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ORIGINAL CONTRIBUTIONS

Effect of Sleeve Gastric Surgery on Body Weight and Hypothalamic-Pituitary Axis Hormone Levels in Patients with Polycystic Ovary Syndrome

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Abstract

Background Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine disorder in women of reproductive age. It is difficult for patients with PCOS to achieve weight loss with conventional treatment. The aim of this study was to investigate weight loss and changes in hypothalamic-pituitary axis hormone levels in patients with PCOS combined with obesity after sleeve gastrectomy.

Methods A retrospective analysis of 12 patients without PCOS and 24 patients with PCOS who underwent bariatric surgery at Beijing Luhe hospital from 2020 to 2022 was performed. The study assessed the changes in body weight and hormonal indexes of the hypothalamic-pituitary axis before and six months after the surgery.

Results Patients with PCOS experienced greater weight loss compared to those without the condition. Following surgery, individuals with PCOS showed lower levels of postoperative testosterone, prolactin, and free testosterone indices compared to preoperative levels. Additionally, postoperative LH and FSH levels were higher than preoperative levels. Analysis of thyroid axis hormone levels revealed that FT3 and TSH levels were notably reduced in patients with PCOS postoperatively. Furthermore, growth hormone levels were found to be elevated in patients with PCOS following surgery.

Conclusion Bariatric surgery enhances hormone levels in the hypothalamic-pituitary axis in women with PCOS, leading to greater improvements in patients with PCOS compared to those with simple obesity.

Keywords Polycystic ovary syndrome · Bariatric surgery · Sex hormones · Thyroid hormones · Growth hormone

Introduction

Polycystic ovary syndrome (PCOS) is a common hormonal and metabolic disorder that affects 5–15% of women of reproductive age [1]. The symptoms of PCOS include androgen excess, ovulatory dysfunction, and polycystic ovaries, and are often accompanied by insulin resistance [2]. Dysfunction of the hypothalamic-pituitary-ovarian axis is an important factor in the development of PCOS, which is characteristic by abnormal secretion of gonadal hormones, mainly in the guise of decreased FSH and increased LH and testosterone (T). In addition to gonadal hormones, there are hormonal abnormalities in other axes in patients with PCOS. Studies have found lower basal and stimulatory GH secretion in patients with PCOS [3]. Regarding the findings of changes in the thyroid axis in patients with PCOS, there is growing evidence of a potential link between them [4].

PCOS is a puzzling condition that is widespread but difficult to treat. Current treatment options for PCOS involve

Shuting Li and Jing Ke share equal contribution to the study.

Key Points
1. Both individuals with and without PCOS experienced notable weight reduction following the surgical procedure, patients with PCOS experienced greater weight loss compared to those without the condition.
2. Patients with PCOS experience more significant alterations in hormone levels of the hypothalamic-pituitary axis after surgery compared to patients without PCOS.
3. Bariatric surgery recommended for PCOS patients.

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lifestyle changes and medication. Making adjustments to one's lifestyle, such as modifying diet, increasing physical activity, and implementing behavioral strategies to enhance weight management, are seen as essential components in treating PCOS. But adherence to diet and physical activity recommendations for lifestyle intervention is challenging, actual outcomes of lifestyle interventions may be significantly reduce over time [5]. There are no specific pharmaceuticals for the treatment of PCOS, and current treatments include improving menstruation drugs, combined contraceptives (COCs); improving metabolism, such as metformin, GLP-1 agonists; and androgen receptor antagonist. Medication can only improve part of the symptoms and cannot achieve a comprehensive treatment effect [6]. Weight loss improves all features of PCOS and weight control is recommended as the first line of treatment for PCOS [7].

