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## Retrospective Study

Effects and mechanisms of nutritional interventions on  
extradigestive complications in obese patients

Li Jiang, Lu-Lian Xu, Yang Lu, Ke-Feng Gu, Shu-Yi Qian, Xi-Ping Wang, Xu Xu

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Children's Hospital, No. 299 Qingyang Road, Liangxi District, Wuxi 214023, Jiangsu Pro-  
vince, China. [xuxu02202@126.com](mailto:xuxu02202@126.com)**Abstract****BACKGROUND**

Obesity is associated with an increased risk of multiple extradigestive complications. Thus, understanding the global epidemiology of obesity and its relationship with extradigestive complications, such as cardiovascular disease, type 2 diabetes mellitus, and non-alcoholic fatty liver disease is important. However, nutritional intervention can positively manage issues associated with obesity. Hence, the identification of the current high prevalence of extradigestive complications among patients with obesity and the potential role of nutritional interventions is also essential.

**AIM**

To determine the relationship between obesity and extradigestive complications and emphasize the importance of nutritional interventions in the management of patients with obesity.

**METHODS**

Overall, 110 patients with obesity admitted to our hospital from February 2020 to November 2022 and 100 healthy individuals were included in the present study. Information of the study population, including demographic characteristics, such as age, sex, body mass index, indicators of extradigestive complications, dietary intake, and biomarkers was collected. The study design, participant selection, interventions, and development of the nutritional intervention program were described. The collected data were analyzed to assess the effect of nutritional interventions on extradigestive complications.

**RESULTS**

As a part of nutritional intervention, the dietary structure was modified to decrease the saturated fatty acid and cholesterol intake and increase the dietary fiber and polyunsaturated fatty acid intake to improve the blood lipid levels and cardiovascular health. Mechanistic studies showed that these nutritional inter-

ventions positively affected mechanisms that regulate lipid metabolism, improved inflammatory markers in the blood, and improved vascular functions.

## CONCLUSION

The study discusses the consistency of the present results with previous findings to assess the clinical significance of the present findings. The study provides direction for future research on improving nutritional intervention strategies.

**Key Words:** Obesity; Nutritional interventions; Extradigestive complications; Cardiovascular disease; Type 2 diabetes; Non-alcoholic fatty liver disease

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**Core Tip:** Nutritional interventions positively impact extradigestive complications in patients with obesity by modifying the dietary structure to improve lipid metabolism, inflammatory markers, and vascular functions. These findings emphasize the importance of nutritional interventions in managing obesity-related conditions, such as cardiovascular disease, type 2 diabetes, and non-alcoholic fatty liver disease, providing valuable insights for future research on optimizing intervention strategies.

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## INTRODUCTION

Obesity is a metabolic disease correlated to an increased risk of multiple extradigestive complications. Nutritional intervention, a crucial management tool, can positively affect weight management, associated disease risk control, and the occurrence of extradigestive complications in patients with obesity by modifying the dietary structure and providing appropriate nutrients[1-5]. The global prevalence of obesity is increasing and is closely related to the development of extradigestive complications, such as cardiovascular disease (CVD), type 2 diabetes mellitus, and non-alcoholic fatty liver disease (NAFLD). Thus, nutritional intervention is clinically important as a nonpharmacological treatment strategy. By modifying the dietary structure and providing appropriate nutrients, nutritional interventions can help with weight management, control of the risk of associated diseases, and reduction in the occurrence of extradigestive complications[6-8].

Introduction to obesity and its worldwide epidemiological data and trends: The relationship between obesity and extradigestive complications has been discussed, highlighting their relevance and importance. Nutritional interventions are important tools for managing patients with obesity patients and preventing complications[9-11]. The association between CVD and obesity has been studied. Nutritional intervention strategies, such as limiting the energy intake, modifying fat and cholesterol intake, and increasing the dietary fiber and polyunsaturated fatty acid (PUFA) intake, are essential to reduce the risk of CVDs. The underlying mechanisms, such as improved lipid metabolism, reduced inflammatory responses, and improved vascular function may help achieve the desired effect of nutritional interventions. Furthermore, nutritional intervention strategies may play a role in improving the insulin sensitivity and glucose metabolism by controlling the glycemic response, weight management, and high-sugar food intake. The possible underlying mechanisms are improving insulin signaling, reduced insulin resistance, and fat accumulation. Additionally, nutritional intervention strategies may play a role in improving hepatic fat accumulation and reducing hepatic inflammation and fibrosis by reducing the fat and sugar intake and increasing the intake of dietary fiber and antioxidants. The possible underlying pathways may be the modulation of fatty acid synthesis and oxidation, amelioration of the hepatic inflammatory response, and reduction in oxidative stress. To summarize the important findings of studies on the effects and mechanisms of nutritional interventions on extradigestive complications in patients with obesity[12-15]. Thus, in the present study, we aimed to investigate the effect of nutritional interventions on extradigestive complications in patients with obesity and the mechanisms underlying this effect. Furthermore, we emphasized the potential and importance of nutritional interventions in preventing and managing obesity and obesity-related complications.

