

# Effects of different weight loss dietary interventions on body mass index and glucose and lipid metabolism in obese patients

Yahui Ma, MD<sup>a,\*</sup>, Lina Sun, MD<sup>a</sup>, Zhijing Mu, PhD<sup>a</sup>

#### Abstract

To investigate the effects of different weight loss interventions on body mass index (BMI) and glucose and lipid metabolism in obese patients. Obese patients (n = 135) admitted to our hospital between December 2020 and August 2022 were divided into 3 groups, according to their diet patterns: calorie-restricted diet (CRD) group (n = 39), high-protein diet (HPD) group (n = 28), and 5+2 intermittent fasting (IF) group (n = 68). Body weight, body fat rate, BMI, hip circumference, and waist circumference were measured before and 60 days after implementation of the respective diet plan. Glycosylated hemoglobin (HbA1c), fasting blood glucose (FBG), 2h postprandial blood glucose (2hPG), triglyceride (TG), total cholesterol, low-density lipoprotein, high-density lipoprotein, and adverse events were evaluated. Following the dietary intervention, the weight (P = .005 for CRD, P < .001 for HPD, and P = .001 for IF), body fat rate (P = .027 for CRD, P = .002 for HPD, and P = .011 for IF group), BMI (P = .017 for CRD, P < .001 for HPD, and P = .002 for IF group), hip circumference (P < .001 for CRD, P = .013 for HPD, and P = .032 for IF group), waist circumference (P = .005 for CRD, P < .001 for HPD, and P = .028 for IF group), HbA1c (P = .014 for CRD, P = .002 for HPD, and P = .029 for IF group), FBG (P = .017 for CRD, P < .001 for HPD, and P = .033 for IF group), and 2hPG (P = .009 for CRD, P = .001 for HPD, and P = .012 for IF group), were significantly decreased. TG (P = .007 for CRD, P < .001 for HPD, and P = .018for IF group), TC (P = .029 for CRD, P = .013 for HPD, and P = .041 for IF group), LDL-C (P = .033 for CRD, P = .021 for HPD, and P = .042 for IF group), and LDL-C (P = .011 for CRD, P < .001 for HPD, and P = .027 for IF group) improved significantly in the 3 groups, when compared to that before treatment. The HPD had the best effect on reducing blood lipids, followed by the CRD; the effect of IF was slightly lesser. Short-term HPD, CRD, and IF can reduce the weight and body fat of overweight/obese individuals and improve blood lipid and blood sugar levels. The effect of HPD on weight loss, body fat, and blood lipid levels was greater than that of CRD or IF.

**Abbreviations:** 2Hpg = 2h postprandial blood glucose, BMI = body mass index, CRD = calorie-restricted diet, FBG = fasting blood glucose, HbA1c = glycosylated hemoglobin, HPD = high protein diet, IF = 5+2 intermittent fasting, LDL-C = low-density lipoprotein cholesterol, T2DM = type 2 diabetes mellitus, TC = cholesterol, TG = triglyceride.

Keywords: 5+2 intermittent fasting, calorie restricted diet, high protein diet, medical weight loss

### 1. Introduction

Over the past 20 years, the prevalence of overweight/obesity in China has increased continuously; this is largely attributed to lifestyle changes.<sup>[1]</sup> According to data from the China Health and Nutrition Survey, the prevalence of overweight/ obesity among adults increased from 13.4% to 26.4% in the 17 years from 1993 to 2009, indicating that the prevalence of overweight/obese adults nearly doubled.<sup>[2]</sup> The prevalence of abdominal obesity in adults has increased from 18.6% to 37.4%, with an average annual growth rate of 1.1%, which is significantly higher than the growth rate of overweight/ obesity.<sup>[3]</sup> According to the 2019 data, the incidence rate of general obesity among Chinese adults was 14.0%, and the incidence rate of abdominal obesity was 31.5%.<sup>[4]</sup> Overweight

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

and obesity will lead to the occurrence and development of a series of diseases. Obesity is a potential risk factor for diabetes, cardiovascular diseases, other metabolic diseases, and tumors.<sup>[5,6]</sup> Obesity treatment includes lifestyle (diet and exercise) adjustment, drugs, and surgical treatment. Although drug and surgical treatments are effective, they are harmful to human health.<sup>[7–9]</sup> Scientific and reasonable nutritional treatment combined with exercise intervention is still the most effective and safe.<sup>[10]</sup> In recent years, the international community has reached a consensus on the nutritional management of obesity/overweight. However, obesity/overweight management, with nutrition and lifestyle interventions as the core, should be adapted to the dietary habits and social culture of specific regions.

How to cite this article: Ma Y, Sun L, Mu Z. Effects of different weight loss dietary interventions on body mass index and glucose and lipid metabolism in obese patients. Medicine 2023;102:13(e33254).

