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ORIGINAL CONTRIBUTIONS

Essential Fatty Acid Plasma Profiles Following Gastric Bypass and Adjusted Gastric Banding Bariatric Surgeries

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Abstract
Background Although patients experience hair loss and dry skin which may be attributable to deficiency in essential fatty acids (EFAs), the impact of bariatric surgeries on EFA status is unknown.
Methods This study aimed to assess plasma phospholipid fatty acid profiles following adjustable gastric banding (AGB), which restricts dietary fat intake, versus Roux-en-Y gastric bypass (RYGB), which also promotes fat malabsorption. Serial measures were obtained before and 1 and 6 months from women undergoing RYGB (N=13) and AGB (N=5). Measures included the composition of plasma fatty acids in phospholipids, dietary intake, and body fat mass. Friedman and Mann–Whitney tests were used to assess differences over time and between groups, respectively, $p<0.05$.
Results Dietary intake of fats decreased equally at 1 and 6 months following RYGB and AGB. By 6 months, the RYGB group lost more body fat. There were no remarkable changes in EFA in plasma phospholipids following AGB. However, following RYGB, a transient increase in 20:4N6 (+18 %) and a decrease in 20:3N6 at 1 (−47 %) and 6 months (−47 %) were observed. Similar changes were observed in N3 fatty acids following RYGB, including a transient increase in 22:6N3 (+11 %) and decreases in 20:5N3 (−79 and −67 % at 1 and 6 months, respectively). EFA status improved following surgery in the RYGB group.
Conclusions We demonstrate alterations in plasma EFA following RYGB. The status of EFA improved, but the decrease in 20:5N3, the precursor for anti-inflammatory eicosanoids, may be a concern.

Keywords Essential fatty acid deficiency · Female · Gastric bypass · Long chain fatty acids · Weight loss surgery

Clinical Trial Registry: ClinicalTrials.gov #NCT00228579

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Abbreviations

EFA	Essential fatty acids
RYGB	Roux-en-Y gastric bypass
AGB	Adjustable gastric banding
AA	Arachidonic acid
EPA	Eicosapentaenoic acid
DHA	Docosahexaenoic acid
LA	Linoleic acid
ALA	Alpha-linolenic acid
A-CTSI	Atlanta Clinical and Translational Science Institute
BMI	Body mass index
CRP	C-reactive protein
FFA	Free fatty acids

Introduction

Essential fatty acids (EFAs) are polyunsaturated fatty acids that must be obtained from the diet [1] and are important for the function of cell membranes, development of the brain and nervous systems, and the production of eicosanoids [2]. Very

long chain EFAs including arachidonic acid (AA, 20:4N6), eicosapentaenoic acid (EPA, 20:5N3), and docosahexaenoic acid (DHA, 22:6N3) are highly active in these functions and are synthesized from dietary EFA precursors, linoleic acid (LA, 18:2N6) and alpha-linolenic acid (ALA, 18:3N3), through the activity of delta-5 and delta-6 desaturases [3]. Lower activities of desaturase enzymes, and a resulting lower composition of AA, EPA, and DHA in plasma phospholipids, have been demonstrated in humans and rodents who are obese when compared to normal weight controls [4–7]. The health consequences of the modification of fatty acid composition by obesity are not yet clear but may include greater susceptibility to inflammation [8].

Typically, for individuals undergoing calorically restricted diets, intake of essential fatty acids is lower than the recommended levels [9–11]. In addition, stores of EFA in adipose tissue are decreased during dieting due to β-oxidation [12, 13]. People undergoing weight loss due to very low calorie dieting and patients with anorexia nervosa have reduced serum concentrations of phospholipids LA and ALA compared to normal weight controls as well as have demonstrated signs of EFA deficiency [14–16]. On the other hand, in individuals with obesity, phospholipid concentrations of EPA and DHA are increased following weight loss, suggesting normalization of desaturase enzyme activity [4, 13, 14, 17]. Thus, studies suggest that energy restriction diets impact both negatively and positively on the fatty acid composition of circulating plasma and tissue phospholipids; negatively due to reduced EFA intake and increased oxidation of EFAs to meet energy needs and positively by the normalization of desaturase enzyme activity.