## MATERIALS AND METHODS

### Research design

The present study was conducted on 110 patients with obesity admitted to our hospital from February 2020 to November

2022 and 100 normal individuals. We selected the study design of “randomized controlled trial” to evaluate the effects and mechanisms of nutritional interventions on extradigestive complications in patients with obesity. The participants were randomized into the following two groups: An intervention group and a control group.

### Research subjects

Patients with obesity meeting the following criteria were selected as study subjects: age range, 18-60 years, and diagnostic criterion, body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>. The exclusion criteria were as follows: Patients with other important underlying diseases, including metabolic diseases and CVDs and patients undergoing other interventions, such as taking medications for other health conditions.

### Nutritional intervention program

In the intervention group, a specific nutritional intervention program was implemented, which involved the following: Energy control: Individualized energy intake targets were set based on the participants’ body composition, activity levels, and metabolic needs and dietary composition. The diets of the participants were modified to limit saturated fatty acid (SFA) and cholesterol intake and increase the dietary fiber and PUFA intake. Nutritional education and individualized dietary guidance were provided to help the patients understand and adopt healthy eating habits. The control group received routine standard care and non-interventional general advice such as general dietary guidance or lifestyle advice.

### Observation indicators

(1) Pre and post-intervention data collection included, but was not limited to, the following demographic characteristics: age, sex, and BMI; (2) Indicators of extradigestive complications included information on the occurrence and severity of several extradigestive complications associated with obesity, such as the indicators of CVD risk, diabetes mellitus, and liver function; (3) Dietary intake data: Information on the patients’ diets, including energy, fat, fiber, and other nutrients, was collected using the methods of recording food intake or dietary review, and (4) Biomarkers: Blood markers, such as lipid and blood glucose levels, liver function indicators, and urine markers.

### Data analysis

Means and standard deviations were calculated to statistically analyze the demographic characteristics of the groups and baseline data. Changes in the indicators of extradigestive complications between the intervention and control groups were compared by statistical methods, such as the independent samples *t*-test and chi-square test. The relationship between the indicators of extradigestive complications and dietary intake data after the intervention was explored by calculating the pearson’s correlation coefficient. Differences were considered statistically significant at  $P < 0.05$ .

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## RESULTS

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### General information

No statistically significant difference was observed between the intervention and control groups in terms of age ( $52.4 \pm 1.0$  years) *vs.* ( $51.2 \pm 1.3$  years), body weight, BMI, literacy level, and the monthly household income ( $P > 0.05$ ). No difference was observed regarding the use of antihypertensive medications between the two groups at baseline. The dosage and frequency of drug consumption remained unchanged for the subjects throughout the trial, and no adverse effects or reactions were reported. None of the participants withdrew from the study for any reason. The baseline characteristics of the patients are summarized in [Table 1](#).

### Indicators of CVD risk

No difference in diastolic blood pressure was observed between the subjects in the two groups after the intervention, whereas the systolic blood pressure of the subjects in the intervention group was lower than that of the subjects in the control group ( $P < 0.05$ ). After four weeks of dietary intervention, the systolic and diastolic blood pressures of the subjects in both groups decreased; however, the decrease observed in the intervention group was more pronounced, with a statistically significant difference ([Table 2](#)).

### Nutrient intake of subjects in the control and intervention groups

The mean intake of protein, carbohydrates, dietary fiber, potassium, calcium, and magnesium in the intervention group was higher than that in the control group. Additionally, the mean intake of energy, fat, cholesterol, SFA, monounsaturated fatty acid, PUFA, and sodium in the intervention group was lower than that in the control group ( $P < 0.05$  for both) ([Table 3](#)).

### Comparison of liver function indices between the two groups before and after intervention

No statistically significant differences in the serum alanine transaminase (ALT) and aspartate aminotransferase (AST) levels were observed between the intervention and control groups before the intervention. After four weeks of dietary intervention, the ALT and AST levels in the intervention group were lower than those before the intervention, and the differences were statistically significant ( $P < 0.05$ ) ([Table 4](#)).

