

## Original Article

**Association of nutritional level with remission and nutritional advice in obesity surgery****Zongwen Shen<sup>1#</sup>, Henggong Pan<sup>2,3#</sup>, Ling-Yan Su<sup>2,3#</sup>, Jiaxue Sun<sup>4#</sup>, Jianwu Xiong<sup>1</sup>, Xiongxiang Chen<sup>1</sup>, Lei Yang<sup>1</sup>, Yu Xu<sup>4</sup>, Huayou Luo<sup>4\*</sup>, Yingxu Li<sup>1\*</sup>, Hejiang Zhou<sup>2,3\*</sup>**<sup>1</sup>Qujing Second People's Hospital of Yunnan Province, Qujing 655000, Yunnan, China.<sup>2</sup>College of Food Science and Technology, Yunnan Agricultural University, No. 452 Fengyuan Road, Kunming 650000, Yunnan, China.<sup>3</sup>Yunnan Provincial Key Laboratory of Precision Nutrition and Personalized Food Manufacturing, Yunnan Agricultural University, Kunming 650000, Yunnan, China.<sup>4</sup>First Affiliated Hospital of Kunming Medical University, Kunming 650000, Yunnan, China.

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## STUDY IMPORTANCE QUESTIONS

\* **What is already known about this subject?**

Iron and multivitamins are given to people undergoing bariatric surgery to ensure long-term postoperative success.

\* **What are the new findings in your manuscript?**

1. Iron and VB12 harmed surgical remission after obesity surgery.
2. The levels of folic acid, UA, and Hcy, especially before surgery, can greatly influence remission after obesity surgery.

\* **How might your results change the direction of research or the focus of clinical practice?**

1. VB12 should not be given to BS patients.
2. Iron supplementation should be given unless the patient is iron deficient.
3. Folic acid supplementation and UA downregulation should continue for 12 months after surgery.

### Abstract

**Aim:** To provide clinical nutritional guidance for BS patients, the effect of nutrient levels on remission at different time points up to one year after surgery was investigated.

**Methods:** A cohort study included 870 participants aged 18 years or older with severe obesity who were undergoing BS for the first time. All participants underwent surgery between January 2021 and November 2023. They were followed up until November 2023 for this report.

**Results:** Participants were predominantly female (76%), with a median age of 33 years. 454, 156, 156, and 65 patients completed a follow-up of 1, 3, 6, and 12 months, respectively. BMI and clinical characteristics are improved after surgery. Albumin had a

positive effect on surgical remission only one month after surgery. Iron and VB12 harmed surgical remission. The levels of folic acid, UA, and Hcy, especially before surgery, can greatly influence remission. As folic acid has a positive effect on remission and UA and Hcy have a negative effect, we suggest that folic acid supplementation and UA downregulation should continue for 12 months after surgery.

**Conclusions:** The study suggests that short-term postoperative protein supplementation, lifelong folic acid supplementation, and reducing UA and Hcy improve postoperative health.

**Keywords:** Bariatric surgery, weight surgery, nutritional guidelines, nutrition

## INTRODUCTION

The WHO criteria for defining overweight (BMI 25-29.9 kg/m<sup>2</sup>) and obesity (BMI > 30 kg/m<sup>2</sup>) and the associated health risks are based on the body mass index (BMI), the ratio of weight to height squared<sup>[1]</sup>. Obesity remains a major national and global public health crisis, both in clinical and economic terms<sup>[2]</sup>. It poses a serious threat to the economy of national health systems due to the increasing costs of treating its complications, including direct costs (medications, hospitalizations, associated diseases) and indirect costs (lost days of work, lost years in health)<sup>[3-6]</sup>. Currently, the most effective treatment for achieving sustained weight loss and reducing comorbidity and mortality associated with severe obesity is considered to be BS<sup>[7,8]</sup>. Although the decision should be based on a risk-benefit analysis, it is the treatment of choice for high-risk obese patients and is considered effective and safe. The two most commonly performed BS are sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB)<sup>[9]</sup>.

