



WEBER STATE UNIVERSITY

STEWART LIBRARY

WEBER STATE UNIVERSITY
INTERLIBRARY LOAN
STEWART LIBRARY
2901 UNIVERSITY CIRCLE
OGDEN, UT 84408-2901

VOICE: (801) 626-6384/7820
FAX: (801) 626-8521
ARIEL: 137.190.51.43
E-mail: interlibrary@weber.edu

FOR RESEARCH ONLY
Further reproduction of this item may
infringe on the copyrights of the author.

DOCUMENT # _____ Has the following problem(s):

Missing pages (page numbers): _____

Edges cut off (page numbers): _____

Illegible (page numbers): _____

Other: _____

Please return this form to us via ARIEL or FAX and we will fix the problem right away.

Thank You.

Borrower: UUE

Call #: Electronic

Lending String: *UUO,WUM,ALM,ALM,JHW

Location:

Patron: Brown, Carol

ARIEL

Journal Title: Surgery for obesity and related diseases

Charge

Maxcost: \$11IFM

Volume: 1 Issue: 2
Month/Year: 2005 Pages: 77-80

Shipping Address:

Eccles Health Sciences Library - ILL
University of Utah
10 N. 1900 E
Salt Lake City, UT 84112-5890

Article Author:

Article Title: Eid GM; Effective treatment of Polycystic

Fax: 801-581-3632

Ariel: 137.190.51.43 or 155.100.78.2

WEBER STATE UNIVERSITY

Imprint: [Amsterdam ; New York] ; Elsevier, 2005 OCT 07 2007

ILL Number: 35734157



Weber State University ILL



ILLiad TN: 70813



ELSEVIER

Original article

Effective treatment of polycystic ovarian syndrome with Roux-en-Y gastric bypass

George M. Eid, M.D.^{a,b,*}, Daniel R. Cottam, M.D.^a, Laura M. Velcu, M.D.^a,
Samer G. Mattar, M.D.^a, Mary T. Korytkowski, M.D.^c, Gabriella Gosman, M.D.^d,
Pooneh Hindi, M.D.^a, Philip R. Schauer, M.D.^a

^aDepartment of Surgery, University of Pittsburgh and UPMC Minimally Invasive Surgery Center, Pittsburgh, Pennsylvania

^bDepartment of Surgery, Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, Pennsylvania

^cDepartment of Medicine, Division of Endocrinology, University of Pittsburgh, Pittsburgh, Pennsylvania

^dDepartment of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, University of Pittsburgh, Pittsburgh, Pennsylvania

Abstract

Purpose: Many women with polycystic ovarian syndrome (PCOS) are overweight. This study investigated the impact of weight loss surgery on the clinical manifestations of this disorder in morbidly obese women with PCOS—a major risk factor for the development of heart disease, stroke, and type II diabetes.

Methods: We reviewed the outcomes of women diagnosed with PCOS who had undergone weight loss surgery at the University of Pittsburgh between July 1997 and November 2001. We evaluated the changes in menstrual cycles, hirsutism, infertility, and type II diabetes.

Results: A total of 24 women with PCOS were included in the study. Their mean age was 34 ± 9.7 years. The mean preoperative body weight was 306 ± 44 lb, with a body mass index of 50 ± 7.5 . All patients were oligomenorrheic. Of the 24 patients, 23 were hirsute. All women underwent elective laparoscopic gastric bypass surgery. The mean follow-up period was 27.5 ± 16 months. The mean excess weight loss at 1 year of follow-up was $56.7\% \pm 21.2\%$. All women resumed normal menstrual cycles after a mean of 3.4 ± 2.1 months postoperatively. Of the 23 women with hirsutism, 12 (52%) had complete resolution at a mean follow-up of 8 ± 2.3 months, 6 (25%) had moderate resolution at a mean of 21 ± 18 months, and 3 had minimal resolution at 34 ± 14 months. Two women reported no change in their hirsutism at 32 ± 7 months. Five women were able to conceive after surgery without the use of clomiphene.