**Table 1** Baseline characteristics of the control and intervention groups (mean ± SE)

Variant	Control group (n = 110)	Intervention group (n = 110)	P value
Age (yr)	28-63 (51.2 ± 1.3)	36-68 (52.4 ± 1.0)	0.488
Sex [cases (%)]			
Males	25 (22.73)	27 (24.55)	0.605
Females	85 (77.27)	83 (75.45)	
Weight (kg)	67.7 ± 1.7	69.2 ± 1.6	0.526
Height (cm)	170.7 ± 1.4	172.4 ± 1.3	0.385
BMI (kg/m <sup>2</sup> )	25.1 ± 0.4	25.1 ± 0.4	0.959
SBP (mmHg)	141.4 ± 1.4	141.9 ± 1.4	0.788
DBP (mmHg)	89.7 ± 1.5	89.5 ± 1.7	0.913
MDA (nmol/L)	4.24 ± 1.7	4.74 ± 1.5	0.196
GSH (μmol/L)	7.95 ± 3.2	6.93 ± 3.4	0.251
SOD (U/mL)	74.21 ± 12.3	67.66 ± 13.4	0.051
Heart rate (time/min)	78.1 ± 1.6	78.9 ± 1.3	0.693
<sup>1</sup> Educational level	3:16:16	4:18:14	0.827
<sup>2</sup> Monthly household income	8:14:13	6:15:15	0.799

<sup>1</sup>University/undergraduate and above: High school/junior high school: primary school and below.

<sup>2</sup>\$20,000 and above: \$10,000 to \$20,000:\$10,000 and below. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MDA: Mobile device assistant; GSH: Glutathione; SOD: Superoxide dismutase.

**Table 2** Post-intervention changes in the blood pressure between the intervention and control groups (mean ± SE)

Norm	Control subjects	Intervention group	P value	
DBP (mmHg)	Start of intervention	86.4 ± 1.4	83.9 ± 1.7	0.241
	End of intervention	82.8 ± 1.6	76.6 ± 1.6	0.007
	Amount of change before and after intervention	3.6 ± 1.1	7.3 ± 1.1	0.000
SBP (mmHg)	Start of intervention	137.3 ± 1.4	133.2 ± 1.1	0.021
	End of intervention	131.1 ± 1.6	116.3 ± 1.5	0.000
	Amount of change before and after intervention	6.2 ± 2.0	16.9 ± 1.4	0.022

SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

### Logistic multifactorial regression analysis of factors affecting the occurrence of extradigestive complications in patients with obesity

A logistic multifactorial regression analysis was performed on the dependent variables associated with extradigestive complications that occurred in patients with lacunar cerebral infarction. The indices with *P* < 0.05 in the above univariate analysis were used as independent variables. The results showed that a history of high blood pressure and high levels of low-density lipoprotein-C, platelet endothelial cell adhesion molecule (PECAM)-1, and fibroblast growth factor (FGF)21 were identified as risk factors for extradigestive complication occurrence in patients with lacunar cerebral infarction (*P* < 0.01), whereas high levels of low-density lipoprotein (HDL)-C and growth differentiation factor (GDF)11 were identified as protective factors (*P* < 0.05). High levels of HDL-C, PECAM-1, and FGF21 were identified as risk factors for extradigestive complication development in patients with lacunar cerebral infarction (*P* < 0.01), whereas high levels of serum HDL-C and GDF11 were identified as protective factors (*P* < 0.05) (Table 5).

### Diagnostic value of serum PECAM-1, GDF11, and FGF21 levels for extradigestive complications in patients with obesity

The receiver operating characteristic (ROC) curve showed that the area under the curve (AUC) values of serum PECAM-1, GDF11, and FGF21 levels as well as the combination of these three diagnostic indicators for carotid atherosclerosis were

**Table 3 Nutrient intake in the control and intervention groups (mean ± SE)**

Original proposal	Control subjects	Intervention group	P value
Energy (kcal)	2033.74 ± 19.45	1953.01 ± 18.55	0.036
Fat (g)	94.21 ± 1.13	50.79 ± 0.75	0.001
Protein (g)	76.42 ± 0.97	97.72 ± 0.89	0.017
Carbohydrates (g)	226.79 ± 3.29	275.03 ± 4.21	0.029
Dietary fiber (g)	10.28 ± 0.11	25.22 ± 1.59	0.005
Cholesterol (mg)	554.96 ± 3.84	473.30 ± 7.33	0.012
SFA (g)	47.58 ± 1.21	27.83 ± 0.28	0.006
MUFA (g)	29.5 ± 0.37	12.44 ± 0.10	0.001
PUFA (g)	20.20 ± 0.21	12.34 ± 0.28	0.013
Sodium (mg)	4347.28 ± 46.34	2284.86 ± 12.43	0.001
Potassium (mg)	1663.15 ± 11.14	3088.78 ± 67.37	0.001
Calcium (mg)	483.84 ± 14.09	864.32 ± 21.60	0.001
Magnesium (mg)	259.97 ± 2.28	479.05 ± 14.12	0.014

SFA: Saturated fatty acid; MUFA: Modulation of fatty acid; PUFA: Polyunsaturated fatty acid.

