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Bariatric Surgery in Adolescents: Is routine nutrient supplementation sufficient to avoid anemia following bariatric surgery?

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Abstract

Background—Anemia following bariatric surgery is a known complication. To prevent nutrient deficiencies, adolescent patients require multivitamin supplementation following bariatric surgery. The purpose of this study was to investigate if routine multivitamin supplementation is sufficient to prevent anemia in adolescents undergoing bariatric surgery, particularly sleeve gastrectomy (SG), a procedure that may induce nutrient malabsorption.

Methods—We conducted a retrospective review of medical records of pediatric patients who underwent SG (34 patients) and laparoscopic adjustable gastric banding (LAGB) (141 patients) (1/2006–12/2013). We examined anemia marker levels (iron, ferritin, folate, B_{12}, hemoglobin and hematocrit) at first visit, 3, 6, and 12 months post-surgery by repeated measures analysis adjusting for weight loss.

Results—Following SG, folate levels decreased 3 and 6 months post-surgery, however returned to baseline levels at 12 months. Furthermore, SG patients demonstrated lower folate levels compared to LAGB at 3 and 6 months. B_{12} levels decreased 6 months post-SG, however returned to baseline at 12 months. Following LAGB, B_{12} levels decreased 12 months post-surgery compared baseline. Ferritin levels decreased 3 months post-LAGB, however returned to baseline levels at 6 months. There were no changes within groups or differences between groups in iron, hemoglobin or hematocrit.

Conclusions—While anemia did not occur in any patients while on recommended routine supplementation, folate levels were significantly reduced following SG and were lower in SG compared to LAGB patients. Additional folate supplementation seemed to improve folate levels,

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which highlights the importance of ongoing surveillance by primary care providers and the need for additional folate supplementation following SG.

Keywords

bariatric surgery; anemia; pediatrics

Introduction

With the high prevalence of childhood and adolescent obesity in the United States, bariatric surgery is increasingly being performed in adolescents to deal with severe obesity and its comorbidities[1–3]. While effective for long-term weight loss, bariatric surgery can cause or exacerbate nutritional deficiencies leading to anemia[1,4,5]. As a result, patients may develop weakness, fatigue, shortness of breath, and reduced cognitive performance[6]. To prevent nutrient deficiencies, adolescent bariatric patients require multivitamin supplementation following surgery. Standardization in nutrition management, however, is lacking[7]. Currently, patients are managed post-operatively according to best practice guidelines[7]. In order to standardize nutrition management following bariatric surgery, further empirical evidence is required[7].

There are two types of bariatric procedures: malabsorptive and restrictive. Malabsorptive procedures induce weight loss by bypassing segments of the small intestine, thus decreasing nutrient absorption[8]. Restrictive procedures promote weight loss by limiting food intake[8,9]. Previous research indicates a higher prevalence of nutrient deficiencies following malabsorptive compared to restrictive procedures[9].

In contrast with previous research, recent studies have found similar proportions of nutrient deficiency following sleeve gastrectomy (SG), a primarily restrictive procedure, compared to Roux-en-Y gastric bypass (RYGB), a procedure encompassing both malabsorptive and restrictive features[10,11]. While SG is considered mainly restrictive, the removal of 60–80% of the stomach may lead to deficiencies in gastric acid and intrinsic factor-secreting parietal cells necessary for effective absorption of iron, B_{12}, and folate.[12–14] It is therefore plausible that SG encompasses malabsorptive characteristics.

To assess if routine multivitamin supplementation is sufficient to prevent anemia in adolescent patients undergoing bariatric surgery, this study examined and compared anemia marker levels (iron, ferritin, B_{12}, folate, hemoglobin (Hgb) and hematocrit (Hct)) following SG to those following LAGB, a known restrictive procedure. We hypothesized that patients undergoing SG would present with greater reductions in anemia markers than those who undergo LAGB, due to the potential malabsorptive characteristics of the procedure, and will therefore require additional multivitamin supplementation.

Methods

Subjects

One hundred seventy-five patients who underwent LAGB (141 patients) or SG (34 patients) at Columbia University Medical Center (CUMC) between January 2006 and December 2013

were included in this study. Patients were referred to the Center for Adolescent Bariatric Surgery and received nutrition and exercise counseling prior to surgery. From 2006 through 2010, patients were offered LAGB as the surgical procedure. Beginning in 2010, a gradual transition to SG began, and since 2011, patients were offered almost exclusively SG. This change resulted from changes in clinical practice as SG increased in popularity among bariatric surgeons. The same surgeon performed all surgeries. This study was approved by the IRB of CUMC. All patients and their parents or legal guardian gave written informed consent and assent for ongoing collection of data prospectively in the bariatric program prior to participation.

