Long-term Evolution of Nutritional Deficiencies After Gastric Bypass

An Assessment According to Compliance to Medical Care

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Objective: To study long-term nutritional deficits based on adherence to a standardized nutritional care after gastric bypass (GBP).

Background: Long-term prospective data on nutritional complications after GBP are missing. It is not known whether severe deficiencies are prevented by standard multivitamin supplementation and what parameters are influenced by patient adherence to nutritional care.

Design: One hundred forty-four consecutive subjects from our prospective database (90% women, initial body mass index: 48 ± 15 kg/m^2, age: 43 ± 10 years) who underwent GBP more than 3 years before the study were assessed. Multivitamins were systematically prescribed after GBP, and additional supplements were introduced if deficiencies were recorded during follow-up. We identified a group of 66 compliant subjects who attended yearly medical visits and a group of 32 noncompliant subjects who were recalled because they had not attended any visit for more than 2 years.

Results: Weight loss was 42 ± 14 kg at 3 years or later. The number of nutritional deficits per subject was 3.2 ± 2.3 before surgery and did not significantly increase between 1 and 3 years or later after GBP (3.4 ± 2.0 and 3.5 ± 2.3, respectively). However, specific nutritional deficits occurred despite long-term multivitamin supplementation, including vitamins B_1, B_{12}, and D and iron. Noncompliant subjects had more deficits than compliant subjects (4.2 ± 1.9 vs 2.9 ± 2.0 deficits per patient, $P < 0.01$) and the number of deficits correlated with the time from last visit ($r = 0.285$, $P < 0.01$).

Conclusions: Lifelong medical care is required to maintain a good nutritional status after GBP. Monitoring of nutritional parameters is necessary to add supplementation for deficits that are not prevented by multivitamin preparations.

Keywords: adherence, nutritional care, nutritional deficiencies, Roux-en-Y gastric bypass, vitamin supplementation

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Bariatric surgery is now recognized as the procedure of choice for the treatment of morbid obesity. Gastric bypass (GBP), which associates restriction and mild malabsorption, [1] is the most frequent bariatric procedure worldwide [2,3] because of its long-term effectiveness on weight loss, well-being, and health.[4] However, GBP also induces nutritional deficiencies that may have adverse effects on health.[5,6] The most common deficiencies concern iron, calcium, and several vitamins, including vitamins D, B_1, B_9, and B_{12}.[7] These deficiencies are responsible for anemia, osteopenia, and neurological symptoms. Less frequently, other malnutrition-related complications have been described after GBP, including protein malnutrition and vitamin A deficiency with ocular complications.[8,9]

Few studies have prospectively evaluated the incidence of nutritional complications after GBP [10,11] and very few prospective data are available after 2 years of postoperative follow-up.[5,6] Divergent results were observed depending on the type of supplementation, the duration of the study, or the type of monitoring. It has not really been determined whether standard vitamin supplementation is sufficient or whether assessment of nutritional parameters is required to adjust supplementation. The Endocrine Society has published recommendations concerning screening and supplementation of nutritional deficiencies after bariatric surgery.[12] Whether currently suggested laboratory blood tests performed at least once yearly (including iron, folate, vitamin B_{12}, calcium, vitamin D, parathyroid hormone, zinc and vitamin A) identify all clinically relevant nutrient deficiencies and whether suggested supplementation (with multivitamins, calcium, and vitamin D) are sufficient in the long term for all patients who have undergone GBP remains to be determined.[6]

In a previous prospective 1-year study[13] we observed that nutritional deficiencies such as iron and vitamin D deficits were frequent in obese subjects already before surgery. In that study,[13] we also found that worsening of nutritional status could generally be avoided after GBP by systematic supplementation with multivitamins. However, some parameters required specific care, like vitamin B_{12}. In this study, we asked whether nutritional deficits worsen at 3 years or later after GBP as compared with 1-year and if nutritional monitoring is required to adjust nutritional supplementation. Our hypothesis was that adherence to medical care is crucial to avoid nutritional complications after GBP. Our aim was thus to study the long-term evolution of nutritional deficits depending on the compliance to medical care, in patients receiving standardized nutritional care after GBP.

