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Immune marker reductions in black and white Americans following sleeve gastrectomy in the short term phase of surgical weight loss

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Abstract:	Background Surgical weight loss procedures like vertical sleeve gastrectomy (SG) are sufficient in resolving obesity comorbidities and are touted to reduce the burden of pro-inflammatory cytokines and augment the release of anti-inflammatory cytokines. The goal was to determine if early changes to immunoglobulins and general markers of inflammation occur similarly after SG in Black Americans (BA) and White Americans (WA). Methods Personal information, anthropometric data, and plasma samples were collected from 58 participants (24 BA and 34 WA) before and 6 weeks after SG for the measurement of immunoglobulin A (IgA), IgG, IgM, C-reactive protein (CRP), and transforming growth factor (TGFβ). Results Collectively, IgG, TGFβ, and CRP were all significantly reduced at six weeks following SG. Both IgG and CRP were significantly elevated in BA in comparison to WA prior to weight loss. CRP levels in BA were reduced to a similar extent as WA, but IgG levels were more dramatically reduced in BA than WA despite the overall higher starting concentration. No change was observed in IgA and IgM. Conclusions These data suggest that SG improves markers of immune function in both BA and WA. More diverse markers of immune health should be studied in future work.
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Ethics Statement Enter an ethics statement for this submission. This statement is required if the study involved: • Human participants • Human specimens or tissue • Vertebrate animals or cephalopods • Vertebrate embryos or tissues • Field research Write "N/A" if the submission does not require an ethics statement. General guidance is provided below. Consult the submission guidelines for detailed instructions. **Make sure that all information entered here is included in the Methods section of the manuscript.**	. All procedures were performed in accordance per the 1964 Declaration of Helsinki ethical standards. Written informed consent was obtained from each participant before formally entering this IRB approved study, Predictors of Weight Loss (POWL), at the University of Mississippi Medical Center (UMMC), Jackson, MS (IRB# 2014-0047).

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Title: Immune marker reductions in black and white Americans following sleeve gastrectomy in the short term phase of surgical weight loss

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Running Title: Racial changes in inflammation after bariatric surgery

ABSTRACT

Background. Surgical weight loss procedures like vertical sleeve gastrectomy (SG) are sufficient in resolving obesity comorbidities and are touted to reduce the burden of pro-inflammatory cytokines and augment the release of anti-inflammatory cytokines. The goal was to determine if early changes to immunoglobulins and general markers of inflammation occur similarly after SG in Black Americans (BA) and White Americans (WA). **Methods**. Personal information, anthropometric data, and plasma samples were collected from 58 participants (24 BA and 34 WA) before and 6 weeks after SG for the measurement of immunoglobulin A (IgA), IgG, IgM, C-reactive protein (CRP), and transforming growth factor (TGFβ).

Results. Collectively, IgG, TGFβ, and CRP were all significantly reduced at six weeks following SG. Both IgG and CRP were significantly elevated in BA in comparison to WA prior to weight loss. CRP levels in BA were reduced to a similar extent as WA, but IgG levels were more dramatically reduced in BA than WA despite the overall higher starting concentration. No change was observed in IgA and IgM.

Conclusions. These data suggest that SG improves markers of immune function in both BA and WA. More diverse markers of immune health should be studied in future work.

Keywords: immune markers, bariatric surgery, vertical sleeve gastrectomy, immunoglobulins, weight loss surgery

INTRODUCTION

Obesity and its associated comorbidities continue to present a strain on health care around the world. Obesity is a disease of excess adiposity accompanied by chronic low-grade inflammation. The expanding size and number of adipocytes stress the surrounding tissues causing active secretion of cytokines from the adipose and endothelial cells and infiltration of immune cells into the surrounding tissues. Over time, inflammatory markers are elevated enough to be reliably measurable in circulation. The elevated inflammation further drives both systemic and local immune cell activation and cytokine secretion resulting in diverse negative impacts on various organ systems including immuno-hematologic parameters.

Black Americans (BA) carry a larger burden of obesity-related diseases than White Americans (WA). BA women have the greatest prevalence of obesity in the United States [1]. Among BA women, 80% are overweight or obese in comparison to only 62.4% of WA women [2]. 34.6% of AA women are Class II and III Obese compared to 17.6% of WA women [2]. Further, among BA men and women, the age-adjusted prevalence of hypertension is 39.6% and 43.1%, respectively [3]. In WA men and women, the prevalence is 31.4% and 28.7%, respectively [3]. Racial disparities also exist in the incidence of T2DM; 18.7% of all BA >20 years of age have T2DM compared to 7.1% of WA [4]. As a whole, BA suffer from a higher rate of metabolic-related diseases in comparison to WA.

In the U.S., BA also carry a higher burden of inflammation than WA. In a study of racial and ethnic disparities in children, the risk of inflammation is higher in BA children in comparison to WA children [5]. Low parental education and elevated child BMI were

partial mediators of this higher association [5]. In a cross-sectional investigation of ethnicity and blood levels of inflammatory markers in non-smoking, church-goers, BA had higher CRP and IL-6 than WA [6]. Further, in a study comparing inflammatory markers and breast cancer risk factors, BA women had higher levels of inflammatory cytokines IL-6 and interferon γ [7]. In a study of the effect of sleep and loss of immunity, BA participants had higher levels of Il-6 and IL-10 than WA [8]. Taken together, significant evidence in a variety of different sectors of population suggests that BA have higher levels of inflammatory mediators than WA.

