

# 중년 후반의 체질량지수 변화와 고혈압 발생률: 우리나라 전국민 코호트 연구

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## Changes of Body Mass Index and the Incidence of Hypertension in Late Middle Age: A Nationwide Cohort Study in South Korea

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**Background:** Previous studies revealed weight gain is an independent risk factor for hypertension. Hypertension in late middle age increases the risks of dementia and cardiovascular diseases. We aimed to analyze the difference in the risk of hypertension in the late middle age according to the change of body mass index (BMI) using nationwide cohort data of South Korea.

**Methods:** We used 64,136 individuals from National Health Insurance Service-Health Screening Cohort in South Korea. The primary endpoint is newly diagnosed hypertension after observation start date, which was defined as the date of first examination after 50. BMI changes were measured between two consecutive health examinations before and after 50. Cox proportional hazard regression analysis was performed to evaluate the association between the change of BMI and the risk of hypertension.

**Results:** During the mean follow-up period of 3.4±1.9 years, 8,676 individuals were diagnosed with hypertension. Both normal-to-obese group and obese-to-obese group had 19% higher risk for hypertension, and obese-to-normal group had 10% higher risk for hypertension in late middle age, compared to normal-to-normal group.

**Conclusions:** We confirmed becoming obese and maintaining obese increase the risk of hypertension in late middle age. Thus, clinicians need to assess obese patients regularly for the possibility of new onset hypertension and take preventive measure to reduce the risk by losing weights before late middle age.

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**Keywords:** Hypertension, Body mass index, Incidence rate

## INTRODUCTION

Multiple studies found that weight or body mass index (BMI) change was associated with the incidence of hypertension. Xie et al.<sup>1)</sup> found that weight change is an independent risk factor for later-life blood pressure and hypertension. Qu et al.<sup>2)</sup> reported that increased BMI is a risk factor of hypertension with dose-response relationship.

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In regards to changes of BMI, Shihab et al.<sup>3)</sup> reported the rate of change in BMI over the life span increased the risk of new-onset hypertension with a dose-response manner. Similarly, Ren et al.<sup>4)</sup> reported that non-overweight participants at baseline had higher risk of hypertension with odds ratio of 1.47 (95% confidence interval [CI], 1.08-1.99) when they became overweight.

The incidence rates of hypertension also increase with age.<sup>5)</sup> According to a population-based cohort research in South Korea by Lee et al.,<sup>6)</sup> the incidence rate of systolic hypertension measured by 1,000 person-years was 6.4, 9.8, 18.6, and 32.6 in the age group of under 45, 45-54, 55-64, and 65 or older, respectively. A Spanish study revealed that the incidence rate of hypertension was 4.6, 9.1, 11.8, and 43.8 respectively for women and 8.7, 22.6, 32.9, and 55.6 respectively for men in the age group of 25-34, 35-44, 45-54, and 55-64.<sup>7)</sup> In the two studies, the incidence of hypertension was increased 47-186% from the age group of 45-54 to 55-64, which was most significant than other age transitions.

In terms of a life-span development, middle age is divided into the early-middle-aged group, defined as those between the ages of 40 and 50, and the late-middle-aged group, defined as those between the ages of 50 and 60.<sup>8)</sup> Late middle age is a critical time in terms of health because health problems connected to the cumulative consequences of unhealthy behaviors frequently emerge at this age.<sup>9)</sup> Obesity, diabetes, alcoholism, dyslipidemia, hypertension, heart disease, and a variety of other causes and factors to mortality are becoming increasingly prevalent.<sup>10)</sup> In particular, the prevalence of obesity increases rapidly from the age of 50 and the prevalence of obesity is highest in the 50 to 65 age group across all age groups.<sup>11)</sup>

Regarding hypertension in late middle age, Walker et al.<sup>12)</sup> found that hypertension sustained from midlife to late life was associated with increased risk of subsequent dementia. Another meta-analysis of 12 studies by Hughes et al.,<sup>13)</sup> in which the average age of participants was 69±5.4, reported that lowering blood pressure with antihypertensive medications was significantly related to a lower risk of incident cognitive impairment or dementia. In addition, Wang et al.<sup>14)</sup> found that increased risks of all-cause mortality and cardiovascular diseases in patient who had new-onset hypertension in late middle age were still high compared to patient who had hypertension before late middle age. Thus, early recognition, control, and prevention of new onset hy-

pertension in late middle age is needed to avoid dementia and cardiovascular complications of hypertension.<sup>15)</sup>