Weight loss following bariatric surgery is effective in reducing the risk of obesity-related disease including type 2 diabetes, atherosclerosis, and cancer [18–20]. However, reduced dietary intake and absorption of essential nutrients following surgery can promote malnutrition in protein, vitamin D, iron, as well as others [21–24]. Although signs and symptoms such as hair loss and dry, rashy skin that may be attributable to deficiency in EFA are common following bariatric surgery [25, 26], the impact of bariatric surgery on EFA status has been investigated only minimally [27]. Bariatric surgery can be classified into procedures that promote weight loss primarily through restriction of food intake and procedures that also promote macronutrient malabsorption. The effect of surgeries that promote energy restriction, such as adjustable gastric banding (AGB), on EFA status would be expected to be similar to conventional dieting. However, the impact of Roux-en-Y gastric bypass (RYGB), a combined restrictive/malabsorptive procedure, on EFA status may be more complex, since ingested food is diverted from the digestion fluids until the distal jejunum, and maldigestion and malabsorption of fat has been reported [28, 29]. A study, by Elizondo et al., reported decreased precursor LA concentration in erythrocytes phospholipids but increased concentration of the desaturase product, AA, at 3 months following RYGB [27]. In this study, the responses to surgery of fatty acids in the n-3 series were mixed, and biochemical indices of EFA deficiency were not assessed. The previous study also did not explore the role of changes in body fat, dietary intake, and metabolic measures as mediators of alterations in phospholipid fatty acid composition. We have shown previously that following RYGB, as body fat decreased, inflammation and oxidative stress decreased concomitantly [30, 31]. Thus, it is possible that phospholipid fatty acid profiles are affected by a number of factors that occur following bariatric surgery including changes in dietary fat intake, weight loss, and decreases in systemic inflammation and oxidative stress.

The population of patients who are receiving bariatric procedures is upwards of 1.5 million in the USA [24], so it is important to determine whether patients are at risk for deficiency in EFA and whether the risk varies between surgeries. Thus, the objective of this current study was to describe, for the first time, compositional changes in plasma phospholipids during 6 months following bariatric surgery procedures that mediate weight loss using caloric restriction versus caloric restriction/malabsorption. The role of potential mediators including dietary intake, body adiposity, and systemic inflammatory response on alterations in fatty acid profiles was assessed. Compared to AGB, we expected to observe more unfavorable changes in EFA profiles following RYGB due to the greater reduction in body adiposity and dietary fatty intake promoted by this malabsorptive surgery.

Subjects and Methods

Participants

Study participants were a convenient and consecutively recruited sample of obese women who were scheduled to undergo RYGB or AGB bariatric procedures at Emory Bariatric Clinic, Atlanta, GA, between March 2007 and March 2009. Informed consent was obtained from all individual participants included in the study. Before the surgery was performed, patients underwent testing to determine medical and psychological fitness for surgery and nutritional counseling as per guidelines for accreditation as a Bariatric Surgery Center of Excellence [32]; the surgical procedure that was chosen was a decision between the patient and the provider. Laparoscopic surgery procedures were followed for each case using methodology published elsewhere [33]. Thirteen participants underwent RYGB, which was categorized as malabsorptive surgery. Five participants received AGB. Race/ethnicity of participants was obtained by self-report. Subjects were excluded from the study if they were (1) male gender, (2) age younger than 18 years or older than 65 years of age, and (3)

with preoperative body mass index (BMI) less than 35 kg/m^2. Participants diagnosed with type 2 diabetes (using criteria from the American Diabetes Association [34]) were included in the study. All study measures were obtained during inpatient visits at the Atlanta Clinical and Translational Science Institute (A-CTSI) at Emory University at baseline (before surgery) and at 1 and 6 months following surgery. Data is presented for participants who completed procedures at all three time points (total N=18). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The IRB Boards at Emory University and Purdue University had approved the study (no. 333-2002 and no. 1204012169, respectively). The study is registered at ClinicalTrials.gov, #NCT00228579.

Body Fat Composition

Body fat mass was measured by air displacement plethysmography (BOD-POD, Life Instruments, Concord, CA), a gold standard measure, in the morning with subjects in fasted condition and in light clothing [35]. Body fatness was also estimated using anthropometrical measures including body weight and height, waist circumference, and sagittal abdominal diameter [35].

Metabolic Measures

Plasma free fatty acids (FFA) were measured by ARUP Laboratories (Salt Lake City, UT), a reference laboratory. C-reactive protein was measured using SYNCHRON LX20 high sensitivity immunoassay (Beckman Coulter, Fullerton, CA). The sensitivity of the assay is 0.07 mg/dL. Oxidative stress was assessed by measuring plasma hydroxyperoxides as described [30, 36].