Conclusion: Gastric bypass surgery and its consequent weight loss results in significant improvement of multiple clinical problems related to PCOS. © 2005 American Society for Bariatric Surgery. All rights reserved.

Keywords: Polycystic ovarian syndrome; Laparoscopy; Gastric bypass surgery; Weight loss; Treatment; Obesity; Surgery

Polycystic ovarian syndrome (PCOS) affects approximately 6% of reproductive-age women in the United States and is a leading cause of infertility [1,2]. PCOS is characterized by chronic anovulation with biochemical and/or

clinical evidence of androgen excess and without other specific diseases of the adrenal, thyroid, or pituitary glands that can produce similar manifestations. The clinical manifestations of PCOS include menstrual dysfunction, hirsutism, acne, alopecia, obesity, infertility, increased libido, and a high rate of miscarriage. The endocrine abnormalities of PCOS include elevated serum androgen concentrations, elevated mean serum concentrations of luteinizing hormone, normal or low levels of follicle-stimulating hormone, elevated luteinizing hormone/follicle-stimulating hormone ra-

G. Eid, P. Schauer, D. Cottam, and L. Velcu were supported by a grant from U.S. Surgical; and P. Schauer was also supported by grants from Computer Motion, Inc., Stryker Corporation, and Berchtold Corporation.

*Reprint requests: George M. Eid, M.D., Magee Women's Hospital, Suite 5500, 300 Halket Street, Pittsburgh, PA 15213.

E-mail: EidGM@msx.upmc.edu

Table 1
Criteria to diagnose PCOS

Primarily a clinical diagnosis; the patient must be:

- Anovulatory (no menses >3 months of the previous year)
- Hirsute

Normal plasma concentrations of:

- 17-hydroxyprogesterone
- Prolactin
- Thyroid hormones
- Growth hormone
- Cortisol
- FSH

Patient must not have been taking any of the following medications for six months prior to diagnosis

- Synthetic glucocorticoids
- Adrenocorticotrophic hormone
- Metypalone
- Anabolic steroids
- Levonorgestrel-containing oral contraceptive pills
- Maternal use of synthetic progestational agents

tios, and hyperinsulinemia. The diagnosis of PCOS is not based primarily on pathologic changes in the ovaries or plasma hormone disturbances, but is instead a clinical diagnosis based on the coexistence of chronic anovulation and varying degrees of hirsutism [3]. PCOS is not only a disease of infertility, but is also associated with an increased risk of type II diabetes, gestational diabetes, stroke, hyperlipidemia, coronary artery disease, and endometrial carcinoma [4–6]. The etiology of PCOS is unclear. Proposed hypotheses of the pathogenesis of PCOS include a central-primary defect in the hypothalamic/ pituitary axis; an ovarian-primary abnormality of steroidogenesis; and insulin resistance.

Since 1935, when Stein and Leventhal [7] first described the syndrome, obesity has been recognized as a major factor in the pathogenesis of PCOS. Estimates of the prevalence of obesity in women with PCOS vary from 35% to 60% [8,9]. Weight loss has been recognized as an important treatment for women with obesity and PCOS, but nonsurgical weight loss is often temporary and has not resulted in complete resolution of the symptoms [10].

In an attempt to determine the effect of sustained weight loss on PCOS, we reviewed the clinical outcomes of laparoscopic Roux-en-Y gastric bypass in women with PCOS.

Methods

This was a retrospective study. The patients were identified from a prospectively maintained database. A chart review was performed of all women with the diagnosis of PCOS seen between July 1997 and November 2001 at the University of Pittsburgh Medical Center who had undergone laparoscopic Roux-en-Y gastric bypass and had at least 1 year of follow-up. All women in the study were diagnosed with PCOS by their endocrinologist using established criteria (Table 1) [3]. All patients underwent laparoscopic Roux-en-Y gastric bypass. In brief, the surgical ap-

proach involves construction of an isolated small gastric pouch (15-cm³) with an antecolic, antegastric Roux limb (75 cm) and stapled gastrojejunostomy and jejunojunostomy. We extend the Roux limb length to 150–250 cm for the superobese (body mass index [BMI] ≥ 60).