In a cohort study conducted in China, the incidence of hypertension was significantly increased in all age groups including late middle age if the body weight at follow-up was obese regardless of whether the body weight at baseline was normal or obese.<sup>16)</sup> However, there is no study that analyzed the effect of weight change on hypertension in late-middle-aged Koreans. Therefore, this nationwide cohort study aimed to investigate the risk of new-onset hypertension based on changes of BMI in late middle age in South Korea.

## METHODS

### 1. Study design and population

We used the National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) in this retrospective cohort analysis. In South Korea, NHIS is a single government insurer that covers 97 percent of the South Korean population, and the medical aid program serves the remaining 3% of the lowest-income people. NHIS database includes qualification data such as age, sex, region, and income, as well as claim data including diagnosis code based on the International Classification of Disease, 10th revision (ICD-10) and treatment history. In addition, all insured individuals have biennial National Health Screening Program (NHSP) (National Health Insurance Service, Wonju, Korea), consists of anthropometric measurements, laboratory testing, and a self-reported questionnaire about health behavior such as smoking, drinking, and exercise.

The present study initially included 514,866 subjects, which were included in the NHIS-HEALS cohort. We defined the observation start date as the date of first examination after 50. To measure BMI changes, we collected those who had two consecutive health examination records before and after 50. Therefore, 304,312 subjects who didn't have two consecutive health examination were excluded among them. Those who had previous hypertension before the observation start date (n=89,333) were also excluded. Since smoking habit and physical activity information were self-administered, those who did not respond to any of these questions were also excluded from the study population (n=49,873) as a result, 64,136 individuals were in-

cluded as study cohort (Figure 1).

## 2. Definition of outcome

The primary endpoint is newly diagnosed hypertension based on operational definition from the observation start date (Figure 2). We used blood pressure records of each health examination as well as diagnosis and medication re-

ords to find new incidence of hypertension during observation period. The definition of hypertension was adopted from a previous study: systolic blood pressure  $\geq 140$  or diastolic blood pressure  $\geq 90$  at each health examination, as well as at least one claim/year for antihypertensive medication under ICD-10 code of I10-I13 and I15.<sup>17)</sup> Antihypertensive medication included thiazide, loop diuretics, beta-blocker, calcium-channel blockers, angiotensin converting enzyme in-

