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MIDLIFE BODY MASS INDEX TRAJECTORY AND RISK OF FRAILTY 8 YEARS LATER IN TAIWAN

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Abstract: *Objectives:* Few studies have focused on weight change and frailty, especially in Asia. This research aimed to evaluate midlife body mass index (BMI) trajectory and assess its relationship with frailty 8 years later in Taiwan. *Design:* A prospective cohort study. *Setting and Participants:* Data were retrieved from the Taiwan Longitudinal Study on Aging conducted from 1999 to 2007. The analysis was restricted to respondents aged between 50 to 69 years old, who were not frail in 1999 and were alive in 2007 (n=1609). *Measurements:* Frailty was defined using the Fried criteria. The group-based model of trajectory was used to estimate BMI trajectories among elderly participants. Logistic regression analysis was used to examine the association between BMI change and frailty. *Results:* Four trajectory classes were identified and each remained stable during the 8-year follow-up. There were 316 participants (20.3%) in the low-normal weight group (baseline BMI=20.38 kg/m2), 737 participants (44.7%) in the high-normal weight group (baseline BMI=23.22 kg/m2), 449 participants (28.4%) in the overweight group (baseline BMI=26.24 kg/m2), and 107 participants (6.6%) in the obesity group (baseline BMI=30.65 kg/m2). After adjustment for confounding factors, the low-normal weight group and obesity group were associated with increased frailty compared with the high-normal weight group. *Conclusion:* Our results showed that the BMI trajectories of midlife individuals tended to be constant and those in both the low-normal weight group and obesity group had an increased risk of developing frailty in later life. Therefore, an optimal weight-targeting strategy should be considered for Asian elderly individuals.

Key words: Body mass index, obesity, trajectory, frailty.

Introduction

Frailty is a geriatric condition characterized by an increased vulnerability and decreased ability to maintain homeostasis. This condition may be related to a number of adverse health outcomes and poor quality of life (1, 2). The pathophysiology of frailty is complex, including mitochondrial dysregulation, decreased energy generations, neuroendocrine alterations, insulin resistance, activation of inflammatory pathways, etc. Some of the mechanisms involved in this condition are similar to those observed in obesity (1, 3, 4) and several studies have evaluated the relationship between body weight and frailty.

One cross-sectional study performed in England has shown that for individuals aged >65 years, a low and very high body mass index (BMI) was associated with a higher risk for the development of frailty (5). An analysis of two cohort studies conducted in Spain (3.5-year follow-up) demonstrated that higher waist circumference and obesity increased the risk of developing frailty (6). Another study performed in Finland revealed that overweight or obese midlife individuals were linked to an increased risk for pre-frailty and frailty compared with those in the normal weight group (22.2-year follow-up) (7).

However most of these studies examined the BMI at one particular time point and subsequently predicted future outcomes. In these studies, the change in body weight with time was not considered. Recently, researchers attempted to map the BMI trajectories and evaluate their relationship with health outcomes. A Canadian study showed that individuals in the overweight-stable, obesity I-stable, and obesity II-stable groups experienced more asthma, arthritis, hypertension, diabetes, heart disease, cognitive impairment, and reduced self-rated overall health than those in the normal-stable group (8). For frailty, only one study performed in the USA has shown that weight change and obesity increased the risk of frailty (9).

A study showed that Asians have a higher percentage of body fat than Caucasians with the same BMI level (10). Of note, the BMI is defined differently in Asia or Taiwan (Table 1). Nevertheless, currently, there are limited data regarding the relationship between change in midlife BMI and frailty in Asians. The aim of this study was to estimate the trajectory of BMI among midlife individuals in Taiwan and determine its relationship with the incidence of frailty in later life.

Materials and Methods

Data source

In this long-term prospective cohort study, data were obtained from the Taiwan Longitudinal Study on Aging (TLSA), which has been conducted by the Health promotion ministration since 1989 involving adult individuals aged >60 years residing in non-aboriginal townships of Taiwan. The

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Table 1
Classification of Body Mass Index in different areas

	WHO	Asia-Pacific	Taiwan
Underweight	BMI<18.5	BMI<18.5	BMI<18.5
Normal weight	18.5≤BMI<25	18.5≤BMI<23	18.5≤BMI<24
Overweight	25≤BMI<30	23≤BMI<25	24≤BMI<27
Mild Obesity	30≤BMI<35	25≤BMI<30	27≤BMI<30
Moderate Obesity	35≤BMI<40	30≤BMI<35	30≤BMI<35
Severe Obesity	BMI≥40	BMI≥35	BMI≥35

respondents were followed every 3 to 4 years (1989, 1993, 1996, 1999, 2003, and 2007). Two fresh samples were added in 1996 and 2003 to maintain the representativeness of the younger age cohort and extend that of the cohort aged ≥50 years. Since the population of this study comprised middle-aged individuals, we initially attempted to use data from wave 3 group 2, followed the weight trajectory using the BMI values obtained in 1996, 1999, 2003, and 2007, and explored its relationship with frailty in 2007. However, after examining the questionnaire in each wave, we found that BMI data were not collected in 1996. Eventually, we obtained data only from 1999, 2003, and 2007 for mapping the BMI trajectories.