Clinical Assessments

Physical examination and biological analyses were routinely performed on patients prior to surgery at the initial visit, in addition to 3 months, 6 months, and 12 months post-surgery. Patient demographic, physical, and biological data were recorded in the patient medical record. All patients were advised to take an over the counter multivitamin supplement once per day following surgery. Low values of iron, vitamin B12 or folate were supplemented with additional iron, B-complex or B12/folate supplements. Compliance was monitored by serial measurements of serum levels. If low values were obtained, supplements were reinforced or increased.

In a retrospective review of medical records, a database was constructed, recording the patients' age, sex, height, weight, BMI, iron, ferritin, B_{12}, folate, Hgb and Hct levels at each visit. Pre-specified primary outcomes included changes within groups and differences between groups in anemia marker levels including, iron, ferritin, B_{12}, folate, Hgb and Hct post-surgery over a 12-month period.

Assessment of Anemia Marker Levels

The Clinical Chemistry Laboratory of CUMC measured iron and ferritin by a liquid chemistry assay (Olympus AU2700™). The Specialty Laboratory of CUMC measured B_{12} and folate by chemiluminescense (Elecsys® 2010). The Hematology Laboratory of CUMC measured Hgb and Hct using Sysmex XE-5000™ instruments. Reference ranges indicated by the Clinical Laboratory at CUMC determined low anemia marker level cutoffs.

Statistical Analysis

The results of this study are reported as means and standard deviations unless otherwise noted. Differences between group means at baseline were assessed with independent t-tests. Differences in frequencies were assessed with Chi-Square or Fisher's Exact tests. To analyze group differences in the absolute level (Table 3) or percent change (Figure 1) in anemia marker levels over the period of follow-up, we used a linear mixed model for repeated measures for each dependent variable. Each model included fixed effects for procedure (LAGB vs. SG), time (3, 6, 12 months post-surgery) and procedure by time interaction with the pre-surgical level of the dependent variable entered as a continuous covariate. Analyses shown in Table 3 additionally employed percent weight loss from baseline as a time-dependent covariate. An ARIMA(1) covariance structure was empirically determined to best fit the within-subject autocorrelation. Model estimated means, standard errors, and 95%

confidence intervals were used to compare the procedure's effect on each dependent variable at specific time. To evaluate the potential for bias from dropout, we used t-tests and chi-square tests to assess whether baseline characteristics correlated with patients' completing follow-up. The same linear mixed models were applied to the subset of patients completing the study to examine if the analysis results would be biased by patients' dropout. We performed all analyses using SAS v9.4 (SAS Institute, Cary, NC). A $p<0.05$ was used as the minimum level of statistical significance.

Results

Baseline Characteristics

Mean age, weight, height, BMI as well as sex distribution and ethnicity are listed in Table 1. All patients were Tanner 4 or 5 pubertal stages. There were no differences in baseline characteristics except in ethnic distribution (p=0.03) between the LAGB and SG groups (Table 1).

There were no differences in frequency of patients who presented with low anemia marker levels at the initial visit between the LAGB and SG groups. Iron deficiency was present in 22% of patients in both groups and low Hgb was present in 15% and 24% of patients in the LAGB and SG groups, respectively. Deficiency for each nutrient was defined using the following cutoffs (conversion factor for SI units in parentheses[14]): Iron [male, female]: 41, 41 µg/dL (0.1791 µmol/L); ferritin: 29, 10 ng/mL (1.0 µg/L); B_{12}: 279, 279 pg/mL (0.7378 pmol/L); folate: 5.4, 5.4 ng/mL (2.266 nmol/L); Hgb: 13, 12 g/dL (10.0 g/L); Hct: 37, 35.4% (Table 2).

There were no differences in anemia marker levels (iron, ferritin, B12, folate, Hgb, or Hct) at the initial visit between the LAGB and SG groups (Table 3).

Anemia Marker Levels Post-Surgery

Within Group Differences in Anemia Marker Levels—Folate levels were lower 3 and 6 months post-SG compared to the initial visit, however returned to baseline levels at 12 months. B_{12} levels were lower 6 months post-SG compared to 3 months, though not different from levels at the initial visit, and returned to baseline levels at 12 months. There were no changes in iron, ferritin, Hgb or Hct following SG at long-term time points (Table 3).

