Cardiometabolic health among gastric bypass surgery patients with polycystic ovarian syndrome

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The majority of the sample was Hispanic (66%, 25% NHB, 9% NHW). Mean body mass index significantly improved 1 year post-surgery for all ethnic groups (45.5 to 35.5 kg/m² for Hispanics, 46.8 to 37.7 kg/m² for NHB and 45.7 to 36.7 kg/m² for NHW, P < 0.001). Among Hispanic women mean total cholesterol (198.1 to 160.2 mg/dL), low-density lipoproteins (LDL) cholesterol (120.9 to 91.0 mg/dL), triglycerides (148.6 to 104.8 mg/dL), hemoglobin A1c (6.2% to 5.6%), alanine aminotransferase (28.1 to 23.0 U/L) and aspartate aminotransferase (23.5 to 21.6 U/L) decreased significantly (P < 0.001). Among NHB, mean total cholesterol (184.5 to 154.7 mg/dL), LDL cholesterol (111.7 to 88.9 mg/dL) and triglycerides (99.7 to 70.0 mg/dL) decreased significantly (P < 0.05). Among NHW, mean total cholesterol (200.9 to 172.8 mg/dL) and LDL cholesterol (124.2 to 96.6 mg/dL), decreased significantly (P < 0.05). Pairwise ethnic group comparisons of all cardiometabolic outcomes adjusted for age and type of surgery before and 1 year after surgery showed no statistical difference between the three groups for any outcome.

CONCLUSION: Cardiometabolic disease risk improvements vary by ethnicity and obesity may impact glucose tolerance and liver function changes more in Hispanic women with PCOS vs non-Hispanic women.

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Key words: Bariatric surgery; Polycystic ovary syndrome; Cardiometabolic outcomes; Weight outcomes; Morbid obesity

Core tip: Morbidly obese women with polycystic ovary syndrome (PCOS) who have undergone Roux-en-Y...
gastric bypass surgery show improvement in cardiometabolic disease risk at one year after the procedure. All women demonstrated a decrease in cardiometabolic disease risk factors including body mass index, glycated hemoglobin A1c (HgA1c), alanine aminotransferase (ALT), total cholesterol (TC), low-density lipoproteins (LDL) and triglyceride (TG). However, only Hispanic women showed a significant decreasing HgA1c and ALT, TC, LDL and TG one year after surgery. These ethnic group differences suggest there may be more comprehensive benefits in terms of cardiometabolic disease risk reduction after bariatric surgery in Hispanic women with PCOS vs other ethnic groups.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex condition strongly associated with obesity, diabetes, coronary heart disease, and certain cancers[1-3]. Often presents in adolescents and is probably the most common endocrinopathy in women. PCOS affects 5%-10% of women of reproductive age and up to 28% of overweight or obese women[4-6]. Diagnostic features consist of clinical evidence of anovulation and clinical or biochemical evidence of hyperandrogenism after exclusion of other etiologies of hyperandrogenism. Consequently, it is the most common cause of anovulatory infertility, oligomenorrhea, amenorrhea, and hirsutism[7].

It is widely reported that women with PCOS have a higher prevalence of cardiometabolic disease risk factors and overt disease compared to non-PCOS women[7]. Specifically, obesity, insulin resistance, metabolic syndrome, diabetes, dyslipidemia and nonalcoholic fatty liver disease (NAFLD) are commonly seen in women with PCOS[7]. Limited studies have shown that weight loss after bariatric surgery in women with PCOS results in improvement or elimination of the symptoms of PCOS and associated cardiometabolic risk factors[8-10]. For example, women with PCOS following surgery have demonstrated normalization of menses, hirsutism score, serum androgens, and insulin sensitivity. However, it is less clear how effective bariatric surgery is on the resolution of pre-diabetes, hypertension and dyslipidemia in affected women with PCOS following bariatric surgery, and in multiethnic women in particular. Hispanics have a higher prevalence of obesity, impaired glucose tolerance, type 2 diabetes and NAFLD compared to their NHW counterparts, and consequently a higher risk for subsequent cardiovascular disease[11-13]. Therefore, weight loss in obese Hispanic women with PCOS may improve the risk of diabetes more substantially compared to non-Hispanic black (NHB) and NHW subjects but these comparisons are largely unknown. The objective of this analysis was to examine the effect of weight loss after bariatric surgery on cardiometabolic disease risk factors in a primarily Hispanic population of women with PCOS.