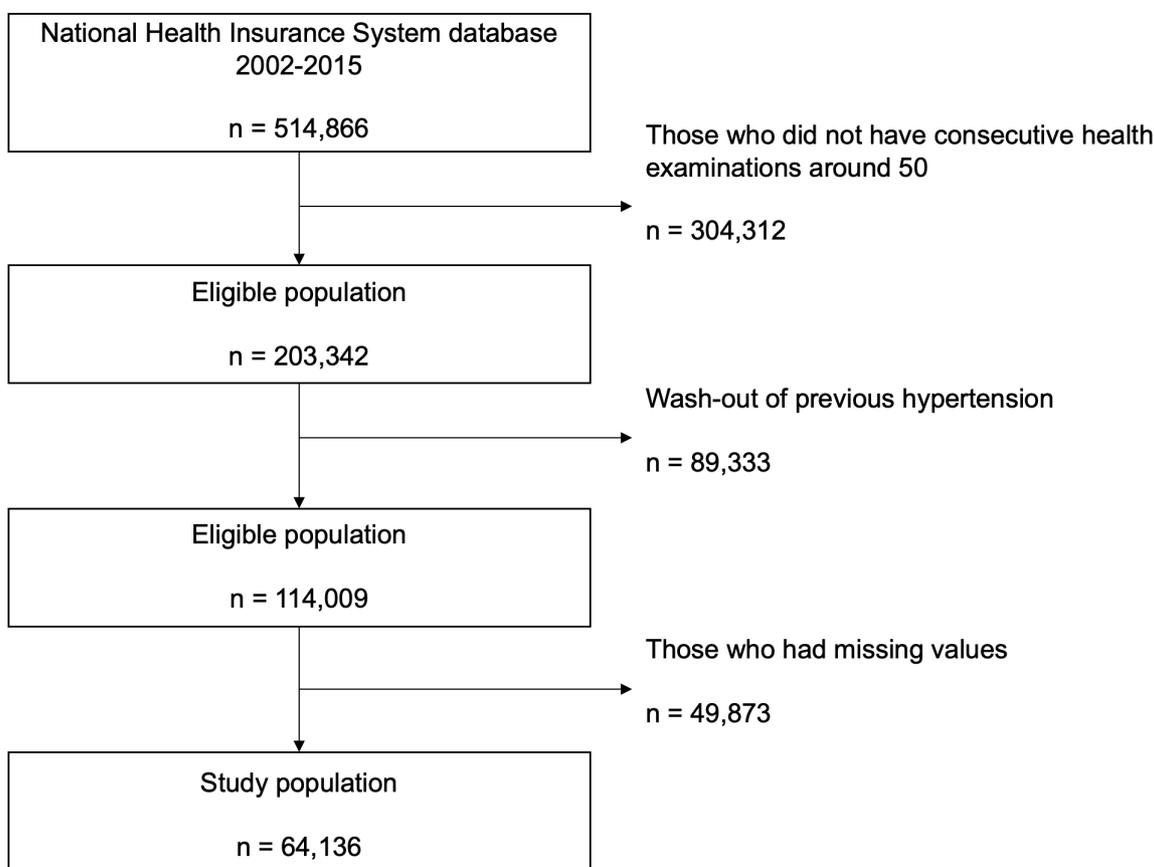


Figure 1. Study participants.

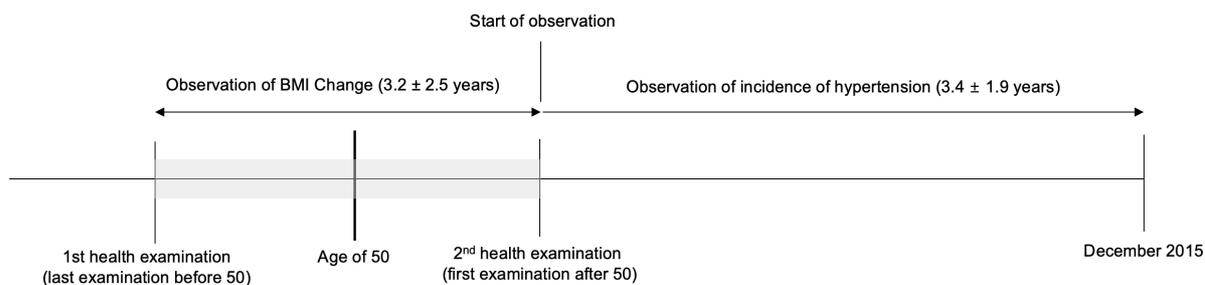


Figure 2. Schematics diagram of observation period. BMI, body mass index.

hibitors, and angiotensin receptor blocker. Blood pressure was examined on the right arm of participants by trained nurses using a standard mercury sphygmomanometer with appropriate-sized cuffs after sitting at least 5 minutes. At least, two measurements were collected and the mean of the two measurements was calculated. BMI was defined as weight in kilograms divided by square of height in meters. BMI  $\geq 25$  kg/m<sup>2</sup> is considered as obese, and BMI  $< 25$  kg/m<sup>2</sup> is considered as normal according to the criteria of obesity in Asia pacific region.<sup>18)</sup> Study participants were categorized into four groups by the change of BMI between two consecutive health examinations before and after 50: 1) normal to normal, 2) normal to obese, 3) obese to normal, and 4) obese to obese. The study cohort were followed up from the observation start date to the earliest date of hypertension diagnosis, or the end of follow-up (December 31, 2015), whichever came first. To explore the association of the change of BMI around age of 60 and the incidence of hypertension after 60, the same analysis is conducted for those who have no hypertension before 60 using two consecutive health examination records before and after 60.