Bariatric surgery has been recognized as a potential treatment for PCOS because this procedure improves glycolipid metabolism, hirsutism, hyperandrogenemia, and menstrual irregularities in women with PCOS [8]. Existing research suggests that bariatric surgery can improve gonadal hormone production, including estradiol, FSH, LH, and testosterone, but the conclusions are not consistent [9]. However, less is known about the changes in the thyroid and growth hormone axes after surgery in patients with PCOS. Currently, the procedure is only recommended for patients with a body mass index (BMI) greater than or equal to 37.5 kg/m^2 or greater than 32.5 kg/m^2 with comorbidities, and whether polycystic ovary syndrome should be considered an indication remains controversial.

Therefore, this study aimed to characterize the effect of bariatric surgery on the hypothalamic-pituitary axis in patients with PCOS, and to compare the effects of bariatric surgery on women with and without polycystic ovary syndrome.

Materials and Methods

Participants

Inclusion of the patients with PCOS and Simple obesity in women without PCOS who had undergone sleeve gastrectomy at Beijing Luhe hospital were recruited from 2020.3.15 and 2022.12.30. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Beijing Luhe hospital (2022-LHKY-024–01), and informed consent was obtained from all individual participants included in the study. The specific inclusion criteria were as follows:

Inclusion criteria:

(1) Patients with obesity aged 18–45 years;
(2) Indications for bariatric surgery refer to the criteria of the Chinese Guidelines for the Surgical Treatment of Obesity and Type 2 Diabetes [7];
(3) Diagnostic criteria for PCOS are based on the Chinese Guidelines for the Treatment of Polycystic Ovary Syndrome.

Exclusion criteria

(1) Patients with secondary obesity caused by hypothyroidism and Cushing's syndrome;
(2) Patients with contraindications to bariatric surgery: patients with intellectual disability and inability to control their own behavior; patients with unrealistic expectations of surgery; patients unwilling to bear the risk of potential complications; patients who are unable to cooperate with postoperative dietary and lifestyle changes and have poor adherence; patients with poor general condition and unable to tolerate general anesthesia or surgery.

Measurement of Clinical Indicators

(1). Height measurement: Subjects stand barefoot and upright on the base of the height measuring device, with the torso straight, eyes looking straight ahead, both upper limbs naturally drooping, both lower limbs straight, in a "three-point-one-line" standing position, and height is measured in centimeters, with an accuracy of 0.1 cm.
(2). Weight measurement: The weight was measured on a fixed digital scale with the subject wearing short clothes and pants, barefoot, standing in the middle of the scale, keeping the body stable, and recording the value after the display was stabilized, with an accuracy of 0.1 kg.
(3). Body mass index: BMI is calculated by dividing weight by the square of height (kg/m^2).
(4). Weight change is expressed as the percentage of total body weight loss (TWL%), which is calculated as TWL% = (W(kg) initial − W(kg) final)/(W(kg) initial) *100%.

Blood Sampling and Laboratory Analysis

Peripheral venous blood was drawn from all patients on the following morning after 8 h of night fasting. Female gonadal hormones were drawn: on the second day of menstruation for subjects with regular menstruation, and on a random date for subjects with menstrual disorders or menopause. Testosterone (T), estradiol (E2), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), thyroxine (T4), triiodothyronine (T3), thyrotropin (TSH), free triiodothyronine (FT3), free thyroxine (FT4), growth hormone (GH), and insulin-like growth factor-1 (IGF-1) were measured using a Roche electrochemiluminescent automated immunoassay system (Roche COBAS e601, Roche, Switzerland) for the assay. Free testosterone index (FAI) was calculated: FAI = total testosterone (ng/mL) * 347/SHBG (nmol/L) * 100%. Follow-ups were conducted before bariatric surgery, 1 month, 3 months, and 6 months after bariatric surgery, and the above indicators were repeated.

