



Sleeve Gastrectomy for Obesity in Polycystic Ovarian Syndrome: a Pilot Study Evaluating Weight Loss and Fertility Outcomes

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Abstract

Purpose Polycystic ovarian syndrome (PCOS) is a common endocrine disorder associated with obesity and infertility. Gastric bypass has been shown to be effective in treating these symptoms. However, the efficacy of vertical sleeve gastrectomy (VSG) has not been studied in the PCOS population. This study analyzed weight loss and fertility outcomes of VSG in this population.

Methods A retrospective review of patients with PCOS and without PCOS (CON) undergoing VSG from 2008 to 2016 was performed at two bariatric centers. BMI and percent excess weight loss (%EWL) were collected at 3, 6, and 12 months postoperatively. Patient characteristics and postoperative pregnancy status were compared between the two cohorts.

Results One hundred nineteen PCOS patients were compared to 119 CON patients. Similar attrition rates were seen between cohorts at 3-month (5 vs 8%), 6-month (13 vs. 14%), and 12-month (18 vs. 13%) evaluation. PCOS patients had greater Δ BMI at 3 months (-7.64 vs. -6.82 ; $p=0.05$), 6 months (-10.56 vs. -9.49 ; $p=0.02$), and 12 months (-12.43 vs. -11.49 ; $p=0.04$). PCOS patients also had greater %EWL at 12 months compared to CON (66 vs 60%; $p=0.05$). Twenty-two percent of PCOS patients became pregnant within 12 months, 69% of which were previously nulliparous.

Conclusion Compared to non-PCOS patients, PCOS patients had greater postoperative Δ BMI and %EWL at 1 year. The majority of patients becoming pregnant after VSG were previously nulliparous. This study shows that VSG is effective for weight loss in PCOS patients with obesity and may positively augment effect fertility rates.

Keywords PCOS · Sleeve gastrectomy · Fertility · Weight loss · Obesity

Introduction

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder present in approximately 5–10% of the population [1–3]. While it is primarily associated with menstrual irregularity, infertility, and androgen abnormalities, it has extensive

metabolic manifestations. These include obesity, insulin insensitivity, and metabolic syndrome [3]. The incidence of central obesity is found to have a much higher prevalence in patients with PCOS than in patients without PCOS [1–4]. The higher levels of insulin and androgens contribute to the increased prevalence of obesity and the central body fat

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deposition, which also perpetuates increased hormonal abnormalities [2]. Additionally, it is also seen that obese patients have more severe manifestations of their PCOS. In addition to the widely appreciated obesity-related metabolic comorbidities such as diabetes and hypertension, obesity-related PCOS can markedly impair both hormonal balance and fertility among females of child-bearing age.

Since 30–40% of patients will achieve regression of PCOS symptoms with normalization of body weight, weight loss stands as a mainstay of treatment for patients suffering from PCOS [1, 5]. Structured diet and exercise therapy should be the first-line treatment for PCOS [3]. Metformin has also been used prophylactically to treat insulin resistance and normalize androgen levels. Oral contraceptives may be used to help regulate dysmenorrhea. Despite attempt at medical management of symptoms and comorbidities, many patients eventually develop obesity [2]. Among patients with class 2 or higher obesity, there is a high incidence of failure with standard lifestyle and medical interventions to achieve significant and sustained weight loss and to improve fertility. Bariatric surgery in this patient cohort has clearly shown superior long-term weight loss and symptom management in PCOS patients compared to lifestyle modifications and medical management alone, and infertility is an increasingly frequent reason for referral [3]. In addition to just simple weight loss, bariatric surgery has shown to have a number of metabolic and hormonal effects that positively impact PCOS, including decreased insulin and androgen levels thought to attribute to the symptoms of PCOS [1]. However, these findings have primarily been demonstrated among patients undergoing gastric bypass surgery.

Vertical sleeve gastrectomy (SG) is an increasingly common bariatric procedure in the USA and worldwide, but it has not been extensively studied in the PCOS population. Weight loss after gastric bypass in PCOS patients has proven to be beneficial for obesity and other PCOS-related symptoms [1, 5, 6]. Since PCOS affects a wide range of metabolic and hormonal changes not common to all bariatric patients, the benefits of a primarily restrictive procedure for weight loss may be different than those seen with the combined restrictive/malabsorptive procedures. The primary objective of this pilot study was to evaluate weight loss outcomes among a large cohort of patients with diagnosed PCOS who underwent sleeve gastrectomy. A secondary objective was to analyze the impact on fertility in PCOS patients following sleeve gastrectomy.