However, BS does result in a significant reduction in the resting metabolic rate and in postoperative energy intake, which can lead to clinically significant nutrient deficiencies<sup>[10-12]</sup>. All of the BS procedures have varying degrees of impact on nutritional status and have the potential to cause clinically significant nutrient

deficiencies<sup>[13,14]</sup>. Without adequate follow-up, BS carries long-term risks, including poor nutrition and weight regain, which may be severe<sup>[15,16]</sup>. For example, malnutrition has been reported to lead to night blindness, cardiomyopathy, and neuropathy, in some instances leading to permanent disability or death<sup>[17]</sup>. Inadequate follow-up or non-adherence to supplements is often cited as a contributing factor in these case reports<sup>[18]</sup>.

The importance of follow-up care has been the subject of clinical guidelines. Since the 2014 British Obesity and Metabolic Surgery Society nutritional guidelines, several other nutritional guidelines have been issued for caring for BS patients<sup>[19-22]</sup>. In general, the recommended post-surgery dietary composition includes protein-rich food, vitamins, and minerals<sup>[23,24]</sup>. However, the effects of different nutrients at different times after surgery on remission in BS patients have not yet been described. As it has been reported that most of the overall weight change is in the first year after the operation, we aim to investigate the effect of nutrient levels on remission at different stages up to one year after surgery and to find out which nutrients were beneficial for remission and when to start supplementing, which will provide clinical nutrition guidance to BS patients.

## **METHODS**

### **Participants**

Participants were aged 18 years or older undergoing first-time BS at the Second People's Hospital of Qujing, Yunnan Province, China. They underwent surgery between January 2021 and November 2023, and all gave written informed consent to participate. They were followed up for this report until November 2023. Institutional review boards approved the protocol and informed consent forms.

### **Assessments and outcome measures**

Outcome data were collected by trained staff. Weight and other clinical data were collected within 3-15 days before surgery, and at 1, 3, 6, and 12 months after surgery, respectively. Means of weight and other clinical data and percentages of nutrient

deficiencies are reported. Deficiencies of albumin, iron, folic acid, and vitamin B12 were defined as blood concentrations below 35 g/L, 10.7 mM for men and 9.1 mM for women, 4.5 nM, and 200 pg/mL respectively. Patients taking anti-diabetes medication such as metformin (12 patients) or taking a lipid-lowering medication (2 patients) were not included in the analysis of the diabetes and lipid-related indicators.

### **Statistical analysis**

Descriptive statistics summarize the weight and clinical characteristics of the BS patients. Means, standard deviations, and percentages of nutritional deficiencies are reported for continuous data. One-way analysis of variance (ANOVA) followed by Dunnett's post-test was used for statistical comparison of multiple groups of samples. Correlations were analyzed using Pearson's *r* coefficient. Analyses were performed using GraphPad Prism 8.3 (GraphPad). *P* values less than 0.05 are considered to be statistically significant.

## **RESULTS**

### **Descriptive statistics**

There are 870 participants (mean [SD] age, 33.7 [10.2] years; 667 women [76%]), 79 undergoing RYGB, 37 undergoing SAGB, 747 undergoing SG, and 7 participants undergoing the less common procedures [Table 1]. 454, 156, 156, and 65 patients were followed for 1, 3, 6, 12 months respectively.

