



Underweight and mortality

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Abstract

Objective: According to most prospective studies, being underweight (BMI <18.5 kg/m²) is associated with significantly higher mortality than being of normal weight, especially among smokers. We aimed to explore in a generally lean population whether being underweight is significantly associated with increased all-cause mortality.

Design: Prospective cohort study.

Setting: Korea Medical Insurance Corporation study with 14 years of follow-up.

Subjects: After excluding deaths within the first 5 years of follow-up (1993–1997) to minimize reverse causation and excluding participants without information about smoking and health status, 94 133 men and 48 496 women aged 35–59 years in 1990 were included.

Results: We documented 5411 (5.7%) deaths in men and 762 (1.6%) in women. Among never smokers, hazard ratios (HR) for underweight individuals were not significantly higher than those for normal-weight individuals (BMI = 18.5–22.9 kg/m²): HR = 0.87 (95% CI 0.41, 1.84, *P* = 0.72) for underweight men and HR = 1.12 (95% CI 0.76, 1.65, *P* = 0.58) for underweight women. Among ex-smokers, HR = 0.86 (95% CI 0.38, 1.93, *P* = 0.72) for underweight men and HR = 3.77 (95% CI 0.42, 32.29, *P* = 0.24) for underweight women. Among current smokers, HR = 1.60 (95% CI 1.28, 2.01, *P* < 0.001) for underweight men and HR = 2.07 (95% CI 0.43, 9.94, *P* = 0.36) for underweight women.

Conclusions: The present study does not support that being underweight *per se* is associated with increased all-cause mortality in Korean men and women.

Keywords
Thinness
Mortality
Smoking
Obesity
Korea

The relationship between BMI and all-cause mortality has been extensively explored in several studies. Obesity has generally been shown to be associated with significantly increased all-cause mortality in many previous studies⁽¹⁾. However, there is still substantial inconsistency regarding the risks of mortality among underweight persons. Indeed, several epidemiological studies have suggested no significant increase in all-cause mortality among individuals in the low BMI category^(2–9), while many other studies do^(10–20).

In Asia, where general populations tend to be leaner and being underweight is highly prevalent, understanding the health outcomes associated with being underweight has become particularly important. Nevertheless, large prospective studies have yet to confirm the relationship between underweight and all-cause mortality, especially in a modern context, where mortality from tuberculosis

and other infectious diseases is low. Therefore we aimed to investigate the associations between being underweight and mortality in Korean men and women.

Methods

Study population

The Korea Medical Insurance Corporation (KMIC) provides health insurance to civil service workers, teachers and their dependants in Korea. Of the entire Korean population (approximately 43 million in 1990), 4 603 361 (11%) were insured by KMIC, including 1 213 594 workers and 3 389 767 dependants. All insured workers are required to participate in biennial medical examinations performed by KMIC. In 1990 and 1992, respectively 95% and 94% of workers

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completed the biennial examinations. The KMIC study comprised a 25 % systematic random sample of male workers and all female workers, drawn from insured members ordered by national identification numbers. The study comprised 108 461 men and 64 119 women, aged 35–59 years, who underwent physical examinations twice in 1990 and 1992. Ethical approval was given by the Institutional Review Board of Severance Hospital at Yonsei University.

Measurements

The KMIC biennial examinations were conducted in a standardized fashion by medical staff at local hospitals. In 1990, examinations were conducted at 416 hospitals. A questionnaire was administered to each participant three to four days before physical examination, and completed questionnaires were reviewed and edited by trained staff. Smoking history, alcohol consumption, physical activity and health status were assessed in 1992. Age was documented in 1990. Height, weight, fasting glucose, total cholesterol, systolic blood pressure and diastolic blood pressure were measured in 1990 and 1992, and were averaged for analysis. BMI was calculated as weight in kilograms divided by the square of height in metres (kg/m^2). BMI groups were divided according to the WHO recommendations for Asians: underweight, $<18.5 \text{ kg}/\text{m}^2$; normal range, $18.5\text{--}22.9 \text{ kg}/\text{m}^2$; overweight at risk, $23.0\text{--}24.9 \text{ kg}/\text{m}^2$; obese I, $25.0\text{--}29.9 \text{ kg}/\text{m}^2$; and obese II, $\geq 30.0 \text{ kg}/\text{m}^2$ ⁽²¹⁾. Participants were classified as current smokers if they were smoking, ex-smokers if they smoked at least one cigarette during their whole life but quit, and never smoker if they never smoked even one cigarette.

