

The Association Between Body Mass Index and All-Cause Mortality in Patients With Type 2 Diabetes Mellitus

A 5.5-Year Prospective Analysis

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Abstract: Abundances of study in different population have noted that obese cardiovascular disease (CVD) patients have a better prognosis than leaner patients, which refer to the phenomenon of obesity paradox. However, data on the association between body mass index (BMI) and mortality among Asian patients are limited, especially in patients with type 2 diabetes mellitus (T2DM). We investigate the association between BMI and all-cause mortality in Taiwanese patients with T2DM to define the optimal body weight for health.

We conducted a longitudinal cohort study of 2161 T2DM patients with a mean follow-up period of 66.7 ± 7.5 months. Using Cox regression models, BMI was related to the risk of all-cause mortality after adjusting all confounding factors.

A U-shaped association between BMI and all-cause mortality was observed among all participants. Those with BMIs $< 22.5 \text{ kg/m}^2$ had a significantly elevated all-cause mortality as compared with those with BMIs 22.5 to 25.0 kg/m^2 , (BMIs 17.5 – 20.0 kg/m^2 : hazard ratio 1.989, $P < 0.001$; BMIs 20.0 – 22.5 kg/m^2 : hazard ratio 1.286, $P = 0.02$), as did those with BMIs $> 30.0 \text{ kg/m}^2$ (BMIs 30.0 – 32.5 kg/m^2 : hazard ratio 1.670, $P < 0.001$; BMIs 32.5 – 35.0 kg/m^2 : hazard ratio, 2.632, $P < 0.001$). This U-shaped association remained when we examined the data by sex, age, smoking, and kidney function.

Our study found a U-shaped relationship between all-cause mortality and BMI in Asian patients with T2DM, irrespective of age, sex, smoking, and kidney function. BMI $< 30 \text{ kg/m}^2$ should be regarded as a potentially important target in the weight management of T2DM.

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Abbreviations: A1C = glycosylated haemoglobin, ACR = albumin/creatinine ratio, BMI = body mass index, Chol = cholesterol, CI = confidence interval, CKD = chronic kidney disease, CV = coefficient of variation, CVD = cardiovascular disease, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, ESRD = end stage renal disease, HDL-C = high-density lipoprotein cholesterol, HPFS = Health Professionals Follow-up Study, HR = hazard ratio, ICD = International Classification of Disease, JDCS = Japan Diabetes Complications Study, J-EDIT = Japanese Elderly Diabetes Intervention Trial, LDL-C = low-density lipoprotein cholesterol, NHS = Nurses' Health Study, OAD = oral antidiabetic drug, SBP = systolic blood pressure, SD = standard deviation, T2DM = type 2 diabetes, TG = triglyceride, WHO = World Health Organization.

INTRODUCTION

Obesity is associated with a variety of cardiometabolic diseases, such as type 2 diabetes mellitus (T2DM), hypertension, hyperlipidemia, metabolic syndrome, and cardiovascular disease (CVD), all of which contribute to increased mortality.¹ In addition, in a number of epidemiologic surveys, even in people deemed otherwise healthy and lacking any identifiable diseases or health risks, there is a higher risk for cardiometabolic dysfunction and mortality if they are overweight or obese.²

The World Health Organization (WHO) has recommended classifications of body weight based on body mass index (BMI), calculated as weight in kilograms divided by height in meters squared (kg/m^2), as a proxy for thinness and fatness. The WHO BMI classifications are intended for international use to identify risk of T2DM and CVD. However, the prevalence and incidence of metabolic disorder vary among ethnic groups, particularly in Asians who have been found to have a higher rate than whites with similar BMIs.^{3,4} Many factors, including belonging to particular cultural and ethnic subgroups, degree of urbanization, and social and economic conditions, have contributed to differences in metabolic disorder rates with BMI in Asian countries. As a result, different optimal cutoff points for BMIs have been proposed in different Asian countries.^{5,6} Most individuals with T2DM are also obese, and the 2 medical problems have both been associated with increased morbidity and mortality. However, a large number of studies of obesity in different population have noted what has come to be known as the obesity paradox, which refers to the phenomenon in which obese CVD patients have a better prognosis than leaner patients.⁷ Recently, whether obesity paradox exists in T2DM is presently under investigation.⁸ The paradox has put weight reduction recommendations in daily clinical practice in doubt, especially for those with cardiometabolic diseases. There are still conflicting data on the phenomenon in diabetic patients.^{9,10}

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Data on the association between BMI and mortality among Asian patients are limited,^{11–13} especially in T2DM patients.^{14–16} Findings regarding the modification by sex, age, and smoking of the association between BMI and the risk of death are also diverse. In this prospective observational study, we investigate the association between BMI and all-cause mortality in Taiwanese patients with T2DM to define the optimal body weight for health.

