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Association between adult height, myocardial infarction, heart failure, stroke and death: a Korean nationwide population-based study

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Abstract

Background: The association between adult height and cardiovascular (CV) events and mortality has been suggested, albeit inconsistently. We sought to discover the comprehensive relationship between height, CV-related morbidity and all-cause death according to age.

Methods: We investigated the association between adult height and myocardial infarction (MI), heart failure (HF), stroke incidence and mortality in 16 528 128 Korean patients who underwent regular health check-ups (2005–08). Height was stratified by decile according to age (20–39 years, 40–59 years and $\geq$60 years) and gender.

Results: During a 9-year follow-up period, 590 346 participants died and 232 093 were admitted to hospital for MI, 201 411 for HF and 267 566 for stroke. An inverse relationship between height and MI, HF, stroke and all-cause death was observed in the overall cohort analysis. The association was unchanged after adjusting for CV risk and behavioural and adulthood socioeconomic factors. Both male and female sex showed an inverse relationship with height in adulthood, CV events and mortality. Adult height showed an inverse association in all CV events and mortality, especially in the older groups ($\geq$40 years). In a subgroup analysis of body mass index, there was an inverse relationship between height, CV events and mortality in each group.

Conclusions: Shorter height in adulthood was strongly related to an increased risk of MI, HF, stroke and all-cause death. A suitable environment and appropriate nutrition early in life could influence adult height and eventually reduce the risk of CV events and mortality.

Key words: Height, myocardial infarction, heart failure, stroke, prognosis

Key Messages

- Adult subjects with short height showed a higher incidence of MI, HF, stroke and all-cause death compared with taller adults, after adjusting for various conventional CV risk factors.
- Both male and female sex showed an inverse relationship with adulthood height and CV events and mortality.
- Adult height showed an inverse association in all CV events and mortality in the older group (age $\geq$ 40 years), but this tendency was attenuated in the younger group (20–39 years).
- The prognostic implication of BMI for CV events and mortality within the same height decile varied across the height deciles.

Introduction

Cardiovascular (CV) events such as myocardial infarction (MI), heart failure (HF) and stroke are prevalent diseases and are important causes of morbidity and mortality.[1,2] Although the prevalence and incidence of HF have been lower in Asian countries than in Western countries, they are rapidly increasing.[3] Owing to the social disease burden of these events, various attempts have been made to identify their potential risk factors.[4–6] Despite improvement in the control of CV risk factors, the disease burden is unacceptably high and there is still a need for better stratification of the risk for CV diseases.

Height in adulthood, one of the basic anthropometric data, is easy to measure and is determined by a complex interaction among genetic endowment, nutritional status and other factors. A previous study reported that coronary heart disease was associated with low stature in middle-aged men, whereas the association between height and stroke was weak,[7] Although another study demonstrated that there was a higher risk of stroke in both middle-aged men and women.[8] Nelson *et al.* showed that there was a relationship between genetically determined height and coronary artery disease.[9] The stature of Western people compared with that of Asian people and stature between young and old people are quite different, and information about these associations in an Asian population is scarce. In addition, the clinical association between height and HF incidence has not been sufficiently evaluated yet.

In this study, we aimed to investigate the association between height and the incidence of CV events, using a large medical insurance database of the entire Korean population.

Methods

Data source and study population

The national health insurance system (NHIS) in the Republic of Korea began in 1963 with the passing of the Medical Insurance Act. After the National Health Insurance Act was passed in 1999, the NHIS became the single insurer of Korean patients in 2000. It has also provided regular health check-up programmes for the public. Adults who subscribe to the health insurance service are recommended to undergo this check-up at least biennially. Details on the NHIS system were published elsewhere.[10] In addition, the Health Insurance Review and Assessment Service (HIRA), a public institution which serves quality control and evaluates all health care performance from diagnosis to treatment, is present. The databases of both NHIS and HIRA are linked, checked and supervised by the Ministry of Health and Welfare which in turn provides the reliability and accuracy of the database. The NHIS database is available to researchers, and the data are supplied in an anonymous form if an official review committee has approved the study protocol. The need to obtain informed consent from subjects was waived in this study because we only used data from the NHIS (No. NHIS-2016-1-174). This study was conducted according to the Declaration of Helsinki and approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 1611-064-807).

Database contents

There are several data subsets of the NHIS database, including the qualification database, claim database, health check-up database and death information database.[10] Together, these databases include comprehensive information about demographics, disease diagnosis (according to the 10th revision of the International Classification of Diseases [ICD-10] codes), laboratory examinations and imaging studies, medical treatments, including medication and procedures, and hospitalization. Among these databases, we analysed information from the claim database, health check-up database and death information database.

Establishment of the study cohort

We recruited 17 391 531 subjects who were older than 20 years and who underwent an initial baseline health check-up by the NHIS between 2005 and 2008, among the total population of the Republic of Korea. This cohort was then followed up to 2015. From this initial population, we excluded 863 403 subjects who were diagnosed with MI, HF or stroke more than once within the first 3 years after the initial health check-up, after inception of the database. This policy was to secure adequate washout periods of previously diagnosed clinical endpoints. Therefore, 16 528 128 subjects were finally included in the baseline cohort and followed up.