Analysis of Plasma Phospholipids

Blood samples were obtained from participants in the morning after a 10-h fast, and plasma was fractionated and stored at −80 °C, until analysis. Plasma phospholipids were extracted and separated using solid phase extraction cartridges (SPE columns, Fisher Scientific, Pittsburgh, PA), using established methodology with minor deviations [37, 38]. Methylated phospholipids were analyzed by capillary gas chromatography [38] using a HP 5890 Series II gas chromatograph equipped with a flame ionization detector (Model 7673, Hewlett-Packard Co, Avondale, PA). Retention times for eluted fatty acids were validated using commercial fatty acid mixtures (Supelco Standard, Sigma-Aldrich, PA and Mead Acid Standard, Matreya LLC, Pleasant Gap, PA), which were run on each day of analysis. Fatty acid concentrations were calculated using area under the curve with computing integrator, and values are expressed in molarity percent. Essential fatty acid status was assessed using the Holman index, which is characterized by an increase in 20:3N9, and defined by 20:3N9/20:4N6 [39]. A Holman index >0.2 is indicative of EFA deficiency [39].

Analysis of Dietary Intake

Dietary and supplement intake were obtained using 3-day food records which were self-reported. At each study visit, the study dietitian reviewed the records with the participant to improve accuracy and to obtain missing information. Records were analyzed using Nutritional Data System for Research software, version 2005 (University of Minnesota, Minneapolis, MN). At each study visit, participants received counseling from a registered dietitian regarding post-operative nutritional care [40]. The counseling provided by the dietitian did not differ for the different surgical types.

Statistical Analysis

The statistical software packages STATISTICA (StatSoft, Inc, Tulsa, OK) and SPSS (version 22, IBM Corp., Armonk, NY) were used. For descriptive data, continuous variables are presented as mean±standard error if normally distributed and median (25 %, 75 %) if the data were skewed. To compensate for the small sample size, non-parametric statistical tests were used. The analysis conducted compared RYGB as a malabsorptive surgery and AGB as a restrictive surgery. Group differences were determined using Mann–Whitney U tests for continuous and chi-squared test for categorical variables. Within group differences among baseline and first and sixth month measurements were explored by Friedman test. Post hoc analyses were performed by running Wilcoxon signed rank tests on different combinations on related groups. Relationships between fatty acid concentrations and dietary intake or body adiposity variables were assessed using Spearman correlations using data that were analyzed by each surgical group separately. Significance was set at $p<0.05$. However, to adjust for multiple comparisons, post hoc analyses were conducted with a Bonferroni correction (0.05/3= 0.017), resulting in a significance level set at $p<0.017$.

Results

Baseline Characteristics

Of the total population of study participants, 72 % underwent RYGB and the remainder received restrictive surgeries. The race/ethnicity of the population was equally African American

and Caucasian American. Mean age of women was 36.6± 2.3 years, while their BMI was 44.0±1.0 kg/m^2. Forty-four percent of women were diagnosed with diabetes, and 83 % were pre-menopausal. Both RYGB and AGB groups were comparable in terms of demographics and other baseline characteristics including dietary intake. For example, prevalence of diabetes, body adiposity, plasma phospholipid fatty acid profiles, and metabolic indices were similar between both surgical groups (Table 1). Within the RYGB group, there were no differences in age, adiposity, intake of macronutrients and EFA, and metabolic measures between patients who had diabetes and those without (data not shown). None of the participants in either group exhibited Holman index above 0.2, which is a marker of EFA deficiency.

Changes in Body Adiposity and Dietary Intake Following RYGB and AGB

During the 6 months following surgery, although both groups experienced weight loss (both $p<0.05$), there were differences between surgical groups. During the first month, participants undergoing RYGB experienced a larger decrease in body

