

HHS Public Access

Author manuscript Obes Surg. Author manuscript; available in PMC 2022 March 01.

Published in final edited form as: Obes Surg. 2021 March ; 31(3): 1004–1012. doi:10.1007/s11695-020-04938-x.

Cardiovascular Risk Factors Following Vertical Sleeve Gastrectomy in Black Americans Compared to White Americans

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Abstract

Objective: Bariatric surgery presents a long-term solution for clinical obesity. Given that Black Americans (BA) carry a greater burden of obesity-related comorbidities than White Americans, (WA), understanding the racial disparities regarding remission of obesity-comorbidities following the most common bariatric surgery, sleeve gastrectomy (SG). The goal of the current study was to provide quantitative values related to cardiovascular and lipid outcomes following SG and determine if racial disparities exist between BA and WA.

Methods: Data was collected from de-identified electronic medical records for patients receiving SG surgery at the University of Mississippi Medical Center in Jackson, MS, USA.

Results: Of 464 patients who obtained SG from (2013-2019), 64% were WA, and 36% were BA. Before surgery, BA had significantly greater body weight (BW), body mass index (BMI), and systolic (SBP) and diastolic (DBP) blood pressure (BP) in comparison to WA. Compared to WA, BA were predicted to lose 5.1 kg less BW than WA at 1-year follow-up. Reduction in SBP (−0.96 vs. −0.60 mmHg/doubling of days) and DBP (−0.51 vs. −0.26 mmHg/doubling of days) was significantly higher in WA compared to BA. There was no racial difference in the change to total

The authors have no conflicts of interest.

Informed Consent Statement

Informed consent does not apply.

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Conflict of Interest Statement

Ethical Approval Statement

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. For this type of retrospective study formal consent is not required.

cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL) cholesterol, or triglycerides by race. When normalized to weight loss, the racial disparity in BP reduction was mitigated.

Conclusions: These data indicate that BA lose less body weight following SG; however, loss of excess body weight loss is associated with improvement to BP similarly in both BA and WA.

Keywords

Bariatric Surgery; Blood Pressure; Cardiovascular Risk; Lipids

INTRODUCTION

According to the National Health and Nutrition Examination Survey from 2017-2018, obesity and its various comorbidities affect over 40% of the U.S. population. For obesity treatment, surgical weight loss is the most successful strategy to reduce the burden of excess body weight, diabetes, dyslipidemia, and hypertension [1]. Although more than 250,000 individuals undergo surgical weight loss procedures per year in the U.S. alone [2], the underpinnings of the mechanisms of action to produce positive benefit remain elusive. The mechanism is far more complex than merely limiting the volume of the stomach and concomitantly reducing food intake. As a result, some individuals appear refractory to the long-term improvements of surgical weight loss by covariates that remain unknown [3–5]. Thus, the severe gaps in knowledge of the mechanisms of weight loss surgery preclude our ability to optimally further assist obese patients in long-term weight management. A recent JAMA Surgery study of >14,000 subjects reported that Black Americans (BA) have less resolution of excess body weight than White Americans (WA) even though many obesity comorbidities appear resolved following the procedures [6]. Other reports show similar findings [7–9]. The reasons that may underlie the refractory improvements by surgical weight management for BA are of great clinical importance.

BA carry a greater burden of obesity-related comorbidities than WA [10–12]. Work is ongoing to understand the metabolic, genetic, nutritional, environmental, and behavioral risk factors that alter body-weight regulation in BA. Studies comparing metabolic features in BA and WA populations have identified differences in lean/fat mass distribution [13, 14], bone density, [15, 16], metabolic rate [13, 17, 18], hormones [19–21], and lipid metabolism [22] that could account for the reduced efficacy of surgical weight loss in BA. These previously identified differences overlap as contributing mechanisms that are co-opted in bariatric surgery to produce positive metabolic benefits. Thus, by default, these surgeries may not work optimally in BA.