Surgical Technique

The patients included in this study were all patients who underwent laparoscopic sleeve gastrectomy (LSG). The specific surgical approach was to enter the surgical grasping forceps laparoscopically, free the large omental vessels and short gastric vessels along the greater curvature of the stomach to the left side of the gastric cardia with an ultrasonic hemostat, place a gastric support tube through the mouth to the pylorus, probe the gastric support tube, and then tightly adhere to the gastric support tube along the greater curvature of the stomach to the left above the cardia at about 4 cm from the pyloric canal, use a laparoscopic linear cutting anastomosis, use a staple bin 60 m to disconnect the gastric wall, and cut off the gastric wall from the cardia at the gastric wall of the greater curvature was dissected at the angle of His, immediately adjacent to the gastric support tube, and the gastric margin was sufficiently hemostatic to remove the greater curvature specimen.

Statistical Analysis

Data entry was performed using Epidata software, and statistical analysis was performed using IBM SPSS 26.0; normality of the distribution of continuous variables was tested using one-sample Kolmogorov–Smirnov analysis; continuous variables with normal distribution were expressed as mean ± standard deviation; variables that did not conform to normal distribution were expressed as median (interquartile range); paired-sample *t* test or Wilcoxon rank sum test was used to compare the changes of clinical indexes, biochemical indexes and hormone levels of hypothalamic-pituitary axis in patients with PCOS before and 1, 3 and 6 months after the weight reduction intervention, and the changes of patient indexes between the patients without PCOS group and PCOS group were compared using independent sample t test or Wilcoxon rank sum test, and $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 12 simple obesity in women without PCOS and 24 patients with PCOS were included according to the inclusion and exclusion criteria. Age, preoperative weight, and BMI did not differ between the two groups of patients, and the baseline data of the two groups differed in terms of fasting C-peptide. The rest of the baseline data are shown in Table 1.

Table 1 Baseline table for bariatric surgery patients

	Non-PCOS	PCOS
N	12	24
Age (year)	32.25 ± 9.27	28.63 ± 7.35
Weight (kg)	104.48 ± 15.71	111.03 ± 21.99
BMI (kg/m^2)	38.61 ± 5.33	40.34 ± 7.58
TG (mmol/L)	1.49 ± 0.59	1.39 ± 0.53
TC (mmol/L)	4.61 ± 0.90	4.62 ± 0.99
HDL (mmol/L)	1.16 ± 0.28	1.11 ± 0.22
LDL (mmol/L)	3.00 ± 0.66	3.07 ± 0.78
Glu (mmol/L)	5.56 ± 0.64	5.27 ± 0.67
HbA1c (%)	6.06 ± 1.22	5.89 ± 0.58
Insulin (mU/L)	26.62 ± 17.02	31.43 ± 11.63
C-Peptide (ng/mL)	3.31 ± 1.02	4.23 ± 1.01*
T3 (ng/mL)	1.18 ± 0.19	1.18 ± 0.21
T4 (ug/dL)	8.15 ± 1.53	7.44 ± 1.40
FT3 (pg/mL)	3.05 ± 0.44	3.12 ± 0.41
FT4 (ng/dL)	1.27 ± 0.13	1.19 ± 0.18
TSH (uIU/m)	2.56 ± 1.30	3.47 ± 1.91
T (ng/mL)	0.36 ± 0.23	0.47 ± 0.29
E2 (pg/mL)	26.34 ± 10.93	78.96 ± 94.56
LH (mlu/mL)	12.49 ± 10.94	7.36 ± 4.08
FSH (mlu/mL)	14.27 ± 15.52	4.93 ± 1.37
PRL (ng/mL)	47.50 ± 60.19	25.30 ± 8.79
GH (ng/mL)	0.74 ± 1.33	0.66 ± 0.91
IGF-1 (ng/mL)	153.50 ± 32.91	139.98 ± 34.75

*$P < 0.05$ compared with the non-PCOS group

Weight Loss

The results of the analysis showed that patients in both groups showed persistent weight and BMI loss after surgery, which was significantly lower than that before surgery ($P < 0.01$), and the TWL% of patients in both groups continued to increase after surgery (Fig. 1). Independent *t*-test was applied to discuss the weight loss at 6 months after surgery in the group of simple obese women versus the PCOS group, and the results showed that the weight loss in the PCOS group was greater than that in the obesity group (25.13 ± 4.87 vs. 21.50 ± 4.85, $P = 0.027$), the difference was statistically significant (Fig. 2).