### 3. Covariates

Sex, age, BMI, blood pressure, fasting blood glucose, familial history of hypertension, proteinuria measured as  $\geq 1+$  in urine dip stick test, smoking, and exercise habit were included as covariates. Smoking habits were classified into the categories of “none,” “light,” “moderate,” or “heavy” smoking. For current smokers, quantitative frequencies of smoking were also calculated to determine an average daily smoking frequency. Amount of smoking was categorized into three groups based on the frequency of smoking at the time of the first examination after 50: 1) light ( $< 10$  cigarettes/day), 2) moderate (10-19 cigarettes/day), and 3) heavy ( $\geq 20$  cigarettes/day) smokers. Regular exercise was defined as moderate level physical activity for  $> 30$  min/day and  $> 5$  days during the past week.

### 4. Statistical analysis

Incidence rates were estimated as the numbers of new-onset hypertension measured as 1,000 person-years. Cox proportional hazard regression analysis was conducted to evaluate the relationship between the change of BMI and the

risk of hypertension. Hazard ratio (HR) and 95% CI were analyzed. Three different models were fitted: unadjusted model, adjusted model for sex and age, and fully adjusted model for all covariates. All statistical analyses were conducted using R software (version 4.1; R foundorlion) and SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA).

### 5. Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

## RESULTS

During the follow-up period (mean,  $3.4 \pm 1.9$  years), 8,676 individuals were diagnosed with new-onset hypertension. The mean age at baseline was  $47.6 \pm 1.7$  years. Hypertension patients had higher baseline BMI ( $24.1 \pm 2.9$  vs.  $23.1 \pm 2.6$  kg/m<sup>2</sup>), higher baseline blood pressure (systolic blood pressure,  $120.3 \pm 10.2$  vs.  $113.9 \pm 11.1$  mmHg and diastolic blood pressure  $75.9 \pm 7.2$  vs.  $71.5 \pm 8.0$  mmHg), had higher proportion of family history of hypertension (9.9% vs. 6.8%) and proteinuria (1.8% vs. 1.3%). Additionally, compared to non-hypertension group, there were more patients who reported being current smokers (24.4% vs. 21.0%) and less patients who exercised with light degree or more (75.0% vs. 77.4%) in hypertension group (Table 1).

According to change of body mass index, more males were included in obese to normal and obese to obese group. Baseline blood pressure was higher in obese-to-obese group and normal-to-obese group compared to normal-to-normal group (Table 2).

#### 1. Risk of new-onset hypertension by changes in BMI

Compared to normal-to-normal group, normal-to-obese group, obese-to-normal, and obese-to-obese group had an increased risk of hypertension (HR, 1.19; 95% CI, 1.09-1.29; HR, 1.10; 95% CI, 1.00-1.22; and HR, 1.19; 95% CI, 1.11-1.29 in the fully adjusted model) in two consecutive examinations before and after 50 (Table 3).

No association was found between the change of BMI and the risk of hypertension in the analysis of two consecutive examinations before and after 60 (Supplementary Table 1).

**Table 1.** Baseline of study participants

	Total (n=64,136)	Non-hypertension (n=55,460)	Hypertension (n=8,676)	P <sup>a</sup>
Sex (male)	37.2	36.2	43.4	<0.01
Age, y	47.6±1.7	47.6±1.7	47.4±1.8	<0.01
BMI, kg/m <sup>2</sup>	23.3±2.7	23.1±2.6	24.1±2.9	<0.01
SBP	114.8±11.2	113.9±11.1	120.3±10.2	<0.01
DBP	72.1±8.0	71.5±8.0	75.9±7.2	<0.01
Family history of hypertension	7.2	6.8	9.9	<0.01
Urine dipstick ≥1+	1.3	1.3	1.8	<0.01
Current smoking				<0.01
None	80.1	80.8	75.6	
Light	3.1	3.0	3.9	
Moderate	9.8	9.5	12.3	
Heavy	6.9	6.7	8.2	
Exercise				0.02
None	22.7	22.6	25.0	
Low	40.2	40.4	38.1	
Middle	35.2	35.3	34.2	
High	1.8	1.7	2.7	

Values are presented as mean±standard deviation for numerical variables and number (%) for categorical variables.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

<sup>a</sup>Chi-squared test or Fisher exact test for categorical variables, as appropriate.