Received: 13 December 2022 / Received in final form: 22 February 2023 / Accepted: 22 February 2023

http://dx.doi.org/10.1097/MD.00000000033254

<sup>&</sup>lt;sup>a</sup> Department of Endocrine, Xuanwu Hospital Capital Medical University, Beijing, China.

<sup>\*</sup> Correspondence: Yahui Ma, Department of Endocrine, Xuanwu Hospital Capital Medical University, Beijing 100053, China (e-mail: nfmmyh@163.com).

Copyright © 2023 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is

permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Based on the 2016 consensus of the Chinese overweight/ obesity medical nutrition treatment experts, the nutrition professional field widely uses the calorie-restricted diet (CRD), high protein diet (HPD), and 5+2 intermittent fasting (IF) diet.<sup>[11-13]</sup> CRD limits daily total energy intake.<sup>[14]</sup> It reduces energy intake per day to 500 to 800 kcal, based on the target recommended intake or daily energy demand. The daily energy supply range is 1000 to 1500 kcal, which is usually above 1200 kcal.<sup>[15]</sup> The HPD increases the protein intake in the daily diet to 20% to 30% of the daily total energy or 1.5 to 2.0 g/kg body weight.<sup>[16]</sup> Protein is an important component of all cells and tissues in the human body and forms the material basis of life.<sup>[17,18]</sup> The human body needs to consume sufficient protein every day to meet the body demand. HPD can not only meet the nutritional needs of the body for protein, but can also help control and lose weight. The working mechanism of the IF diet is to periodically limit energy intake, strengthen the interventions against unhealthy dietary habits, and regularly influence and tame the body fat set point located in the hypothalamus. This enables the hypothalamus to induce the body to return to the original set point by regulating metabolism, through mobilizing the stored fat in the body, to ensure weight management.[19]

These 3 dietary patterns have beneficial effects on weight loss. CRD prevents and reverses the harmful effects of excessive body fat and obesity.<sup>[20,21]</sup> Result from epidemiological studies have shown HPD can result in greater weight loss.<sup>[22,23]</sup> Weigle et al found a significant increase in satiety, an average decrease of  $441 \pm 63$  kcal in daily energy intake compared to preintervention, and a  $4.9 \pm 0.5$  kg decrease in body weight, accompanied by a decrease in adiposity through a 12-week short-term HPD intervention.<sup>[24]</sup> Long-term weight maintenance after weight loss was better in the HPD group compared to that in the low-protein and normal diet groups in 256 subjects, after weight loss for a 12-month period.<sup>[25]</sup> In a randomized pilot study published in 2018, Conley et al compared IF with daily calorie restriction in 24 obese male patients over 6 months and the results showed that IF was more effective for weight loss.<sup>[26]</sup> In addition, IF is a new diet that is more flexible, safe, and compliant than traditional calorie restriction diets.<sup>[27]</sup> However, few studies have directly compared their weight loss effects and their effects on metabolic disorders and other health indicators in obese patients. Therefore, this study aimed to investigate the effects of 3 different dietary interventions (CRD, HPD, and IF) on body weight, BMI, body fat, glucose, and lipid metabolism, to provide a reference for overweight/obese people to choose appropriate methods.

#### 2. Materials and methods

#### 2.1. General information

A total of 135 obese patients admitted to our hospital between December 2020 and August 2022 were included in this retrospective study and divided into 3 groups based on the different dietary interventions: the CRD group (n = 39), HPD group (n = 28), and IF group (n = 68). The inclusion criteria were as follows: BMI  $\ge 25 \text{ kg/m}^2$ , first-visit patients, and age  $\le 65 \text{ years}$ , with sports ability. Exclusion criteria were as follows: pregnancy or lactation; taking hormones or other drugs that may affect metabolism for a long time; movement, digestion, and absorption disorders; type 2 diabetes mellitus (T2DM)-related complications; and other acute and chronic diseases, such as malignant tumor, diseases of the blood system, nervous system, reproductive system, and others. All patient data were obtained from the electronic medical records at our hospital. The study was reviewed and approved by the Medical Ethics Committee of Xuanwu Hospital Capital Medical University (approval no.: 2022035).