METHODS

Patients and Surgical Procedures

Subjects were selected from a prospective database started in 2004. The present assessment was conducted between June 2010 and June 2011. We included all subjects who had undergone GBP surgery in our obesity center at Hôpital Louis Mourier 3 or more years before this assessment and for whom data were available at least before and 1 year after surgery. The subjects who did not attend routine yearly follow-up visits in our department for more than 1 year were systematically recalled by phone and mail. At the end of June 2011, the subjects who had not responded neither to the phone call nor to the mail, and therefore had no visit for 2 years or more were considered as lost to follow-up (LFU). Finally, among the subjects for whom

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data were available more than 3 years after surgery were classified into 2 groups; 1 group of "compliant" subjects (CS) who had been seen yearly (time between 2 visits <18 months) for a medical visit in our department after surgery and 1 group of "noncompliant" subjects (NCS) for whom the last 2 visits were spaced 24 months or later. This study included the 49 subjects studied in our previous prospective study concerning the nutritional deficiencies at 1 year after GBP.[13,14] All data presented in this manuscript were collected for medical care. All patients signed an informed consent before surgery, and the data collection was approved by our hôpital Louis Mourier and the local ethics committee (institutional review board of "Assistance Publique des Hôpitaux de Paris").

GBP procedure was performed laparoscopically, as previously described[14] and in accordance with the recommendations of international committees and consensus conferences.[15,16] The length of the alimentary limb and of the biliopancreatic limb were 150 and 70 cm, respectively, in all patients.

Dietary recommendations were systematically given before surgery, in the days after surgery, at 1 and 6 months, and then yearly after surgery to obtain a balanced diet with emphasis on proteins, milk products, vegetables, and fresh fruits. Patients were also advised to eat slowly, chew well, and limit the consumption of sweets to avoid food intolerance or dumping syndrome. Multivitamin supplements were systematically prescribed after GBP. ELEVIT B9 (1 tablet per day, containing 1.6 mg of vitamin B_1, 0.8 mg of folic acid, 100 mg of vitamin C, 4000 IU vitamin A, 15 mg of vitamin E, 500 IU vitamin D_3, 125 mg of calcium, and 60 mg of iron; Bayer Santé, Gaillard, France) was first prescribed, but AZINC optimal (2 capsules per day, containing 1.4 mg of vitamin B_1, 0.2 mg of folic acid, 120 mg of vitamin C, 10 mg of vitamin E, 200 IU vitamin D_3, 220 mg of calcium, and 8 mg of iron; Arkopharma, Carros, France) was prescribed instead in some subjects who did not tolerate large tablets. Intramuscular vitamin B_{12}, 1000 μg monthly, was prescribed after GBP when a deficiency was observed. Additional oral supplements and notably vitamin B_1, vitamin D, calcium, and iron were prescribed depending on biological data obtained before surgery, at 6 and 12 months after surgery, and then yearly.

Clinical and Biological Assessments

All the patients underwent routine physical examination and systematic fasting biological analyses at each assessment. Patients were systematically asked about clinical symptoms of nutritional deficiencies (hair and skin abnormalities, muscle pains, paresthesias, or other neurological symptoms) or digestive disturbances (including dumping syndrome, abdominal pain, vomiting, diarrhea, or constipation). Nutritional supplements were systematically recorded. Food intake was assessed by a dietician. Biochemical parameters were measured using routine techniques.[13,14] Biological nutritional deficiencies were defined as a result below the low normal value of the manufacturer.

Statistical Analysis

Nutritional and metabolic parameters were studied before and after surgery. Quantitative parameters were compared in univariate analysis before and after surgery using paired or unpaired Student *t* test and between groups, using unpaired Student *t* test or nonparametric tests when the distribution was not normal. The number of nutritional deficiencies in each group and other qualitative parameters were compared by the Pearson χ^2 test. Correlations between parameters were analyzed by Pearson correlation or linear regression. Results are expressed as mean ± SD or percentage when indicated. *P* values were considered significant when less than 0.05.

RESULTS

Baseline Characteristics of the Patients and Follow-up Categories

Among the 165 subjects who underwent GBP more than 3 years before this study, 147 subjects (89%) attended the 1-year postsurgical visit (9–15 months). Three women were excluded from analysis because they were pregnant at the 1-year visit. The baseline characteristics of the 144 remaining patients are detailed in Table 1. For the first 31 subjects, only partial data were available before surgery (missing data were vitamins B_1 and C and fat-soluble vitamins), but complete data were available at 1 year and long-term visits for these subjects. Twenty-nine subjects (20%) were LFU after the first year; 1 died by committing suicide, 6 had moved to another part of the country, 17 were unreachable, 5 were contacted but refused to come for a new visit. For 3 women who were pregnant at the last visit, the data of the last visit (but >3 years) before pregnancy were carried forward. Thus, we obtained data at 3 years or later in 115 subjects. Sixty-six subjects (46%) attended to planned yearly visits during follow-up and thus met the criteria of CS. In 32 subjects (22%), the last 2 follow-up visits were spaced by more than 2 years; these subjects were classified as NCS. Finally, 17 subjects (12%) were unclassifiable, and their data were not used in the analysis of influence of compliance on nutritional outcomes. In the last 17 subjects, although the last 2 visits were spaced by less than 24 months, they had an erratic follow-up with gaps of more than 18 months between 2 visits. (The consort flow diagram is available in Supplemental Digital Content Figure 1, available at http://links.lww.com/SLA/A458).