Table 1 Baseline characteristics of study participants

	RYGB (n=13)	AGB (n=5)	Significance (p)
Race			
Black	5 (38 %)	4 (86 %)	0.11
White	8 (62 %)	1 (14 %)	
Age (years)	39.2±2.5	29.8±4.1	0.139
BMI (kg/m^2)	45.4±0.9	40.5±2.6	0.115
Diabetes prevalence			
Yes	7	1	0.20
No	6	4	
Fat (kg)	69.0±3.3	57.5±7.1	0.126
Daily dietary intake			
Caloric intake (kcal)	1,773±179	2,236±247	0.155
Protein intake (g)	78.4±7.6	91.5±7.9	0.429
Carbohydrate intake (g)	214.6 (152.5, 217.6)	247.8 (196.8, 255.4)	0.429
Fat intake (g)	61.0±8.3	93.1±12.3	0.126
N-6 intake (g)	5.26±1.34	7.01±1.70	0.370
N-3 intake (g)	0.58 (0.15, 0.80)	0.82 (0.56, 0.85)	0.317
Plasma phospholipids (percentage by molarity of total fatty acid phospholipids)			
16:0	30.19 (28.55, 31.21)	29.29 (29.13, 29.71)	0.657
18:0	17.15 (16.37, 18.31)	17.25 (17.17, 18.89)	0.693
18:1N-9	9.08 (8.24, 10.22)	8.73 (7.67, 8.79)	0.237
20:3N-9	0.30 (0.06, 0.33)	0.35 (0.21, 0.40)	0.375
18:2N-6	18.67 (17.44, 24.21)	19.78 (18.33, 20.20)	0.921
20:3N-6	3.19 (2.70, 3.66)	3.37 (2.52, 3.38)	0.493
20:4N-6	12.28 (10.44, 13.78)	13.23 (12.6, 14.27)	0.115
18:3N-3	0.00 (0.00, 0.13)	0.00 (0.00, 0.10)	0.844
20:5N-3	0.41 (0.32, 0.55)	0.41 (0.00, 0.46)	0.402
22:6N-3	2.48 (2.26, 2.83)	3.12 (2.31, 4.11)	0.375
Holman index	0.02 (0.01,0.03)	0.02 (0.02, 0.03)	0.730
Metabolic indicators			
Free fatty acids (mmol/L)	0.71 (0.43, 0.87)	0.53 (0.41, 0.63)	0.258
C-reactive protein (mg/dL)	1.06 (0.89, 2.39)	0.79 (0.63, 1.01)	0.188
Hydroperoxides (dROMS units)	0.61±0.10	1.10±0.25	0.126

Differences in baseline characteristics between participants undergoing Roux-en-Y gastric bypass (RYGB) versus adjustable gastric banding (AGB) were compared using chi-squared analysis (for categorical variables) or Mann–Whitney U tests (for continuous variables). For descriptive data, continuous variables are presented as mean±standard error if normally distributed and median (25 %, 75 %) if the data were skewed. Holman index is defined as the ratio of 20:3N9/20:4N6

BMI body mass index

weight (−10 % of initial) compared to those undergoing AGB (−7.5 %). Also by the sixth month, participants who obtained RYGB had lost more weight (−28 %) compared to those who had AGB surgeries (−13 %, Table 2). Similarly, at 6 months following surgery, participants who had received RYGB lost more body fat mass compared to those who had AGB (−43 versus −2.1 %, respectively). Participants decreased their daily macronutrient intake and consequently total energy intake, for the first and sixth month periods following surgery, and there were no differences between groups (Table 2). Following the surgical procedures, the decrement in fat intake was comparable between groups. Following surgery, participants in the RYGB group had a transient decrease in their dietary intake of N-6 fatty acids. Dietary intake of N-3 fatty acids including 18:3N3 (0.079±0.030 g/day for RYGB and 0.060±0.029 g/day for AGB) was low compared to recommended levels (1.1 g/day [11]) before surgery, and this remained low after surgery with no differences between groups.

Changes in Plasma Phospholipids Following RYGB and AGB

Within plasma phospholipids, compared to baseline, transient changes were observed after surgery in saturated fatty acids, 16:0 (+10 % at 1 month) and 18:0 (−7 % at 1 month), and this did not differ between surgical groups (Table 3). In the N-9 fatty acid series, which are non-essential, we found an increase in the precursor, 18:1N9, in the RYGB group (+20 %) but not the AGB group at 6 months after surgery. However, 20:3N9, the product of 18:1N9, which is a marker of EFA deficiency when elevated, tended to decrease in the RYGB group at 1 and 6 months following surgery (−9 and −54 %, respectively). For EFA in the N-6 series, 18:2N6 fatty acid in plasma phospholipids decreased at 1 month (−16 and −14 % for RYGB and AGB surgery groups, respectively); however, this change was transient. The intermediary product, 20:3N6, decreased (both −47 %) in the RYGB group at 1 and 6 months following surgery, while no changes were observed in the AGB group. Despite the decrease in precursors, there was a transient increase in 20:4N6 (+18 %) observed in the RYGB group at 1 month following surgery. Alterations in profiles of N-3 fatty acids in plasma phospholipids were similar to those observed for N-6 fatty acids. The concentration of 18:3N3 did not change in response to either surgery. However, a sustained decrease was observed in the intermediary product, 20:5N3 (−79 and −67 % at 1 and 6 months, respectively), for participants undergoing RYGB. Moreover, at 1 month for participants undergoing RYGB, a transient increase in 22:6N3 (+11 %) was observed. Measures of EFA status showed improvement (by a decreased 20:3N9 concentration and a decreased Holman Index ratio) in RYGB group, at 1 and 6 months following surgery. EFA status did not change in participants who underwent AGB. Consistent with these observations, deficiency in EFA did not develop within 6 months after surgery for participants in either group.