Definition of the events and other variables

The CV endpoints were *de novo* occurrence of MI, HF, stroke and death during the follow-up period. The definition of each CV disease has been described in our previous reports and in Supplementary Table 1, available as Supplementary data at *IJE* online.[11,12] Comorbidities such as hypertension, diabetes mellitus, dyslipidaemia, chronic obstructive lung disease and end-stage renal disease were also defined using ICD-10 codes with additional information.

Considering that height is dependent on age and sex, we divided the population into deciles according to adult height for each age group (20–39 years, 40–59 years and ≥60 years) and sex. The deciles from the six different age and sex groups were merged into a single decile. We analysed these merged deciles based on CV outcomes and mortality. The definition of each decile according to age and sex is presented in Table 1 and in Supplementary Figure 1, available as Supplementary data at *IJE* online. To adjust for the effect of body weight, we calculated the participants' body mass index (BMI) and categorized participants as follows: BMI < 18.5, BMI 18.5–22.9, BMI 23.0–24.9, BMI 25.0–29.9 and BMI ≥ 30.0.[13] At the time of height and weight measurement, systolic and diastolic blood pressure, fasting blood glucose, haemoglobin and total cholesterol levels were also obtained, after overnight fasting. A detailed medical history including smoking history and alcohol drinking habits was obtained by questionnaire.

Statistical analysis

Data are presented as numbers and frequencies for categorical variables and as mean ± standard deviation. For comparisons between groups, the chi-square test (or Fisher's exact test when any expected cell count was <5 for a 2 × 2 table) was used for categorical variables, and an unpaired Student's t-test was applied for continuous variables. The annual event incidence rates (IR) were calculated as the number of events per 1000 person-years. Cox proportional hazard models were used to estimate the hazard ratios (HR) and the corresponding 95% confidence intervals (CI) for the association between height and CV endpoints. Two-sided *P*-values < 0.05 were considered statistically significant. Statistical tests were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA) and Stata statistical software release 12 (StataCorp, College Station, TX, USA).

Results

Baseline characteristics of study subjects

The study cohort consisted of 16 528 128 subjects who were seen at baseline between 2005 and 2008 and followed until 2015. The baseline characteristics according to height group are presented in Table 2. In brief, the mean age of the total population at baseline was 45.2 ± 14.2 years, and 8 856 661

Table 1. Reference value of height deciles based on age and sex groups

Sex	Age group	Height									
		D1	D2	D3	D4	D5	D6	D7	D8	D9	D10
Male	20–39 years (n = 3 771 508)	<165	165 ∼ 168	168 ∼ 170	170 ∼ 171	171 ∼ 173	173 ∼ 174	174 ∼ 176	176 ∼ 177	177 ∼ 180	>180
	40–59 years (n = 3 714 497)	<162	162 ∼ 164	164 ∼ 166	166 ∼ 167	167 ∼ 169	169 ∼ 170	170 ∼ 172	172 ∼ 174	174 ∼ 176	>176
	≥60 years (n = 1 370 656)	<158	158 ∼ 160	160 ∼ 162	162 ∼ 164	164 ∼ 165	165 ∼ 167	167 ∼ 168	168 ∼ 170	170 ∼ 172	>172
Female	20–39 years (n = 2 337 225)	<154	154 ∼ 156	156 ∼ 158	158 ∼ 159	159 ∼ 160	160 ∼ 162	162 ∼ 163	163 ∼ 165	165 ∼ 167	>167
	40–59 years (n = 3 752 003)	<150	150 ∼ 152	152 ∼ 154	154 ∼ 155	155 ∼ 156	156 ∼ 158	158 ∼ 159	159 ∼ 161	161 ∼ 163	>163
	≥60 years (n = 1 582 239)	<144	144 ∼ 147	147 ∼ 149	149 ∼ 150	150 ∼ 152	152 ∼ 153	153 ∼ 155	155 ∼ 156	156 ∼ 159	>159