Long-term Evolution of Weight and Nutritional Parameters After Surgery

As shown in Table 2, mean weight was significantly reduced 1 year after GBP with a very slight additional decrease at 3 years or later. Energy intake was drastically reduced at 1 year and remained stable thereafter. In contrast, protein intake significantly increased between the 1-year visit and the visit at 3 years or later. Serum albumin and prealbumin concentrations remained stable with time, and the decrease of serum creatinine concentration that was observed at 1 year was no longer significant at 3 years or later. The percentage of subjects taking multivitamins did not statistically differ between the 1-year visit and the visit at 3 years or later but the prescription of other supplements and notably intramuscular vitamin B_{12} increased with follow-up. The increase in serum concentration of vitamin B_{12} after 1 year paralleled that of vitamin B_{12} supplementation. The increase in vitamin B_6, B_9, and C concentrations observed at 1 year were maintained during follow-up. Conversely, the increase in transferrin saturation and vitamin B_1 concentration observed at 1 year were no longer observed at later follow-up. The decrease in fat-soluble

TABLE 1. Baseline Characteristics of the Subjects

N	144
Sex (M/F)	14/130
Age (yr)	42.9 ± 9.9
Weight (kg)	125.9 ± 25.7
BMI (kg/m^2)	48.2 ± 15.4
Current smokers	28 (19)
Treatment of	
Diabetes	27 (19)
Hypertension	53 (37)
Lipid disorders	27 (19)
Sleep apnea	74 (51)

Values are expressed as mean ± SD or number of subjects (%).

TABLE 2. Long-term Evolution of Nutritional Parameters

	Before Surgery, N = 144	At 1 yr, N = 144	≥3 yr, N = 115
Time from surgery (mo)	—	12.5 ± 1.7	52.5 ± 15.7*
Weight (kg)	125.9 ± 25.7	89. 1 ± 19.5†	86.7 ± 19.9†
BMI (kg/m^2)	48.2 ± 15.4	34.1 ± 10.4†	32.4 ± 6.8†
Weight loss (kg)	—	36.9 ± 12.7	38.6 ± 13.4‡
Dietary energy intake (kcal/24 hr)	1993 ± 704	1272 ± 401†	1350 ± 409†
Carbohydrates (%)	44.2 ± 7.4	46.4 ± 9.3	43.7 ± 8.2
Proteins (%)	16.8 ± 3.3	16.0 ± 3.3§	18.7 ± 5.0*
Lipids (%)	38.4 ± 6.0	38.0 ± 6.9	37.6 ± 7.7
Patients taking, n (%)			
Multivitamin supplements	0 (0)	130 (90)†	98 (85)†
Other complements per os	9 (6)	36 (25)†	44 (39)†‡
Intramuscular vitamin B_{12}	0 (0)	38 (26)†	46 (40)†‡
Prealbumin (mg/L)	275.6 ± 47.7	254.5 ± 54.6	250.0 ± 62.9
Albumin (g/L)	37.3 ± 3.0	37.9 ± 2.9	37.5 ± 3.8
Creatinine (μmol/L)	70.0 ± 15.0	62.4 ± 14.9†	66.1 ± 1.9
Transferrin saturation (%)	19.4 ± 7.5	24.0 ± 12.0†	20.6 ± 11.3‡
Vitamin B_1 (nmol/L)	153.9 ± 43.9	176.6 ± 62.1§	155.3 ± 54.8¶
Vitamin B_6 (nmol/L)	29.1 ± 20.2	51.1 ± 41.4†	42.1 ± 31.5†
Vitamin B_9 (μg/L)	6.6 ± 3.4	16.5 ± 7.6†	15.7 ± 24.4†
Vitamin B_{12} (ng/L)	396.9 ± 187.9	303.7 ± 131.5†	409.6 ± 261.3*
Vitamin C (mg/L)	6.2 ± 3.8	10.4 ± 6.0†	10.5 ± 4.5†
TC (mmol/L)	5.0 ± 0.9	4.55 ± 0.81†	4.7 ± 0.83†
TG (mmol/L)	1.5 ± 0.88	0.96 ± 0.59†	0.88 ± 0.41†
Vitamin A (μmol/L)	2.66 ± 3.7	2.08 ± 0.83‖	2.01 ± 0.87‖
Vitamin E (μmol/L)	29.7 ± 8.3	26.5 ± 7.1§	25.9 ± 5.7†
Vitamin A/(TC + TG) (μmol/mmol)	0.35 ± 0.13	0.38 ± 0.15	0.36 ± 0.16
Vitamin E/(TC + TG) (μmol/mmol)	5.0 ± 4.6	5.4 ± 4.6	4.8 ± 1.2
Serum calcium (mmol/L)	2.27 ± 0.20	2.24 ± 0.09	2.21 ± 0.19
Urinary calcium/creatinine	0.34 ± 0.21	0.31 ± 0.18	0.27 ± 0.18
Vitamin 25OHD (μg/L)	11.5 ± 8.4	18.7 ± 10.4†	23.1 ± 13.8†¶
Hemoglobin (g/dL)	13.0 ± 1.3	12.6 ± 1.3§	12.7 ± 1.4
Parathyroid hormone (pg/mL)	60.0 ± 29.8	57.5 ± 26.2	66.2 ± 36.7‡