Classification of study participants

This study included middle-aged individuals who participated in the TLSA in 1999. Individuals who were frail in 1999 or had unreasonable weight or height data at each of the three study time points were excluded. In addition, we retrieved data from the Death Registration of the Ministry of Interior in Taiwan and excluded those who died in 2007. Eventually, 1609 individuals were included in this study (831 males and 778 females).

Research variables

From 1999, we collected data for variables that were considered risk factors of frailty in previous studies (i.e., age, sex, level of education, income, social participation, self-rated health, smoking, drinking, and number of diseases (11, 12). The level of education was classified into four groups: illiterate (0 years), elementary school (1–6 years), junior-to-senior high school (7–12 years), and college or above (>12 years). The level of income was determined through a question posed to the participants: Are you satisfied with your income? Three groups were formed: good (very satisfied/satisfied), fair, and poor (unsatisfied and very unsatisfied). Individuals who had either paid or voluntary work or participated in community activities were considered as having social participation. Moreover, individuals were divided into three groups according to self-rated health: good (very good/good), fair, and poor (poor/very poor). The recorded diseases (number of diseases) included hypertension, diabetes, cardiovascular disease, stroke, cancer, chronic respiratory diseases, arthritis or rheumatoid diseases, gastric diseases, hepatobiliary diseases, and kidney diseases.

The BMI was calculated as weight divided by the square of height (kg/m^2). The BMI criteria established by the Ministry of Health and Welfare of Taiwan in 2002 were used in the present study. A comparison of Taiwan's standard with that of the World Health Organization (WHO) is listed in Table 1.

Frailty was defined according to the Fried criteria (13). Individuals who met at least three of five symptoms (i.e., shrinking, weakness, exhaustion, slowness, and low physical activity) were considered frail. Because we retrieved data from the questionnaire, we used substitute evaluations on this five domains (14). Regarding the nutritional status of individuals, we used the parameter of decreased appetite instead of body weight loss. Individuals who reported poor appetite often in the previous week were classified as having experienced the symptom of shrinking. For mobility, we used walking/moving in and around the house instead of gait speed. Individuals who had difficulty or were unable to walk a distance of 200–300 m were considered slow. For strength, we used the parameter of lifting heavy groceries instead of hand grip strength. Individuals who had difficulty or were unable to carry 12 kg of groceries were considered weak. For physical activity, we used the frequency of leisure time/physical activities per week instead of the level of physical activity. Individuals who did not do gardening, take a walk, jog, hiking, or participate in other outdoor activities at least once or twice a week were considered to have low activity. To determine the level of energy, we used the questionnaire of the Center for Epidemiologic Studies Depression Scale (CES-D). Individuals who reported, "I could not get going" or "I felt everything I did was an effort" often or most of the time in the previous week were considered exhausted (11).

Statistical analysis

A group-based analysis model was applied to determine the BMI trajectories. We chose the most appropriate model groups based on the Bayesian Information Criterion (15). This model has been used in several geriatric research studies (11, 16-18). The demographic and clinical characteristics of each group were descriptively analyzed. We used the analysis of variance

Table 2
Estimates of growth curve parameters for Body Mass Index trajectories, 1999–2007

Body Mass Index trajectory	Parameter			
	Intercept, kg/m²		Linear slope, kg/m²	Group %
	Estimate	95% CI		
Low-normal weight	20.38	20.10–20.66	–0.017	20.3
High-normal weight	23.22	22.99–23.46	0.027	44.7
Overweight	26.24	26.01–26.46	0.078	28.4
Obesity	30.65	30.30–31.00	0.101	6.6

and the chi-squared test to analyze continuous and categorized variables, respectively. The logistic regression model was used to analyze the relationship between the BMI trajectory groups and frailty after adjusting for the factors of age, sex, education, level of income, social participation, self-rated health, smoking status, drinking status, and number of diseases. All data were analyzed using the SAS 9.4 (SAS Institute, Cary, North Carolina, USA). Statistical significance was set at the $p < 0.05$ level.

