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# Investigation of the Impact of Body Mass Index in the 20s on Chronic Metabolic Diseases and Their Progression Rate After the Age of 65 Years

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## ABSTRACT







**Background:** In this study, we aimed to evaluate the relationship between the body mass index (BMI) of participants in their 20s (20s\_BMI) and the risk of developing various chronic metabolic diseases when they were over the age of 65 years. We also investigated how quickly these values worsened after 65 years of age.

**Methods:** This 8-year prospective cohort study targeted elderly people aged 65 years or older with three healthcare visits at 3–4 to year intervals. Participants were divided into four groups according to their 20s\_BMI and the occurrence and changes in body weight and fatty liver were observed for approximately 8 years.

**Results:** A total of 1,130 people aged 65 years or older were included. In the 65–69 years age group, as the 20s\_BMI increased, weight, BMI, waist circumference, and hip circumference all significantly increased (all  $P < 0.001$ ); furthermore, the incidence of metabolic syndrome also significantly increased ( $P < 0.05$ ). In particular, the rates of deterioration in weight, BMI, waist circumference, and waist-to-hip ratio were high in people aged 75 years and older (all  $P < 0.001$ ). The Framingham Steatosis Index and Hepatic Steatosis Index tended to increase as the 20s\_BMI increased; moreover, they all showed a worsening trend toward the second and third visit.

**Conclusion:** We found that a high 20s\_BMI continued to be high even after the age of 65 years and had a negative impact on the occurrence and worsening of metabolic dysfunction-associated steatotic liver disease. This suggests that weight management starting in the 20s is important to prevent the progression of chronic diseases after the age of 65 years.

**Keywords:** Body Mass Index; Bone Density; Fatty Liver; Metabolic Syndrome; Age

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#### Disclosure

The authors have no potential conflicts of interest to disclose.

#### Author Contributions

Conceptualization: Kim KJ, Kim H, Kim HS, Kim CO. Data curation: Kim KJ, Kim H, Sun E, Yun YM, Park YS, Shinn J, Jung DY, Kim HS, Kim CO. Formal analysis: Kim KJ, Kim H, Sun E, Yun YM, Park YS, Jung DY, Kim HS, Kim CO. Funding acquisition: Kim KJ, Kim HS. Investigation: Kim HS, Kim CO. Methodology: Kim HS, Kim CO. Software: Kim HS, Kim CO. Validation: Kim KJ, Kim H. Visualization: Kim HS, Kim CO. Writing - original draft: Kim KJ, Kim H, Kim HS. Writing - review & editing: Yim HW, Kim CO.

## INTRODUCTION

Body mass index (BMI), a measure of obesity, is associated with various chronic diseases.<sup>1,2</sup> In particular, a high BMI increases the prevalence of various metabolic syndromes related to diabetes mellitus, hypertension, and dyslipidemia.<sup>2-5</sup> Ultimately, it increases the risk of various cardiovascular diseases,<sup>6</sup> chronic renal failure,<sup>7</sup> and death due to metabolic syndrome.<sup>6-8</sup> Surprisingly, the BMI in youth is important<sup>9,10</sup> as it can continue to influence the occurrence of chronic metabolic diseases, such as obesity, metabolic dysfunction-associated steatotic liver disease (MASLD), and osteoporosis, even after becoming elderly. This means that obesity in youth can act as a major risk factor for various chronic metabolic diseases, even in old age. However, the relationship between the BMI of patients in their 20s (20s\_BMI) and adverse outcomes in old age is not well known. Moreover, it is not well known whether 20s\_BMI affects the rate of deterioration of variables that constitute metabolic diseases in old age.

Therefore, in this study, we aimed to investigate the relationship between 20s\_BMI and the risk of various chronic metabolic diseases that occur in old age. Furthermore, we compared the rates at which various indicators of chronic metabolic diseases worsened with age after 65 years of age.

## METHODS

### Study population

This study utilized 8 years of prospective cohort data established at Yonsei University Hospital, targeting elderly participants aged 65 years or older. The participants included those who first visited the hospital and underwent a health examination between 2012 and 2015 (baseline). Subsequently, the participants underwent health checkups at least twice at 3–4 year intervals. The second health check-up was conducted between 2016 and 2019 (Visit\_4Y), and the third was conducted between 2020 and 2022 (Visit\_8Y). Consequently, each patient underwent a health checkups at least three times at 3–4 year intervals. New information, such as changes in contact information and address, occurrence of major serious diseases, hospitalization, and changes in health status, were collected and managed through a telephone survey targeting cohort participants every year; moreover, continuous data quality management was conducted.

### Study design

As data was collected through memory-based recollections of the past, the average weight and height of those in their 20s during the three visits over 8 years were calculated for the three surveys. The 20s\_BMI was calculated based on recalled height and weight. These were then divided into four groups according to the average BMI of people in their 20s: under-weight (Under\_BMI group, BMI < 18.5 kg/m<sup>2</sup>), normal weight (Normal\_BMI group 18.5 ≤ BMI < 23.0 kg/m<sup>2</sup>), over-weight (Over\_BMI group, 23.0 ≤ BMI < 25.0 kg/m<sup>2</sup>), and obesity groups (Obese\_BMI, BMI ≥ 25.0 kg/m<sup>2</sup>).<sup>11</sup> As this study targeted participants over 65 years of age, they were divided into three groups based on the time of examination (65–69 years, 70–74 years, and 75 years or older). Additionally, we compared the changes in the variables for each BMI group twice over 3 years from baseline, for a total of 8 years.

To determine the basic conditions of the participants, age, sex, height, weight, BMI, waist circumference, hip circumference, systolic blood pressure (BP), and diastolic BP were

measured according to standardized health examination protocols. To check general health status, glucose, glycated hemoglobin (HbA1c), blood urea nitrogen, creatinine, glomerular filtration rate (GFR), aspartate aminotransferase, alanine aminotransaminase, alkaline phosphatase, insulin, calcium, phosphorus, 25-hydroxy-vitamin D, protein, albumin, uric acid, total bilirubin, high sensitivity C-reactive protein, total cholesterol, triglyceride, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C) were measured. Based on these values, the presence of metabolic syndrome was confirmed.<sup>12</sup>

Various formulae were used to determine whether MASLD was present according to 20s\_BMI. These included the: Framingham Steatosis Index (FSI),<sup>13</sup> which diagnoses fatty liver using abdominal computed tomography in the Framingham cohort study; the hepatic steatosis index (HSI),<sup>14</sup> a diagnostic method for fatty liver development in Koreans diagnosed by ultrasound; and the non-alcoholic fatty-liver disease fibrosis score (NFS),<sup>15</sup> a fatty liver diagnostic model using various biochemical variables to predict liver fibrosis. Furthermore, to check bone mineral density (BMD), the L1-L4 and total hip T-scores were measured using 3-dimensional quantitative computed tomography.