Table 2. Baseline characteristics according to height group

Variables	Height				
	1st decile (n = 1 637 617)	2nd decile (n = 1 541 247)	3rd to 8th decile (n = 9 969 744)	9th decile (n = 1 797 889)	10th decile (n = 1 581 631)
Demographic data					
Age at baseline	47.3 ± 15.3	47.6 ± 14.1	45.0 ± 14.1	43.3 ± 13.9	44.1 ± 13.6
Male	900 615 (55.0)	907 352 (58.9)	5 238 468 (52.5)	1 031 072 (57.4)	779 154 (49.3)
Past medical history					
Diabetes mellitus	130 856 (7.99)	128 539 (8.34)	707 591 (7.1)	120 485 (6.7)	106 506 (6.73)
Hypertension	443 172 (27.06)	422 290 (27.4)	2 401 457 (24.09)	402 068 (22.36)	358 565 (22.67)
Dyslipidaemia	240 410 (14.68)	226 735 (14.71)	1 344 378 (13.48)	212 982 (11.85)	191 286 (12.09)
Chronic obstructive lung disease	187 032 (11.42)	176 083 (11.42)	1 058 414 (10.62)	180 610 (10.05)	166 089 (10.5)
End-stage renal disease	403 (0.02)	412 (0.03)	2 156 (0.02)	353 (0.02)	319 (0.02)
Social hsitory					
Smoking					
Never smoker	1 115 564 (68.12)	1 004 970 (65.2)	6 647 148 (66.67)	1 136 572 (63.22)	1 064 805 (67.32)
Ex-smoker	117 260 (7.16)	135 713 (8.81)	821 542 (8.24)	169 904 (9.45)	133 843 (8.46)
Current smoker	404 793 (24.72)	400 564 (25.99)	2 501 054 (25.09)	491 413 (27.33)	382 983 (24.21)
Drinking					
Never or rarely	913 874 (55.81)	807 724 (52.41)	5 169 443 (51.85)	850 623 (47.31)	808 759 (51.13)
2 ∼ 3 times/month	280 090 (17.1)	274 459 (17.81)	1 939 584 (19.45)	377 885 (21.02)	318 558 (20.14)
1 ∼ 2 times/weekly	290 830 (17.76)	294 871 (19.13)	1 969 238 (19.75)	394 531 (21.94)	317 911 (20.1)
3 ∼ 4 times/weekly	97 172 (5.93)	105 193 (6.83)	621 391 (6.23)	124 785 (6.94)	98 686 (6.24)
Almost daily	55 651 (3.4)	59 000 (3.83)	270 088 (2.71)	50 065 (2.78)	37 717 (2.38)
Blood pressure					
Systolic blood pressure	123.9 ± 17.0	123.8 ± 16.7	122.6 ± 16.0	122.2 ± 15.5	122.2 ± 15.5
Diastolic blood pressure	77.1 ± 10.8	77.2 ± 10.8	76.6 ± 10.6	76.5 ± 10.4	76.4 ± 10.4
Laboratory examinations					
Total cholesterol	195 ± 38.3	194.7 ± 37.8	192.6 ± 37.2	189.8 ± 36.2	189.9 ± 36.4
Fasting glucose	95.8 ± 26.2	96.3 ± 26.1	95.0 ± 24.2	94.7 ± 23.5	94.8 ± 23.5
Body mass index (kg/m^2)					
<18.5	62 415 (3.81)	54 238 (3.52)	404 130 (4.05)	86 616 (4.82)	76 029 (4.81)
18.5–22.9	640 064 (39.09)	600 159 (38.94)	4 046 708 (40.59)	755 751 (42.04)	661 280 (41.81)
23–24.9	403 733 (24.65)	390 980 (25.37)	2 417 634 (24.25)	419 826 (23.35)	381 096 (24.1)
25–39.9	474 526 (28.98)	449 679 (29.18)	2 796 861 (28.05)	480 713 (26.74)	414 428 (26.2)
30+	56 879 (3.47)	46 191 (3)	304 411 (3.05)	54 983 (3.06)	48 798 (3.09)
Low income level	428 391 (26.16)	358 948 (23.29)	2 153 478 (21.6)	361 501 (20.11)	314 522 (19.89)
Outcomes					
Myocardial infarction	29 671 (1.81)	26 863 (1.74)	135 407 (1.36)	21 821 (1.21)	18 331 (1.16)
Heart failure	30 550 (1.87)	23 743 (1.54)	114 676 (1.15)	17 443 (0.97)	14 999 (0.95)
Stroke	38 355 (2.34)	33 116 (2.15)	154 555 (1.55)	22 722 (1.26)	18 818 (1.19)
All-cause death	97 838 (5.97)	76 429 (4.96)	326 165 (3.27)	50 151 (2.79)	39 763 (2.51)

Values are presented as number (%).

subjects (53.6%) were male. Among them, 6.9% had diabetes mellitus, 23.4% had hypertension, 12.9% had dyslipidaemia, 10.3% had chronic obstructive lung disease and 2.1% had end-stage renal disease. During follow-up (mean 9.1 ± 1.4 years), 590 346 (3.6%) participants died. Among those who survived, 232 093 experienced MI (1.3%), 201 411 experienced HF (1.2%) and 267 566 experienced stroke-related events (1.6%). The overall incidence rates of MI, HF, stroke and all-cause death among the total population were 1.56, 1.35, 1.80 and 3.94, respectively, per 1000 person-years. The distribution of height in this study population is shown in Supplementary Figure 2, available as Supplementary data at *IJE* online.

Inverse association betweenhHeight and CV events

We analysed the relative risk of CV events according to height deciles, after stratifying the groups. Figure 1 demonstrates the HRs of MI, HF, stroke and all-cause death with