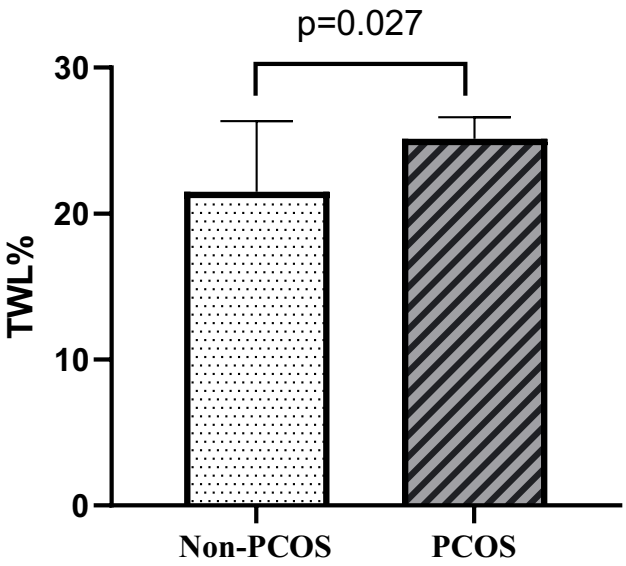

Fig. 2 Changes in TWL% between different groups at 6 months after bariatric surgery

Changes in Gonadal Hormone Levels

The paired t-test was applied to analyze the changes of gonadal hormone levels in patients without PCOS after surgery, and the results showed that the changes of gonadal hormones in patients without PCOS were not significant compared with those before. The results of the analysis of gonadal hormone levels in patients with PCOS before surgery and 6 months after surgery showed that the T and PRL levels of patients decreased compared with those before, and the free testosterone levels decreased significantly compared with those before, and the differences were statistically significant. LH and FSH levels were higher than before, and LH/FSH levels were also slightly higher than before surgery, but the differences were not statistically significant (Table 2). The results of comparing the values of gonadal hormone changes between the two groups showed that there were differences in the values of LH and FSH changes between the patients without PCOS and PCOS groups (Fig. 3).

Changes in Thyroid Hormone Levels

The results of thyroid axis hormone levels showed a significant decrease in FT3 in patients without PCOS compared to before, and a significant decrease in FT3 and TSH levels in patients with PCOS compared to before. There were no statistically significant differences in the values of thyroid hormone changes between the two groups (Table 3).

Changes in Ghrelin Levels

The results of growth hormone changes were analyzed, and the changes of GH and IGF-1 in patients without PCOS at 6 months after surgery were not significant compared with those before. GH levels in patients with PCOS increased compared with those before, and IGF-1 was not significantly higher than before. The changes between the two groups were not statistically different (Table 4).

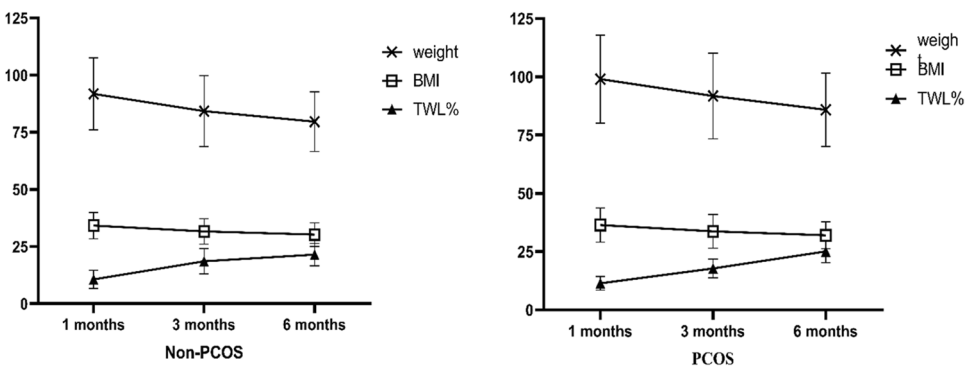

Fig. 1 Changes in weight, BMI, and TWL% after bariatric surgery in different patients