Surgical weight loss procedures are sufficient in the resolution of obesity comorbidities such as excess weight, diabetes, and hypertension [9]. However, recent studies suggest that BA have reduced improvements to body weight loss and percentage of total weight loss in comparison to WA [10]. Higher overall rates of complications and health care resource utilization in BA have also been reported within 30 days of surgery in comparison to controls [10]. Bariatric surgeries are touted to reduce the burden of pro-inflammatory cytokines and augment release of anti-inflammatory cytokines [11,12]. Immunoglobulins (Ig) are reduced by bariatric surgery [13] in addition to several inflammatory cytokines and markers levels [14,15]. Moreover, bariatric surgery alters immune cell function and proliferation [16-18]. Nevertheless, the impact of surgery on inflammation in BA surgical recipients has not been reported.

Given that the burden of obesity-related disease is substantial in BA, and inflammation is higher in BA independent of this, understanding the effect of surgical weight loss outcomes in BA is important. The focus of this study was to determine if bariatric surgery ameliorates obesity-related inflammation in BA to a similar extent as

seen in WA subjects. Vertical sleeve gastrectomy (SG) is the most common surgery currently performed in the U.S. Here we report some key differences in the early changes of inflammatory markers after SG in a patient population of Mississippi, a state with one of the highest burdens of obesity-related comorbidities. Using anthropometric data and plasma samples from patients before and six weeks following SG, we investigated specific inflammatory markers IgG, IgM, IgA, TGFβ, and CRP.

MATERIALS AND METHODS

Assurances. All procedures were performed in accordance per the 1964 Declaration of Helsinki ethical standards. Written informed consent was obtained from each participant before formally entering this IRB approved study, Predictors of Weight Loss (POWL), at the University of Mississippi Medical Center (UMMC), Jackson, MS (IRB# 2014-0047).

Study Design. This is a non-randomized prospective study of obese patients receiving elective SG surgery through the Weight Management Clinic, UMMC were consented. The inclusion criteria for this study comprised of men and women between the ages of 21-65 years, BMI ≥35 kg/m^2, and undergoing first-time bariatric procedures between June and December 2016. Exclusion criteria for participation in this study were as follows: 1) Individuals with major organ system failure like: cirrhosis, hepatic insufficiency, portal hypertension, severe renal insufficiency or on dialysis, severe arterial insufficiency, dementia, or the inability to give informed consent. 2) Individuals who are pregnant or lactating. 3) Individuals with prior surgical weight loss procedure.

REDCap electronic record. Study data were collected and managed using REDCap (Research Electronic Data Capture) tools [19] hosted at the University of Mississippi Medical Center. REDCap is a secure, web-based application designed to support data

capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Plasma Analytes**.** Blood was collected in EDTA coated tubes, processed for plasma and stored at -80 ºC until further use. The following kits were used: C-reactive protein (#80955, CrystalChem, Elk Grove Village, IL), immunoglobulin A (#88-50600, Thermofisher, Waltham, MA), immunoglobulin G (#88-50550, Thermofisher, Waltham, MA), immunoglobulin M (#88-50620, Thermofisher, Waltham, MA), and tumor growth factor beta (#RAB0460, SigmaAldrich, St. Louis, MO). All assays were performed according to the manufacturers' specifications.

Statistical Analysis. Descriptive statistics were compiled where appropriate. For comparing post vs. pre-operative characteristics of participants, paired student's T tests and two-way analysis of variance with repeated measures for time were used followed by Tukey's post hoc test for variables of race and time with results are given as means ± SEM. Models for pre-op immune markers consisted of generalized linear models with gamma families to account for right skewness of the markers and identity link to facilitate ease of interpretation. In addition to the adjusters listed below, these models were adjusted for pre-op systolic and diastolic blood pressures. Weight change was modeled using ordinary least squares on the difference in weight post-op vs. pre-op. Similar models were used to model immune marker change, additionally adjusting for BMI change, systolic change, and diastolic change. All models were adjusted for age, sex, race, hypertension, hyperlipidemia, sleep apnea, and diabetes. Multivariable

fractional polynomials were used as a first step in modeling to account for potential nonlinearities. All linearity assumptions were found to be valid. Results were considered statistically significant when $p < 0.05$. All statistical analyses were performed with GraphPad Prism v8.1.2 (GraphPad Software, San Diego, California) and Stata v16.1 (StataCorp, College Station, Texas).