Mortality follow-up

The follow-up period, which lasted 14 years, was from 1 January 1993 to 31 December 2006. Death certificates from the National Statistical Office were issued according to identification numbers that were assigned to the participants at birth. The causes of death were coded according to the International Classification of Diseases, 10th revision (ICD-10): CVD were categorized by ICD-10 codes I00–I99; cancers were classified by ICD-10 codes C00–C97; and respiratory diseases were coded by ICD-10 codes J00–J99. Other causes of deaths were defined as deaths from other causes than cardiovascular, cancer and respiratory causes.

Statistical analysis

We excluded 8317 men and 4561 women who had known diseases at baseline, and further excluded 2041 men and 329 women who died during 1993–1997 to minimize the impact of reverse causality. We also excluded 3970 men and 10 733 women who had no information on smoking. Finally, we included 94 133 men and 48 496 women for analysis. All statistical analyses were performed separately for men and women. Baseline characteristics of the participants are listed

according to BMI categories. Cox's proportional hazards regression models were used to calculate hazard ratios (HR) and 95 % CI to investigate the association between BMI and all-cause mortality after adjusting for age and alcohol consumption. In order to investigate whether being underweight is associated with all-cause mortality independently from smoking status, we calculated HR and 95 % CI separately for never smokers, ex-smokers and current smokers. The Cox's regression models were adjusted for age, alcohol consumption and cigarettes smoked per day (only for current smokers). As an exploratory analysis, we also calculated HR and 95 % CI for cause-specific mortality: CVD, cancer, respiratory disease and other causes. All statistical procedures were performed using the statistical software package SAS version 9.2 and all *P* values less than 0.05 were considered statistically significant.

Results

The general characteristics of the study participants are presented according to BMI category in Table 1. For men, the numbers of individuals in each BMI group ($<18.5 \text{ kg}/\text{m}^2$, $18.5\text{--}22.9 \text{ kg}/\text{m}^2$, $23.0\text{--}24.9 \text{ kg}/\text{m}^2$, $25.0\text{--}29.9 \text{ kg}/\text{m}^2$, $\geq 30.0 \text{ kg}/\text{m}^2$) were 974 (1.0 %), 40 254 (42.8 %), 29 369 (31.2 %), 22 946 (24.4 %) and 590 (0.6 %), respectively. For women, the numbers in those groups were 2199 (4.5 %), 29 209 (60.2 %), 11 028 (22.7 %), 5841 (12.0 %) and 219 (0.5 %), respectively. Male participants who were underweight had relatively lower mean values for blood pressure, fasting glucose and total cholesterol; they were also more likely to be current smokers, non-drinkers and physically inactive, compared with those in higher BMI categories. Female participants who were underweight had relatively lower mean age, blood pressure, fasting glucose and total cholesterol; they were also more likely to be non-drinkers and physically inactive, compared with women in higher BMI categories.

In Table 2, analyses adjusted for age and alcohol consumption revealed a significantly higher HR for total mortality in underweight men (HR = 1.48; 95 % CI 1.21, 1.82) compared with individuals with normal BMI. Men in the obese II category were also associated with higher all-cause mortality (HR = 1.28; 95 % CI 0.96, 1.70) compared with those with normal BMI, although the association was not statistically significant. Underweight (HR = 1.20; 95 % CI 0.83, 1.74) and obese II (HR = 1.55; 95 % CI 0.73, 3.29) women showed higher mortality than women with normal BMI, although these associations were not statistically significant.