Table 2 Gonadal hormone changes after bariatric surgery in two groups of patients

	Non-PCOS		PCOS		P^a
	Preoperative	6 months post-op	Preoperative	6 months post-op	
T (ng/mL)	0.36 ± 0.23	0.35 ± 0.28	0.47 ± 0.29	0.36 ± 0.19*	0.825
E2 (pg/mL)	26.34 ± 10.93	65.77 ± 50.64	78.96 ± 94.56	101.72 ± 80.72	0.449
LH (mlu/Ml)	12.49 ± 10.94	10.03 ± 12.89	7.36 ± 4.08	13.72 ± 17.11	0.048[b]
FSH (mlu/Ml)	14.27 ± 15.52	13.38 ± 20.02	4.93 ± 1.37	6.38 ± 3.54	0.044[b]
PRL (ng/Ml)	47.50 ± 60.19	20.97 ± 20.96	25.30 ± 8.79	16.75 ± 8.65*	0.319
FAI			7.93 ± 6.25	4.02 ± 3.06*	

*Value for $P < 0.05$ compared with preoperative; [a]P value for the difference in thyroid hormone changes after surgery for non-PCOS and PCOS; [b]value for a difference in sex hormone changes between the non-PCOS group and the PCOS group

Discussion

The current epidemic of obesity and related comorbidities has posed a significant threat to human health, and studies have shown that a 5–10% reduction in body weight can reduce the severity of obesity and its comorbidities [10]. There are numerous methods to lose weight, such as managing diet, exercise, and using medications. While dietary changes and lifestyle adjustments are crucial for weight loss, they are often not enough to maintain weight loss for most individuals. The impact of anti-obesity medications is limited and comes with various side effects [11]. As a result, bariatric surgery remains the most effective treatment for obesity and the most effective treatment available for obesity and its complications.

The results of a study including 13,900 patients undergoing SG surgery showed that the TWL% at 1 year postoperatively was 23.0% [12], this study did not specifically report TWL values at six months postoperatively, but similar weight loss was seen in our study at 6 months. Earlier research indicated that the TWL% six months after surgery for patients with PCOS was 24.2%. Similarly, our study found that the TWL% at the same time point was 25.13% ± 4.87 for patients with PCOS, our results are better than previous studies. A study including 90 Chinese women showed a TWL% of 30.1% (26.3–38.7) at 1 year postoperatively in patients with LSG with PCOS [13]; however, our research did not extend over a long duration, preventing comparisons to be made. We also calculated postoperative percentage of excess weight lost (EWL% its calculation method: first according to the standard BMI of 25 kg/m^2 to calculate the standard weight, calculate EWL% = (original weight − current weight)/(original weight − standard weight) × 100%) in patients with PCOS. The results of our trial showed that the patient's EWL% was 58.91% ± 17.74 at 6 months postoperatively. The results of the Shilpa Bhandari study showed an EWL% of 58.37% ± 11.41 at 6 months after SG in patients with PCOS [14] and another study reported an EWL% of 49% ± 10.62 at 6 months after surgery in patients with PCOS [15]. In this study, patients experienced greater weight loss post-surgery, possibly due to the personalized intervention plan provided to those who underwent bariatric surgery. This plan included tailored surgical methods, dietary and exercise guidance, and ongoing monitoring with adjustments based on individual progress.