#### 2.2. Research methods

2.2.1. Physical examination. Height and weight were measured before and after the intervention. This was recorded on an empty stomach, empty stool and urine, and no strenuous exercise; each subject was barefoot and dressed in single clothes. Body composition and height were measured using a body composition analyzer and a standard height meter. When measuring the height, a mechanical height meter was used. The subject stood on the bottom plate of the height meter with his back facing the XXX, eyes looking straight in front, trunk straight, head straight, upper limbs naturally drooping, heels close together, toes separated by 60°, heel, sacrum, and the area between the 2 scapulae contacting the column. The measurer stood on the right side, gently pressed the head of the subject, and read the measurement at the same height as the plane of the plate, accurate to 0.1 cm. The average of 2 measurements were considered. If the error was >0.5 cm, a third measurement was obtained, and the average of the 2 values that are close to each other was recorded. The InBody270 (InBody, Tokyo, Japan) body composition analyzer was used to measure the body weight and body fat content, accurate to 0.1 kg, and the average value of the 2 measurements was considered. If the error was >0.5 kg, a third measurement was obtained, and the average value of the 2 readings that are close to each other was recorded.

**2.2.2. Biochemical inspection.** Fasting venous blood was collected from all subjects before and at the end of the intervention. The fully automatic biochemical analyzer (Hitachi, model 7600, Japan) was used. Fasting blood glucose (FBG), 2h postprandial blood glucose (2hPG), and glycosylated hemoglobin (HbA1c) were evaluated using Bole BIO-RAD VAR ANT 11 A 1 c meter, respectively. The CardioChekPA automatic blood lipid detector (PTS Company) was used to quantitatively determine triglyceride (TG), cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol levels. The kit was purchased from Annuolun (Beijing) Biotechnology Co. Ltd.

2.2.3. Recipe design. Both the CRD and HPD groups were provided with diets with low GI, high-quality protein, and high dietary fiber. The daily energy supply ratios were 25% for breakfast, 30% for lunch, 25% for dinner, and 10% at 2 o'clock. Energy and macronutrient ratio: the daily total energy is calculated based on the standard weight, and the daily total energy is controlled between 25 and 30 kcal/kg (1 kcal = 4.184 kJ). In the HPD group, the daily protein heat supply ratio was 30%, the fat heat supply ratio was 20% to 30%, and the carbohydrate heat supply ratio was 40%. In the CRD group, the protein, fat, and carbohydrate heat supply ratios were 15% to 20%, 20% to 30%, and 40% to 55%, respectively. The intervention period was 60 days. The IF group ate normally for 5 days in a week and followed intermittent fasting for 2 days discontinuously. On the normal eating days, women ate 1200 to 1500 kcal/d and men ate 1500 to 1800 kcal/d, which included 45% to 50% carbohydrate, 20% protein, and 30% to 35% fat. They consumed 500 kcal/d and at least 50g of protein/d on a light fasting day. It was recommended to exercise at least 3 times a week for at least 150 minutes. Two nutritionists were responsible for diet and exercise guidance, and they recorded discomfort symptoms during the study.

#### 2.3. Quality control

To ensure the quality of this study, the following quality control measures were taken. Every day, patients participating in this study were required to report their personal information through the WeChat platform or telephone communication. If they did not follow the method, they were deemed to have automatically withdrawn from this study. In case of drastic changes

Table 1			
Baseline i	nformation of	included	patients.

Variables	Calorie restrict diet	High protein diet	5+2 intermittent fasting	Р
Age (yr)	32.90 ± 8.76	32.57 ± 5.39	33.41 ± 9.75	.981
Gender, n (%)				.956
Male	10 (25.6%)	8 (28.5%)	19 (27.9%)	
Female	29 (74.4%)	20 (71.5%)	49 (72.1%)	
Nationality, n (%)				.971
Han	38 (97.4%)	27 (96.4%)	66 (97.1%)	
Others	1 (2.6%)	1 (3.6%)	2 (2.9%)	
Waistline (cm)		× ,	X Z	
Male	107.1 ± 8.7	$108.1 \pm 9$	$107.6 \pm 8.8$	.651
Female	$99.6 \pm 8.9$	98.7 ± 15.6	$99.2 \pm 12.2$	.195
Blood pressure (mm Hg)				
Systolic	124.87 ± 14.83	123.72 ± 17.29	124.23 ± 15.69	.129
Diastolic	$78.73 \pm 10.34$	81.39 ± 11.25	$80.26 \pm 10.94$	.693
Educational level				.744
College degree and above	19	12	35	
High school and below	20	16	33	
Underlying diseases				
Hypertension	13	11	29	.637
Dyslipidemia	25	22	41	.229
Diabetic mellitus	16	17	38	.209

in weather or when it was not possible to perform outdoor sports, alternative indoor sports with the same intensity should be adopted. Once a month visit to the hospital so that the medical staff can fully understand the dynamic changes and basic condition of the patient. Patients wearing exercise bracelets were required to take photos or short videos after exercise every day and send them to medical staff through the WeChat platform to ensure that the specified exercise intensity was reached. Patients without exercise bracelets were supervised by their families to ensure that they operated according to the treatment method. Remind patients of the importance of this study, so that they are honest, trustworthy, and report the facts.