Sleeve Gastrectomy (SG), a procedure that removes >80% of the stomach and creates a tube linking the esophagus to the duodenum, is the most common (53.6%) of the weight loss surgeries obtained world-wide currently and is the surgery of choice for many patients [23]. SG has been performed over the last 15 years. As such, one of the strengths of the literature is that SG is often included in longitudinal studies of bariatric surgery. However, stratified data comparing SG directly to other forms of surgical weight loss is less common than other surgeries. Additionally, reporting the effects of specific surgeries on minority populations,

such as BA, is limited by the availability of demographics at the site of the particular study. Mississippi carries one of the highest burdens of metabolic disease in the U.S. for both BA and WA [24]. The goal of the current study was to determine the effectiveness of SG to improve body weight and other obesity-related comorbidities, particularly blood pressure and plasma lipids, in BA vs. WA (37.7% BA and 58.6% WA) in a cohort that closely resembles the population of the state of Mississippi, and to provide quantitative targets for weight loss in both BA and WA. We hypothesize that BA will have less of an improvement in body weight and other metabolic risk factors compared to WA.

METHODS

Database extraction.

This retrospective study was performed using data extracted from the University of Mississippi Medical Center Patient Cohort Explorer (PCE). The PCE contains de-identified patient data derived from the electronic health record used on-site, EPIC, from 1 January 2013 through 30 June 2019. Data were obtained for all patients coded for "vertical sleeve gastrectomy" as a surgical procedure. The data warehouse from which the information for this study is derived has been de - identified and date-shifted so that it does not include any protected health information (PHI). Data is extracted from the PCE in a Comma-separated values file and then uploaded into Strata statistics program. Number of patients from each zip code and insurance status was provided by an independent working group to maintain de-identified data. Median income of zip codes containing at least 5 patients was obtained from United States Census data. All procedures performed in studies involving human participants were approved by the Institutional Review Board and performed 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.

Output measure extraction.

Body mass index (BMI), blood pressure, triglycerides, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol data were obtained from the PCE. Data were prepared for analysis by an automated procedure to guarantee reproducibility. The data were separated into patients via a patient identification number, and each patient's data was abstracted individually. Surgery date was obtained by searching the "Procedure ID" feature for the key phrase "vertical sleeve gastrectomy". The date of surgery for a patient was denoted as time 0, and the date of all other data entries were reset relative to this point. The features of interest (lab reports, weights, and vital signs) were extracted with the dates they were recorded and organized into a ragged array. Additionally, a demographic vector was reported for each patient, containing sex, age at surgical date (the PCE algorithm adds a uniformly distributed random factor added for additional assurance of patient privacy), and race.

Statistical Analysis.

After preparing the data for analysis in Excel, summary statistics were compiled for baseline (time point 0) measures. Means, standard deviations, and t-tests were used for continuous variables, and count percentages, and chi-squared tests for categorical. Patient count data for

insurance status was analyzed by a chi-squared test to determine if there is a difference in proportions between BA and WA.

Due to the potential for high non-linearities in the data, exploratory fractional polynomial models were constructed for all outcomes. These revealed that an appropriate modeling framework would consist of placing a spline knot at the surgery date, keeping the time horizon before this knot on the linear scale, and post-surgery performing a log-transform for time since surgery. A base-2 log transform was used to facilitate interpretability into a "per doubling unit of time". Post-transformation linearity was then confirmed. These two-time variables were interacted with race, and all relevant linear combinations were calculated in models estimating change in the outcome over time. Similar models were used to estimate the effect of weight loss (per 5 kg decrease) on cardiovascular outcomes. The difference for this analysis was that two triple interaction terms (race interacted with weight interacted with either of the time variables) were used.

All models are mixed models, specifically random intercept-slope models with exchangeable correlation structures to account for patient-level variation, without which standard error model estimates would be incorrect due to independence assumption violations. All models are adjusted for age and sex. Due to the nature of data extracted from hospital databases, a non-ignorable amount of missingness for various variables was present. There was no reason to assume these were not missing at random (NMAR), so the missing at random (MAR) assumptions of the mixed models are valid. All statistical analyses were performed with Stata v16.1.