Postoperatively, all women were followed up in our clinical center. Information about the patient's current weight, medical comorbidities, medications used, hirsutism, acne, fertility status, and any current menstrual cycle irregularities were gathered. All descriptive statistical analysis was done using Sigma Stat Software.

The diagnosis of hypertension was made when the average of two or more diastolic blood pressure measurements on at least two subsequent visits was ≥ 90 mm Hg or when the average of multiple systolic blood pressure readings on two or more subsequent visits was consistently >140 mm Hg. Type II diabetes mellitus was defined as a fasting plasma glucose measurement from venous blood of ≥ 140 mg/dL combined with the need for medication. Amenorrhea was defined as absence of menses for >3 months of the previous year. Infertility was defined as the inability of a couple to achieve a pregnancy after 1 year of regular unprotected sexual relations or the inability of a woman to carry a pregnancy to a live birth.

Results

A total of 30 patients with PCOS were identified from the pool of patients who had undergone weight loss surgery between July 1997 and November 2001. Of these, 24 patients were included for analysis; 6 patients were excluded owing to incomplete follow-up data or the use of medications (steroids, oral contraceptive pills). Preoperatively, these patients had a mean age of 34 ± 9.7 years (range 22–48) and a mean BMI of 50 ± 7.5 (range 36–66). In addition to PCOS, 21 of the 24 patients had at least three other weight-related comorbid conditions, including dyslipidemia. The mean number of medications per patient was 2.5, with 11 patients having three or more prescriptions. All patients were oligomenorrheic. Of the 24 patients, 23 (96%) had hirsutism, 5 (20%) had acne, and 12 (50%) had undergone preoperative ultrasonography of their ovaries that showed multiple cysts.

Postoperatively, these patients were followed up for a mean of 27.5 ± 16 months (range 12–57). Immediate postoperative gastrointestinal bleeding developed in 1 patient but resolved without any surgical intervention. The mean excess weight loss was $56.7\% \pm 21.2\%$ (range 12–93%) at 1 year, with a mean postoperative BMI of 30 ± 4.5 (range 25–38). This was a decrease from a mean BMI of 50 preoperatively. At follow-up, 20 (83%) of the 24 patients were free of medication. All 11 patients with type II diabetes mellitus preoperatively were normoglycemic at follow-up. Of the 9 patients with a history of hypertension, 7 (78%) became normotensive without the help of antihypertensive

Table 2
Patient characteristics pre- and post-gastric bypass

	Pre-operative	Post-operative	% change
Age (yr)	34 ± 9.7	N/A	N/A
Weight (lb)	306 ± 44	201 ± 30	
BMI (kg/m ²)	50 ± 7.5	30 ± 4.5	
HTN	9	2	77
DM	11	0	100
HA1C (%)	8.2	5.14	62*
GERD	12	0	100
Dyslipidemia	12	1	92
Hirsutism	23	5	79
Depression	10	0	100
Menstrual dysfunction	24	0	100
Medications per hypertensive	1.3 (9 patients on 12 medications)	0.67 (2 patients on 3 medications)	N/A
Diabetic medication	1.1 (11 patients on 12 medications)	0	100
Medications per patient	2.5	0.6	75

BMI = body mass index; HTN = hypertension; DM = diabetes mellitus; HA1C = hemoglobin A1C; GERD = gastroesophageal reflux disease.

* This data based on five patients who had preoperative HA1c levels and postoperative HA1C levels.

medications. Similarly, 11 (92%) of 12 patients with dyslipidemia no longer required medication based on the reported normalization of their cholesterol or triglyceride level. Of the 23 patients with hirsutism, 12 (52%) had complete resolution at a mean follow-up of 8 ± 2.3 months (range 5–12), six (25%) had moderate resolution at a mean of 21 ± 18 months (range 6–46), and 3 had minimal resolution at 34 ± 14 months (range 21–49). Finally, 2 (8.7%) of the 23 patients reported no change in their hirsutism at 27 and 37 months. All patients had complete resolution of their menstrual abnormalities (Table 2). The mean time to normalization of the menstrual cycle postoperatively was 3.4 ± 2.1 months (range 1–10).