**1 Table 1. BMI and Clinical characteristics before surgery and during the 12-month follow-up.**

	before surgery	after surgery			
	0 m	1 m	3 m	6 m	12 m
Age (years) ( <i>n</i> )	33.71 ± 10.2 (871) a	33.17 ± 10.26 (454) a	33.58 ± 10.53 (156) a	33.51 ± 10.2 (156) a	35.25 ± 11.06 (65) a
Sex					
Female, <i>n</i> (%)	667 (76)	326 (72)	121 (78)	108 (69)	50 (77)
BMI (kg/m <sup>2</sup> ) ( <i>n</i> )	35.83 ± 5.54 (858) a	31.76 ± 5.147 (400) b	28.5 ± 4.211 (139) c	25.99 ± 3.737 (155) d	24.9 ± 4.051 (64) d
HgB (g/L) ( <i>n</i> )	151 ± 19.82 (871) a	150 ± 18.78 (439) a	143.6 ± 16.33 (151) b	141.7 ± 22.5 (153) b	134.7 ± 25.07 (65) b
ALT (U/L) ( <i>n</i> )	41.52 ± 33.22 (836) a	38.97 ± 31.75 (437) a	20.79 ± 14.98 (151) b	16.48 ± 12.09 (152) b	17.88 ± 10.15 (64) b
AST (U/L) ( <i>n</i> )	31.12 ± 21.68 (836) a	33.44 ± 16.84 (438) a	22.02 ± 8.16 (151) b	19.54 ± 7.878 (152) b	23.06 ± 18.72 (65) b
Cr (mM) ( <i>n</i> )	62.01 ± 24.03 (870) b	66.17 ± 20.3 (438) a	61.2 ± 15.9 (152) b	61.45 ± 14.46 (153) b	61.18 ± 14.49 (65) b
cholesterol (mM)	5.195 ± 1.681 (870) a	4.575 ± 2.39 (436) b	4.862 ± 1.029 (150) b	4.795 ± 0.8796 (153)	4.634 ± 0.887 (64)

(n)				b	b
LDL (mg/L) (n)	3.138 ± 0.6975 (869) a	2.808 ± 0.679 (433) b	3.057 ± 0.7642 (150) ab	2.972 ± 0.651 (153) ab	2.78 ± 0.6871 (64) b
HDL (mM) (n)	1.143 ± 0.231 (870) b	1.037 ± 0.266 (433) a	1.178 ± 0.257 (150) b	1.31 ± 0.256 (153) c	1.441 ± 0.267 (64) d
Triglycerides (mg/L) (n)	2.419 ± 2.091 (870) a	1.506 ± 0.528 (436) b	1.435 ± 0.5773 (150) b	1.086 ± 0.375 (153) bc	1.054 ± 0.421 (64) b
HbA1c (mM) (n)	6.644 ± 3.138 (852) a	5.648 ± 1.267 (380) b	5.232 ± 0.762 (132) b	5.144 ± 0.392 (147) b	5.217 ± 0.471 (58) b
Glucose (mM) (n)	8.112 ± 3.162 (134) a	5.082 ± 0.855 (394) b	5.03 ± 0.737 (138) b	4.519 ± 0.558 (149) c	4.581 ± 0.666 (63) c
Insulin (mIU/mL) (n)	34.47 ± 44.14 (140) a	17.15 ± 10.79 (77) b	12.77 ± 5.654 (38) b	11.39 ± 5.303 (54) b	8.409 ± 4.067 (20) b
CRP (ng/mL) (n)	4.325 ± 2.157 (140) a	3.351 ± 1.511 (76) b	2.659 ± 0.7473 (37) b	2.498 ± 0.9788 (54) c	1.974 ± 0.731 (20) c
<i>Nutrition and Metabolites</i>					
Iron (mM) (n)	16.35 ± 6.627 (860) a	15.49 ± 6.11 (368) a	15.8 ± 6.39 (136) a	17.28 ± 7.11 (150) a	15.22 ± 7.588 (64) a

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						a
Albumin (g/L) ( <i>n</i> )						41.88 ± 6.443 (65)
	43.02 ± 4.296 (871) a	43.21 ± 4.606 (441) a	42.77 ± 5.789 (151) a	43.02 ± 4.652 (152) a	a	
VB12 (pg/mL) ( <i>n</i> )						504.9 ± 184.9 (60)
	486.1 ± 194.1 (827) a	696.2 ± 367 (388) b	527.9 ± 206.6 (138) a	495.1 ± 249.4 (146) a	a	
Folic acid (ng/mL)						
( <i>n</i> )	8.908 ± 4.509 (824) a	11.15 ± 5.411 (386) b	12.25 ± 6.689 (137) b	11.27 ± 6.644 (146) b	11.5 ± 5.914 (60) b	
UA (mM) ( <i>n</i> )	445.2 ± 119.8 (870) b	475.3 ± 179.4 (441) a	392.6 ± 114.6 (153) bc	363.7 ± 108.5 (154) c	356 ± 96.52 (65) c	
Hcy (mM) ( <i>n</i> )						11.45 ± 5.357 (59)
	13.11 ± 9.995 (854) a	12.75 ± 7.567 (350) a	14.43 ± 10.19 (131) a	15.27 ± 12.15 (150) a	a	

