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The strategy of vitamin supplementation in Chinese patients with gastric cancer after gastrectomy: a prospective cohort study

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This study investigated the effects of oral multivitamin supplementation on vitamin levels in Chinese gastric cancer patients after gastrectomy, aiming to provide a basis for postoperative vitamin supplementation strategies. A total of 78 patients who underwent radical gastrectomy were divided into an experimental group (41 patients, receiving oral multivitamins) and a control group (37 patients). Levels of folic acid, vitamin B_{12}, vitamin B_1, and 25-hydroxyvitamin D were compared before and one month after surgery. Results showed that the level of vitamin B_1 in the experimental group was substantially higher than that in the control group when comparing the difference value between the preoperative and 1-month postoperative periods ($P < 0.05$). Although the deficiency rates of 25-hydroxyvitamin D and vitamin B_1 were relatively high in both groups, the vitamin B_1 deficiency rates of the experimental group 1 month postoperatively were significantly lower than preoperative rates ($P < 0.05$). Subgroup analysis revealed that partial gastrectomy patients in the experimental group had increased vitamin B_1 levels and decreased deficiency rates compared to the control group ($P < 0.05$). The study suggests that systematic multivitamin supplementation should be routinely administered to Chinese gastric cancer patients following gastrectomy, with particular emphasis on initiating vitamin B_1 and vitamin D supplementation upon resumption of semi-solid oral intake. Patients after total gastrectomy may require additional vitamin B_1 supplementation. Further studies with larger sample sizes and longer follow-up periods are needed to confirm these findings.

Keywords Gastric cancer, Radical gastrectomy, Folic acid, Vitamin B_{12}, Vitamin D, Vitamin B_1

Despite a gradual drop in mortality as medical therapy improves, gastric cancer remains the fifth most common malignancy in the world and the fifth largest cause of cancer-related death globally[1]. According to the World Health Organization's (WHO) World Cancer Report 2020 on gastric cancer statistics[2]China's stomach cancer incidence and mortality are the highest in the world. According to *Cancer Incidence and Mortality in China in 2022* reported by theNCCRC (National Central Cancer Registry of China), gastric cancer is a highly prevalent tumor in China. The mortality rates of gastric cancer in China are more than three times the world average

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(26.04%, 8.6%)[3]. Because the early signs of stomach cancer are so subtle and difficult for patients to recognize, the majority of patients are diagnosed with advanced gastric cancer. According to the GLOBOCAN cancer estimates 2022[1], the typical survival time for people with advanced stomach cancer is less than one year. With the advancement of medical technology and the maturation of minimally invasive surgery, radical resection is now the most significant treatment for gastric cancer[4].

Gastric cancer patients' physiological condition following gastrectomy is difficult to recover from, frequently resulting in weight loss, vitamin deficiencies, and other nutrition-related issues[5]. Folic acid, vitamin B_{12}, vitamin B_1, and vitamin D insufficiency were frequently reported[6–9]. Because the role of vitamin B_{12} in cell metabolism is closely connected to that of folic acid, vitamin B_{12} insufficiency and folic acid shortage can result in megaloblastic anemia and associated neurological disorders[10,11]. Furthermore, vitamin B_{12} insufficiency can result in gastrointestinal symptoms such as nausea, vomiting, diarrhea, limb numbness, and mental disorders[12]. However, a deficiency of vitamin B_1 will lead to initial symptoms such as poor appetite, nausea, and fatigue, which are similar to the early symptoms of chemotherapy and are not easily detected by gastric cancer patients[13]. It can also lead to further complications such as peripheral neuropathy and heart failure, and even Wernicke's encephalopathy in severe cases[14]. Therefore, if the supplementation of vitamin B_1 after gastrectomy for gastric cancer patients is ignored, it may lead to serious consequences. Vitamin D insufficiency has been linked to osteoporosis and immune system problems[15]. As a result, vitamin supplementation following gastrectomy for patients with stomach cancer can prevent related complications, increase chemotherapy tolerance, and improve patients' quality of life.

The consensus on nutritional and multi-disciplinary management for bariatric surgery in 2018[16] suggested that for patients who have undergone Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy, it is recommended that all multivitamin and trace element supplements be administered in orally chewable or liquid form during the early postoperative period (e.g., within the first 3 months). However, there is no standardized guideline on whether multivitamin preparations should be routinely supplemented after gastrectomy for stomach cancer, and when to begin supplementing. There are currently relatively few relevant studies that can be retrieved. Taiwan Nutritional Consensus on the Nutrition Management for Gastric Cancer Patients Receiving Gastrectomy[17] recommends corresponding vitamin B_{12} and vitamin D supplementation for patients undergoing total gastrectomy for gastric cancer according to different surgical methods. 2025 Gastric Cancer NCCN Clinical Practice Guidelines in Oncology[18] recommends Follow-up with appropriate practitioners or specialists should be established for lifelong monitoring and management of potential nutritional sequelae of gastrectomy, which may include, but are not limited to, vitamin B_{12}, iron, zinc, calcium, and vitamin D deficiencies. Consider routine supplementation with a daily multivitamin/mineral complex, vitamin B_{12}, calcium, and vitamin D. Chinese patients with gastric cancer and clinicians generally do not pay enough attention to nutrition at the present stage, and routine postoperative follow-up nutrition indicators are incomplete. When the researchers conducted nutritional follow-up 1 month after surgery, most patients in the control group paid more attention to nutrition and began to spontaneously switch to the experimental group. To ensure the accuracy of clinical research results, the trend of vitamin levels within one month following vitamin supplementation was evaluated in Chinese patients with gastric cancer after gastrectomy.