In Table 3 we present the HR for all-cause mortality among the BMI groups stratified according to smoking status, with adjustment for age and alcohol consumption. The reference group comprised participants with normal BMI within the same stratum of smoking status. Among male never smokers, being underweight was not associated with all-cause mortality (HR = 0.87; 95 % CI 0.41, 1.84); obese I (HR = 1.15;

Table 1 Baseline characteristics of participants by sex: men (*n* 94 133) and women (*n* 48 496) aged 35–59 years in 1990, Korea Medical Insurance Corporation study

Characteristic	BMI (kg/m ²)																			
	Men										Women									
	<18.5 (<i>n</i> 974)		18.5–22.9 (<i>n</i> 40 254)		23.0–24.9 (<i>n</i> 29 369)		25.0–29.9 (<i>n</i> 22 946)		≥30.0 (<i>n</i> 590)		<18.5 (<i>n</i> 2199)		18.5–22.9 (<i>n</i> 29 209)		23.0–24.9 (<i>n</i> 11 028)		25.0–29.9 (<i>n</i> 5841)		≥30.0 (<i>n</i> 219)	
Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	
Age (years)	45.6	7.2	44.5	6.7	44.9	6.6	44.8	6.5	45.2	6.7	39.6	5.1	41.0	5.5	43.4	6.3	45.3	6.4	46.1	6.7
BMI (kg/m ²)	17.9	0.5	21.4	1.1	24.0	0.6	26.4	1.1	31.2	1.2	17.8	0.6	21.0	1.2	23.9	0.6	26.4	1.1	31.4	1.5
SBP (mmHg)	118.7	12.1	122.3	13.0	125.9	13.6	128.9	14.1	135.7	15.9	110.9	10.0	113.8	10.8	118.1	12.6	123.0	14.2	132.4	17.6
DBP (mmHg)	77.2	8.6	79.9	8.9	82.5	9.2	84.7	9.5	89.5	10.5	71.6	7.5	73.8	8.0	76.9	9.0	80.3	9.7	86.5	11.5
FG (mg/dl)	89.2	13.4	90.3	16.3	92.4	17.9	94.2	18.9	98.2	20.5	84.1	9.8	84.9	10.0	86.9	12.3	89.1	14.0	92.6	19.8
TC (mg/dl)	180.3	28.4	188.2	31.3	196.4	32.6	201.3	33.5	205.6	34.5	179.1	28.2	184.8	30.3	193.3	33.2	200.8	34.9	205.0	34.9
Smoking status (<i>n</i> , %)																				
Never smoker	191	19.6	7785	19.3	6498	22.1	5435	23.7	148	25.1	2169	98.6	28 868	98.8	10 899	98.8	5746	98.4	214	97.7
Ex-smoker	139	14.3	7683	19.1	6446	22.0	5224	22.8	127	21.5	17	0.8	237	0.8	88	0.8	67	1.2	1	0.5
Current smoker	644	66.1	24 786	61.6	16 425	55.9	12 287	53.6	315	53.4	13	0.6	104	0.4	41	0.4	28	0.5	4	1.8
<20 cigarettes/d	456	46.8	17 475	43.4	11 147	38.0	7959	34.7	191	32.4	11	0.5	93	0.3	37	0.3	25	0.4	4	1.8
≥20 cigarettes/d	188	19.3	7311	18.2	5278	18.0	4328	18.9	124	21.0	2	0.1	11	0.04	4	0.04	3	0.1	0	0.0
Alcohol consumption (<i>n</i> , %)																				
No	364	37.5	10 231	25.5	6556	22.4	4819	21.1	139	23.6	2000	92.5	26 184	90.5	9832	90.2	5064	87.9	182	84.3
Yes	606	62.5	29 906	74.5	22 733	77.6	18 067	78.9	451	76.4	163	7.5	2745	9.5	1068	9.8	700	12.1	34	15.7
Physical activity (<i>n</i> , %)																				
No	746	78.0	27 967	70.5	19 484	67.2	15 203	67.1	396	68.3	1900	86.9	24 463	84.3	8995	82.4	4753	82.4	185	85.3
Yes	210	22.0	11 727	29.5	9507	32.8	7461	32.9	184	31.7	286	13.1	4563	15.7	1925	17.6	1019	17.7	32	14.8

SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; TC, total cholesterol.