**Table 4 Comparison of the levels of oxidative stress indicators between the intervention and control groups (mean ± SE)**

Norm	Control subjects	Intervention group	P value	
ALT (nmol/L)	End of intervention	115.29 ± 1.2	63.94 ± 1.4	0.001
	Amount of change before and after intervention	21.25 ± 0.2	20.6 ± 0.1	0.015
AST (µmol/L)	End of intervention	157.15 ± 3.5	59.00 ± 2.8	0.017
	Amount of change before and after intervention	20.6 ± 0.2	22.17 ± 0.1	0.021

ALT: Alanine transaminas; AST: Aspartate aminotransferase.

**Table 5 Logistic multifactorial regression analysis of factors affecting the occurrence of extradigestive complications in patients with obesity**

Variables	β-value	SE value	Wald value	P value	OR value	95%CI
History of hypertension	1.296	0.421	9.470	0.002	3.654	1.601-8.343
TC high	0.226	0.138	2.685	0.101	1.254	0.957-1.643
TG high	0.305	0.211	2.091	0.148	1.356	0.897-2.051
HDL-C high	-0.247	0.123	4.002	0.045	0.781	0.613-0.995
LDL-C high	0.909	0.254	12.787	< 0.001	2.481	1.508-4.085
PECAM-1 high	0.070	0.019	12.930	< 0.001	1.073	1.032-1.114
GDF11 high	-0.008	0.003	9.199	0.002	0.992	0.987-0.997
FGF21 high	0.024	0.007	13.062	< 0.001	1.024	1.011-1.038

OR: Odds ratio; CI: Confidence interval; TC: Total cholesterol; TG: Triacylglycerol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; PECAM-1: Platelet endothelial cell adhesion molecule-1; GDF11: Growth differentiation factor 11; FGF21: Fibroblast growth factor 21.

**Table 6 Receiver operating characteristic curve analysis of the serum levels of platelet endothelial cell adhesion molecule-1, growth differentiation factor 11, and fibroblast growth factor 21 in predicting the occurrence of extradigestive complications in patients with obesity**

Indicators	Cut-of value	AUC (95%CI)	Sensitivity	Specificity	Jordon index
PECAM-1	40 µg/L	0.798 (0.595-0.974)	0.824	0.744	0.568
GDF11	650 µg/L	0.716 (0.509 -0.929)	0.716	0.733	0.449
FGF21	160 ng/L	0.813 (0.671-0.940)	0.811	0.791	0.602
Tripartite		0.909 (0.850-0.958)	0.919	0.884	0.803

AUC: Area under the curve; CI: Confidence interval; PECAM-1: Platelet endothelial cell adhesion molecule-1; GDF11: Growth differentiation factor 11; FGF21: Fibroblast growth factor 21.

0.798, 0.716, 0.813, and 0.909, respectively. Furthermore, the efficacy of the combination was higher than that of each indicator alone ( $Z/P = 2.097/0.036, 2.290/0.022, 2.005/0.045, 0.022, \text{ and } 2.005/0.045$ ) (Table 6).

## DISCUSSION

Patients with obesity often show symptoms, such as high blood pressure, cholesterol, and blood glucose levels, which are considered CVD risk factors[16-18]. Nutritional interventions, such as limiting the energy intake and improving diet quality can reduce the risk of CVD. For instance, reducing the saturated fat and cholesterol intake, and increasing the dietary fiber and whole grain intake can help improve lipid and glycemic control.

Patients with obesity often suffer from disease. Nutritional interventions, such as limiting the energy intake can improve NAFLD by improving the lipid metabolism and reducing liver fat accumulation. A diet limiting the consumption of high-sugar and high-fat foods, increasing the antioxidant and anti-inflammatory food intake, and reducing alcohol consumption can positively affect liver health[19].

Obesity is an important risk factor of insulin resistance and type 2 diabetes. Nutritional interventions that reduce the energy intake, control the carbohydrate intake, and aid in the consumption of foods with a low glycemic index can reduce the risk of insulin resistance and diabetes by improving insulin sensitivity[20].