Materials and methods

Study design and participants

A prospective cohort study was conducted on patients diagnosed with gastric cancer and who underwent radical gastrectomy, who were admitted to Nanjing Drum Tower Hospital between May 2019 and May 2021. The individuals were all between the ages of 18 and 80, diagnosed with gastric cancer and required surgical intervention. 122 patients were eliminated for the reasons mentioned in Fig. 1. In this institution, the vitamin B1 testing is an additional paid service. Due to variations in patients' emphasis on postoperative vitamin supplementation and differences in health awareness, 41 participants in the experimental group and 37 in the control group underwent vitamin B1 testing. A total of 78 patients were enrolled, with an average age of 57.38 years, comprising 50 men and 28 women. Members of Nanjing Drum Tower Hospital's gastric surgery department medical team conducted the procedure. Gastrectomy procedures included partial and total radical gastrectomy. Patients were divided into an experimental group (oral multivitamin preparation) and a control group (no oral multivitamin preparation) based on whether they received an oral multivitamin preparation from the initiation of a semi-liquid diet (postoperative day 7) to 1 month after surgery, implementing identical clinical pathways and standardized perioperative management protocols. The researchers collected general patient information, such as sex, age, diagnosis, surgical information, and pathological stage. Simultaneously, the relevant personnel were organized to conduct regular postoperative telephone follow-up visits to the patients weekly to ensure their medication compliance. Preoperatively and 1 month postoperatively, two groups of patients were referred to the Pharmacy Clinic for nutritional indicator evaluation, including serum folic acid level, serum vitamin B_{12} level, serum vitamin B_1 level, serum 25-hydroxyvitamin D level, food intake, and other nutritional indicators. All patients were questioned by a clinical pharmacist to ensure that patients in the test group were taking the multivitamin preparation daily after surgery as prescribed. This study was approved by the Ethics Committee of Nanjing Drum Tower Hospital (IRB#2019-173-01) on 24 July 2019. The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants prior to their inclusion in the study. The study has been registered with the Chinese Clinical Trial Registry (https://www.chictr.org.cn/; Registration number: ChiCTR2400087619; date: 31/07/2024). A statement to confirm that all methods were carried out in accordance with relevant guidelines and regulations.

For all patients scheduled for gastrectomy, nutritional risk screening using the Nutritional Risk Screening 2002 (NRS 2002) was performed within 24 h of admission. Patients without preoperative nutritional risk (NRS 2002 < 3) received no immediate nutritional intervention but underwent repeat NRS 2002 assessment after

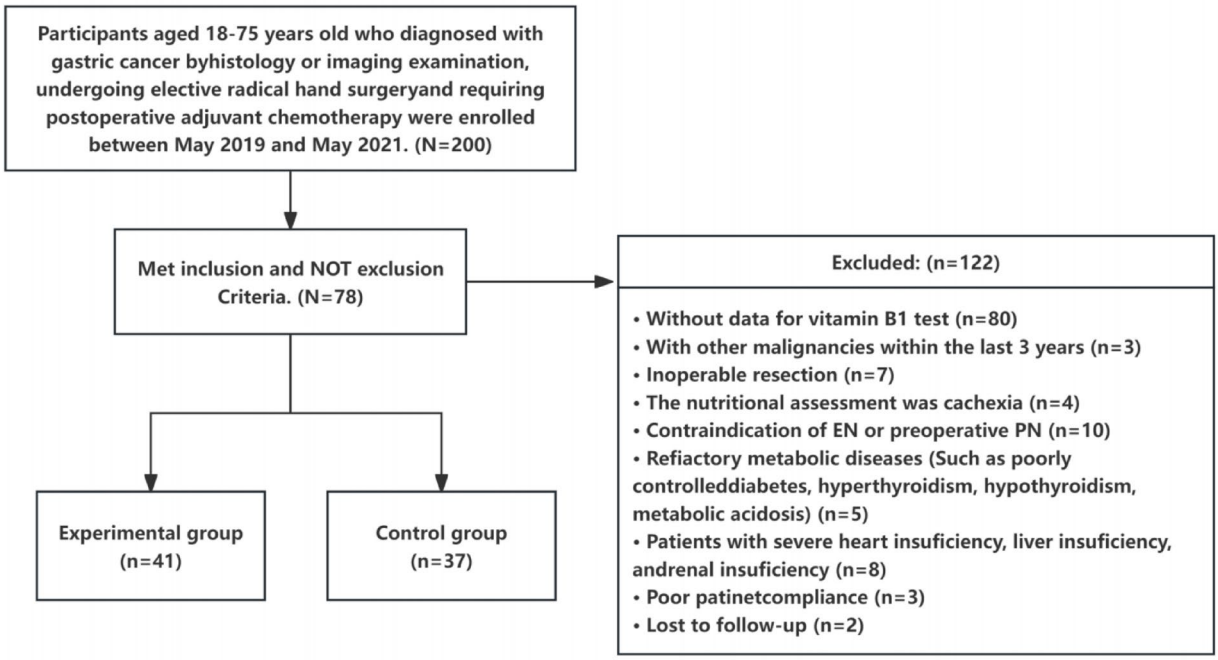

Fig. 1. Flowchart of patient eligibility and study design.

one week. Those identified with nutritional risk (NRS 2002 ≥ 3) were provided nutritional support, preferably via oral enteral nutrition. Postoperatively, both cohorts were maintained nil per os (NPO), with nutritional support transitioning from parenteral nutrition (PN) to enteral nutrition (EN), ultimately advancing to oral intake. All patients received intravenous vitamin administration, including one bottle of Water-soluble Vitamin for Injection and one bottle of Fat-Soluble Vitamin Injection (II). A standardized perioperative management regimen and identical intravenous vitamin administration protocol were maintained for both patient cohorts throughout the study period.