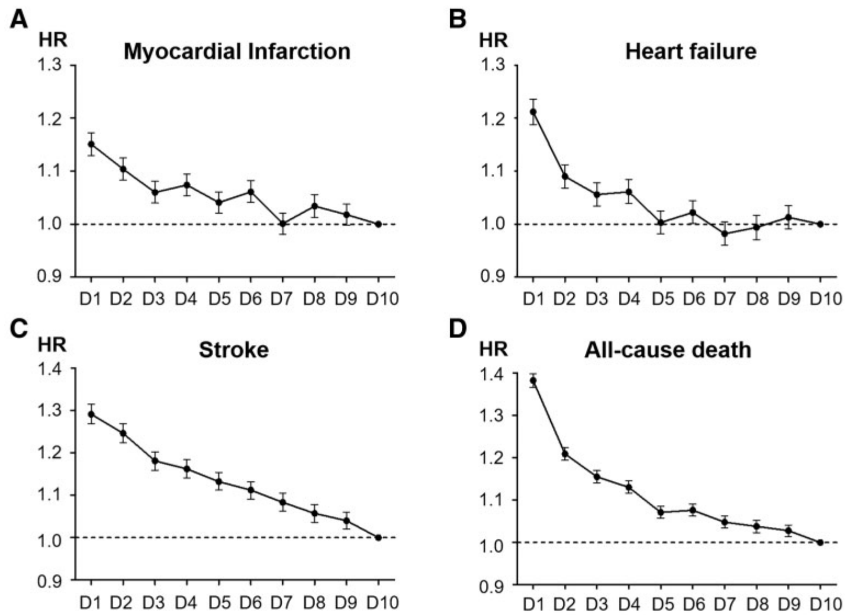

Figure 1. Hazard ratios for cardiovascular events in overall cohort. Data are from National Insurance Health Serve of South Korea. The reference category of height was the tallest 10th decile. Analysis results are demonstrated for myocardial infarction (A), heart failure (B), stroke (C) and all-cause death (D). D = height deciles from 1st to 10th; HR = hazard ratio.

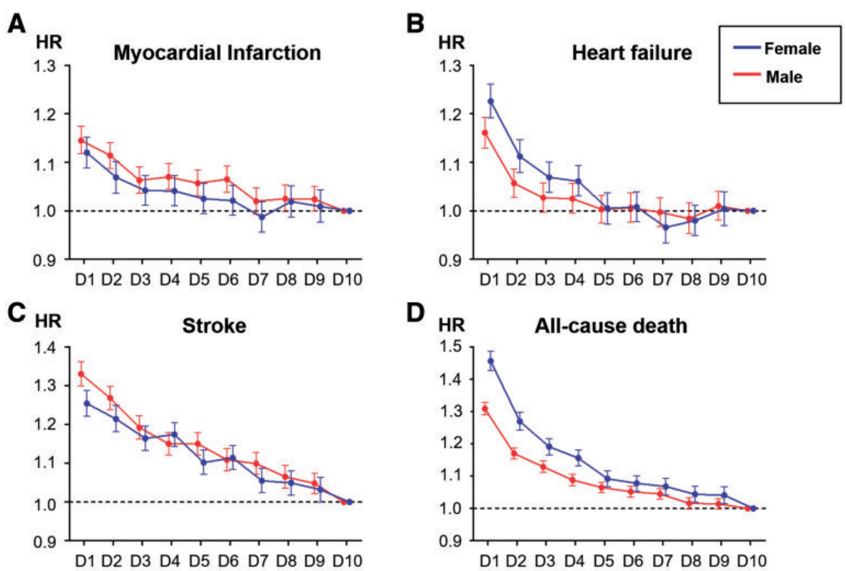

Figure 2. Hazard ratios for cardiovascular events according to sex. With the reference category as the tallest 10th decile, the hazard ratios of myocardial infarction (A), heart failure (B), stroke (C) and all-cause deaths (D) are demonstrated. D = height deciles from 1st to 10th; HR = hazard ratio.

the highest decile (D10) as a reference category. For MI and HF, short stature tended to be associated with an increased risk of MI (HR up to 1.15) and HF (HR up to 1.21). Regarding stroke (HR up to 1.29) and all-cause death (HR up to 1.38), all other groups had a significantly higher risk of poor prognosis compared with those in the highest decile.

The association between height and the risk of CV events had a similar pattern when subjects were classified according to sex. Regardless of sex, subjects with short stature had worse CV events. The HRs of MI, HF, stroke and all-cause death were increased up to 1.15, 1.16, 1.33 and 1.31, respectively, for men and up to 1.12, 1.23, 1.25 and 1.46, respectively, for women (Figure 2).

We also analysed the association between height and CV events according to age subgroups (20–39 years, 40–59 years and ≥60 years) (Figure 3; and Supplementary Table 2, available as Supplementary data at *IJE* online). In subjects aged ≥60 years, the incidence of MI, HF, stroke and all-cause death showed an inverse relationship with height; the HR increased up to 1.20, 1.24, 1.39 and 1.36, respectively, when compared with those in the highest decile.

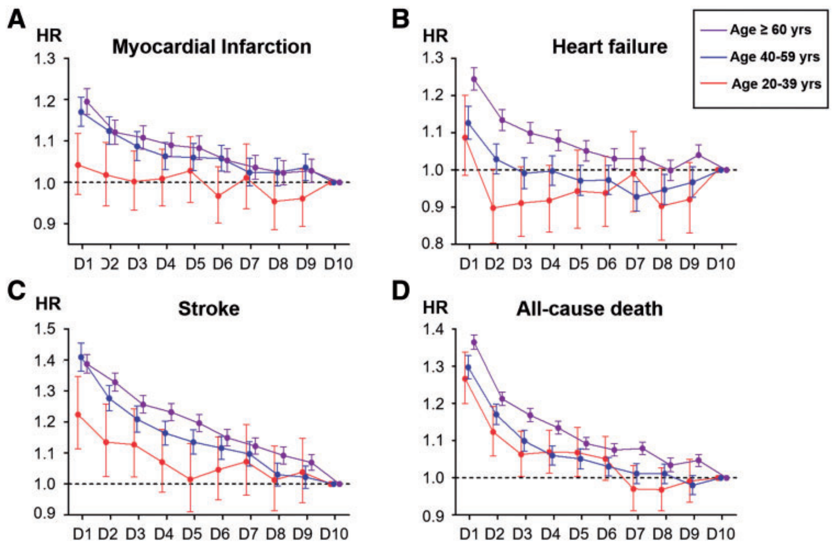

Figure 3. Hazard ratios for cardiovascular events according to age. With the reference category as the tallest 10th decile, the hazard ratios of myocardial infarction (A), heart failure (B), stroke (C) and all-cause deaths (D) are demonstrated. D = height deciles from 1st to 10th; HR = hazard ratio.