RESULTS

Baseline Characteristics of Participants. The total number of participants for the current study was 58 individuals of which 24 self-identified as BA and 34 self-identified as WA. Of the BA participants, all 24 were female, comprising 41.3% of the total; we were unable to enroll any BA males. Of the 34 WA participants, 28 or 48.2% were females and 6 participants or 10.3% of the total were WA males. There was no difference in the average age of female BA and WA participants (average age ± SEM, 45.5±2.0 years and 46.9±2.0 years respectively) or WA males (average age of 43.8±2.7 years)**.** BA participants had significantly higher levels of hypertension in comparison to WA patients, $p<0.001$, (**TABLE 1**)**.** No difference was measured in the instances of hyperlipidemia, diabetes, or obstructive sleep apnea between BA and WA **(TABLE 1).**

Pre-operative Characteristics of BA and WA Participants. There were no differences in pre-operative body weight or BMI of BA vs. WA participants enrolled in the study (**TABLE 2**). Further, there was no difference in waist circumference of BA and WA participants (**TABLE 2**); however, hip circumference was significantly higher pre-operatively in BA, $p<0.05$ (**TABLE 2**). Blood pressure and pulse did not differ significantly between BA and WA (**TABLE 2**). Liver enzymes, ALT and AST, were significantly higher in WA participants compared to BA, although there was no

difference observed in bilirubin, $p<0.001$ (**TABLE 2**). Creatinine and glucose were not different between BA and WA (**TABLE 2**). There was no difference in WBC count, though hematocrit percentage was significantly higher in WA, $p<0.01$, and platelets were significantly higher in BA, $p<0.05$ (**TABLE 2**).

Pre-operative Inflammatory markers in BA and WA Participants. Age did not influence inflammatory markers CRP, IgA, IgG, IgM, or TGFβ at the pre-operative time point (**TABLE 3**). BA participants had on average 1377.36 mg/dL higher IgG levels than WA participants pre-operatively, $p=0.001$ (**TABLE 3**). There was no influence of hypertension or sleep apnea status on the inflammatory markers tested pre-operatively (**TABLE 3**). However, the presence of diabetes was associated with a 17.33 mg/dL reduction on average of IgA in comparison to non-diabetics, $p<0.05$, and hyperlipidemia was associated with 1.20 mg/dL lower CRP, $p=0.001$ (**TABLE 3**).

Pre-operatively, BMI did not influence the circulating levels of immune markers measured in this cohort (**TABLE 3**). Additionally, pre-operative systolic blood pressure was not an influence on circulating levels of immune markers (**TABLE 3**). However, higher pre-operative diastolic blood pressure was associated with a significant, albeit subtle, reduction in circulating pre-operative CRP levels by 0.04 mg/L, $p<0.05$ (**TABLE 3**).

Comparison of BA and WA six weeks after SG.. As anticipated, 6 weeks following SG, both BA and WA lost a significant amount of body weight ($p<0.0001$), with no difference in weight change identified by race (**TABLE 2**). When percent excess body weight (%EWL) is calculated, based on ideal weight, WA participants (Mean ±SEM) (20.55 ± 1.327) had a greater amount of excess bodyweight loss in comparison to BA

participants (24.15 ± 0.86), p<0.05. Percent weight loss (%WL) was not significant (BA 11.24 ± 0.56 vs. WA 12.44 ± 0.34), nor was the change in BMI (BA 5.32 ± 0.27 vs. WA 5.547 ± 0.20) or percent excess BMI loss (%EBMIL) (BA 25.2 ± 2.07 vs. WA 29.53 ± 1.15).

Further, BMI (p<0.0001), waist circumference (p<0.0001), and hip circumference (p<0.0001) were all reduced at 6 weeks post SG with no differences identified by race (**TABLE 2**). Pulse rate (p<0.0001) and systolic blood pressure (p<0.0001) significantly reduced following SG with no differences specified by race (**TABLE 2**). Diastolic blood pressure did not change six weeks after SG as a function of time (**TABLE 2**). However, a significant racial difference in diastolic blood pressure at 6 weeks post-surgery was measured with BA having less of a reduction than WA, p<0.05 (**TABLE 2**).

Overall, weight and BMI changes did not correlate with race or the presence of the comorbidities we reported, such as hypertension, hyperlipidemia, sleep apnea, or diabetes mellitus (**TABLE 3**). On the other hand, greater reduction in both weight and BMI were correlated with age, such that younger participants lost weight at an average of 0.10 kg more per year younger and 0.04 points of BMI per year younger than older participants, *p*<0.05 (**TABLE 3**).

Effect of SG on circulating immune markers. Plasma IgA and IgM were not altered because of SG (**FIGURE 1**), and there was no impact of race on immunoglobulin A and M levels (**FIGURE 1**). Alternately, there was a significant reduction in plasma IgG after SG, *p*<0.001 (**FIGURE 1**). Plasma IgG varied significantly by race with BA having higher levels of IgG than WA, *p*<0.001 (**FIGURE 1**). Furthermore, BA had greater reductions in IgG, with an average reduction of 1108 mg/dL as a result of SG in comparison to WA

(**TABLE 5**). Age did not impact the change of any of the cytokines during the first six weeks post-operatively, except for TGFβ, such that for every year older, there was a 0.35 mg/dL increase in TGFβ, $p<0.05$ (**TABLE 5**).