Methods

After multicenter IRB approval, a retrospective review of all SGs performed on female patients at two tertiary military bariatric centers from 2008 to 2016 was performed. All female patients of reproductive age with PCOS undergoing a SG

were included. PCOS status was defined as having a written diagnosis in the electronic medical chart. Patients undergoing revisional bariatric surgery, over the age of 50 years, and who were lost to follow-up before 3 months were excluded from the study. Identified PCOS patients were compared to a control cohort. The control group was an equal number of randomly selected non-PCOS (CON) female patients of reproductive age undergoing a SG during the same time period. Preoperative height, weight, BMI, bariatric-related comorbidities, age, and postoperative pregnancy status were collected and compared between the two groups. Bariatric-related comorbidities were identified as having a documented ICD-9/10 diagnosis in the electronic medical chart. Postoperative BMI and Δ BMI were collected at 3-, 6-, and 12-month intervals during routine postoperative clinic visits at those time periods. A loss of BMI was recorded as a negative Δ BMI and a gain in BMI was recorded as a positive Δ BMI. Percent excess weight lost (%EWL) was calculated using the recorded preoperative weight and the calculated ideal body weight (BMI equivalent of 25 kg/m²) as measured at their final preoperative clinic appointment within 30 days of surgery. These were compared between cohorts.

A student's *t* test was utilized to compare continuous variables between cohorts. Δ BMI and weight loss as denoted by %EWL were compared using a Tukey-Kramer least square. All analysis was performed using STATA software (StataCorp, College Station, TX, USA). Statistical analysis was defined as a *p* value of < 0.05.

Results

One thousand three hundred eighty-five patients were identified and reviewed. Among these, 119 eligible patients were found to have PCOS and were compared to 119 case-matched CON. The mean age for all patients was 35.5 ± 10.7 years in age and the mean pre-operative BMI was 41.9 ± 5.2. Two hundred twenty two (93%) patients had a postoperative visit at 3 months and demonstrated an average Δ BMI of -6.8 kg/m² and 38.1 ± 11.6 %EWL at 3 months. Two hundred six (89%) patients were seen at 6 months and demonstrated an average Δ BMI of -10.1 kg/m² and 52.9 ± 15.2 %EWL. Finally, 200 (84%) patients were seen at 12 months and demonstrated an average Δ BMI of -12.1 kg/m² and 62.9 ± 21.1 %EWL.

The descriptive statistics characterizing our two cohorts can be seen with comparison *p* values in Table 1. While the PCOS group was younger (31.5 vs. 39.4 years; *p* ≤ 0.01), there was no difference in preoperative BMI between groups (42.2 vs. 41.5; *p* = 0.31). The PCOS group had fewer patients with preoperative hypertension (24 vs. 41%; *p* < 0.01), but no differences were seen between groups regarding hyperlipidemia, pseudotumor cerebri, obstructive sleep apnea, and diabetes.

Table 1 Demographics of PCOS and CON groups

Variable	PCOS (total n = 119)	CON (total n = 119)	p
Age (±sem)	31.5 ± 1.08 years	39.5 ± 0.69 years	< 0.01
Preoperative BMI	42.2	41.5	0.31
Diabetes	19% (n = 22)	14% (n = 17)	0.39
HTN	24% (n = 29)	41% (n = 49)	0.01
HLD	20% (n = 24)	29% (34)	0.17
Pseudotumor	1.7% (n = 2)	0.8% (n = 1)	1
OSA	7.6% (n = 9)	11% (n = 13)	0.5

PCOS polycystic ovarian syndrome, CON control group without polycystic ovarian syndrome, BMI body mass index, HTN hypertension, HLD hyperlipidemia, OSA obstructive sleep apnea

Of the 119 PCOS patients, 113 (95%) had ΔBMI/%EWL calculated at 3 months, 104 (87%) at 6 months, and 97 (82%) at 12 months. The CON group had 109 (92%), 102 (86%), and 103 (87%) patients with calculated ΔBMI/%EWL at 3-, 6-, and 12-month intervals, respectively (Table 2). A difference was seen between cohorts regarding postoperative ΔBMI, as shown in Table 3. Compared to the CON groups, the PCOS cohort had a greater ΔBMI at 3 months (− 7.64 vs. − 6.82; *p* = 0.05), 6 months (− 10.56 vs. − 9.49; *p* ≤ 0.05), and 12 months (− 12.43 vs. 11.49; *p* ≤ 0.05).