However, the predictive value of height was attenuated in the youngest group (aged 20–39 years) due to fewer events.

Relationship between height and CV events according to body mass index

There were 683 428 (4.1%) subjects with a BMI < 18.5 kg/mg^2, 6 703 962 (40.6%) subjects with a BMI 18.5–22.9 kg/m^2, 4 013 269 (24.3%) subjects with a BMI 23.0–24.9 kg/m^2, 4 616 207 (27.9%) with a BMI 25.0–29.9 kg/m^2 and 51 162 (3.1%) with a BMI ≥ 30 kg/m^2. The incidence rates per 1000 person-years are demonstrated in Figure 4. In each BMI group, shorter subjects tended to have increased incidence rates of MI, HF, stroke and all-cause death. Regarding the effect of BMI within each height decile, BMI tended to have a linear correlation with the risk of MI, HF and stroke. However, this correlation diminished, especially in deciles with shorter adults. Underweight participants (BMI < 18.5 kg/m^2) showed a similar or higher risk of MI, stroke and HF as obese participants (BMI ≥ 30 kg/m^2), especially in the lowest height decile. Underweight subjects in all height deciles showed the highest risk of mortality. This finding was more prominently observed at lower height deciles compared with higher height deciles; the IR per 1000 person-years differed from 17.5 to 4.7 in the lowest height decile, whereas the IR in the highest decile group across BMI groups differed from 3.7 to 2.5.

Independent predictive value of height for CV events

In a multivariate analysis (Table 3) which was adjusted for age, sex, BMI and additional comorbidities such as smoking history, drinking history, diabetes mellitus, hypertension, dyslipidaemia and low income level, low height was an independent risk factor for MI (HR up to 1.15; 95% CI 1.13–1.17), HF (HR up to 1.21; 95% CI 1.19–1.24, stroke (HR up to 1.29; 95% CI 1.27–1.31) and all-cause death (HR up to 1.38; 95% CI 1.36–1.40) compared with those in the highest group. With same models of Table 3, the hazard risk for cardiovascular events per 5-cm increase in height are also analysed. Table 4 demonstrates the hazard ratio and confidence interval per 5-cm height increment for cardiovascular events; they were constantly significant in both male and female subgroups.

Discussion

Main findings

To the best of our knowledge, this is the largest study that has included more than 16 million subjects and reported the relationship between height in adulthood and CV events and mortality. The major findings of this study are as follows: (i) adult subjects with shorter height showed a higher incidence of MI, HF, stroke and all-cause death compared with taller adults, after adjusting for various conventional CV risk factors; (ii) both male and female sex showed an inverse relationship with adulthood height and CV events and mortality; (iii) adulthood height showed an inverse association with all CV events and mortality in the older group (age ≥ 40 years), but this tendency was attenuated in the younger group (20–39 years); and (iv) the prognostic implication of BMI for CV events and mortality within the same height decile varied across the height deciles.

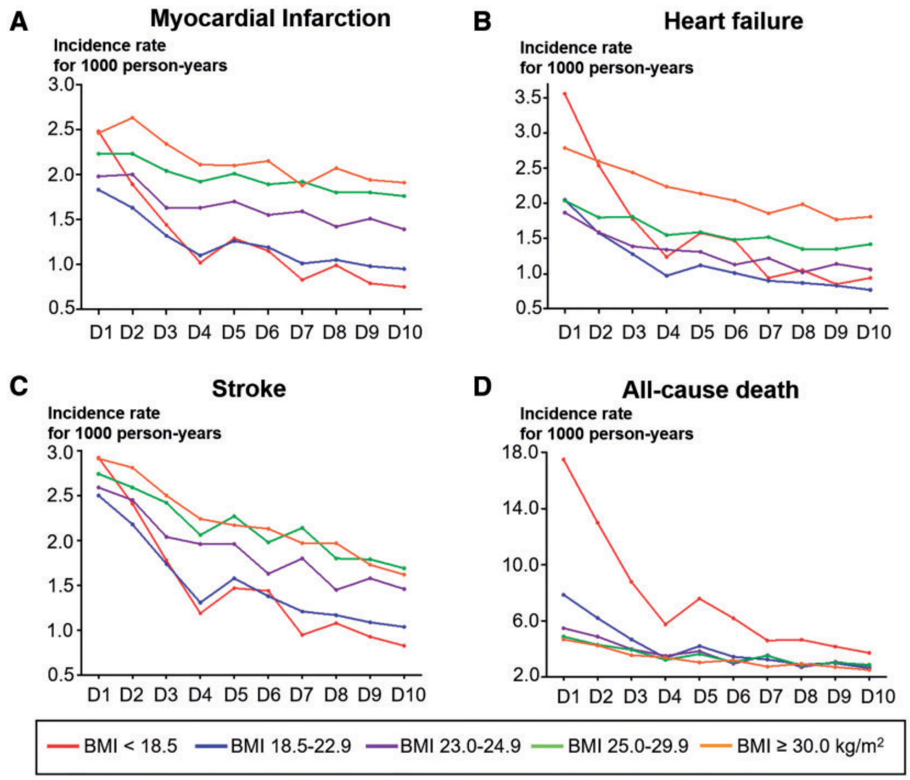

Figure 4. Incidence rates of cardiovascular events according to height and body mass index.nThe incidence rates of cardiovascular events are demonstrated according to height after being stratified by the body mass index: myocardial infarction (A), heart failure (B), stroke (C) and all-cause deaths (C). BMI = body mass index; D = height deciles from 1st to 10th.