The presence of pre-operative hypertension or sleep apnea status did not contribute to changes in any of the immune markers measured (**TABLE 5**). However, in participants who had diabetes mellitus pre-operatively, SG promoted a greater change, on average, of 23.81 mg/dL in IgM levels than those who did not have diabetes, $p<0.05$ (**TABLE 5**). Change over the 6 weeks following SG in BMI, systolic blood pressure, and diastolic blood pressure did not correlate significantly with any of the shifts in the markers of inflammation tested (**TABLE 5**).

DISCUSSION

Obesity is a condition of excess adiposity that results in chronic low-grade inflammation. Surgical weight loss procedures produce robust improvements in metabolic indices and increase the quality and longevity of life for the obese individual that is burdened with an array of metabolic comorbidities [20]. In the current study, we asked whether inflammatory markers were altered in BA SG recipients differentially than in WA participants and whether these changes accounted for any variation in change in BMI in the six week time frame following bariatric surgery.

Pre-operatively, BA and WA participants were not significantly different overall; however, there were a few notable differences between the groups. BA participants had a significantly higher hip circumference contributing to a lower waist-to-hip ratio than WA participants. A high waist-to-hip ratio is associated with visceral adiposity whereas a

low waist-to-hip ratio is associated with greater subcutaneous fat [21]. Larger proportions of visceral fat lend to an increased risk for cardiovascular disease. Interestingly, WA participants did not have a significant difference in blood pressure or pulse rate in comparison to BA participants, regardless of their larger initial levels of visceral adiposity. This may be due to both groups having a substantial BMI rendering waist-to-hip ratio as a less reliable marker for cardiovascular dysfunction.

Though within the normal range for both groups, there were markedly lower liver enzymes in BA participants compared to liver enzymes of WA participants. ALT and AST are liver enzymes whose elevations are indicative of liver damage. While obesity is associated with an elevation of liver enzymes, black populations tend to have lower liver enzymes when compared to white populations [22]. Additionally, liver enzymes are generally elevated in men in comparison to women [22,23]. Despite variations in diagnostic tools, blacks have the lowest prevalence of non-alcoholic fatty liver disease (NAFLD), [24] and non-alcoholic steato-hepatitis (NASH) is inversely associated with being African American, though this finding is somewhat limited by non-histologic diagnosis [25]. Further, the temporal severity of advanced fibrosis is elevated in non-Hispanic whites, whereas in non-Hispanic blacks, the trajectory of severity is reduced [26].

Further, a variant of PNPLA3, a pro-steatotic gene that carries with it a higher incidence of NAFLD occurs with the greatest frequency in Hispanics, followed by non-Hispanic whites, and least in African Americans, may explain the lower prevalence of NAFLD in African Americans despite the prevalence of obesity and diabetes in this population [27]. Despite having lower intrahepatic triglyceride accumulation, once

NAFLD develops, NASH occurs as frequently and as severe as in Caucasian patients [28].

BA participants enrolled in the present study had a lower hematocrit percentage than WA participants, corresponding in pattern to literature showing hematocrit lower in African-Americans than in whites [29]. Though potentially caused by a variety of factors, anemia is a common contributor to low hematocrit and has a higher prevalence in the black population [30]. Platelet counts were also higher in the BA group compared to WA. This is similar to an earlier study in which black women had significantly higher platelet counts than white women [31], particularly applicable to our study as there were no male BA participants.

As expected, participants had noticeable weight loss in comparison to baseline weight with appreciable improvements in BMI, waist circumference, and hip circumference following SG. A recent JAMA Surgery report suggests that BA do not realize the same positive benefits to excess loss of weight as WA [10]. Undoubtedly, given the small sample size of the current study, this facet regarding race was not captured in the data set, though %EWL was greater in the WA participants. Bariatric surgeries are also purported to reduce blood pressure and provide resolution of hypertension along with improvements in heart rate [32,33], as seen in our cohort. It is unknown whether this improvement to cardiovascular health is the result of weight-dependent changes or if the improvement comes from other neural, hormonal, or chemical changes that are weight-independent.

In the current study, IgA and IgM levels were highly variable among participants, both pre-operatively and after six weeks. There was no change to IgA or IgM as a

function of surgery in this short time frame. However, the presence of diabetes pre-operatively was linked with lower IgA levels. Poor glycemic control appears associated with an increase in IgA serum antibodies [34]. Within our data set, the patients identified as diabetic may have more controlled glucose, associated with a reduced IgA in comparison to those individuals who had not been identified to be diabetic. With respect to IgG, BA individuals had higher concentrations at both time points compared to WA, but overall, IgG was dramatically reduced as a result of surgery. IgG is the most common circulating immunoglobulin in the humoral immune system. It binds to pathogens and protects the body from infection by developing a memory of exposure to specific invaders. Black subjects have previously reported to have higher IgG levels in a variety of studies, regardless of context [35,36]. The reason for the higher IgG levels in black subjects remains unknown. The reduction of IgG levels following surgical weight loss is not currently understood.

IgG-specific antibody mediated reactions are a body's natural defensive reaction to infiltrating food antigens [37]. Following an elimination diet (targeting foods which specifically increased IgG levels), overweight or obese adults were able to decrease IgG antibody titers [38]. Thus, the possibility exists that either as a result of diet choice or genetic factors associated with gastrointestinal permeability, BA have greater levels of IgG that are ameliorated with SG.