Values are mean ± SD or number (%) of subjects when indicated.
*$P < 0.001$ versus 1 yr.
†$P < 0.001$ versus baseline.
‡$P < 0.05$ versus 1 yr.
§$P < 0.01$ versus baseline.
¶$P < 0.01$ versus 1 yr.
‖$P < 0.05$ versus baseline.
TC indicates total cholesterol; TG, triacylglycerol.

vitamin A and E concentrations was sustained over time after surgery. However, the decrease of these fat-soluble vitamins paralleled that of lipids concentration, so that the ratio of vitamin A or vitamin E to serum lipids (the sum of triacylglycerol + cholesterol) was unchanged. By contrast, serum vitamin D concentration increased with follow-up. Parathyroid hormone increased after 1 year, whereas serum and urinary calcium tended to decrease, although this decrease did not reach significance. Overall, the average concentration of nutritional parameters rather improved after GBP in our cohort, even in the long term.

As shown in Table 3, deficiencies were frequent before surgery notably for vitamin D, iron, and vitamin C. The prevalence of some deficiencies (vitamins B_6, C, and D) decreased after surgery. However, vitamin D deficit remained very common after surgery. We observed an increase in the prevalence of some specific deficiencies after surgery. Vitamin B_{12} deficiencies increased at 1 year but not thereafter. In contrast, the prevalence of iron, vitamin B_1 and E deficiencies increased with follow-up. The prevalence of anemia also increased with time (Table 3). The concentration of hemoglobin at the last visit strongly correlated with transferrin saturation ($R = 0.792$, $P < 0.001$) but not with folate or vitamin B_{12} concentrations. Overall, the total number of biological nutritional deficiencies did not significantly increase during follow-up (Table 3).

Long-term Evolution of Nutritional Parameters According to Compliance

The baseline characteristics and the preoperative nutritional parameters of the NCS, CS, and LFU subjects did not substantially differ (see Supplemental Digital Content Table 1, available at http://links.lww.com/SLA/A457). At 1 year, there was no clinical difference between these groups of subjects, except for a higher percentage of patients with snacking habits in NCS than in CS (see Supplemental Digital Content Table 2, available at http://links.lww.com/SLA/A457). The nutritional parameters of the 3 groups were similar except for vitamins B_6 and D that were lower in NCS than in CS (see Supplemental Digital Content Table 2, available at http://links.lww.com/SLA/A457).

Long-term nutritional parameters in CS and NCS are detailed in Table 4. Time from last visit was significantly higher in NCS with a gap of 22 months than CS (Table 4). Food consumption was similar except for a higher percentage of carbohydrates consumption in CS. The difference in snacking observed at 1 year between the 2 groups did not reach significance at 3 years or later. Symptoms of nutritional deficiencies were more frequent in NCS, whereas weight loss and food avoidances were similar in the 2 groups. At 3 years or later (Table 4), vitamin B_{12} and D concentrations and transferrin saturation were lower in NCS than CS. We also observed higher homocystein

TABLE 3. Evolution of Nutritional Deficiencies During Follow-up

	Before Surgery, N = 144	At 1 yr, N = 144	≥3 yr, N = 115
Percentage of subjects with parameters < normal value			
Albumin <34 g/L	8	6	7
Serum calcium <2.12 mmol/L	5	6	1
Hemoglobin <11.5 g/dL	6	12	13*
Tranferrin saturation <20%	42	34†	50‡
Vitamin B_1 <126 nmol/L	22	16*	27‡
Vitamin B_6 <20 nmol/L	24	17†	17†
Vitamin B_9 <3 μg/L	2	4	1
Vitamin B_{12} <190 ng/L	5	16*	11*
Vitamin C < 5 mg/L	33	14§	11§
Vitamin A < 1.5 μmol/L	10	19	14
Vitamin E < 21 μmol/L	15	23	26*
Vitamin 25OHD <30 μg/L	92	86†	71†‡
Total no. of deficiencies (n)	3.2 ± 2.3	3.4 ± 2.0	3.5 ± 23