**Table 2.** Baseline characteristics of study participants according to change of body mass index

	Normal to normal (n=44,456)	Normal to obese (n=4,244)	Obese to normal (n=3,289)	Obese to obese (n=12,147)	P <sup>a</sup>
Sex (male)	34.4	35.8	47.1	45.4	<0.01
Age, y	47.7±1.7	47.3±1.9	47.4±1.9	47.5±1.8	<0.01
BMI, kg/m <sup>2</sup>	21.9±1.7	24.0±1.0	25.9±1.3	27.1±1.8	<0.01
SBP	113.7±11.2	115.1±11.0	117.5±10.9	117.9±40.6	<0.01
DBP	71.4±8.1	72.4±7.9	73.8±7.9	74.1±7.6	<0.01
FHx of hypertension (yes)	7.0	8.3	7.2	7.7	<0.01
Urine Dipstick ≥1+ (yes)	1.3	1.2	1.3	1.6	0.03
Current smoking					<0.01
None	81.3	80.5	74.8	77.0	
Light	3.0	3.1	3.3	3.4	
Moderate	9.4	9.9	12.1	10.9	
Heavy	6.3	6.5	9.8	8.7	
Exercise					0.36
None	22.4	23.7	25.5	23.3	
Low	40.6	37.7	38.3	39.7	
Middle	35.1	36.7	34.1	35.5	
High	1.9	1.9	2.1	1.5	

Values are presented as mean±standard deviation for numerical variables and number (%) for categorical variables.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FHx, family history; SBP, systolic blood pressure.

<sup>a</sup>Chi-squared test or Fisher exact test for categorical variables, as appropriate.

**Table 3.** Difference in the incidence of hypertension according to changes of body mass index between consecutive health examinations before and after 50

Group	Number	Event	Duration	IR	Model 1 <sup>a</sup>		Model 2 <sup>a</sup>		Model 3 <sup>a</sup>	
					HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Normal to normal	44,456	4,821	153,792.9	31.3	1 (ref.)		1 (ref.)		1 (ref.)	
Normal to obese	4,244	780	13,221.2	59.0	1.78 (1.65-1.92)	<0.01	1.78 (1.65-1.92)	<0.01	1.19 (1.09-1.29)	<0.01
Obese to normal	3,289	468	11,231.8	41.7	1.25 (1.14-1.38)	<0.01	1.25 (1.14-1.38)	<0.01	1.10 (1.00-1.22)	0.04
Obese to obese	12,147	2,607	39,144.3	66.6	2.02 (1.92-2.11)	<0.01	2.02 (1.92-2.11)	<0.01	1.19 (1.11-1.29)	<0.01

Abbreviations: CI, confidence interval; HR, hazard ratio; IR, incidence rate; ref., reference.

<sup>a</sup>Model 1: unadjusted; model 2: adjusted for age and sex; model 3: adjusted for age, sex, body mass index, fasting blood glucose, presence of proteinuria (urine dipstick  $\geq 1+$ ), family history of hypertension, systolic blood pressure, diastolic blood pressure, smoking history, and exercise history.

## 2. Association between covariates and the risk of new-onset hypertension

In the multivariate cox regression analysis for the fully adjusted model, baseline age (adjusted HR [aHR], 1.03; 95% CI, 1.01-1.04), BMI (aHR, 1.02; 95% CI, 1.01-1.03), systolic blood pressure (aHR, 1.04; 95% CI, 1.04-1.04), diastolic blood pressure (aHR, 1.10; 95% CI, 1.09-1.10), and family history of hypertension (aHR, 1.12; 95% CI, 1.05-1.19) were associated with increased risk of hypertension. On the contrary, regular exercise was associated with decreased risk of new-onset hypertension (aHR, 0.92; 95% CI, 0.88-0.97) (Supplementary Table 2).

## DISCUSSION

This nationwide population-based cohort research analyzed the risks for new-onset hypertension in late middle age according to changes of BMI. Both normal-to-obese group and obese-to-obese group had 19% higher risk for hypertension, and obese-to-normal group had 10% higher risk for hypertension, compared to normal-to-normal group. Same analysis was conducted for BMI change before and after 60 and there was no association between BMI change and the risk of hypertension in the period. To our knowledge, this is the first research that revealed that the changes of BMI affect the risk of hypertension differently during and after late middle age.