There were no changes in folate at any time point post-LAGB. B_{12} levels were lower 12 months post-LAGB compared to levels at 6 months and levels at the initial visit. Ferritin levels were lower 3 months post-LAGB compared to the initial visit, however, returned to baseline levels at 6 months (Table 3). There were no changes within groups in iron, Hgb or Hct following LAGB at long-term time points (Table 3).

The results from the unadjusted analysis did not differ from the adjusted for weight loss analysis with one exception: Ferritin levels were lower 12 months post-SG compared to the initial visit (40.0±145.1 ng/mL vs. 57.8±95.8, p=0.03).

Between Group Differences in Anemia Marker Levels—SG patients demonstrated lower folate levels compared to LAGB patients 3 and 6 months post-surgery, though showed no differences between groups at 12 months (Table 3). There were no other between-group differences in anemia marker levels.

Between Group Differences in Percent change of Anemia Marker Levels—SG patients demonstrated a greater percent decrease in folate than LAGB patients 3 months (−31.0±185.7 vs. 3.6±93.7, p=0.006) and 6 months (−22.9±174.7 vs. 10.3±80.4, p=0.005) post-surgery compared to the initial visit (Figure 1). There were no other between-group differences in percent change of anemia marker levels.

Assessment for Potential Bias from Patients Lost to Follow up

There was no significant association between procedure type and patients lost to follow up. There was no significant association between baseline nutrient levels and patients lost to follow up. When the statistical analysis assessing anemia marker levels was restricted to only those patients who completed the study and compared with our original analysis, there was no significant change in results.

Discussion

Bariatric surgery is the most effective method of long-term weight loss for adolescents with severe obesity[3]. Micronutrient deficiencies, however, often develop following surgery. As a result, patients commonly present with anemia[1]. To prevent deficiencies from arising, patients are advised to take multivitamin supplements. Although previous research has investigated nutrient deficiencies following bariatric surgery, the literature is not extensive enough for the development of standardized nutrition management guidelines[7]. It is known that adolescents with obesity are already at an increased risk for developing anemia pre-operatively[15–18]. Similarly, patients included in the current study demonstrated a high prevalence of iron deficiency and anemia (defined by low Hgb levels) prior to surgery. Thus, monitoring micronutrient levels following bariatric surgery and supplementing accordingly is crucial. Our patients were advised to take one tablet of an over the counter multivitamin supplement daily. We sought to investigate if this routine supplementation was sufficient to prevent reductions in anemia markers following bariatric surgery, and particularly following SG, as this surgery may encompass malabsorptive characteristics.

Our results indicated that folate levels in SG patients were significantly reduced 3 and 6 months following surgery compared to the initial visit despite all patients being advised to take multivitamin supplements. Furthermore, folate levels were significantly lower in SG compared to LAGB patients. With SG, a large proportion of gastric acid secreting parietal cells are removed, whereas with LAGB, parietal cells are maintained. Gastric acid is required for effective folate absorption, thus, it is not surprising that folate levels would be reduced to a greater extent following SG compared LAGB[12]. These results are consistent with previous research that found that bariatric procedures, including SG and RYGB, can be associated with folate deficiency[19,20]. Previous research has also found that the odds of folate deficiency in the first year following bariatric surgery are higher for malabsorptive compared to restrictive surgeries, similar to our findings[21].

In our patients, identification of deficiencies resulted in supplementation of that nutrient. Previous research indicates that folate deficiency can be successfully corrected with oral supplementation[22]. Our research showed that folate levels returned to baseline levels 12 months post-operatively, indicating that with monitoring and additional supplementation as needed, deficiencies can be corrected successfully.

Folate plays a major role in cell division, cell maintenance, construction and repair of DNA, and DNA methylation required for epigenetic gene expression[23,24]. Folate deficiency can result in macrocytic anemia[23]. Additionally, folate deficiency in pregnant women increases the risk of neural tube defects in offspring[24]. In our study, folate levels significantly decreased 3 and 6 months following SG. This represents a potentially serious problem as our study sample included 114 adolescent women (65%) who are likely to become pregnant in the future. Effective supplementation is therefore critical in this group of patients. Importantly, our patient population had a high missed appointment rate. Thus, primary care practitioners need to be particularly aware that adolescent bariatric patients are at risk for folate deficiency so that they can prescribe additional supplements accordingly and manage this complication successfully.