Values are percentage of subjects with deficiencies defined as values below the low normal value of the laboratory.
*$P < 0.05$ versus baseline.
†$P < 0.01$ versus baseline.
‡$P < 0.05$ versus 1 yr.
§$P < 0.001$ versus baseline.

concentrations in NCS. The concentration of homocystein correlated with that of vitamin B_{12} ($R = 0.326$, $P = 0.0014$) and vitamin B_9 ($R = 0.197$, $P = 0.005$) in the whole cohort at the visit at 3 year or later.

Nutritional deficiencies were more common in NCS than in CS. Notably, deficiencies in vitamins B_1, B_{12}, and D were more frequent in NCS than in CS (Table 5). The increase in prevalence of anemia in NCS did not reach significance. The number of subjects with more than 5 deficits was dramatically higher in NCS (Table 5, Fig. 1). Furthermore, in the whole cohort, we found a positive correlation between the number of biological deficiencies and the time from last visit (Fig. 2) whereas there was no correlation with weight loss or time from surgery. More CS than NCS took multivitamins and other nutritional complements but this did not reach statistical significance. Nevertheless, in the entire cohort, the number of biological nutritional deficiencies at 3 years or later was higher among subjects who did not take multivitamins than in subjects taking multivitamins (number of deficits was 4.58 ± 2.2 vs 3.16 ± 2.0, $P = 0.0267$). Interestingly, the number of biological deficiencies in the long term decreased with age at the last visit in the whole cohort ($R = -0.273$, $P = 0.0071$). In contrast, this number of deficiencies increased with postsurgical body mass index ($R = 0.224$, $P = 0.0285$). Furthermore, in subjects who regained weight (delta weight between the 1-year visit and the last visit was >0, n = 51), the number of nutritional deficiencies was higher than in subjects who were stable or had lost weight (delta weight ≤ 0, n = 64): 3.93 ± 2.21 vs 3.06 ± 2.08 deficits, respectively ($P = 0.00462$). We found no correlation between the number of deficiencies and energy intake, homeostatic model assessment-insulin resistance (HOMA-IR) index, or C-reactive protein.

DISCUSSION

Nutritional deficiencies have been frequently reported after bariatric surgery[5–9] and could affect the benefits of bariatric surgery on long-term health.[17] However, nutritional parameters are not always monitored in clinical practice,[17] and very few studies have prospectively evaluated the prevalence of nutritional deficits in large surgical series[10,11,18,19], especially in the long term, more than 2 years after surgery.[20,21] Nutritional deficits are common before bariatric surgery[6] but are often not assessed before GBP. It is therefore not easy to distinguish postoperative deficiencies that are caused by surgery from those due to obesity, preexisting to surgery.[13] Indeed, obesity is often not fully corrected by surgery and could have a negative effect on vitamin status by increasing vitamin need due to oxidative stress, intestinal bacterial overgrowth,[6] or trapping of vitamins in adipose tissue.[22, 23]

Furthermore, the question of whether nutritional deficits worsen with time has not been answered. Finally, the recommendations of Endocrine Society concerning supplementation are based on very little prospective data. Thus, there remains the question of whether standard supplementation is sufficient to prevent nutritional deficiencies and whether monitoring is required to adjust nutritional supplements.

We previously showed that obesity is associated with a high prevalence of iron, thiamine, vitamin D, and vitamin C deficits that were not worsened at 1 year after GBP.[13, 14] On the contrary, the prevalence of these deficiencies was decreased 1 year after GBP in patients taking multivitamin supplements. However, GBP was associated with specific deficiencies at 1 year such as fat-soluble vitamins and vitamin B_{12} deficiencies.[13,14]

The results of our study show that overall nutritional status does not worsen at 3 years or later after GBP in patients receiving dietary recommendations and multivitamin preparations. Some parameters even improved during follow-up. For example, as also reported by others[7,20], we previously found an increase of stigmata of protein malnutrition 1 year after surgery.[13,14] In this study, plasma albumin remained stable during the follow-up to 3 years or later, and protein intake significantly increased between the first year and the long-term follow-up, presumably due to the decrease of postsurgical protein avoidance with time. In the same line, we observed a decrease of serum creatinine concentration at 1 year, which may be related to a decrease of muscular mass.[13] However, serum creatinine measured after 3 years of follow-up was close to preoperative values.