MATERIALS AND METHODS

A retrospective medical chart review identified women with a history or diagnosis of PCOS who underwent Roux-en-Y gastric bypass surgery (n = 389) in one private practice from 2001-2009. Diagnosis of PCOS was self reported and confirmed by an endocrinologist or gynecologist. Pre-surgery and 12 mo post-surgical cardiometabolic risk factors and ethnicity were collected for comparative analysis. Cardiometabolic risk factors included weight, height, body mass index (BMI), total cholesterol (TC), high- and low-density lipoproteins (HDL and LDL), triglyceride (TG), glycated hemoglobin A1c (HbA1c), and alanine aminotransferase (ALT) and aspartate aminotransferase (AST). This study was approved by and in accordance with the ethical standards of the Institutional Review Board.

Data collection

We abstracted data collected before and 1 year after surgery. In addition to data on sex, race, and ethnicity, these data included BMI and concentrations of HbA1c, HDL, LDL, TC, TG, AST and ALT. Pre-operative comorbidities and surgical complications were also recorded.

Measurements

Height and weight were measured during routine clinical visits by practice nursing staff. Weight was measured to the nearest 0.1 pound (and converted to kilograms for analyses) using a digital scale with the participants wearing light clothing and no shoes. Height was measured to the nearest 0.5 cm using an Accustat Genentech stadiometer. Body mass index was calculated as body weight in kilograms divided by height in meters squared (kg/m²). Excess weight loss (EWL) was calculated as show in the following equation: EML (%) = (Preoperative weight - follow up weight)/(Preoperative weight - ideal body weight) × 100%. Ideal body weight was calculated in base of the 1983 Metropolitan Life Insurance tables for gender and height. All blood samples were collected, processed, stored at -20 °C, and shipped to the laboratory for analysis. HbA1c was analyzed by turbidimetric immunoinhibition with commercially available reagents. TC, LDL, HDL, TG were analyzed enzymatically with commercially available reagents. TC, LDL, HDL, TG, AST and ALT. Pre-operative comorbidities and surgical complications were also recorded.

Surgery criteria

All patients met the National Institutes of Health criteria for bariatric surgery[14]. Thus, all patients had a BMI
after surgery. All patients were scheduled for routine post-operative visits at 1, 3, 6 and 12 mo post-surgery.

Patients had a Roux limb length of either 125 or 150 cm, depending on the patient’s baseline BMI. The Roux limb was brought up in an antecolic, antegastric manner. The jejunal-jejunal mesenteric defect was closed with a permanent running suture. The entire gastrojejunostomy was over-sewn with a circumferential permanent running suture. All patients went to the bariatric floor postoperatively and were started on liquids after a normal upper gastrointestinal study on post-operative day 1. All patients were discharged home on a standard bariatric liquid diet for 1 wk.

**Statistical analysis**

Separate repeated measures linear mixed models were fit using the MIXED procedure to assess change in cardiometabolic disease risk factors (TC, HDL, LDL, BMI, HbA1c, AST and ALT) before and 1 year after bariatric surgery were evaluated by ethnicity (Hispanic, NHB and NHW).

### RESULTS

The majority of the sample was Hispanic (n = 257, 66%), 25% (n = 97) were NHB and 9% (n = 35) were NHW; mean age was 40.9 years, (SD 12.9, range 16-74 years). BMI significantly improved from before to 1 year after surgery for all ethnic groups (P < 0.0001). Among Hispanic women all before-after differences in cardiometabolic disease risk factors were statistically significant (P < 0.0001) with the exception of HDL cholesterol and AST (not significant). Among NHB, HDL Cholesterol, HbA1c, ALT and AST did not decrease significantly 1-year after surgery. Among NHW, all differences were statistically significant (P < 0.05), except for HDL cholesterol, triglycerides, HbA1c, ALT and AST (not significant) (Table 1). Pairwise ethnic group comparisons adjusted for age and type of surgery of before and 1 year after surgery cardiometabolic outcomes showed no statistical difference between the three groups for any outcome (Table 2).

### Limitations

Our study has some limitations. In the evaluation of hepatic steatosis, we were not able to evaluate liver ultrasound or liver biopsy prior to and after bariatric surgery which may be more specific to detect pathology. Blood pressures were not available in all patients to assess hypertension as an additional cardiovascular disease risk factor. Finally, we were unable to assess potential confounders such as lifestyle factors (physical activity and diet) because this information was not assessed in patients.