Changes in Metabolic Indices Following RYGB and Restrictive Surgery

The concentration of plasma FFA was increased (+62 %) in the RYGB group at 1 month following surgery, which is evidence of the increased catabolic state of this group, but values were restored to baseline by 6 months following surgery (Table 3). Plasma concentration of C-reactive protein (CRP), an indicator of inflammation, was not observed to change compared to baseline in either surgical group at 1 month,

Table 2 Changes in body adiposity and dietary intake following surgery

	RYGB			AGB			Group differences	
	Baseline	1 month	6 months	Baseline	1 month	6 months	Δ 1 month	Δ 6 months
BMI (kg/m^2)	45.4±0.9	41.1±1.1*	32.6±1.2*, **	40.5±2.6	37.5±2.6	35.2±2.9	0.027	0.001
Fat (kg)	69.0±3.3	60.9±3.5*	39.3±3.4*,**	57.5±7.2	52.8±5.9	47.2±6.8	0.256	0.001
Daily dietary intake								
Caloric intake (kcal)	1,773±179	650±80*	905±96*	2,236±247	974±345	1,354±224	0.916	0.916
Protein intake (g)	78.4±7.6	49.8±5.7	55.0±5.1	91.5±7.9	54.2±17.8	60.1±8.7	0.673	1.000
Carbohydrate intake (g)	214.6 (152.5, 217.6)	65.5 (53.9, 98.6)*	86.9 (76.7, 126.7)*	247.8 (196.8, 255.4)	109.1 (37.9, 169.2)	202.7 (131.3, 204.4)	0.292	0.292
Fat intake (g)	61.0±8.3	16.9±3.58*	29.8±3.6*	93.1±12.3	24.6±8.0	51.7±12.1	0.171	0.461
N-6 intake (g)	5.26±1.34	1.37±0.23*	4.16±0.73**	7.01±1.70	1.79±0.58	4.57±1.33	0.673	0.833
N-3 intake (g)	0.58 (0.15, 0.80)	0.19 (0.08, 0.36)	0.71 (0.35, 0.92)	0.82 (0.56, 0.85)	0.18 (0.06, 0.22)	0.47 (0.40, 0.52)	0.527	0.206

Within group differences among baseline, first month, and sixth month measurements were explored by Friedman test. Post hoc analyses were performed by running Wilcoxon signed rank tests on different combinations on related groups. Group differences in changes from baseline between patients who underwent RYGB and AGB were explored using Mann–Whitney *U* test. A Bonferroni was applied to correct for multiple comparisons, resulting in a significance level set at $p<0.017$

*=$p<0.017$, 1 or 6 months versus baseline; **=$p<0.017$, 6 versus 1 month

Table 3 Changes in plasma phospholipid fatty acid profile and metabolites in participants undergoing RYGB and AGB surgeries

