISCUSSION

The results of the present study demonstrated that both regular PA and physical fitness are inversely associated with the risk of death among relatively healthy men.

The extent how much the beneficial effects of PA on health are mediated through one's fitness level has been a matter of debate. The association between PA pattern and fitness was reported with a correlation of 0.3-0.6 (20) and 0.09 (5) in different studies. Roman et al. examined the relationship between VO₂ max and PA energy expenditure using doubly labeled water method in free living older individuals (21). They reported a low order of correlation ($r=0.37$) and only 13% of shared variance between VO₂ max and PA energy expenditure. They also suggested that fitness and PA may act in a unique and independent manner to improve cardiovascular and metabolic health (21).

Few studies have addressed both fitness and PA in the same study in subjects with clinical data. In this study, the association between fitness and mortality was significant among men who did not engage in regular PA, but not among those

who did. We observed that the subjects in the no regular PA group with the highest level of fitness showed a significant 51% risk reduction in all-cause mortality; meanwhile the risk of death in the subjects in the regular PA group with the highest level of fitness was attenuated by 23%, compared to the lowest level of fitness, but this effect was not statistically significant. These finding might be originated from the result that the number of subjects who engaged in regular PA was relatively small (38.1% of total subjects), and the incidence rate of mortality in the men engaging in regular PA was lower than that in the men with no regular PA (484.02 per 100,000 person-years for lowest fitness in regular PA group, 853.39 per 100,000 person-years for lowest fitness in no regular PA group).

Regular PA in this study was defined as leisure time PA (engaging in any kind of leisure time PA for 30 min at least three times a week) over one month prior to the assessment of fitness. All subjects not included in the regular PA group were included in the no regular PA group. Regular PA in this study reflected regularly spent leisure time PA-related energy expenditure regardless of intensity of leisure time PA. In regular PA, strength and power training like indoor golf or weight lifting and stretching exercise like yoga were all included based upon the frequency and duration of activity. These activities are not enough to increase fitness level, but enough to spend PA-related energy expenditure and reduce total mortality related to non-CV causes such as fall, fracture and depression etc. Although there is a genetic component to fitness, the major modifiable determinant of fitness is physical activity intense enough to increase heart rate above resting levels and deliver more oxygen to the tissue.

Our study showed that all-cause mortality was affected by regular PA than fitness level. Regular PA is known to influence not only metabolic health including improving insulin sensitivity and reducing body fatness, but also improving cardiopulmonary fitness (22). They also reported that PA-related energy expenditure, or the total dose of physical activity is more important for health benefits than is the specific type of PA performed (e.g., walking, running, cycling) (22).

In general, the dose-response relationship between fitness and activity and the risk of death showed a relatively greater benefit in the lower fitness group than in the higher fitness group (23-24). In Korea, the 2001 Korean National Health and Nutrition Survey performed with a representative sample of 7,838 subjects who completed questionnaires on PA and were over 20 yr old showed that 71.8% of the subjects did not exercise at all (25). However, the public transportation system and walkways in Korea are well developed, and people in Korea spend an average 65.8 (± 73.6) min per day walking (25). Therefore regardless of regularity of leisure time PA, Korean people might spend much time walking on average. This phenomenon might explain why the effect of fitness level on mortality was attenuated in subjects in the regular PA group.

We also assessed the influence of smoking status on the association between fitness level, regular PA and all-cause mortality. The risk of mortality in men who did not engage in regular PA with higher level of fitness, compared to the lowest level of fitness, was significantly reduced in all smoking categories. In the regular PA group, an increased fitness level seemed to have a protective effect on death risk reduction, but this was statistically significant only in the current smokers.

Smoking is widely recognized as a major risk factor for all-cause mortality, as is physical inactivity (26). Cigarette smoking has been known to contain more than 4,000 toxic substances, and engaging in physical activities that are intense enough to increase one's fitness level would increase their body heat and eliminate the water-soluble toxic substances found in cigarettes from their body by heat dissipation (sweating). Even the detrimental effect of smoking on all-cause mortality might be preventable with strenuous physical activity. Physical activity also provides the advantages of increased body fluid for heat dissipation (sweating) and thermoregulatory stability as well as a larger vascular volume for greater cardiac filling and stroke volume and cardiovascular stability during exercise and orthostatic challenges (27). Therefore, PA and fitness may be protective against reduced blood volume and the subsequent development of disease associated with aging. These findings suggest that human beings might be born with an innate need to be physically active to live healthy. We observed that physical fitness reduced the risk of all-cause mortality, especially in the high-risk group, such as those who did not engage in regular PA. According to our study results, men who do not engage in regular PA could reduce their mortality risk by engaging in daily activities that are intense enough to increase their fitness level.

Our study has several limitations. The study population was composed of relatively healthy people and did not include women because the number of female smokers was too small. Although the sample size of this study was not small, the number of deaths may not have been large enough to obtain enough statistical power to demonstrate the health benefit of increased the fitness level of healthy subjects who engage in regular PA. Because the cause-specific mortality has been classified accurately since 2000, it might have chance of being misclassified between 1995 and 1999.

However, our study results are not different from those of previous studies that investigated physical fitness or activity separately (28-30). Few researches have focused on the association between fitness level and all-cause mortality according to smoking status, mostly in former and current smokers. To the best of our knowledge, this is the first large study to directly measure VO_2 max by graded exercise testing in order to assess physical fitness in Korean men.

In conclusion, we observed that regular PA and physical fitness, as assessed by VO_2 max, were inversely associated with all-cause, CV and cancer mortality in Korean men. In

this study, the regular PA is more important than fitness in predicting the mortality. The combined effect of fitness and PA on mortality was more pronounced in the subjects who did not engage in regular PA. Our study suggested that even in the current smokers especially who did not engage in regular PA, increasing one's fitness level by participating intense activities such as running, fast walking or climbing stairs during normal daily activities, might provide health benefits to reduce the risk of mortality. Further studies are needed to investigate the association between free living PA and fitness on all-cause and cause-specific mortalities.

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