Height in adulthood and CV events and mortality

Previous reports on Western populations demonstrated that coronary artery disease, stroke and heart failure had a relationship with height.[7–9,14–16] However, previous Asian studies regarding height in adulthood and CV events were controversial. In the Japanese population, only female and not male sex showed an independent relationship between height and stroke mortality among a cohort of healthy participants.[17] A study of the Chinese population reported that only stroke mortality but not iscahemic heart disease-related mortality and all-cause mortality were associated with height.[18] A study of middle-aged Koreans reported that there was an association among height and all-cause and stroke-related mortality, but there was no statistical association between height and mortality due to coronary heart disease in either middle-aged men or women.[19,20] Although the previous study recruited a relatively large number of subjects, only the association between height and cause-specific mortality was reported, without studying the incidence of each CV event. In this study, we analysed the largest number of subjects of both sexes with a wide age range. In addition, we analysed not only the mortality, but also various CV outcomes including MI, HF and stroke.

Mechanisms of the relationship between adult height and CV events

Although we did not explore the sophisticated biological mechanism of height in adulthood and CV events, there are several possible explanations for our results, which include genetic and environmental factors. Multiple gene and environmental factors control height in adulthood.[21] The heritability of height in adulthood was estimated at up to 80%, whereas 20% could be attributable to environmental factors. A recent study[9] reported an increased risk of coronary artery disease in people with genetically determined shorter height, to explain the association between shorter height and an adverse lipid profile. Another study also revealed that people with a genetic predisposition to be taller in adulthood had a lower risk of coronary heart disease, possibly because of favourable lung function and metabolic profiles.[22] Environmental factors, especially during childhood, were suggested to have an influence on both height and CV diseases.[23–25] One report revealed that there was an association between adult height shrinkage and CV disease.[26] An additional, traditional physiological mechanism might also elucidate the relationship between height and CV disease. For instance, shorter subjects had faster heart rates, increased pulsatile effort of the left ventricle[27]

Table 3. Multivariate Cox regression analysis according to height deciles

Height decile	Events/observed	Person-years	Incidence rates per 1 000 person-years	Hazard ratio (95% confidence interval)	
				Model 1[a]	Model 2[b]
Myocardial infarction					
1st decile	29 671/1 637 617	14 638 764	2.03	1.14 (1.12–1.16)	1.15 (1.13–1.17)
2nd decile	26 863/1 541 247	13 846 676	1.94	1.11 (1.09–1.13)	1.10 (1.08–1.13)
3rd–8th decile	135 407/9 969 744	90 077 680	1.50	1.05 (1.04–1.07)	1.05 (1.03–1.06)
9th decile	21 821/1 797 889	16 222 266	1.35	1.02 (1.00–1.04)	1.02 (1.00–1.04)
10th decile	18 331/1 581 631	14 236 191	1.29	1 (reference)	1 (reference)
Heart failure					
1st decile	30 550/1 637 617	14 669 850	2.08	1.20 (1.17–1.22)	1.21 (1.19–1.24)
2nd decile	23 743/1 541 247	13 889 479	1.71	1.09 (1.07–1.11)	1.09 (1.07–1.11)
3rd–8th decile	114 676/9 969 744	90 314 223	1.27	1.03 (1.01–1.05)	1.02 (1.01–1.04)
9th decile	17 443/1 797 889	16 265 539	1.07	1.02 (0.99–1.04)	1.01 (0.99–1.04)
10th decile	14 999/1 581 631	14 271 258	1.05	1 (reference)	1 (reference)
Stroke					
1st decile	38 355/1 637 617	14 611 837	2.62	1.27 (1.25–1.29)	1.29 (1.27–1.31)
2nd decile	33 116/1 541 247	13 829 851	2.39	1.24 (1.22–1.27)	1.25 (1.22–1.27)
3rd–8th decile	154 555/9 969 744	90 048 988	1.72	1.13 (1.11–1.15)	1.13 (1.11–1.14)
9th decile	22 722/1 797 889	16 228 852	1.40	1.04 (1.02–1.06)	1.04(1.02–1.06)
10th decile	18 818/1 581 631	14 242 463	1.32	1 (reference)	1 (reference)
All-cause death					
1st decile	97 838/1 637 617	14 747 316	6.63	1.40 (1.38–1.41)	1.38 (1.36–1.40)
2nd decile	76 429/1 541 247	13 949 809	5.48	1.22 (1.21–1.24)	1.21 (1.19–1.22)
3rd–8th decile	326 165/9 969 744	90 615 088	3.60	1.10 (1.09–1.11)	1.09 (1.08–1.10)
9th decile	50 151/1 797 889	16 311 007	3.07	1.03 (1.02–1.05)	1.03 (1.01–1.04)
10th decile	39 763/1 581 631	14 311 787	2.78	1 (reference)	1 (reference)