Previous studies have shown higher EWL% at 6 months postoperatively in patients with PCOS compared to patients with non-PCOS (58.37% ± 11.41 vs 54.84% ± 11.58) [14]

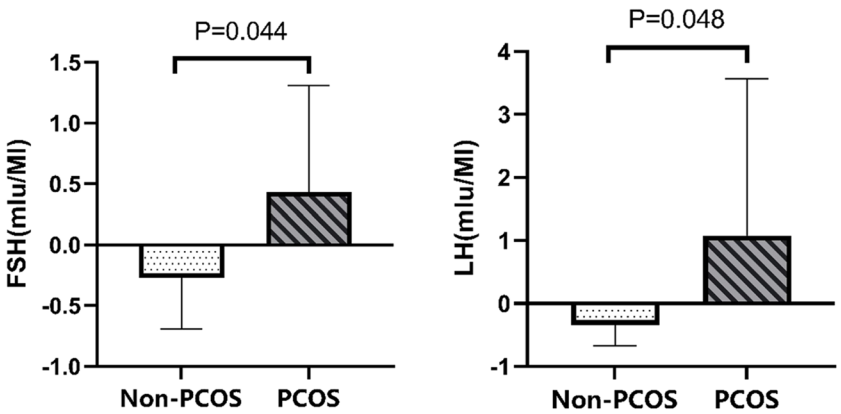

Fig. 3 Differences in gonadal hormone changes between non-PCOS and PCOS group

Table 3 Thyroid hormone changes after bariatric surgery in two groups of patients

	Non-PCOS		PCOS		P^a
	Preoperative	6 months post-op	Preoperative	6 months post-op	
T3 (ng/mL)	1.18 ± 0.19	1.07 ± 0.17	1.18 ± 0.21	1.06 ± 0.17	0.915
T4 (ug/dl)	8.15 ± 1.53	8.04 ± 1.34	7.44 ± 1.40	7.17 ± 1.17	0.620
FT3 (pg/mL)	3.05 ± 0.44	2.76 ± 0.29*	3.12 ± 0.41	2.85 ± 0.30*	0.845
FT4 (ng/dL)	1.27 ± 0.13	1.22 ± 0.12	1.19 ± 0.18	1.21 ± 0.13	0.148
TSH (uIU/m)	2.56 ± 1.30	2.38 ± 1.45	3.47 ± 1.91	2.49 ± 1.30*	0.187

*$P < 0.05$ compared with preoperative; [a]P value for the difference in thyroid hormone changes after surgery for non-PCOS and PCOS

Table 4 Growth hormone changes after bariatric surgery in two groups of patients

	Non-PCOS		PCOS		P^a
	Preoperative	6 months post-op	Preoperative	6 months post-op	
GH (ng/mL)	0.74 ± 1.33	2.75 ± 3.15	0.66 ± 0.91	3.50 ± 3.13*	0.479
IGF-1 (ng/mL)	153.50 ± 32.91	171.50 ± 52.29	139.98 ± 34.75	170.08 ± 61.09	0.600

*$P < 0.05$ compared with preoperative; [a]P value for the difference in growth hormone changes after surgery for non-PCOS and PCOS

and more significant weight loss, which is the same as our findings. It has also been confirmed that patients with PCOS 1 year after SG surgery lost more weight (36.28% ± 2.93 vs 33.04% ± 6.84) [16]. This could be linked to the notable enhancement in insulin resistance levels, or it might be because the bariatric surgery corrected the abnormal hormone levels in the patients and helped them move towards a healthier weight.