PATIENTS AND METHODS

Population

Our study comprised 2161 T2DM patients under follow-up in the outpatient department of Metabolism Division at Changhua Christian Hospital during September 2003 and April 2005. The details of the design, methods, and procedures of the survey have been described in a recent publication.¹⁷ In a few words, we made a study to appraise the relationship between all-cause mortality and BMI in T2DM patients. We excluded patients who had acute myocardial infarction, heart failure, or stroke within 12 months. Patients who had end-stage renal disease (ESRD) defined by estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m² or under regular dialysis, loss of follow-up within 6 months were also removed from consideration.

The protocol for our study was ratified by the hospital's Human Research Ethics Committees. All participants provided written informed consent.

Baseline Investigation

The baseline survey for each participant included medical history, physical examination, and laboratory evaluation. Laboratory tests consisted of plasma glucose, glycosylated haemoglobin (A1C) (if not available within past 3 months), fasting lipid profile (including triglyceride [TG], total cholesterol, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C]), and creatinine using a biochemistry automatic analyser (Beckman-Coulter Inc, Fullerton, CA). The A1C test was performed in whole blood using ion-exchange high-performance liquid chromatography (VAR-IANTM II Turbo; BIO-RAD, Hercules, CA).

We assessed urinary albumin and creatinine using a spot urine sample (overnight first void urine) from each patient to calculate their albumin/creatinine ratio (ACR).

The eGFR of each patient was estimated from the Modified Diet in Renal Disease equation.

Follow-Up Investigation

We followed up every patient regularly every 2 to 6 months. The laboratory evaluations at each visit were the same as at baseline.

Assessment of BMI

Weight and height were measured during the outpatient visit by means of a calibrated scale. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²).

Primary Outcome: All-Cause mortality

Specific causes of death were categorized according to the International Classification of Disease (ICD) 9th revision: cancer (140–208), cardiopulmonary disease (401–429), diabetes (250), infection (001–139, 320, 321, 326, 421, 460–466, 480–487, 510, 513, 551, 567, 590, 599, 680–686, 711, 730), digestive disease (520–579, excluding 551), accidents (800–949), and other causes (codes other than above).

Statistical Analysis

The baseline clinical and biochemical characters of our patients were delineated as mean ± standard deviation (SD) or ratios. To evaluate the risk factors for all-cause mortality, Cox regression models were used and hazard ratios (HRs) with 95% confidence intervals (CI) were calculated. BMI was first regarded as a continuous variable; for further inquiry on the non-linear relationship between BMI and mortality, the baseline BMI was classified into: 17.5–20.0 kg/m², 20.0–22.5 kg/m², 22.5–25.0 kg/m², 25.0–27.5 kg/m², 27.5–30.0 kg/m², 30.0–32.5 kg/m², 32.5–35.0 kg/m². BMI of 22.5–25.0 kg/m² group was used as the reference BMI to calculate HRs. Potential confounders, including sex, age at enrollment, baseline parameters (blood pressure, A1C, fasting plasma glucose and lipid profile, creatinine, eGFR, ACR), and mean follow-up A1C, were adjusted in the models using strata defined by propensity score quintiles. The propensity quintiles were figured out by logistic regression analysis as clarified by D'Agostino.¹⁸ Because the distributions of TG and ACR were highly right-skewed, natural log transformation of these 2 variables were used in the logistic regression model for manufacturing the propensity score quintiles. All statistical operations were carried out using SAS version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

Study Participants

Table 1 summarizes the baseline characteristics of our patients, stratified according to the life status at the end of follow-up. The mean age of the cohort was 63.5 ± 11.9 years, and 57% were women. The mean BMI was 25.8 ± 3.6 kg/m². The mean follow-up period was 66.7 ± 7.5 (range 21–80) months, and the mean number of follow-up visits was 15.7 ± 3.4 kg/m² (range 9–23) times. One hundred and nineteen patients died during the follow-up period; these people were older and had significantly higher mean SBP, serum creatinine, and eGFR than those who were alive at the end of follow-up. More of patients who died were receiving insulin therapy and antihypertensive treatment than those who remained alive at follow-up.