Assessment of vitamin level

The vitamin levels of the subjects were examined by electrochemical method (LK3000V, Lanbiao, Tianjin, China) in the Nanjing Drum Tower Hospital. Fig. 2 lists the vitamin components of the multivitamin formulation used in this study. The determination of folic acid deficiency was based on serum folic acid level < 2ng/mL[19], while vitamin B_{12} deficiency was determined by serum vitamin B_{12} < 200 pg/mL[20], vitamin B_1 deficiency was determined by serum vitamin B_1 < 50 nmol/L (According to the reference guidelines, vitamin B1 deficiency is defined as a serum vitamin B1 level of < 70 nmol/L. However, due to variations in laboratory assay methodologies, the hospital defines the deficiency as a level < 50 nmol/L.)[20], and vitamin D deficiency was determined by 25-hydroxyvitamin D < 20 ng/mL[21,22].

Statistical analysis

Prior to the study, the primary endpoints were predefined as serum levels of vitamin B_{12}, folate, vitamin D, and vitamin B_1 at 1-month postoperatively. Given the absence of existing data comparing vitamin B_1 levels between supplemented and non-supplemented cohorts in Chinese gastric cancer patients during this critical postoperative window, the sample size was determined per pilot study guidelines[23] recommending 10–40 participants per group. Accounting for practical constraints, a minimum of 30 subjects per cohort was established. Statistical analysis was performed using SPSS 26.0 (IBM, USA). The chi-square test was used for comparison of counting data, and the independent sample *t* test was used for comparison of measurement data with a normal distribution. The data were expressed as mean ± standard deviation. The Wilcoxon rank-sum test was used for non-normal distribution, and data were expressed as median (interquartile spacing). The level of significance was set at 5%.

Results

General characteristics

After obtaining informed consent, 78 patients undergoing gastrectomy for gastric cancer were finally included. There were 41 patients in the experimental group and 37 patients in the control group with an average age of 57.38 years. The participants' baseline characteristics are shown in Table 1, and the results demonstrate that there is no significant difference between the two groups ($P > 0.05$). The biochemical findings and other details of the research participants are shown in Table 2.

The composition of Centurm Silver (per pill)			
Vitamin A	4000 IU	**chlorine**	72 mg
Vitamin D	400 IU	**magnesium**	100 mg
Vitamin E	45 IU	**iron**	9 mg
Vitamin B_1	1.5mg	**copper**	2 mg
Vitamin B_2	1.7mg	**zinc**	15 mg
Vitamin B_6	3mg	**manganese**	2.5 mg
Vitamin C	60mg	**iodine**	150 μg
Vitamin B_{12}	25 μg	**chromium**	100 μg
Vitamin K_1	10 μg	**molybdenum**	25 μg
Folic acid	200 μg	**selenium**	25 μg
calcium	200 mg	**nickel**	5 μg
phosphorus	48 mg	**silicon**	10 μg
potassium	80 mg	**vanadium**	10 μg

Fig. 2. List of multivitamin ingredients (Centrum Silver).

Project	Experimental group ($N = 41$)	Control group ($N = 37$)	P-value[a]
Sex (Male/Female)	28/13	22/15	0.417
Age	56.39 ± 12.66	58.49 ± 9.84	0.421
BMI (kg/m^2)			
< 18.5	0	0	0.549
18.5–24	26	21	
> 24	15	16	
NRS 2002 (score)			
< 3	20	20	0.642
≥ 3	21	17	
PG-SGA (score)			
< 4	6	9	0.278
≥ 4	35	28	
Surgical method			
Distal gastrectomy	18	15	0.874
Proximal gastrectomy	3	2	
Total gastrectomy	20	20	
Tumor staging			
Stage Ⅰ	11	13	0.191
Stage Ⅱ and Stage Ⅲ	27	24	
Stage Ⅳ	3	0	

Table 1. Baseline characteristics of patients with gastric cancer undergoing gastrectomy. [a]Calculated by the Wilcoxon rank sum test or Pearson's chi-square test. BMI: Body Mass Index; NRS 2002: Nutritional Risk Screening 2002; PG-SGA: Patient-Generated Subjective Globe Assessment.