No difference was seen in postoperative BMI at 3, 6, and 12 months between the two groups (Table 3). The mean %EWL at 3 months was similar between PCOS and CON groups (39.4 vs. 36.8%; *p* = 0.3). The difference in %EWL between

Table 3 Difference between postoperative BMI, ΔBMI, and %EWL between cohorts

Difference between postoperative values			
Mean postoperative BMI	PCOS ± std. dev	CON ± std. dev	p
3 months	34.34 ± 6.1	34.63 ± 4.5	0.22
6 months	31.63 ± 5.4	31.97 ± 5.1	0.76
12 months	29.55 ± 5.7	29.85 ± 5.2	0.71
Mean postoperative ΔBMI	PCOS	CON	p
3 months	7.64 ± 4	6.82 ± 2.5	0.05
6 months	10.56 ± 3.1	9.49 ± 4	0.02
12 months	12.43 ± 4.2	11.49 ± 4.2	0.04
Mean postoperative %EWL	PCOS	CON	p
3 months	39.38 ± 12.3	36.77 ± 10.8	0.30
6 months	55.41 ± 15.5	50.33 ± 14.5	0.06
12 months	65.83 ± 21.8	60.83 ± 20.2	0.05

PCOS polycystic ovarian syndrome, CON control group without polycystic ovarian syndrome, BMI body mass index

PCOS and CON groups approached significance at 6 months (55.4 vs. 50.3%; *p* = 0.06) and showed more %EWL in the PCOS group at 12 months compared to the CON group (65.8 vs. 60.1%; *p* = 0.05). Figure 1 graphically displays the %EWL and comparison data between the two cohorts. Figure 2 graphically displays the ΔBMI between the two cohorts.

Results regarding fertility can be found in Fig. 1. Significantly more PCOS patients became pregnant within 12 postoperative months compared to the CON group (22 vs. 3%;

Table 2 Postoperative ΔBMI/EWL between groups

PCOS	Obs	Variable	N	Mean	Std Dev	Minimum	Median	Maximum
No	119	3 months %EWL	109	36.77	10.79	9.00	36.00	63.20
		6 months %EWL	102	50.33	14.45	8.10	47.80	87.00
		12 months %EWL	103	60.06	20.20	9.00	56.80	112.00
		BMI 3 months	109	34.63	4.46	27.28	33.69	47.73
		BMI 6 months	102	31.97	5.10	9.74	31.58	44.69
		BMI 12 months	103	29.85	5.17	20.10	29.06	47.97
		ΔBMI 3 months	109	6.82	2.52	− 1.51	6.69	14.12
		ΔBMI 6 months	102	9.49	4.00	− 1.26	9.55	30.01
		ΔBMI 12 months	103	11.49	4.20	1.92	11.53	19.20
Yes	119	3 months %EWL	113	39.38	12.30	13.00	37.00	86.30
		6 months %EWL	104	55.41	15.54	20.50	54.80	90.50
		12 months %EWL	97	65.83	21.79	19.90	63.00	121.00
		BMI 3 months	113	35.58	7.89	15.00	34.30	70.50
		BMI 6 months	104	31.73	5.46	23.50	30.05	45.50
		BMI 12 months	97	29.55	5.72	20.70	28.50	45.20
		ΔBMI 3 months	113	6.40	7.17	− 1.97	6.69	24.24
		ΔBMI 6 months	104	10.47	3.45	3.70	10.63	21.11
		ΔBMI 12 months	97	12.43	4.15	1.10	12.61	23.80

PCOS polycystic ovarian syndrome, Obs observed in data sample, %EWL percent of excess weight loss, Std Dev standard deviation, ΔBMI change in body mass index, BMI body mass index

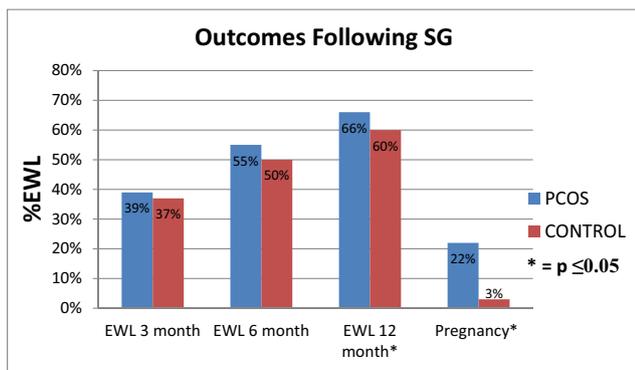


Fig. 1 Outcomes after SG. PCOS: polycystic ovarian syndrome. %EWL: percent excess weight loss. EWL: excess weight loss