All-Cause Mortality

Cox regression analysis revealed a U-shaped association between BMI and all-cause mortality among all participants (Figure 1). Those with BMIs <22.5 kg/m² had a significantly elevated all-cause mortality as compared with those with BMIs 22.5 to 25.0 kg/m², (BMIs 17.5–20.0 kg/m²: HR 1.989, *P* < 0.001; BMIs 20.0–22.5 kg/m²: HR 1.286, *P* = 0.02), as did those with BMIs >30.0 (BMIs 30.0–32.5 kg/m²: HR 1.670, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 2.632, *P* < 0.001). Those with BMIs 25.0 to 30.0 kg/m² were not found to be at added risk of mortality.

Effect modification of Age

Among adults older than 65 years at baseline, both those with BMIs <20.0 and those with BMIs >30.0 kg/m² had a significantly increased all-cause mortality as compared with participants with BMIs 22.5 to 25.0 (BMIs 17.5–20.0 kg/m²: HR 1.800, *P* < 0.001; BMIs 30.0–32.5 kg/m²: HR 1.622, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 2.579, *P* < 0.001) (Figure 2A). A U-shaped trend between BMI and all-cause mortality was also noted among adults younger than 65 years at baseline with even higher HRs for those with extremely low or

TABLE 1. Baseline Characteristics of Patients According to Outcome (All-Cause Mortality)

	Total (n = 2161)	Status at the End of Follow-up		P
		Death (n = 119)	Live (n = 2042)	
Sex (male/female)	936/1225	59/60	877/1165	.16
Age	63.5 ± 11.9	70.9 ± 10.8	63.1 ± 11.8	.001
BMI	25.8 ± 3.6	25.9 ± 3.8	25.8 ± 3.6	.65
A1C, %	7.70 ± 1.70	7.84 ± 2.11	7.69 ± 1.67	.46
Fasting glucose, mg/dL	149.6 ± 52.5	149.7 ± 57.2	149.6 ± 52.3	.98
SBP, mmHg	134.6 ± 18.8	139.0 ± 19.9	134.3 ± 18.7	.007
DBP, mmHg	77.9 ± 11.5	77.3 ± 10.7	77.9 ± 11.6	.54
TG, mg/dL	155.3 ± 134.2	163.9 ± 119.8	154.8 ± 135.0	.48
Chol, mg/dL	185.6 ± 38.6	191.6 ± 52.5	185.3 ± 37.6	.20
HDL-C, mg/dL	49.5 ± 13.0	49.2 ± 14.5	49.5 ± 12.9	.78
LDL-C, mg/dL	104.2 ± 28.4	106.1 ± 35.8	104.1 ± 27.9	.56
Creatinine, mg/dL	1.07 ± 0.38	1.32 ± 0.62	1.06 ± 0.35	.001
eGFR, mL/min/1.73 m ²	64.93 ± 23.94	50.05 ± 20.29	65.79 ± 23.86	.001
ACR	98.783 ± 44.93	229.01 ± 837.44	91.09 ± 290.35	.08
Glucose-lowering drugs				<.001
Diet control only, No. (%)	32 (1.5%)	2 (1.7%)	30 (1.5%)	
OAD only, No. (%)	1246 (58%)	48 (40%)	1198 (59%)	
Insulin only, No. (%)	210 (10%)	21 (18%)	189 (9%)	
OAD + insulin, No. (%)	673 (31%)	48 (40%)	625 (31%)	
Antihypertensive drugs, No. (%)	1701 (79%)	108 (91%)	1593 (78%)	.001
ACEI or ARB, No. (%)	1572 (73%)	103 (87%)	1469 (72%)	<.001
Diuretics, No. (%)	971 (45%)	87 (73%)	884 (43%)	<.001
CCB, No. (%)	835 (39%)	79 (66%)	756 (37%)	<.001
Beta-blocker, No. (%)	498 (23%)	33 (28%)	465 (23%)	.22
Statin, No. (%)	1275 (59%)	70 (59%)	1205 (59%)	.96
Fibrate, No. (%)	358 (17%)	21 (18%)	337 (17%)	.75