### Statistical analysis

Values are presented as numbers (percentages) for categorical variables and as means (standard deviations) for continuous variables. *P* values were calculated using the  $\chi^2$  test or Fisher's exact test for categorical variables and the one-way analysis of variance for continuous variables. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and *P* < 0.05 was considered statistically significant.

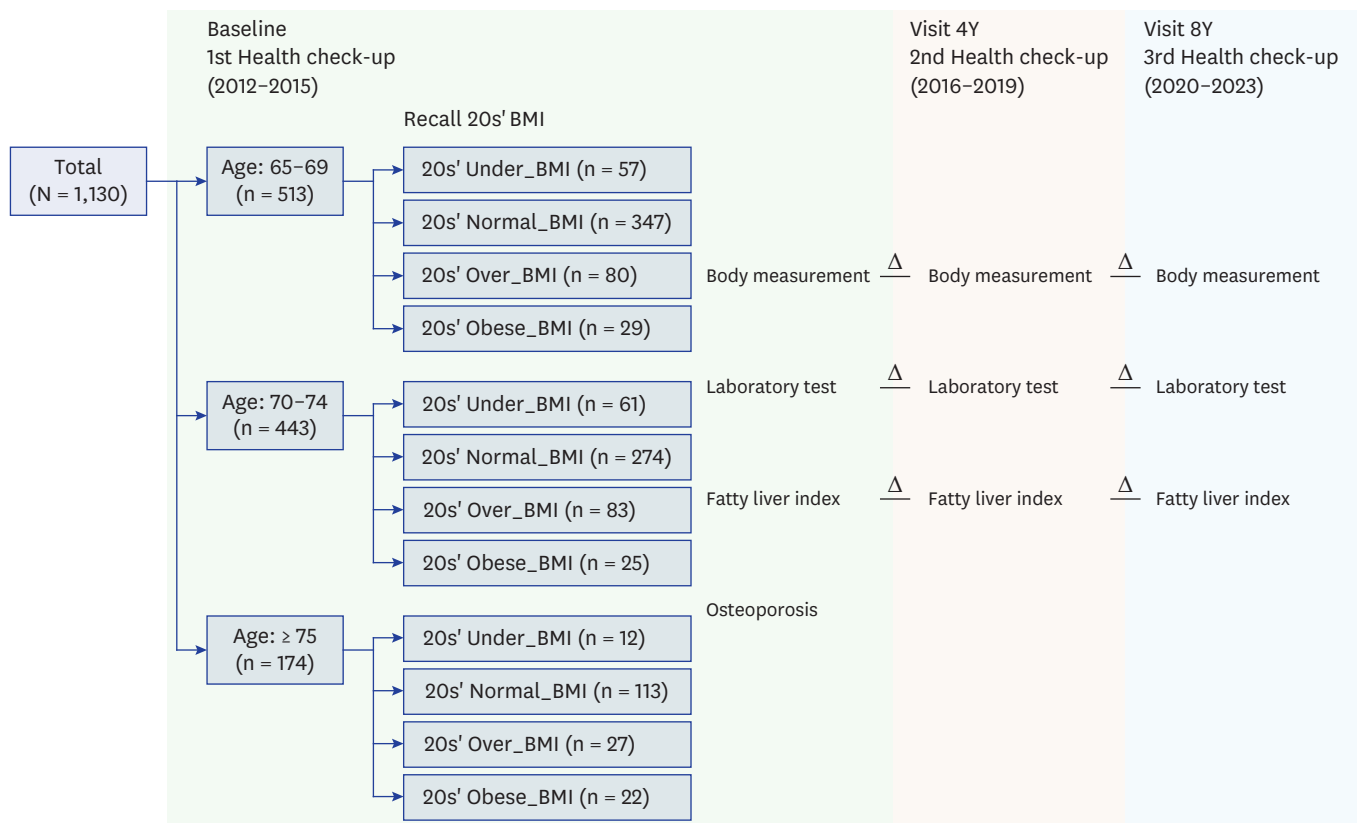
### Ethics statement

This study utilized the "Geriatric Disease Prevention and Management Cohort Data," which was previously approved by the Yonsei University Institutional Review Board (IRB) in 2012, and all informed consents were obtained from the participants at the inclusion time. All personal identifiers were deleted for statistical analysis, and because this study was conducted on a new topic utilizing already constructed data, additional patient consent was not required. Additional approval was obtained by the Clinical Research Ethics Committee of Yonsei University (IRB number: 4-2024-0569) separately from the previous IRB.

## RESULTS

### Patient characteristics

Among the 3,517 participants who underwent health check-ups at baseline (2012–2015), this study targeted 1,147 participants who attended both Visit\_4Y and Visit\_8Y. This study analyzed the healthcare check-up data for 1,147 participants for a total of 8 years, with a total of three visits, including baseline, at 3–4 year intervals. Among these, 17 participants who were unable to recall their BMI in their 20s were excluded from the study. Consequently, a total of 1,130 participants were included in this study (Fig. 1). Among them, 45.4% (513/1,130) were between 65 and 69 years old, 39.2% (443/1,130) were between 70 and 74 years old, and 15.4% (174/1,130) were 75 years old or older. Among those aged between 65 and 69 years of age, 20s\_BMI was Under\_BMI in 11.1% (57/513), Normal\_BMI in 67.6% (347/513), Over\_BMI in 15.6% (80/513), and Obese\_BMI in 5.7% (29/513). Among those aged between 70 and 74 years, 20s\_BMI was Under\_BMI in 13.8% (61/443), Normal\_BMI in 61.9% (274/443), Over\_BMI in 18.7% (83/443), and Obese\_BMI in 5.6% (25/443 people). Among



**Fig. 1.** Schematic diagram of the research flow.  
BMI = body mass index.

those aged 75 years or older, 20s\_BMI was Under\_BMI in 6.9% (12/174), Normal\_BMI in 64.9% (113/174), Over\_BMI in 15.5% (27/174), and Obese\_BMI in 12.6% (22/174).