$p \leq 0.01$). Although the difference in fertility rates between groups showed statistical significance, this is of little clinical importance. Since the groups were not equal in age or PCOS status, the design of the study was not meant to directly compare fertility rates between the two groups. The results are not meant to show that PCOS patients are more likely to become pregnant compared to non-PCOS patients; the difference in age and PCOS status would skew the data and prevent a true conclusion. Rather, it simply points out the high postoperative fertility rate and date of conception of PCOS patients following SG. The average date of conception was 10.8 postoperative months, despite preoperative counseling regarding the need to delay pregnancy for at least 12 months. Of those who became pregnant, 69% of the PCOS group were previously nulliparous prior to the SG. In contrast, none of those who became pregnant in the CON group were nulliparous.

Discussion Bariatric surgery has proven to be a promising treatment for obesity in the PCOS population [1, 3, 5–7]. Many studies show the postoperative benefits of gastric bypass in PCOS patients [1]. However, there is a paucity of data specifically related to SG in those with PCOS. Wang et al. demonstrated more weight loss and an improvement in clinical symptoms of PCOS after SG compared to lifestyle modifications [3]. However, the groups compared were not equal,

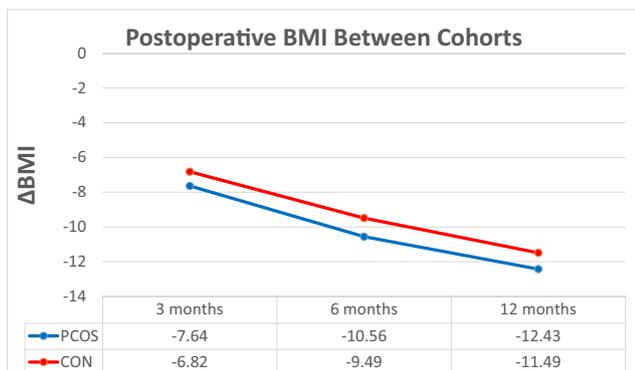


Fig. 2 Postoperative BMI between cohorts. ΔBMI: change in body mass index

as those in the lifestyle modification group would not have met criteria for bariatric surgery based on an average BMI < 35. Multiple studies involving murine models have demonstrated weight loss and symptom management after SG [6, 7]. However, the exogenous hormones required to cause the PCOS-like physiology in the murine models might not be translatable to human populations.

Obesity is a condition that affects up to one third of the population in the USA [6]. It incurs a significant effect on the health care system with many associated comorbidities. Gastric bypass procedures have been well known to ameliorate many obesity-related hormonal and metabolic comorbidities [8]. Despite the benefits of gastric bypass, SG has been gaining popularity and is becoming increasingly more common. Although there may be some hormonal contribution [9], SG is a primarily restrictive procedure by reducing the volume of the stomach. Regarding endocrine abnormalities of obesity such as diabetes, gastric bypass has shown superior postoperative management compared to SG [10]. This has led many to choose bypass procedures in patients with obesity-related metabolic and hormonal comorbidities as a tailored weight loss approach. PCOS has been associated with a female-specific metabolic syndrome [7].

This pilot study directly compares the postoperative weight loss effects after SG in patients with and without PCOS. The results of this study show that SG is an efficacious weight loss strategy. Traditionally, a successful bariatric surgery has been defined as %EWL > 50% at 12 months [11, 12]. The mean weight loss in the PCOS cohort was 55.4% at 6 months and 65.8% at 12 months. By obtaining a mean %EWL > 50% at 12 months, SG was shown to provide adequate weight loss in PCOS patients [11]. The presence of PCOS does not seem to negatively affect the expected weight loss after SG. In contrast, the PCOS group lost significantly more %EWL than the CON group at 12 months and a greater ΔBMI throughout the 12-month postoperative period. This increased weight loss in the PCOS group could be due to a synergistic effect of weight loss’ effect on PCOS comorbidities. The evidence of improved fertility in the PCOS cohort bolsters this theory. Prospective androgen levels could be followed and may validate this theory.