CRP is an acute phase, hepatically-derived immune marker for generalized inflammation. As with other markers of inflammation, obesity is associated with higher levels of CRP [39]. Bariatric surgery reduces CRP levels at three months following gastric bypass and as far as twelve months in SG patients [13,40]. Participants in the

current study showed a reduction in CRP levels at six weeks in both BA and WA, although BA individuals had overall higher CRP levels. Interestingly, the change in the reduction of CRP levels at six weeks was comparable in BA and WA when the differential CRP starting levels were controlled for. Overall, this aligns with literature suggesting that black subjects have higher CRP levels when compared to white subjects, and further, that CRP levels are higher in women than in men [41].

TGFβ is an immune cell-derived chemokine which regulates a variety of growth, differentiation, and adhesion cellular processes, in particular the chemotaxis of immune cells. TGFB levels are correlated with obesity in humans [42], and reports show that RYGB decreases TGFβ at one year following surgical weight loss [15]. We show very early reductions in TGFβ in the current work with no differences by race. Circulating levels of TGFβ reductions are not as great as age increased, with older recipients of SG have higher levels of TGFβ. The role of both age and potentially sex in TGFβ production remains to be further studied.

Strengths and Limitations.

The study presented here encompassed patients that were consecutively enrolled in the study. The data collected are representative of short-term weight loss and no information is available about the changes to the immune markers at times greater than six weeks. The trajectories of change in excess weight loss and immune markers may change over time for the population's samples. One of the significant failures of the study is the consent of BA males. Not only do men seek bariatric surgery at reduced rates compared to women, the historical context of BA male utilization in medical studies functions as a barrier to enrollment for this study.

Overall, the sample size is small and given the current trajectories, some parameters may have benefited from increasing the power of the study. While we focused on a limited number of markers, there are vast numbers of others that may have also been interesting to test and are important for future studies.

Conclusions.

In a subset of patients receiving SG representing the demographics of our region of the country, there were no differences in the magnitude of weight loss following SG at six weeks. BA had greater starting levels of cardiovascular dysfunction, but lower levels of liver dysfunction and reduced tendency for obesity-related lipid disorders. CRP, TGFβ, and IgG were all reduced as a result of SG. IgG was initially elevated in BA in comparison to WA. However, IgG was substantively reduced in BA than WA in the early phase of weight loss. The higher levels of both IgG and CRP in obese BA have significance, given the greater morbidity and mortality of BA individuals in the current viral pandemic [43] where elevations in inflammation appear to exacerbate the severity of symptoms in the BA population [44]. These data suggest that in the early surgical weight loss time frame, markers of immune function are positively improved with SG for both BA and WA but may be improved more so for BA given their higher starting point. Further work is necessary to understand this relationship more adequately.

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Formal Analysis: CLP, TTL, SL, and BEG
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Investigation: CLP, KDV, and BEG
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Project Administration: KDV and BEG
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Conflicts of interest

CLP, BAW, AD, TTL, STL, SCG, KDV, and BEG have no financial, personal, or professional conflicts of interest.

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FIGURE LEGENDS

Table 1: Baseline comorbidities of study participants. Data presented as percentages. Comparisons made using Chi-squared test.

Table 2: Pre-operative and post-operative characteristics of participants. Data presented as mean ± SEM. Pre-operative values between BA and WA compared using student T test (Column A vs. B). Two-way Anova was used to compare variables of race and time. Boldface designates statistical significance 0.05. BP (blood pressure); ALT (alanine transaminase); AST (aspartate aminotransferase); WBC (white blood cells).

Table 3: Modelling results of pre-operative immune markers. Displayed are beta coefficients, p-values, and 95% confidence intervals. Coefficients for age, BMI, SBP, and DBP correspond to one-unit increases. BMI (body mass index); SBP (systolic blood pressure); DBP (diastolic blood pressure); CRP (c-reactive protein); IgA (immunoglobulin A); IgG (immunoglobulin G); IgM (immunoglobulin M); TGFB (transforming growth factor beta).

Table 4: Modelling results for weight change. Displayed are beta coefficients, p-values, and 95% confidence intervals. Change was defined as post-op minus pre-op, ergo a positive coefficient indicates, on average, less weight loss. Coefficient for age corresponds to one year increase. DM (diabetes mellitus).

Figure 1: Immunoglobulins and immune markers pre- and post-SG. (**A**) Plasma IgA (**B**) Plasma IgG (**C**) IgM (**D**) CRP (**E**) TGFβ. Data presented as mean ± SEM. Two-way Anova was used to compare variables of race and time. IgA (immunoglobulin A); IgG (immunoglobulin G); IgM (immunoglobulin M); CRP (c-reactive protein); TGFB (transforming growth factor beta).