#### 2.4. Statistical analysis

SPSS 22.0 was used for the data analysis. Normally distributed data were expressed as mean (standard deviation, SD) and were analyzed using analysis of variance (ANOVA) or *t* test. nonnormally distributed data were presented as median (interquartile range, IQR) and were analyzed using the Kruskal-Wallis or Mann-Whitney test. Counting data were expressed as frequency or rate (%) and were analyzed using the  $\chi^2$  test or Fisher exact test. *P* < .05 was considered statistically significant.

#### 3. Results

#### 3.1. Patient information

A total of 135 subjects were included in this study, including 39 in the CRD group (10 males and 29 females), 28 in the HPD group (8 males and 20 females), and 68 in the IF group (19 males and 49 females). The mean age of the CRD group was 32.90 (SD  $\pm$  8.76), the mean age of the HPD group was  $32.57 \text{ (SD} \pm 5.39$ ), the mean age of the IF diet group was 33.41 $(SD \pm 9.75)$ . In terms of education level, 19 subjects (50.0%) had a college degree or above, and 20 subjects (50.0%) had a high school degree or below, in the CRD group; 12 subjects (42.9%) had a college degree or above and 16 subjects (57.1%) had a high school degree or below, in the HPD group; 35 subjects (51.5%) had a college degree or above, and 33 subjects (48.5%) had high school degree or below, in the IF diet group. In terms of underlying diseases, 13 subjects (33.3%) had hypertension, 25 (64.1%) had dyslipidemia, 16 (41.0%) had diabetes mellitus, in the CRD group; 11 (39.3%) had hypertension, 22 (78.6%) had dyslipidemia, 17 (60.7%) had diabetes mellitus, in the HPD group; 29 subjects (42.6%) had hypertension, 41 (60.3%) had dyslipidemia, and 38 (55.9%) had diabetes mellitus, in the IF diet group. There were no significant differences among the 3 groups in terms of age (P = .981), sex (P = .956), nationality (P = .971), waistline (P = .651 for male and P = .195 for female), blood pressure (P = .129 for systolic blood pressure and P = .693 for diastolic blood pressure), educational level (P = .744), or underlying diseases (P = .637 for hypertension, P = .229 for dyslipidemia, and P = .209 for diabetes mellitus) (Table 1).

#### 3.2. Body weight and body fat changes

Before treatment, there were no significant differences in weight (P = .516), body fat rate (P = .843), BMI (P = .788), hip circumference (P = .115), and waist circumference (P = .262), among the 3 groups (Table 2). After treatment, the weight (P = .005 for CRD, P < .001 for HPD, and P = .001 for IF group), body fat rate (P = .027 for CRD, P = .002 for HPD, and P = .011 for IF group), BMI (P = .017 for CRD, P < .001 for HPD, and P = .011 for IF group), BMI (P = .032 for IF group), and waist circumference (P = .002 for IF group), hip circumference (P < .001 for CRD, P = .003 for IFD, and P = .003 for IFD, and P = .032 for IF group), and waist circumference (P = .005 for CRD, P < .001 for HPD, and P = .028 for IF group) were significantly decreased among the 3 groups when compared to that before treatment. The effect in the HPD group was the best, followed by that in the CRD group; the effect in the IF group was slightly lower.

#### 3.3. Comparison of metabolic indicators

**3.3.1. Comparison of glucose metabolism indicators.** HbA1c, FBG, and 2hPG levels of the 3 groups before and 60 days after treatment were compared. The results are presented in Table 3 and Figure 1. The results showed that there was no significant difference in HbA1c (P = .584), FBG (P = .927), and 2hPG (P = .385) levels among the 3 groups before treatment. After the treatment, the HbA1c (P = .014 for CRD, P = .002 for HPD, and P = .029 for IF group), FBG (P = .017 for CRD, P < .001 for HPD, and P = .033 for IF group), and 2hPG (P = .009 for CRD, P = .001 for HPD, and P = .012 for IF group) levels were significantly decreased in the 3 groups when compared to that before treatment (Table 3 and Fig. 1). The HPD group exhibited the best hypoglycemic effect, followed by the CRD group; the effect in the IF group was slightly lower.