All 5 patients who desired to conceive were able to do so postoperatively without the use of clomiphene.

Discussion

PCOS is a complex endocrine disorder that is associated with, and aggravated by, obesity. Weight loss has been demonstrated to decrease insulin and androgen levels, as well as to improve the clinical manifestations of PCOS [1–18].

Our data support the hypothesis that weight loss results in resolution of the symptoms associated with PCOS. This weight loss, induced by surgical means, was followed by significant improvements in menstrual dysfunction and hirsutism. Our 75% rate of moderate to complete resolution of hirsutism is superior to that of alternate methods of treatment described in the literature [19]. In addition, marked improvement has been achieved in the treatment of comorbid conditions commonly associated with PCOS, including type II diabetes mellitus, hypertension, and dyslipidemia.

The phenomenon of resumed menstruation after surgically induced weight loss was also observed in the era of the jejunoileal bypass, before the abandonment of this surgical

option because of its long-term metabolic consequences [20]. The current mainline surgical options of Roux-en-Y gastric bypass [21] or the adjustable silicone gastric band (Inamed, Santa Barbara, CA) [22] have far fewer metabolic side effects and have been shown to be highly effective in reversing the insulin resistance associated with type II diabetes mellitus [21,23–25]. The metabolic effects of insulin have been implicated as a key mediator in PCOS syndrome [26].

Our experience with patients who conceived after weight loss is not unique [15,27–30]. However, pregnancy following weight loss surgery, among women who have been previously diagnosed with infertility, has only been reported by Doldi et al. [31]. We believe it is noteworthy that all 5 patients who were infertile before surgery were able to conceive without the aid of clomiphene. Surgery in these instances is beneficial, as it is the only durable method of obtaining sustained weight loss [32,33], thereby improving the chances for successful conception and gestation.

Our study had some limitations, including the small size of the group and the retrospective nature of the analysis.

Conclusion

Our results suggest that obese patients with PCOS who undergo gastric bypass will experience a significant improvement in multiple clinical problems related to the disorder. Larger prospective studies are needed to confirm further the benefit of surgically induced weight loss in the treatment of women with PCOS.

References

- [1] Patel S, Korytkowski M. Polycystic ovary syndrome: how best to establish the diagnosis. *Women's Health Primary Care* 2000;3:55–67.