For some nutritional parameters including vitamin B_6, B_9, C, and D concentrations, the improvement observed at 1 year after GBP was maintained during follow-up, probably reflecting both the high efficacy of standard multivitamin preparations and the beneficial effect of weight loss on these parameters. Indeed, we observed a decrease in the number of deficits while body mass index dropped after surgery. However, some of these parameters, although

TABLE 4. Long-term Nutritional Parameters According to Compliance

Groups	NCS, N = 32	CS, N = 66
Time from surgery (mo)	57.4 ± 14.2	49.0 ± 15.4*
Time from last visit (mo)	34.1 ± 8.3	11.9 ± 1.5†
Weight (kg)	90.0 ± 18.6	85.0 ± 22.0
BMI (kg/m^2)	33.2 ± 6.5	31.8 ± 7.5
Weight loss (kg)	37. 1 ± 14.6	40.4 ± 13.6
Dietary energy intake (kcal/24 hr)	1382 ± 475	1348 ± 341
Carbohydrates (%)	40.8 ± 9.5	44.3 ± 6.9‡
Proteins (%)	19.8 ± 4.3	18.3 ± 3.7
Lipids (%)	39.6 ± 7.7	37.4 ± 6.4
Percentage of subjects with		
Snacking habits (%)	41	30
Food intolerances (%)	22	20
Symptoms of deficiencies (%)	75	53‡
Intake of multivitamin (%)	78	92
Intake of other supplements (%)	16	53
IM vitamin B_{12} (%)	25	48
Prealbumin (mg/L)	251.1 ± 72.9	256.1 ± 57.3
Albumin (g/L)	38.3 ± 3.2	37.5 ± 4.1
Creatinine (μmol/L)	65.8 ± 17.1	70.0 ± 22.3
Tranferrin saturation (%)	16.8 ± 7.9	22.5 ± 11.4‡
Vitamin B_1 (nmol/L)	151.3 ± 55.3	160.8 ± 45.8
Vitamin B_6 (nmol/L)	40.8 ± 31.2	46.1 ± 34.1
Vitamin B_9 (μg/L)	12.7 ± 6.6	14.1 ± 6.2
Vitamin B_{12} (ng/L)	342 ± 222	457 ± 288‡
Vitamin C (mg/L)	10.1 ± 3.6	10.7 ± 4.7
Vitamin A (μmol/L)	2.0 ± 0.8	2.0 ± 0.9
Vitamin E (μmol/L)	25.0 ± 5.5	26.1 ± 5.7
Serum calcium (mmol/L)	2.24 ± 0.08	2.20 ± 0.22
Urinary calcium /creatinine	0.323 ± 0.18	0.248 ± 0.19
Vitamin 25OHD (μg/L)	17.1 ± 13.6	26.3 ± 13.1*
Hemoglobin (g/dL)	12.8 ± 1.8	12.8 ± 1.1
Homocystein (μmol/L)	12.7 ± 5.1	10.3 ± 4.4‡
Parathyroid hormone (pg/mL)	66.3 ± 32.4	62.9 ± 32.1

Values are Mean ± SD or percentage of subjects when indicated.
*$P < 0.01$ versus noncompliant subjects.
†$P < 0.001$ versus noncompliant subjects.
‡$P < 0.05$ versus noncompliant subjects.
NCS indicates noncompliant subjects; CS, compliant subjects; IM, intramuscular.

TABLE 5. Numbers of Nutritional Deficiencies According to Compliance at Long Term

Groups	NCS, N = 32	CS, N = 66
Percentage of subjects with Parameters < normal value		
Albumin <34 g/L	6	5
Serum calcium <2.12 mmol/L	6	9
Hemoglobin <11.5 g/dL	16	8
Tranferrin saturation <20%	56	46
Vitamin B_1 <126 nmol/L	41	15*
Vitamin B_6 <20 nmol/L	16	15
Vitamin B_9 <3 μg/L	0	2
Vitamin B_{12} <190 ng/L	19	6†
Vitamin C <5 mg/L	9	12
Vitamin A <1.5 μmol/L	34	23
Vitamin E <21 μmol/L	22	9
Vitamin 25OHD <30 μg/L	94	59*
Total no. of deficiencies (n)	4.2 ± 1.9	2.9 ± 2.0*
Subjects with ≥5 deficiencies (%)	44	15*

Values are percentage of subjects with deficiencies defined as values below the low normal value of the laboratory.
*$P < 0.01$ versus noncompliant subjects.
†$P < 0.05$ versus noncompliant subjects.
NCS indicates noncompliant subjects; CS, compliant subjects.