Table 2 Hazard ratios for mortality according to BMI category by sex: men (*n* 94 133) and women (*n* 48 496) aged 35–59 years in 1990, follow-up period 1 January 1993 to 31 December 2006, Korea Medical Insurance Corporation study

BMI (kg/m ²)	No. of deaths	% of deaths	Adjusted HR*	Adjusted 95 % CI*
Men				
<18.5	93	9.6	1.48	1.21, 1.82
18.5–22.9	2440	6.1	1.00	Reference
23.0–24.9	1608	5.5	0.87	0.82, 0.93
25.0–29.9	1222	5.3	0.86	0.80, 0.91
≥30.0	48	8.1	1.28	0.96, 1.70
Women				
<18.5	31	1.4	1.20	0.83, 1.74
18.5–22.9	393	1.4	1.00	Reference
23.0–24.9	189	1.7	1.03	0.86, 1.23
25.0–29.9	142	2.4	1.26	1.03, 1.54
≥30.0	7	3.2	1.55	0.73, 3.29

HR, hazard ratio.

*Adjusted for age and alcohol consumption.

95 % CI 0.96, 1.36) and obese II (HR=1.98; 95 % CI 1.11, 3.53) men showed a higher risk of mortality, with the association for obese I men being nearly significant. Among male ex-smokers, none of the BMI groups showed significantly increased mortality risk. Among male current smokers, being underweight was associated with a significantly higher risk of mortality (HR=1.60; 95 % CI 1.28, 2.01). Among female never smokers, being underweight was not significantly associated with mortality (HR=1.12; 95 % CI 0.76, 1.65); obese I (HR=1.30; 95 % CI 1.07, 1.60) women showed a significantly higher risk of mortality. Among female ex-smokers and current smokers, the number of deaths in each BMI category was too small to properly assess the relationship between BMI and mortality.

We additionally assessed cause-specific mortalities to investigate causes contributing to the increased mortality risk observed in underweight male participants who smoke cigarettes. Among male current smokers, being underweight was associated with an increased risk of death from cancer, respiratory disease and other causes, but not from CVD, compared with males with normal BMI (data presented in online supplementary material, Supplemental Table 1).

Discussion

In the present large-scale and long-term prospective study of middle-aged Korean men and women, no significant associations between being underweight and all-cause mortality were observed among never smokers.

Previous studies have reported that underweight people with disease or poor health exhibit different patterns of mortality than healthy underweight people. Moreover, underweight individuals with one of several prevalent diseases also show marked increases in mortality, compared with their normal-weight counterparts^(22–24). Thus, the inclusion of participants with underlying disease

or poor health may limit analyses^(8,10,11,25,26). Accordingly, we excluded participants with underlying disease and those who died within the first 5 years of follow-up to reduce bias associated with reverse causality.

The physiological characteristics of smokers are not the same as those of the general population. In particular, smokers tend to have lower BMI⁽²⁷⁾. Smoking is also one of the major leading risk factors for all-cause mortality worldwide^(28,29). Associations between BMI and mortality should therefore be separately analysed according to smoking status. Some prospective studies undertaken in Western and Chinese populations have suggested that mortality is not increased in never smokers of the lowest BMI category^(2–9). In contrast, other studies have found an increased risk of mortality in the leanest of participants who did not smoke^(10,12–20). There could be several explanations for this difference. First, participants with underlying diseases were not adequately excluded. In fact, some of the studies did not exclude participants with underlying disease^(12–19). Second, the validity of information on BMI may have been compromised. While repeated measurements can reduce measurement error, few of these previous studies measured height and weight twice. Third, the associations between being underweight and mortality could differ according to the age distribution of participants. Many studies included participants of ages 60 years or more^(10,12–20). These older participants may more likely carry co-morbidities, leading to low BMI and introducing bias to the results.

One previous study performed in Korea suggested that male never smokers (HR=1.3; 95 % CI 1.2, 1.4) and ever smokers (HR=1.4; 95 % CI 1.3, 1.4) with low BMI (<18.5 kg/m²) exhibit higher mortality than reference males (BMI=23.0–24.9 kg/m²). Among female never smokers, those with low BMI showed higher mortality (HR=1.2; 95 % CI 1.1, 1.3) than the reference category⁽¹⁰⁾. We were unable to clearly determine what made our study findings different from those of the previous Korean study.