### DISCUSSION

This analysis shows that Roux-en-Y gastric bypass surgery results in a significant decrease in BMI among Hispanic, NHWs and NHBs with a history or diagnosis greater than 35 kg/m² and at least one other risk factor for cardiometabolic disease (e.g., elevated blood pressure, hypercholesterolemia, and so on) or a BMI greater than 40 kg/m². Patients received group and individual education from an interdisciplinary group of providers about surgical and nonsurgical treatments, outcomes, complications, and necessary lifestyle changes. All patients underwent psychological and nutritional evaluation and testing before surgery.

**Surgical procedure**

All patients underwent Roux-en-Y gastric bypass surgery. The majority of patients spent one night in the hospital before surgery. All patients were scheduled for routine post-operative visits at 1, 3, 6 and 12 mo post-surgery.

Patients had a Roux limb length of either 125 or 150 cm, depending on the patient's baseline BMI. The Roux limb was brought up in an antecolic, antegastric manner. The jejunal-jejunal mesenteric defect was closed with a permanent running suture. The entire gastrojejunostomy was over-sewn with a circumferential permanent running suture. All patients went to the bariatric floor postoperatively and were started on liquids after a normal upper gastrointestinal study on post-operative day 1. All patients were discharged home on a standard bariatric liquid diet for 1 wk.
of PCOS. Several ethnic group differences in pre-post change in individual cardiometabolic disease risk factors were found. Specifically, while all ethnic groups showed improvement in HbA1c and ALT, the decrease was significant only in Hispanic subjects. Additionally, all ethnic groups showed improvement in TC, LDL and TG one year after surgery. However, improvement in TC and TG were only significant for Hispanics and NHW subjects. Decrease in LDL was only significant in Hispanic and NHW subjects.

Our results are similar to previous studies of much smaller sample sizes that have shown that weight loss after bariatric surgery improves cardiometabolic disease risk among women with PCOS including insulin resistance and dyslipidemia, as well as biochemical features we did not include such as hyperandrogenism and oligomenorrhea. Specifically, Escobar-Morreale et al. followed 12 Caucasian women of European ancestry with PCOS after bariatric surgery and found significant improvements in hirsutism and normalization of serum androgens in 91% of subjects at follow up (mean 12 mo, range 7-26 mo). All patients had regular menses after weight loss and 10 subjects had confirmed ovulation. They also found normalization of insulin sensitivity based on homeostasis model assessment (HOMA) in all patients. Similarly, Eid et al. followed 24 American women, whom were primarily Caucasian, with PCOS after Roux-en-Y gastric bypass (mean follow up 27 mo, range 12-57 mo). All subjects had normalization of menses and 77% had significant improvement or resolution of hirsutism. Eleven of the 24 subjects had type 2 diabetes prior to surgery and all 11 were normoglycemic at follow up without glucose lowering medications. Likewise, eleven patients with dyslipidemia prior to surgery no longer required cholesterol lowering medications at follow up. The most recent study by Jamal et al followed 20 American women with PCOS after Roux-en-Y gastric bypass (mean follow up 46.7 mo, range 15-123 mo). They found similar improvements in menses, hirsutism and type 2 diabetes. Six patients that desired pregnancy were able to conceive. These studies indicate weight loss through bariatric surgery significantly improved symptoms of PCOS and associated cardiometabolic disease risk and confirm our findings.

Hispanic ethnicity is associated with an increased cardiometabolic disease risk. In the Diabetes Prevention Trial, Hispanic adults with impaired glucose tolerance were found to have a higher HbA1c and HOMA after adjusting for BMI compared with white subjects with similar fasting plasma glucose levels. Similarly, in the Nurse’s Health Study the relative risk of type 2 diabetes among Hispanic women was 2.18 compared to white women after adjusting for BMI. In addition, relative risk for type 2 diabetes is higher in Hispanics than in African-Americans. Obesity further amplifies this risk; it has been reported that for every 5 point increase in BMI the relative risk for diabetes in Hispanic women is 2.36 vs 1.96 in NHW women. Furthermore, obese Hispanic women are at a higher risk of diabetes compared to NHW and NHB women. Therefore, weight loss in obese Hispanic women with PCOS may improve the risk for overt diabetes more substantially compared to NHB and NHW subjects. Our results here showed significant ethnic group differences in the post-surgery improvement in HbA1c. While HbA1c improved in all groups, the improvement was only significant among Hispanic women with PCOS. This specific finding suggests that obesity may impact glucose tolerance more in Hispanic women with PCOS vs non-Hispanic women.