Data are mean ± SD. ACR = urinary albumin creatinine ratio, BMI = body mass index, Chol = cholesterol, DBP = diastolic blood pressure, eGFR = estimated glomerular filtration rate, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, OAD = oral antidiabetic drugs, SBP = systolic blood pressure, TG = triglyceride.

high BMI (BMIs 17.5–20.0 kg/m²: HR 3.040, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 4.730, *P* < 0.001) (Figure 2B).

Effect modification of Sex

Among the female participants, those with BMIs <22.5 kg/m² had significantly elevated all-cause mortality as compared with participants with BMIs 22.5 to 25.0 (BMIs 17.5–20.0 kg/m²: HR 2.647, *P* < 0.001; BMIs 20.0–22.5 kg/m²: HR 1.487, *P* = 0.02), as did those with BMIs >30.0 kg/m² (BMIs 30.0–32.5 kg/m²: HR 2.061, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 3.822, *P* < 0.001) (Figure 3A). However, those with BMIs 25.0 to 30.0 kg/m² were not found to be at further increased mortality risk. A similar U-shaped trend between BMI and all-cause mortality was noted in male participants, but with less statistical significance (Figure 3B).

Effect Modification of Smoking

A U-shaped association between BMI and all-cause mortality was observed among participants who had never smoked. Compared with participants' BMIs 22.5 to 25.0 kg/m², all BMI categories revealed increased mortality risk except BMI of 25.0 to 30.0 kg/m² (Figure 4A). A similar U-shaped trend between BMI and all-cause mortality was also noted among participants who had smoked, with even higher HRs for those with extremely low or high BMI (BMIs 17.5–

20.0 kg/m²: HR 3.491, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 9.296, *P* < 0.001) (Figure 4B).

Effect Modification of Kidney Function

A similar U-shaped relationship between BMI and all-cause mortality was also found among the participants with

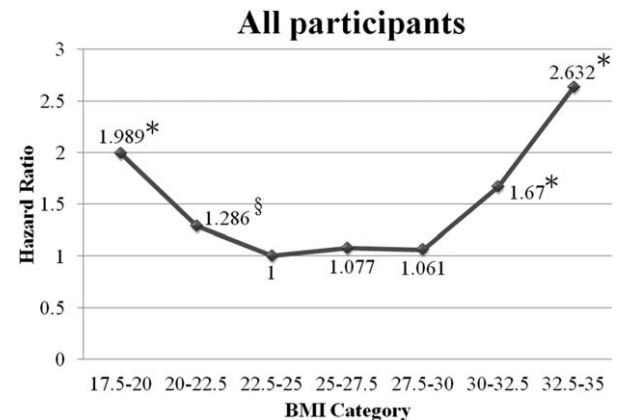


FIGURE 1. Association between BMI and all-cause mortality among all participants.