### Differences in BMI according to 20s\_BMI

In the 65–69 years age group, as the 20s\_BMI increased, the weight, BMI, waist circumference, hip circumference, and waist-to-hip (W/H) ratio all significantly increased (all trends  $P < 0.001$ ) (Table 1, Supplementary Table 1). Likewise, the systolic ( $P = 0.189$ ) and diastolic BP ( $P = 0.014$ ) also showed that the higher the 20s\_BMI of individuals, the higher the BP of those aged between 65 and 69 years. Similarly, in the 70–74 years age group, the higher the 20s\_BMI, the more the weight ( $P < 0.001$ ), BMI ( $P = 0.001$ ), waist circumference ( $P = 0.006$ ), hip circumference ( $P = 0.032$ ), and GFR ( $P < 0.001$ ). In people over 75 years of age, there were no items other than LDL-C that showed a significant association with 20s\_BMI. In the case of metabolic syndrome between the ages of 65 and 69 years, the rate was found to increase significantly as the 20s\_BMI increased ( $P = 0.024$ ). The same trend was observed in people aged more than 70 years; however, the difference was not statistically significant. Moreover, as the 20s\_BMI increased, fasting glucose (trend  $P = 0.181$ ), HbA1c (trend  $P = 0.054$ ), and fasting insulin levels (trend  $P = 0.963$ ) all tended to increase; however, the difference was not statistically significant. The same trend was observed across all age groups. The same trend was also observed for uric acid levels; however, the difference was not statistically significant.