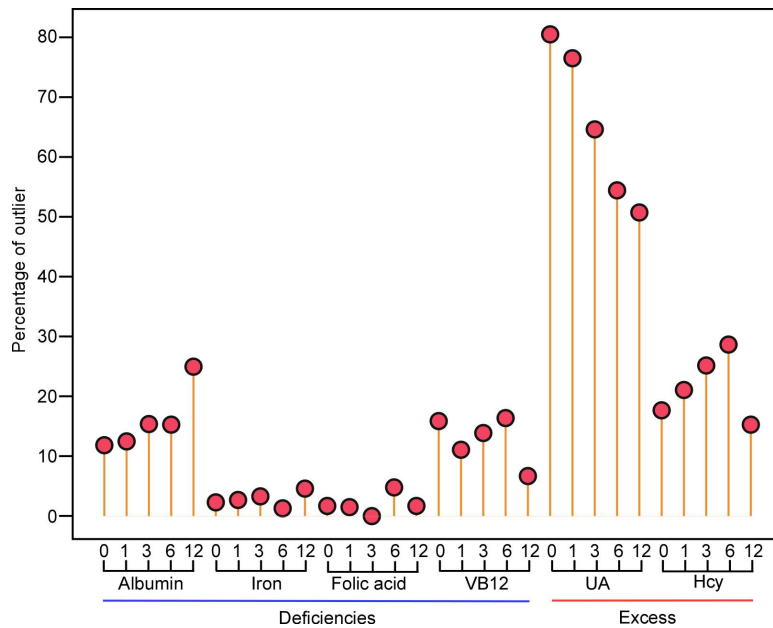
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### **Changes in weight and clinical characteristics**

The weight and clinical characteristics of the patients were recorded at four follow-up time points. The BMI showed a continuous decrease from a mean value of 35.8 before the operation to 24.9 12 months after the operation [Table 1]. The mean values of HgB, ALT, and AST were high preoperatively and showed a significant decrease to normal values three months after the operation. Lipids (cholesterol, LDL, and triglycerides) were significantly reduced one month after surgery, while HDL was significantly increased six months after surgery. As diabetes is one of the most common complications of obesity, indicators of diabetes were also assessed. The indicators (HbA1c, glucose, insulin, and CRP) were significantly reduced at one month after surgery, with further reductions in glucose and CRP at six months after surgery. Overall, BMI and clinical characteristics improved significantly 12 months after BS.

### **Changes in the level of nutrition**

We also observed an increase in vitamin B12 and folic acid levels after surgery, due to the medically prescribed vitamin supplements that patients need after surgery. However, nutritional deficiencies remain before and after surgery. Deficiencies of albumin and vitamin B12 are relatively rare, occurring in less than 5% of patients, while deficiencies of iron and folic acid are more common [Figure 1]. Iron deficiencies were 11.9%, 12.5%, 15.4%, 15.3%, and 25% before and after 1, 3, 6, and 12 months, respectively. Folic acid deficiencies were 15.9%, 11.1%, 13.9%, 16.4% and 6.7%. The metabolites UA and Hcy also showed higher accumulation in BS patients both before and after surgery. In 15 to 30 percent of patients, abnormal Hcy accumulation was found at various times. UA abnormalities were found in up to 80 percent of patients before surgery and in more than 50 percent of patients after surgery.