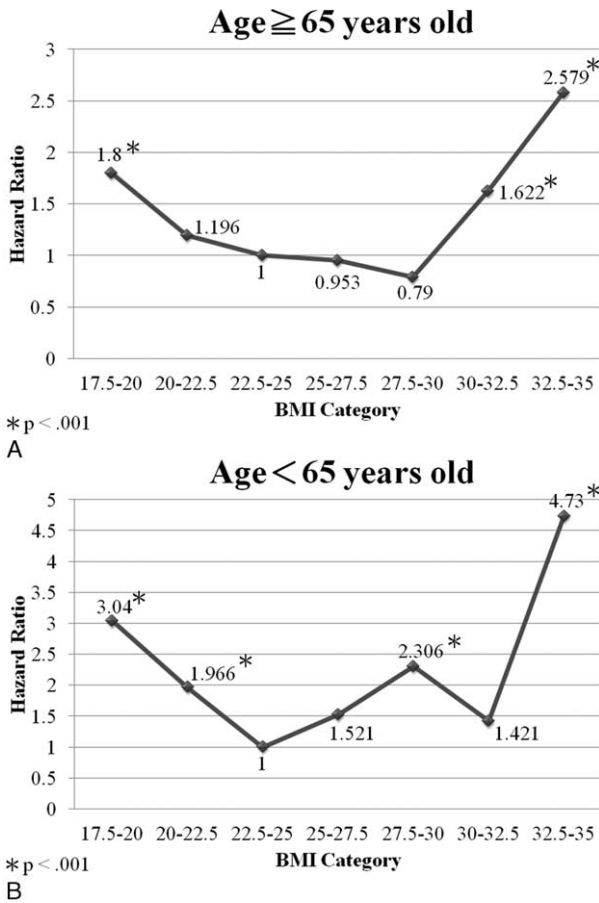


FIGURE 2. Association between BMI and all-cause mortality among participants aged ≥65 years (A) and those aged <65 years (B).

eGFR 15 to 59 mL/min/1.73 m²; both the lowest BMI category (BMIs 17.5–20.0 kg/m²: HR 1.759, *P* < 0.001) and BMIs >27.5 kg/m² (BMIs 27.5–30.0 kg/m²: HR 1.409, *P* = 0.005; BMIs 30.0–32.5 kg/m²: HR 1.718, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 3.378, *P* < 0.001) had significantly elevated all-cause mortality as compared with the referent category (BMIs 22.5–25.0 kg/m²) (Figure 5A). Among the participants with eGFR ≥60 mL/min/1.73 m², BMIs >30.0 kg/m² were associated with greater all-cause mortality (BMIs 30.0–32.5 kg/m²: HR 2.376, *P* < 0.001; BMIs 32.5–35.0 kg/m²: HR 4.336, *P* < 0.001) (Figure 5B).

DISCUSSION

This study found a U-shaped relationship between all-cause mortality and BMI in patients with T2DM in Taiwan. Compared with those with BMIs 22.5 to 25.0 kg/m², those with BMI <22.5 or ≥30 kg/m² had a significant increase in risk of mortality. Except for those younger than 65 years, no excess risk of mortality was observed in the group with BMIs 25.0 to 30.0 kg/m².

Our findings are consistent with the results of several studies of BMI and mortality among participants with diabetes.^{14,19,20} Prospective cohort studies from Hong Kong¹⁴ and Ukraine¹⁹ have reported a V- or U-shaped association between BMI and total mortality in patients with T2DM. The

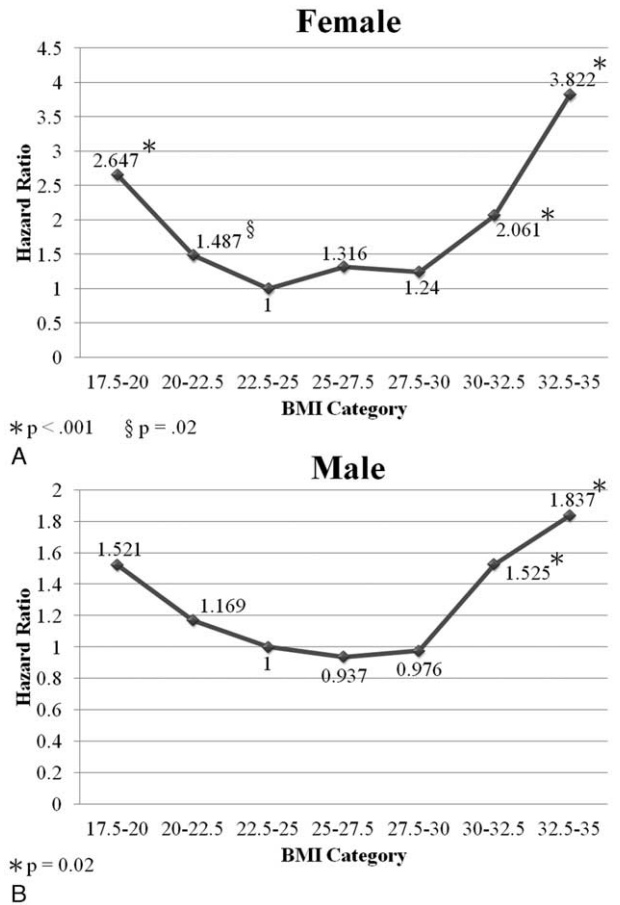


FIGURE 3. Association between BMI and all-cause mortality among females (A) and males (B).

nadirs of the risk curves were at BMI of 26 kg/m² in Hong Kong and BMI of 27 kg/m² in Ukraine. A study by Tobias et al²⁰ reported results similar to ours with a J-shaped association across BMI categories for all-cause mortality in participants with incident diabetes who were free of cardiovascular disease and cancer at the time of a diagnosis of diabetes. Compared with those with BMIs 22.5 to 24.9 kg/m², those in the lowest BMI category (18.5–22.4 kg/m²) and the highest BMI category (30.0–34.9 kg/m²) had significantly elevated risk of all-cause mortality.