Variables	Calorie restrict diet	High protein diet	5+2 intermittent fasting	P*
Weight (kg)				
Before	87.33 ± 10.17	$90.64 \pm 8.59$	94.20 ± 10.75	.516
After	$76.06 \pm 10.31$	$71.52 \pm 9.44$	82.93 ± 10.32	.031
Р	.005	<.001	.001	
The rate of body fat (%)				
Before	39.21 ± 2.22	$40.72 \pm 2.21$	41.17 ± 2.93	.843
After	$36.05 \pm 2.74$	$35.37 \pm 2.96$	36.37 ± 2.24	.027
Р	.027	.002	.011	
BMI (kg/m²)				
Before	$30.47 \pm 0.68$	$31.23 \pm 0.61$	31.11 ± 0.53	.788
After	$28.87 \pm 0.70$	$27.4 \pm 0.01$	29.72 ± 0.61	.016
Р	.017	<.001	.002	
Waistline (cm)				
Before	97.37 ± 9.75	$96.38 \pm 8.06$	98.87 ± 7.41	.262
After	$90.11 \pm 8.96$	87.83 ± 7.59	93.24 ± 8.72	.022
Р	.005	<.001	.028	
Hipline (cm)				
Before	$109.66 \pm 8.39$	$107.44 \pm 5.06$	$106.96 \pm 7.48$	.115
After	$102.33 \pm 9.78$	$101.72 \pm 5.16$	$104.30 \pm 7.46$	.003
Р	<.001	.013	.032	

BMI = body mass index.

\*Compared between the 3 groups.

## Table 3 Comparison of sugar metabolism indexes.

Variables	Calorie restrict diet	High protein diet	5+2 intermittent fasting	<b>P</b> *
FBG (mmol/L)				
Before	$10.10 \pm 1.25$	$10.08 \pm 1.20$	$10.13 \pm 1.32$	.927
After	$6.50 \pm 0.61^*$	$5.35 \pm 0.67^*$	$7.22 \pm 0.77^*$	.004
Р	.017	<.001	.033	
2hPG (mmol/L)				
Before	$14.96 \pm 2.10$	$14.54 \pm 2.12$	$14.38 \pm 2.32$	.385
After	$8.05 \pm 1.43^*$	$7.38 \pm 1.32^*$	$9.25 \pm 1.46^*$	<.001
Р	.009	.001	.012	
HbA1c (%)				
Before	$9.82 \pm 1.05$	9.75 ± 1.11	$9.84 \pm 1.03$	.584
After	$6.29 \pm 0.62^{*}$	$5.97 \pm 0.55^{*}$	$6.92 \pm 0.63^{*}$	.032
Р	.014	.002	.029	

2Hpg = 2h postprandial blood glucose, FBG = fasting blood glucose, HbA1c = glycosylated hemoglobin. \*Compared between the 3 groups.

**3.3.2.** Comparison of lipid metabolism indicators. TG, TC, LDL-C, and high-density lipoprotein cholesterol levels in the 3 groups before and 60 days after treatment were compared. The results showed no significant differences in TG (P = .286), TC (P = .717), LDL-C (P = .981), and LDL-C (P = .477) among the 3 groups before treatment (Table 4). After treatment, TG (P = .007 for CRD, P < .001 for HPD, and P = .018 for IF group), TC (P = .029 for CRD, P = .013 for HPD, and P = .041 for IF group), LDL-C (P = .033 for CRD, P = .021 for HPD, and P = .042 for IF group), and LDL-C (P = .011 for CRD, P < .001 for HPD, and P = .042 for IF group), and LDL-C (P = .011 for CRD, P < .001 for HPD, and P = .027 for IF group) levels were improved significantly in the 3 groups when compared to that before treatment (Table 4 and Fig. 2). The HPD group had the best effect in terms of reducing blood lipids, followed by the CRD group; the effect in the IF group was slightly lower.

#### 3.4. Adverse events

In the IF group, 1 case of hypoglycemia improved after having food and fructose, and no serious adverse events such as coma or ketoacidosis occurred. The rate of incidence of adverse events in the IF group was 1.5% (1/68). No adverse events were observed in the CRD and HPD groups. There were no significant differences in the adverse events among the 3 groups.

#### 4. Discussion

With the improvement of people living conditions and the increase in life pressure, the incidence rates of obesity, T2DM, and other basic diseases are increasing. This not only affects the beauty and health of patients but also poses a great threat to their health. BMI is closely related to glucose and lipid metabolism.<sup>[28]</sup> Obese patients not only have a high BMI, but may also have glucose metabolism and lipid metabolism disorders.<sup>[29]</sup> Therefore, effective measures should be taken to manage the BMI of patients and regulate their glucose and lipid metabolism. In recent years, with the development of medical technology, a variety of weight loss drugs have emerged; however, they have little effect on many obese patients.<sup>[30-32]</sup> Therefore, it is important to explore effective and safe intervention strategies that meet the medical weight loss needs of obese patients.