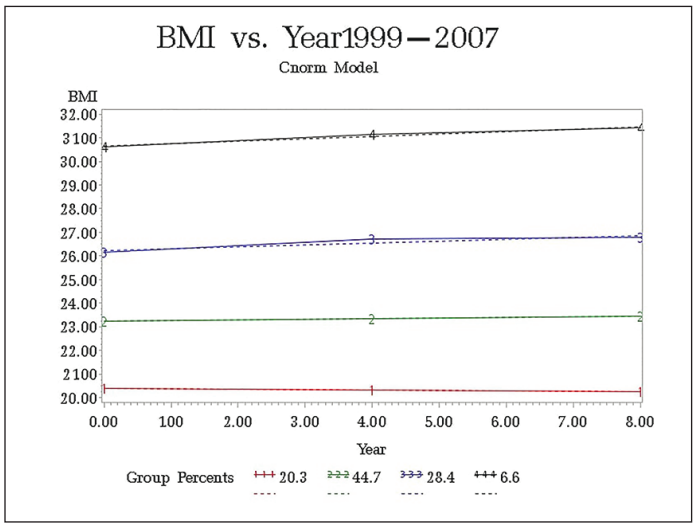
Results

A total of 1609 individuals were involved in this study and the BMI trajectories were divided into four groups according to the results of the model. There were 316 individuals (20.3%) in the low-normal weight group (average BMI: 20.38 kg/m², 737 individuals (44.7%) in the high-normal weight group (average BMI: 23.22 kg/m², 449 individuals (28.4%) in the overweight group (average BMI: 26.24 kg/m², and 107 individuals (6.6%) in the obesity group (average BMI: 30.65 kg/m2 (Figure 1, Table 2).

The demographic and clinical characteristics of each group are shown in Table 3. The study population consisted of 831 males and 778 females, with an average age of 61.13 years. The level of education of most participants was low, with 73% of those educated for <6 years. A fair level of satisfaction with income, high social participation, and less smoking/drinking status was noted. The average number of diseases was 1.16.

The univariate logistic regression analysis showed that all variables –except for social participation –were significantly associated with frailty (Table 4). After removing the irrelevant factor, a multivariate logistic regression analysis was performed. The results showed that those in the low-normal weight and obesity groups had a higher risk of frailty. For individuals in the overweight group, the odds ratio (OR) was 0.959 (not statistically significant). Furthermore, being older, female, with a low level of education, less satisfied with income, in poor self-rated health, and with a higher number of diseases were high-risk factors of frailty (Table 5).

Figure 1
Trajectories of Body Mass Index between 1999 and 2007



Discussion

This long-term prospective study analyzed the BMI trajectories of midlife individuals in Taiwan. After 8 years of follow-up, the BMI trajectories tended to be maintained to near constant and within the normal range. Thus far, there have been only a few studies focusing on the BMI trajectories of middle-aged individuals and most of these studies were conducted in the USA (9, 19-21). Compared to our study, >70% of subjects were overweight and obese in the studies conducted in USA according to the criteria of the WHO and the results were consistent with those observed in studies performed in Canada (8) and Austria (22). In Asia, only one study investigating BMI trajectories has been performed in Japan. It followed up individuals aged >60 years for 19 years (1987–2006). Four BMI trajectories were identified: "low-normal weight, decreasing" (baseline BMI: 18.7; 23.8% of individuals); "mid-normal weight, decreasing" (baseline BMI: 21.9; 44.6% of individuals); "high-normal weight, decreasing" (baseline BMI: 24.8; 26.5% of individuals); and "overweight, stable" (baseline BMI: 28.7; 5.2% of individuals) (18). Compared with these studies, the