[a]Model 1 was adjusted for age, sex and body mass index.
[b]Model 2 was adjusted for age, sex, body mass index, smoking history, drinking history, diagnosis of diabetes mellitus, hypertension, dyslipidaemia and low income level.

and narrower vessel diameter[28] and showed more arterial occlusive events.[29]

Adulthood height, BMI and CV events

Although adulthood height, CV events and mortality showed an inverse relationship, similar height in adulthood showed a direct relationship with BMI (Figure 4). The J-curve association between BMI and all-cause mortality has been reported repeatedly,[30,31] and an association between BMI and CV mortality and other causes except cancer showed a similar pattern in a previous study which was performed in Denmark.[31] However, malignancy and respiratory disease, which were also major causes of death in Korea,[32] showed a substantially higher risk of mortality in subjects with lower BMI,[33,34] and it might compensate for the effect of CV disease on the association between all-cause death and BMI. Smoking and drinking habits, which are well-known confounders, did not show a clinically significant difference across the height deciles.

Strengths and limitations

Our study has several important strengths. We analysed an entire nationwide cohort, which included both men and women, as well as young and elderly people. The follow-up duration was long enough to discover significant discrepancies in each clinical event. We analysed not only the incidence rates of MI, HF and stroke, but also demonstrated a significant difference in all-cause mortality rates. However, there are also limitations to our study. This is an observational study of a prospective cohort, albeit a very large one, rather than a randomised, controlled trial; therefore, there could be unmeasured confounding factors. The biological mechanism to explain the association between height and CV events was not available, as we did not use a genetic approach or perform a twin study. Although we classified and adjusted the height deciles according to age and sex, there might be some limitation in aspects of height tendency according to age groups. The diagnosis of MI and stroke was based on the ICD codes, which might have a possibility of underestimation or overestimation; we used the MI and stroke definitions which had been validated in

Table 4. Multivariate Cox regression analysis according to 5-cm increment in height

	Hazard ratio (95% confidence interval)	
	Model 1[a]	Model 2[b]
Myocardial infarction		
Total	0.961 (0.957–0.964)	0.961 (0.958–0.965)
Male	0.962 (0.958–0.967)	0.966 (0.961–0.970)
Female	0.975 (0.969–0.980)	0.961 (0.956–0.967)
Heart failure		
Total	0.947 (0.944–0.951)	0.950 (0.947–0.954)
Male	0.961 (0.956–0.966)	0.968 (0.963–0.973)
Female	0.946 (0.941–0.951)	0.937 (0.931–0.942)
Stroke		
Total	0.924 (0.921–0.927)	0.924 (0.921–0.927)
Male	0.920 (0.916–0.924)	0.923 (0.919–0.927)
Female	0.936 (0.931–0.941)	0.924 (0.920–0.929)
All-cause death		
Total	0.914 (0.912–0.916)	0.923 (0.921–0.925)
Male	0.925 (0.922–0.927)	0.935 (0.932–0.937)
Female	0.908 (0.904–0.912)	0.908 (0.904–0.912)

[a]Model 1 was adjusted for age, sex and body mass index.
[b]Model 2 was adjusted for age, sex, body mass index, smoking history, drinking history, diagnosis of diabetes mellitus, hypertension, dyslipidaemia and low income level.

previous studies to avoid overestimation.[35] We also excluded those patients who had only one diagnosis in outpatient clinics, to exclude overestimation, which might have led to underdiagnosis of MI and stroke events.

Finally, we did not deal with environmental childhood factors that could affect height.[23,24] Although we adjusted for smoking history, drinking history and income level in the multivariate analysis, health and nutritional status during childhood, rather than adulthood, might be associated with height.

Conclusions

In this large, Korean, nationwide cohort study, we found that shorter height in adulthood was strongly related to an increased risk of MI, HF, stroke and all-cause death. This association was persistently found in a subgroup analysis, as well as in a multivariate analysis. Although adult height is mostly influenced by heredity, a suitable environment and appropriate nutrition early in life could influence adult height and eventually reduce the risk of CV events and mortality.

Supplementary Data

Supplementary data are available at *IJE* online.

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References

1. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol* 2009;**8**:355–69.
2. Mozaffarian D, Benjamin EJ, Go AS *et al*. Heart disease and stroke statistics – 2015 update: a report from the American Heart Association. *Circulation* 2015;**131**:e29–322.
3. Lee JH, Lim NK, Cho MC, Park HY. Epidemiology of heart failure in Korea: present and future. *Korean Circ J* 2016;**46**:658–64
4. Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. *Lancet* 2014;**383**:1973–80.
5. Held C, Iqbal R, Lear SA *et al*. Physical activity levels, ownership of goods promoting sedentary behaviour and risk of myocardial infarction: results of the INTERHEART study. *Eur Heart J* 2012;**33**:452–66.
6. Vazir A, Claggett B, Jhund P *et al*. Prognostic importance of temporal changes in resting heart rate in heart failure patients: an analysis of the CHARM program. *Eur Heart J* 2015;**36**:669–75.
7. Wannamethee SG, Shaper AG, Whincup PH, Walker M. Adult height, stroke, and coronary heart disease. *Am J Epidemiol* 1998;**148**:1069–76.
8. Njolstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women. A 14-year follow-up of the Finnmark Study. *Circulation* 1996;**94**:2877–82.
9. Nelson CP, Hamby SE, Saleheen D *et al*. Genetically determined height and coronary artery disease. *N Engl J Med* 2015;**372**: 1608–18.
10. Song SO, Jung CH, Song YD *et al*. Background and data configuration process of a nationwide population-based study using the Korean national health insurance system. *Diabetes Metab J* 2014;**38**:395–403.
11. Kang SH, Choi EK, Han KD *et al*. Underweight is a risk factor for atrial fibrillation: A nationwide population-based study. *Int J Cardiol* 2016;**215**:449–56.
12. Lee SR, Choi EK, Rhee TM *et al*. Evaluation of the association between diabetic retinopathy and the incidence of atrial fibrillation: A nationwide population-based study. *Int J Cardiol* 2016; **223**:953–57.
13. World Health Organization. *The Asia-Pacific Perspective: Redefining Obesity and Its Treatment*. Geneva: WHO, 2000.
14. Paajanen TA, Oksala NK, Kuukasjarvi P, Karhunen PJ. Short stature is associated with coronary heart disease: a systematic review of the literature and a meta-analysis. *Eur Heart J* 2010;**31**: 1802–09.