Several studies have found an inverse correlation between BMI and all-cause mortality (obesity paradox) in patients with T2DM.^{15,21–24} An analysis of pooled data from 5 large US cohorts²¹ concluded that adults who were of normal weight (BMIs 18.5–24.9 kg/m²) at the time of incident diabetes had higher mortality than adults who are overweight or obese (BMI of ≥25 kg/m²). Tseng et al¹⁵ conducted a 12-year follow-up of a nationally representative cohort of patients with T2DM in Taiwan and concluded that underweight patients (BMI of <18.5 kg/m²) might have a significantly higher risk of mortality. The obesity paradox was mainly observed in non-cancer mortality. Studies from the United States²² and France²³ have reported a positive association between BMI and mortality in adults without diabetes, but an inverse association among participants with diabetes. Analyzing the data from the United

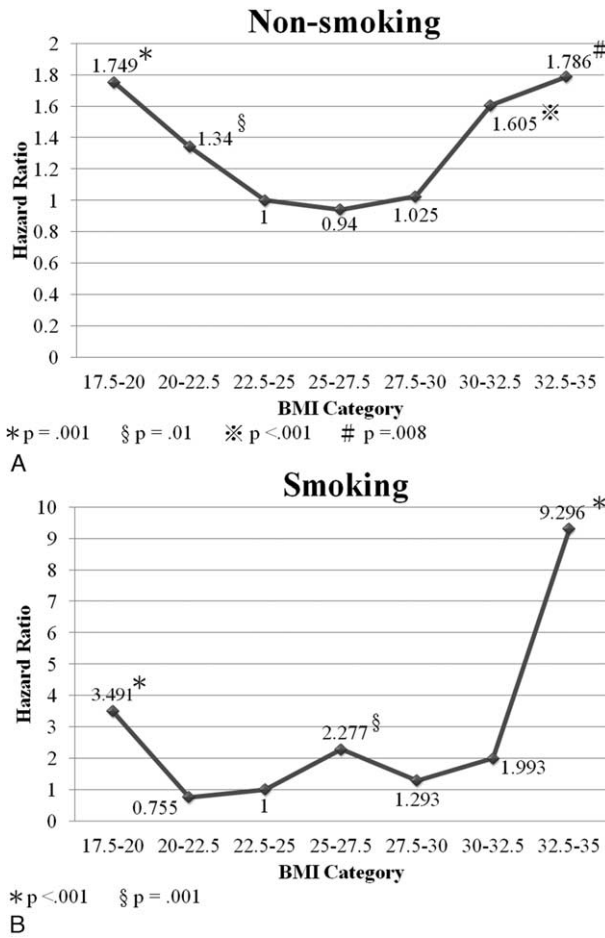


FIGURE 4. Association between BMI and all-cause mortality among non-smoking (A) and smoking participants (B).

Kingdom primary care, Thomas et al²⁴ reported that adults with normal weight (BMI of >18.5 and <25.0 kg/m²) at the diagnosis of T2DM were at significantly higher mortality risk compared with those who are obese (BMI of ≥30 kg/m²), with significant interactions between age, BMI, and A1C.