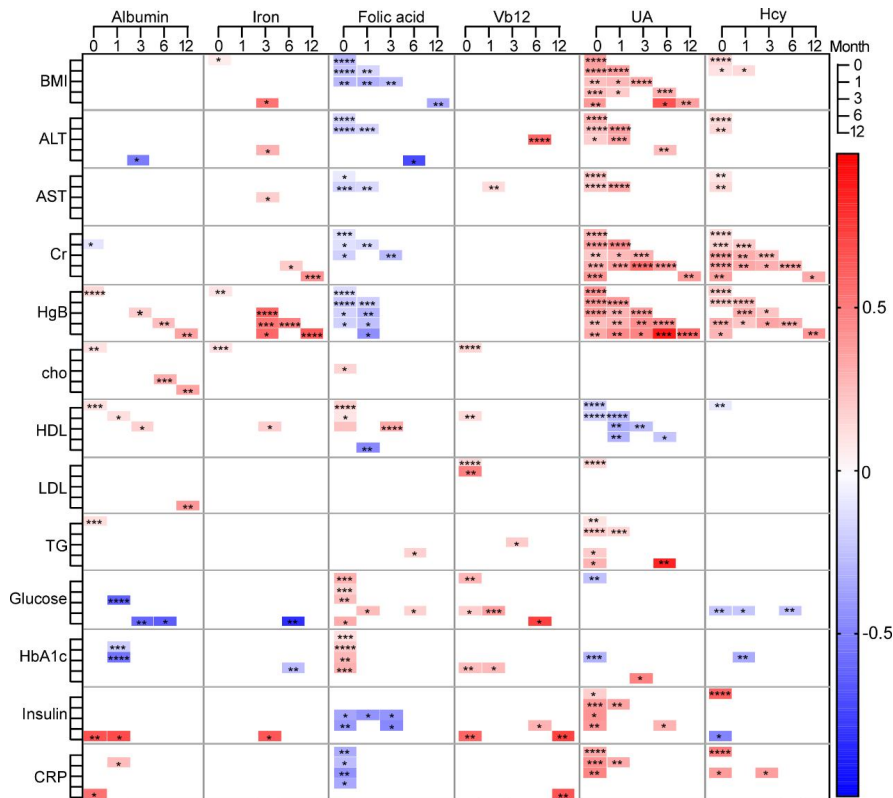


**Figure 1.** Percentage of patients with nutrient deficiencies and metabolite excesses before surgery and during the 12-month follow-up. 0 is the time of the operation, and 1, 3, 6, and 12 refer to the months following the operation.

**Association of nutritional level with remission**

We analyzed the relationships between individual levels of nutrition (iron, albumin, vitamin B12, and folic acid) or metabolites (UA and Hcy) and pre- and post-operative outcomes [Figure 2]. We found that preoperative albumin levels correlated positively with HgB, cho, HDL, TG, insulin, and CRP; 6-12 months postoperative levels also correlated positively with HgB, cho, and LDL; whereas 1-3 months postoperative levels were negatively correlated with ALT, glucose and HbA1c. Combined with the fact that more than 95% of patients do not have an albumin deficiency, we believe that BS patients do not have to be supplemented with a high-protein diet, except for 3 months after surgery. Preoperative iron levels were positively correlated with BMI, HgB, and cho, and levels 3 to 12 months postoperatively were also positively correlated with BMI, ALT, AST, Cr, HgB, LDL, and insulin. Given the data that between 10 and 30 percent of patients are iron deficient, we do not believe that iron supplementation is necessary for all patients except those who are iron deficient. Folic acid levels, especially before surgery and within one month after surgery, were negatively correlated with several indicators (BMI, ALT, AST, Cr, HgB, Insulin, and CRP). Despite the positive