15. Schmidt M, Botker HE, Pedersen L, Sorensen HT. Adult height and risk of ischemic heart disease, atrial fibrillation, stroke, venous thromboembolism, and premature death: a population based 36-year follow-up study. *Eur J Epidemiol* 2014;**29:**111–18.
16. Akinkuolie AO, Aleardi M, Ashaye AO, Gaziano JM, Djousse L. Height and risk of heart failure in the Physicians' Health Study. *Am J Cardiol* 2012;**109:**994–97.
17. Hozawa A, Murakami Y, Okamura T *et al.* Relation of adult height with stroke mortality in Japan: NIPPON DATA80. *Stroke* 2007;**38:**22–26.
18. Wang N, Zhang X, Xiang YB *et al.* Associations of adult height and its components with mortality: a report from cohort studies of 135 000 Chinese women and men. *Int J Epidemiol* 2011;**40:** 1715–26.
19. Song YM, Davey Smith G, Sung J. Adult height and cause-specific mortality: a large prospective study of South Korean men. *Am J Epidemiol* 2003;**158:**479–85.
20. Song YM, Sung J. Adult height and the risk of mortality in South Korean women. *Am J Epidemiol* 2008;**168:**497–505.
21. Lango Allen H, Estrada K, Lettre G *et al.* Hundreds of variants clustered in genomic loci and biological pathways affect human height. *Nature* 2010;**467:**832–38.
22. Nuesch E, Dale C, Palmer TM *et al.* Adult height, coronary heart disease and stroke: a multi-locus Mendelian randomization meta-analysis. *Int J Epidemiol* 2016;**45:**1927–37.
23. Silventoinen K, Zdravkovic S, Skytthe A *et al.* Association between height and coronary heart disease mortality: a prospective study of 35,000 twin pairs. *Am J Epidemiol* 2006;**163:**615–21.
24. Yarnell JW, Limb ES, Layzell JM, Baker IA. Height: a risk marker for ischaemic heart disease: prospective results from the Caerphilly and Speedwell Heart Disease Studies. *Eur Heart J* 1992;**13:**1602–05.
25. Davey Smith G, Hart C, Upton M *et al.* Height and risk of death among men and women: aetiological implications of associations with cardiorespiratory disease and cancer mortality. *J Epidemiol Community Health* 2000;**54:**97–103.
26. Batty GD, Shipley MJ, Gunnell D *et al.* Height loss and future coronary heart disease in London: the Whitehall II study. *J Epidemiol Community Health* 2011;**65:**461–64.
27. Smulyan H, Marchais SJ, Pannier B, Guerin AP, Safar ME, London GM. Influence of body height on pulsatile arterial hemodynamic data. *J Am Coll Cardiol* 1998;**31:**1103–09.
28. Lemos PA, Ribeiro EE, Perin MA *et al.* Angiographic segment size in patients referred for coronary intervention is influenced by constitutional, anatomical, and clinical features. *Int J Cardiovasc Imaging* 2007;**23:**1–7.
29. West NE, Ruygrok PN, Disco CM *et al.* Clinical and angiographic predictors of restenosis after stent deployment in diabetic patients. *Circulation* 2004;**109:**867–73.
30. Aune D, Sen A, Prasad M *et al.* BMI and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ* 2016;**353:**i2156.
31. Afzal S, Tybjaerg-Hansen A, Jensen GB, Nordestgaard BG. Change in body mass index associated with lowest mortality in Denmark, 1976–2013. *JAMA* 2016;**315:**1989–96.
32. Oh CM, Won YJ, Jung KW *et al.* Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2013. *Cancer Res Treat* 2016;**48:**436–50.
33. Jee SH, Sull JW, Park J *et al.* Body-mass index and mortality in Korean men and women. *N Engl J Med* 2006;**355:**779–87.
34. Song YM, Sung J. Body mass index and mortality: a twelve-year prospective study in Korea. *Epidemiology* 2001;**12:** 173–79.
35. Kang SH, Choi EK, Han KD *et al.* Risk of ischemic stroke in patients with non-valvular atrial fibrillation not receiving oral anticoagulants – Korean Nationwide Population-Based Study. *Circ J* 2017;**81:**1158–64.