The term “obesity paradox” has been found to only apply to all-cause mortality and not the risk of obesity-related chronic diseases and morbidity.²⁵ This paradox generally does not apply to more severe degrees of obesity, wherein most studies show adverse prognosis with BMI >35 kg/m².²⁶ In a pooled analysis of 20 prospective studies from the United States, Sweden, and Australia, Class III obesity (BMIs 40.0–59.9 kg/m²) was associated with substantially elevated rates of total mortality, with most of the excess deaths due to heart disease, cancer, and diabetes, and major reductions in life expectancy compared with normal weight (BMIs 18.5–24.9 kg/m²).²⁷

One possible explanation for the obesity paradox might include methodological bias from different BMI cut points. In the studies demonstrating obesity paradox, broad BMI categories were used for obesity group (ie, only ≥30.0 kg/m² for obesity group in most studies). For example, Tseng et al¹⁵ demonstrated a mortality advantage in obese patients with T2DM in Taiwan with BMI classified as <18.5, 18.5 to 22.9, 23.0 to 24.9, 25.0 to 29.9, and ≥30.0 kg/m². However,

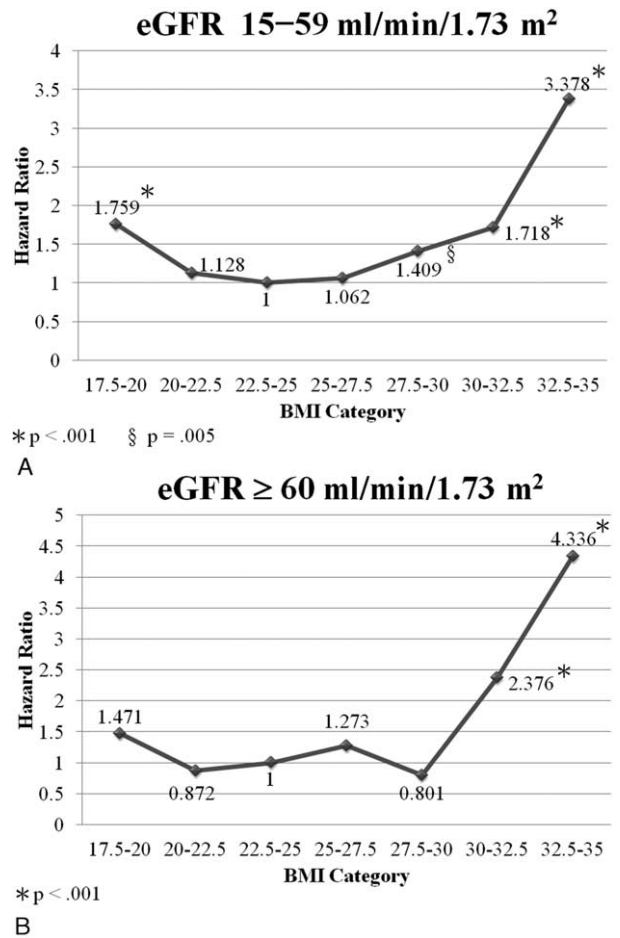


FIGURE 5. Association between BMI and all-cause mortality among participants with estimated glomerular filtration rate (eGFR) 15–59 mL/min/1.73 m² (A) and with eGFR ≥60 mL/min/1.73 m².

if we use finer BMI categories for obesity group (in our study we divide into 17.5–20.0, 20.0–22.5, 22.5–25.0, 25.0–27.5, 27.5–30.0, 30.0–32.5, and 32.5–35.0 kg/m²), a U-shaped relationship between all-cause mortality and BMI develops. Similar findings have been reported by the Nurses’ Health Study (NHS) and the Health Professionals Follow-up Study (HPFS).²⁰

Data on the association between BMI and mortality among Asian patients are limited, especially in T2DM patients. Lin et al¹² found a U-shaped association between BMI and all-cause mortality in a 10-year prospective cohort study among 58738 men and 65718 women in Taiwan. In that study, the lowest risk of death was observed among men and women who had BMIs 24.0 to 25.9 kg/m². A 15-year prospective study of 220,000 men in China revealed a U-shaped association between BMI and all-cause mortality with the lowest mortality at 22.5 to 25.0 kg/m².¹³ The relationship between death from any cause and BMI followed a J-shaped pattern in a 12-year prospective cohort study of 12,138,29 Koreans.¹¹ The risk of death from any cause was lowest among patients with a BMI of 23.0 to 24.9 kg/m². In a pooled analysis of 2620 Japanese patients with T2DM followed for 6.3 years, the lowest mortality rate was observed among patients with BMI 18.5 to 24.9 kg/m² and obesity had no

benefits regarding mortality.¹⁶ The associations between BMI and mortality observed in our study are consistent with these relationships, with the lowest risk of death seen around 22.5 to 25.0 kg/m².