	RYGB	AGB	*p*	RYGB	AGB	*p*
	Change from baseline to 1 month			Change from baseline to 6 months		
Saturated						
16:0	3.98 (1.67, 6.13)	1.17 (−0.14, 3.68)	0.127	0.48 (−1.31, 3.15)	−0.94 (−2.31, 1.16)	0.292
18:0	−1.63 (−3.28, −0.94)	−0.27 (−0.36, 1.14)	0.009	−1.83 (−2.96, −0.10)	0.31 (−0.09, 0.72)	0.045
Polyunsaturated—non-essential						
18:1N-9	0.51 (−0.90, 1.42)	1.27 (0.18, 2.25)	0.278	2.52 (1.16, 3.03)	0.67 (−3.97, 1.66)	0.045
20:3N-9	−0.10 (−0.3, 0.0)	−0.09 (−0.31, 0.11)	0.805	−0.21 (−0.31, 0.12)	0.14 (−0.03, 0.18)	0.126
Polyunsaturated—essential fatty acids						
18:2N-6	−3.25 (−5.89, −0.92)	−1.18 (−5.63, −0.57)	0.657	−2.25 (−5.19, 0.95)	−0.15 (−2.87, 0.62)	0.598
20:3N-6	−1.44 (−1.92, −0.99)	−0.16 (−1.22, 0.38)	0.026	−1.14 (−1.43, 0.61)	0.42 (−0.15, 0.71)	0.002
20:4N-6	2.74 (1.09, 3.88)	0.52 (−6.74, 2.96)	0.183	0.53 (−1.15, 2.89)	0.33 (−0.28, 0.34)	0.883
18:3N-3	0.00 (−0.13, 0.09)	0.00 (−0.13, 0.08)	1.000	−0.05 (−0.13, 0.00)	0.00 (−0.13, 0.08)	0.332
20:5N-3	−0.29 (−0.55, −0.19)	0.00 (−0.15, 0.27)	0.008	−0.29 (−0.48, −0.12)	0.14 (−0.16, 0.79)	0.015
22:6N-3	1.19 (0.81, 1.49)	0.11 (−0.74, 0.55)	0.007	0.46 (−0.05, 1.08)	0.04 (−1.06, 0.74)	0.225
Holman index	−0.01 (−0.03, 0.00)	−0.01 (−0.02, 0.01)	0.805	−0.02 (−0.03, 0.01)	0.01 (−0.01, 0.01)	0.092
FFA	0.41 (0.19, 0.65)	0.16 (−0.02, 0.01)	0.301	0.03 (−0.38, 0.26)	0.10 (−0.11, 0.42)	0.375
CRP	−0.61 (−1.17, 0.71)	0.25 (−0.34, 0.49)	0.218	−0.83 (−1.85, −0.44)	−0.33, −0.71, −0.12	0.094
Hydroperoxides	−0.01 (−0.31, 0.16)	−0.21 (−0.54, 0.01)	0.364	−0.05 (−0.21, −0.03)	−0.55 (−1.46, −0.25)	0.013

Data presented as median (25 %, 75 %). Differences between patients who underwent RYGB versus those who underwent adjustable gastric banding surgery were explored by Mann–Whitney *U* test

FFA plasma free fatty acids, *CRP* C-reactive protein

and it was found to decrease at 6 months following both restrictive and malabsorptive surgeries. Plasma concentrations of lipid hydroxyperoxides, a marker of oxidative stress, did not change at 1 month following RYGB or restrictive surgery. However, at 6 months following surgery, lipid hydroxyperoxides decreased in both RYGB and AGB groups (−18 and −68 %, respectively). .

Relationships Among Changes in Plasma Phospholipids, Dietary Intake, Body Adiposity, and Metabolic Indices

We assessed whether changes observed in EFA phospholipid profiles were related to the changes in dietary fatty acid intake or in body adiposity (Table 4). Most of the alterations in plasma phospholipid concentrations occurred following RYGB during the first month period, so longitudinal associations with diet and adiposity during this period were of interest. A positive but non-significant correlation was found between decreased dietary intake of N-6 fatty acids and the decrease observed in 20:3N6 in plasma phospholipids (r=0.52, p<0.08) at 1 month following RYGB. In addition, a correlation was found between intake of N-3 fatty acids and the decrease in plasma phospholipid 20:5N3 content (r=0.69, p=0.01). The observed increase in 20:4N6 in plasma phospholipids was associated with a decrease in dietary intake of N-6 fatty acids (r=−0.67, p=0.02) and also a decrease in dietary intake of N-3 fatty acids (r=−0.89, p=0.00). There was no relationship between dietary intake of N3 fatty acids and plasma phospholipid 22:5N3 content. No significant relationships were found between changes in body fat and EFA profiles in plasma phospholipids (data not shown). We also assessed whether markers of metabolism (such as plasma free fatty acids) or metabolic risk (CRP) were associated with changes in EFA. In patients who had RYGB surgery, there was a positive correlation between the changes in plasma concentrations of CRP and 22:6N3 at 1 month (r=0.62, p=0.023). No other notable relationships between phospholipid concentrations and metabolic indicators were observed (data not shown).