**Table 1.** Differences in body index according to BMI in the 20s

Variables	65-69 yr					70-74 yr					Over 75 yr				
	Under_BMI	Normal_BMI	Obese_BMI	P value		Under_BMI	Normal_BMI	Obese_BMI	P value		Under_BMI	Normal_BMI	Obese_BMI	P value	
No. of participants	57	347	80			61	274	83			12	113	27		
Weight, kg	56.8 ± 6.4	58.7 ± 8.6	63.7 ± 7.7	70.3 ± 11.1 < 0.001		57.4 ± 8.2	59.9 ± 7.8	63.5 ± 8.9	65.8 ± 11.1 < 0.001		57.9 ± 8.1	59.3 ± 8.0	60.1 ± 9.3	64.0 ± 10.3	0.106
BMI, kg/m <sup>2</sup>	23.2 ± 2.5	24.0 ± 2.9	25.2 ± 2.6	26.7 ± 3.1 < 0.001		23.8 ± 2.7	24.2 ± 2.7	24.8 ± 2.4	26.1 ± 2.7	0.001	24.3 ± 4.0	23.9 ± 2.9	23.7 ± 2.3	25.4 ± 2.6	0.163
Waist circumference, cm	79.6 ± 7.6	81.7 ± 8.5	85.6 ± 8.0	88.9 ± 8.2 < 0.001		82.4 ± 7.1	84.2 ± 7.8	85.1 ± 7.6	88.7 ± 8.4	0.006	85.1 ± 10.1	84.6 ± 7.8	83.5 ± 7.6	86.9 ± 8.5	0.527
Hip circumference, cm	91.8 ± 4.7	92.7 ± 5.9	94.4 ± 4.9	96.4 ± 6.4 < 0.001		92.9 ± 5.3	93.4 ± 5.5	94.3 ± 5.2	96.3 ± 5.9	0.032	93.1 ± 6.8	92.4 ± 5.6	91.4 ± 4.9	95.5 ± 5.6	0.067
W/H ratio	0.87 ± 0.06	0.88 ± 0.07	0.91 ± 0.06	0.92 ± 0.06 < 0.001		0.89 ± 0.06	0.90 ± 0.06	0.90 ± 0.06	0.92 ± 0.06	0.129	0.91 ± 0.07	0.91 ± 0.06	0.91 ± 0.06	0.91 ± 0.07	0.989
Systolic BP, mmHg	124 ± 18	127 ± 15	128 ± 13	131 ± 15	0.189	130 ± 18	128 ± 15	130 ± 14	129 ± 18	0.653	139 ± 13	130 ± 15	123 ± 19	130 ± 16	0.027
Diastolic BP, mmHg	73 ± 9	74 ± 8	77 ± 8	78 ± 10	0.014	74 ± 9	73 ± 9	75 ± 10	75 ± 9	0.209	75 ± 9	72 ± 8	71 ± 8	73 ± 9	0.524
Body fat percentage	33.6 ± 5.4	32.6 ± 7.2	32.1 ± 8.1	32.8 ± 7.0	0.685	34.0 ± 6.4	32.3 ± 7.7	30.5 ± 7.7	32.7 ± 8.3	0.059	31.5 ± 9.2	31.8 ± 8.0	30.4 ± 6.7	33.7 ± 5.8	0.542
Metabolic syndrome, yes	17 (29.8)	105 (30.3)	37 (46.3)	13 (44.8)	0.024	24 (39.3)	97 (35.4)	28 (33.7)	13 (52.0)	0.359	8 (66.7)	48 (42.5)	11 (40.7)	7 (31.8)	0.269
ALP, U/L	75 ± 25	70 ± 21	71 ± 19	65 ± 16	0.234	69 ± 17	70 ± 21	68 ± 18	71 ± 20	0.842	78 ± 16	73 ± 18	72 ± 23	75 ± 21	0.758
AST, U/L	29 ± 64	22 ± 12	22 ± 9	25 ± 15	0.231	21 ± 7	22 ± 12	23 ± 13	20 ± 6	0.500	19 ± 7	24 ± 18	19 ± 6	18 ± 8	0.318
ALT, U/L	31 ± 46	25 ± 8	26 ± 8	25 ± 9	0.197	25 ± 6	26 ± 9	28 ± 16	25 ± 5	0.159	23 ± 4	27 ± 13	23 ± 6	23 ± 6	0.168
BUN, mg/dL	17.2 ± 4.2	16.8 ± 4.1	17 ± 4.5	17.5 ± 3.8	0.761	17.2 ± 3.8	17.0 ± 4.0	17.5 ± 4.9	20.0 ± 6.9	0.011	22.2 ± 7.0	19.0 ± 6.5	17.5 ± 4.8	19.1 ± 6.8	0.204
Creatinine, mg/dL	0.9 ± 0.1	1.0 ± 0.1	1.0 ± 0.2	1.0 ± 0.2	0.007	1.0 ± 0.1	1.0 ± 0.2	1.0 ± 0.2	1.1 ± 0.4	0.015	1.1 ± 0.2	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.950
GFR, mL/min/1.73 m <sup>2</sup>	55 ± 9	56 ± 10	60 ± 12	67 ± 12	< 0.001	50 ± 7	53 ± 9	57 ± 10	55 ± 14	< 0.001	43 ± 8	46 ± 9	46 ± 8	48 ± 10	0.215
Glucose, mg/dL	93 ± 9	96 ± 16	99 ± 21	98 ± 30	0.181	99 ± 16	98 ± 18	97 ± 21	95 ± 11	0.854	103 ± 19	99 ± 18	97 ± 10	102 ± 42	0.781
HbA1c, %	5.6 ± 0.4	5.8 ± 0.7	5.9 ± 0.9	5.9 ± 1.1	0.054	5.9 ± 0.7	5.8 ± 0.7	5.9 ± 1.1	5.8 ± 1.1	0.741	6.2 ± 0.9	5.9 ± 0.8	5.7 ± 0.6	5.8 ± 0.5	0.314
Insulin, uIU/mL	6.8 ± 3.6	6.7 ± 4.9	6.9 ± 4.9	7.0 ± 3.8	0.963	8.4 ± 6.4	7.5 ± 5.1	7.1 ± 6.9	11.5 ± 19	0.038	7.4 ± 4.6	7.4 ± 4.6	6.6 ± 3.3	7.3 ± 3.7	0.833
Calcium, mg/dL	9.5 ± 0.3	9.5 ± 0.3	9.5 ± 0.3	9.5 ± 0.3	0.621	9.5 ± 0.3	9.4 ± 0.3	9.4 ± 0.4	9.5 ± 0.4	0.017	9.7 ± 0.5	9.4 ± 0.4	9.4 ± 0.4	9.5 ± 0.3	0.021
Phosphorus, mg/dL	3.8 ± 0.4	3.8 ± 0.5	3.8 ± 0.5	3.6 ± 0.5	0.110	3.9 ± 0.5	3.7 ± 0.5	3.7 ± 0.5	3.7 ± 0.5	0.026	3.7 ± 0.4	3.6 ± 0.5	3.6 ± 0.4	3.5 ± 0.3	0.670
25(OH)Vit-D	17.7 ± 7.7	18.2 ± 8.1	16.9 ± 7.2	18.1 ± 6.5	0.607	18.9 ± 7.6	17.5 ± 7.4	18.9 ± 8.4	18.5 ± 6.9	0.321	19.6 ± 9.3	18.9 ± 8.1	16.7 ± 7	18.4 ± 8	0.615
Protein, g/dL	7.4 ± 0.3	7.3 ± 0.4	7.4 ± 0.3	7.3 ± 0.3	0.641	7.4 ± 0.4	7.3 ± 0.4	7.3 ± 0.4	7.3 ± 0.3	0.097	7.4 ± 0.3	7.4 ± 0.4	7.3 ± 0.4	7.2 ± 0.3	0.046
Albumin, d/dL	4.4 ± 0.2	4.4 ± 0.2	4.4 ± 0.2	4.4 ± 0.2	0.687	4.4 ± 0.2	4.4 ± 0.2	4.4 ± 0.2	4.4 ± 0.2	0.108	4.5 ± 0.2	4.4 ± 0.2	4.4 ± 0.2	4.3 ± 0.2	0.205
Uric acid, mg/dL	4.5 ± 1.1	4.8 ± 1.1	4.9 ± 1.3	5.4 ± 1.3	0.016	4.8 ± 1.2	5.0 ± 1.3	5.3 ± 1.6	5.2 ± 1.4	0.150	5.5 ± 1.4	5.4 ± 1.5	5.7 ± 1.7	5.6 ± 1.4	0.888
Total bilirubin, mg/dL	0.8 ± 0.3	0.8 ± 0.3	0.8 ± 0.3	0.8 ± 0.3	0.235	0.7 ± 0.2	0.8 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	0.081	0.8 ± 0.2	0.8 ± 0.3	0.8 ± 0.2	0.7 ± 0.2	0.791
CRP, mg/dL	1.6 ± 3.6	1.4 ± 2.7	1.3 ± 2.3	1.3 ± 1.9	0.925	1.2 ± 1.7	1.4 ± 4.5	1.5 ± 4.0	1.8 ± 3.3	0.942	1.7 ± 2.1	2.2 ± 4.3	1.9 ± 5.4	1.0 ± 0.8	0.659
Total cholesterol, mg/dL	195 ± 35	186 ± 34	186 ± 32	193 ± 31	0.231	185 ± 33	181 ± 34	174 ± 38	174 ± 35	0.223	203 ± 31	169 ± 34	174 ± 28	165 ± 25	0.004
Triglyceride, mg/dL	134 ± 58	123 ± 58	137 ± 68	123 ± 51	0.166	124 ± 52	127 ± 66	118 ± 56	118 ± 57	0.684	152 ± 96	121 ± 61	146 ± 81	115 ± 49	0.138
HDL-C, mg/dL	53 ± 13	52 ± 12	51 ± 17	49 ± 10	0.372	51 ± 10	51 ± 12	48 ± 11	47 ± 9	0.053	50 ± 10	49 ± 13	46 ± 9	45 ± 8	0.341
LDL-C, mg/dL	115 ± 30	110 ± 29	108 ± 30	120 ± 24	0.149	110 ± 30	105 ± 29	103 ± 31	104 ± 32	0.552	123 ± 23	95 ± 29	101 ± 29	97 ± 25	0.017
MASLD index	-6.1 ± 0.8	-6.0 ± 1.0	-5.8 ± 1.0	-5.9 ± 0.8	0.245	-6.1 ± 0.9	-5.7 ± 1.0	-5.7 ± 1.1	-5.4 ± 0.9	0.012	-5.6 ± 1.0	-5.5 ± 0.8	-5.8 ± 0.7	-5.4 ± 1.2	0.368
NFS	10.4 ± 2.0	10.8 ± 3.0	10.6 ± 2.5	11.4 ± 2.7	0.421	11.0 ± 2.5	10.4 ± 2.7	10.1 ± 2.5	10.4 ± 2.3	0.229	10.4 ± 3.1	10.3 ± 3.1	9.6 ± 2.0	10.2 ± 2.9	0.773
FSI	-6.6 ± 0.6	-6.5 ± 0.8	-6.2 ± 0.8	-6.3 ± 0.8	0.023	-6.4 ± 0.7	-6.3 ± 0.8	-6.4 ± 0.7	-6.2 ± 0.6	0.718	-6.0 ± 1.0	-6.2 ± 0.8	-6.2 ± 0.8	-6.2 ± 0.6	0.905

Values are numbers (percentages) for categorical variables and means ± standard deviation for continuous variables.

The P values are calculated using  $\chi^2$  test or Fisher's exact test for categorical variables and ANOVA test for continuous variables.