correlation with glucose and HbA1c levels, we believe that folic acid is an essential nutrient for weight loss patients, especially preoperatively and in the first month postoperatively. The level of VB12 level before surgery was positively correlated with indicators of lipid and diabetes levels, and the level between 1 and 12 months after surgery was also positively correlated with diabetes indicators. Therefore, it is our opinion that VB12 supplementation should not be an option for patients with weight loss. The level of UA, especially before the operation and within one month after the operation, was positively correlated with numerous indicators (BMI, ALT, AST, Cr, HgB, LDL, TG, insulin, and CRP). In addition, UA levels in weight loss patients are generally high, especially before surgery, and more than 80% of patients have abnormally elevated UA levels, which is why we recommend that weight loss patients take UA-lowering drugs and reduce intake of purine-rich foods that metabolize UA. The pre-surgery Hcy level was positively correlated with many indicators (BMI, ALT, AST, Cr, HgB, insulin, and CRP), and the level of 12 months postoperatively with Cr and HgB. In patients with abnormally high levels of Hcy (between 10 and 30 percent of patients), we believe that B vitamins other than VB12 should be supplemented to increase metabolism and reduce Hcy levels.

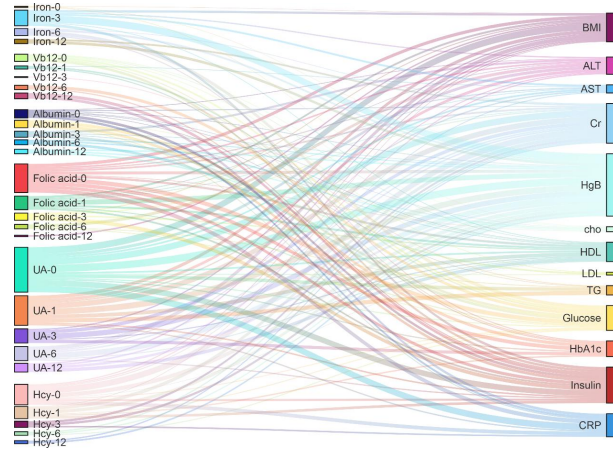


**Figure 2.** A heat map showing the association of nutrition and metabolite abundance with BMI and clinical characteristics. Correlations were analyzed using Pearson’s *r* coefficient. 0 is the time of the operation, and 1, 3, 6, and 12 refer to the months following the operation. \*, *P* < 0.05; \*\*, *P* < 0.01; \*\*\*, *P* < 0.001; \*\*\*\*, *P* < 0.0001.

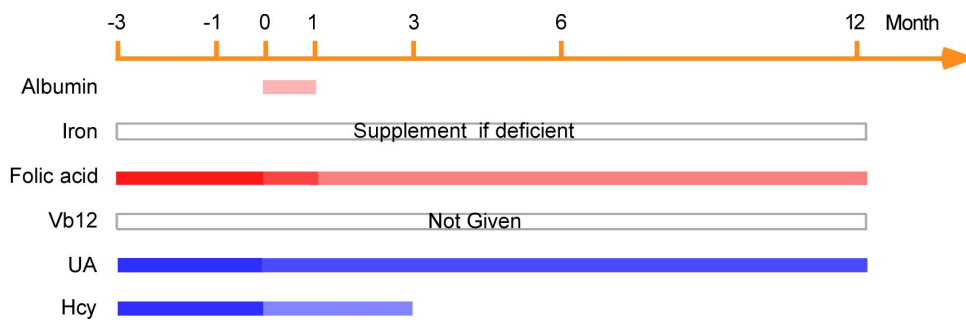
### Nutritional advice in obesity surgery

The Sankey diagram shows that levels of folic acid, UA, and Hcy are more important for surgical remission, while albumin, iron, and VB12 are less important [Figure 3]. Taken together with the data in Figure 2, it can be seen that albumin has a positive effect on surgical remission only one month after surgery, whereas iron and VB12 levels hurt surgical remission. Therefore, we believe that a high-protein diet can be supplemented one month after surgery and that VB12 should not be given to BS patients [Figure 4]. Although iron hurts surgical remission, we do not believe that iron supplementation should be given unless the patient is iron deficient, given the anemia seen in those BS patients. The levels of folic acid, UA, and Hcy, especially before surgery, can have a major impact on the remission of obesity. We suggest that folic acid supplementation,

less purine-rich food, and UA and Hcy-lowering drugs are needed before surgery, considering that folic acid mostly has a positive effect on remission and UA and Hcy have a negative effect. Folic acid supplementation and UA lowering should be continued for 12 months following surgery.