improved, remained in the low to normal range and require specific supplementation in addition to standard multivitamin supplementation. For example, vitamin D concentration improved after surgery but remained insufficient in most subjects, as we previously showed in the short-term after GBP.[24] Vitamin D deficiency is a major clinical concern after bariatric procedures.[6] Low vitamin D concentrations perpetuate the inadequate calcium absorption and the secondary hyperparathyroidism, observed during follow-up by us and others[25,26] with deleterious effects on bone. In contrast, the improvement of other parameters including transferrin saturation or vitamin B_1, that was observed 1 year after surgery, was not sustained at 3 years or later. The same kinetic of iron deficiency was observed by Blume et al,[27] that is improvement at 1 year and worsening at 3 years. The beneficial effect of weight loss on hepcidin expression, an inhibitor of iron transport overexpressed in obesity,[28] may thus be counterbalanced by a decrease of iron absorption.[29] Severe iron deficits that require intravenous supplementation have been described after GBP.[30] Furthermore, we showed that both at 1 year[13] and in this long-term study, iron deficit is the main determinant of hemoglobin concentration. As anemia remains one of the most frequent long-term complications of bariatric surgery with a prevalence as high as 70% in some series,[8,20] it is important to monitor iron status in the long term after surgery, especially in premenopausal women. In the same line, severe complications of vitamin B_1 deficit have been described after GBP such as Wernicke encephalopathy[31] that justify, continued monitoring of the serum concentration of this vitamin.

Other parameters that were decreased at 1 year, such as vitamins A and E, remained lower during follow-up than before surgery. Deficits in fat-soluble vitamins have previously been described after GBP.[10,18,32] Because the decrease of vitamin A and E concentrations paralleled the decrease of plasma lipids after GBP, it is not clear whether lower concentration reflects true deficits or decrease of the plasmatic carriers, that is lipoproteins.[33] Because of large stores, vitamin B_{12} deficiency is often delayed after GBP with a prevalence exceeding 60% in the long term.[5] In this study, the decrease of vitamin B_{12} observed at 1 year was prevented at 3 years or later by intramuscular supplementation. Some authors have stressed that commercial multivitamins preparations alone are not sufficient to prevent nutritional deficiencies induced by GBP in studies with short follow-up.[34,35] The need of specific supplements is required in the long term, as illustrated by the increase in the number of additional nutritional supplements prescribed with time in this study.

It was previously shown that adherence to multivitamin supplementation is poor in the long term after bariatric surgery.[36] As we previously observed for adherence to multivitamins,[13] the adherence to medical visits influences nutritional status, as illustrated by the positive correlation between the number of deficiencies and the time from last visit in our cohort. In addition, although nutritional status in the first year after surgery was similar in CS and NCS, nutritional deficiencies were more common at 3 years or later in NCS than in CS. Notably, we observed a greater frequency of vitamin B_1, B_{12}, and D deficits and a lower transferrin saturation, associated with an increased prevalence of symptoms of nutritional deficiencies in subjects who did not adhere to medical monitoring.

Interestingly, the higher proportion of snackers among NCS during follow-up may reflect a lower ability to apply dietary recommendations. This could negatively influence nutritional status especially as food choices for snacking are oriented toward high fat foods and sugary foods with low nutritional value.[6,37] The positive correlation between body mass index at 3 years or later and the number of nutritional deficits and the higher number of deficits in patients