BMI = body mass index. W/H ratio = waist-to-hip ratio, BP = blood pressure, ALP = alkaline phosphatase, AST = aspartate aminotransferase, ALT = alanine aminotransferase, BUN = blood urea nitrogen, GFR = glomerular filtration rate, HbA1c = glycosylated hemoglobin, 25(OH)Vit-D = 25-hydroxyvitamin D, CRP = C-reactive protein, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, MASLD = metabolic dysfunction-associated steatotic liver disease, NFS = non-alcoholic fatty liver disease fibrosis score, HSI = hepatic steatosis index, FSI = Framingham Steatosis Index.



In the 65–69 years age group, the follow-up test results of Visit\_4Y, 3 years after baseline, showed that the higher the 20s\_BMI, the lower the increase in weight (trend  $P = 0.043$ ), BMI (trend  $P = 0.075$ ), waist circumference (trend  $P = 0.044$ ), hip circumference (trend  $P = 0.146$ ), and W/H ratio (trend  $P = 0.113$ ) compared with the low 20s\_BMI group (Table 2, Supplementary Table 2). However, in people over 75 years of age, the change in weight (trend  $P = 0.041$ ), BMI (trend  $P = 0.047$ ), waist circumference (trend  $P = 0.021$ ), hip circumference (trend  $P = 0.435$ ), and W/H ratio (trend  $P = 0.031$ ) increased. However, the results of Visit\_8Y, a follow-up test 6 years after the baseline, showed a generally similar trend to the follow-up test results of Visit\_4Y; however, the differences were not statistically significant.

### Differences in MASLD according to 20s\_BMI

The presence of MASLD was checked in individuals over 65 years of age according to their 20s\_BMI (Table 1). The NFS, which predicts liver fibrosis, also increased as the 20s\_BMI increased; however, this was only statistically significant in the age group between 70 and 74 years ( $P = 0.012$ ). The HIS ( $P = 0.421$ ) and FSI ( $P = 0.023$ ), which are diagnostic indicators for MASLD, tended to increase as the 20s\_BMI increased. This pattern was similar in those aged between 70 and 74 years; however, the difference was not statistically significant.

In the 65–69 years age group, from Visit\_4Y to Visit\_8Y, the NFS, HIS, and HIS values all showed a worsening trend (Fig. 2A–C). In particular, in the case of Visit\_4Y, 3 years after the baseline, the NFS showed a tendency to decrease as the 20s\_BMI increased; however, this was not statistically significant. As the 20s\_BMI increased, the decrease in the HSI was significantly smaller ( $P = 0.012$ ), which also showed the same significant difference at Visit\_8Y ( $P = 0.001$ ). As the 20s\_BMI increased, the FSI also tended to decrease; however, there was no statistically significant difference among the four groups. This pattern was the same even in the 70–74 years age group (Fig. 2D–F). In particular, the NFS showed that as the 20s\_BMI increased, the decrease in HSI also decreased ( $P < 0.05$ ). The same trend was

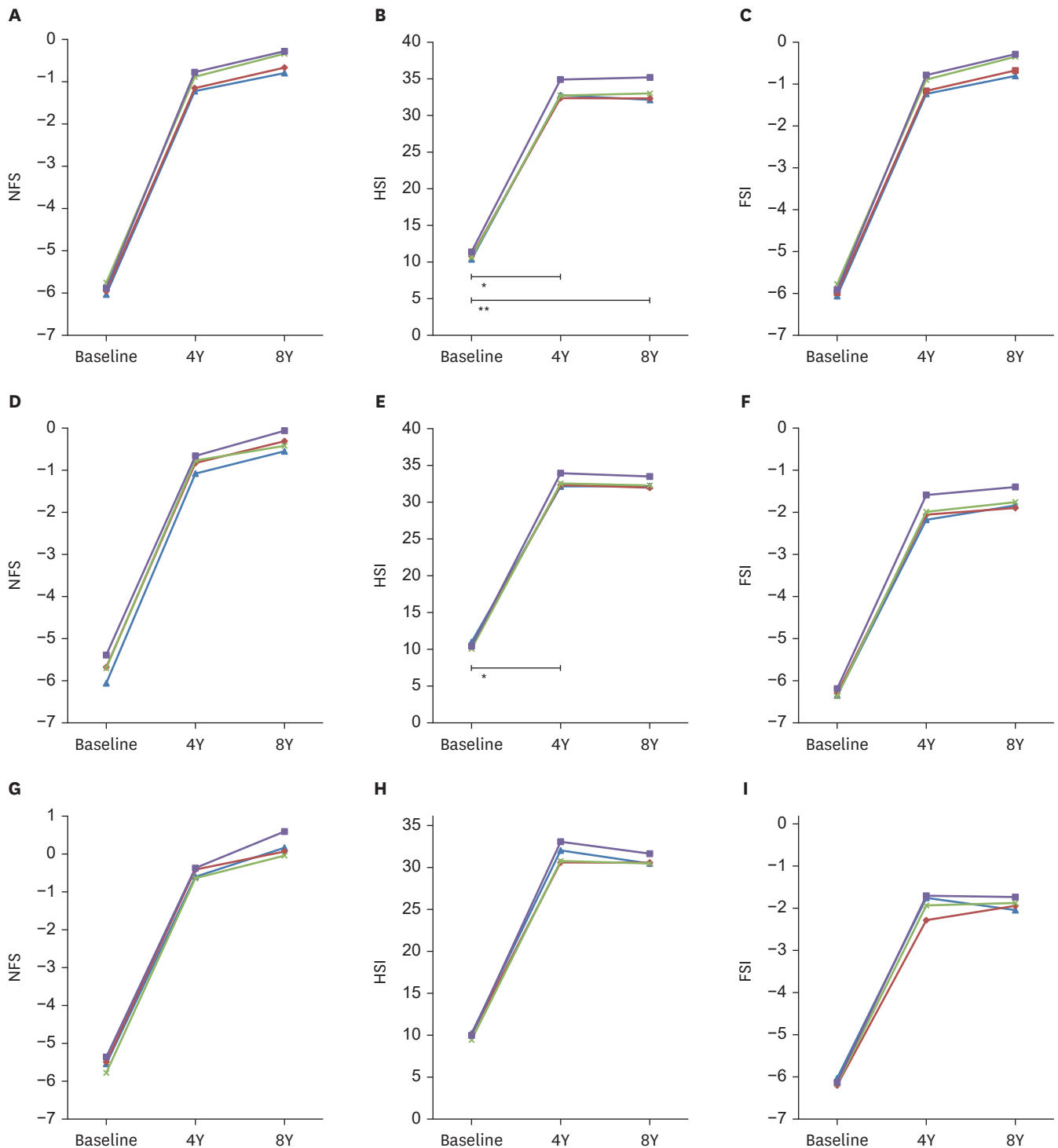
**Table 2.** Change of difference in body index according to BMI in the 20s