Table 5: Modelling results for immune marker change. Displayed are beta coefficients, p-values, and 95% confidence intervals. Change was defined as post-op minus pre-op, ergo a positive coefficient indicates, on average, less reduction. Coefficients for age, BMI, SBP, and DBP correspond to one-unit increases. HTN (hypertension); DM (diabetes mellitus); BMI (body mass index); SBP (systolic blood pressure); DBP (diastolic blood pressure); CRP (c-reactive protein); IgA (immunoglobulin A); IgG (immunoglobulin G); IgM (immunoglobulin M); TGFB (transforming growth factor beta).

TABLE 1

Participant Characteristics	BA	%	WA	%	Statistics
Hypertension (Y/Total)	22/58	*91.6%*	15/58	*44.1%*	*chi^2=13.77;* ***p<0.001***
Hyperlipidemia (Y/Total)	4/58	*16.7%*	13/58	*38.2%*	*chi^2=3.16; p=0.07*
Diabetes (Y/Total)	9/58	*37.5%*	7/58	*20.5%*	*chi^2=2.01; p=0.16*
Obstructive Sleep Apnea (Y/Total)	11/58	*45.8%*	13/58	*38.2%*	*chi^2=0.33; p=0.56*

TABLE 2

	BA Pre-op (A) Mean ± SEM n=24	WA Pre-op (B) Mean ± SEM n=24	BA 6 wks post-op (C) Mean ± SEM n=24	WA 6 wks post-op (D) Mean ± SEM n=24	STATISTIC Student's T A vs B	STATISTIC Two-way ANOVA time =AB vs CD; race= AC vs. BD
Body weight (kg)	127.6 ± 4.09	123.8 ± 4.02	113.4 ± 3.73	108.4 ± 3.52	p=0.5206	***p(time)<0.0001***; p(race)=0.4292
Body Mass Index (BMI)	47.5 ± 1.27	44.7 ± 1.03	42.9 ± 1.50	39.5 ± 1.09	p=0.0934	***p(time)<0.0001***; p(race)=0.0659
Waist Circumference (cm)	124.5 ± 2.87	128.0 ± 2.73	115.2 ± 2.83	123.7 ± 2.52	p=0.4047	***p(time)<0.0001***; p(race)<0.1826
Hip Circumference (cm)	134.8 ± 2.78	128.2 ± 1.99	112.9 ± 2.32	122.5 ± 1.87	***p<0.05***	***p(time)<0.0001***; p(race)<0.8606
Systolic BP (mm Hg)	143.3 ± 4.31	138.6 ± 1.91	134.1 ± 2.65	127.7 ± 3.03	p=0.2744	***p(time)<0.0001***; p(race)<0.1230
Diastolic BP (mm Hg)	85.4 ± 1.97	81.6 ± 2.06	84.8 ± 1.55	77.4 ± 2.69	p=0.2051	p(time)=0.1850; ***p(race)<0.05***
Pulse (bpm)	83.6 ± 3.42	79.1 ± 2.05	80.0 ± 2.81	74.4 ± 1.99	p=0.2386	***p(time)<0.05***; p(race)=0.0661
Temperature (◦ C)	97.7 ± 0.17	97.5 ± 0.14	97.6 ± 0.13	96.8 ± 0.94	p=0.3567	p(time)=0.5813; p(race)= 0.278
ALT (IU/L)	18.0 ± 1.69	36.5 ± 3.82	N/A	N/A	***p=0.0005***	N/A
AST (IU/L)	17.7 ± 1.15	29.6 ± 3.05	N/A	N/A	***p=0.0033***	N/A
Billirubin (mg/dL)	0.4 ± 0.06	0.5 ± 0.04	N/A	N/A	p=0.3286	N/A
Creatinine (mg/dL)	0.8 ± 0.03	0.8 ± 0.02	N/A	N/A	p=0.3576	N/A
Glucose (mg/dL)	104.9 ± 5.11	113.6 ± 5.88	N/A	N/A	p=0.2996	N/A
WBC (x10 /ul)	8.0 ± 0.54	7.3 ± 0.30	N/A	N/A	p=0.2053	N/A
Hematocrit %	38.7 ± 0.77	41.9 ± 0.63	N/A	N/A	***p=0.0026***	N/A
Platelets (x10 /ul)	312.5 ± 16.28	266.0 ± 12.13	N/A	N/A	***p=0.0234***	N/A