In this research, it was discovered that the testosterone levels and free testosterone indices of individuals with PCOS decreased notably 6 months after undergoing bariatric surgery compared to before the surgery. The study also revealed that bariatric surgery effectively reduced hyperandrogenemia, which has been clearly confirmed in previous studies [8, 15, 17]. This improvement in hyperandrogenemia post-surgery may be attributed to factors such as insulin resistance, adipokines, and inflammatory mediators. Furthermore, we also discovered that the levels of postoperative PRL in patients with PCOS were lower compared to their levels before the surgery. There have been limited research studies on the postoperative changes in PRL levels in patients with PCOS. However, a meta-analysis of 32 observational studies from various countries revealed that individuals with PCOS had notably elevated PRL levels compared to those without PCOS [18], probably due to the higher GnRH/LH pulsatility in patients with PCOS. It has been suggested that the higher levels of estradiol produced as a result of the stimulating impact of recombinant human follicle-stimulating hormone in individuals with PCOS could result in elevated PRL levels. Bariatric surgery helps alleviate hormone irregularities in patients. In the current research, it was observed that LH and FSH levels were higher postoperatively compared to before the surgery, with a slight increase in LH/FSH levels as well. Past studies have presented varying results, with some indicating a rise in FSH levels and a decline in LH levels and the LH/FSH ratio following surgery [19]. A study involving 522 patients with PCOS found that there was a notable reduction in LH levels 3 months after surgery. However, there were no significant changes in FSH levels or the LH/FSH ratio post-surgery [20]. Following bariatric surgery, the drop in testosterone levels typically triggers a shift in the secretion of gonadotropins (specifically LH/FSH inversion). However, our findings revealed a rise in FSH levels only 6 months post-surgery. The lack of statistical significance in this change could be attributed to the limited sample size and the short duration of follow-up. In comparison to women with obesity, patients with PCOS showed an increase in LH and FSH levels following surgery, with statistically significant differences noted. This was linked to the abnormal hormone levels seen in PCOS patients prior to surgery, indicating that weight loss surgery can help correct these hormone imbalances. Additionally, the weight loss in PCOS patients was more pronounced compared to those with simple obesity, suggesting a potential connection between the extent of weight loss and changes in hormone levels.

The present study also found a significant decrease in FT3 and TSH levels in patients with PCOS after surgery compared with before. There are few studies on the hormonal changes in the thyroid axis in patients with PCOS after treatment. Previous studies have found a higher prevalence of thyroid

dysfunction and autoimmune diseases in women with PCOS [21, 22]. Preoperative FT3 levels were statistically significantly higher in the PCOS group than in the control group, possibly as a compensatory defense mechanism for weight gain. We believe it was the bariatric surgery that lowered the weight and therefore changed the FT3 levels. Previous clinical reports have shown that some PCOS symptoms were alleviated or even eliminated by restoring thyroid function [23], but whether other mechanisms are involved is still unclear.

In addition, the present study found an increase in postoperative growth hormone levels in patients with PCOS. Previous studies have suggested that excess androgens in patients with PCOS may lead to a decrease in GH secretion because testosterone directly stimulates the release of growth hormone [3, 24]. Insufficient GH production disrupts ovarian function, leading to problems with sexual maturation, the menstrual cycle, and fertility in women. Previous studies have shown studies have shown that exogenous growth hormone supplementation improves GC mitochondrial dysfunction and oocyte quality in patients with polycystic ovary syndrome [25]. Therefore, we speculate that androgens as well as weight loss in patients after bariatric surgery contribute to the increase in GH compared with the previous period, changes in GH secretion after bariatric surgery may have beneficial effect on ovarian function and fertility in PCOS, but there are still few studies on the changes in growth hormone after PCOS treatment, and more studies are needed to further support this in the future.

In summary, bariatric surgery not only facilitates weight loss but also helps normalize abnormal hormone levels in various axes of patients with PCOS. Changes in the thyroid and growth hormone axes can also contribute to the improvement of patients with PCOS conditions. Therefore, for patients with PCOS who have not responded well to conventional therapies, bariatric surgery may be a viable treatment option. However, our study has several limitations. Firstly, we only observed short-term changes post-surgery and did not investigate long-term effects. Secondly, the sample size was small and should be expanded in future studies. Lastly, we focused solely on post-surgical changes and did not delve into the underlying mechanisms involved.

Conclusion

According to these results, individuals with PCOS show more favorable outcomes in weight loss and hormone level improvement compared to individuals without PCOS. Patients with PCOS not only saw alterations in their gonadal hormone levels, but also changes in their thyroid and growth hormone levels following bariatric surgery.

Data Availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical Approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

Conflict of Interest The authors declare no competing interests.

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