B_{12} deficiency following LAGB and SG has been previously reported[1,9]. One study found that the prevalence of B_{12} deficiency between 3 and 12 months following SG was 14%[22]. Reductions in B_{12} levels can be attributed to reduced intake of B_{12} containing foods, such as meat, as well as reduced gastric acid and intrinsic factor associated with malabsorption[19]. Consistent with previous research, our results indicated that B_{12} levels decreased in both groups following surgery. B_{12} levels were reduced 6 months post-SG compared to 3 month levels, however, were corrected by 12 months, demonstrating that additional oral supplementation was successful.

Interestingly, B_{12} levels following LAGB were significantly reduced 12 months following LAGB, however were not reduced at earlier time points. It is likely that this reduction in B_{12} relates to poor quality of eating, which is characterized by food intolerance, frequent vomiting and subjective satisfaction of eating ability[25]. Previous research has shown that patients who have undergone LAGB have a lower quality of eating than patients who have undergone SG and RYGB[25]. Importantly, LAGB patients show the lowest quality of eating around 6–12 months or later following the procedure, and have particular difficulty tolerating red meat. This could accounts for the reduction in B_{12} that was demonstrated in our patient population 12 months following LAGB[25]. Future research should investigate the relative contribution of malabsorption versus food intolerance to specific nutrient deficiencies following different bariatric procedures across time points to elucidate this pattern of results further.

Iron deficiency is frequently observed following bariatric surgery with a prevalence as high as 14% and 18% following LAGB and SG, respectively[26]. However, at least two other studies found a very low prevalence of iron deficiency following SG[6,20]. Similarly, our results indicated that there were no significant reductions in iron levels following surgery in either groups, or differences between SG and LAGB patients.

Ferritin was measured to assess levels of iron in storage. Similar to iron levels, there were no significant decreases in ferritin following SG or differences between SG and LAGB groups at any time points post-surgery. Following LAGB, ferritin was lower at 3 months compared to the initial visit, however returned to baseline levels by 6 months. Our results therefore suggest that that iron stores were not reduced[27].

Hgb and Hct levels are used as indicators for anemia[28]. Previous studies have found that bariatric surgery is associated with reductions in Hgb and Hct, although, levels are usually maintained within the normal range[29,30]. Our results showed no significant reductions in Hgb and Hct levels after surgery or differences between LAGB and SG patients, which is consistent with our results on iron and ferritin levels.

The unadjusted analysis showed similar results to the adjusted analysis across all anemia marker variables, except for further reductions in ferritin in LAGB patients. This difference that disappeared with the adjustment for weight loss indicates that weight loss with associated decreased intake contributed to ferritin changes in LAGB patients, rather than the actual procedure.

To our knowledge, this study is the first to compare anemia marker levels following LAGB to those following SG in the adolescent population. This comparison provided an opportunity to examine the potential malabsorptive characteristics of SG and to assess if routine nutrient supplementation is sufficient to prevent deficiencies post-operatively. These investigations are crucial for guiding physicians in prescribing nutritional supplements and monitoring nutrient deficiencies.

We acknowledge limitations in our study. All patients included in the study were advised to take multivitamin supplements daily, although it is unclear if all patients adhered to physicians' prescription of supplements. Given the development of deficiencies in B_{12} and folate despite the recommendation for routine supplementation, it must be concluded that patients are either non-adherent or need greater amounts than are provided in a general multivitamin and that periodic monitoring for nutrient deficiencies is important, particularly during year one after a bariatric procedure. Additionally, patients were lost to follow-up at later time points in the study. To assess if patient dropout biased our results, we performed several statistical analyses. First, we found that procedure type was not associated with patients lost to follow up. We also tested for baseline differences in the characteristics of those who completed 12-month follow-up and those who did not and found no statistically significant differences. Further, when we compared the analysis of anemia marker levels based on the entire cohort to the analysis restricted to those who provided 12-month data, all previously significant findings remained so and previous findings that were not significant did not attain significance. These analyses suggest a lack of impact on outcome due to loss to follow-up. However, given the need for additional supplementation demonstrated by those who did return, a potential for more significant deficiencies is possible and warrants evaluation by practitioners seeing these patients for routine health care.