TABLE 3

Models for PreOp Immune Markers

	CRP	IgA	IgG	IgM	TGFB
Age	0.01 p=0.741 (-0.03, 0.05)	0.25 p=0.442 (-0.39, 0.89)	27.25 p=0.202 (-14.65, 69.14)	-2.03 p=0.219 (-5.25, 1.20)	-0.10 p=0.333 (-0.31, 0.11)
Black	-0.1 p=0.829 (-1.01, 0.81)	3.70 p=0.566 (-8.95, 16.37)	1377.36 p=0.001 (569.83, 2184.89)	-22.78 p=0.625 (-114.11, 68.55)	-0.72 p=0.729 (-4.82, 3.37)
Hypertension	-0.06 p=0.879 (-0.85, 0.73)	3.45 p=0.637 (-10.86, 17.76)	-326.06 p=0.440 (-1154.00, 501.88)	28.6 p=0.537 (-62.30, 119.49)	2.10 p=0.480 (-3.71, 7.91)
Hyperlipidemia	-1.20 p=0.001 (-1.88, -0.51)	8.14 p=0.279 (-6.60, 22.88)	634.20 p=0.133 (-193.05, 1461.43)	-20.84 p=0.614 (-101.77, 60.09)	3.71 p=0.220 (-2.22, 9.65)
Sleep Apnea	0.03 p=0.945 (-0.79, 0.85)	7.90 p=0.266 (-6.04, 21.85)	-228.24 p=0.597 (-1074.56, 618.08)	-14.01 p= 0.634 (-71.72, 43.71)	-0.89 p=0.721 (-5.78, 4.00)
Diabetes	0.46 p=0.170 (-0.20, 1.13)	-17.33 p=0.029 (-32.88, -1.79)	-610.98 p=0.152 (-1446.08, 224.12)	-18.68 p=0.664 (-102.91, 65.55)	1.29 p=0.670 (-4.64, 7.22)
PreOp BMI	0.06 p=0.224 (-0.03, 0.14)	-0.01 p=0.978 (-1.03, 1.00)	59.37 p=0.110 (-13.36, 132.09)	-0.49 p=0.901 (-8.28, 7.29)	-0.08 p=0.710 (-0.49, 0.34)
PreOp SBP	0.00 p=0.731 (-0.02, 0.03)	-0.29 p=0.230 (-0.78, 0.19)	1.73 p=0.916 (-30.32, 33.78)	-0.87 p=0.534 (-3.62, 1.88)	0.07 p=0.447 (-0.10, 0.23)
PreOp DBP	-0.04 p=0.032 (-0.08, 0.00)	0.03 p=0.933 (-.65, .71)	15.22 p=0.422 (-21.94, 52.39)	1.35 p=0.453 (-2.17, 4.87)	-0.06 p=0.586 (-0.29, 0.17)

TABLE 4

Models for Weight Change

	Weight Change (kg)	BMI Change
Age	0.10 ***p*=0.045** (0.00, 0.20)	0.04 ***p=0.047*** (0.00, 0.07)
Black	-0.09 p=0.935 (-2.24, 2.07)	-0.15 p=0.703 (-0.90, 0.61)
Hypertension	0.67 p=0.543 (-1.54, 2.88)	0.53 p=0.180 (-0.25, 1.31)
Hyperlipidemia	0.75 p=0.479 (-1.37, 2.88)	-0.20 p=0.585 (-0.95, 0.54)
Sleep Apnea	-1.28 p=0.223 (-3.36, .80)	-0.19 p=0.599 (-0.93, 0.54)
DM	0.18 p=0.869 (-2.03, 2.40)	0.05 p=0.899 (-0.73, 0.83)

FIGURE 1

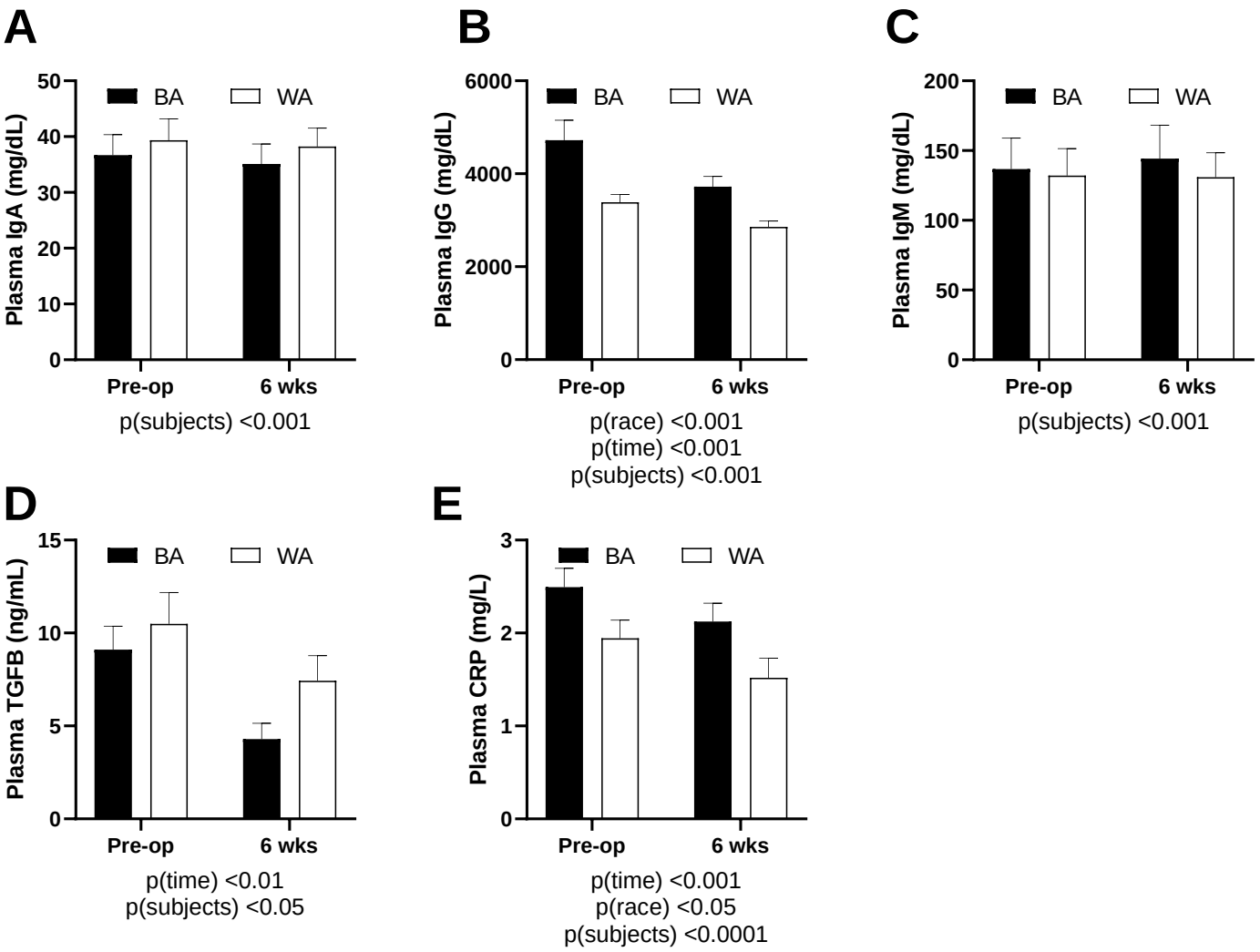
A
Plasma IgA (mg/dL)
50
40
30
20
10
0
BA
WA
Pre-op
6 wks
p(subjects) <0.001
B
Plasma IgG (mg/dL)
6000
4000
2000
0
BA
WA
Pre-op
6 wks
p(race) <0.001
p(time) <0.001
p(subjects) <0.001
C
Plasma IgM (mg/dL)
200
150
100
50
0
BA
WA
Pre-op
6 wks
p(subjects) <0.001
D
Plasma TGFB (ng/mL)
15
10
5
0
BA
WA
Pre-op
6 wks
p(time) <0.01
p(subjects) <0.05
E
Plasma CRP (mg/L)
3
2
1
0
BA
WA
Pre-op
6 wks
p(time) <0.001
p(race) <0.05
p(subjects) <0.0001