**Figure 3.** Sankey diagram showing the effect of nutrition and metabolites on BMI and clinical characteristics. 0 is the time of the operation, and 1, 3, 6, and 12 refer to the months following the operation.



**Figure 4.** Nutritional recommendations for BS patients at different time points. -1, -3 are the number of months before the operation, 0 is the time of the operation, and 1, 3, 6, and 12 refer to the months following the operation. Red means it needs to be replenished, green means it needs to be reduced, and the shade indicates the degree of change.

## DISCUSSION

We measured the clinical characteristics and nutrient levels in the serum of patients who

underwent BS to analyze the relationship between serum nutrients and remission at different stages of BS. Substantial weight loss was observed at 1-year follow-up after BS, consistent with previous results and further demonstrating that BS is an effective therapy for long-term weight loss<sup>[25-27]</sup>. Indicators of liver function (ALT and AST), diabetes (HbA1c, glucose, insulin, and CRP), and lipids (cho, LDL, HDL, and TG) all improved to some extent.

We further analyzed the improvements in health after BS as a function of the nutritional level. The results showed that one month after surgery albumin levels and folic acid were positively correlated with health improvement, iron and VB12 were negatively correlated with remission to a lesser degree, and the metabolites UA and Hcy were significantly negatively correlated with remission. Accordingly, nutritional recommendations include folic acid supplementation pre- and post-operatively, protein supplementation in the first month after surgery if not deficient, and reduction of UA and Hcy pre- and post-operatively in patients with weight loss. Given the other functions of serum iron, iron supplementation is recommended for patients with iron deficiency, whereas there is no need for VB12 supplementation at all. Previous studies have concluded that patients should be given short-term post-surgical protein supplements after surgery and lifelong multivitamin and mineral supplements because of the obvious nutritional deficiencies in BS patients after surgery<sup>[23,24]</sup>. Consistent with previous studies, our trials showed that protein supplementation should be given in the month after surgery. In contrast to previous studies, we believe that long-term multivitamin and mineral supplementation is not necessary. Vitamins affect remission differently. Based on their effects, we believe that folic acid is a must and that there should be no supplementation of VB12. Iron should only be given to deficient people, which does not exceed 30%. Our results highlight the influence of pre-surgical nutritional levels on post-surgical remission, which underlines the need for a preoperative supplementation with folic acid and a reduction of the UA and Hcy levels.

In conclusion, our data confirm that nutritional levels are associated with significant

improvements in weight and health at one-year post-surgery in a followed-up BS population. Short-term protein supplementation after surgery, lifelong folic acid supplementation, and reductions in UA and Hcy were associated with improved health outcomes. Our findings provide a clinical theory to guide the nutritional management of patients with BS.

### **Limitations of the study**

Conclusions regarding the long-term efficacy of BS in relation to the level of nutritional levels are limited. Analyzing follow-up remission with nutritional levels is a strength of the current study. Despite its efforts, our study did not achieve the complete personal follow-up needed to measure clinical and nutritional characteristics. This underlines that sustained efforts are needed to maximize retention and tracking, one of the major challenges of large, multi-center, observational clinical studies of BS. Another weakness is the under-reporting of nutrient categories in the data collection. To provide more effective nutritional advice, more nutrients should be covered and more data on vitamins and minerals should be included.

### **DECLARATIONS**

#### **Authors' contributions**

Designed the research: Z.H., L.Y., and L.H;

Supervised patient recruitment and data collection: L.Y., L.H;

Performed the patient recruitment, the patient examination, the experimental work and data collection: S.Z., S.J., X.J., C.X., Y.L., X.Y;

Analyzed and interpreted the data: S.L. and Z.H;

Wrote the paper: Z.H.

#### **Availability of data and materials**

All data associated with this study are present in the main text or the Supplementary Information. Raw data for the main figures and supplementary figures are available from the corresponding author upon request.

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### **Conflict of interest**

The authors declare no competing financial interests.

### **Ethical approval and consent to participate**

Not applicable.

### **Consent for publication**

Not applicable.

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