Table 3
Demographic and clinical characteristics of the participants

Characteristics		Total n=1609	BMI Trajectory Group 1 n=316	Group 2 n=737	Group 3 n=449	Group 4 n=107	P value
Age		61.13(4.7)	61.59(4.9)	61.28(4.7)	60.65(4.8)	60.75(4.2)	0.03
Sex							0.0002
	Male	831(51.6%)	163(51.6%)	405(55%)	229(51%)	34(31.8%)	
	Female	778(48.4%)	153(48.4%)	332(45%)	220(49%)	73(68.2%)	
Body Mass Index			20.38(1.5)	23.22(1.5)	26.24(1.7)	30.65(2.4)	<0.0001
Level of education							0.1333
	Illiterate	358(22.2%)	61(19.3%)	167(22.7%)	101(22.5%)	29(27.1%)	
	1–6 years	817(50.8%)	160(50.6%)	359(48.7%)	236(52.6%)	62(57.9%)	
	7–12 years	323(20.1%)	68(21.5%)	156(21.2%)	86(19.2%)	13(12.2%)	
	>12 years	111(6.9%)	27(8.5%)	55(7.5%)	26(5.8%)	3(2.8%)	
Income							0.1763
	Poor	326(20.6%)	63(20.4%)	154(21.3%)	87(19.6%)	22(21.2%)	
	Fair	713(45.1%)	128(41.6%)	332(45.9%)	196(44.1%)	57(54.8%)	
	Good	541(34.2%)	117(38%)	238(32.8%)	161(36.3%)	25(24%)	
Social participation							0.0084
	No	380(23.6%)	96(30.4%)	157(21.3%)	98(21.8%)	29(27.1%)	
	Yes	1229(76.4%)	220(69.6%)	580(78.7%)	351(78.2%)	78(72.9%)	
Self-rated health							0.1091
	Poor	273(17%)	43(13.6%)	126(17.1%)	83(18.5%)	21(19.6%)	
	Fair	579(36%)	126(39.9%)	252(34.2%)	154(34.3%)	47(43.9%)	
	good	757(47%)	147(46.5%)	359(48.7%)	212(47.2%)	39(36.5%)	
Smoking							0.0071
	No	1185(73.7%)	220(69.6%)	532(72.2%)	342(76.2%)	91(85%)	
	Yes	424(26.3%)	96(30.4%)	205(27.8%)	107(23.8%)	16(15%)	
Alcohol							0.4195
	No	1106(68.7%)	224(70.9%)	495(67.2%)	308(68.6%)	79(73.8%)	
	Yes	503(31.3%)	92(29.1%)	242(32.8%)	141(31.4%)	28(26.2%)	
Numbers of diseases		1.16(1.25)	1.04(1.25)	1.1(1.22)	1.21(1.24)	1.68(1.38)	<0.0001

Data in tables are numbers(%) for categorical variables and means (SD) for continuous variables; *Group 1: Low-normal weight; Group 2: High-normal weight; Group 3: Overweight; Group 4: Obesity

BMI in Taiwan was between those reported in Japan and Western countries and was similar to the Japanese data. The observed differences may be attributed to racial differences, lifestyle, and diet habits. Two studies involving BMI trajectory analysis of middle-aged individuals, have suggested racial differences between Whites, Blacks, and Hispanics (20, 23). Moreover, body weight change analysis in a national longitudinal study of adolescent health in the USA found that Chinese, Filipino, and adolescents of other Asian origins had a significantly lower BMI and slower BMI increases in adulthood compared with Whites, even in the same environment (24). Racial differences may play an important role in this topic. Further studies are warranted to investigate BMI change and its effects in Asian and non-Asian populations of middle-aged individuals.

In the survey for the risk of frailty, the low-normal weight and obesity groups were associated with a higher risk after adjusting for confounding factors and the OR in the overweight group was 0.959 (not statistically significant). In the USA, Briana Mezuk analyzed data from the Health and Retirement

Table 4
Univariate logistic regression analysis of demographic and clinical characteristics predicting frailty

		Frailty		
		OR	**95% CI**	**P value**
Age		1.121*	1.076–1.169	<.0001
Sex				
	Male	Ref		<.0001
	Female	2.519*	1.674–3.592	
Level of education				
	Illiterate	Ref		
	1–6 years	0.486*	0.322–0.734	<.0001
	7–12 years	0.213*	0.105–0.430	0.0006
	>12 years	0.06*	0.008–0.438	<.0001
Income satisfaction				
	Good	Ref		
	Fair	2.204*	1.319–3.682	0.00025
	Poor	2.958*	1.683–5.2	0.0002
Social participation				
	Yes	Ref		
	No–	1.507	0.996–2.280	0.0522
Self-rated health				
	Good	Ref		
	Fair	3.399*	1.971–5.864	<.0001
	Poor	8.542*	4.909–14.864	<.0001
Smoking				
	Yes	0.602*	0.369–0.981	0.0415
	No	Ref		
Drinking	Yes	0.56*	0.352–0.890	0.0142
	No	Ref		
Body Mass Index trajectory				
	Group 1	1.554	0.949–2.546	0.0798
	Group 2	Ref		
	Group 3	0.905	0.546–1.5	0.6991
	Group 4	2.565*	1.391–4.731	0.0026
Numbers of diseases		1.469*	1.290–1.674	<.0001