Variables	$\Delta$ (Visit 4Y – Baseline)					$\Delta$ (Visit 8Y – Baseline)				
	Under_BMI	Normal_BMI	Over_BMI	Obese_BMI	<i>P</i> value	Under_BMI	Normal_BMI	Over_BMI	Obese_BMI	<i>P</i> value
Weight, kg										
65–69 yr	1.06 ± 2.51	0.42 ± 2.45	0.17 ± 2.60	−0.54 ± 3.95	0.043	0.12 ± 3.67	−0.40 ± 4.65	−0.47 ± 3.72	−1.16 ± 4.77	0.646
70–74 yr	0.37 ± 2.47	0.10 ± 2.31	−0.16 ± 2.63	−0.15 ± 4.84	0.642	−0.19 ± 3.86	−0.99 ± 3.53	−1.15 ± 4.21	−1.01 ± 5.22	0.453
≥ 75 yr	−1.55 ± 1.77	−0.67 ± 3.22	0.24 ± 2.01	1.08 ± 4.20	0.041	−2.90 ± 4.00	−1.78 ± 4.54	−1.66 ± 3.86	−0.12 ± 4.79	0.321
BMI, kg/m <sup>2</sup>										
65–69 yr	0.57 ± 1.07	0.31 ± 0.97	0.26 ± 1.02	−0.02 ± 1.48	0.075	0.37 ± 1.55	0.11 ± 1.97	0.10 ± 1.34	−0.07 ± 1.77	0.707
70–74 yr	0.30 ± 1.02	0.22 ± 0.93	0.15 ± 1.00	0.18 ± 1.80	0.834	0.27 ± 1.54	0.01 ± 1.45	−0.04 ± 1.62	0.04 ± 2.02	0.636
≥ 75 yr	−0.43 ± 0.77	−0.05 ± 1.25	0.30 ± 0.91	0.60 ± 1.58	0.047	−0.76 ± 1.68	−0.28 ± 1.81	−0.31 ± 1.59	0.25 ± 1.76	0.437
Waist circumference, cm										
65–69 yr	3.10 ± 6.73	1.36 ± 5.97	0.50 ± 4.45	0.12 ± 4.99	0.044	5.43 ± 8.02	4.70 ± 7.36	3.02 ± 6.25	3.35 ± 6.29	0.155
70–74 yr	0.87 ± 5.82	0.89 ± 5.75	1.11 ± 5.29	0.52 ± 7.72	0.975	4.17 ± 7.54	4.42 ± 7.58	5.21 ± 6.35	3.78 ± 6.25	0.762
≥ 75 yr	−1.13 ± 7.14	−0.25 ± 5.59	1.23 ± 5.52	3.68 ± 6.09	0.021	1.03 ± 4.70	3.19 ± 8.21	2.86 ± 7.20	4.36 ± 5.44	0.687
Hip circumference, cm										
65–69 yr	1.55 ± 3.45	−0.00 ± 3.79	0.20 ± 3.92	0.74 ± 6.14	0.146	0.97 ± 6.94	1.43 ± 5.18	0.84 ± 5.88	0.90 ± 8.63	0.802
70–74 yr	−0.42 ± 4.19	0.20 ± 3.59	−0.45 ± 3.54	0.26 ± 4.46	0.411	0.87 ± 7.22	1.24 ± 5.32	1.58 ± 5.65	1.82 ± 3.59	0.847
≥ 75 yr	−1.29 ± 3.46	0.04 ± 3.99	0.92 ± 4.18	0.06 ± 3.31	0.435	0.78 ± 5.65	1.02 ± 6.86	2.80 ± 3.59	2.08 ± 3.98	0.528
W/H ratio										
65–69 yr	0.02 ± 0.06	0.01 ± 0.06	−0.00 ± 0.05	−0.01 ± 0.07	0.113	0.06 ± 0.13	0.04 ± 0.08	0.03 ± 0.10	0.03 ± 0.10	0.285
70–74 yr	0.01 ± 0.06	0.01 ± 0.06	0.02 ± 0.05	−0.00 ± 0.08	0.557	0.04 ± 0.11	0.04 ± 0.08	0.04 ± 0.06	0.02 ± 0.06	0.791
≥ 75 yr	−0.00 ± 0.07	−0.00 ± 0.06	−0.00 ± 0.06	0.04 ± 0.05	0.031	0.01 ± 0.07	0.02 ± 0.08	−0.00 ± 0.07	0.03 ± 0.06	0.498

Values are mean ± standard deviation for continuous variables.

The *P* values are calculated using ANOVA test for continuous variables.

BMI = body mass index, W/H ratio = waist-to-hip ratio.



**Fig. 2.** Differences in metabolic dysfunction-associated steatotic liver disease according to BMI in the participants 20s. (A) NFS in the 65–69 years age group, (B) HSI in the 65–69 years age group, (C) FSI in the 65–69 years age group, (D) NFS in the 70–74 years age group, (E) HSI in the 70–74 years age group, (F) FSI in the 70–74 years age group, (G) NFS in the ≥ 75 years age group, (H) HSI in the ≥ 75 years age group, and (I) FSI in the ≥ 75 years age group. NFS = non-alcoholic fatty-liver disease fibrosis score, HSI = hepatic steatosis index, FSI = Framingham Steatosis Index.

\* $P < 0.05$ , calculated using ANOVA test for continuous variables.

\*\* $P < 0.005$ , calculated using ANOVA test for continuous variables.