RESULTS

Baseline Characteristics.

The cohort of patients had no statistical difference in age at the time of surgery between WA and BA (Table 1). In the cohort, which was primarily female $(p<0.01)$, BA-SG patients had significantly higher BMI ($p<0.001$) and body weight ($p<0.01$) than WA at the appointment closest to surgery. BA had significantly higher systolic blood pressure (SBP) (p<0.001) and diastolic blood pressure (DBP) $(p<0.01)$ in comparison to WA (Table 1). There were no statistical differences in total cholesterol, high-density lipoprotein (HDL), or low-density lipoprotein (LDL) between groups (Table 1). BA had significantly lower serum triglycerides (p<0.001) compared to WA prior to surgery (Table 1).

Socio-economic Data.

More than 99% of the patients undergoing SG were from Mississippi. Of the 254 patients (or 54.7% of total patients) for whom we were able to obtain residential zip codes, 52% lived in a zip code in which the median income was less than the median income for the United States, 31% lived in a zip code in the which median income was near the median income for the United States, and only 17% lived within a zip code above the median income for the United States (Figure 1A). The only major difference between BA and WA in terms of insurance status is that out of 99 patients who paid out of pocket (self-pay), 85 percent were WA, and 15 percent were BA (Figure 1B).

Pre-surgical trajectories.

Leading up to surgery, there was a minimal change in BMI for WA and BA that was statistically significant, but not clinically relevant ($p<0.001$) and ($p<0.01$) respectively (Figure 2, Table 2). There was also a significant increase in percentage of body weight change in WA (p<0.05) but not BA (Figure 2, Table 2). Conversely, prior to surgery, WA but not BA has improvement to DBP ($p=0.001$), total cholesterol ($p=0.001$), HDL ($p<0.01$) and LDL $(p<0.05)$ (Table 2). Furthermore, prior to surgery, there was a small, but significant reduction in plasma triglycerides in WA ($p<0.05$) but BA had a slight increase in triglyceride levels, approximately 0.34 mg/dl/month (Table 2).

Post-surgical trajectories.

WA and BA had significant improvement in many parameters of interest following surgical weight loss (Table 2). WA had significantly greater improvement in BMI per doubling of days since surgery compared to BA body weight $(p<0.001)$ and percent body weight change (p<0.001) (Table 2). Per doubling of days following SG, WA had a greater reduction in both SBP ($p<0.001$) and DBP ($p<0.001$) compared to BA (Table 2). There is no statistical difference between BA and WA with respect to the improvement of total cholesterol, HDL and LDL (Table 2). Table 3 indicates expected mean values at various time points following SG of all cardiovascular risk factor modelled. The data provide theoretical targets for BA and WA undergoing SG.

Cardiovascular risk factor modelling.

We next determined whether weight loss *per se* improves cardiovascular risk factors associated with obesity, and whether there is a racial disparity in cardiovascular risk improvement following weight reduction. Relative to body weight loss, both WA and BA had significant reductions in SBP, $(p<0.001)$ and $(p<0.001)$ respectively, per 5 kg of body weight loss (Table 4). More importantly, both WA and BA had a significant increase in HDL $(p<0.001)$ with no significant difference in total cholesterol or LDL per 5 kg of body weight loss (Table 4). Interestingly, when looking at the data relative to weight loss, there were no statistical differences between WA and BA in SBP, DBP, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides (Table 4) BUN, or blood creatinine per 5 kg of body weight loss (**data not shown**).