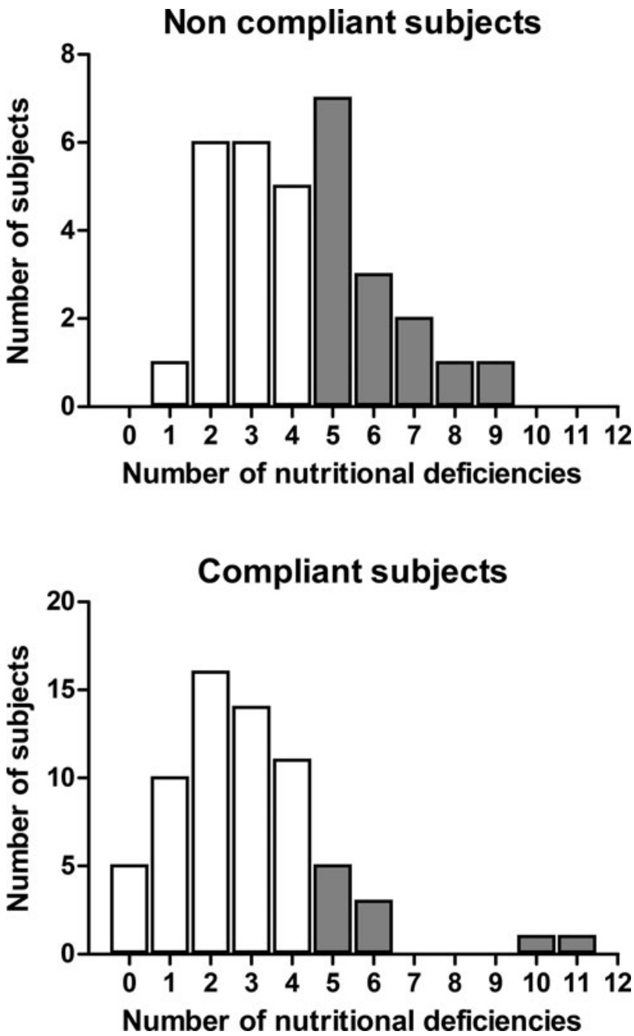

FIGURE 1. Frequency of nutritional deficiencies according to compliance. The bars represent the number of subjects with each number of deficiencies (defined as values below the low normal value of the laboratory), under 5 (open bar), and above 5 (filled bar) deficiencies, in noncompliant subjects (n = 32, upper graph) and compliant subjects (n = 66, lower graph).

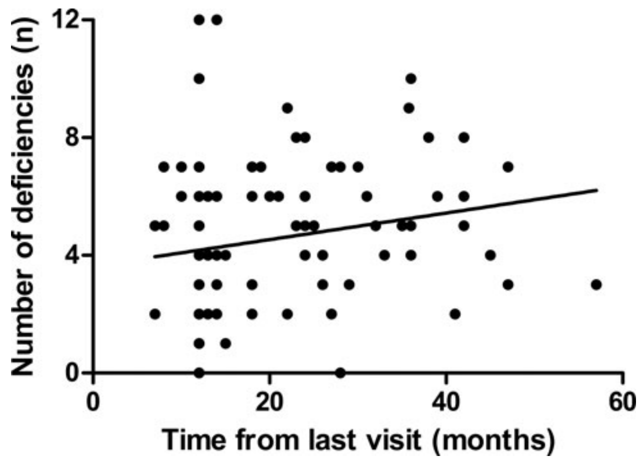

FIGURE 2. Correlation between the frequency of nutritional deficiencies and the time from last visit. The number of biological nutritional deficiencies (defined as values below the low normal value of the laboratory) correlated positively ($R = 0.285$, $P = 0.0045$) with the number of months between the last 2 visits in the whole cohort (n = 115).

with weight regain could also reflect the deleterious effect of a less balanced diet both on weight and nutritional status. In the same line, the negative correlation between the number of deficits and age could reflect the greater difficulty of young subjects to adhere to medical care as observed in other chronic diseases.[38] We also observed a trend, although not significant, to a lower proportion of NCS taking multivitamins and specific nutritional supplements during follow-up. The number of nutritional deficits in the whole cohort was higher in subjects who did not take multivitamins than in subjects taking multivitamins. However, folate concentration, that we previously used as a marker of adherence to multivitamin supplementation,[13] did not differ between NCS and CS. Thus, adherence to standard multivitamins did not seem to explain the higher prevalence of nutritional deficiencies in subjects who did not adhere to long-term medical visits. The poorer nutritional status in NCS could rather be explained by difference in use of specific supplements adjusted to monitoring. In this line, the higher homocystein level in NCS, which was better correlated with serum vitamin B_{12} concentration than to folate concentration could reflect a lower use of specific B_{12} supplements.

The principal limits of this study are: (1) It is not a randomized study but it does not seem ethical to leave patients without nutritional supplements or nutritional monitoring after surgery. (2) The sample size of the study is small and 90% of our subjects are female. Thus, the results may not be extrapolated to the male population. (3) Twenty percent of the subjects were LFU despite our efforts to contact all the operated subjects for this study. (4) Zinc, copper, and selenium assays were not included in this study because their assessment was too recent in our monitoring program.

CONCLUSIONS

The main finding of this long-lasting, prospective study is that nutritional status does not worsen after GBP in subjects taking nutritional supplementation, even in the long term. Indeed, the total number of deficiencies did not increase after surgery, and some deficiencies observed in obese subjects before surgery even improved after GBP. However, some specific nutritional deficits were not adequately corrected by standard commercial multivitamin preparations, including vitamin B_{12}, vitamin D, and iron deficits.

Factors like young age, snacking, and residual obesity could negatively affect nutritional status. Furthermore, the number of nutritional deficiencies was higher in subjects with low compliance to medical visits than subjects with good compliance. Lifelong medical care is thus necessary to maintain a good nutritional status after GBP. Notably, monitoring of nutritional parameters will permit to adjust supplementation for deficits that are not corrected by standard multivitamin preparations.

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