**Table 3.** Differences in BMD according to BMI in the 20s

Variables	65–69 yr					70–74 yr					Over 75 yr				
	Under_ BMI	Normal_ BMI	Over_BMI	Obese_ BMI	P value	Under_ BMI	Normal_ BMI	Over_BMI	Obese_ BMI	P value	Under_ BMI	Normal_ BMI	Over_BMI	Obese_ BMI	P value
No. of participants	57	347	80	29		61	274	83	25		12	113	27	22	
L1-L4 T-score	-1.8 ± 1.2	-1.5 ± 1.2	-1.0 ± 1.4	-0.6 ± 1.4	< 0.001	-1.6 ± 1.2	-1.3 ± 1.4	-0.8 ± 1.7	-0.7 ± 1.7	0.004	-1.4 ± 1.2	-1.3 ± 1.4	-0.9 ± 1.9	-0.5 ± 2.1	0.195
L1-L4 Z-score	0.3 ± 1.0	0.3 ± 0.8	0.5 ± 0.9	0.5 ± 0.9	0.363	0.5 ± 0.9	0.5 ± 1.0	0.5 ± 1.0	0.6 ± 1.0	0.902	0.6 ± 0.8	0.5 ± 0.9	0.6 ± 1.1	0.8 ± 1.2	0.550
Neck T-score	-1.6 ± 0.8	-1.5 ± 0.9	-1.2 ± 1.0	-0.7 ± 1.1	< 0.001	-2.0 ± 0.7	-1.7 ± 0.9	-1.4 ± 1.0	-1.1 ± 1.1	< 0.001	-1.8 ± 1.2	-1.8 ± 1.0	-1.5 ± 1.2	-1.6 ± 1.1	0.634
Neck Z-score	0.4 ± 1.0	0.3 ± 0.9	0.4 ± 1.0	0.8 ± 1.0	0.046	0.1 ± 0.8	0.2 ± 1.0	0.3 ± 0.9	0.6 ± 1.1	0.127	0.4 ± 1.3	0.2 ± 1.0	0.3 ± 1.0	0.3 ± 1.0	0.892
Total hip T-score	-0.7 ± 0.8	-0.7 ± 0.9	-0.5 ± 0.9	-0.0 ± 0.9	0.001	-1.1 ± 0.7	-0.8 ± 0.8	-0.6 ± 1.1	-0.2 ± 1.1	< 0.001	-1.2 ± 1.2	-0.9 ± 0.9	-0.7 ± 1.1	-0.8 ± 1.3	0.578
Total hip Z-score	0.5 ± 0.8	0.4 ± 0.9	0.5 ± 1.1	0.8 ± 0.7	0.177	0.3 ± 0.8	0.4 ± 0.8	0.4 ± 0.9	0.8 ± 0.9	0.097	0.4 ± 1.1	0.4 ± 0.9	0.6 ± 0.9	0.5 ± 1.1	0.865
vBMD, mg/mL	79.2 ± 24.7	79.6 ± 26.8	85.4 ± 34.6	92.7 ± 28.5	0.046	68.0 ± 25.5	74.7 ± 27.7	79.6 ± 32.2	80.2 ± 24.1	0.087	68.3 ± 20.7	65.5 ± 31.1	68.4 ± 35.6	72.1 ± 35.4	0.837

Values are mean ± standard deviation for continuous variables.

The *P* values are calculated using  $\chi^2$  test or Fisher's exact test for categorical variables and ANOVA test for continuous variables.

BMD = bone mineral density, BMI = body mass index, vBMD = volumetric bone mineral density.

also observed in individuals aged 75 years and older; however, the values were not statistically significant (Fig. 2G-I).

### Differences in BMD according to 20s\_BMI

As the 20s\_BMI increased, the BMD T-score in L1-L4 significantly increased in those aged between 65–69 ( $P < 0.001$ ) and 70–74 years ( $P = 0.004$ ) (Table 3, Supplementary Table 3). This trend was the same in people over 75 years ( $P = 0.195$ ); however, the difference was not statistically significant. Similarly, in the T-score of the neck, the BMD significantly increased as the 20s\_BMI increased in the 65–69 ( $P < 0.001$ ) and 70–74 years age groups ( $P < 0.001$ ). This trend was similar for the total hip-T score in the 65–69 ( $P = 0.001$ ) and 70–74 years age groups ( $P < 0.001$ ). However, there was still no statistical difference in people aged over 75 years. As the 20s\_BMI increased, lumbar spine volume ( $P = 0.046$ ) at the age of 65–69 years also increased significantly; however, this was not significant over the age of 70 years.

## DISCUSSION

The relationship between BMI and waist circumference, hip circumference, and BP have already been proven in many cross-sectional studies.<sup>16,17</sup> However, this was a prospective cohort study analyzing 20s\_BMI from two aspects over a period of 8 years: obesity-related indicators when a person becomes older than 65 years, and the amount of change over time thereafter.

In this study, a high 20s\_BMI remained high even in those aged over 65 years and had an effect on the occurrence and worsening of MASLD. Obese men in their 20s remain obese over time; however, the rate of normal-weight men who later become obese is significantly lower.<sup>18</sup> This indicates that obesity in young people in their 20s is a risk factor for various chronic diseases in the elderly and ultimately acts as a risk factor for cardiovascular diseases. Ultimately, to prevent the progression of these adverse effects, it is important to reduce eating habits characterized by increased consumption of fats and calories starting in the 20s and increase physical activity to prevent weight gain starting in the 20s and 30s.



The novelty of this study lies in its confirmation of the amount of change in various indicators according to 20s\_BMI. We found that the higher the 20s\_BMI, the smaller the amount of weight gain in elderly people over 65 years of age; however, this weight gain increased when people were over 75 years of age. It is difficult to rely simply on body weight as an obesity criterion for seniors aged over 65 years. This is because muscle mass decreases and visceral fat increases.<sup>19</sup> When people reach the age of 65 years, the hip and thigh muscles decrease significantly.<sup>20</sup> This means that the older an individual gets, the faster the muscles shrink.<sup>19</sup> Therefore, the W/H ratio was used to evaluate obesity in elderly individuals.<sup>21</sup> We found that as the 20s\_BMI increased in people aged over 75 years, the W/H ratio also tended to increase significantly. Interestingly, the increase in W/H ratio decreases as 20s\_BMI increases in the age group between 65 and 69 years, but increases significantly in the 75 years or older age group. This also applies to weight, BMI, and waist circumference. This implies that the increase in obesity among Koreans becomes noticeable after the age of 75 years; hence, more attention should be paid to healthcare after the age of 75 years. This highlights the need for large-scale randomized controlled studies to determine a clear causal relationship between 20s\_BMI and weight gain later in life.

After humans reach their 20s and 30s, fat mass increases, and muscle mass gradually decreases.<sup>19</sup> In addition, even if energy intake does not increase with age, energy expenditure gradually decreases, leading to increased fat mass.<sup>22</sup> According to the present study, 20s\_BMI had an effect on MASLD when people were over 65 years of age. In the case of the foreign FSI for diagnosing fatty liver disease and HSI developed in Korea, 20s\_BMI increases, FSI and HSI tend to increase together in people over 65 years of age. Unfortunately, there was no statistical difference regarding the HSI developed in Korea, but it showed a tendency to have a high overall correlation; therefore, additional research is needed. The NFS, which predicts liver fibrosis, also increased as the 20s\_BMI increased; however, this was only statistically significant in the 70–74 years age group. As liver fibrosis progresses over a long period with age, it is presumed that this is significant in older participants. Although, the relationship between BMI in their 20s and various MASLD index was reduced in the age of 70 or older. Therefore, the interpretation of the results of this study may be perceived as exaggerated, however, the changes between Visit\_4Y and Visit\_8Y became less pronounced compared to those between Baseline and Visit\_4Y due to aging, it is important to note that the progression is still ongoing. As the average life expectancy increases overall, healthcare management in this area is necessary. Diseases in the elderly develop slowly and progress to chronic levels.<sup>23</sup> Therefore, early detection and prevention of disease in individuals in their 20s is of utmost importance.