* P<0.05

Study, showing that the weight gain group was linked to the highest likelihood for the development of frailty (OR: 3.61, 95% confidence interval [CI]: 2.39–5.46), with the overweight group used as reference. The obesity and weight loss groups had a similarly elevated risk (9). In the Helsinki Businessmen Study, the OR in the overweight group was 1.6 (not statistically significant) (CI: 0.7–3.5), with the normal weight group used as reference. However, the risk of mobility-related disability increased (OR: 1.9, CI: 1.1–3.2) in the overweight group (25). Another study performed in USA communities also found that an increasing BMI was associated with a slower late-life gait speed than a stable baseline BMI of 22.5 (26). Although some studies of weight trajectory and mortality (18, 27) indicated that overweight might be a protective factor compared to normal weight, this phenomenon was not noted in studies of frailty and overweight individuals had a higher risk of mobility-related

Table 5
Multivariate logistic regression analysis of demographic and clinical characteristics predicting frailty

		Frailty		
		OR	**95% CI**	**P value**
Age		1.124*	1.072–1.177	<.0001
Sex				
	Male	Ref		
	Female	1.862*	1.060–3.270	0.0304
Level of education				
	Illiterate	Ref		
	1–6 years	0.733	0.458–1.171	0.1933
	7–12 years	0.402*	0.185–0.871	0.0209
	>12 years	0.176	0.023–1.354	0.0952
Income satisfaction				
	Good	Ref		
	Fair	1.820*	1.051–3.152	0.0326
	Poor	2.387*	1.291–4.415	0.0055
Self-rated health				
	Good	Ref		
	Fair	2.512*	1.412–4.470	0.0017
	Poor	4.885*	2.637–9.050	<.0001
Smoking				
	Yes	1.049	0.549–2.006	0.8846
	No	Ref		
Drinking	Yes	1.025	0.585–1.794	0.9315
	No	Ref		
Body Mass Index trajectory				
	Group 1	1.794*	1.050–3.065	0.0325
	Group 2	Ref		
	Group 3	0.959	0.559–1.644	0.8783
	Group 4	2.013*	1.013–4.001	0.046
Numbers of diseases		1.196*	1.032–1.388	0.0177

* P<0.05

disability (25, 26, 28). The benefits of higher metabolic reserves on life expectancy after being frail or disabled may be a reason for this (29, 30); however, further studies are warranted to test this hypothesis. Maintaining a normal BMI for better physical ability appears to be a better suggestion.

Among other variables, being older, female, with a low level of education, less satisfied with income, a poor self-rated health, and a high number of diseases was associated with a higher risk for the development of frailty. Hui-Chuan Hsu has reported that older age, female sex, and a low level of education were risk factors for frailty, whereas high satisfaction with income and high social participation were protective factors (11). Research conducted in Brazil showed that older age, the administration of more medications and the presence of chronic diseases, the inability to perform activities of daily living or Instrumental Activities of Daily Living, a poor self-rated health, and depression increased the risk of frailty (12). Future studies are warranted to investigate factors that were not examined in the present study.

This is the first study in Asia to evaluate the relationship between the BMI trajectories of midlife individuals and frailty. Moreover, this prospective study included a large, nationwide

representative, randomly selected population and had extremely highly response rates. Thus, these results may be used as the basis for other studies and have higher generalizability. With the advancement of medicine and technology, life expectancy is extended and a good quality of life is pursued. Using this national BMI data as a standard, these results may be applied to the Taiwanese population and influence policy making in terms of risk stratification and the provision of effective interventions to prevent frailty.

There were some limitations in this study. Firstly, the height and weight data reported in the questionnaire were either measured on the scene or self-reported. Thus, recall bias may exist for some data. Secondly, we used substitutes to evaluate frailty instead of measuring actual grip strength and walking speed. There may be differences between these two assessment tools. Thirdly, BMI is not the most accurate method to evaluate the muscle/adipose composition of the human body. A high BMI is not equal to having excess fat tissue, which was attributable to frailty. However, individuals can easily perform the measurement of BMI at home or in health care facilities. Moreover, it has been included in the free medical examination provided by the government of Taiwan for individuals aged >40 years. This study may provide clinicians more information in health education.

In conclusion, midlife BMI trajectories in Taiwan tended to remain stable and most were within the normal range. Individuals in the obesity and low-normal weight group were associated with a higher risk for the development of frailty. Notably, the overweight group was not linked to a higher risk or protection from frailty. It may be revealed that obesity paradox is not applicable when it comes to frailty. For Asian elderly individuals, an optimal weight-targeting strategy should be considered.

Conflict of Interest: There are no conflicts of interest to declare.

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Ethical Standards: TLSA was initiated by the government and the protocols were approved with the Institutional Review Board. We obtained the data following the laws and informed consent was also obtained from all the participants.

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