DISCUSSION

Racial disparities in various health parameters are becoming increasingly evident [25–28]. BA carry substantial burden of Metabolic Syndrome (MetS)-related diseases leading to increased risk for stroke, heart failure, and peripheral artery disease among BA in comparison to WA [11, 29, 30]. 80% of BA women are overweight or obese in comparison to only 62.4% of WA women [29]. Further, among BA men and women, the age-adjusted prevalence of hypertension is 39.6 and 43.1%, respectively, whereas, in WA men and women, the prevalence is 31.4 and 28.7%, respectively [30]. In the current study, BA undergoing SG had significantly higher BMI at baseline compared to WA even though the average age was similar. In addition, predicted weight loss was 5.1 kg more for WA compared to BA. Reduced blood pressure following SG was directly related to the amount

of body weight loss; therefore, BA on average had less of a reduction in blood pressure compared to WA.

A major finding of the current study is that BA did not lose as much body weight, or benefit from as much percent change in body weight or reduction in BMI compared to WA. This phenomenon has been shown in previous studies [6–9], but what is novel about the present work is that it specifically reports this dampened improvement following SG, which according to the American Society of Metabolic and Bariatric Surgery is the most common of the surgical weight loss procedures currently. It is widely assumed that weight loss following SG is primarily due to reductions in caloric intake; however, hormonal, dietary, and environmental factors may impact the amount of weight loss following surgery [32]. Identifying vulnerable populations at risk for reduced surgical efficacy will aid our understanding of these factors contributing to weight loss following bariatric surgery.

Two recent studies highlight the racial disparity in weight loss following bariatric surgery. Wood et al. provided a comprehensive assessment of clinical outcomes following all bariatric surgeries and compared differences between BA and WA in Michigan [6]. This study found the BA had reduced body weight loss compared to WA following both SG and Roux-en-y. BA also had lower rates of remission of hypertension compared to WA. In addition, Sheka et al. reported the same finding using data from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program [33]. This study used patient reported clinical outcomes from a national database whereas in contrast to the data in the current manuscript which utilizes data from clinical visits. However, the population of both BA and WA reported by Wood *at al.* were quite different from our study in that mean age at the time of surgery was six years younger than the mean age of bariatric patients in Mississippi [6]. In addition, the BMI of the Michigan cohort for WA was 5.5 points lower, and for BA, almost 2 points lower than the Mississippi cohort [6]. These data show that the Mississippi cohort presented reflects the greater MetS burden typically reported in the Southern United States [34, 35].

Weight loss is typically associated with a reduction in blood pressure [36]; therefore, it was predicted that following SG surgery, there would be a significant reduction in arterial pressure for both WA and BA. The Michigan cohort mentioned previously had a significant portion of the population with resolved hypertension [6] and this was reported to be less in BA compared to WA. In the current study, WA and BA had a similar percentage of patients on hypertensive medications; however, in Mississippi, BA do not have the same cardiovascular benefit from SG as WA. This disparity appears to be because they did not lose a similar amount of body weight, and thus, have reduced improvement in both SBP and DBP compared to WA since the improvement to blood pressure is associated to the amount of body weight lost. The cause of the difference in body weight loss are not known. These data suggest that mechanisms promoting weight loss following bariatric surgery should be properly identified to improve outcomes in bariatric patients. This may also be specific to SG; RYGB is considered the gold standard for the resolution obesity comorbidities, and SG may not rival RYGB in this parameter or even particularly for BA patients interested in bariatric surgery.

Obesity is a major risk factor for hypertension and cardiovascular disease risk [37]; however, it is becoming more and more apparent that visceral adipose abundance is associated with greater risk more so than subcutaneous fat [38]. BA are reported to have more subcutaneous adipose compared to WA [39]. This data would suggest that WA may be more apt to lose visceral adipose, while BA are most likely to lose more subcutaneous adipose. Our data suggest that reductions in blood pressure following SG is associated to weight loss; however, this difference in visceral vs. subcutaneous fat loss may be one mechanism by which WA have better outcomes related to other cardiovascular risk factors following bariatric surgery compared to BA. Unfortunately, the data set does not contain information on adipose distribution, and more studies are needed to test this hypothesis.