Table 3 Hazard ratios for mortality according to BMI category and smoking status by sex: men (n 94 133) and women (n 48 496) aged 35–59 years in 1990, follow-up period 1 January 1993 to 31 December 2006, Korea Medical Insurance Corporation study

BMI (kg/m ²)	Never smoker			Ex-smoker			Current smoker					
	No. of deaths	% of deaths	Adjusted HR*	Adjusted 95% CI*	No. of deaths	% of deaths	Adjusted HR*	Adjusted 95% CI*	No. of deaths	% of deaths	Adjusted HR†	Adjusted 95% CI†
Men												
<18.5	7	3.7	0.87	0.41, 1.84	6	4.3	0.86	0.38, 1.93	80	12.4	1.60	1.28, 2.01
18.5–22.9	285	3.7	1.00	Reference	362	4.7	1.00	Reference	1793	7.2	1.00	Reference
23.0–24.9	270	4.2	1.08	0.92, 1.28	314	4.9	0.99	0.85, 1.15	1024	6.2	0.85	0.79, 0.92
25.0–29.9	245	4.5	1.15	0.96, 1.36	228	4.4	0.87	0.74, 1.03	749	6.1	0.86	0.79, 0.94
≥30.0	12	8.1	1.98	1.11, 3.53	9	7.1	1.32	0.68, 2.56	27	8.6	1.22	0.83, 1.78
Women												
<18.5	28	1.3	1.12	0.76, 1.65	1	5.9	3.77	0.42, 32.29	2	15.4	2.07	0.43, 9.94
18.5–22.9	379	1.3	1.00	Reference	6	2.5	1.00	Reference	8	7.7	1.00	Reference
23.0–24.9	186	1.7	1.06	0.88, 1.27	2	2.3	0.83	0.17, 4.15	1	2.4	0.27	0.03, 2.17
25.0–29.9	140	2.4	1.30	1.07, 1.60	0	0.0	–	–	2	7.1	0.80	0.17, 3.81
≥30.0	6	2.8	1.40	0.63, 3.15	0	0.0	–	–	1	25.0	4.21	0.51, 34.46

HR, hazard ratio.

*Adjusted for age and alcohol consumption.

†Adjusted for age, alcohol consumption and cigarettes per day.

The two studies are, nevertheless, distinct in a few aspects. First, the previous study enrolled insured workers and their family members of a wider age range (35–95 years)⁽¹⁰⁾, while our study enrolled only insured workers of ages 35 to 59 years. Second, the previous study enrolled participants who had undergone at least one health screening examination between 1992 and 1995, while our study enrolled participants who had undergone two health screening examinations in both 1990 and 1992, allowing us to use the means of two measurements for analysis to reduce measurement errors. Lastly, the reference categories were different: BMI = 23.0–24.9 kg/m² in the previous study and BMI = 18.5–22.9 kg/m² in our analysis.

Concerning current smokers, most previous studies have reported that underweight individuals are at a significantly increased risk of mortality^(2,9,10,12,13,16–18). This was also reflected in our results. We speculate that being thin may indicate a greater susceptibility to the adverse effects of smoking and particular smoking behaviours, such as deep inhalation.

The strengths of our study include the use of data from a large prospective study in Korea, which is, in general, a lean population. Second, we excluded participants with underlying disease or who died within the first 5 years of follow-up. Third, our study used average BMI, which was measured twice at baseline years (1990 and 1992); thus, our data on BMI might be more reliable and less subject to measurement error. Information on deaths was also accurate, since deaths were confirmed from the National Statistical Office via use of identification numbers assigned to participants at birth.

Our study has several limitations that warrant consideration. First, we performed the study in only middle-aged Korean men and women, which may limit the generalizability of our results to other populations. Nevertheless, our data from a population with a much lower average BMI than most Western populations enabled us to robustly explore associations that may not be prevalent in other cohorts. Second, a considerable number of women were excluded from the analysis, because they did not report their smoking status. If smoking women with poor health status were less likely to report their smoking status than healthy smoking women, selection bias might occur and distort our study findings. Notwithstanding, we did perform sensitivity analyses classifying participants with unknown smoking status into never smokers and the results were very close to our initial results. Third, we did not assess the effect of weight changes after baseline evaluation. If an underweight participant was to gain weight and a normal-weight participant was to lose weight, the difference in BMI between the two groups might become smaller. Thus, we could not completely exclude the possibility of a bias towards the null.

In conclusion, the present study does not support that being underweight *per se* is associated with higher mortality than being of normal weight.

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Supplementary material

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