Comparison of vitamin levels

Fig. 3 depicts the serum vitamin levels of two groups of patients preoperatively and 1 month postoperatively. When comparing the serum vitamin levels of two groups patients preoperatively and 1 month postoperatively, there were no significant differences in preoperative levels of folic acid, vitamin B_{12}, vitamin B_1, and 25-hydroxyvitamin D between the two groups ($P > 0.05$). It was discovered that the level of vitamin B_1 in the experimental group was substantially higher than that in the control group when comparing the difference value between the preoperative and 1-month postoperative periods ($P < 0.05$). The experimental group's level of

Project	Preoperative		*P*-value[a]	One-month postoperative		*P*-value[a]
	Experimental group (*N* = 41)	Control group (*N* = 37)		Experimental group (*N* = 41)	Control group (*N* = 37)	
ALT U/L	14.40 (10.70–22.00)	18.60 (13.55–29.55)	0.097	23.20 (17.60–31.50)	21.70 (14.70–36.40)	0.990
AST U/L	18.80 (13.10-22.95)	20.08 (17.23–25.63)	0.090	20.00 (15.80–29.60)	20.45 (15.50-26.45)	0.995
ALB g/L	39.00 (36.85–40.75)	39.65 (37.50–41.60)	0.465	41.20 (39.78–43.13)	42.45 (40.50–43.50)	0.226
TBil umol/L	7.90 (6.00-12.85)	10.10 (6.70–14.20)	0.205	10.60 (8.30–13.70)	10.40 (8.95–12.55)	0.739
DBil umol/L	1.80 (1.15–2.20)	1.90 (1.10–2.40)	0.419	2.30 (1.55–3.10)	2.00 (1.40–2.60)	0.237
TBA umol/L	3.90 (2.45–5.45)	3.80 (2.40–4.90)	0.552	1.30 (0.90–3.70)	1.80(0.80–3.45)	0.812
Hb g/L	125.34 ± 24.91	129.78 ± 18.35	0.382	123.53 ± 14.60	121.55 ± 12.49	0.541
PAB mg/L	218.56 ± 46.91	220.09 ± 40.50	0.884	198.91 ± 52.83	199.88 ± 40.23	0.937
ChE/L	6.94 ± 1.58	7.36 ± 1.96	0.305	6.20 (5.10–6.70)	5.90 (5.25–6.80)	0.785
Food-intake[b]	–	–	–	1182.00 (857.50-1697.50)	1039.00 (900.00-1225.00)	0.130

Table 2. Values of preoperative biochemical indicators and nutrient intake of patients undergoing gastrectomy. [a]Calculated by parametric (*t*-test) or nonparametric (Wilcoxon) as appropriate. [b]The average estimated daily energy intake (kcal). ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ALB: Albumin; TBil: Total bilirubin; DBil: Direct Bilirubin; TBA: Total Bile Acid; Hb: Hemoglobin; PAB: Prealbumin; ChE: Cholinesterase.

vitamin B_1 was significantly increased at 1-month postoperative compared to preoperative periods, and other specific data are shown in Table 3.

Table 4 shows the comparison of vitamin deficiency rates between the two groups preoperatively and 1 month postoperatively. The deficiency rates of 25-hydroxyvitamin D and vitamin B_1 were relatively high in both groups, while the deficiency rates of folic acid and vitamin B_{12} were low in both groups. There were no significant differences in the preoperative vitamin deficiency rates between the two groups ($P > 0.05$). The vitamin B_1 deficiency rates of the experimental group 1 month postoperatively were significantly lower than preoperative rates ($P < 0.05$). Furthermore, we compared the folate, vitamin B12, and vitamin D levels in patients with unavailable vitamin B1 measurements ($N = 80$). No statistically significant differences were observed in the difference value of these vitamins or in the rates of their deficiencies($P > 0.05$). Detailed data are provided in Supplementary Tables 1, 2, and 3.

Subgroup analyses

Considering that the operation may have an impact on vitamin levels in patients after gastrectomy, the 78 patients were divided into two subgroups according to the type of surgery: partial gastrectomy (including distal and proximal gastrectomy) and total gastrectomy. This analysis compared whether there were differences in vitamin levels between the oral multivitamin preparation group and the non-oral multivitamin preparation group under the conditions of the same surgical procedure. There were 40 total gastrectomy patients and 38 partial gastrectomy patients. There were no statistically significant differences between the two groups in terms of baseline characteristics ($P > 0.05$). Specific data are shown in Table 5.

The results showed that there was no significant difference in the preoperative levels of folic acid, vitamin B_{12}, vitamin B_1, and 25-hydroxyvitamin D between the two groups in the total gastrectomy group ($P > 0.05$). The experimental group's levels of vitamin B_{12}, and vitamin B_1 were increased at the 1-month postoperative period compared to the preoperative period, whereas the control group's levels of folic acid were increased at the 1-month postoperative period compared to the preoperative period ($P < 0.05$). There were no significant differences in the rates of vitamin deficiency between the two groups at the preoperative period ($P > 0.05$), and there were no significant differences in the rates of folic acid, vitamin B_{12}, vitamin B_1 and 25-hydroxyvitamin D deficiency between the two groups at the 1-month postoperative period ($P > 0.05$).

In the group of partial gastrectomy, there was no significant difference in the preoperative levels of folic acid, vitamin B_{12}, vitamin B_1 and 25-hydroxyvitamin D between the two groups ($P > 0.05$). It was discovered that the vitamin B_1 level in the experimental group was significantly higher than that in the control group when comparing the difference value at the 1-month postoperative period compared to the preoperative period ($P < 0.05$). There were no significant differences in the preoperative vitamin deficiency rates between the two groups ($P > 0.05$). The vitamin B_1 deficiency rates of the experimental group at the 1-month postoperative period were significantly lower than preoperative rates ($P < 0.05$), while the deficiency rates of folic acid, vitamin B_{12}, vitamin B_1 and 25-hydroxyvitamin D of the control group at the 1-month postoperative period were not significantly different from the preoperative rates ($P > 0.05$). Specific data are shown in Tables 6 and 7.