Conclusion

The current study showed that although anemia per se did not occur in any of our patients while on recommended routine supplementation, folate levels were significantly reduced following SG and were lower in SG compared to LAGB patients. This complication is particularly concerning for female patients because of the potential impact of folate deficiency in pregnancy. Our study demonstrates that SG encompasses malabsorptive characteristics and as a result, routine nutrient supplementation is not necessarily sufficient to prevent nutrient deficiency following bariatric surgery. Additional folate supplementation seemed to improve folate levels, which highlights the importance of ongoing surveillance by general practitioners and further folate supplementation following SG.

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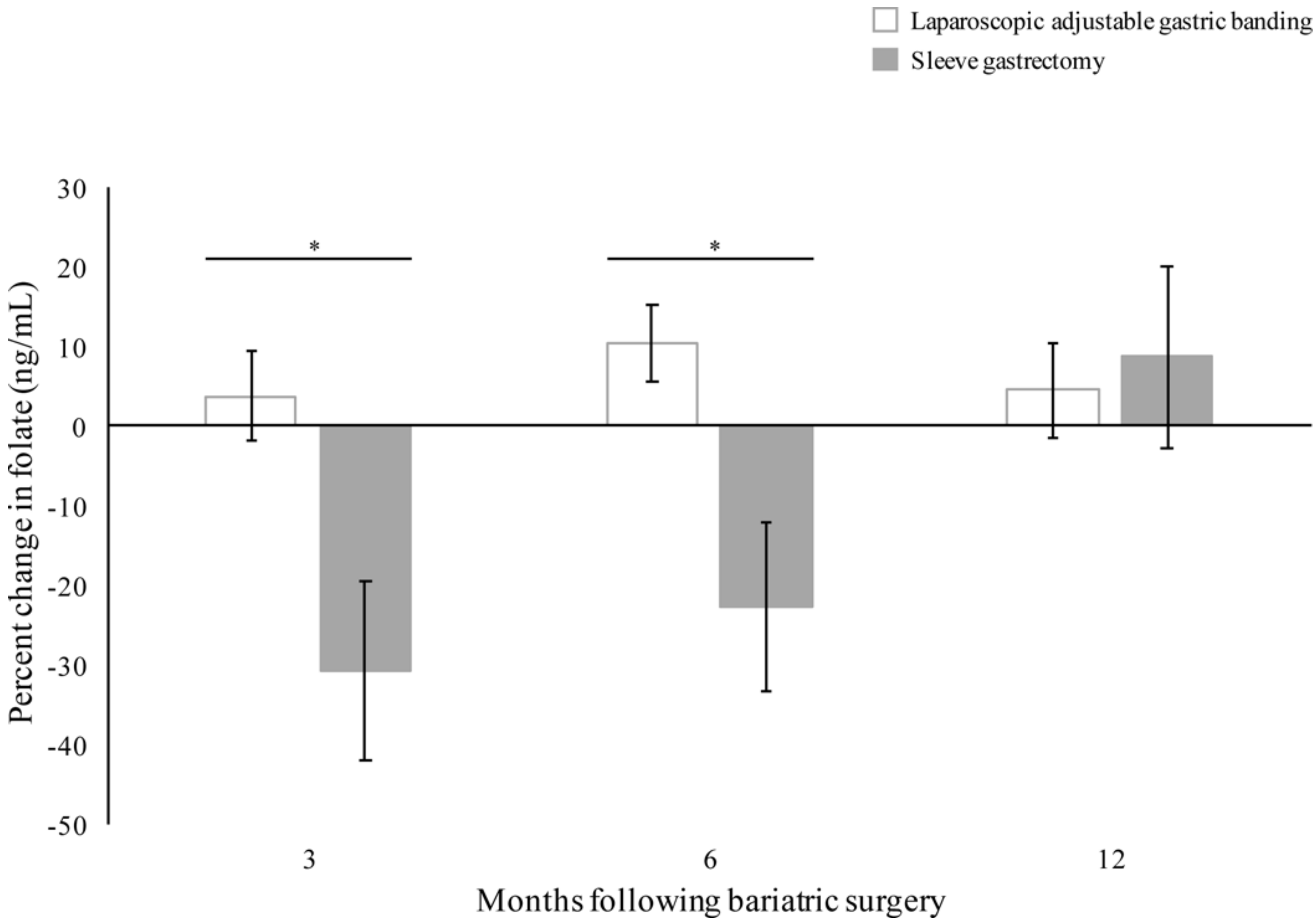

Figure 1.

Mean percent change in folate from the initial visit following laparoscopic adjustable gastric banding and sleeve gastrectomy. *between group differences, *P<0.05*. Error bars represent standard error.