Hispanics also have a higher prevalence of NAFLD which is associated with obesity, insulin resistance and increased metabolic risk. NAFLD represents a spectrum of fat accumulation in the liver from steatosis to cirrhosis and is the most common cause of elevated liver

### Table 2: Ethnic group comparison of change in mean cardiometabolic disease risk factors among women with polycystic ovary syndrome 12 mo, after gastric bypass surgery performed between 2001 and 2010

| Anthropometric measures | Group | Estimated change 12 mo after surgery (SE) | P value | P value | Ethnic group comparisons |
|-------------------------|-------|-------------------------------------------|---------|---------|--------------------------|
| BMI (kg/m²)             | Overall | 9.7 (0.3) | <0.0001 | NHB | NHW |
| Hispanic | 10.1 (0.3) | <0.0001 | 0.09 | 0.19 |
| NHW | 9.1 (0.5) | <0.0001 | - | 0.87 |
| Weight (kg)             | Overall | 25.7 (0.7) | <0.0001 | NHB | NHW |
| Hispanic | 26.1 (0.8) | <0.0001 | 0.49 | 0.40 |
| NHW | 25.0 (1.3) | <0.0001 | - | 0.76 |
| Total cholesterol       | Overall | 35.3 (3.6) | <0.0001 | NHB | NHW |
| Hispanic | 37.9 (4.2) | <0.0001 | 0.36 | 0.21 |
| NHW | 29.7 (7.8) | <0.0001 | - | 0.63 |
| HDL cholesterol (mg/dL) | Overall | -0.1 (1.2) | 0.95 | NHB | NHW |
| Hispanic | 0.7 (1.5) | 0.64 | 0.26 | 0.96 |
| NHW | -2.4 (2.6) | 0.40 | - | 0.36 |
| LDL cholesterol (mg/dL) | Overall | 27.8 (3.4) | <0.0001 | NHB | NHW |
| Hispanic | 29.9 (4.3) | <0.0001 | 0.32 | 0.89 |
| NHW | 22.9 (6.2) | 0.01 | - | 0.51 |
| Triglycerides (mg/dL)   | Overall | 40.1 (7.6) | <0.0001 | NHB | NHW |
| Hispanic | 43.8 (10.4) | 0.0003 | 0.36 | 0.26 |
| NHW | 29.7 (7.5) | 0.01 | - | 0.64 |
| Hemoglobin (g/dL)       | Overall | 22.7 (12.8) | 0.13 | 0.64 |
| Hispanic | 22.7 (12.8) | 0.13 | 0.64 |
| NHW | 22.7 (12.8) | 0.13 | 0.64 |
| ALT (U/L)               | Overall | 4.9 (1.1) | <0.0001 | NHB | NHW |
| Hispanic | 5.1 (1.3) | 0.0002 | 0.16 | 0.38 |
| NHW | 2.6 (1.4) | 0.08 | - | 0.16 |
| AST (U/L)               | Overall | 7.9 (3.7) | 0.06 | 0.16 |
| Hispanic | 1.9 (1.1) | 0.07 | 0.37 | 0.66 |
| NHW | 0.6 (1.1) | 0.56 | - | 0.40 |
| NHB | 2.9 (2.8) | 0.33 | 0.40 | - |

NHB: Non-Hispanic black; NHW: Non-Hispanic white; BMI: Body mass index; EWL: Estimated weight loss; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase.
enureses. The estimated United States prevalence of NAFLD is approximately 25% in the general population, but has been found to be as high as 45% in some Hispanic populations vs 33% among NHW and 25% among NHB. The prevalence of hepatic steatosis on ultrasound among NHW women with PCOS is 55% and may be as high as 90% in some obese cohorts. Hispanic women with PCOS also had a higher prevalence of NAFLD compared to Caucasian subjects. Women with PCOS have a low prevalence of elevated transaminases despite radiographic evidence of hepatic steatosis. Gambarin-Gelwan et al. determined that only 15% of women with PCOS and steatosis on ultrasound had abnormal liver enzymes. We found in our population of women with PCOS that Hispanic and NHW subjects had a higher baseline ALT compared to NHB subjects. Post-surgery, Hispanic women with PCOS had a significant decrease ALT, whereas the decrease in ALT in NHW and NHB subjects was not significant. This decrease in ALT in the Hispanic population may indicate improvement of fatty infiltration after surgery and therefore, weight loss in obese Hispanic women with PCOS may have a greater impact on hepatic steatosis compared to NHW and NHB subjects.