The increased risk of hypertension in normal-to-obese group in our study was consistent with results from previous studies. Shihab et al.<sup>3)</sup> found that men who were normal weight at age 25 but became overweight or obese by age 45 faced an increased risk of hypertension compared to

men who remained normal weight at both ages (HR, 1.57; 95% CI, 1.20-2.07). Men who were overweight or obese at the age of 25 but returned to a normal weight by the age of 45 did not face an increased risk of hypertension (HR, 0.91; 95% CI, 0.43-1.92).<sup>3)</sup> This is similar to our study results that BMI gain affected increased risk of hypertension. On the contrary, obese participants before late middle age had still higher risk of hypertension even though they lose weight, which is the first that reported becoming obese or sustained obese are both risk factors for new onset compared to those who maintained normal BMI. In addition, Li et al.<sup>19)</sup> reported that overweight at the age of 50-59 increased the risk of hypertension with HR 1.27 (95% CI, 1.09-1.49), but there was no association between onset of overweight at  $\geq 60$  years of age and the risk of hypertension. Our research also revealed that BMI reduction around age of 60 was not effective for preventing hypertension. This results may be because obesity is a major cause of hypertension until age 60, but after age 60, other causes, rather than obesity, are the main cause of hypertension.

It is well known that increased adiposity, whether measured by a higher BMI, increased weight, or a larger waist circumference (WC), is strongly associated with elevated blood pressure and hypertension development.<sup>20-25)</sup> In the previous study by Shihab et al.,<sup>3)</sup> loss of weight between young adulthood and middle age posed no additional risk for the incidence of hypertension. However, becoming normal is insufficient to reverse the development of hypertension if they were already obese before late middle age in our study. This means maintaining normal weight may be more effective for the prevention of hypertension in early middle age than in late middle age, or prevention of hypertension may require more weight reduction than being

slightly out of the obesity range as in our study.

In regard to association between physical activity and the risk of hypertension, our study found that regular exercise at moderate level or more reduce the risk of hypertension at 8% in late middle age. According to a review article by Diaz and Shimbo,<sup>26)</sup> the available evidence strongly suggests that physical activity plays a role in hypertension prevention, however, the optimal prescription for the prevention of hypertension still remains uncertain. In another study of 3,148 participants whose mean age was 42.3, Lee et al.<sup>27)</sup> reported that those who maintained or improved their fitness level had a 26% and 28% lower risk of incident hypertension, respectively, compared to those who decreased their fitness level. Our result indicate that physical activity is still helpful to decrease new onset of hypertension in late middle age, even though it is not as much as in early middle age.

There are several limitations in this study. First, we analyzed those who participated in national health examinations; this indicates that the study population was generally healthier. Second, self-reported smoking habits and physical activity may be underestimated, resulting in a weaker relationship. Third, WC was not included as covariates because there were so many missing values. WC is associated with body fat ratio; thus, future study is needed to measure the relationship between increased WC and the risk of hypertension in the late middle age.

In conclusion, we confirmed becoming obese and maintaining obese increase the risk of hypertension in late middle age. Thus, clinicians need to assess obese patients regularly for the possibility of new onset hypertension and take preventive measure to reduce the risk by becoming normal weights before late middle age and maintaining normal weights during late middle age.

## ACKNOWLEDGEMENTS

All data used in this study can be presented to researchers who have an approval by NHIS.

## 요 약

연구배경: 예전 연구에 따르면 체중 증가가 고혈압의 독립적인 위험인자임이 알려져 있다. 특히, 중년 후반의 고혈압은 치매와 심혈관 질환의 위험을 증가시킨다. 체질량지수

(BMI)의 변화가 중년 후반 시기에 고혈압 발병에 어떤 영향을 미치는지를 우리나라 전국 코호트 자료를 이용하여 분석하고자 하였다.

방법: 국민건강보험공단 건강검진 코호트로부터 64,136명의 데이터를 사용하였다. 1차 평가변수는 50세 이후의 첫 검진 날짜로 정의되는 관찰 시작일 이후 새로 고혈압으로 진단받았는지 여부로 하였다. BMI 변화는 50세 전후의 두 번 연속으로 받은 건강검진 때 측정하였다. BMI의 변화와 고혈압 진단 사이의 연관성을 평가하기 위해 cox proportional hazard regression 분석을 수행하였다.