Discussion

Although there is no consensus on the evaluation, prevention and treatment of postoperative vitamin deficiency in patients with gastrectomy for gastric cancer, according to the ASMBS Comprehensive Health and Nutrition Guidelines for Surgical Weight Loss Patients[20] patients undergoing gastrectomy who have lost weight require routine screening and supplementation of folic acid and vitamin B_{12} as well as routine screening and

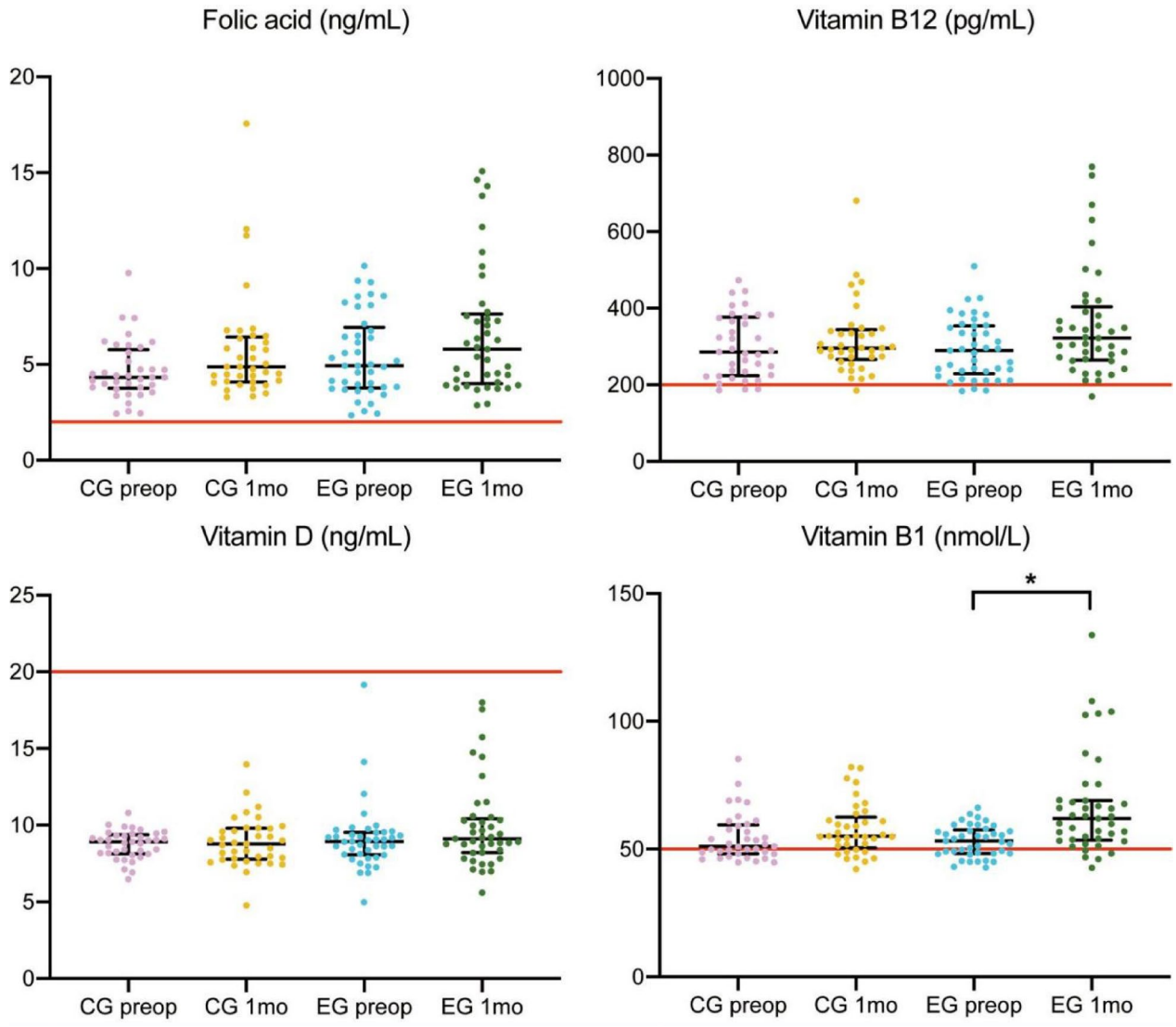

Fig. 3. Serum vitamin levels of the control group (CG) and experimental group (EG) during the preoperative (preop) period and 1-month (1 mo) postoperative period. *$P < 0.05$.

Project	Time	Experimental group	Control group	*P*-value[a]
Folic acid (ng/mL)	Preoperative	4.94 (3.78–6.94)	4.33 (3.76–5.77)	0.139
	1-month postoperative	5.79 (4.00-7.64)	4.88 (4.09–6.43)	0.252
	Difference value	0.65 (-0.39-2.23)	0.10 (-0.71-2.42)	0.674
Vitamin B_{12} (pg/mL)	Preoperative	289.71 (228.87-354.24)	286.36 (223.96-376.17)	0.749
	1-month postoperative	322.28 (264.90-404.10)	295.98 (266.60-344.09)	0.265
	Difference value	41.18 (-11.98-136.05)	20.51 (-82.24-69.92)	0.113
25-hydroxyvitamin D(ng/mL)	Preoperative	8.94 (8.08–9.54)	8.91 (8.15–9.38)	0.719
	1-month postoperative	9.12 (8.21–10.43)	8.78 (7.80–9.80)	0.193
	Difference value	0.41 (-0.84-1.27)	0.15 (-0.78-0.79)	0.435
Vitamin B_1 (nmol/L)	Preoperative	55.34 (48.95–60.19)	52.06 (48.22–61.59)	0.708
	1-month postoperative	62.18 (53.85–68.84)*	55.18 (51.34–64.89)	0.069
	Difference value	9.23 (0.87–17.18)	1.69 (-3.72-12.98)	0.045*

Table 3. Comparison of serum vitamin levels between the preoperative and 1-month postoperative period. **P*-value < 0.05 versus preoperative serum vitamin levels in the experimental group or control group. [a]Calculated by the Wilcoxon rank sum test.