Discussion

The objectives of this study were to compare the impact of restrictive versus malabsorptive bariatric surgery on plasma phospholipid profiles and determine relationships between concomitant changes in dietary fatty acid intake and adiposity following surgery. Findings were that RYGB, but not AGB surgery, was associated with alterations in essential fatty acids within plasma phospholipids including decreases in precursors and intermediary fatty acids (18:2N6, 20:3N6, 20:5N3) and transient increases in products (20:4N6 and 22:6N3). Following RYGB, phospholipid fatty acid composition was restored to baseline levels by 6 months post-surgery, except for a sustained decrease in content of 20:5N3. For patients

Table 4 Longitudinal relationships during 1 month following surgery between plasma phospholipid concentrations and dietary intake of N3 and N6 fatty acids

	Δ Dietary N6 fatty acid intake		Δ Dietary N3 fatty acid intake	
	r	*p*	*r*	*p*
RYGB group				
Δ 18:2N6	0.14	0.65	−0.17	0.59
Δ 20:3N6	0.52	0.08	0.23	0.47
Δ 20:4N6	**−0.67**	**0.02**	**−0.89**	**≤0.01**
Δ 18:3N3	0.30	0.35	0.38	0.23
Δ 20:5:N3	0.45	0.14	**0.69**	**0.01**
Δ 22:6N3	0.23	0.47	0.16	0.62
AGB group				
Δ 18:2N6	0.20	0.74	−0.50	0.39
Δ 20:3N6	−0.30	0.62	0.30	0.62
Δ 20:4N6	−0.30	0.62	0.30	0.62
Δ 18:3N3	−0.62	0.27	−0.05	0.93
Δ 20:5:N3	−0.30	0.62	0.30	0.62
Δ 22:6N3	−0.50	0.39	−0.10	0.87

Analysis was performed using Spearman's correlations. Data is analyzed separately for each surgical group. Δ = change at 1 month following surgery compared to baseline value

Values depicted in bold are significantly correlated, $p < 0.05$

undergoing RYGB, reductions in dietary intake of N-6 and N-3 fatty acids explained the decreased plasma concentrations of precursor fatty acids observed but not the reciprocal increase in AA and DHA. Finally, contrary to our hypothesis, deficiency did not develop in any patient during the initial 6 months following RYGB or AGB surgery, and in fact, EFA status improved during the course of the study.

Plasma phospholipid concentrations are responsive to changes in diet and adipose tissue depots [41]. Since bariatric surgery is known to induce a dramatic reduction in dietary fat intake as well as in body adiposity [30, 42], an objective of the study was to examine effects of changes in these variables on the fatty acid composition of plasma phospholipids. In addition, studies have shown mild to moderate degrees of fat malabsorption following RYGB [28, 43]. In the current study, as has been shown following weight loss through conventional dieting, content of LA within plasma phospholipids was decreased, presumably due to reduction of dietary fat and therefore intake of EFA [14, 17, 44–46] or due to increased beta-oxidation [12, 13]. In support of a dietary explanation for the alterations in EFA, we observed in the current study that the plasma phospholipid content of 20:3N6 and 20:5N3 tended to correlate with intake levels of 18:2N6 and 18:3N3, respectively, suggesting that decreased dietary intake was responsible for the observed decrease in precursor EFAs. Paradoxically, despite decreases in precursor EFAs, we observed concurrent increases in concentrations of derivatives, AA and DHA, in plasma phospholipids, a finding that is consistent with findings in some studies [14, 17, 47–49] but not others [45, 46]. Since we found no relationship between dietary intake and plasma content of AA and DHA, and since such a relationship has not been reported by others, it seems these fatty acids are not sensitive to changes in dietary intake during weight loss. We therefore surmised that the increase observed in AA and DHA could be due to increased β-oxidation following adipose tissue lipolysis. In support of this theory, an increase in free fatty acids was observed in the RYGB group. Alternatively, elevated concentrations of AA and DHA could have been the result of increased activity of desaturase enzymes, as has been previously shown in obese individuals undergoing weight loss [17, 50, 51]. The catalytic rate of desaturase enzymes is activated by free fatty acids [52] which, as aforementioned, were increased following RYGB. Of interest is our finding that changes in plasma concentrations of CRP and DHA were associated; thus, it is possible that inflammatory processes could regulate the expression of desaturase enzyme activity, and such mechanisms could be explored in a future study. Although we did not find relationships between plasma phospholipid fatty content and decreasing adiposity, evidence for such relationships may be observed by directly examining adipose tissue; however, this was not done in the current study.