결과: 평균 3.4±1.9년의 추적 관찰 기간 동안 8,676명이 고혈압 진단을 받았다. 중년 후반에 정상-정상군에 비해 정상-비만군과 비만-비만군 모두 고혈압 위험이 19% 더 높았고, 비만-정상군은 고혈압 위험이 10% 더 높았다.

결론: 정상인이 비만이 되어지거나 비만 환자가 비만인 상태를 유지하면 중년 후반에 고혈압의 위험이 증가함을 확인하였다. 따라서 임상 의사는 비만 환자에서 새로운 고혈압 발병 가능성에 대해 정기적으로 평가하고 중년 후반 이전에 체중을 감량하여 위험을 줄이기 위한 예방 조치를 취해야 한다.

중심 단어: 고혈압, 체질량지수, 발생률

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**Supplementary Table 1.** Difference in the incidence of hypertension according to changes of body mass index between consecutive health examinations before and after 60

Group	Number	Event	Duration	IR	Model 1 <sup>a</sup>		Model 2 <sup>a</sup>		Model 3 <sup>a</sup>	
					HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Normal to normal	23,366	2,982	69,969.5	42.62	1 (ref.)		1 (ref.)		1 (ref.)	
Normal to obese	2,011	382	5,751.0	66.42	1.54 (1.38-1.71)	<0.01	1.52 (1.37-1.69)	<0.01	1.00 (0.88-1.12)	0.95
Obese to normal	1,892	329	5,885.8	54.87	1.32 (1.18-1.48)	<0.01	1.28 (1.14-1.44)	<0.01	1.03 (0.91-1.15)	0.66
Obese to obese	8,285	1,805	23,992.4	75.23	1.76 (1.66-1.86)	<0.01	1.75 (1.65-1.85)	<0.01	1.08 (0.98-1.19)	0.12

Abbreviations: CI, confidence interval; HR, hazard ratio; IR, incidence rate; ref., reference.

<sup>a</sup>Model 1: unadjusted; model 2: adjusted for age and sex; model 3: adjusted for age, sex, body mass index, fasting blood glucose, presence of proteinuria (urine dipstick  $\geq 1+$ ), family history of hypertension, systolic blood pressure, diastolic blood pressure, smoking history, and exercise history.

**Supplementary Table 2.** Multivariate cox regression analysis for the risk of hypertension

Variable	Model 1		Model 2		Model 3	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
<b>BMI group</b>						
Normal-to-normal	1 (ref.)		1 (ref.)		1 (ref.)	
Normal-to-obese	1.83 (1.69-1.97)	<0.01	1.78 (1.65-1.92)	<0.01	1.19 (1.09-1.29)	<0.01
Obese-to-normal	1.32 (1.20-1.46)	<0.01	1.25 (1.14-1.38)	<0.01	1.10 (1.00-1.22)	0.04
Obese-to-obese	2.09 (1.99-2.19)	<0.01	2.01 (1.92-2.11)	<0.01	1.19 (1.11-1.29)	<0.01
<b>Sex</b>						
Female			1 (ref.)		1 (ref.)	
Male			1.27 (1.22-1.33)	<0.01	1.03 (0.98-1.09)	0.23
Age			1.13 (1.11-1.15)	<0.01	1.03 (1.01-1.04)	<0.01
BMI					1.02 (1.01-1.03)	<0.01
SBP					1.04 (1.04-1.04)	<0.01
DBP					1.10 (1.09-1.10)	<0.01
Proteinuria					1.30 (1.14-1.47)	<0.01
<b>FHx of hypertension</b>						
No					1 (ref.)	
Yes					1.12 (1.05-1.19)	<0.01
<b>Smoking</b>						
No					1 (ref.)	
Yes					1.02 (0.96-1.08)	0.61
<b>Regular exercise</b>						
No					1 (ref.)	
Yes					0.92 (0.88-0.97)	<0.01

Model 1: unadjusted; model 2: adjusted for age and sex; model 3: adjusted for age, sex, BMI, SBP, DBP, fasting blood glucose, proteinuria, FHx of hypertension, smoking habit, and regular exercise.

Proteinuria was defined as urine dipstick  $\geq 1+$ ; regular exercise was defined as weekly physical activity  $\geq 600$  metabolic equivalent of task.

Abbreviations: BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; FHx, family history; HR, hazard ratio; ref., reference; SBP, systolic blood pressure.