It is well known that factors related to osteoporosis in the elderly include BMI, age, age at menarche, smoking, and drinking.<sup>24,25</sup> Studies on BMI and osteoporosis are well-known. Although this study was conducted once at baseline, as the 20sBMI increased, BMD significantly increased in elderly individuals over 65 years of age. Human bones recognize mechanical stimuli through osteocytes and suppress sclerostin and receptor activator of NF-kappaB ligand, which are harmful to bones.<sup>26</sup> Hence, when a person with obesity walks, more load is placed on the bones; ultimately, this increased mechanical load helps stimulate bone formation and increases bone density.<sup>27</sup> Additionally, in the case of underweight individuals, it can be estimated that BMD decreases due to hormonal imbalance and a relative lack of nutrition intake, including calcium and vitamin D.<sup>28</sup> Moreover, as more hormones that are beneficial for bones, such as estrogen, are produced in the fat of people with obesity, this may also be beneficial for the bones.<sup>29</sup> However, fat generates good and bad

adipokines; hence, their net effects on bones remain controversial. Adipokines are an issue, but owing to mechanical loading and estrogen synthesis in fat, people with obesity have good bones.<sup>30</sup> Furthermore, because fat acts as padding, fractures are less likely if you fall (BMD increases). Although the results of this study are already well known, they are consistent with well-known information; therefore, it can be assumed that the cohort in this study is a well-verified and good cohort. We found that 20s\_BMI, rather than body weight at the time of BMD measurement, was of greater importance because it affected BMD in older adults. Unfortunately, since the BMD test was conducted only at the first visit, differences between visits could not be observed.

Obesity is a major cause of various complications such as diabetes, high BP, and cardiovascular diseases. People with a high BMI in their youth were more likely to develop liver diseases, such as non-alcoholic fatty-liver disease, or die from it as they grew older.<sup>31</sup> Considerable research has been conducted on weight loss in early adulthood and various diseases that occur in old age. Being overweight in early adulthood increases the risk of developing pancreatic<sup>32</sup> or stomach cancer.<sup>33</sup> In pancreatic cancer, the onset time is earlier and the survival period is shorter.<sup>32</sup> However, since this study defined early overweight as being between the ages of 20 and 49 years, its definition of the early 20s is different in that the impact of BMI in early adulthood is more limited. This study is significant as it does not simply look at obesity at one age, but also confirms changes in values over time. In particular, body weight has been shown to have a significant impact on the development of fatty liver, emphasizing the importance of body weight in one's 20s. In an obesity study conducted in children and adolescents, 50% of those who were obese during childhood and 80% of those who were obese during adolescence were obese even as adults.<sup>34</sup> This can lead to complications such as diabetes, high BP, Metabolic syndrome, fatty liver, and cardiovascular disease. In the end, like this study, it has been proven that weight management, not only for children and adolescents but also for those in their early 20s, must be done on a continuum to be able to maintain health after becoming elderly.

This was a prospective follow-up study for the prevention and management of high-risk groups for cardiovascular diseases, meaning that it was conducted with the clear objective of tracking the occurrence of cardiovascular diseases. Prospective cohort studies have the advantage of accurately identifying temporal sequences of disease occurrence, which is beneficial for establishing causality.<sup>35</sup> Undeniably, bias due to drop-out of participants during the follow-up period may occur, which could reduce the generalizability of the study results.<sup>36</sup> To address this potential issue in this study, we maintained continuous contact with the participants to build the cohort and prevent mid-study drop-outs. To minimize drop-out rates, the investigators either invited participants to personally visit the center for surveys or gave them the option to be assessed at their own home. Importantly, we want to reiterate that this was not a retrospective cohort study based on pre-established data, but a prospective cohort study clearly designed with the goal of prevention and management of high-risk groups for cardiovascular diseases.

In addition, this study contains various types of bias inherent to cohort studies. First, a major limitation was recall bias, because, to calculate the 20s\_BMI, elderly people over the age of 65 years had to recall their height and weight from memory.<sup>37</sup> However, an effort was made to minimize bias by calculating the average height and weight measured three times at 3-year intervals. To enhance the reliability of the study results, additional prospective cohort studies with stronger evidence are needed. Second, this study had an average duration of

eight years. Therefore, major confounding variables such as eating habits, physical activity, smoking, drinking, the presence of chronic diseases (medications), and socioeconomic conditions were not appropriately considered in the analysis. Consequently, it is difficult to clearly establish causality based on this study.<sup>38</sup> Third, because this study only included participants aged 65 years and older, the uneven distribution of data is a limitation. In reality, the data distribution differs among 65–69 years, 70–74 years, and  $\geq 75$  years groups, as well as among under\_BMI, normal\_BMI, over\_BMI, and obese\_BMI groups, which may have influenced the statistical results. In particular, sex hormones such as estrogen and testosterone are important factors in chronic metabolic diseases in older adults. However, the uneven distribution of sex in this study may have limited the accuracy and generalizability of the findings. Fourth, a formula was used to diagnose fatty liver disease. Nonetheless, the FSI is a widely known method utilizing abdominal computed tomography based on the Framingham cohort study,<sup>13</sup> while the HSI is a formula calculated using ultrasound for Koreans.<sup>14</sup> Therefore, using these two formulae may have improved credibility. Finally, regarding BMD, the amount of change could not be calculated because it was only assessed one time at baseline.

While obesity education typically focuses on children and adolescents, there is a relative lack of counseling and education targeting adults in their early 20s. Hence, this study is of great significance because it provides epidemiological evidence for the importance of weight control among Koreans in their 20s. In modern society, the importance of managing obesity, which is rapidly increasing among all age groups, should be emphasized, especially for people in their early 20s who are considered new to adulthood. Future large-scale, prospective randomized controlled studies are needed to further validate our findings.

## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

Differences in body index in male and female according to BMI in the 20s

### Supplementary Table 2

Change of difference in body index in male and female according to BMI in the 20s

### Supplementary Table 3

Differences in BMD in male and female according to BMI in the 20s

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