We expected that plasma phospholipid concentrations would be impacted more by RYGB compared to restrictive surgeries, since RYGB induces more weight loss compared to AGB [42] and also promotes fat malabsorption [28]. As we hypothesized, RYGB induced more alterations in fatty acid profiles—especially during the first month following surgery. However, our findings do not provide evidence for a direct role of adipose tissue regulation of the profile of plasma phospholipid content. Other than higher systemic concentrations of

FFA at 1 month in the RYGB group, there were no other distinguishable responses to surgery (including inflammation or oxidative stress) between groups. By 6 months following surgery, we found that RYGB induced superior reduction in body mass and adiposity compared to AGB, which some other groups have shown [19, 53–56]. However, the differential in weight loss response did not produce differences in fatty acid profiles between groups. Furthermore, by 6 months following surgery, despite substantial weight loss, most phospholipid fatty acid concentrations were restored to baseline concentrations in both RYGB and AGB groups, which is further evidence that changes in adiposity may not directly mediate fatty acid profiles.

A persistent decrease in plasma phospholipid concentrations of EPA was observed in patients during 6 months following RYGB, but the long-term impact of a systemic decrease is unclear. Eicosapentaenoic acid is beneficial due to its anti-inflammatory property; however, in the context of reduced inflammation and oxidative stress during weight loss, a decrease in EPA may not be a concern. While the effects of a decrease in 20:5N3 are unclear, there was a favorable response in terms of the status of other EFAs. The Holman index improved following RYGB, probably due to a decrease in plasma concentrations of long chain N-9 fatty acids and a reciprocal increase in N-6 long chain EFA, and this index did not change in the patients who underwent restrictive surgeries. Taken together, our findings suggest that over the short-term, malabsorptive and restrictive bariatric surgeries do not have a negative impact on EFA within plasma phospholipids. The findings in the current study are consistent with those of Elizondo at al., which demonstrated decreases in 18:2N6 and 20:5N3 and increases in desaturase products 20:4N6 and 22:6N3 in erythrocyte phospholipids at 3 months following RYGB. To our knowledge, the current study is the first to report that the changes observed in plasma phospholipid fatty acid profile are unique to RYGB surgery and are mostly transient. Studies with a follow-up beyond 6 months are necessary to determine the long-term impact of RYGB on EFA status and the functional consequences of the alterations.

In this current study, we provide information on the responses of plasma fatty acid profiles during the initial 6 months following commonly performed bariatric surgeries. Limitations are that males were not studied, and although men represent a small proportion of those who undergo weight loss surgery, future studies should determine whether similar findings would be observed in men. Also, we did not obtain tissue samples for determination of phospholipid content, although several studies have shown that plasma and tissue phospholipid concentrations are highly correlated. For example, a similar pattern of fatty acid alterations as we report in the current study was found in erythrocytes following gastric bypass surgery in the Elizondo study [27]. It should also be noted that dietary information was obtained using 3-day food records, which were self-reported. Food records are subject to systematic bias, although this could be mitigated by having a dietitian review the records with the participant to improve accuracy [57], as we did in the study. Another of the limitations is that the population in this study was not randomized and was a sample of convenience of women recruited between 2007 and 2009 that resulted in relatively small groups of women in both surgery groups. We acknowledge that such a study design can be affected by selection bias. Also, it is possible that some of the statistically non-significant differences between RYGB and AGB groups may have been due to a small sample size. In future studies, analyses should be repeated on a larger sample size of women who underwent RYGB and AGB. Despite these limitations, this study is the first to assess the impact of various bariatric surgeries on status of fatty acids, in a multiethnic population, and to include covariates such as dietary fat intake, adipose tissue mass, and systemic inflammatory response. The clinical relevance of our findings is that despite decreased dietary intake of essential fatty acids in the first 6 months following common bariatric surgeries, patients undergoing gastric bypass experienced favorable changes in essential fatty acids, with the exception of eicosapentaenoic acid. Although the clinical consequences of decreased systemic concentrations of EPA are not yet clear, it may be prudent to advise patients to increase their dietary intake of N-3 fatty acids following bariatric surgery.

In conclusion, the results of our study indicate that, following RYGB surgery, there is a decrease in precursor and intermediary fatty acids including 20:5N3 and a transient increase in the long chain fatty acids, AA and DHA. These changes were unique to RYGB and suggested an upregulation of desaturase enzyme activity. Future studies are needed to confirm whether the catabolic processes that occur acutely following malabsorptive bariatric surgery can induce the biosynthesis of long chain EFA, as well as the functional and long-term consequences of alterations in these bioactive compounds.

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Conflict of Interest The authors declare that they have no competing interests.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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