Group	Project	Quantity (Deficiency/Normal)		X^2	*P*-value[a]
		Preoperative [b]	1-month postoperative		
Experimental group	Folic acid	0/41	0/41	0.000	1.000
	Vitamin B_{12}	3/38	1/40	0.263	0.608
	25-hydroxyvitamin D	41/0	41/0	0.000	1.000
	Vitamin B_1	16/25	5/36	7.746	0.005*
Control group	Folic acid	0/37	0/37	0.000	1.000
	Vitamin B_{12}	3/34	1/36	0.264	0.607
	25-hydroxyvitamin D	37/0	37/0	0.000	1.000
	Vitamin B_1	17/20	10/27	4.893	0.091

Table 4. Comparison of vitamin deficiency rates between the preoperative and 1-month postoperative period. [a]Calculated by Pearson's Chi square test. [b]There was no significant difference in preoperative vitamin deficiency rates between the two groups. *P-value < 0.05.

Project	Total gastrectomy CG ($N = 20$)	Total gastrectomy EG ($N = 20$)	*P*-value[a]	Partial gastrectomy CG ($N = 17$)	Partial gastrectomy EG ($N = 21$)	*P*-value[a]
Sex (Male/Female)	12/8	14/6	0.507	10/7	14/7	0.618
Age	60.30 ± 10.92	58.75 ± 11.51	0.665	56.35 ± 8.21	54.74 ± 13.36	0.640
BMI (kg/m^2)						
< 18.5	0	0	1.000	0	0	0.491
18.5–24	10	10		11	16	
> 24	10	10		6	5	
NRS 2002 (score)						
< 3	10	11	0.752	10	9	0.328
≥ 3	10	9		7	12	
PG-SGA (score)						
< 4	5	1	0.184	4	5	1.000
≥ 4	15	19		13	16	
Tumor staging						
Stage Ⅰ	4	1	0.180	9	10	0.449
Stage Ⅱ and Stage Ⅲ	16	18		8	9	
Stage Ⅳ	0	1		0	2	

Table 5. Baseline characteristics of the subgroup analysis patients. [a]Calculated by Pearson's Chi square test, parametric (*t*-test) or nonparametric (Wilcoxon) as appropriate.

supplementation of vitamin D. Furthermore, the study by Koike[14] suggested that postoperative monitoring of vitamin B_1 should be paid attention to gastrectomy patients complicated with polyneuropathy.

In recent years, most of the discussions on postoperative vitamin deficiency in patients with gastrectomy for gastric cancer have focused on supplementary treatment after corresponding nutritional complications, and few patients with gastrectomy for gastric cancer are provided with routine preventive supplementation strategies. In patients at high risk of folic acid deficiency, further measures such as oral folic acid supplementation or food fortification should be used to correct the folic acid deficiency status[24]. Intramuscular injection of vitamin B_{12} used to be the only known treatment for patients with vitamin B_{12} deficiency after gastrectomy, however Hyoung-il[25] found that oral vitamin B_{12} was one of the safe and effective alternative treatments. This provides a theoretical basis for this study to supplement vitamin B_{12} with oral multivitamin preparation. Most studies now use active vitamin D preparations for supplemental treatment of vitamin D deficiency. Vitamin B_1 deficiency poses significant risks for postgastrectomy patients due to limited bodily reserves (≈ 30 mg) and a short biological half-life (10–20 days), predisposing individuals to deficiency through inadequate intake, malabsorption, or increased metabolic demands[26]. Consequently, consistent dietary vitamin B_1 replenishment is imperative. The sequelae of vitamin B_1 deficiency span neurological, cardiovascular, and gastrointestinal systems, potentially causing irreversible organ damage or mortality. The most prevalent manifestation is wet beriberi—a cardiomyopathy characterized by edema and lactic acidosis. Vitamin B_1 deficiency is also implicated in neurodegenerative pathologies including Alzheimer's, Parkinson's, and Huntington's diseases[27]. Consequently, we recommend initiating vitamin B_1 supplementation upon resumption of semi-solid oral intake in postgastrectomy gastric cancer patients, coupled with regular serum vitamin B_1 monitoring. Maintenance of levels > 70 nmol/L is clinically advisable[20]. However, a study[21] pointed out that vitamin D supplementation with oral multivitamin preparations is also feasible, considering that ordinary vitamin D has more targets of