Twenty-two percent of the PCOS group became pregnant within 12 months after SG; 69% of these pregnancies were in previously nulliparous women. Obesity from PCOS is known to inhibit fertility [2]. With > 50% EWL seen in the PCOS group after 6 months, an increase in fertility is not surprising. However, current guidelines recommend that pregnancy should be avoided for the first 12–18 months after bariatric surgery [13]. Additionally, the bariatric surgeons and obstetricians at both centers stress these guidelines. Many patients with PCOS may chose not to be on an adequate birth control regimen after SG as they often demonstrate years of previous infertility. This study may indicate that the weight loss seen

after SG can lead to fertility sooner than patients expect, especially in nulliparous patients. Another cause for early fertility may lie in the patients' overall goal. Since weight loss has been shown to increase fertility rates in the PCOS population, some patients may be choosing bariatric surgery with the hope of a subsequent pregnancy as the main reason. While only anecdotal, some patients may choose to forego the recommendations pursue post-operative fertility as soon as possible. Despite this seemingly high fertility rate, no definitive stance can be made from the data in this study as the use of pre- and postoperative patient birth control regimens could not be assessed. While there was a difference in postoperative fertility rates between cohorts, this does not truly represent a clinically relevant difference, as the two cohorts were not similar in their preoperative fertility status (i.e., difference in age, unknown contraceptive use, and unknown hysterectomy/menopause status). Thus, it is impossible to say that postoperative fertility in the PCOS group is purely from weight loss. This study was not intended to determine the efficacy of SG on fertility; the design was only meant to characterize the postoperative pregnancy status on PCOS patients as fertility may be an influencing factor on PCOS patient pursuing SG for weight loss. However, the results presented do seem promising and should be followed with dedicated research on PCOS postoperative fertility after SG.

Despite the fact that PCOS causes multiple endocrine imbalances, we found that a primarily restrictive procedure proved to be equally successful in the PCOS population and the non-PCOS population. The significant impact gastric bypass has on the metabolic derangements seen in diabetic patients may impact the decision to perform gastric bypass instead of SG in those patients. However, regarding weight loss alone, SG appears to be equally effective in PCOS and non-PCOS patients.

In addition to retrospective bias, this pilot study was not without inherent limitations. Patients were followed for a relatively short period of 12 months. There is a known subset of patients who regain weight after 12 months [12–14]; thus, monitoring BMI and %EWL at 24 months would have added to the strength of this study. Since the mean age of the PCOS cohort in this study was relatively young (mean = 32 years old), determining long-term weight loss would be ideal. With the designation as a pilot study, the main factor evaluated was postoperative weight loss. SG may show even more promise if PCOS symptoms were controlled postoperatively as effectively as the weight loss seen. This evaluation would be especially beneficial in patients with insulin resistance on metformin not yet diagnosed with diabetes mellitus. In fact, the true rate of PCOS patients with insulin resistance is likely higher than this retrospective observational study can show. This pilot study opens the door for future studies of that nature.

The symptoms and effects of PCOS are more encompassing than only obesity and include infertility, hormonal and menstrual irregularities, diabetes, and metabolic syndrome. Since weight loss can decrease the severity of these symptoms [1, 5], bariatric surgery can simultaneously treat multiple symptoms of the disease. Future studies are needed to evaluate the effects on these symptoms after SG in the PCOS population.

Conclusions

PCOS is a common disease process that can exacerbate obesity and negatively impact fertility. This study shows that the presence of PCOS does not negatively affect the weight loss seen after SG. No difference in 3-, 6-, and 12-month postoperative BMI was seen between the two groups. Compared to non-PCOS patients, PCOS patients experienced similar %EWL at 3 and 6 months and had greater weight loss at 1 year. Many PCOS patients became pregnant following SG, the majority of which were previously nulliparous. This study shows that SG is effective for weight loss in PCOS patients with obesity and may positively augment fertility.

Author Contributions Study design and development: Dilday, Ahnfeldt, Sanders, Bader.

Data collection: Dilday, Derickson, Kuckelman.

Data analysis: Dilday, Derickson, Kuckelman, Reitz, Ahnfeldt, Martin, Sanders.

Manuscript writing: Dilday, Derickson, Kuckelman, Reitz, Martin, Sanders.

Critical revisions: Dilday, Derickson, Kuckelman, Ahnfeldt, Martin, Sanders.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval For this type of study, formal consent is not required.

Informed Consent Does not apply.

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