Though improvement to body weight vary with BP changes, there may be intermediate processes that are directly responsible for this relationship. With the resection of the stomach and the loss of excess body fat, there are changes to myriads of hormones, and alterations to neural networks throughout the body, including the gut-brain axis. These in fact, may vary in parallel to body weight and could be ultimately responsible for the improvement in cardiovascular outcomes. More work, in both humans and animal models are necessary to uncover these complex relationships.

Caveats and obstacles to interpretation.

These data are reflective of the Mississippi cohort of patients undergoing SG, where there was no statistical difference in age between BA and WA. However, the average BMI for BA was 3.8 points higher than WA, and SBP and DBP were significantly higher before surgery. Notably, our cohort of 36% BA and 64% WA closely resembles the population of the state of Mississippi. This current work was a retrospective study using de-identified hospital records. Because this was not from a clinical study protocol, code was written to match and estimate the time interval of physician-patient interactions and, therefore, an inherent variability of the timing of visits is present within the dataset. In addition, there is no way to verify the method by which blood pressure was taken at the clinic visit, a topic a high debate [40]. We were also not able to verify the length of time that patients were administered antihypertensive pharmacologic therapies; we were only able to verify that at one point during their treatment, they had been prescribed anti-hypertensive medication. We were not able to identify the specific anti-hypertensive treatment and if there were racial differences in the treatment of choice. Another drawback to the current study is that we did not have information regarding diet or frequency of consumption of types of foods and salt intake. We cannot further analyze the influence that racial dietary preferences in particular in Mississippi that may affect the starting BMI and resolution of excess weight and effect on blood pressure.

Conclusions

Cardiovascular benefits of bariatric surgery have been well documented and include reductions in blood pressure and improved plasma lipids [41]. The short-term cardiovascular risk improvement is due to the drastic weight loss [42]. The current data set indicates that BA lose less body weight than WA following bariatric surgery, and that a relationship exists

between long-term cardiovascular improvement following surgery and the amount of body weight lost. Therefore, the potential approach to improve racial disparities in cardiovascular outcomes following bariatric surgery is to understand the mechanism behind why BA do not lose as much weight as WA. Beyond these racial differences, we lack a comprehensive understanding of why such a significant variability of outcomes exist with surgical procedures that are well controlled for, yet garner a vast range of long-term weight loss.

Acknowledgements:

We would like to thank Fremel Backus and Jimmy Flint for their efforts in providing insight and assistance in attaining the data for this manuscript.

Funding: J.S.S is supported by National Heart, Lung, and Blood Institute grants R00 HL127178, P01 HL051971, and National Institute of General Medicine Sciences grant P20GM104357. B.E.G. is supported by awards from the Office of the Assistant Secretary of Defense for Health Affairs supported by Award No. W81XWH-16-1-0349 and W81XWH-16-1-0387. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense. The Mississippi Center of Excellence in Perinatal Research MS COBRE P20GM121334, also supported B.E.G. The content of the manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. STL is partially supported by the Mississippi Center for Clinical and Translational Research and Mississippi Center of Excellence in Perinatal Research COBRE funded by the National Institute of General Medical Sciences of the National Institutes of Health under Award Numbers 5U54GM115428 and P20GM121334.

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FIGURE 1:

Socio-economic data of patients who underwent bariatric surgery. A) The number of patients living within a zip code of the specified median income range and B) patient count of insurance status divided into BA and WA. Chi-squared test on insurance status indicates a significant difference in the propor

FIGURE 2:

A) Body weight and B) Percent of body weight relative to the date of vertical sleeve gastrectomy surgery in white American (green) and black Americans (orange). Solid line represents modeled data.

TABLE 1:

Participant Characteristics at date closest to surgery. Data are presented as mean ± SD.

TABLE 2:

Change in weight or cardiovascular marker pre-post bariatric surgery. Data are presented as mean \pm SD.

* All estimates adjusted for age and sex

TABLE 3:

Expected means of cardiovascular risk factor in BA and WA at various time points following bariatric surgery.

TABLE 4:

Expected change in cardiovascular risk markers per 5kg decrease in body weight. Data are presented as mean \pm SD.