This study compared the weight loss effect and safety of 3 different dietary interventions in obese patients. The HPD, CRD, and IF diets can effectively improve the weight, body fat, and

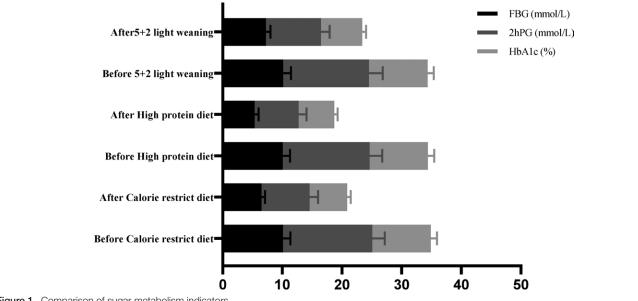


Figure 1. Comparison of sugar metabolism indicators.

Table 4	
Comparison of lipid metabolism indexes.	

Variables	Calorie restrict diet	High protein diet	5+2 intermittent fasting	<b>P</b> *
TG (mmol/L)				
Before	$1.29 \pm 0.30$	$1.31 \pm 0.33$	$1.30 \pm 0.31$	.286
After	$0.86 \pm 0.20^{*}$	$0.74 \pm 0.19^{*}$	$1.00 \pm 0.23^{*}$	.005
Р	.007	<.001	.018	
TC (mmol/L)				
Before	$5.92 \pm 1.06$	$5.89 \pm 1.10$	$5.79 \pm 1.13$	.717
After	$4.14 \pm 0.33^{*}$	$3.60 \pm 0.55^*$	$4.63 \pm 0.71^{*}$	.019
Р	.029	.013	.041	
LDL-C (mmol/L)				
Before	$3.10 \pm 0.65$	$3.08 \pm 0.61$	$3.09 \pm 0.51$	.981
After	$1.85 \pm 0.33^{*}$	$1.68 \pm 0.34^{*}$	$2.10 \pm 0.43^{*}$	<.001
Р	.033	.021	.042	
HDL-C (mmol/L)				
Before	$0.95 \pm 0.30$	$0.93 \pm 0.18$	$0.96 \pm 0.23$	.477
After	$1.84 \pm 0.37^{*}$	$2.02 \pm 0.41^{*}$	$1.65 \pm 0.34^{*}$	.006
Р	.011	<.001	.027	

 $\mathsf{HDL-C} = \mathsf{high-density} \ \mathsf{lipoprotein} \ \mathsf{cholesterol}, \ \mathsf{TC} = \mathsf{cholesterol}, \ \mathsf{TG} = \mathsf{triglyceride}$ 

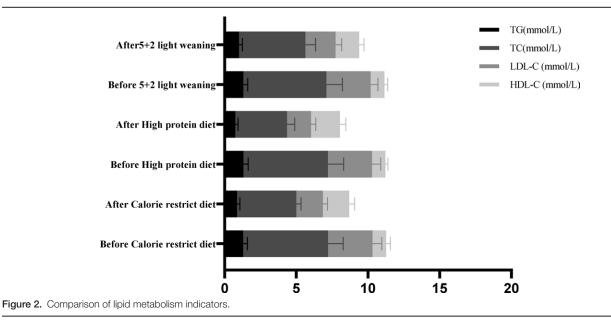
\*Compared between the 3 groups.

blood lipids of overweight/obese people. The HPD diet is better than the CRD and IF diet interventions in improving weight and blood lipid levels.

Both HPD and standard protein diet (protein energy supply ratio 12%-16%) can effectively improve the weight and body fat of obese people; the former is more effective than the latter.<sup>[24]</sup> Protein is superior to carbohydrates in promoting satiety and increasing energy consumption; this enables those who lost weight better ensure negative energy balance and promote weight loss.<sup>[28,30,33]</sup> A prospective cohort study showed that, the risk of T2DM can be reduced by 16% for every 1 kg of weight loss.<sup>[34]</sup> A meta-analysis showed that a weight loss intervention (average total weight loss using different intervention times was 2.56-3.42 kg) could reduce the risk of all-cause death by 18%.[31] We speculate that HPD increases fish, poultry, meat, and eggs in food selection, which makes it easy for overweight/obese people to accept, thus improving the compliance of people with weight loss. This is more conducive to weight loss and could bring a series of health benefits.[35]

The total fat heat supply ratio of the HPD is higher than that of the energy limited balanced diet, and the total fat intake is also higher than that of the CRD.<sup>[36]</sup> Excessive fat intake is a risk factor for dyslipidemia.<sup>[37]</sup> However, HPD improves TC and TCHLO more significantly than the standard protein diet.<sup>[33,35,38,39]</sup> In this study, both weight loss methods effectively improved blood lipids, and the HPD group was better than the CRD group in improving blood lipids. The difference in the TG levels between the 2 groups was as high as 0.12 mmol/l. With every 1 mmol/l increase in TG, the risk of cardiovascular disease death and all-cause death increases by 13% and 12%, respectively.<sup>[40,41]</sup> In this study, the incidence of adverse events in the 3 groups were similar, suggesting that the 3 weight loss interventions will not increase the risk of adverse events in obese patients, and have a certain degree of safety.