We also found differential improvements in cholesterol among the Hispanic and NHB subjects. The majority of American women with PCOS have a lipid abnormality. Most display an atherogenic lipid profile including high triglyceride concentrations, high LDL and low HDL. Browning et al. found in a sample of 12 women the majority with PCOS that required cholesterol lowering medication prior to surgery were able to discontinue medication at follow up based on improvements in total cholesterol and triglycerides. We found that all ethnic groups showed improvement in total cholesterol, LDL and TG after surgery. However, total cholesterol and triglycerides showed significant improvement only for Hispanics and NHB subjects, and improvement in LDL was only significant for Hispanics and NHW subjects one year after surgery. We also found NHB subjects had significantly lower baseline triglycerides compared to Hispanics and NHB subjects. This is consistent with other adult and adolescent studies which found lower triglycerides levels among NHB subjects compared to Hispanics and NHW subjects.

In conclusion, morbidly obese women with PCOS who have undergone Roux-en-Y gastric bypass surgery show improvement in cardiometabolic disease risk at one year after the procedure. All women demonstrated a decrease in cardiometabolic disease risk factors including BMI, HbA1c, ALT, TC, LDL and TG. However, only Hispanic women showed a significant decreasing HbA1c and ALT, TC, LDL and TG one year after surgery. These ethnic group differences suggest there may be more comprehensive benefits in terms of cardiometabolic disease risk reduction after bariatric surgery in Hispanic women with PCOS vs other ethnic groups.

ACKNOWLEDGMENTS

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COMMENTS

Background

It is widely reported that women with polycystic ovarian syndrome (PCOS) have a higher prevalence of cardiometabolic disease risk factors and overt disease compared to non-PCOS women. However, it is less clear how effective bariatric surgery is on the resolution of pre-diabetes, hypertension and dyslipidemia in affected women with PCOS following bariatric surgery, and in multiethnic women in particular.

Research fronts

This analysis shows that Roux-en-Y gastric bypass surgery results in a significant decrease in body mass index (BMI) among Hispanic, non-Hispanic black (NHB) and white (NHW) with a history or diagnosis of PCOS. Several ethnic group differences in pre-post change in individual cardiometabolic disease risk factors were found. Specifically, while all ethnic groups showed improvement in hemoglobin A1c (HbA1c) and alanine aminotransferase (ALT), the decrease was significant only in Hispanic subjects. Additionally, all ethnic groups showed improvement in total cholesterol (TC), low-density lipoproteins (LDL) and triglyceride (TG) one year after surgery. However, improvement in TC and TG were only significant for Hispanics and NHB subjects. Decrease in LDL was only significant in Hispanic and NHW subjects.

Innovations and breakthroughs

This is one of the first studies to demonstrate improvement in cardiometabolic health at one year after the procedure in a large multiethnic sample of morbidly obese women with PCOS. All women demonstrated a decrease in cardiometabolic disease risk factors including BMI, HbA1c, ALT, TC, LDL and TG. However, only Hispanic women showed a significant decreasing HbA1c and ALT, TC, LDL and TG one year after surgery. These ethnic group differences suggest there may be more comprehensive benefits in terms of cardiometabolic disease risk reduction after bariatric surgery in Hispanic women with PCOS vs other ethnic groups.

Applications

Post-surgery, Hispanic women with PCOS had a significant decrease ALT, whereas the decrease in ALT in NHW and NHB subjects was not significant. This decreased in ALT in the Hispanic population may indicate improvement of fatty infiltration after surgery and therefore, weight loss in obese Hispanic women with PCOS may have a greater impact on hepatic steatosis compared to NHW and NHB subjects. This finding suggests multiple improvements post-bariatric surgery among Hispanic women in particular not previously reported.

Terminology

Obesity, insulin resistance, metabolic syndrome, diabetes, dyslipidemia and nonalcoholic fatty liver disease are commonly seen in women with PCOS. Limited studies have shown that weight loss after bariatric surgery in women with PCOS results in improvement or elimination of the symptoms of PCOS and associated cardiometabolic risk factors. For example, women with PCOS following surgery have demonstrated normalization of menopause, hirsutism score, serum androgens, and insulin sensitivity.

Peer review

The paper may add some new knowledge to the literature.

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