Subgroup	Project	Time	Control group	Experimental group	*P*-value[a]
Total gastrectomy (*N* = 40)	Folic acid (ng/mL)	Preoperative	4.33(3.17–4.74)	4.61 (3.73–8.23)	0.194
		1-month postoperative	4.88 (4.08–5.84)*	4.54 (3.91–7.27)	0.735
		Difference value	1.28 ± 2.81	0.57 ± 3.37	0.472
	Vitamin B_{12} (pg/mL)	Preoperative	264.30 (219.27-321.47)	243.29 (210.65-294.37)	0.675
		1-month postoperative	295.98 (269.71–330.10)	302.72 (272.12-390.66)*	0.198
		Difference value	14.09 ± 102.76	82.06 ± 112.86	0.053
	25-hydroxyvitamin D (ng/mL)	Preoperative	9.06 (8.31–9.51)	8.91 (7.85–9.77)	0.665
		1-month postoperative	8.29 (7.74–9.44)	8.79 (7.45–11.45)	0.440
		Difference value	-0.46 (-1.42-0.66)	-0.07 (-1.00-1.49)	0.542
	Vitamin B_1 (nmol/L)	Preoperative	57.92 ± 2.72	52.57 ± 1.35	0.059
		1-month postoperative	55.18 (49.79–59.68)	57.00 (51.59–65.12)*	0.453
		Difference value	-1.57 (-3.88-5.04)	7.27 (-2.22-11.73)	0.078
Partial gastrectomy (*N* = 38)	Folic acid (ng/mL)	Preoperative	4.42 (3.90–6.10)	5.34 (3.96–6.63)	0.378
		1-month postoperative	4.76 (4.01–6.50)	6.36 (4.63–9.88)	0.106
		Difference value	-0.30 (-1.10-2.14)	0.88 (-0.12-3.34)	0.182
	Vitamin B_{12} (pg/mL)	Preoperative	318.60 ± 78.68	320.81 ± 79.37	0.932
		1-month postoperative	292.55 (248.59-422.12)	344.28 (233.96-427.71)	0.692
		Difference value	14.08 (-91.36-111.31)	4.79 (-25.73-111.44)	0.670
	25-hydroxyvitamin D (ng/mL)	Preoperative	8.64 (7.98–9.28)	9.03 (8.25–9.45)	0.394
		1-month postoperative	9.02 (7.98–9.88)	9.54 (8.74–10.43)	0.258
		Difference value	0.15 (-0.35-1.08)	0.58 (-0.58-1.27)	0.500
	Vitamin B_1 (nmol/L)	Preoperative	49.94 (46.51–54.05)	55.43 (49.79–59.53)	0.126
		1-month postoperative	54.83 (50.74–64.62)	66.80 (58.30–81.50)*	0.013†
		Difference value	5.73 ± 2.78	19.63 ± 5.93	0.045†

Table 6. Comparison of serum vitamin levels between the preoperative and 1-month postoperative period in subgroup analysis. **P*-value < 0.05 versus preoperative serum vitamin levels within the experimental group or the control group. [a]Calculated by parametric (*t*-test) or nonparametric (Wilcoxon) as appropriate. †*P*-value < 0.05.

Subgroup	Group	Project	Quantity (Deficiency/Normal)		X^2	*P*-value[a]
			Preoperative [b]	1-month postoperative		
Total gastrectomy	Experimental group (*N* = 20)	Folic acid	0/20	0/20	0.000	1.000
		Vitamin B_{12}	3/17	0/20	1.441	0.230
		25-hydroxyvitamin D	20/0	20/0	0.000	1.000
		Vitamin B_1	11/13	5/19	3.375	0.066
	Control group (*N* = 20)	Folic acid	0/20	0/20	0.000	1.000
		Vitamin B_{12}	2/18	1/19	0.000	1.000
		25-hydroxyvitamin D	20/0	20/0	0.000	1.000
		Vitamin B_1	7/8	5/10	0.558	0.710
Partial gastrectomy	Experimental group (*N* = 21)	Folic acid	0/21	0/21	0.000	1.000
		Vitamin B_{12}	0/21	0/21	0.000	1.000
		25-hydroxyvitamin D	21/0	21/0	0.000	1.000
		Vitamin B_1	5/12	0/17	7.798	0.044*
	Control group (*N* = 17)	Folic acid	0/17	0/17	0.000	1.000
		Vitamin B_{12}	1/16	0/17	0.000	1.000
		25-hydroxyvitamin D	17/0	17/0	0.000	1.000
		Vitamin B_1	7/15	4/18	0.485	0.486

Table 7. Comparison of vitamin deficiency rates between the preoperative and 1-month postoperative period in subgroup analysis. [a]Calculated by Pearson's Chi square test. [b]There was no significant difference in preoperative vitamin levels between the two groups. **P*-value < 0.05.

action than active vitamin D, has a good safety profile, is clinically monitorable, and can be a preferred option for vitamin D supplementation.

The lack of oral vitamin supplement absorption due to altered digestion and impaired nutrition absorption may develop following total or subtotal gastrectomy. The vitamin deficiencies are attributed to malabsorption, rapid gastrointestinal transit time and bacterial overgrowth[17]. Since water-soluble vitamins are stored less in the body, patients may develop deficiency as early as 24 h after the operation. Moreover, fat-soluble vitamins will also be rapidly depleted during the surgical procedure. Consequently, we recommend routine oral multivitamin supplementation commencing upon initiation of semi-solid diets in postgastrectomy gastric cancer patients, with prioritized administration of vitamin B_1 and vitamin D. Periodic monitoring of vitamin status is essential. For patients failing to achieve optimal serum concentrations with maximally tolerated oral dosing, intramuscular administration of vitamin B_1 and vitamin D represents an alternative therapeutic strategy. It can be seen from the research results that the level of vitamin B_1 in the experimental group was significantly higher than that in the control group when comparing the difference value between preoperatively and 1 month postoperatively, and the deficiency rate of vitamin B_1 in the experimental group 1 month postoperatively significantly decreased compared with that preoperatively. In conclusion, oral multivitamin preparation within 1 month after gastrectomy can effectively improve the level of serum vitamin B_1 and significantly reduce the rate of vitamin B_1 deficiency in patients with gastric cancer. Subgroup analyses showed that in partial gastrectomy patients, the difference value of vitamin B_1 level between the preoperative and 1-month postoperative periods in the experimental group was greater compared with that in the control group, the deficiency rate of vitamin B_1 in the experimental group was similarly decreased at 1 month postoperatively compared with preoperatively. The reason may be that part of the gastric function is preserved for gastric cancer patients undergoing partial gastrectomy, which is conducive to the absorption of vitamin B_1. These patients after total gastrectomy may require additional vitamin B_1 supplementation.