This study had some limitations. First, the sample size is a major limitation. Second, this was a single-center study. Third, excessive intake of protein and its processing through renal metabolism will increase the renal burden, and could even damage the renal function. Therefore, it is necessary to further study



the impact of the 3 weight loss methods on renal function, regularly monitor renal function, and determine the amount of protein and start weight loss time.

In conclusion, this study showed that short-term HPD was more effective than CRD or IF diets in reducing body weight, BMI, body fat, glucose control, and lipid metabolism. Further large-scale, multicenter, and well-designed studies are needed to verify our findings and further investigate the effects of the 3 different dietary interventions (CRD, HPD, and IF) on body weight, BMI, body fat, glucose, and lipid metabolism.

#### **Author contributions**

Conceptualization: Lina Sun.

- Data curation: Lina Sun.
- Formal analysis: Lina Sun.
- Funding acquisition: Lina Sun.
- Investigation: Lina Sun.
- Methodology: Lina Sun, Zhijing Mu. Project administration: Lina Sun, Zhijing Mu.
- Resources: Lina Sun, Zhijing Mu.
- Software: Lina Sun, Zhijing Mu.
- Supervision: Ya'hui Ma, Zhijing Mu.
- Validation: Ya'hui Ma, Zhijing Mu.
- Visualization: Ya'hui Ma, Zhijing Mu.
- Writing original draft: Ya'hui Ma, Zhijing Mu. Writing – review & editing: Ya'hui Ma.

#### References

- [1] Wang Y, Wang L, Qu W. New national data show alarming increase in obesity and noncommunicable chronic diseases in China. Eur J Clin Nutr. 2017;71:149-50.
- [2] Chen Y, Peng Q, Yang Y, et al. The prevalence and increasing trends of overweight, general obesity, and abdominal obesity among Chinese adults: a repeated cross-sectional study. BMC Public Health. 2019;19:1293.
- [3] Xi B, Liang Y, He T, et al. Secular trends in the prevalence of general and abdominal obesity among Chinese adults, 1993-2009. Obes Rev. 2012;13:287-96.
- [4] Zhang X, Zhang M, Zhao Z, et al. Geographic variation in prevalence of adult obesity in China: results from the 2013-2014 national chronic disease and risk factor surveillance. Ann Intern Med. 2020;172:291-3.
- [5] Lee CMY, Goode B, Nørtoft E, et al. The cost of diabetes and obesity in Australia. J Med Econ. 2018;21:1001-5.

- [6] Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. Nat Rev Endocrinol. 2018:14:513-37
- [7] Chen W, Jiang H. Interpretation of consensus of Chinese overweight/ obesity medical nutrition treatment experts in 2016. Chin J Pract Intern Med. 2017;37:430-3.
- Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guide-[8] line for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart association task force on practice guidelines and the obesity society. Circulation. 2014;129:S102-38.
- [9] Giusti J, Rizzotto JA. Interpreting the joslin diabetes center and joslin clinic clinical nutrition guideline for overweight and obese adults with type 2 diabetes. Curr Diab Rep. 2006;6:405-8.
- [10] Yamada Y, Uchida J, Izumi H, et al. A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. Intern Med. 2014;53:13-9.
- [11] Jiang S, Ji S, Tang X, et al. A comparison study on the therapeutic effect of high protein diets based on pork protein versus soybean protein on obese mice. Foods. 2022;11:1227
- [12] Maekawa S, Niizawa M, Harada M. A comparison of the weight loss effect between a low-carbohydrate diet and a calorie-restricted diet in combination with intragastric balloon therapy. Intern Med. 2020:59:1133-9.
- [13] Carter S, Clifton PM, Keogh JB. The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Res Clin Pract. 2016;122:106-12.
- [14] Liu P, Li Y, Ma L. Caloric restriction may help delay the onset of frailty and support frailty management. Front Nutr. 2021;8:731356.
- [15] Heilbronn LK, de Jonge L, Frisard MI, et al. Effect of 6-month calorie restriction on biomarkers of longevity, metabolic adaptation, and oxidative stress in overweight individuals: a randomized controlled trial. JAMA. 2006;295:1539-48.
- [16] Leidy HJ, Clifton PM, Astrup A, et al. The role of protein in weight loss and maintenance. Am J Clin Nutr. 2015;101:S1320-S1329.
- [17] Wang B, Chen P, Huang DS, et al. Predicting protein interaction sites from residue spatial sequence profile and evolution rate. FEBS Lett. 2006;580:380-4.
- [18] Zhao XM, Cheung YM, Huang DS. A novel approach to extracting features from motif content and protein composition for protein sequence classification. Neural Netw. 2005;18:1019-28.
- [19] Welton S, Minty R, O'Driscoll T, et al. Intermittent fasting and weight loss: systematic review. Can Fam Physician. 2020;66:117-25.
- [20] Fontana L. The scientific basis of caloric restriction leading to longer life. Curr Opin Gastroenterol. 2009;25:144-50.
- [21] de Souza Nunes FM, Pimentel VE, Helaehil JV, et al. Caloric restriction overcomes pre-diabetes and hypertension induced by a high fat diet and renal artery stenosis. Mol Biol Rep. 2022;49:5883-95.
- [22] Golbidi S, Daiber A, Korac B, et al. Health benefits of fasting and caloric restriction. Curr Diab Rep. 2017;17:123.