Finally, the ROC curve analysis showed that the serum levels of PECAM-1, GDF11, and FGF21 possessed high diagnostic values for extradigestive complications in patients with obesity, and the diagnostic value was further improved when the combination of the three indicators was considered (AUC = 0.909). The diagnostic sensitivity, specificity, and accuracy of the combination were 0.919, 0.884, and 0.900, respectively. Nutritional intervention is a clinically important non-pharmacological treatment strategy. By modifying the dietary structure and providing appropriate nutrients, nutritional interventions help control body weight, manage the risk of associated diseases, and reduce the incidence of extragastrointestinal complications. Despite the creativity of the study, it is not yet possible to list all the possibilities due to the limitations of the sample size and research model; future studies should expand the sample size and age structure to exclude these limitations.

## CONCLUSION

In conclusion, the levels of PECAM-1, GDF11, and FGF21 are related to cerebral arterial hemodynamic parameters in extradigestive complications in patients with obesity; thus, they can be considered as factors affecting the extradigestive complications in patients with obesity. Moreover, the combination of the three has a better diagnostic value for extradigestive complications in patients with obesity.

## ARTICLE HIGHLIGHTS

### Research background

Obesity is associated with an increased risk of multiple extradigestive complications. Thus, understanding the global epidemiology of obesity and its relationship with extradigestive complications, such as cardiovascular disease, type 2 diabetes mellitus, and non-alcoholic fatty liver disease, is important. Nutritional interventions can also positively manage obesity-associated issues.

### Research motivation

In the present study, we aimed to determine the relationship between obesity and extradigestive complications and

emphasize the importance of nutritional interventions in managing patients with obesity.

### Research objectives

Hence, identification of the current high prevalence of extradigestive complications among patients with obesity and the potential role of nutritional interventions are essential.

### Research methods

Overall, 110 patients with obesity admitted to our hospital from February 2020 to November 2022 and 100 healthy individuals were included in the present analysis. Information regarding demographic characteristics, such as age, sex, body mass index, indicators of extradigestive complications, dietary intake, and biomarkers, was collected. The study design, participant selection, interventions, and development of the nutritional intervention program were described. The collected data were analyzed to assess the effects of nutritional interventions on extradigestive complications.

### Research results

As part of the nutritional intervention, the dietary structure was modified to decrease the saturated fatty acid and cholesterol intake and increase the dietary fiber and polyunsaturated fatty acid intake to improve the blood lipid levels and cardiovascular health. Mechanistic studies have shown that nutritional interventions positively affect mechanisms that regulate lipid metabolism, improve inflammatory markers in the blood, and improve vascular function.

### Research conclusions

The present study explains the possible mechanisms by which nutritional interventions affect extradigestive complications in patients with obesity. Moreover, we discuss the consistency of the present results with previous findings to assess the clinical significance of the present findings.

### Research perspectives

The study provides directions for future research on improving nutritional intervention strategies.

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## FOOTNOTES

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**Co-first authors:** Li Jiang and Lu-Lian Xu.

**Author contributions:** Jiang L, Xu LL, Lu Y, Gu KF, Qian SY, Wang XP, and Xu X designed the research study; Jiang L, Xu LL, Lu Y, Gu KF, Qian SY, Wang XP, and Xu X performed the research; Jiang L, Xu LL, and Xu X contributed new reagents and analytic tools; Jiang L, Xu LL, and Xu X analyzed the data and wrote the manuscript; All authors have read and approved the final manuscript. Jiang L and Xu LL contributed equally to this work as co-first authors. The reasons for designating Jiang L and Xu LL as co-first authors are threefold. First, the research was performed as a collaborative effort, and the designation of co-first authors accurately reflects the distribution of responsibilities and burdens associated with the time and effort required to complete the study and the resultant paper. This also ensures effective communication and management of post-submission matters, ultimately enhancing the paper's quality and reliability. Second, the overall research team encompassed authors with a variety of expertise and skills from different fields, and the designation of co-first authors best reflects this diversity. This also promotes the most comprehensive and in-depth examination of the research topic, ultimately enriching readers' understanding by offering various expert perspectives. Third, Jiang L and Xu LL contributed efforts of equal substance throughout the research process. The choice of these researchers as co-first authors acknowledges and respects this equal contribution, while recognizing the spirit of teamwork and collaboration of this study. In summary, we believe that designating Jiang L and Xu LL as co-first authors of is fitting for our manuscript as it accurately reflects our team's collaborative spirit, equal contributions, and diversity.

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