TABLE 5

Models for Immune Marker Change

	Δ CRP	Δ IgA	Δ IgG	Δ IgM	ΔTGFB
Age	-0.01 p=0.292 (-0.04, 0.01)	0.12 p=0.636 (-0.37, 0.60)	6.36 p=0.767 (-36.60, 49.32)	0.01 p=0.980 (-1.07, 1.09)	0.35 p=0.030 (0.04, 0.66)
Black	0.22 p=0.366 (-0.27, 0.71)	-0.14 p=0.977 (-9.87, 9.59)	-1108.04 p=0.012 (-1963.49, -252.60)	3.13 p=0.771 (-18.38, 24.65)	0.91 p=0.771 (-5.34, 7.15)
HTN	-0.14 p=0.579 (-0.65, 0.36)	-2.39 p=0.633 (-12.42, 7.63)	606.87 p=0.173 (-274.93, 1488.67)	-2.48 p=0.823 (-24.66, 19.70)	-6.28 p=0.055 (-12.71, 0.15)
Hyperlipidemia	0.22 p=0.374 (-0.27, 0.71)	-4.76 p=0.329 (-14.47, 4.95)	-608.68 p=0.158 (-1462.35, 244.99)	-17.47 p=0.108 (-38.94, 4.00)	-3.75 p=0.232 (-9.98, 2.48)
Sleep Apnea	-0.25 p=0.291 (-0.72, 0.22)	0.62 p=0.895 (-8.77, 10.01)	-235.55 p=0.569 (-1061.37, 590.28)	16.51 p=0.116 (-4.25, 37.29)	-0.08 p=0.978 (-6.11, 5.94)
DM	0.15 p=0.560 (-0.36, 0.65)	0.09 p=0.986 (-9.89, 10.07)	745.39 p=0.094 (-132.33, 1623.10)	23.81 p=0.035 (1.74, 45.88)	1.09 p=0.734 (-5.32, 7.49)
BMI Δ	-0.12 p=0.223 (-0.31, 0.07)	0.05 p=0.979 (-3.73, 3.83)	301.21 p=0.074 (-30.90, 633.32)	-5.39 p=0.201 (-13.74, 2.97)	-0.75 p=0.537 (-3.17, 1.67)
SBP Δ	-0.01 p=0.145 (-0.02, 0.00)	0.07 p=0.633 (-0.21, 0.35)	11.41 p=0.355 (-13.18, 36.00)	-0.13 p=0.684 (-0.74, 0.49)	0.11 p=0.233 (-0.07, 0.29)
DBP Δ	0.01 p=0.322 (-0.01, 0.03)	0.02 p=0.915 (-0.33, 0.37)	5.88 p=0.705 (-25.14, 36.89)	-0.22 p=0.569 (-1.00, 0.56)	-0.07 p=0.542 (-0.30, 0.16)