Table 1

Baseline characteristics of LAGB and SG patients expressed as mean (SD) except for sex, ethnicity and anemia marker levels expressed as number (%)

	LAGB n = 141	SG n = 34	*P*
Sex			0.79
Male	48 (34)	13 (38)	
Female	93 (66)	21 (62)	
Age (y)	16.2 (1.2)	15.8 (1.6)	0.13
Weight (kg)	132.9 (27.5)	134.5 (22.7)	0.76
Height (cm)	167.2 (8.2)	166.7 (9.0)	0.76
BMI (kg/m^2)	47.4 (8.3)	48.3 (6.7)	0.55
Ethnicity *			0.03
African American	19 (13)	3 (9)	
Asian	0 (0)	2 (6)	
Caucasian	51 (36)	7 (21)	
Hispanic	53 (38)	20 (59)	
Mixed ethnicity	14 (10)	2 (6)	
Not specified	4 (3)	0 (0)	

*Percentages in the SG group add up to > 100% due to rounding.

Table 2

Low anemia marker levels at baseline in LAGB and SG patients expressed as number (%)

	LAGB	**SG**	***P***
	n=134	n=33	
Folate (ng/mL)	2 (1)	1 (3)	0.49
	n=136	n=30	
B_{12} (pg/mL)	6 (4)	1 (3)	1.00
	n=135	n=34	
Ferritin (ng/mL)	6 (4)	3 (9)	0.39
	n=137	n=32	
Iron (μg/dL)	30 (22)	7 (22)	1.00
	n=140	n=34	
Hgb (g/dL)	21 (15)	8 (24)	0.30
	n=140	n=34	
Hct (%)	3 (2)	1 (3)	0.58

Table 3

Anemia marker levels in LAGB and SG patients (adjusting for weight loss) expressed as mean (SD)

		Initial Visit	3 Months	6 Months	12 Months	Group*Time ***P***
Folate (ng/mL)		n=134	n=55	n=75	n=52	<0.001
	LAGB	12.7 (7.9)	**12.7 (11.3)**	**13.1 (9.8)**	12.3 (12.0)	
		n=33	n=15	n=17	n=15	
	SG	12.5 (15.2)	**7.5 (24.3)**[a]	**9.1 (25.7)**[a]	13.9 (26.0)[bc]	
B_{12} (pg/mL)		n=136	n=55	n=75	n=54	0.002
	LAGB	639.1 (353.8)	610.7 (509.3)	613.8 (441.5)	547.7 (535.2) [ac]	
		n=30	n=15	n=18	n=15	
	SG	644.4 (716.6)	696.7 (1102.0)	531.1 (1124.7)[b]	643.9 (1200.7)	
Ferritin (ng/mL)		n=135	n=56	n=77	n=55	<0.001
	LAGB	56.0 (52.0)	46.9 (72.3)[a]	53.3 (63.3)	49.1 (77.3)	
		n=34	n=16	n=17	n=15	
	SG	57.4 (98.3)	54.9 (154.3)	46.4 (164.9)	41.2 (173.7)	
Iron (μg/dL)		n=137	n=57	n=77	n=55	0.57
	LAGB	64.2 (45.4)	63.2 (65.1)	75.1 (55.8)	68.1 (67.8)	
		n=32	n=15	n=18	n=15	
	SG	62.7 (89.3)	74.4 (136.2)	77.0 (142.6)	65.4 (149.7)	
Hgb (g/dL)		n=140	n=58	n=74	n=55	0.64
	LAGB	13.2 (2.7)	13.2 (4.0)	13.4 (3.6)	14.0 (4.2)	
		n=34	n=16	n=19	n=17	
	SG	13.2 (5.4)	13.5 (8.5)	13.4 (8.8)	13.4 (9.0)	
Hct (%)		n=140	n=58	n=74	n=55	0.71
	LAGB	40.9 (4.5)	40.4 (6.4)	40.8 (5.1)	40.3 (6.2)	
		n=34	n=16	n=19	n=17	
	SG	40.9 (8.9)	40.9 (12.8)	40.3 (14.7)	40.6 (14.4)	

Hgb, hemoglobin; Hct, hematocrit

Bolded values are significant between-group differences at indicated follow-up time.

[a] within-group significant differences at time from baseline.

[b] within-group significant differences at time from 3 months.

[c] within-group significant differences at time from 6 months.

"Group*Time" values indicate if LAGB and SG groups differ with respect to time.