- [2] Franks S, White DM. Prevalence of and etiological factors in polycystic ovarian syndrome. *Ann NY Acad Sci* 1993;687:112–14.
- [3] Carr BR. Disorders of the ovaries and female reproductive tract. In Williams RH (ed): *Williams' Textbook of Endocrinology*. Philadelphia: WB Saunders; 1998, pp 787–90.
- [4] Talbott E, Guzick D, Clerici A, et al. Coronary heart disease risk factors in women with PCOS. *Arterioscler Thromb Vasc Biol* 1995; 15:821–6.
- [5] Talbott E, Clerici A, Berga SL, et al. Adverse lipid and coronary heart disease risk profiles in young women with polycystic ovary syndrome: results of a case-control study. *J Clin Epidemiol* 1998;51: 415–22.
- [6] Parham KJ. Adenocarcinoma of the endometrium associated with the Stein-Leventhal syndrome. *Am J Obstet Gynecol* 1969;105:113–5.
- [7] Stein IF, Leventhal ML. Amenorrhea associated with bilateral polycystic ovaries. *Am J Obstet Gynecol* 1935;29:181–91.
- [8] Balen AH, Conway GS, Kaltsas G, et al. Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. *Hum Reprod* 1995;10: 2107–11.
- [9] Legro RS. The genetics of obesity: lessons for polycystic ovary syndrome. *Ann NY Acad Sci* 2000;900:193–202.
- [10] Asuncion M, Calvo RM, San Millan JL, et al. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. *J Clin Endocrinol Metab* 2000;85:2434–8.
- [11] Futterweit W. Polycystic ovary syndrome: clinical perspectives and management. *Obstet Gynecol Surv* 1999;54:403–13.
- [12] Guzick DS, Wing R, Smith D, et al. Endocrine consequences of weight loss in obese hyperandrogenic anovulatory women. *Fertil Steril* 1994;61:598–604.
- [13] Hoeger K. Obesity and weight loss in PCOS. *Obstet Gynecol Clin North Am* 2001;28:85–97.
- [14] Harlass FE, Plymate SR, Fariss BL, et al. Weight loss is associated with correction of gonadotropin and sex steroid abnormalities in the obese anovulatory female. *Fertil Steril* 1984;42:649–52.
- [15] Pasquali R, Antenucci D, Casimirri F, et al. Clinical and hormonal characteristics of obese amenorrheic hyperandrogenic women before and after weight loss. *J Clin Endocrinol Metab* 1989;68:173–9.
- [16] Kopelman PG, White N, Pilkington TR, et al. The effect of weight loss on sex steroid secretion and binding in massively obese women. *Clin Endocrinol* 1981;15:113–6.
- [17] Kiddy DS, Sharp PS, White DM, et al. Differences in clinical and endocrine features between obese and nonobese subjects with PCOS: an analysis of 263 cases. *Clin Endocrinol* 1990;32:213–20.
- [18] Holte J, Bergh T, Berne C, et al. Restored insulin sensitivity but persistently increased early insulin secretion after weight loss in obese women with PCOS. *J Clin Endocrinol Metab* 1995;80:2586–93.
- [19] Kiddy DS, Hamilton-Fairley D, Bush A, et al. Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome. *Clin Endocrinol* 1992;36: 105–11.
- [20] Hey H, Niebuhr-Jorgensen U. Jejuno-ileal bypass surgery in obesity: gynecological and obstetrical aspects. *Acta Obstet Gynecol Scand* 1981;60:135–40.
- [21] Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg* 1995;222:339–52.
- [22] Favretti F, Cadiere GB, Segato G, et al. Laparoscopic banding: selection and technique in 830 patients. *Obes Surg* 2002;12:385–90.
- [23] Schauer PR, Burguera B, Ikramuddin S, et al. Effect of laparoscopic roux-en-Y gastric bypass on type II diabetes mellitus. *Ann Surg* 2003;238:467–85.
- [24] Houmard JA, Tanner CJ, Yu C, et al. Effect of weight loss on insulin sensitivity and intramuscular long chain fatty acyl-CoAs in morbidly obese subjects. *Diabetes* 2002;51:2959–63.
- [25] O'Brien PE, Dixon JB, Brown W, et al. The laparoscopic adjustable gastric band (Lap-Band): a prospective study of medium-term effects on weight, health and quality of life. *Obes Surg* 2002;12:652–60.
- [26] Marsden PJ, Murdoch AP, Taylor R. Tissue insulin sensitivity and body weight in polycystic ovary syndrome. *Clin Endocrinol* 2001;55: 191–9.
- [27] Dixon JB, Dixon ME, O'Brien PE. Pregnancy after Lap-Band surgery: management of the band to achieve healthy weight outcomes. *Obes Surg* 2001;11:59–65.
- [28] Clark AM, Ledger W, Galletly C, et al. Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women. *Hum Reprod* 1995;10:2705–12.
- [29] Hollmann M, Runnebaum B, Gerhard I. Effects of weight loss on the hormonal profile in obese infertile women. *Hum Reprod* 1996;11: 1884–91.
- [30] Bates GW, Whitworth NS. Effect of body weight reduction on plasma androgens in obese infertile women. *Fertil Steril* 1982;38:406–9.
- [31] Doldi SB, Micheletto G, Latuada E, et al. Adjustable gastric banding: a 5 year experience. *Obes Surg* 2000;10:171–3.
- [32] Brolin RE. Update: NIH Consensus Conference Gastrointestinal Surgery for Severe Obesity. *Nutrition* 1996;12:403–4.
- [33] NIH. Gastrointestinal surgery for severe obesity. *Ann Intern Med* 1991;115:956–61.