The timing of the onset of each of these vitamin deficiencies may be related to the time it takes to deplete the body's stores of each vitamin. When folic acid is not ingested in the diet by those with adequate nutritional status, the body's storage capacity can be maintained for at least 3 months without deficiency[28]. The liver stores a large amount of vitamin B_{12}, but people on a restricted diet may develop vitamin B_{12} deficiency in about three years[10]. Since the body is unable to synthesize vitamin B_1, we must meet our body's vitamin B_1 needs through our diet. For people with a dietary deficiency of vitamin B_1, the body's stores of vitamin B_1 only last for a maximum of 18 days. After about 3 weeks of vitamin B_1 deficiency, blood levels of vitamin B_1 also decline[29,30]. Therefore, in order to maintain the normal content of vitamin B_1 in tissues, regular replenishment is needed. The results of a Chinese study[31] showed that in a total of 963 healthy adults aged 45 years or older, the serum vitamin B_1 level was 99.73 (83.10, 140.62) nmol/L, which was significantly higher than the preoperative and 1-month postoperative serum vitamin B_1 levels of the gastric cancer patients in the present study (52.12 nmol/L, 57.67 nmol/L). Therefore, considering the short storage time of vitamin B_1 in the body, serum vitamin B_1 levels in gastric cancer patients were significantly lower than those in the normal population, and vitamin B_1 deficiency may lead to serious complications such as Wernicke's encephalopathy or even increase the risk of death[32] combined with the finding of the present study that gastric cancer patients who underwent gastrectomy can effectively improve their serum vitamin B_1 levels and significantly reduce the rate of vitamin B_1 deficiency through supplementation within 1 month after surgery, we think targeted vitamin B_1 supplementation is advisable within one month post-surgery.

At the same time, in a multi-center study of 2173 healthy adults from five cities in China[33] vitamin D deficiency was observed to be prevalent in all age groups , with the average 25-hydroxyvitamin D level of all participants being 19.4 ± 6.4ng/mL, and it was also significantly higher than the serum 25-hydroxyvitamin D levels of the gastric cancer patients in this study (9.45 ng/mL, 10.47 ng/mL) in the preoperative and 1-month postoperative periods. In addition, gastric cancer patients who need chemotherapy may also further increase the risk of vitamin D deficiency by not being able to spend long periods in the sun. Based on the findings of this study and the high rate of vitamin D deficiency in the Chinese population, it is recommended that Chinese patients with gastric cancer receive vitamin D supplements after gastrectomy.

Due to the deficiency of folic acid storage in vivo for about 3 months[34] according to the original trial design, patients' vitamin levels would be collected up to 3 months later. However, due to the large number of lost follow-up patients, it is necessary to increase the number of cases and extend the monitoring period in order to effectively evaluate the need for oral multivitamin preparation. Based on our study, we recommend implementing systematic multivitamin supplementation as standard care for Chinese gastric cancer patients post-gastrectomy, with prioritized administration of vitamin B_1 and vitamin D initiated upon resumption of semi-solid oral intake. This strategy can prevent Wernicke encephalopathy and mitigate neurogastrointestinal symptoms, including anorexia, nausea, vomiting, abdominal distension, and altered bowel habits. These non-specific symptoms often mimic inherent postgastrectomy dysfunction, yet may exacerbate nutritional deterioration through diagnostic challenges.

Conclusion

Systematic multivitamin supplementation should be routinely administered to Chinese gastric cancer patients following gastrectomy, with particular emphasis on initiating vitamin B_1 and vitamin D supplementation upon resumption of semi-solid oral intake. Patients after total gastrectomy may require additional vitamin B_1 supplementation. Meanwhile, vitamin levels can be regularly monitored, and vitamin supplementation schemes can be adjusted in a timely manner. Considering the time of occurrence of other vitamin deficiencies and the small number of follow-up patients at the later stage of this study, it is necessary to further expand the number of cases and extend the monitoring time to verify the necessity of multivitamin supplementation.

Data availability

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation. For data inquiries, please contact the corresponding author (Xiaojie Bian, 18061678828@189.cn).

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Author contributions

Conceptualization: X.B., X.L. and W.G. : software: X.B. and X.L.: Validation: D.l., M.Z. and X.C.: investigation: D.L. M.Z. X.C. Y.E., l.H. T.W. and W.G.: Resources: W.G. and X.C.: Data Curation: Land Y.Y.: Formal Analysis: X.B. and X.L.: Proiect Administration: X.B. : All authors haveread and approved the final manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study protocol was approved by the Ethics Committee of Nanjing Drum Tower Hospital (IRB#2019-173-01) on 24 July 2019.

Additional information

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