The modification by sex, age, smoking and kidney function of the association between BMI and the risk of death has been controversial. In our study, we found similar U-shaped associations between BMI and all-cause mortality among men and women. This was consistent with the analysis from the cohorts in Korea,¹¹ Taiwan,¹² and the United States.²⁰ A direct linear trend among participants younger than 65 years but a null linear association among participants 65 years of age or older were observed in subgroup analysis of NHS and HPFS.²⁰ However, in the reports of the Japan Diabetes Complications Study (JDACS) and the Japanese Elderly Diabetes Intervention Trial (J-EDIT), the HRs of patients with BMI ≥ 18.5 kg/m² tended to be higher among patients aged 75 years or older, but the BMI–age interaction was not significant.¹⁶ In our study, we found a U-shaped association between BMI and all-cause mortality among participants older than 65 years and a weakened relationship among participants younger than 65 years. Our study observed that smokers had a steeper U-shaped curve than those who reported never having smoked. In the NHS and HPFS, the relationship between BMI and all-cause mortality was nonlinear and all-cause mortality was nonlinear and among those who had ever smoked it was linear.²⁰ The HRs of patients who were smokers were higher in subgroup analysis of JDACS and J-EDIT, but the BMI–smoking interaction was not significant.¹⁶ Obesity paradox have been demonstrated in surveys of patients on dialysis.²⁸ Data are limited and diverse among patients in the earlier stages of chronic kidney disease (CKD), much less in diabetic kidney disease.^{29,30} Our study disclosed a U-shaped association between BMI and all-cause mortality among the participants with eGFR 15 to 59 mL/min/1.73 m² (stage 3–4 CKD). A similar trend was noted among eGFR ≥ 60 mL/min/1.73 m² (stage 1–2 CKD) except the relationship was no longer significant within the lowest BMI category. The possible explanations of the discrepancy include protein-energy wasting and inflammation that render diabetic patients with advanced kidney disease more susceptible to higher mortality when BMI is low (reverse causation).³¹

Our study found that T2DM patients with BMIs 25.0 to 30.0 kg/m² had no excess risk of mortality as compared with other BMI categories. However, this does not mean that overweight individuals do not need to lose weight, as fatness and fitness are proven to modify the association between BMI and mortality. In fact, modest weight loss can improve glycemic control and reduce cardiovascular disease risk factors in overweight and obese individuals with prediabetes and T2DM.³² Weight management in T2DM should not only be based on the application of BMI cutoff points for individual patients, but it should also take metabolic health status into consideration. For patients to achieve modest weight loss, it is recommended that they receive counseling about nutrition, physical activity, and other related behaviors.³³

The present study has several strengths. First, this cohort study has a relatively large sample size, detailed phenotyping, and a relatively long prospective observational period (average 5.5 years). Second, our study recruited 1225 female patients of T2DM in Taiwan. To date, only few studies discuss the relationship between obesity and mortality in woman. A J-shaped association between BMI and all-cause mortality was observed among 8970 female participants with incident diabetes from the NHS.²⁰ Those in the highest BMI categories

(≥ 35 kg/m²) had the highest risk of all-cause mortality with multivariable-adjusted HR 1.39 (1.17–1.65) in total and 1.46 (1.11–1.92) in those who never smoked. However, another analysis, which included 2421 French women with incident diabetes, supported the obesity paradox.²³ This difference may be due to bias result from use of different BMI categories.

This study also has several limitations. First, this study was of patients with T2DM visiting the diabetic clinic in our hospital. Their duration of diabetes varied and we could not calculate their BMI with body weight at the time of diagnosis of diabetes. Weight change due to reverse causation, life style changes, or pharmacologic treatments could not be excluded and bias might develop. Second, there is evidence that fat distribution and cardiorespiratory fitness modify the association between obesity and mortality. However, we did not have access to such data to adjust for these parameters. Third, this study was not randomized. We categorized patients according to their calculated BMI at baseline of the study. This could lead to possible sources of confounding. However, as much as possible, we tried to adjust for these confounders.

CONCLUSION

Our study found a U-shaped relationship between all-cause mortality and BMI in patients with T2DM in Taiwan, irrespective of age, sex, and smoking status. Those with BMI of ≥ 30 kg/m² are at higher risk of mortality and weight management should be strongly recommended.

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