- [23] Yu D, Tomasiewicz JL, Yang SE, et al. Calorie-restriction-induced insulin sensitivity is mediated by adipose mTORC2 and not required for lifespan extension. Cell Rep. 2019;29:236–248.e3.
- [24] Weigle DS, Breen PA, Matthys CC, et al. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. Am J Clin Nutr. 2005;82:41–8.
- [25] Aller EE, Larsen TM, Claus H, et al. Weight loss maintenance in overweight subjects on ad libitum diets with high or low protein content and glycemic index: the DIOGENES trial 12-month results. Int J Obes (Lond). 2014;38:1511–7.
- [26] Conley M, Le Fevre L, Haywood C, et al. Is two days of intermittent energy restriction per week a feasible weight loss approach in obese males? A randomised pilot study. Nutr Diet. 2018;75:65–72.
- [27] Park SJ, Yang JW, Song YJ. The effect of four weeks dietary intervention with 8-hour time-restricted eating on body composition and cardiometabolic risk factors in young adults. Nutrients. 2021;13:2164.
- [28] Astrup A, Raben A, Geiker N. The role of higher protein diets in weight control and obesity-related comorbidities. Int J Obes (Lond). 2015;39:721–6.
- [29] Ohira M, Yamaguchi T, Saiki A, et al. Laparoscopic sleeve gastrectomy significantly increases serum lipoprotein lipase level in obese patients. Obes Facts. 2019;12:357–68.
- [30] Wycherley TP, Moran LJ, Clifton PM, et al. Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials. Am J Clin Nutr. 2012;96:1281–98.
- [31] Ma C, Avenell A, Bolland M, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017;359:j4849.

- [32] Layman DK, Boileau RA, Erickson DJ, et al. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. J Nutr. 2003;133:411–7.
- [33] Liu J, Zeng FF, Liu ZM, et al. Effects of blood triglycerides on cardiovascular and all-cause mortality: a systematic review and meta-analysis of 61 prospective studies. Lipids Health Dis. 2013;12:159.
- [34] Teunissen-Beekman KF, Dopheide J, Geleijnse JM, et al. Effect of increased protein intake on renal acid load and renal hemodynamic responses. Physiol Rep. 2016;4:e12687.
- [35] Johnston CS, Day CS, Swan PD. Postprandial thermogenesis is increased 100% on a high-protein, low-fat diet versus a high-carbohydrate, lowfat diet in healthy, young women. J Am Coll Nutr. 2002;21:55–61.
- [36] Ha K, Nam K, Song Y. A moderate-carbohydrate diet with plant protein is inversely associated with cardiovascular risk factors: the Korea national health and nutrition examination survey 2013-2017. Nutr J. 2020;19:84.
- [37] Anuradha R, Hemachandran S, Ruma D. The waist circumference measurement: a simple method for assessing the abdominal obesity. J Clin Diagn Res. 2012;6:1510–3.
- [38] Knight EL, Stampfer MJ, Hankinson SE, et al. The impact of protein intake on renal function decline in women with normal renal function or mild renal insufficiency. Ann Intern Med. 2003;138:460–7.
- [39] Ko GJ, Obi Y, Tortoricci AR, et al. Dietary protein intake and chronic kidney disease. Curr Opin Clin Nutr Metab Care. 2017;20:77.
- [40] Flechtner-Mors M, Boehm BO, Wittmann R, et al. Enhanced weight loss with protein-enriched meal replacements in subjects with the metabolic syndrome. Diabetes Metab Res Rev. 2010;26:393–405.
- [41] Campos-Nonato I, Hernandez L, Barquera S. Effect of a high-protein diet versus standard-protein diet on weight loss and biomarkers of metabolic syndrome: a randomized clinical trial. Obes Facts. 2017;10:238–51.